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**ALL, AML, MDS & bone marrow failure**

**BSH2021-OR-001**

**Management of Meningococcal Disease Risk in Patients with Paraoxymsal Nocturnal Hemoglobinuria (PNH) on Complement Inhibitors: 18 Years’ Experience from the UK National PNH Service in Leeds**

Louise Arnold*, Ray Burrow, Kathryn Riley, Talha Munir, Richard Kelly, Alexandra Pike, Rachael Jones, Jennifer Gachev, Briony Forrest, Petra Muus, Peter Hillmen, Morag Griffin

Abstract Content: Eculizumab treatment for paroxysmal nocturnal hemoglobinuria (PNH) C5 inhibitors increase susceptibility to encapsulated microorganisms (*Neisseria meningitidis*). The PNH National service has 18 years of experience. The risk of *N. meningitidis* is mitigated by vaccination, ciprofloxacin (500 mg bd) days 1–13 we moved to vaccination day one of complement inhibitor, and prophylaxis (penicillin/erythromycin). Since a case of sepsis with penicillin-resistant meningococci, patients also have course ciprofloxacin. Education, prompt action in case of fever and a 24-hour on-call service are equally important.

Until 2010, patients were revaccinated with MenACWY 3 yearly. MenB vaccine added in 2015. With Public Health England Meningococcal Reference Unit, a program was developed to monitor titers after vaccination. It is technically not possible to assay for meningococcal serogroup B antibody titers when on Eculizumab therapy.

**Methods:** Antibody titers were assayed following vaccination. Unprotective titers led to revaccination. We evaluate practice of nine meningococcal infections in eight patients. We present disease characteristics, serogroup and outcome, vaccination history, and antibody status.

**Results:** Between 2002 and 2020, 324 patients commenced complement inhibitor treatment for PNH. Eighty one hundred and one vaccinations with MenACWY were administered: median of 2 vaccinations per patient (range 1–10). A total of 1,671 antibody titer assessments were conducted in 294 patients, median of 4 tests per patient (range 1–15). Every test assessed antibodies against all four serogroups.

Titer were not assessed in 9% of patients (30), due to vaccination prior to change in practice or recent commencement. Protective response after first vaccination was observed in 170/294 patients (57.8%) and a partial response (three serotypes) in 51/294 (17.3%). Revaccination of 51 partial responders resulted an additional 21 patients with a full response. Revaccination of 73 non-responders (antibodies to 0–2 serotypes) resulted in 32 more partial/full responses. Two hundred and eighty-seven of 324 patients received MenB vaccinations: median of 2 vaccinations per patient (range 1–4). Eight of 324 (2%), median age 22.5 years, developed meningococcal sepsis (see table); patient 5 had two episodes. Three of five cases with serogroup B infection were before serogroup B vaccination. Four episodes in three patients were due to Y, C, W meningococci, in one the serogroup is unknown. All except patient 1 were compliant with antibiotic prophylaxis. Patient 7 died from meningococcemia, a delay in seeking medical attention may have contributed (a penicillin-resistant strain).

**Discussion:** The largest experience of managing meningococcal risk in complement inhibitor for PNH. Despite proactive management, we had nine cases of meningococcal sepsis, one fatal infection. Recently practice of prompt treatment with ciprofloxacin if pyrexic on prophylaxis will prevent cases – patient 7 with a penicillin-resistant strain. Three patients had a meningococci sepsis serogroups C, W and Y; one patient had no titers due to recent commencement on treatment, titers of 2 suggested protective immunity.

A full antibody response can be obtained on second vaccination in most if first one failed. If no response is achieved, then MenACWY vaccination is not likely to be successful. Current practice significantly mitigates the risk of meningococcal disease; however, it is essential that patients are vigilant for fever, seeking immediate medical attention stating their diagnosis of PNH on complement inhibitor therapy.

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**BSH2021-OR-002**

**Long-term survivors and gilteritinib safety beyond 1 year in patients with FLT3-mutated relapsed or refractory acute myeloid leukemia: ADMIRAL trial follow-up**

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**Abstract Content:** The phase 3 ADMIRAL trial showed that gilteritinib was superior to salvage chemotherapy in patients with FLT3-mutated relapsed or refractory acute myeloid leukemia (Perl AE, et al.
N Engl J Med. 2019;381(18):1728–1740). This follow-up of the ADMIRAL trial assessed long-term survivors and gilteritinib safety beyond 1 year. A data cut was performed 1 year after the primary analysis. Response outcomes in long-term survivors (overall survival ≥18 months) in the gilteritinib arm, and safety during and after 12 months of gilteritinib therapy were assessed. At 1 year after the primary analysis, median follow-up for overall survival was 29.2 months. Median overall survival remained longer with gilteritinib (9.3 months) than with salvage chemotherapy (5.6 months; hazard ratio for death: 0.679 [95% confidence interval: 0.527, 0.875], nominal P = 0.0026); 18-month overall survival rates were 27% and 15%, respectively (Table). Of 49 censored patients in the gilteritinib arm, 20 continued treatment; 13 of these 20 patients underwent hematopoietic stem cell transplantation and received post-transplant gilteritinib maintenance therapy. Median gilteritinib exposure was 4.1 months (interquartile range, 2.1–8.2); 12% (n = 30/246) of patients had ≥18 months of drug exposure. A total of 63 gilteritinib-treated patients had overall survival ≥18 months (median exposure, 17.6 months [interquartile range, 3.1–25.7 months]). A high proportion of these long-term survivors achieved remission before transplantation (Table). After a median of 3.5 months, 35 of 63 (56%) long-term survivors underwent transplantation; 25 of these 35 patients (71%) received post-transplant gilteritinib maintenance therapy. Of 28 patients who did not undergo transplantation, 15 (54%) received gilteritinib for ≥18 months. The most common grade ≥3 adverse events during the first 12 months of gilteritinib therapy were febrile neutropenia (45%), anemia (40%), and thrombocytopenia (23%); rates of these grade ≥3 adverse events decreased to 8%, 10%, and 0, respectively, after 12 months of treatment. The most common adverse events during the first 12 months of gilteritinib therapy were acute myeloid leukemia (11%), infections (11%), and cardiac disorders (3%); after 12 months of treatment, rates of these fatal adverse events were 6%, 8%, and 2%, respectively. Results from this ADMIRAL trial follow-up suggest long-term survival in patients receiving gilteritinib is related to ongoing remission, subsequent transplantation, or post-transplant gilteritinib maintenance therapy. The safety profile of gilteritinib beyond 1 year was stable.

Abstract Table:

<table>
<thead>
<tr>
<th>Gilteritinib (n = 247)</th>
<th>Salvage Chemotherapy (n = 124)</th>
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<tbody>
<tr>
<td>Deaths, n (%)</td>
<td>198 (80)</td>
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<tr>
<td>Overall Survival Rates (%)</td>
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<tr>
<td>12-month</td>
<td>37</td>
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<tr>
<td>18-month</td>
<td>27</td>
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<tr>
<td>24-month</td>
<td>20</td>
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<tr>
<td>Pre-Transplant Remission Rates in Gilteritinib Long-term Survivors (n = 63), n (%)</td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>20 (32)</td>
</tr>
<tr>
<td>CRi/CRp</td>
<td>25 (40)</td>
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<tr>
<td>CRc*</td>
<td>45 (71)</td>
</tr>
<tr>
<td>CRh</td>
<td>10 (16)</td>
</tr>
<tr>
<td>CR/CRh</td>
<td>30 (48)</td>
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</tbody>
</table>

Abbreviations: CR, complete remission; CRc, composite complete remission; CRh, complete remission with partial hematologic recovery; CRi, complete remission with incomplete hematologic recovery; CRp, complete remission with incomplete platelet recovery.

Bold font indicates aggregate responses.

*Defined as the sum of patients who achieved CR, CRi, and CRp.


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SARS-CoV-2 antibody responses in patients with acute leukaemia

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Abstract Content: Patients with acute leukaemia represent a high-risk group who are reported to have some of the poorest outcomes of COVID-19. The development of antibody responses to SARS-CoV-2 is an indicator of seroconversion and affords protection from infection. In addition, antibody responses to SARS-CoV-2 following natural infection or vaccination will clearly be a key factor in preventing and controlling COVID-19, as well public health surveillance. It has been presumed that antibody responses to SARS-CoV-2 will be impaired in patients with aggressive haematological malignancies due to underlying immunological dysfunction caused by malignancy or systemic anti-cancer treatment (SACT), placing them at increased risk. This has led to recommendations to reduce the risk of COVID-19 in these patients, including dramatic restructuring of clinical services, prolonged periods of shielding and alterations in therapy. Thus, understanding the humoral immune response to SARS-CoV-2 in this patient group is critical to help inform treatment decisions, shielding advice and vaccination policies.

Here we analysed longitudinal SARS-CoV-2 serum samples and antibody responses in a cohort of nine hospitalised patients with acute leukaemia and COVID-19 receiving systemic anti-cancer therapy (SACT) at University College London Hospital during the first wave of the pandemic. Five patients had AML, three B-ALL and one T-ALL. All patients in our cohort received SACT within 28 days of developing COVID-19. Median time between symptom onset and PCR diagnosis was 3 days (0–35 days), median duration of PCR positivity was 18.5 days (8–59 days). Longitudinal serum samples were collected a median of 9.5 days after positive PCR test and subsequent serum samples were collected up to 103 days post onset of COVID-19 symptoms. Total immunoglobulin levels and antibodies to SARS-CoV-2 external Spike glycoprotein (S1 subunit) and internal nucleoprotein (N) were measured by ELISA. We found that the majority (7/8) of patients with PCR confirmed SARS-CoV-2 infection seroconverted and developed antibodies to the major SARS-CoV-2 antigens (S1 and N), a seroconversion rate of 88% which is similar to the general population. However, seroconversion appeared delayed in general population. However, seroconversion appeared delayed in patients with acute leukaemia.
by day 28, compared to 90%). The temporal dynamics of SARS-CoV-2 antibody responses in patients was measured and the overall magnitude and persistence was as expected for acute infection. We then assessed whether the antibodies generated by patients with acute leukaemia were functional and able to inhibit SARS-CoV-2 infection, using an established pseudotyped SARS-CoV-2 neutralisation assay. The majority of the patients who seroconverted (67%) produced neutralising antibody responses. Importantly anti-S1 IgG titres and neutralising responses broadly correlated with clinical COVID-19 disease severity, although this was not absolute. Again, this is in keeping with studies in the general population and patients with haematological diseases. Our key findings are that patients with acute leukaemia on SACT can make functional antibody responses to SARS-CoV-2 and that the temporal dynamics of these responses are broadly similar to those previously reported for non-cancer patients. These have important implications for patient management and serological monitoring of SARS-CoV-2 in this high-risk group.

Disclosure of Interest: None Declared

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Novel algorithmic approach to generate consensus guidelines in AML

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Abstract Content: Treatment options for acute myeloid leukaemia (AML) have become more complex with the licensing of 4 new drugs for 1st line treatment. Clinicians have the dual challenge of establishing a patients’ eligibility for each drug and assessing their relative effectiveness in different clinical scenarios.

To help solve this problem, we developed an algorithmic approach to identify the different treatment paradigms for AML and surveyed UK experts to understand the degree of consensus for each scenario.

We created a series of decision trees (DTs) to cover the eligibility criteria for upfront AML treatments into a digital format, based on NICE guidance. A DT was also designed to replicate the ELN risk group and drug eligibility. All cases were classified by the DTs and assigned to one of 20 paradigms, based on ELN risk group and drug eligibility. All cases were eligible for daunorubicin + cytarabine (DA).

One representative case from each paradigm was identified for review by 9 AML experts who were asked to select their preferred induction chemotherapy for a 40- and 65-year-old patient, both with good performance status and no major comorbidities. A second question asked if FLAG-IDA was preferred over the initial choice. A threshold for establishing a strong consensus was arbitrarily set as >=85% agreement on 1st line choice and a weak consensus of >=75% agreement. To compare the outcomes of the survey to an existing guideline, the ESMO Clinical Practice Guideline was converted into a DT as above and applied to the selected cases to give a recommended ESMO treatment.

The survey revealed that for a 40-year-old patient, there is a strong consensus in 13/20 paradigms, a weak consensus in 2/20 paradigms and no consensus in 5/20 paradigms. For a 65-year-old, there is a strong consensus in 11/20 paradigms, a weak consensus in 3/20 paradigms and no consensus in 6/20 paradigms.

In 16/24 of the paradigms with a strong consensus in the survey, the ESMO recommendation is the same. In 4 paradigms where DA+gemtuzumab (GO) is the preferred option, the ESMO guidance is less specific with DA+/– GO recommended. ESMO recommended treatment is different in 2 paradigms (DA over CPX in a 40-year-old with intermediate risk AML and prior MDS, and CPX over DA+Midostaurin in a 65-year-old with intermediate risk AML). For 2 paradigms, there is no recommendation by ESMO as that clinical scenario is not included in the guideline.

At least 3 of the clinicians surveyed preferred FLAG-IDA as 1st line therapy in 5 paradigms for a 40-year-old and in one scenario for a 65-year-old. In the ESMO guidance FLAG-IDA was suggested as an option in 2 and one paradigms, respectively.

Our algorithmic approach successfully assigned all cases to the 20 treatment paradigms and highlighted 2 paradigms that were not covered by an existing guideline. Consensus was established in the majority of scenarios, but barriers included rigidity of drug approval or lack of evidence for rarer clinical/genetic paradigms. The survey suggests there are some differences in current treatment practices in the UK compared to those published by ESMO, and formal guidelines are needed to reflect this. This survey is the first part of a Delphi method approach to generate a UK consensus guideline.

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General Haematology including ITP and Myeloproliferative Disorders

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Pevomedistat + azacitidine versus azacitidine alone in patients with higher-risk myelodysplastic syndromes/chronic myelomonocytic leukemia or low-blast acute myelogenous leukemia: a phase 2 randomized study
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Abstract Content: Pevomedistat (P), the first small-molecule inhibitor of the NEDD8-activating enzyme, disrupts proteasomal degradation of select proteins, causing cell death. P, combined with azacitidine (A), has been well tolerated, with promising clinical activity in acute myelogenous leukemia (AML). This phase 2, randomized, open-label trial (NCT02610777) evaluated the efficacy and safety of P+A versus A in patients (pts) with higher-risk myelodysplastic syndromes (MDS)/chronic myelomonocytic leukemia (CMML) or low-blast (LB) AML.

Pts with higher-risk MDS/CMML (Revised International Prognostic Scoring System risk ≥3) or LB AML, who were naive to hypomethylating agents, were randomized 1:1 to receive intravenous (IV) P (20 mg/m² on days 1, 3 and 5) + IV/subcutaneous A (75 mg/m² on days 1–5, 8 and 9) or A alone in 28-day cycles until unacceptable toxicity, relapse, transformation to AML or progression. The study was powered on an original primary endpoint of event-free survival (EFS; time from randomization to death/transformation to AML), which changed to overall survival (OS) when enrollment was complete. Secondary endpoints included EFS, overall response rate (ORR) and safety. Pt-reported health-related quality of life (HRQoL) and response rate by baseline mutational profiling data were assessed.

Baseline characteristics were mostly balanced between the P+A (n = 58) and A (n = 62) arms. In the intent-to-treat population (n = 120), EFS trended longer with P+A than with A (median 21.0 vs. 16.6 months; hazard ratio [HR] 0.67; 95% confidence interval [CI] 0.42–1.05; P = 0.076) and was longer in pts with higher-risk MDS with P+A versus A (median 20.2 vs. 14.8 months; HR 0.54; 95% CI 0.29–1.00; P = 0.045). Median OS with P+A versus A was 21.8 vs. 19.0 months (HR 0.80; 95% CI 0.51–1.26; P = 0.334; median follow-up 21.4 vs. 19.0 months). By disease subgroup, median OS with P+A vs. A was 23.9 vs. 19.1 months (HR 0.70; 95% CI 0.39–1.27; P = 0.240) in pts with higher-risk MDS (n = 67) and 23.6 vs. 16.0 months (HR 0.49; 95% CI 0.22–1.11; P = 0.081) in pts with LB AML (n = 36). ORR in response-evaluable pts was 71% (n = 39/55; 46% complete remission [CR] + CR with incomplete blood count recovery [CRi], 5% partial response [PR], 20% hematological improvement [HI]) with P+A vs. 61% (n = 32/53; 38% CR+CRi, 8% PR, 15% HI) with A. In pts with higher-risk MDS, ORR was 79% with P+A vs. 57% with A, and the CR rate with P+A was nearly double that with A (52% vs. 27%; P = 0.050). Pts received a median of 13.0 cycles of P+A vs. 8.5 cycles of A; median A dose intensity was 97% with P+A vs. 98% with A. Grade ≥3 adverse events were reported in 90% of pts receiving P+A vs. 87% of pts receiving A, the most common being neutropenia (33% vs. 27%), febrile neutropenia (26% vs. 29%), anemia (19% vs. 27%) and thrombocytopenia (19% vs. 23%). Of the pts receiving P+A, 9% died on study vs. 16% of pts receiving A. HRQoL assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 was maintained with P+A, and there was no difference vs. A. Similar mean scores were sustained from study entry to treatment end in both arms. Clinical activity of P+A was observed in pts with higher-risk MDS or LB AML harboring poor prognostic mutations.
P+A vs. A led to longer EFS and double the CR rate in pts with higher-risk MDS and had a comparable safety profile and no increased myelosuppression; A dose intensity was maintained. A randomized phase 3 trial (NCT03268954) is further evaluating P+A vs. A.

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BH2021-OR-006
Changes in the incidence and overall survival of patients with myeloproliferative neoplasms between 2002 and 2016 in the United States

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Abstract Content: Patients (pts) with myeloproliferative neoplasms (MPNs), including polycythemia vera (PV), essential thrombocythemia (ET), and myelofibrosis (MF), have reduced overall survival (OS) compared with the general population. Previous reports have shown MPN incidence rates of 0.9–1.1, 0.7–1.0, and 0.3 per 100,000 person-years for PV, ET, and primary MF (PMF), respectively, with evidence of increasing incidence over time. The median OS for pts with PV, ET, and PMF has been previously reported in the literature as 13.5, 19.8, and 5.2–5.9 years, respectively. Contemporary analyses of MPN incidence and survival are needed, as the most recent real-world analyses were conducted on time periods up to 2012. The objective of this analysis was to describe trends in incidence and OS among pts with MPNs in the United States using data through 2016 from the Surveillance, Epidemiology, and End Results (SEER) database.

Adult pts with PV, ET, or PMF were identified from the SEER 18 registry (2002–2016) using the primary site of bone marrow (C421) and International Classification of Diseases for Oncology (ICD-O) histology codes (ICD-O-3: 9950 [PV], 9962 [ET], and 9961 [PMF]). Pts aged <18 y on the index date (date of diagnosis) or with missing demographic or survival information were excluded. Age-adjusted incidence rates (per 100,000 person-years) were standardized to the 2000 US population by dividing the incidence rates among adult pts per year by the adult US population in the year 2000. Confidence intervals for rates and rate ratios were calculated using the Tiwari method (Tiwari et al. Stat Methods Med Res. 2006;15[6]:547). Kaplan–Meier methodology was used to compare mortality rates by diagnosis year, categorized into three groups: 2002–2006, 2007–2011,

Abstract Table:
Table 1. Annual Incidence (per 100,000 Person-Years) and Kaplan-Meier Estimation of Mortality Rates for PV, ET, and PMF in the United States between 2002 and 2016 (SEER 18).

<table>
<thead>
<tr>
<th>Incidence</th>
<th>PV (n = 15,141)</th>
<th>ET (n = 14,676)</th>
<th>PMF (n = 4214)</th>
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<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Rate (95% CI)</td>
<td>Cases</td>
</tr>
<tr>
<td>Total*</td>
<td>15,261</td>
<td>1.57 (1.55–1.60)</td>
<td>14,793</td>
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<tr>
<td>Age &lt;65 y (PMF)/&lt;60 y (PV/ET)</td>
<td>5586</td>
<td>0.72 (0.70–0.74)</td>
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<tr>
<td>≥65 y (PMF)/≥60 y (PV/ET)</td>
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<td>4.54 (4.45–4.64)</td>
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<tr>
<td>Sex Female</td>
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<tr>
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<td>1727</td>
</tr>
<tr>
<td>American Indian/Alaska native</td>
<td>71</td>
<td>0.65 (0.50–0.84)</td>
<td>77</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>923</td>
<td>1.03 (0.96–1.10)</td>
<td>1075</td>
</tr>
<tr>
<td>Unknown</td>
<td>243</td>
<td>NA</td>
<td>332</td>
</tr>
<tr>
<td>Year of diagnosis 2002–2006</td>
<td>4793</td>
<td>1.65 (1.61–1.70)</td>
<td>3564</td>
</tr>
<tr>
<td>2007–2011</td>
<td>4847</td>
<td>1.52 (1.48–1.56)</td>
<td>5090</td>
</tr>
<tr>
<td>2012–2016</td>
<td>5501</td>
<td>1.55 (1.51–1.59)</td>
<td>6022</td>
</tr>
<tr>
<td>Mortality*</td>
<td>PV (n = 15,141)</td>
<td>ET (n = 14,676)</td>
<td>PMF (n = 4214)</td>
</tr>
<tr>
<td>5-y mortality rate, n/N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years 2002–2006</td>
<td>575/4725 (12.2)</td>
<td>378/3555 (10.6)</td>
<td>420/1097 (38.3)</td>
</tr>
<tr>
<td>Years 2007–2011</td>
<td>577/4780 (12.1)</td>
<td>702/5076 (13.8)</td>
<td>496/1410 (35.2)</td>
</tr>
<tr>
<td>Years 2012–2016</td>
<td>604/5438 (11.1)</td>
<td>723/6008 (12.0)</td>
<td>614/1702 (36.1)</td>
</tr>
</tbody>
</table>

*Total incidence was calculated in the population prior to exclusions (ie, index myelofibrosis with subsequent ET/PV diagnosis or index ET/PV with subsequent PV/ET diagnosis) for additional analyses.

1Patients with missing values for survival were excluded from the mortality analysis (PV, n = 198; ET, n = 37; PMF, n = 5).

2*n* represents the number of deaths; “N” represents the number of patients available for analysis in each time period.
and 2012–2016. Pts were censored at the end of each 5-year analysis timeframe.

Data for 34,031 pts (mean age, 65 y; female, 50.5%) were included in this analysis (PV, n = 15,141; ET, n = 14,676; PMF, n = 4,214). Over the entire study period, incidence rates (95% CI) for PV, ET, and PMF were 1.57 (1.55–1.60), 1.55 (1.52–1.57), and 0.44 (0.43–0.45) per 100,000 person-years, respectively. The annual incidence rates of PV and PMF were higher for male versus female pts (1.94 vs. 1.23 and 0.59 vs. 0.33, respectively); however, the ET incidence rate was higher for female pts (1.73 vs. 1.34; Table 1). ET incidence was highest among black pts (1.81 vs. 1.51 for white pts). ET incidence increased across the three time periods, whereas PV and PMF incidence remained relatively stable.

Over the three time periods, mortality rates decreased for PV and PMF, but not for ET (Table 1). Improved OS was observed in pts with PMF over time (median [95% CI]: 2002–2006, 3.3 [2.4–3.6] y; 2007–2011, 3.6 [3.3–4.3] y; 2012–2016, 3.8 [3.5–4.2] y). The median (95% CI) OS for the entire time period investigated was 12.0 (11.7–12.4) years for pts with PV, 12.0 (11.7–12.3) years for those with ET, and 3.6 (3.4–3.8) years for pts with PMF.

In this nationally representative real-world study, incidence of ET appeared to increase over time from 2002 to 2016. Median OS in pts with PV, ET, and PMF was shorter than previous reports. A trend of improved survival over time was observed in pts with PV and PMF, which was not observed in pts with ET. Further investigation into the varying OS rates between MPN subtypes is needed, as these data may suggest that ET is lacking improvements in supportive care strategies or therapies that exist for PV and MF.


BSH2021-OR-007

Results from PIONEER: a randomized, double-blind, placebo-controlled, phase 2 study of avapritinib in patients with indolent systemic mastocytosis

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1Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom, 2University of Antwerp and Antwerp University Hospital, Antwerp, Belgium, 3Brigham and Women's Hospital, Harvard Medical School, Boston, 4University of Michigan, Ann Arbor, United States, 5University Medical Center Groningen, University of Groningen, Groningen, Netherlands, 6Huntsman Cancer Institute, University of Utah, 7ARUP Laboratories, University of Utah, Salt Lake City, 8Blueprint Medicines Corporation, Cambridge, 9DanaFarber Cancer Institute, Boston, 10Stanford Cancer Institute/Stanford University School of Medicine, Stanford, United States

Abstract Content: Systemic mastocytosis (SM) is driven by the KIT D816V mutation in ~95% of cases. Patients with indolent SM (ISM), a variant of SM, suffer from debilitating and potentially life-threatening symptoms caused by mast cell (MC) proliferation/

hyperactivation. There are no approved disease-modifying therapies for patients with ISM. Avapritinib, a highly potent and selective KIT D816V inhibitor, markedly reduced MC burden in the phase 1 EXPLORER study (NCT02561988) in patients with advanced SM. PIONEER (NCT03731260) is a randomized, double-blind, placebo-controlled, 3-part, phase 2 study of avapritinib in patients with ISM and symptoms inadequately controlled by supportive care. Objectives included identifying recommended phase 2 dose (RP2D) in part 1 (25 mg, 50 mg, 100 mg once daily vs. placebo), safety, and comparing efficacy of avapritinib at RP2D versus placebo in part 2, based on change in total symptom score (TSS) assessed by the ISM Symptom Assessment Form (scores ranging from 0 to 110). Changes in serum tryptase, KIT D816V mutational burden, and marrow MC burden were also measured. Part 1 completed enrollment with 39 patients with ISM, treated with 25 mg (n = 10), 50 mg (n = 10), or 100 mg avapritinib (n = 10), or placebo (n = 9) in 4-week cycles; 77% were female, with median age of 51 (range 21–75) years. As of 27 December 2019, 95% of patients remained on study with a median of 18 (range 1–36) weeks. At baseline, median TSS was 52 (range 19–100), serum tryptase was 45 ng/mL (range 6–416), and 95% of patients were KIT D816V-positive in peripheral blood with median variant allele fraction of 0.36% (range 0–30) digital droplet PCR (central lab); median bone marrow MC infiltrate was 10% (range 1–60). Most common adverse events (AEs) of any grade (placebo; avapritinib all doses) were nausea (22%; 37%), dizziness (22%; 33%), headache (11%; 30%), diarrhea (11%; 23%), and fatigue (11%; 20%). Grade 3 AEs occurred in 22% of placebo- and 20% of avapritinib-treated patients. None of the 10 patients treated at 25 mg had grade 3 AEs or dose modifications; of patients receiving 50 mg (n = 10) and 100 mg (n = 10), 20% and 40% had grade 3 AEs, and 30% and 30% had dose modifications, respectively. A significant mean % reduction in TSS was observed at cycle 5 day 1 in avapritinib-treated patients (all cohorts combined) versus placebo (P = 0.001). Improvements in all individual TSS symptoms assessed were observed at cycle 5 day 1 with 25 mg avapritinib. Across avapritinib dose cohorts, mean reductions in symptoms were similar; TSS trends observed in ongoing patients in the 25-mg dose group up to cycle 5 indicate that symptom burden reached similar levels to the 100-mg dose group over time. Based on tolerability and efficacy findings, 25 mg was selected as the RP2D for part 2. Analysing the 25-mg avapritinib group in more detail, 7 of 10 patients exhibited a ≥50% reduction in serum tryptase, 6 of 10 cleared or had a ≥50% reduction in blood KIT D816V allele fraction, and 7 of 10 cleared marrow MC aggregates and/or had a ≥50% reduction of marrow MCs. At 25 mg (RP2D), avapritinib was well tolerated with no grade ≥5 reductions in any grade ≥5 AEs or dose modifications. Furthermore, patient-reported reductions from baseline in SM symptoms versus placebo were associated with decreased levels of serum tryptase, KIT D816V allele fraction in peripheral blood, and marrow MC aggregates. Part 2 of PIONEER will assess the safety and efficacy of avapritinib 25 mg (RP2D) vs. placebo, with a target enrollment of 204 patients.

Disclosure of Interest: D. H. Radia Conflict with: Dr. Radia has received funding from Blueprint Medicines Corporation, V. Sabato Conflict with: Dr. Sabato's institution has received funding from Blueprint Medicines Corporation for this trial, M. Castells Conflict with: Dr. Castells has served as consultant for Blueprint Medicines Corporation. She has received funding from Blueprint Medicines Corporation for research support, C. Akin Conflict with: Dr. Akin has received funding from Blueprint Medicines Corporation for consultation and research support., H. O. Elberink Conflict with: Dr. Elberink has served on an advisory board for Blueprint Medicines Corporation. Dr. Elberink has received an institutional grant from Novartis for an investigator-initiated trial with midostaurin. T. Tashi:
None Declared. T. I. George Conflict with: Dr. George has received no funding for this research. ARUP Laboratories, owned by the University of Utah, has received funding from Blueprint Medicines Corporation. Dr. George has received consulting fees from Blueprint Medicines Corporation during the past 12 months; she is also a consultant for Deciphera, but has not received financial compensation for the past 12 months. M. Roche Conflict with: Maria Roche reports other from Epizyme, outside the submitted work and is a current employee and shareholder of Blueprint Medicines Corporation. D. J. DeAngelo Conflict with: Dr. DeAngelo has served as a consultant for Amgen, Autolos, Agios, Blueprint Medicines Corporation, Forty-Seven, Incyte, Jazz, Novartis, Pfizer, Shire, and Takeda. Dr. DeAngelo has received research funding from AbbVie, Glycomimetics, Novartis, and Blueprint Medicines Corporation, J. Gotlib Conflict with: Dr. Gotlib has received funding for administration of the trial from Blueprint Medicines Corporation.

**BSH2021-OR-008**

**Addition of parsaclisib (INC050465), a PI3Kδ inhibitor, in patients with suboptimal response to ruxolitinib: a phase 2 study in patients with myelofibrosis**

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1University of Kansas Medical Center, Kansas City, 2Roswell Park Comprehensive Cancer Center, Buffalo, New York, 3Memorial Sloan Kettering Cancer Center, New York, 4Oregon Health & Science University, Portland, Oregon, 5Mount Sinai Hospital, New York, 6City of Hope Comprehensive Cancer Center, Duarte, 7Massachusetts General Hospital, Boston, 8University of Southern California, Los Angeles, 9Incyte Corporation, Wilmington, 10University of Texas MD Anderson Cancer Center, Houston, United States

**Abstract Content:** Ruxolitinib improves outcomes in patients with myelofibrosis (MF); however, suboptimal response may occur due to persistent PI3K/AKT pathway activation despite continued JAK inhibition. This phase 2 study (NCT02718300) evaluated optimal dosing and efficacy of add-on parsaclisib, a potent, highly selective next-generation PI3Kδ inhibitor, in patients with MF and suboptimal ruxolitinib response.

Patients had primary/secondary MF, ECOG ≤2, and suboptimal response (palpable spleen > 10 cm below subcostal margin [LSM]; or palpable spleen 5–10 cm below LSM and active symptoms) after ≥6 months of ruxolitinib (5–25 mg BID; stable dose, ≥8 weeks). Patients remained on their stable ruxolitinib dose and were randomized to add-on parsaclisib QD/QW (10 or 20 mg QD for 8 weeks and same dose QW thereafter) or parsaclisib QD (5 or 20 mg QD for 8 weeks and 5 mg QD thereafter). The primary endpoint was baseline-to-week-12 spleen volume change by MRJ/CT; secondary endpoints were spleen length and symptom changes (Myelofibrosis-Symptoms Assessment Form Total Symptom Score [MFSAF-TSS]).

At data cut-off (1/20/2020), 33 patients received parsaclisib QD/QW; 20 received QD (median treatment duration, 197 days; median average daily doses: parsaclisib, 4.9 mg/day; ruxolitinib, 30.0 mg/day). Baseline median (range) spleen volume (cm³) was 2333 (327–5324) in QD/QW (n = 30) and 1890 (434–3741) in QD (n = 17); median MFSAF-TSS was 10.8 (n = 28) and 18.7 (n = 17).

In QD/QW and QD, median percent spleen volume change was −2.3 (n = 30) and −15.4 (n = 17) at week-12; −2.5 (n = 24); −25.4 (n = 9) at week-24. See Table 1 for week-12 and week-24 spleen volume reductions. Median percent change in MFSAF-TSS at week-12 was −14.0 (n = 21) in QD/QW; −39.6 (n = 12) in QD.

Nonhematologic AEs were primarily grade 1/2. Grade 3/4 treatment-related, nonhematologic AEs included disseminated tuberculosis, enteritis, fatigue, hypertension, increased alanine aminotransferase, and increased aspartate aminotransferase in QD/QW and stomatitis in QD. In QD/QW and QD, 6/33 and 6/20 patients had new-onset grade 3 thrombocytopenia; 7/33 and 0/20 patients had grade 4 thrombocytopenia; hemoglobin levels remained steady during the study in both groups. Serious treatment-related AEs were stomatitis, herpes zoster infection, varicella zoster infection, and disseminated tuberculosis (each n = 1). No colitis/dose-limiting diarrhea/rash occurred. In QD/QW and QD, 18/33 and 10/20 patients interrupted parsaclisib, and 4/33 and 4/20 interrupted ruxolitinib for AEs.

Add-on parsaclisib showed efficacy in patients with MF experiencing suboptimal ruxolitinib response; QD dosing appeared more efficacious than QD/QW dosing. Combination therapy demonstrated acceptable safety with limited grade 3/4 AEs and no dose-limiting AEs.

**Abstract Table:**

<table>
<thead>
<tr>
<th>Week 12</th>
<th>n (%)</th>
<th>Daily/Weekly Dosing</th>
<th>All Daily Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10% reduction</td>
<td>10 (33)</td>
<td>10</td>
<td>17</td>
</tr>
<tr>
<td>≥25% reduction</td>
<td>1 (3)</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>≥35% reduction</td>
<td>0</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Week 24</td>
<td>n = 0</td>
<td>n = 14</td>
<td></td>
</tr>
<tr>
<td>≥10% reduction</td>
<td>6 (20)</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>≥25% reduction</td>
<td>4 (13)</td>
<td>5</td>
<td>36</td>
</tr>
<tr>
<td>≥35% reduction</td>
<td>1 (3)</td>
<td>1</td>
<td>7</td>
</tr>
</tbody>
</table>

BSH2021-OR-009
BCX9930, an oral factor D inhibitor for the potential treatment of paroxysmal nocturnal hemoglobinuria and other alternative pathway mediated diseases, inhibits the alternative pathway in healthy subjects
Matthew Davidson1,*, Amanda Mathis1, Stuart Mair2, Diane Gesty-Palmer3, Sylvia Dobo1, Melanie Compropst1, William Sheridan1, Saritha Muppa3, Fugang Zhu3, Cynthia Parker3, David Reynolds1, Jessica Best1, Yarlagadda Babu3, Xilin Chen3
1BioCryst Pharmaceuticals, Inc., Durham, United States, 2Quotient Sciences, Nottingham, United Kingdom, 3BioCryst Pharmaceuticals, Inc., Birmingham, United States

Abstract Content: BCX9930 is a potent and selective orally bioavailable inhibitor of factor D that has the potential to abrogate dysregulation of the complement alternative pathway (AP), including inhibition of both intravascular hemolysis and extravascular hemolysis in paroxysmal nocturnal hemoglobinuria (PNH). This abstract describes results from the completed single ascending dose (SAD) and multiple ascending dose (MAD) evaluations of Study BCX9930-101.

This was a first-in-human randomized, double-blind, placebo-controlled evaluation of the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of oral BCX9930 in healthy subjects. Safety and tolerability were evaluated via clinical and laboratory monitoring. Plasma concentrations of BCX9930 were measured using a validated liquid chromatography-dual mass spectrometry assay; PD effects were assessed using multiple assays, including inhibition of stimulated AP activity in the AP-specific Wieslab assay.

A total of 56 subjects (n = 6 BCX9930 per cohort, n = 2 placebo per cohort) were enrolled into 7 SAD cohorts, with doses ranging from 10 to 2000 mg. A total of 96 subjects (n = 10 BCX9930 per cohort, n = 2 placebo per cohort) were enrolled into 8 MAD cohorts, with doses ranging from 50 to 500 mg every 12 hours (Q12h), and 1000 to 2000 mg every 24 hours (Q24h). The mean age of all enrolled subjects was 34.9 years, and 52.0% were male.

BCX9930 was safe and generally well-tolerated at all SAD and MAD dose levels. In Part 1, 32% (18/56) of subjects reported a treatment-emergent adverse event (TEAE); all were mild. In Part 2, 59% (57/96) of subjects reported a TEAE of these, most (37/57; 65%) reported only mild event(s). No serious adverse events, treatment-related grade 3 or 4 events, or clinically relevant laboratory abnormalities were reported.

Following BCX9930 administration, exposure was approximately linear and dose proportional across all evaluated doses. BCX9930 concentrations were within or above the anticipated therapeutic target range at 12 hours post-dose for SAD doses ≥300 mg and for MAD doses ≥200 mg Q12h and ≥1000 mg Q24h at steady state.

The onset of AP suppression as observed in the AP-Wieslab assay was rapid, occurring ≤1 hour after a single dose. Maximal suppression (>98% relative to predose levels) was achieved following SAD doses ≥100 mg and for all MAD doses. The duration of suppression was dose-dependent, with maximal suppression observed prior to and for at least 1 dosing interval following the last dose at steady state for MAD doses ≥200 mg Q12h and ≥1000 mg Q24h.

BCX9930 was safe and generally well-tolerated following SAD and MAD in healthy subjects, with no serious adverse events or safety signals across the dose range. BCX9930 administration resulted in predictable plasma exposure across the evaluated dose range and exhibited rapid, potent, and dose-dependent inhibition of AP activity. Doses ≥200 mg Q12h and ≥1000 mg Q24h achieved maximal suppression of AP activity throughout the dosing interval. These results support the further development of oral BCX9930 for treatment of AP-mediated diseases such as PNH.

HUMAN erythroid progenitors are directly infected by SARS-CoV-2: implications for emerging erythropoiesis in severe COVID-19 patients
Hector Huerga Encabo* and Haematopoietic Stem Cell Laboratory (The Francis Crick Institute-Dominique Bonnet)

Abstract Content: We document here that intensive care COVID-19 patients suffer a profound decline in haemoglobin levels but show an increase of circulating nucleated red cells, suggesting that SARS-CoV-2 infection either directly or indirectly induces stress erythropoiesis. We show that ACE2 expression peaks during erythropoiesis and renders erythroid progenitors vulnerable to infection by SARS-CoV-2. Early erythroid progenitors, defined as CD34−CD117+CD71−CD235a−, show the highest levels of ACE2 and constitute the primary target cell to be infected during erythropoiesis. SARS-CoV-2 causes the expansion of colony formation by erythroid progenitors and can be detected in these cells after two weeks of the initial infection. Our findings constitute the first report of SARS-CoV-2 infectivity in erythroid progenitor cells and can contribute to understanding both the clinical symptoms of severe COVID-19 patients and how the virus can spread through the circulation to produce local inflammation in tissues, including the bone marrow.

Background: An aberrant increase of erythroid progenitors in circulation have been reported in severe COVID-19 cases and correlates with severity and mortality. The infectivity of SARS-CoV-2 in HSPCs and more particularly in erythroid progenitors have not been characterized. In this report, we have studied HSPCs and different erythroid progenitor populations to assess if they can be infected by SARS-CoV-2.

Aims: Demonstrate that SARS-CoV-2 can infect erythroid progenitors and disrupt erythropoiesis causing the aberrant increase of nucleated red blood cells observed in severe COVID-19 patients.

Methods: Clinical data: A sample of 30 patients who were being treated for COVID-19 on intensive care units at King’s College Hospital; RNAseq data import and analysis of ACE2 expression: RNAseq dataset was downloaded from GSE118537; Isolation of mononuclear cells from human cord blood, bone marrow and peripheral blood; Flow cytometry analysis and cell sorting; mRNA quantification by RT-qPCR; Immunostaining, confocal microscopy and immunofluorescence quantification of ACE2 and TMPRSS2; SARS-CoV-2 production and infection; colony-forming unit (CFU) assay.

Disclosure of Interest: None Declared
Laboratory Haematology and Transfusion

BSH2021-OR-011
Transfusion related mortality in the UK 2014-2019
Simon Carter-Graham*, Shruthi Narayan1, Jeni Davies1, Debbi Poles1
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Introduction: Transfusion of blood components in the UK is generally safe and data during this six-year period shows the risk of death as 0.85 per 100,000 components issued. Serious Hazards of Transfusion (SHOT) is the UK independent haemovigilance scheme. Reactions, errors and events related to transfusions of blood components are reported to SHOT via an electronic reporting system. Non-infectious causes continue to be the leading cause of transfusion related deaths. Most of the incidents reported to SHOT were caused by human errors, some of which resulted in death.

Aims: This review was undertaken to look at any changing trends relating to transfusion related deaths in the UK which were reported to SHOT.

Methods: A retrospective analysis was performed of all cases reported to SHOT where patient death occurred in relation to transfusion of blood products where the imputability was 1 (possibly related to transfusion), 2 (probably related) and 3 (related) during the period 2014–2019.

Abstract Table:

<table>
<thead>
<tr>
<th>Category</th>
<th>Deaths</th>
<th>Imputability 3</th>
<th>Imputability 2</th>
<th>Imputability 1</th>
<th>% of total deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusion-associated circulatory overload (TACO)</td>
<td>48</td>
<td>4</td>
<td>22</td>
<td>22</td>
<td>39.0</td>
</tr>
<tr>
<td>Avoidable, delayed, under(over) transfusion (ADU)</td>
<td>40</td>
<td>4</td>
<td>12</td>
<td>24</td>
<td>32.5</td>
</tr>
<tr>
<td>Transfusion-associated dyspnoea (TAD)</td>
<td>11</td>
<td>0</td>
<td>1</td>
<td>10</td>
<td>9.0</td>
</tr>
<tr>
<td>Haemolytic transfusion reactions (HTR)</td>
<td>8</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>6.5</td>
</tr>
<tr>
<td>Uncommon complications of transfusion (UCT)</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Transfusion-related acute lung injury (TRALI)</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>4.1</td>
</tr>
<tr>
<td>Transfusion-associated necrotising enterocolitis (TANEC)</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>3.3</td>
</tr>
<tr>
<td>Transfusion-transmitted infection (TTI)</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2.4</td>
</tr>
<tr>
<td>Incorrect blood component transfused (IBCT)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>Anti-D Ig administration error</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>Total</td>
<td>123</td>
<td>11</td>
<td>45</td>
<td>67</td>
<td>100%</td>
</tr>
</tbody>
</table>

Results: In the six years of data examined there were 123 deaths, an average of 21.2 deaths per year from 14,771,126 components issued. The main causes of death were TACO (transfusion associated circulatory overload) 48/123 (39.0%) and ADU (avoidable, delayed under or over transfused) 40/123 (32.5%). Deaths occurred mainly in patients between 70–90 years of age 74/123 (60.0%). Paediatric cases accounted for 8/123 (6.5%) of deaths, most often due to TANEC (transfusion associated necrotising enterocolitis) in pre-term neonates.

Emergency/urgent transfusions in high stress/busy clinical areas such as emergency departments, theatres and intensive care units accounted for 73/123 (59.3%) of reports. There were 45/123 (36.5%) routine/elective transfusions and 3/123 (2.4%) were unknown. There were 35/123 (28.4%) delays in transfusion with 14/35 (40.0%) involving MHP (major haemorrhage protocol). Poor communication between the clinical and laboratory teams accounted for 25/32 (78.1%) of reports causing a delay in transfusion. Other errors include under-transfusion and over-transfusion.

In deaths related to TRALI (transfusion related acute lung injury), TAD (transfusion associated dyspnea), HTR (haemolytic transfusion reactions) and IBCT (incorrect blood component transfused) the implicated component was primarily red cells 19/25 (76.0%). In all reports the patients had an average number of four co-morbidities for example chronic anaemia, cardiac failure and renal impairment amongst others.

Summary/Conclusions: Non-infectious complications, especially TACO, continue to be the most common causes of transfusion related deaths in the UK. The past six years has seen an upward trend in reports of delay in transfusion with an average of 90.4 cases reported each year. This changing trend may be attributed to improved detection of errors and better reporting. Improving decision making in transfusion, monitoring patients receiving transfusion, patient education, addressing factors contributing to errors, building safer systems and continued vigilance are vital in improving transfusion safety.

There are still improvements to be made with routine/elective transfusions carried out within normal working hours, where delays have occurred. The information suggests that great care needs to be taken with all transfusions but especially in emergency transfusions of male patients who are aged 70 years or over, have multiple co-morbidities and are outside normal working hours (8 pm–8 am). Several reports demonstrate that there are still misunderstandings about activation of the MHP and robust procedures need to be in place to prevent delays.

BSH2021-OR-012
Platelet transfusions for reversing the effects of antiplatelet drugs at Oxford University Hospital NHS Foundation Trust: a two-year retrospective review
Michael Desborough1,2,*, Julie Staves1, Paolo Polzella1, Sue Pavord1, Richard Siviter3, Mike Murphy1,2,4
1Department of Clinical Haematology, Oxford University Hospitals NHS Foundation Trust, 2Radcliffe Department of Medicine, University of Oxford, 3Neurocritical Care, Oxford University Hospitals NHS Foundation Trust, 4NHS Blood and Transplant, John Radcliffe Hospital, Oxford, United Kingdom

Abstract Content: Introduction: British Society for Haematology guidelines recommend consideration of tranexamic acid and 2–3
Abstract Table:

<table>
<thead>
<tr>
<th>Indication for platelet transfusion</th>
<th>Neurosurgery</th>
<th>Cardiac surgery</th>
<th>Other</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>108 (74%)</td>
<td>24 (17%)</td>
<td>13 (9%)</td>
<td>145</td>
</tr>
<tr>
<td>Platelet count (x10^9/L)</td>
<td>269 ± 116</td>
<td>186 ± 69</td>
<td>237 ± 112</td>
<td>253±113</td>
</tr>
<tr>
<td>Platelet transfusions</td>
<td>183 (76%)</td>
<td>39 (16%)</td>
<td>18 (8%)</td>
<td>240</td>
</tr>
<tr>
<td>Platelet transfusions per patient</td>
<td>1.69 ± 0.57</td>
<td>1.63 ± 0.88</td>
<td>1.38 ± 0.51</td>
<td>1.66±0.62</td>
</tr>
<tr>
<td>1 unit</td>
<td>46 (43%)</td>
<td>14 (58%)</td>
<td>8 (62%)</td>
<td>68 (47%)</td>
</tr>
<tr>
<td>2 units</td>
<td>57 (53%)</td>
<td>6 (25%)</td>
<td>5 (38%)</td>
<td>68 (47%)</td>
</tr>
<tr>
<td>3 or more units</td>
<td>5 (4%)</td>
<td>4 (17%)</td>
<td>0 (0%)</td>
<td>9 (6%)</td>
</tr>
<tr>
<td>Tranexamic acid</td>
<td>29 (27%)</td>
<td>3 (13%)</td>
<td>9 (69%)</td>
<td>41 (28%)</td>
</tr>
<tr>
<td>Bleeding complications</td>
<td>7 (6%)</td>
<td>3 (13%)</td>
<td>2 (15%)</td>
<td>12 (8%)</td>
</tr>
<tr>
<td>Thrombotic complications</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>2 (15%)</td>
<td>3 (2%)</td>
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</tbody>
</table>

adult doses platelets for reversal of antiplatelet drug effects in critical bleeding or prevention of bleeding before emergency surgery. **Aim:** To review platelet transfusion practice for reversal of antiplatelet drugs at Oxford University Hospitals NHS Foundation Trust (OUH), a large acute hospital trust with a tertiary neurosurgical centre. **Methods:** Retrospective review of all platelet transfusions over 24 months between 1 January 2019 and 31 December 2020, where the indication was reversal of antiplatelet drug effect. Patients were included if their primary reason for platelet transfusion was reversal of antiplatelet drug effect and if their platelet count was less than 50 x10^9/L. **Results:** In total, 1671 patients received 7031 units of platelets at OUH over 24 months. A total of 145 patients (9% of all patients transfused with platelets) received 240 adult doses of platelets (3% of all platelet transfusions) for reversal of antiplatelet drugs. 183/240 (76%) adult doses of platelets to reverse antiplatelet drug effect were administered immediately prior to neurosurgery and 24/240 (17%) for bleeding after cardiac surgery. 79/145 (54%) patients were taking single agent aspirin, 38/145 (26%) were taking single agent clopidogrel and 27/145 (19%) were taking dual antiplatelet therapy. The indications for antiplatelet drugs were: acute myocardial infarction or acute ischaemic stroke in the preceding seven days 34/145 (23%), cardiovascular disease secondary prevention 70/145 (48%), cardiovascular disease primary prevention 19/145 (13%), and 22/145 (15%) were taking antiplatelet drugs for other reasons.

One adult dose of platelets was administered in 68/145(47%), two adult doses for 68/145 (47%) and 3 or more adult doses for 9/145 (6%). 41/145 (32%) were given tranexamic acid. Antiplatelet drugs were withheld for at least seven days after giving platelets in 94/145 (65%) cases. 12/145 (8%) patients had significant bleeding complications despite platelet transfusion and 3/145 (2%) had thrombotic events (one provoked deep vein thrombosis four days after platelet transfusion for neurosurgery; one provoked pulmonary embolism eleven days after platelet transfusion for an acute gastrointestinal bleed; and one myocardial infarction 28 days after platelet transfusion for a pulmonary haemorrhage). There were no transfusion reactions. **Conclusion:** There is considerable variation in platelet transfusion practice for reversal of the effects of antiplatelet drugs. The efficacy and safety of platelet transfusions prior to neurosurgery or for bleeding after cardiac surgery is unknown. While the number of transfusions is presently a small proportion of the total doses of platelets transfused, evidence suggesting efficacy, or lack of efficacy, for platelet transfusion before neurosurgery or for bleeding after cardiac surgery, would result in significant changes in platelet prescribing practice.

Disclosure of Interest: M. Desborough Conflict with: Takeda and Portola, Conflict with: Speaker fees for Takeda and Pfizer, J. Staves: None Declared, P. Polzella: None Declared, S. Pavord: None Declared, R. Siviter: None Declared, M. Murphy: None Declared

BSH2021-OR-013

**Sorry I didn’t know – the perils of poor handover in transfusion laboratories**

**Victoria Tuckley**, Emma Milser, Shruthi Narayan, Jennifer Davies, Debbi Poles

1SHOT Office, Serious Hazards of Transfusion, NHS Blood and Transplant, Manchester, United Kingdom

**Abstract Content:** The Serious Hazards of Transfusion (SHOT) haemovigilance scheme collects and analyses anonymised information relating to serious adverse reactions and serious adverse events (SAE) of blood transfusion reported in the United Kingdom. Miscommunication is frequently noted as a contributory factor in SHOT reports and the importance of communication at handover is highlighted in the Transfusion Handbook (2014). Shift work relies on effective information transfer; however, multiple factors prevent safe and effective handovers.

Laboratory incidents reported to SHOT from January 2015-December 2019 were reviewed. Searches were performed with phrases ‘handover’ and ‘shift change’ and their derivatives. The number of incidents containing these phrases was compared to number of incidents reported in each category and the overall number of incidents reported. A total of 113/2267 (5.0%) laboratory incidents were related to the handover, the largest yearly percentage 26/409 (6.4%) occurred in 2017. Most involved transfusions in adults, 95/113 (84.1%) and the majority suffered no or minor adverse outcome, 112/113 (99.1%), there were 0 deaths and 1 case of major morbidity (sensitisation to K antigen in a patient of childbearing potential).

Incidents associated with handover were found in every SAE category. Most were seen in the avoidable, delayed, undertransfusion category, 25/233 (10.7%), followed by handling and storage errors, 28/416 (6.7%). Most 47/113 (41.6%) errors occurred between 8 am and 8 pm and with routine requests 45/113 (39.8%). Handover was contributory in 83/113 (73.5%) of cases and was the main source of error in 30/113 (26.3%). Incidents were further categorised as handover being insufficient, 78/113 (69.0%) or volume of workload impacting handover between shifts, 17/113 (15.0%), and in 15/113 (13.3%) of cases handover was improved as a corrective action. Where insufficient, no handover was completed in 21/78 (26.9%), or was written, 12/78 (15.4%), verbal, 5/78 (6.4%) or other.
Since the 1970s anti-D immunoprophylaxis has been given to prevent RHD isoimmunisation in all RHD-negative mothers. In 2014, a pivotal pilot study in the South West of England recommended cffDNA testing to all RHD-negative women at around 16 weeks gestation to avoid exposure to Anti-D when the foetus is predicted to be RHD negative. However, more recent meta-analysis identified a false negative rate (incorrectly classes as RHD negative) in 0.34% of cases, highlighting the importance of checking RHD status of cord blood at birth. In false negative cases, a Kleihauer test should be performed and anti-D immunoglobulin be administered to avoid RHD isoimmunisation of the mother. cffDNA testing was implemented in Hillingdon Hospital NHS Trust in March 2017. In 2019, a retrospective audit between March 2018 and May 2019 showed that 26.1% of predicted RHD-negative foetuses did not have cord blood testing to confirm RHD status at birth.

These results was highlighted as a patient safety issue and cascaded to relevant stakeholders by the obstetrics and gynaecology audit lead, unfortunately, they could not be formally presented due to the COVID-19 pandemic. To assess improvement after this intervention, further retrospective data were collected from all neonates born between April and September 2020 in The Hillingdon Hospital NHS Trust. Cord blood results of RHD-negative mothers were collected from WINPATH, Sunquest ICE. Miscarriages and deliveries in alternative hospitals were excluded.

A total of 202 RHD-negative women were identified (Table 1). Of these pregnant women, 118 (59.4%) were identified as carrying RHD-positive foetuses, 65 (32.2%) identified as carrying RHD-negative foetuses and 19 (9.4%) had inconclusive RHD status on cffDNA screen. There was one false positive result, where RHD status was positive on cffDNA and negative on cord blood. Cord blood testing for RHD status was performed in 91% of pregnant women carrying RHD-negative foetuses according to cffDNA screen, compared with only 74% in the first audit cycle.

Since the first audit cycle, the multi-disciplinary approach to change practice has resulted in marked improvement (17%) in cord blood testing in RHD-negative mothers to confirm the cffDNA result. Six cases with RHD-negative results on cffDNA were still not confirmed with cord blood testing. Although these cases are few, it could lead to potentially hazardous consequences, and so the reasons behind these situations occurring need to be explored further. Also, RHD-positive mothers do not require cord blood testing to confirm cffDNA (only a Kleihauer) and this is a potential cost saving which should be highlighted to the obstetric and midwifery team. Overall, the results are very promising; however, it is important to note that the second PDSA (plan, do, study, act) cycle has a much smaller sample size than the original. Further investigations into barriers to achieving 100% compliance is required to ensure no cases of potential maternal isoimmunisation are missed.

Abstract Table:

Table 1. Results of first and second audit cycle after intervention to increase confirmation of RHD status with cord blood at delivery.

<table>
<thead>
<tr>
<th></th>
<th>March 2018- April 2019</th>
<th>April – September 2020</th>
</tr>
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<tbody>
<tr>
<td>Total number of patients</td>
<td>433</td>
<td>202</td>
</tr>
<tr>
<td>RHD positive on cffDNA</td>
<td>261</td>
<td>118</td>
</tr>
<tr>
<td>RHD positive confirmed on cord blood (%)</td>
<td>225 (86%)</td>
<td>116 (98%)</td>
</tr>
<tr>
<td>RHD negative on cffDNA</td>
<td>149</td>
<td>65</td>
</tr>
<tr>
<td>RHD negative confirmed on cord blood (%)</td>
<td>110 (74%)</td>
<td>59 (91%)</td>
</tr>
<tr>
<td>Inconclusive/unavailable cffDNA testing</td>
<td>23</td>
<td>19</td>
</tr>
<tr>
<td>Inconclusive results cord bloods checked (%)</td>
<td>20 (87%)</td>
<td>17 (89%)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared
Effectiveness of goal-directed therapy versus massive transfusion protocol in a tertiary care center in South India

Arun V. J*, Ramesh Bhaskaran, Aboobacker Rafi, Susheela Innah, Divya Venugopal

Abstract Content: The aim of the study is to compare the blood component utilization, morbidity & mortality in patients managed by an institutional massive transfusion protocol (MTP) versus goal-directed therapy (GDT) using Rotational thromboelastometry (ROTEM).

A comparative study was done, wherein the retrospective data were collected from the institutional MTP registry and compared with prospective data of patients managed by GDT using ROTEM.

Massive transfusion was defined as per standard guidelines. Goal-Directed therapy was as per the temogram from ROTEM, Which shows clear indication for transfusion of FFP, Platelet, or cryoprecipitate. Red cell transfusion is based on clinical and other lab parameters.

Data pertaining to patient demographics, mode of admission, indication for massive transfusion, blood component usage, morbidity, and mortality were collected and analysed.

The study population comprised a total of 122 patients (61 in each protocol). The mean age of patients managed by MTP and GDT was 33.36 and 46.52 years, respectively. There was no statistical difference in gender, criteria of admission among the comparison groups.

MTP was activated for PPH, trauma and surgery at a rate of 45%, 36.1% and 11.5%. Goal-directed Therapy was initiated mainly for trauma, surgery, PPH and snake bite at a rate of 42.6%, 23%, 19.7% and 4.9% respectively. There was a significant reduction in blood component utilization for PRBC, FFP & platelet($P < 0.05$) in GDT, but cryoprecipitate utilization remained the same.

There was a significant reduction in morbidity measured as length of hospital stay (Sig=$0.038$) for patient managed by GDT (9.39 days) in comparison to those managed by MTP (17.05 days). There was no statistical difference in mortality among the comparison groups.

From the data we were able to conclude that Goal-directed therapy shows a significant reduction in blood component utilization and morbidity without a significant change in mortality among patients in this study. GDT has the potential to impact the care of critically ill patients in many ways, but current evidence for their use is limited. Further high-quality research, including randomized controlled trials are needed to elucidate the role of GDT.

Abstract Table:

<table>
<thead>
<tr>
<th></th>
<th>MTP</th>
<th>GDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRBC</td>
<td>6.92 ± 2.96</td>
<td>3.75 ± 2.23*</td>
</tr>
<tr>
<td>FFP</td>
<td>6.56 ± 2.75</td>
<td>2.38 ± 2.37*</td>
</tr>
<tr>
<td>RDP</td>
<td>6.46 ± 2.71</td>
<td>0.97 ± 2.05*</td>
</tr>
<tr>
<td>CRYO</td>
<td>6.89 ± 5.34</td>
<td>6.15 ± 5.944</td>
</tr>
<tr>
<td>TOTAL</td>
<td>26.82 ± 11.33</td>
<td>13.25 ± 8.62*</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared
Lymphoma, CLL and Myeloma

BSH2021-OR-016
CAR TITUDE-1: Phase 1b/2 study of cilta cabtagene autoleucel in relapsed/refractory multiple myeloma

Deepu Madduri1,2, Jesus Berdeja1,2, Saad Usmani2, Andrzej Jakubowiak3,4, Mounzer Agha5, Adam Cohen6, A Keith Stewart7, Parameswaran Hari8, Myo Htu9, Elizabeth O'Donnell10,11, Nikhil Munshi11,12, David Avigan12, Abhinav Deol13, Alexander Lesokhin14, Indrajeet Singh15, Enrique Zudaire15, Tzu-Min Yeh16, Alicia Allred17, Yunzi Oyslager17, Arban Banerjee15, Jenna Goldberg18, Jordan Schecter16, Carolyn Jackson16, William Deraedt17, Sen Hong Zhuang16, Jeffrey Infante16, Dong Geng16, Xiaoling Wu18, Marlene Carrasco-Alfonso18, Muhammad Akram18, Farah Hossain18, Syed Rizvi18, Frank Fan18, Sundar Jagannath1, Yi Lin20, Thomas Martin21

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Abstract Content: Cilta cabtagene autoleucel (cilta cel) is a chimeric antigen receptor T (CAR-T) cell therapy with 2 B-cell maturation antigen targeting single-domain antibodies designed to confer avidity. We present updated phase 1b data and initial phase 2 data from the CARTITUDE-1 study (NCT03548207).

Eligible patients (pts) had multiple myeloma (MM) per International Myeloma Working Group (IMWG) criteria, measurable disease, received ≥3 prior regimens (or double refractory to a proteasome inhibitor and immunomodulatory drug), and received an anti-CD38 antibody. Bridging therapy was permitted after apheresis. After cyclophosphamide 300 mg/m2 1 day and fludarabine 30 mg/m2 1–5 days, a single cilta cel targeted dose of 3–45 µg/kg was infused. Primary objectives were to characterize the safety and establish the recommended phase 2 dose of cilta cel (phase 1b) and to evaluate efficacy (phase 2). Response was assessed per IMWG criteria and minimal residual disease (MRD) by next-generation sequencing. Adverse events (AEs) were graded using CTCAE v5.0. Cytokine release syndrome (CRS) was graded by Lee et al and neurotoxicity by CTCAE in phase 1b and by American Society for Transplantation and Cellular Therapy (ASTCT) criteria in phase 2. In this combined analysis, Lee et al and CTCAE were mapped to ASTCT criteria for CRS and immune effector cell-associated neurotoxicity syndrome, respectively.

As of 20 May 2020, 97 pts with relapsed/refractory MM received cilta cel (29 in phase 1b; 68 in phase 2). Median follow-up was 8.8 mo (1.5–20.4). Median prior lines of therapy (LoT) was 6 (3–18); 83.5% were penta-exposed, 87.6% triple-refractory, 41.2% penta-refractory, and 97.9% refractory to last LoT. Overall response rate per independent review committee (primary endpoint) was 94.8% (95% CI 88.4–98.3); 55.7% had stringent complete responses, 32.0% had very good partial responses, and 7.2% had partial responses. All pts had reduction in M-protein. Median time to first response was 1.0 mo (0.9–5.8); 80.4% ≤1.0 mo), and median time to ≥complete response was 1.8 mo (0.9–12.5; 74.1% ≤3.0 mo); responses deepened with time. Median duration of response was not reached (NR). Of 52 MRD- evaluable pts, 94.2% were MRD-negative at 12 mo. The 6-mo progression-free survival (PFS) and overall survival (OS) rates (95% CI) were 87.4% (78.9–92.7) and 93.8% (86.7–97.2), respectively; median PFS and OS were NR. Ten deaths occurred during the study; 6 related and 2 unrelated AEs (CRS/hemophagocytic lymphohistiocytosis, neurotoxicity, respiratory failure, sepsis, septic shock, pneumonia, lung abscess, and acute myelogenous leukemia [n = 1 each]), and 2 from progressive disease. AEs (>70% of pts) were CRS (94.8%; grade [gr] 3/4 4.1%), neutropenia (90.7%; gr 3/4 90.7%), anemia (81.4%; gr 3/4 68.0%), and thrombocytopenia (79.4%; gr 3/4 59.8%). Median time to CRS onset was 7.0 d (1–12) and median duration 4.0 d (1–27, excluding n = 1 with 97 d). 20.6% of pts had CAR-T cell–related neurotoxicity (gr 3/4 10.3%). Cilta cel CAR+ T cells showed peak peripheral expansion at 14 d (9–43). Among pts with 6-mo individual follow-up, 67% had cilta cel CAR+ T cells below the level of quantification (2 cells/µl) in peripheral blood.

Preliminary phase 1b/2 data from CARTITUDE-1 indicate a single low-dose infusion of cilta cel leads to early, deep, and durable responses in heavily pretreated pts with MM with safety consistent with LEGEND-2.

Disclosure of Interest: D. Madduri Conflict with: Consultancy/ Honoraria (Foundation Medicine, AbbVie, Celgene, Takeda, Janssen), Conflict with: Consultancy/Honoraria/Advisory Committees/ Speakers Bureau (GSK, Legend, Kinevant), J. Berdeja Conflict with: Research Funding and/or Consultancy (Vivolux, AbbVie, Acetylon, Bluebird, Cellularity, Constellation, CURIS, EMD Serono, Genentech, Glenmark, Kesios, Lilly, Novartis, Poseida, Teva, Amgen, BMS, Celgene, CRISPR Therapeutics, Janssen, Takeda, Bioclinica, Karyopharm, Kite Pharma, Legend, Prothena, Servier), S. Usmani Conflict with: Consultancy, Honoraria, Speaking Fees, and/or Research Funding (Amgen, Takeda, Janssen, BMS/Celgene, Sanofi, AbbVie, SkylineDX, Seattle Genetics, Merck, GSK, Incyte, Pharmacyclics, Array BioPharma), A. Jakubowiak Conflict with: Consultancy/Honoraria, and/or Membership on Board of Directors/ advisory committees (AbbVie, Amgen, BMS/Celgene, GSK, Janssen, Karyopharm, Sanofi, Adaptive, Juno), M. Agha: None Declared, A. Cohen Conflict with: Consultancy (AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Seattle Genetics, Takeda), Conflict with: Research funding (GSK, Novartis), A. K. Stewart Conflict with: Honoraria/Advisory Committees (Janssen, BMS, Sanofi-Genentech, GSK, Tempus, Inc., Genomics England LLC), P. Hari Conflict with: Consultancy/honoraria/research funding (Celgene, Takeda, BMS, Spectrum, Janssen, Kite, AbbVie, Amgen, Sanofi), Conflict with: Current equity holder (Cell Vault), M. Htut Conflict with: Employee (City of Hope Medical Center), E. O’Donnell: None Declared, N. Munshi: None Declared, D. Avigan: None Declared, A. Deol Conflict with: Consultancy (Kite, Novartis), A. Lesokhin Conflict with: Consultancy/Honoraria/Research Funding (BMS, Consultancy/Honoraria (GenMab, Juno, Takeda), Conflict with: Research Funding (Genentech, Janssen), Conflict with: Patents/ Royalties (Serametrix), I. Singh Conflict with: Employee at the time of study (Janssen), E. Zudaire Conflict with: Employee (Janssen), T.-M. Yeh Conflict with: Employee (Janssen), A. Allred Conflict with: Employee (Janssen), Y. Oyslager Conflict with: Employee (Janssen),
BSH2021-OR-017
Iberdomide in combination with dexamethasone and daratumumab or bortezomib in patients with relapsed/refractory multiple myeloma: first results from the CC-220-MM-001 study

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Abstract Content: CC-220-MM-001 is a phase 1/2 study evaluating dose escalations of Iberdomide (IBER; CC-220), an oral, potent novel cereblon E3 ligase modulator (CELMoD) agent, with different treatment combinations in independent cohorts, in patients (pts) with relapsed/refractory multiple myeloma (RRMM) (NCT02773030). Preclinically, IBER has marked synergistic tumoricidal and immune-stimulatory effects in combination with bortezomib (BORT) or daratumumab (DARA). Here, we present results from the IBER+DARA+dexamethasone (DEX) (IberDd) and IBER+BORT+DEX (IberVd) cohorts. Eligible pts had experienced disease progression ≤60 days of last MM therapy, and received ≥2 prior regimens in the IberDd cohort and ≥1 prior regimen in the IberVd cohort, containing lenalidomide or pomalidomide, and a proteasome inhibitor (PI). Escalating oral doses of IBER were given in the IberDd cohort on Day (D)1–21, and in the IberVd cohort on D1–14 of each 21-D cycle. DEX was given weekly. Primary objectives were to evaluate maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), and safety; preliminary efficacy was also assessed. Immune profiling was evaluated by flow cytometry from pt peripheral blood.

As of 18 Jun, 2020, 19 pts had received IberDd and 21 pts IberVd. Baseline characteristics are shown (Table); exposure to prior regimens was heterogeneous. IBER doses ranged from 1.0mg to 1.6mg; MTD/RP2D was not reached in either cohort. Median cycles received was 5 (1–14) and 4.5 (1–17), median follow-up was 5 (0–14) and 3 (0–11) months, and 10 (53%) and 13 (62%) pts continued on treatment, with IberDd and IberVd, respectively.

Grade (G) 3–4 treatment-emergent adverse events (TEAEs) were reported in 14 (78%) and 13 (65%) pts, with IberDd and IberVd, respectively. Most frequent G3–4 TEAEs of interest included neutropenia (50%), leukopenia (22%), and anemia (22%) with IberDd; neutropenia (20%) and thrombocytopenia (20%) with IberVd. Neutropenia was managed with G-CSF. 1 pt (IberDd; 1.2mg) had G4 neutropenic sepsis. Occurrence of G3–4 non-haematological TEAEs was low. 1 pt had G2 infusion-related reaction with IberDd, and 3 pts G1–2 peripheral neuropathy with IberVd. 6 (33%; IberDd) and 4 (20%; IberVd) pts had IBER dose reductions.

With IberDd, overall response rate (ORR) was 35% across dosing groups (2 very good partial responses [VGPRs], 4 partial responses [PRs]); clinical benefit rate (CBR) was 47% and disease control rate (DCR) 88%. With IberVd, ORR was 50% (1 complete response, 3 VGPRs, 6 PRs); CBR was 65% and DCR 85%. Responses were observed irrespective of DARA- and BORT-refractoriness, median time to response was 4.1 (4.1–12.0) and 4.9 (3.0–13.1) weeks, with IberDd and IberVd, respectively.

In both cohorts, dose-dependent decreases in B cells and increases in activated and differentiated T cells were observed with immune profiling. Except for reductions in CD38+ T cells in the IberDd cohort, findings were similar with IBER+DEX.

In heavily pre-treated pts with RRMM, IberDd and IberVd showed a favorable tolerability profile, with promising clinical activity, even among pts refractory to the last prior regimen and previously exposed to immunomodulatory agents, PIs, and anti-CD38 monoclonal antibodies. IBER+DEX is pharmacodynamically active in triplet combination, as confirmed by immune-profiling data. These findings support further development of IBER-based regimens in MM.


Abstract Table: Baseline characteristics, prior therapies, and refractory status

<table>
<thead>
<tr>
<th></th>
<th>IberDd (n = 19)</th>
<th>IberVd (n = 21)</th>
</tr>
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<tbody>
<tr>
<td>Age, median (range), years</td>
<td>66 (40–77)</td>
<td>65 (47–81)</td>
</tr>
<tr>
<td>Time since initial diagnosis, median (range), years</td>
<td>8.0 (3.4–19.1)</td>
<td>7.6 (3.0–16.0)</td>
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</table>

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British Journal of Haematology, 2021, 193, (Suppl. 1), 3–45
Abstract Table. (Continued)

<table>
<thead>
<tr>
<th>Presence of EMP, n (%)</th>
<th>IberDd (n = 19)</th>
<th>IberVd (n = 21)</th>
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<tbody>
<tr>
<td>n (%)</td>
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<tr>
<td>ISS at study entry</td>
<td></td>
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<tr>
<td>Stage I</td>
<td>11 (57.9)</td>
<td>12 (57.1)</td>
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<tr>
<td>Stage II</td>
<td>5 (26.3)</td>
<td>9 (42.9)</td>
</tr>
<tr>
<td>Stage III</td>
<td>2 (10.5)</td>
<td>0</td>
</tr>
<tr>
<td>Prior therapies, median (range)</td>
<td>4 (2 – 12)</td>
<td>6 (1 – 14)</td>
</tr>
<tr>
<td>ASCT, n (%)</td>
<td>16 (84.2)</td>
<td>17 (81.0)</td>
</tr>
<tr>
<td>LEN, n (%)</td>
<td>19 (100)</td>
<td>21 (100)</td>
</tr>
<tr>
<td>POM, n (%)</td>
<td>14 (73.7)</td>
<td>16 (76.2)</td>
</tr>
<tr>
<td>BORT, n (%)</td>
<td>19 (100)</td>
<td>20 (95.2)</td>
</tr>
<tr>
<td>CFZ, n (%)</td>
<td>14 (73.7)</td>
<td>11 (52.4)</td>
</tr>
<tr>
<td>DARA, n (%)</td>
<td>13 (68.4)</td>
<td>17 (81.0)</td>
</tr>
<tr>
<td>Anti-BCMA, n (%)</td>
<td>2 (10.5)</td>
<td>2 (9.5)</td>
</tr>
<tr>
<td>&gt;8 prior regimens, n (%)</td>
<td>4 (21.1)</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>Anti-CD38 mAb-refractory, n (%)</td>
<td>12 (63.2)</td>
<td>16 (76.2)</td>
</tr>
<tr>
<td>DARA, n (%)</td>
<td>12 (63.2)</td>
<td>16 (75.1)</td>
</tr>
<tr>
<td>PI-refractory, n (%)</td>
<td>14 (73.7)</td>
<td>16 (76.2)</td>
</tr>
<tr>
<td>BORT, n (%)</td>
<td>8 (42.1)</td>
<td>9 (42.9)</td>
</tr>
<tr>
<td>IMID-refractory, n (%)</td>
<td>18 (94.7)</td>
<td>16 (76.2)</td>
</tr>
<tr>
<td>Quad-class refractory, n (%)</td>
<td>11 (57.9)</td>
<td>10 (47.6)</td>
</tr>
</tbody>
</table>

ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; BORT, bortezomib; CFZ, carfilzomib; DARA, daratumumab; DEX, dexamethasone; EMP, extramedullary plasmacytoma; IberDd, IBER+DARA+DEX; IberVd, IBER+BORT+DEX; ISS, International Staging System; IMID, immunomodulatory drug; LEN, lenalidomide; mAb, monoclonal antibody; POM, pomalidomide.

*4 patients received both autologous and allogenic stem cell transplant; #Defined as refractory to LEN or POM; $Defined as refractory to ≥1 IMID, 1 PI, 1 anti-CD38 mAb, and 1 glucocorticoid.

Disclosure of Interest: N. W. C. J. van de Donk Conflict with: Amgen, Bristol Myers Squibb, Janssen (membership on an entity’s board of directors or advisory committees, research funding); Bayer, Ferrer, Novartis, Takeda (membership on an entity’s board of directors or advisory committees); R. Popat Conflict with: AbbVie (consultancy, honoraria); GSK, Janssen (consultancy, honoraria, other: travel accommodations, expenses (paid by any for-profit health care company)); Takeda (consultancy, honoraria, other: travel support and research funding); Bristol Myers Squibb, Celgene (consultancy, honoraria); University College London Hospital (current employment), J. Larsen Conflict with: Janssen Oncology, Takeda (consultancy, honoraria and membership on an entity’s board of directors or advisory committees), M. C. Minnema Conflict with: Amgen, Servier (consultancy); Kite, a Gilead Company (speakers bureau); Celgene (research funding, other: travel support), S. Jagannath Conflict with: BMS, Janssen, Karyopharm, Legend Biotech, Sanofi, Takeda (consultancy, A. Orlit Conflict with: Bristol-Myers Squibb (membership on an entity’s board of directors or advisory committees, speakers bureau); Amgen (consultancy, speakers bureau); Janssen (consultancy); GlaxoSmithKline, Sanofi (membership on an entity’s board of directors or advisory committees), J. A. Zonder Conflict with: Celca, Janssen, Prothera); Amgen, Alnylam, Intellia, Oncopetide, Takeda (membership on an entity’s board of directors or advisory committees); BMS (consultancy, research funding), P. G. Richardson Conflict with: Celgene/BMS, Janssen, Karyopharm, Oncopetides, Sanofi, Secura Bio, Takeda, GlaxoSmithKline, Jazz Pharmaceuticals (membership on an entity’s board of directors or advisory committees); Celgene/BMS, Oncopetides, Takeda, Karyopharm (research funding); AbbVie (consultancy); Janssen, Takeda, Celgene, GlaxoSmithKline, SecuraBio, Oncopetides, BMS, Karyopharm, Sanofi (honoraria), P. Rodriguez Otero Conflict with: Sanofi (consultancy, honoraria); Janssen (consultancy, honoraria, other: travel, accommodations, expenses (paid by any for-profit health care company)); Medscape (membership on an entity’s board of directors or advisory committees); Abbvie, Amgen, Kite, Oncopetides (consultancy, honoraria); GlaxoSmithKline (consultancy, current employment, current equity holder in publicly traded company, honoraria), A. Z. Badros Conflict with: University of Maryland (current employment); Amgen (consultancy), E. Stadtmueller Conflict with: Bristol Myers Squibb (consultancy, research funding); Sanofi, Takeda (consultancy); AbbVie (research funding), S. Bringenhe Conflict with: Bristol-Myers Squibb (honoraria); Amgen, Celgene (honoraria, membership on an entity’s board of directors or advisory committees); Janssen (consultancy, honoraria, membership on an entity’s board of directors or advisory committees); Karyopharm (membership on an entity’s board of directors or advisory committees); Takeda (consultancy), E. Campagnaro: None Declared, D. S. Siegel Conflict with: Amgen, BMS, Janssen, Merck, Takeda (consultancy, honoraria, speakers bureau); Karyopharm (consultancy, honoraria); Celularity (current equity holder in publicly traded company), B. Gambari Conflict with: Amgen, Bristol Myers Squibb, Janssen, Sanofi (consultancy, honoraria); GSK (consultancy); M. Girnella Mesa Conflict with: Janssen (consultancy, honoraria); Bristol Myers Squibb (honoraria, speakers bureau), P. Sonneveld Conflict with: Amgen, Bristol-Myers Squibb, Janssen, Karyopharm, Takeda (consultancy, honoraria, research funding); Skyline Dx (honoraria, research funding); Sanofi (consultancy), T. Vi Nguyen Conflict with: Bristol Myers Squibb (current employment, current equity holder in publicly traded company), A. Di Maio Conflict with: Bristol Myers Squibb (current employment, current equity holder in publicly traded company), A. Sorrell Conflict with: Bristol Myers Squibb (current employment, current equity holder in publicly traded company), M. Amatangelo Conflict with: Bristol Myers Squibb (current employment, current equity holder in publicly traded company), E. Kueemberg Conflict with: Celgene International SA, a Bristol Myers Squibb Company, Boudry, Switzerland (current employment), S. Lorial Conflict with: Amgen, GSK, Merck, Novartis (consultancy, honoraria, other: personal fees); Takeda (consultancy, other: personal fees, research funding); BMS (consultancy, honoraria, other: personal fees, research funding); Abbvie, Genentech, JUNO Therapeutics, Karyopharm, Sanofi (consultancy); TG Therapeutics (consulting on an entity’s board of directors or advisory committees); Emory University (current employment); Millennium (consultancy, honoraria); Onyx (honoraria)

BSH2021-OR-018
Impact of age and genetics on outcomes of multiple myeloma treated with autologous stem cell transplant: single centre retrospective review, 2002-2019
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Abstract Content: Autologous stem cell transplant (ASCT) following induction chemotherapy remains standard in suitable newly
diagnosed patients with multiple myeloma (MM). Treatment strategies have evolved over time including the introduction of tandem ASCT for genetically defined high-risk myeloma. Individual high-risk genetic abnormalities confer poorer overall survival (OS) and progression-free survival (PFS), but Boyd (2012) showed that combinations of high-risk lesions were more informative in identifying high-risk disease.

A retrospective review of outcomes following ASCT for myeloma at University Hospital Southampton (UHS) was conducted, focusing on age and genetics. A database of 651 myeloma and plasma cell leukaemia patients treated with ASCT between 2002 and 2019 was collated and analysed for OS. Genetic results were present for 319 patients. 187 patients had additional data available for chart review to determine PFS. Fluorescence in situ hybridisation on CD138 selected bone marrow plasma cells from diagnosis and/or relapse was performed at Wessex Regional Genetics Laboratory to identify high-risk abnormalities t(4;14), t(14;16), t(14;20), del(1p), gain(1q) and del(17p). If only relapse results were available, any IgH translocations detected were assumed present at diagnosis.

629 patients had their first ASCT at UHS. 389 (61.8%) were male and 240 (38.2%) were female. Median age at first ASCT was 61.9 years (range 20.9–76.4 years) which increased from 58.6 in 2002–2004 to 63.2 in 2015–2019. 61 were 70 years or older.

Outcomes were compared between treatment eras. Median OS from date of ASCT increased from 6.28 years [95% CI: 4.77–8.22] for patients treated in 2002–2009 to 8.77 years [95% CI: 7.90–not reached (NR)], P = 0.007, for patients treated in 2010–2019. Median PFS from ASCT increased from 1.85 [95% CI: 1.51–2.20] to 3.12 years [95% CI: 2.53–3.70], P = 0.004, between the same time periods.

Age at ASCT had no significant effect on OS or PFS from ASCT, neither when comparing patients aged 60 and over to those under 60 nor when comparing patients aged 70 and over to those under 70. Transplant-related mortality (TRM) did not differ between those aged 70 and over compared to those less than 70 years, with TRM for the cohort being 1.45%.

A significant difference was found between patients with two or more high-risk genetic abnormalities compared to those with none, with decreases in median OS from ASCT from 11.25 [95% CI: 8.48–NR] to 3.03 years [95% CI: 2.52–6.06], P < 0.001, and in median PFS from ASCT from 3.12 [95% CI: 2.40–4.42] to 1.85 years [95% CI: 0.99-NR], P = 0.013. However, no significant difference was found between patients with one high-risk abnormality compared to those with none.

No significant difference in OS or PFS was found between patients receiving tandem ASCT for high-risk myeloma (del(17p) or 2+ high-risk markers) compared to those receiving a single ASCT, though follow-up is short.

In conclusion, this analysis demonstrates the improvements in ASCT outcomes over time. ASCT outcomes are not affected by age, but there is no standard approach to optimally select more elderly patients. Importantly, this also provides real-world validation of clinical trial data indicating poor outcomes with two or more high-risk abnormalities and the need to evaluate alternate strategies such as tandem ASCT or those explored in clinical trials such as MUK9. However, a single adverse genetic marker may not be sufficient reason to change treatment strategy.

Disclosure of Interest: M. Martine: None Declared, L. Chieccio: None Declared, K. Orchard: None Declared, E. Grand: None Declared, C. Alderman: None Declared, M. Jenner Conflict with: Honoraria and Advisory work: Janssen, Celgene/BMS, Takeda, Amgen, Abbvie, Skyline, Oncopeptides

BSH2021-OR-019
Second interim analysis of the ‘Use Via Early Access to Ixazomib’ study: A European, multicentre, observational, longitudinal cohort study of the effectiveness and safety of ixazomib-based therapy in patients with relapsed/refractory multiple myeloma treated outside of the clinical trial setting via an Early Access Programme: UK subgroup analysis

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Abstract Content: Improving our understanding of routine clinical practice and the effectiveness of new agents outside the clinical trial setting is becoming increasingly important in multiple myeloma (MM) treatment. The ‘Use Via Early Access to Ixazomib’ (UVEA-IXA) study evaluated patients (pts) treated with ixazomib (ixa), the first oral proteasome inhibitor (PI), via an Early Access Programme (EAP) in the Czech Republic, Greece, Hungary, Italy, Slovakia, Slovenia, Spain and United Kingdom (UK). Ixa was available in Europe via the EAP from Nov 2015 until European approval (based on TOURMALINE-MM1 study results; Moreau NEJM 2016) in Nov 2016. We report overall data from the second interim analysis of UVEA-IXA; data from 78 UK pts with two or three prior lines of therapy will be included for presentation.

The UVEA-IXA observation period comprised a retrospective chart review from ixa therapy initiation in the EAP and a 1-year (yr) prospective follow-up period, with quarterly data capture. Eligible pts were in biochemical and/or symptomatic relapse after 1–3 prior lines of therapy, had not received anti-MM therapy for ≥3 cycles (except steroids) at the start of ixa therapy and had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0–2. Lenalidomide (len)- or PI- refractory pts were excluded. The primary endpoints were response and progression-free survival (PFS).

At data cut-off (22 May 2020), 302 of 359 enrolled pts were evaluable; 55% were male; median age at enrolment was 68 yrs (range 36–92), 39% aged ≥70 yrs. At the start of ixa therapy, 36/117 (31%; unknown: n = 185) pts had International Staging System (ISS) stage III disease and 61/301 (20%; unknown: n = 1) had an ECOG PS of 2. Of all 302 evaluable pts, 60% had ≥1 comorbidity, including hypertension (26%), renal disease (23%) and diabetes (10%). Median time from MM diagnosis was 37.0 months (mos; range 36–231.7); 39%, 43% and 18% of pts had received 1, 2 and 3 prior lines of therapy, respectively. The median observation period among 295 pts with available data was 24.9 mos (range 0.2–49.3). Pts received ixa for a median of 10.8 mos (range 0.2–49.3); most pts also received len (97%) and dexamethasone (96%). The overall response rate (ORR) was 60% and median PFS (mPFS) was 15.6 mos; in pts with 1 or ≥2 prior lines of therapy, mPFS was 20.0 and 13.6 mos, respectively (Table). Ixa doses were reduced in 57/302
Lymphoma, CLL and Myeloma

(19%) pts and ixax was discontinued in 219/302 (73%) pts (not recorded: n = 11). Reductions were due to adverse events (AEs) in 42/302 (14%) pts; pts discontinued ixax due to PD (32%)/AEs (16%)/loss or lack of response (10%). In 187 pts who received ≥4 cycles of ixax, rates of any-grade (G) and G≥3 AEs were 60% and 33%; the most common any-G AEs were diarrhoea and thrombocytopenia (14% each); the most common G≥3 AE was thrombocytopenia (6%).

We demonstrate that ixax-based therapy is effective and tolerable outside the clinical trial setting. Outcomes appeared more favourable in pts with 1 versus ≥2 prior lines of therapy. Compared with TOURNALINE-MM1 pts (ixa arm; ORR 78%, mPFS 20.6 mos), UVEA-IXA pts had higher rates of ECOG PS 2 (20 vs. 5%) and ISS stage III MM (31 vs. 12%), and had received more prior lines of therapy (61 vs. 38% had ≥2). The most common AEs were gastrointestinal and hematologic, in line with the well-characterised safety profile of ixax, although data are not directly comparable with clinical trial safety data due to the retrospective/infrequent prospective collection schedule.

Abstract Table:

Table. Best response* to ixax-based therapy and PFS† for pts receiving ixax-based therapy within the EAP, for all evaluable pts and by number of prior lines of therapy.

<table>
<thead>
<tr>
<th>Best response, %</th>
<th>All evaluable pts</th>
<th>1 prior line</th>
<th>≥2 prior lines</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 275</td>
<td>n = 109</td>
<td>n = 166</td>
<td></td>
</tr>
<tr>
<td>ORR</td>
<td>60</td>
<td>64</td>
<td>57</td>
</tr>
<tr>
<td>≥Very good partial response (VGPR)</td>
<td>29</td>
<td>37</td>
<td>23</td>
</tr>
<tr>
<td>Complete response</td>
<td>12</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>VGPR</td>
<td>17</td>
<td>19</td>
<td>16</td>
</tr>
<tr>
<td>Partial response</td>
<td>31</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>PFS</td>
<td>n = 296</td>
<td>n = 114</td>
<td>n = 182</td>
</tr>
<tr>
<td>Events, n</td>
<td>199</td>
<td>72</td>
<td>127</td>
</tr>
<tr>
<td>Median PFS</td>
<td>15.6</td>
<td>20.0</td>
<td>13.6</td>
</tr>
<tr>
<td>(95% confidence interval), mos</td>
<td>(11.8–20.0)</td>
<td>(12.5–27.2)</td>
<td>(10.0–18.1)</td>
</tr>
</tbody>
</table>

*Response was evaluated per International Myeloma Working Group criteria; data collection ongoing for n = 27 pts. †From ixax therapy initiation in the EAP to first documented disease progression/death during the observation period; invalid time or censoring values were deleted for n = 6 pts as last observation date was not available.


BHS2021-OR-020

Patients with plasma cell disorders are able to develop and sustain an antibody response to SARS-CoV-2 following asymptomatic infection and whilst on immunomodulatory therapy

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Abstract Content: Plasma cell disorder (PCD) patients are extremely vulnerable to SARS-CoV-2 infection. Mortality in a large cohort of patients with plasma cell disorders was reported at 33%. The roll-out of COVID-19 vaccines is welcomed; however, there is no information on immune responses to vaccination in these B-cell malignancy patients who suffer with disease-related impaired humoral and cellular immunity, compounded by receipt of repeated rounds of immunosuppressive therapy, and are known to mount suboptimal antibody response to influenza vaccination. Possible negative impact of concurrent systemic anti-cancer therapy (SACT) is a further source of concern. We aimed to investigate the SARS-CoV-2 antibody response in PCD patients, relationship with symptomatic infection, PCD characteristics and receipt of SACT.

SARS-CoV-2 antibody screening with the Elecsys Anti-SARS-CoV-2 assay (Roche Diagnostics, Basel, Switzerland), a semi-quantitative assay of IgG and IgM against the nucleocapsid (N) antigen was introduced for PCD patients at our institution in July 2020. Clinical information was retrieved from medical records. Patients with unexpected positive antibody tests were asked about possible exposure to SARS-CoV-2 and previous symptoms of COVID-19 infection.

Two-hundred and forty-three PCD patients had at least one antibody test. Twenty-six (10.7%) patients tested positive; 12 were patients with known PCR-swap positive-19 disease. In a separate but overlapping cohort, 41 patients had PCR confirmed COVID-19 disease; 20 patients had antibody tests, and 12 (60%) seroconverted. Median time from positive PCR test to positive antibody test was 86.5 days (range 22–256) and 30.5 days (range 5–176 days) in antibody negative patients (included table). Of the 14 (6.3%) screening antibody positive patients with no positive PCR test, 11 (79%) patients had symptomatic multiple myeloma (MM) and 3 had plasmacytomas. Median time since MM diagnosis was 32 months (range 6–233), with median of one (range 0–3) previous line of treatment. Seven (50%) patients were on SACT (including ixazomib, pomalidomide, lenalidomide and dexamethasone) throughout their treatment. Two patients recalled symptoms of cough, high temperature, loss of taste and smell. Twelve (85.7%) described no symptoms. Of these, three lived with relatives who developed symptoms or tested PCR-positive for COVID-19, one has school-
aged children and two describe using public transport and visiting restaurants. Ten antibody positive patients in our antibody positive cohort had serial positive results at median 45 days (range 21–119) apart, demonstrating persistence, but some decline in response over time.

Despite asymptomatic COVID-19 disease, PCD patients retain ability to seroconvert and sustain their antibody response, while on immunomodulatory therapy. Seroconversion rates following symptomatic infection appear lower and may be delayed compared to the general population. The seroprevalence of 10.7% is lower but not dissimilar to that reported in London over a similar time period reflecting shielding behaviours in our patients but also challenges in protecting them during high SARS-CoV-2 incidence in the community. These data support the advice for COVID-19 vaccination to be offered to all PCD patients although the suboptimal humoral response calls for close antibody monitoring of all vaccinated patients and timely booster doses.

**Abstract Table:**

<table>
<thead>
<tr>
<th></th>
<th>All patients with antibody results n = 243</th>
<th>Positive antibody test post PCR positive COVID-19 disease n = 12</th>
<th>Screening positive antibody test only n = 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex (%)</td>
<td>140 (57.6)</td>
<td>7 (58.3)</td>
<td>5 (35.7)</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>129 (53.1)</td>
<td>8 (66.7)</td>
<td>5 (35.7)</td>
</tr>
<tr>
<td>African/Caribbean (%)</td>
<td>38 (15.6)</td>
<td>1 (8.3)</td>
<td>3 (21.4)</td>
</tr>
<tr>
<td>Asian (%)</td>
<td>23 (9.5)</td>
<td>1 (8.3)</td>
<td>4 (28.6)</td>
</tr>
<tr>
<td>Other (%)</td>
<td>22 (9.1)</td>
<td>2 (16.7)</td>
<td>1 (7.1)</td>
</tr>
<tr>
<td>Not disclosed</td>
<td>31 (12.8)</td>
<td>0 (0.0)</td>
<td>1 (7.1)</td>
</tr>
<tr>
<td>MGUS (%)</td>
<td>4 (1.6)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>SMM (%)</td>
<td>15 (6.2)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>MM (%)</td>
<td>212 (87.2)</td>
<td>12 (100.0)</td>
<td>11 (78.6)</td>
</tr>
<tr>
<td>Other (i.e. plasma celloma, AL amyloid, POEMS) (%)</td>
<td>12 (4.9)</td>
<td>0 (0.0)</td>
<td>3 (21.4)</td>
</tr>
<tr>
<td>Median previous lines of therapy [range]</td>
<td>2 [0–8]</td>
<td>3.5 [1–6]</td>
<td>1 [0–3]</td>
</tr>
<tr>
<td>On active treatment (%)</td>
<td>139 (57.2)</td>
<td>7 (58.3)</td>
<td>7 (50.0)</td>
</tr>
<tr>
<td>Immuneparesed (%)</td>
<td>70 (28.8)</td>
<td>3 (25.0)</td>
<td>6 (42.9)</td>
</tr>
</tbody>
</table>

**Disclosure of Interest:** W. Y. Chan: None Declared, E. Sanchez: None Declared, S. Chavda: None Declared, C. Lecat: None Declared, L. Ainley: None Declared, K. Xu: None Declared, B. Wisniowski: None Declared, S. Mahmood: None Declared, X. Papanikolaou: None Declared, C. Kyriakou: None Declared, J. Sive: None Declared, A. Wechalekar: None Declared, R. Popat Conflict with: National Institute for Health Research University College London Hospitals Biomedical Research Centre, N. Rabin Conflict with: Janssen Consultancy, Conflict with: Travel support for meetings and Speakers Bureau outside the submitted work, L. Lee: None Declared, E. Nastosli: None Declared, K. Yong Conflict with: Research funding from National Institute for Health Research University College London Hospitals Biomedical Research Centre, Sanofi, Celgene, Takeda, Janssen and Auto Lake, Conflict with: Receives honoraria from Janssen, Takeda, Sanofi, GSK and Amgen
Red Cell Disorder

BSH2021-OR-021
Early safety and efficacy results with a single dose of autologous CRISPR-Cas9-modified CD34+ hematopoietic stem and progenitor cells in transfusion-dependent ß-thalassemia and sickle cell disease
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3. CRISPR Therapeutics, Cambridge, United States,
4. University of Milan, Milan, Italy,
5. University of Regensburg, Regensburg, Germany,
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7. Children’s Hospital University, University of Tübingen, Tübingen, Germany,
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12. Columbia University New York, United States,
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14. University of Illinois at Chicago, Chicago, Illinois,
15. Joan and Sanford I Weill Medical College of Cornell University, New York,
16. Boston University School of Medicine, Boston, United States,
17. BC Children’s Hospital, University of British Columbia, Vancouver,
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Abstract Content: BCL11A is a key transcription factor that suppresses the production of fetal hemoglobin (HbF) in red blood cells (RBCs). In transfusion-dependent ß-thalassemia (TDT) and sickle cell disease (SCD), elevated levels of HbF are associated with reduced transfusion requirements and diminished clinical complications. To reactivate HbF in RBCs we used the CRISPR-Cas9 platform to edit the erythroid enhancer region of BCL11A in hematopoietic stem and progenitor cells (HSPCs) ex vivo (CTX001). We present safety and efficacy results from all consecutive patients infused with CTX001 with ≥3 months of follow-up.

CLIMB THAL-111 (NCT03655678) and CLIMB SCD-121 (NCT03745287) are multicenter studies of CTX001 for TDT and SCD, respectively. Patients (aged 12–35 years) with TDT (all genotypes) receiving ≥10 units/year of packed RBC transfusions in the previous 2 years, and those with severe SCD (≥2 vaso-occlusive crises (VOCs)/year requiring medical care in the previous 2 years), were eligible. We collected peripheral CD34+ HSPCs by apheresis after mobilization with G-CSF and plerixafor (TDT) or plerixafor alone (SCD). We edited the erythroid enhancer region of BCL11A in the enriched CD34+ cells using a specific CRISPR guide-RNA and Cas9 nuclease. Patients received myeloablative busulfan before CTX001 infusion. Engraftment, adverse events (AEs), total Hb, HbF, hemolysis, F-cells, RBC transfusions (TDT), and VOCs (SCD) were monitored during follow-up.

Seven TDT patients with a median follow-up of 8.9 months (range 3.8–21.5) and 3 SCD patients with a median follow-up of 7.8 months (range 3.8–16.6) have received CTX001. Patients with TDT achieved neutrophil and platelet engraftment at a median of 32 (range 20–39) and 37 (range 29–52) days after CTX001, respectively. Patients with SCD achieved neutrophil and platelet engraftment at a median of 22 (range 17–30) and 30 (range 30–33) days after CTX001, respectively.

In all 10 patients, the safety profile after CTX001 infusion was generally consistent with myeloablative conditioning and autologous bone marrow transplant. Four serious AEs (SAEs) related or possibly related to CTX001 were reported in 1 TDT patient and occurred in the context of hemophagocytic lymphohistiocytosis (HLH): HLH, headache, ARDS, and IPS. All 4 SAEs had resolved at the time of this analysis. No CTX001-related SAEs were reported in the 9 other patients.

All patients received their last transfusion within 2 months after CTX001 infusion and showed increases in Hb and HbF over time (Table). The first patients with TDT and SCD have remained transfusion-free for over 20.5 and 16.0 months, respectively. No SCD patients have had a VOC since CTX001 infusion and the first SCD patient has remained VOC-free for over 16.6 months. Additionally, no SCD patients have evidence of ongoing hemolysis as defined by detectable haptoglobin and improved LDH levels.

CTX001, an investigational CRISPR-Cas9-modified autologous HSPC product, has led to increases in HbF and total Hb in the 10 treated patients. Its post-infusion safety profile is generally consistent with myeloablation. All 7 TDT patients have been transfusion-free since ~2 months after CTX001 and the 3 SCD patients have had no VOCs after CTX001. These early data demonstrate that CTX001 is a potential functional cure for the treatment of TDT and SCD.

Exact text of hemophagocytic lymphohistiocytosis (HLH): HLH, headache, ARDS, and IPS. All 4 SAEs had resolved at the time of this analysis.

No CTX001-related SAEs were reported in the 9 other patients.

Table: Median Hb fractionation and total Hb in patients with TDT (N = 7); pooled analysis

<table>
<thead>
<tr>
<th>Months after CTX001 infusion</th>
<th>Median (range), g/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (n = 7)</td>
<td>10.1 (8.4–12.0)</td>
</tr>
<tr>
<td>Month 1 (n = 7)</td>
<td>8.8 (6.6–13.2)</td>
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<tr>
<td>Month 3 (n = 7)</td>
<td>11.5 (8.5–13.1)</td>
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<tr>
<td>Month 6 (n = 5)</td>
<td>11.6 (10.3–13.4)</td>
</tr>
<tr>
<td>Month 9 (n = 2)</td>
<td>12.2 (11.9–12.5)</td>
</tr>
<tr>
<td>Month 12 (n = 1)</td>
<td>12.7 (12.4)</td>
</tr>
<tr>
<td>Month 15 (n = 1)</td>
<td>14.2 (13.5)</td>
</tr>
<tr>
<td>Month 18 (n = 1)</td>
<td>14.1 (13.1)</td>
</tr>
</tbody>
</table>

Hb fractionation and total Hb in patients with SCD (N = 3); patient-level analysis

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British Journal of Haematology, 2021, 193, (Suppl. 1), 3–45
Hb, hemoglobin; HbA, adult hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin; SCD, sickle cell disease; TDT, transfusion-dependent β-thalassemia.


BSH2021-OR-022

FT-4202, an allosteric activator of pyruvate kinase-R, demonstrates proof of mechanism and proof of concept after multiple daily doses in a phase 1 study of patients with sickle cell disease


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Abstract Content: The hallmark of sickle cell disease (SCD) is hemoglobin S (HbS) polymerization upon deoxygenation, resulting in red blood cell (RBC) sickling, oxidative damage, membrane damage, hemolysis, cell adhesion, and vaso-occlusion. Exacerbating SCD pathogenesis, the HbS RBC has increased 2,3-diphosphoglycerate (2,3-DPG) with corresponding decreased O2 affinity, as well as decreased RBC adenosine triphosphate (ATP). FT-4202, a small-molecule allosteric activator of erythrocyte pyruvate kinase (PKR), increases PKR activity resulting in decreased 2,3-DPG levels and increased ATP levels in RBCs.

FT-4202 is being evaluated in a randomized, double-blind phase 1 study (NCT03815695), which includes cohorts of healthy subjects and patients (pts) with SCD, and several cohorts have reported results. In healthy subjects, FT-4202 was well tolerated and demonstrated physiologic responses (Kalfa et al. Blood 2019). Further, a single-dose cohort of pts with SCD showed a favorable safety profile for FT-4202 and promising pharmacodynamic effects (Estepp et al. EHA 2020). Multiple-dose cohorts for pts with SCD are ongoing.
We report available data as of 16-Nov-2020, at which time, the first 14-day treatment cohort had completed, but data remain blinded. For analyses of biological effects, pts were classified based on FT-4202 plasma levels to maintain blinding.

In the first 14-day treatment cohort, 9 pts were randomized 7:2 to FT-4202 300 mg once daily or placebo for 14 days. Most pts (6/9) had Hb SS genotype, and 6/9 were on stable hydroxyurea. Fifteen treatment-emergent adverse events (TEAEs) were reported in 7 pts. Most TEAEs (8/15) were grade 1, specifically headache (n = 3) and 1 each of nausea, constipation, somnolence, increased LDH, and increased AST; of these 1 AE of headache and 1 of nausea were considered possibly related to study drug. Six TEAEs were grade 2; 1 each of nausea, vomiting, and increased reticulocytes, and 3 uncomplicated sickle pain events (in 2 pts). The pain AEs were consistent with each pt’s SCD pain history, and all were treated with their standard home pain medications (no SAE/no hospitalization). All grade 2 TEAEs were considered unrelated to study treatment.

Levels of RBC 2,3-DPG decreased from baseline and remained at similar levels through the 14-day period (P = 0.031). RBC ATP levels rose more slowly, continuing to increase to day 14 (P = 0.031). The partial pressure of O2 at 30% Hb saturation (PsO2) at day 14 was decreased in treated pts (P = 0.031), reaching values similar to those of untreated healthy subjects. After 14-days, Hb increased (median 1.2 g/dl range 0.2-3.3; 6/7 pts having an increase of >1 g/dl, and there were decreases from baseline in reticulocyte count (median 60% range -39%, -81%), LDH (median 36% range +18%, -57%; 6/7 pts had a decrease), and bilirubin (median 35% range -7%, -63%).

In conclusion, FT-4202 300 mg once daily demonstrated a favorable safety profile in pts with SCD receiving up to 14 days of dosing; consequently, the second multiple-dose cohort in pts with SCD has initiated. In addition, FT-4202 300 mg once daily showed improvements in hematologic and hemolytic parameters, as well as decreased 2,3-DPG and increased ATP in RBCs, which correlated with increased RBC O2 affinity and improved RBC membrane function. Therefore, the study demonstrated proof of concept for FT-4202 300 mg once daily and, based on these results, a phase 2/3 efficacy study is ongoing (NCT04624659).


BSH2021-OR-023

Categorized hematologic response to pegcetacoplan versus eculizumab in patients with paroxysmal nocturnal hemoglobinuria: post hoc analysis of data from a phase 3 randomized trial (PEGASUS)

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Abstract Content: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, hematologic disease characterized by complement-mediated red blood cell (RBC) hemolysis. Eculizumab (ECU) and ravulizumab, both C5 inhibitors, are the standard of care for PNH. Despite treatment with ECU, anemia persists in up to ~70% of patients and is attributed to persistent intravascular hemolysis (IVH), and mostly C3-mediated extravascular hemolysis (EVH). PEGASUS is a phase 3, randomized, open-label, active-comparator controlled study of the efficacy and safety of pegcetacoplan, a C3 inhibitor, versus ECU. PNH patients with hemoglobin (Hb) levels <10.5 g/dL despite stable ECU treatment for ≥5 months were enrolled. This post hoc analysis categorized the hematological response to pegcetacoplan or ECU in patients with PNH.

Hematologic response to treatment was categorized (complete, major, good, partial, minor, or no response) using the number of packed RBC transfusions required, Hb level, lactate dehydrogenase (LDH) level, and absolute reticulocyte count (ARC), per Risitano AM, et al. Front Immunol. 2019;10:1157. Complete response: no transfusions required, stable Hb in the normal range, and no evidence of hemolysis (LDH≤1.5x upper limit of normal [ULN] U/L, ARC≤150,000/μl). Major response: no transfusion, normal hemoglobin, but with evidence of hemolysis (LDH>1.5xULN U/L and/or ARC>150,000/μl). Good response: no transfusions, but with chronic mild anemia or evidence of hemolysis. Partial response: chronic moderate anemia and/or occasional transfusions (<3 units/6 months). Minor response: regular transfusions required (3–6 units/6 months). No response: regular and frequent transfusions required (>6 units/6 months). Nine patients (pegcetacoplan [n = 6]; ECU [n = 3]) did not fit within existing criteria due to the availability of data at Week 16. These patients were manually categorized by the lead and senior author independently, in a blinded manner, but were not included in the final analysis.

The intent-to-treat population was randomized to pegcetacoplan (n = 41) or ECU (n = 39). Four patients in the pegcetacoplan group and 1 in the ECU group were unavailable due to missing data at Week 16. A majority, 61.0% of patients (25/41) in the pegcetacoplan...
group achieved at least a good hematological response, versus 5.1% (2/39) in the ECU group. At Week 16, the distribution of response categories was as follows (Table): in the pegcetacoplan arm and ECU arm, respectively, complete responses were 36.6% and 0.9%, good responses were 24.4% and 5.1%, partial responses were 12.2% and 33.3%, minor responses were 2.4% and 23.1%, and no responses were 0.0% and 28.2%. The addition of 9 manually categorized patients did not significantly alter these response proportions. Factors that may contribute to heterogeneity of hematologic response to treatment include impaired bone marrow function, residual IVH, and residual EVH. Since bone marrow failure was ruled out, and no differences in LDH were observed, one factor that may account for the response differences between pegcetacoplan and ECU treatment is the prevention of C3-mediated EVH (as confirmed by reduction in C3-opsonization of PNH RBCs).

In PEGASUS, treatment with pegcetacoplan resulted in a greater proportion of patients with improved hematological responses compared to ECU. These results support the concept that proximal complement inhibition, through preventing EVH and controlling IVH, leads to clinical improvements in PNH treatment.

Table 1. Performance of the Sickle SCAN test compared to capillary electrophoresis.

<table>
<thead>
<tr>
<th>Response category</th>
<th>Pegcetacoplan % (n/N)</th>
<th>Eculizumab % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>36.6 (15/41)</td>
<td>0.0 (0/39)</td>
</tr>
<tr>
<td>Major</td>
<td>0.0 (0/41)</td>
<td>0.0 (0/39)</td>
</tr>
<tr>
<td>Good</td>
<td>24.4 (10/41)</td>
<td>5.1 (2/39)</td>
</tr>
<tr>
<td>Partial</td>
<td>12.2 (5/41)</td>
<td>33.3 (13/39)</td>
</tr>
<tr>
<td>Minor</td>
<td>2.4 (1/41)</td>
<td>23.1 (9/39)</td>
</tr>
<tr>
<td>No response</td>
<td>0.0 (0/41)</td>
<td>28.2 (11/39)</td>
</tr>
<tr>
<td>Uncategorized</td>
<td>14.6 (6/41)</td>
<td>7.8 (3/39)</td>
</tr>
<tr>
<td>Missing data</td>
<td>9.8 (4/41)</td>
<td>2.6 (1/39)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: A. Risitano Conflict with: Alexion and Amyndas (Consultancy), Conflict with: Novartis, Ahlyam, Alexion, and RA pharma (Grant/Research Support), Conflict with: Novartis, Alexion, Samsung, Biocryx, Achillion, Roche and Apellis (Membership on an entity’s Board of Directors or advisory committees); Novartis, Alexion, Jazz, Pfizer, Apellis (Speakers Bureau), I. C. Weitz Conflict with: Alexion and Apellis (Consultancy), Conflict with: Alexion and Apellis (Honoria); Alexion (Speakers Bureau), C. M. De Castro Conflict with: Apellis (Consultancy), Conflict with: Alexion and Apellis (Grant/Research Support), Conflict with: Novartis (Honoria, Steering Committee); Alexion and Apellis (Honoria); Biocryx (Honoria, Data monitoring committee), J.-J. Kialadjian Conflict with: Abbvie, Novartis, Bristol Myers Squibb, AOP Orphan (Membership on an entity’s Board of Directors or advisory committees), M. Griffin Conflict with: Biocryx (Membership on an entity’s Board of Directors or advisory committees); Alexion (Honoria, conference support), H. Nishimori: None Declared, M. Hamdani Conflict with: Apellis (Current Employment and Current equity holder in publicly traded company), T. Ajayi Conflict with: Apellis (Current Employment and Current equity holder in publicly traded company), S. B. Baver Conflict with: Apellis (Current Employment and Current equity holder in publicly traded company), R. Peffault de Latour Conflict with: Novartis, Pfizer and Alexion (Consultancy), Conflict with: Novartis, Pfizer, Amgen and Alexion (Grant/Research Support), Conflict with: Novartis, Pfizer and Alexion (Honoria)

**Abstract Table:** Table. Hematological Response in Pegcetacoplan-treated or ECU-treated Patients

BH2021-OR-024
Diagnostic accuracy of the Sickle SCAN™ rapid test for neonatal screening for sickle cell disease in Lubumbashi, Democratic Republic of Congo

Tina Katamea, Olivier Mukuku, Oscar Luboya, Léon Tshilolo, Stanis Wembonyama

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Abstract Content: Sickle cell disease is a common and potentially fatal hematologic disease. Its universal screening and early intervention have significantly contributed to reducing child mortality in high-resource countries. However, people living in low-resource settings are often not diagnosed until late childhood when they present with clinical manifestations. The high cost and complexity of conventional sickle cell diagnosis methods limit its newborn screening in sub-Saharan Africa and other resource-poor parts of the world.

We evaluated a prototype immunoassay as a rapid and inexpensive diagnostic device designed to identify HbA, HbS and HbC. Sickle SCAN™ is a rapid, qualitative, lateral flow immunoassay. Samples from 165 newborns were analysed by this rapid method and compared to the results by capillary electrophoresis. This study was carried out on newborns born at University Clinics in Lubumbashi, in the Democratic Republic of Congo.

Sickle SCAN™ correctly identified the hemoglobin (Hb) phenotype in 96.4% of the cases. The sensitivity (99.5%) and specificity (92.5%) for the detection of HbAS were excellent. There were no false positives or false negatives for the detection of HbSS and HbAC, with a sensitivity and specificity of 100%. For HbAA, the sensitivity (97.69%) and specificity (91.43%) were also excellent.

This study demonstrates the potential utility of this rapid test in reducing the overall cost and increasing accessibility to newborn screening for sickle cell disease in resource-limited settings.

Abstract Table:

<table>
<thead>
<tr>
<th>Sample type</th>
<th>Result by reference method</th>
<th>Expected Sickle SCAN pattern</th>
<th>Samples correctly scored</th>
<th>Samples incorrectly scored</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb AA</td>
<td>130 A or FAS</td>
<td>A</td>
<td>127</td>
<td>3 (A, S)</td>
</tr>
<tr>
<td>Hb AS</td>
<td>16</td>
<td>A or FAS</td>
<td>13</td>
<td>3 (A only)</td>
</tr>
<tr>
<td>Hb SS</td>
<td>18</td>
<td>S or FS</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Hb AC</td>
<td>1</td>
<td>AC</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>165</td>
<td></td>
<td>159</td>
<td>6</td>
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Disclosure of Interest: None Declared
BSH2021-OR-025

Longitudinal results of the BELIEVE trial: sustained reductions in red blood cell transfusion burden and transfusion events in patients with beta-thalassaemia receiving luspatercept

Ali T. Taher1,*, Vip Viprakasit2, Olivier Hermine3,4, John B. Porter5, Antonio Piga6, Kevin H. M. Kuo7, Thomas D. Coates1,9, Ersi Voskaridou10, Abderrahim Khelif11, Antonis Kattamis12, Jeevan K. Shetty13, George Zhang14, Yu Olivia Tian15, Dimana Miteva19, Tatiana Zinger15, Derek Tang14, Jay T. Backstrom15, Maria Domenica Cappellini16

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Abstract Content: Luspatercept is a first-in-class erythroid maturation agent approved by the FDA and EMA to treat anaemia in adult patients (pts) with β-thalassaemia requiring regular red blood cell (RBC) transfusions. We report the results of a longitudinal analysis of the benefit of luspatercept on RBC transfusion burden (TB) in the phase 3 BELIEVE trial, evaluating efficacy and safety of luspatercept in pts with β-thalassaemia requiring regular RBC transfusions (NCT02604433).

Eligible pts were adults with β-thalassaemia or haemoglobin (Hb) E/β-thalassaemia requiring regular RBC transfusions of 6–20 RBC units in the 24 weeks before randomisation (no transfusion-free period >35 days). 336 pts were randomised 2:1 to luspatercept 1.0 mg/kg (titrated up to 1.25 mg/kg; n = 224) or PBO (n = 112) subcutaneously every 3 weeks for ≥48 weeks. Mean RBC units transfused and mean change in RBC TB and number of visits were assessed in luspatercept (primary endpoint responders and non-responders) and placebo (PBO) arms Weeks 1–48 weeks. Long-term changes in RBC TB and visits in luspatercept-treated pts remaining on treatment were assessed every 24 weeks from treatment start to data cut-off (1 July 2019).

In the 24 weeks before randomisation, median RBC TB was 14.3 RBC units (range 6.0–26.0) and median pretransfusion Hb level was 9.27 g/dL (range 4.5–11.7). As of 1 July 2019, median duration of treatment for pts in the luspatercept and PBO (pre-crossover) arms was 119.1 and 74.7 weeks, respectively. 62.8% of pts initially randomised to luspatercept were still receiving treatment at the end of 2 years. Pts receiving luspatercept experienced a mean change of –2.20 RBC units/24 weeks transfused vs. +0.72 RBC units/24 weeks in PBO-treated pts in Weeks 1–24 vs. baseline (least squares mean difference [LSMD] = −2.95; 95% confidence interval [CI] −3.59, −2.32; P < 0.001; Table). In Weeks 25–48, mean changes of −2.53 and +0.21 RBC units/24 weeks transfused were reported in luspatercept- and PBO-treated pts, respectively (LSMD = −2.76; 95% CI −3.46, −2.06; P < 0.001). Luspatercept responders (i.e. achieving ≥33% reduction in RBC TB in Weeks 13–24, with a reduction of ≥2 RBC units, vs. baseline) experienced mean transfusion reductions of −5.32 and −4.83 RBC units/24 weeks in Weeks 1–24 and 25–48, respectively, and luspatercept non-responders experienced mean changes of −1.30 and −1.85 RBC units/24 weeks. Luspatercept-treated pts continued to experience sustained, durable reductions in RBC units up to 144 weeks of follow-up (Table). In Weeks 1–24, luspatercept-treated pts experienced mean change of −0.49 in transfusion event frequency vs. +0.32 for PBO-treated pts (LSMD = −0.78; 95% CI −1.16, −0.40; P < 0.001; Table). In Weeks 25–48 mean changes in transfusion visits of −0.54 and +0.14 were experienced by pts in the luspatercept and PBO arms, respectively (LSMD = −0.65; 95% CI −1.03, −0.26; P = 0.001). Luspatercept responders and non-responders reported mean reductions in transfusion visits in Weeks 1–24 (−1.38, P < 0.001 and −0.23, P = 0.006, respectively) and Weeks 25–48 (−1.09, P < 0.001 and −0.38, P = 0.010, respectively) vs. baseline. Sustained reductions in transfusion visits persisted for over 2 years (Table).

Luspatercept treatment was associated with sustained reductions in RBC transfusion units and visits in responders and non-responders during the first 48 weeks versus PBO. Pts receiving luspatercept continued to experience reductions in RBC TB and events over 2 years.

This abstract was previously published (Taher et al., Blood 2020;136(1)45–46).

Disclosure of Interest: A. T. Taher Conflict with: BMS, Novartis Pharmaceuticals, Vifor Pharma (consultancy, research funding); Ionis Pharmaceuticals, Silence Therapeutics (consultancy), V. Viprakasit Conflict with: BMS, Novartis (consultancy, honoraria, research funding, speakers bureau); Agios Pharmaceuticals, Ionis Pharmaceuticals, La Jolla Pharmaceuticals, Protagonist Therapeutics, Vifor Pharma (consultancy, research funding), O. Hermine Conflict with: Roche (consultancy); Celgene BMS (consultancy, research funding); AB Science (consultancy, current equity holder in publicly traded company, honoraria, patents & royalties, research funding); Alexion, Novartis (research funding), J. B. Porter Conflict with: Agios Pharmaceuticals, bluebird bio, Inc., BMS (consultancy, honoraria); La Jolla Pharmaceuticals, Protagonist Therapeutics, Silence Therapeutics, Vifor Pharmaceuticals (consultancy, honoraria), A. Piga Conflict with: BMS, Novartis (research funding), K. H. M. Kuo Conflict with: Agios (consultancy, membership on an entity’s board of directors or advisory committee), Apellis, Bluebird Bio, Celgene (consultancy); Pfizer (consultancy, research funding); Alexion, Novartis (consultancy, honoraria); Bioverativ (membership on an entity’s board of directors or advisory committees), T. D. Coates Conflict with: Celgene, BMS, Sangamo (consultancy, honoraria, membership on an entity’s board of directors or advisory committees); apo pharma, Vifor Pharma (consultancy, honoraria, speakers bureau); Agios pharma (consultancy, honoraria), E. Voskaridou Conflict with: ACCELERON Company, ADDMEDICA Company, BMS, GENESIST Company (consultancy, research funding); NOVARTIS Company, PROTAGONIST Company (research funding), A. Khelif: None Declared, A. Kattamis Conflict with: Novartis (consultancy, honoraria, membership on an entity’s board of directors or advisory committees, research funding, speakers bureau), Genesis Pharma SA, Ionis, Vertex, Vifor (membership on an entity’s board of directors or advisory committees); Apopharma/Chiesi (honoraria, speakers bureau); Celgene/BMS (honoraria, membership on an entity’s board of directors or advisory committees, speakers bureau); Agios (consultancy), J. K. Shetty Conflict with: BMS (current employment, current equity holder in publicly traded company), G. Zhang Conflict with: BMS (current employment), Y. O. Tian Conflict with: BMS (current employment, speakers bureau).
Abstract Table:
Table. Longitudinal reductions in RBC transfusions and visits in the BELIEVE trial.

<table>
<thead>
<tr>
<th>Luspatercept at baseline</th>
<th>Change in RBC units transfused /24 weeks from baseline, mean (SD)</th>
<th>Change in transfusion visits from baseline, mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luspatercept responders</td>
<td>–2.20 (2.8)*</td>
<td>–2.53 (3.3)*</td>
</tr>
<tr>
<td>(n = 210)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Luspatercept non-responders</td>
<td>–5.32 (2.5)*</td>
<td>–4.83 (3.4)*</td>
</tr>
<tr>
<td>(n = 177)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PBO (N = 112)</td>
<td>–1.30 (2.2)*</td>
<td>–1.85 (2.9)*</td>
</tr>
<tr>
<td>RBC units transfused/24 weeks</td>
<td>Mean (SD)</td>
<td>Mean change from baseline (SD)</td>
</tr>
<tr>
<td>Luspatercept at baseline</td>
<td>14.53 (3.6)</td>
<td>–2.20 (2.8)*</td>
</tr>
<tr>
<td>(N = 224)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weeks 1–24</td>
<td>12.27 (4.4)</td>
<td>–2.20 (2.8)*</td>
</tr>
<tr>
<td>(n = 210)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weeks 25–48</td>
<td>11.85 (4.7)</td>
<td>–2.53 (3.3)*</td>
</tr>
<tr>
<td>(n = 201)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weeks 49–72</td>
<td>11.71 (4.5)</td>
<td>–2.67 (3.1)*</td>
</tr>
<tr>
<td>(n = 177)</td>
<td></td>
<td></td>
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<tr>
<td>Weeks 73–96</td>
<td>11.38 (4.6)</td>
<td>–2.83 (3.2)*</td>
</tr>
<tr>
<td>(n = 155)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weeks 97–120</td>
<td>10.93 (4.6)</td>
<td>–3.36 (3.0)*</td>
</tr>
<tr>
<td>(n = 104)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weeks 121–144</td>
<td>10.93 (4.6)</td>
<td>–3.36 (3.0)*</td>
</tr>
</tbody>
</table>

*P < 0.001 by ANCOVA comparing differences between luspatercept (overall, responders, non-responders) with placebo; b P < 0.001 by ANCOVA comparing differences between luspatercept (overall) at baseline with post-baseline.

ANCOVA, analysis of covariance; PBO, placebo; RBC, red blood cell; SD, standard deviation; wk, week.

employment), D. Miteva Conflict with: BMS (current employment), T. Zinger Conflict with: Celgene International, A Bristol-Myers Squibb Company (current employment), D. Tang Conflict with: BMS (current employment, current equity holder in publicly traded company), J. T. Backstrom Conflict with: Acceleron Pharma (current employment, current equity holder in publicly traded company); BMS (current equity holder in publicly traded company), M. D. Cappellini Conflict with: BMS (honoraria); Genzyme/Sanofi (honoraria, membership on an entity’s board of directors or advisory committees); CRISPR Therapeutics, Novartis, Vifor Pharma (membership on an entity’s board of directors or advisory committees).

BSH2021-OR-026
Factors influencing time from initial presentation to start of plasma exchange (PEX) in patients with acute thrombotic thrombocytopenic purpura (TTP)
Tom Bull1*, RORY McCulloch2, Phillip Nicolson3, Rebecca J. Shaw4, Zara Sayar5, Alex Langridge6, Michala Pettit7, Rita Perry7, David Tucker8, Marie Scully9, Haemstar Investigators10
1Haematology, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, 2Haematology, Gloucestershire Hospitals NHS Foundation Trust, Gloucester, 3Haematology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, 4Haematology, Liverpool University Hospitals NHS Foundation Trust, Liverpool, 5Haematology, Whittington Health NHS Trust, London, 6Haematology, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, 7Birmingham Centre for Observational and Prospective Studies, Birmingham Surgical Trials Consortium, Birmingham, 8Haematology, Royal Cornwall Hospitals NHS Trust, Truro, 9Haematology, University College London Hospitals NHS Foundation Trust, London, 10HaemSTAR Network, www.haemstar.org, United Kingdom

Abstract Content: Acute TTP is a life-threatening medical emergency and plasma exchange is the only treatment shown to significantly impact acute mortality (Rock et al, N Engl J Med 1991). Diagnosis can be challenging and therein arrangements for PEX must be made,
with most centres in the United Kingdom (UK) having to co-ordinate transfer to a tertiary site. To understand issues affecting practice the trainee research network HaemSTAR conducted a retrospective nationwide review of patients presenting to UK hospitals with TTP against British Society of Haematology clinical guidelines (Scully et al, B J Haem 2012). Analysis was conducted on the time from first full blood count to initiation of treatment and impact on patient outcomes.

Adults ≥18 years presenting to hospital between 1 June 2014 and 1 June 2019 with first episode acute TTP and ADAMTS13 level <10% were identified by local clinicians. Anonymized data of baseline characteristics and treatment times were submitted via an online secure server. Time to PEX was defined as time from receipt of the first full blood count sample in the laboratory to time of plasma release for PEX from blood bank. Where patients were transferred between sites, data were linked retrospectively. Data on 148 patients treated at 80 UK hospitals were used for analysis (Table 1). The overall median time to PEX from initial presentation was 15 hours (95% CI 11.3–18.7). Availability of on-site PEX was associated with earlier treatment initiation with median time to PEX for those treated on site 10 hrs (95% CI 7.7–12.3) vs. 21 hrs (95% CI 16.8–25.2) for patients transferred. A blood film comment of red cell fragments significantly impacted time to treatment: in 24 cases with no fragments documented median time to PEX was 110 hrs (95% CI 39–181) vs. 10 hrs (95% CI 8.5–11.5) in cases where fragments were reported.

On univariate and multivariate analysis age <60 years, haemoglobin (Hb) <100 g/L, presence of fragments, PEX available on-site and admissions occurring after May 2017 were significant predictors for PEX initiation within 8 hrs. This is the first multi-centre record of time to treatment from initial presentation of acute TTP. Results comply with guidance for rapid initiation of PEX with 61% patients commencing within 24 hrs of presentation and, from June 2017, 34% of patients initiating PEX within 8 hrs. The recent increase in early PEX initiation correlates with initiatives to improve treatment pathway efficiency following diagnosis of TTP. Early use of steroids and rituximab correlated with earlier use of PEX indicating where timely diagnosis was made there was good compliance with guidelines. Inappropriate use of platelets appeared attributable to misdiagnosis. Older patients, those with higher platelet counts and haemoglobin and absence of red cell fragments on film report were more likely to experience prolonged time to initiation of PEX. This does not appear related to PEX access, but most likely the difficulty of making TTP diagnosis in this cohort. That 22% of patients initiated PEX over 48 hrs from admission indicates the issue is relatively common and with several deaths occurring in this group we suggest initiatives to increase early diagnosis should be prioritised.

Abstract Table: Table 1. Numbers of patients meeting key performance indicators in the treatment of acute thrombotic thrombocytopenic purpura.

<table>
<thead>
<tr>
<th>No. of patients (%)</th>
<th>Total included in analysis</th>
<th>148</th>
<th>96</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received PEX (total)</td>
<td>142</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>Received PEX (at site of presentation)</td>
<td>67</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Received PEX (after hospital transfer)</td>
<td>75</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Received PEX within 8 hours of first full blood count</td>
<td>37</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Received PEX within 24 hours of first full blood count</td>
<td>91</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>Died before receiving PEX</td>
<td>6</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. (Continued)

<table>
<thead>
<tr>
<th>No. of patients (%)</th>
<th>Received Steroids within 24 hours of first full blood count</th>
<th>96</th>
<th>65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received Rituximab within 48 hours of first full blood count (of the 128 presenting with cardiac or central nervous system symptoms)</td>
<td>98</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>Received platelet transfusion in the absence of major bleeding</td>
<td>12</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Died within 30 days of presentation</td>
<td>19</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure of Interest: T. Bull: None Declared, R. McCulloch: None Declared, P. Nicolson: None Declared, R. J. Shaw: None Declared, Z. Sayar: None Declared, A. Langridge: None Declared, M. Pettit: None Declared, R. Perry: None Declared, D. Tucker: None Declared, M. Scully: None Declared, H. Investigators Conflict with: Sanofi provided grants to support the running of this project but had no input on project or abstract design.

BSH2021-OR-027
An epidemiological study of the cardiovascular health and thrombotic risk profiles of patients with myeloproliferative neoplasms in primary care across the UK
Frederick Chen1†, Adrian Rabe2,3,4†, Jay Were2, Gavin Chiu2, Annae Liu2
1Barts Health NHS Trust, 2Health IQ Limited, 3Imperial College London, 4Global Health Focus, London, 5Novartis Pharmaceuticals UK Limited, Camberley, United Kingdom

Abstract Content: Patients with myeloproliferative neoplasms (MPN) are at increased risk of venous and arterial thromboembolic events (TEEs). Although MPN-specific treatment is generally delivered by specialist haematology centres in the UK, cardiovascular risk is managed in the primary care setting. In this retrospective cohort study, we interrogated the Clinical Practice Research Datalink (CPRD), a national dataset comprising clinical and prescription records for patients in primary care across the entire UK, for descriptive data on the cardiovascular health and thrombotic risk of all patients with MPN. During the study period (1 January 2012–21 August 2019), adults were identified at the date of first recorded diagnosis for polycythema vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (MF), with a ≥6-month pre-index lookback and ≥24-month post-index follow-up. The study objectives were to determine the MPN epidemiological landscape, extent of co-morbidities (using the Charlson score), thrombotic/cardiovascular risk profiles (before diagnosis) and occurrence of TEEs/cardiovascular events (CVEs) (after diagnosis). MPN diagnoses and co-morbidities were determined using medical and ICD-10 codes; medications were identified using product codes.

Overall, 2,477 patients with MPN (PV, n = 1,315; ET, n = 336; MF, n = 146; unspecified MPN, n = 680) of the 19,474,733 patients in the CPRD were identified with a median age at diagnosis of 68 years (range 7 months–101 years); 56% were male. Among all MPN patients, 96.2% had a low Charlson co-morbidity score of 0–5. The prevalence of MPN was 12.72 per 100,000; PV was the most prevalent MPN subtype (6.75 per 100,000), followed by ET (1.73 per 100,000) and MF (0.75 per 100,000). In the total MPN population, the most prevalent pre-diagnosis risk factors were smoking (59.8%)
and ischaemic heart disease (27.7%); few patients had hypertension (14.6%), diabetes (13.1%), dyslipidaemia (12.8%) or obesity (8.8%). For risk management, most hypertensive (88.9%), dyslipidaemic (82.4%) and diabetic (77.9%) patients were prescribed appropriate medications for management of their blood pressure, dyslipidaemia and diabetes, respectively. Among the patient cohort, 372 TEEs/CVEs occurred after diagnosis (PV, 214 events; ET, 64 events; MF, 9 events; unspecified MPN, 85 events), the most common being stroke (27.2%), deep vein thrombosis (17.7%) and myocardial infarction (MI; 14.8%) (Table). Notably, the occurrence of MI was greater for patients with PV (15.9%) than for those with ET (10.9%) or MF (0%).

This study is the first of its kind to describe the cardiovascular health and thrombotic risk profiles of UK patients with MPN in primary care within the CPRD. The prevalence of PV and MF in this study was largely consistent with most known epidemiological reports, but the prevalence of ET was lower. However, MPN subtype was not specified in the CPRD for a sizeable proportion (680 of 2,477 patients). Importantly, in the UK MPN population, the majority were smokers and a considerable proportion of patients (11.1–22.1%) were not prescribed appropriate medications for management of co-morbidities associated with thrombotic risk (hypertension, dyslipidaemia or diabetes), highlighting a potential unmet need for improved cardiovascular risk management and coordination between primary and secondary care.

Disclosure of Interest: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu Conflict with: F. Chen Conflict with: Received personal fees (consultancy honoraria) from Novartis, outside of the submitted work, A. Rabe: None Declared, J. Were: None Declared, G. Chiu

We present the experience of Birmingham children’s hospital, one of the largest comprehensive haemophilia centers in the UK, about management and outcomes of our cohort of patients who underwent surgical procedures while on emicizumab prophylaxis. Data of 13 patients were included (Table). Their age ranged from 0.72 to 13.2 (Median 5.20) years. Three patients had active factor (F) VIII inhibitors prior to surgery with levels of 491 Bethesda units (BU), 85 BU and 3.0 BU. All patients were on emicizumab for a period ranging from 2 to 62 weeks (Median 38.0) and dose of 3 mg/kg fortnightly except one patient who was on the weekly loading doses. Twelve procedures where considered minor in which only skin, mucous membranes, or superficial connective tissue were manipulated. One patient underwent cleft palate correction which was a major surgery requiring iliac crest bone graft to correct the cleft defect. Line (vascular and central line) removals were the most common surgical procedures (11/13), which was expected due to the transition from intravenous to subcutaneous injections.

Multidisciplinary haemostatic plan was agreed between the haematologists, anaesthesiologists and surgeons prior to surgery. All procedures were managed with preplanned tranexamic acid, 25 mg/kg three times in the pre-procedural day, one intravenous dose 10 mg/kg during induction of anaesthesia and then continued orally after the procedure at a dose of 25 mg/kg three times daily for 7 days. Only three patients required additional haemostatic agents, one inhibitor patient required rFVIII prior to his central line removal and this was due to lack of experiences in management of similar cases, second required rFVIII prior to his dental procedure as he was still on loading doses of emicizumab and the third who underwent cleft palate surgery and thus covering with rFVIII was mandatory. Overall, the procedures were successfully performed in all patients including inhibitor patients and none experienced postoperative bleeding. No unplanned hospital admissions or changes in peri-operative treatment plan were reported.

Our results clearly highlights what we consider to be valuable data to the debate mainly in regard the need for additional haemostatic agents prior to line removals in patients on emicizumab prophylaxis. The authors believe that minor procedures can be safely done without the need of additional clotting factors.

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British Journal of Haematology, 2021, 193, (Suppl. 1), 3–45
Abstract Content: As emicizumab is biochemically different from factor (F) VIII, there is interest in its real-world efficacy in preventing bleeding. It is a more convenient option for prophylaxis in the paediatric patients with haemophilia A (PwHA) as it reduces the burdensome of frequent intravenous infusions. Beyond clinical trials, data are limited on outcomes of patients on emicizumab prophylaxis, especially in children without inhibitors.

We conducted a retrospective cohort study at Birmingham Children’s hospital, on PwHA on emicizumab prophylaxis. Data regarding age, prior treatment, compliance, inhibitor status, compliance, annualized bleeding rate (ABR) and Joint ABR (J-ABR) for each patient were compared before and after starting emicizumab.

Data from 49 PwHA, with baseline FVIII levels < 1% including four patients with active inhibitors were analysed. 91.8% were previously on FVIII/bypassing agents prophylaxis. Median age of emicizumab start was 7.7 (range 0.3–15.3) years. Median time on emicizumab was 13.1 (range 2.7–36.6) months. All patients were compliant to emicizumab which was generally well tolerated. No thromboembolic events, de novo inhibitor development or other serious drug related events were reported.

ABR requiring factor was significantly lower after starting emicizumab \((P < 0.001)\). 85.7% of patients had zero treated bleeding events post emicizumab compared to 28.6% pre-emicizumab \((P < 0.001)\). J-ABR decreased in all patients \((P < 0.001)\). (See table.) Our favorable clinical experience with this novel agent is similar to that reported in clinical trials. In emicizumab era, there is high potential for significant improvements in bleeding prevention and joint health for paediatric PwHA, regardless of the presence of FVIII inhibitors. Ongoing long term follow-up for patients on emicizumab prophylaxis is important to assess its efficacy profile.

Disclosure of Interest: None Declared

Abstract Table: Table.

<table>
<thead>
<tr>
<th>#</th>
<th>Number of doses of emicizumab(^a)</th>
<th>Procedure</th>
<th>Inhibitor/Historical inhibitor</th>
<th>Factor replacement</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>Central line removal</td>
<td>Yes</td>
<td>rFVIIa</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>Central line removal</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>Port removal</td>
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<td>–</td>
</tr>
<tr>
<td>4</td>
<td>30</td>
<td>Port removal</td>
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<td>–</td>
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<td>Port removal</td>
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<td>12</td>
<td>2</td>
<td>Dental procedure</td>
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<td>rFVIII one dose</td>
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<tr>
<td>13</td>
<td>35</td>
<td>Cleft Palate Correction</td>
<td>–</td>
<td>rFVIII one dose pre-surgery then post operatively for 5 days(^c)</td>
</tr>
</tbody>
</table>

\(^a\)At time of procedure \(^b\)Eradiated with ITI \(^c\)twice daily for one day then once daily for 4 days rFVIII: recombinant FVIII(25I U/kg) rFVIIa: recombinant activated FVII (90 mcg/kg)

Disclosure of Interest: None Declared
Mild Factor VII Deficiency: Correlation Between Genotype and Phenotype
Craig Fraser1,2*, Mohammed Khan2
1University of Aberdeen, 2Department of Haematology, Aberdeen Royal Infirmary, Aberdeen, United Kingdom

Abstract Content: Factor VII (FVII) deficiency is the commonest of the rare coagulation disorders with a prevalence of 1 in 500000. It is an autosomal recessive disorder with a heterogenous clinical phenotype. Patients with FVII deficiency can have rare pathogenic mutations in the F7 gene causing a reduction in FVII levels. There are also a number of polymorphisms in the F7 gene which occur relatively frequently in the general population and can lead to decreased FVII levels. It is unclear whether the genetic profile has an impact on the clinical phenotype in those with mild FVII deficiency, or whether the management should differ based on the underlying genotype.

We performed a retrospective review of FVII deficiency cases registered with a Haemophilia Treatment Centre (HTC) in order to assess if there are any differences in the clinical phenotype between those with F7 gene pathogenic variants and those with common F7 gene polymorphisms. Case notes and electronic patient records were reviewed for all patients with a low FVII level recorded on more than one occasion from 2010 to the present. For each patient, genetic testing reports were used to determine the F7 genotype. Only those with pathogenic F7 gene mutations or common polymorphisms were included in this review. For each case, the clinical phenotype was determined by reviewing the records and formulating the International Society of Thrombosis and Haemostasis Bleeding Assessment Tool (ISTH BAT) score. The baseline FVII activity was also recorded for each case. Patient records were reviewed to determine if any treatment for FVII deficiency was received such as Tranexamic Acid or recombinant FVII replacement.

Fifty-four patients were identified as having low FVII levels of which 10 were excluded because they either had acquired FVII deficiency or the data were incomplete. Of the remaining 44 patients, 12 (27.3%) had mutations in their F7 gene and 32 (72.7%) had polymorphisms associated with their F7 gene. The mean FVII level for those with pathogenic mutations was 32% (21%-44%) and 40% (27%-47%) for those with polymorphisms only (p <0.05).

Patients were deemed to have a pathological bleeding score if the ISTH BAT score was >3 for adult males, >5 for adult females and >2 for children. 16.7% patients with an F7 mutation had a pathological bleeding score which was not significantly different to those with polymorphisms and an abnormal bleeding score (18.8%). Only 6 of the total cohort received haemostatic treatment of which 1 had a mutation whilst the remainder had polymorphisms. There was no statistically significant difference between the 2 groups and the need for haemostatic treatment.

In this cohort of patients with mild FVII deficiency, the presence of a pathogenic mutation resulted in lower mean FVII activity. Despite this, the objective bleeding score was no different when compared to those with polymorphisms only. Furthermore there was no difference between the 2 groups as to whether they received haemostatic treatments. These results support mild FVII deficiency being managed with the same approach in those with pathogenic mutations as those with only polymorphisms.

Disclosure of Interest: None Declared

Newborn screening for sickle cell disease in Lubumbashi city, Democratic Republic of Congo: a preliminary study on an update of the disease prevalence
Tina Katamea1,2*, Olivier Mukuku1, Stanis Wembonyama1
1Université de Lubumbashi, 2Institut Supérieur des Techniques Médicales, Lubumbashi, Congo, The Democratic Republic of the

Abstract Content: Introduction: Sickle cell disease is an autosomal recessive hemoglobinopathy. It has reached up to 2% of newborns in some countries in sub-Saharan Africa. In most patients, the incidence of complications can be reduced if screening takes place at the time of birth.

This study was conducted to determine the prevalence of sickle cell disease among a population of newborns in Lubumbashi, Democratic Republic of Congo.

Methods: This prospective cross-sectional study was carried out at the University Clinics of Lubumbashi, in the Democratic Republic of Congo, on newborns. Newborn blood samples were examined by iso-focusing electrophoresis.

Results: Of a total of 338 newborns screened for sickle cell disease, 276 (81.7%) were AA, 37 (10.9%) were AS, 1 (0.3%) was AC and 24 (7.1 %) were SS.

Conclusion: This preliminary work allowed us to analyse data from neonatal screening for sickle cell disease in Lubumbashi. Conducting prenuptial counselling is essential to reduce the prevalence of this haemoglobinopathy. Systematic newborn screening in all maternity hospitals in the country would help assess the prevalence at the national level and improve the quality of life of affected children.

Abstract Table: Table 1. Haemoglobin phenotypes of the babies.

<table>
<thead>
<tr>
<th>Haemoglobin phenotype</th>
<th>n (%)</th>
</tr>
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<tbody>
<tr>
<td>AA</td>
<td>276 (81.7)</td>
</tr>
<tr>
<td>AS</td>
<td>37 (10.9)</td>
</tr>
<tr>
<td>AC</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>SS</td>
<td>24 (7.1)</td>
</tr>
<tr>
<td>Total</td>
<td>338 (100)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

Hibiscus, an adaptive, randomized, placebo-controlled, double-blind, multi-centre study of oral FT-4202, a pyruvate kinase activator in patients with sickle cell disease
Kenneth Wood1, James Geib1, Eric Wu1, Jason Berlin1, Irena Webster1, Kenneth Ataga2, Jo Howard3, Jeremie Estepp4, Marilyn Telen5, Julie Brevard1
1Forma Therapeutics, Inc., Watertown, 2University of Tennessee Health Science Center, Memphis, United States, 3Guy’s and St. Thomas’ Hospital, London, United Kingdom, 4St. Jude Children’s Research Hospital, Memphis, 5Duke University Medical Center, Durham, United States

Abstract Content: The hallmark of sickle cell disease (SCD) is hemoglobin S (HbS) polymerization upon deoxygenation, resulting in red blood cell (RBC) sickling, oxidative damage, membrane damage, haemolysis, chronic anaemia, cell adhesion, vaso-occlusion and inflammation. Exacerbating the pathogenesis of SCD, the HbS RBC has increased (↑) levels of 2,3-diphosphoglycerate (2,3-DPG), resulting in reduced (↓) Hb oxygen affinity (P50), and ↓ATP, essential for RBC homeostasis. FT-4202, an investigational agent, is a potent,
Red Cell Disorder

selective, orally biosavailable allosteric activator of erythrocyte pyruvate kinase (PKR), that \(^1\)PKR activity, and is hypothesized to \(2,3\) DPG and \(4\)ATP. In a phase 1 study (NCT03815695), FT 4202 was well-tolerated, exhibited linear, time-independent pharmacokinetics and pharmacodynamic responses \((2,3\text{-}DPG \text{ and } 4\text{-}ATP)\) without steroidogenic effects. Treatment of patients with SCD for 14 days with once-daily FT 4202 resulted in \(3\)Hb O\(2\) affinity, \(4\)RBC sickling, improved measures of \(5\)BBC haemoglobin and improved haematologic and haemolytic parameters.\(^1\)

Hibiscus (NCT04624659) is a phase 2/3, randomized, double-blind, placebo-controlled global study to investigate the safety and efficacy of FT-4202 in patients with SCD.

Adult and paediatric (≥12 years old) patients with SCD (all genotypes) will be enrolled in a Dose Determination (DD) group and an Efficacy Continuation (EC) group using an adaptive design. Eligible patients must have had ≥2 vaso-occlusive crises (VOCs) in the past year, baseline Hb ≥5.5 and ≤10 g/dL, and if receiving hydroxyurea (HU), be on stable therapy for the previous 90 days. Patients with >10 VOCs in the past year, hospitalized for sickle cell crisis/other vaso-occlusive event within 14 days of consent, receiving routine RBC transfusions, significant hepatic/renal dysfunction, history of unstable or deteriorating cardiac or pulmonary disease, or overt stroke within 2 years will be excluded. Co-primary endpoints are Hb response rate (RR) at Week 24 (increase from baseline >1 g/dL) and annualized VOC rate during the blinded treatment period based on adjudicated VOC review. Secondary endpoints include measures of haemolysis, time to first VOC and the Patient Reported Outcome Measurement Information System fatigue scale. Safety endpoints will also be assessed. Patients will be stratified by number of VOCs, prior/concomitant HU use and age, and randomized 1:1:1 to 200 or 400 mg (once-daily) FT-4202, or placebo in the DD group. At interim analysis (IA) 1, one FT-4202 dose level will be selected based on safety and Hb RR at Week 12 of the first 60 patients. EC group patients will be randomized 1:1:1 to the selected FT-4202 dose or placebo. Once 110 patients randomized to the selected dose or placebo complete 24-week blinded treatment or drop out, IA2 will assess Hb RR (first primary endpoint). At final analysis (52-weeks blinded treatment) annualized VOC rate (second primary endpoint), 24-week Hb RR and all secondary endpoints will be evaluated. Patients may then enter a 52-week open-label extension period at the selected FT-4202 dose. Futility assessments will be conducted (Weeks 12 and 24). Recruitment is ongoing; planned enrolment: ≥344 patients with SCD (DD group, n = 60; EC group, n~274).

This study will evaluate the safety and efficacy of oral, once-daily FT-4202 in adult and paediatric patients (≥12 years old) with SCD.\(^1\)

Brown, ASH2020, abstract, #134269.


**BSH2021-OR-033**

**Epistaxis at presentation as a predictor of subsequent severe bleeding events in immune thrombocytopenia**

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**Abstract Content:** Immune thrombocytopenia (ITP) is an acquired disease characterised by a platelet count drop to under 100 x 109/L. A relatively common paediatric condition, incidence is 1.9–6.4 per 105 children per year. The majority of cases present with mild bleeding symptoms and spontaneously resolve, yet severe bleeding has been reported in up to 20% of cases in the first year of illness. It is established that presenting with cutaneous manifestations alone is associated with lower risk and urinary or gastrointestinal bleeding higher risk of future severe bleeding. Conversely the significance of epistaxis is unclear, despite it being the most common site of mucosal bleed. Higher risk epistaxis is defined as longer than 5 minutes duration by the 2013 ITP-specific bleeding assessment or longer than 15 minutes in the Epistaxis specific element of the Buchanan score. The overall Buchanan score classifies all epistaxis as moderate risk, as was used by the TIKI trial. This trial identified a trend towards increased risk for severe bleeding (defined as any bleed causing a haemoglobin drop over 2 g dL\(^{-1}\)) for untreated patients in the twelve months following presentation with a moderate severity bleed, this risk was reduced by immunoglobulin infusion.

We hypothesised that longer duration of epistaxis at presentation would be associated with a higher risk of future bleeding events.

We used data from the national UK Childhood ITP database, a multi-centre prospective clinical registry of new cases of ITP between 2006 and February 2020. Exposure was defined as no epistaxis, epistaxis lasting under 10 minutes, epistaxis lasting 10 to 30 minutes and epistaxis lasting over 30 minutes. The outcome was bleeding events in the first 12 months following presentation. Overall bleeding severity was classified using the adapted Buchanan bleeding score. We used logistic regression to estimate the association between epistaxis duration at presentation and future bleeding severity. We estimated unadjusted models (model 1) and covariate adjusted models (model 2). The covariates were age at presentation, platelet count less than 10 at presentation, atypical features, number of other bleeding sites and if treatment with steroids or immunoglobulin was received.

The sample included 1793 participants, of which 295 had minor bleeding, 150 moderate bleeding and 22 severe bleeding in the 12 months after presentation. At presentation 334 participants had epistaxis lasting under 10 minutes, 88 lasting 10–30 minutes and 97 over 30 minutes. In model 1 epistaxis over 30 minutes duration was associated with higher odds of subsequent bleeding for both severe bleeds and combined moderate and severe bleeds (Table 1). Bleeding under 30 minutes duration was not associated with increased odds for either outcome; however, a trend for increased risk with increasing duration of epistaxis was statistically significant \((P = 0.01)\). In model 2 the associations remained significant after adjustment for potential confounders. Additionally, number of bleeding sites did not alter odds of bleeding event for severe bleeds alone nor moderate and severe bleeds combined.
We found that the longer the epistaxis, the higher the risk of a subsequent severe bleeding episode. This is mostly driven by a large increase in risk when epistaxis lasts over 30 minutes. Our findings support watch and monitor for children with short duration epistaxis and treatment in epistaxis lasting 30 minutes or more.

Abstract Table: Table 1: Logistic Regression Showing The Association Between Bleeding Outcome And Epistaxis Duration.

<table>
<thead>
<tr>
<th></th>
<th>Model 1a</th>
<th>Model 2b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>Moderate and severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10mins</td>
<td>1.32 (0.87 to 1.99)</td>
<td>1.14 (0.73 to 1.78)</td>
</tr>
<tr>
<td>10–30 mins</td>
<td>1.71 (0.88 to 3.33)</td>
<td>1.37 (0.68 to 2.77)</td>
</tr>
<tr>
<td>&gt;30 mins</td>
<td>2.55 (1.45 to 4.48)</td>
<td>2.07 (1.12 to 3.82)</td>
</tr>
<tr>
<td>Severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10 mins</td>
<td>1.53 (0.48 to 4.92)</td>
<td>1.05 (0.31 to 3.55)</td>
</tr>
<tr>
<td>10–30 mins</td>
<td>1.45 (0.18 to 11.48)</td>
<td>1.13 (0.14 to 9.40)</td>
</tr>
<tr>
<td>&gt;30 mins</td>
<td>5.44 (1.67 to 17.67)</td>
<td>3.61 (1.02 to 12.83)</td>
</tr>
</tbody>
</table>

*aUnadjusted logistic regression, bAdjusted for age at presentation, platelet count less than 10 at presentation, atypical features, number of other bleeding sites and if treatment with steroids or intravenous immunoglobulin was received.*

Disclosure of Interest: None Declared

BSH2021-OR-034

Single center experience on safety and tolerability of emicizumab in the paediatric population with severe haemophilia A

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Abstract Content: Emicizumab has been highly effective novel medication for children with severe hemophilia A (HA) with and without inhibitors. Safety assessment is a crucial component in all phases of development of new drugs. In case of emicizumab, serious safety concerns about thromboembolic events (TEs), and thrombotic microangiopathy (TMA) were raised from clinical trials. However, to date neither TMA nor TEs have been reported paediatric patients, thus suggesting that emicizumab is relatively safe in this age group. On the other hand, minor side effects were reported in more than 90% of emicizumab-treated HA children, including injection site reactions, headache and contusion. In literature, the development of antidrug antibodies (ADA) represent an incidence of about 4–5%. Real-world data on safety and tolerability of emicizumab in paediatric population have not been well explored especially in non-inhibitor patients.

We conducted an observational study in Birmingham Children’s hospital. Data regarding adverse events were collected from a cohort of 49 severe HA patients on emicizumab prophylaxis. Median age of emicizumab start was 7.7 (range 0.3–15.3) years. Median time on emicizumab was 13.1 (range 2.7–36.6) months. Four patients had active inhibitors at the time of the study.

The most common side effects were minor and reported in 8% of the patients after emicizumab injections. Two patients developed headaches, one patient had minimal injection site reaction and one patient had abdominal pain and nausea. Major adverse events were reported in four patients (see table). Patient#1 developed headaches which were severe enough that he discontinued emicizumab and returned to previous prophylaxis. Patient#2 was well controlled on recombinant factor (r) (F) VIII prophylaxis prior to emicizumab with zero annualized bleeding rate and no inhibitors. Although his emicizumab levels were in normal ranges, he developed a significant haematoma behind his hip joint after minimal trauma that required hospitalization for 2 days and treatment with rFVIII for 12 days. Following this event, family decided to return to previous prophylaxis regimen. Patient#3 had emicizumab plasma concentrations persistently lower than normal ranges. Anti-FX anti-emicizumab antibodies were found to be positive at low levels. He was treated with rFVIII three times for joint pains; however, joint bleeding was not confirmed in these occasions as formal review was not possible due to COVID circumstances. He continued emicizumab at a weekly dose instead of fortnightly with close clinical follow-up and monitoring of ADA. Patient#4 had recurrent inhibitors (at low levels) after previous successful immune tolerance. None of the patients developed TEs or TMA.

All of these real-life adverse events highlight that management of HA patients on emicizumab may not be an easy task, despite its efficacy, the convenience of subcutaneous injections and infrequent dosing. Therefore, we believe that additional clinical trials to evaluate long-term safety of emicizumab prophylaxis are mandatory especially in children with HA.

Abstract Table: Table

<table>
<thead>
<tr>
<th>Patient#</th>
<th>Number of doses of emicizumab</th>
<th>Inhibitor status</th>
<th>Adverse Event</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>Negative</td>
<td>Headaches</td>
<td>Stopped emicizumab</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>Negative</td>
<td>Major breakthrough bleeding</td>
<td>emicizumab Continued on emicizumab at higher frequency</td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>Negative</td>
<td>ADA</td>
<td>Continued on emicizumab with advice to give activated rFVII on demand and close follow-up for inhibitor levels</td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>Negative</td>
<td>Recurrence of previously tolerated inhibitors</td>
<td>Stopped</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

BSH2021-OR-035

Laboratory monitoring of paediatric patients on emicizumab prophylaxis: experience from a large comprehensive haemophilia center in the UK

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Abstract Content: Emicizumab is highly effective in bleeding prevention. However, the functional differences between emicizumab and factor VIII (FVIII) in addition to its long half-life make it challenging for laboratories. Recent publications as well as helpful manufacturer insight have provided guidance on how emicizumab can influence haemostasis laboratory tests, measurement of FVIII activity levels and monitoring of emicizumab levels.

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We present laboratory monitoring data from our cohort of 49 patients receiving emicizumab prophylaxis at Birmingham Children’s Hospital. A set of laboratory investigations including emicizumab levels, activated partial thromboplastin time (aPTT), chromogenic FVIII assay (CSA), inhibitor titers, full blood count, liver and renal function tests are done for all patients at the end of loading doses (fifth week of starting emicizumab), monthly for 3 months, then every three months afterwards.

Standard one-stage FVIII activity assays were found to be either insensitive or oversensitive to emicizumab, which excludes their use. Moreover, CSA that contains human FIXα and FX are highly sensitive to the presence of emicizumab resulting in falsely elevated FVIII activity; however, those containing bovine FIXα and FX are unaffected. At Birmingham Children’s Hospital, we use CSA, with bovine sources reagents, a higher plasma dilution and emicizumab specific calibrator (r² diagnostics). Each patient sample is analysed in multiple point dilutions in concordance with standard parallel line assay recommendations to enable accurate quantification of FVIII activity and measurement of emicizumab concentrations. Also, inhibitor levels under concurrent treatment with emicizumab, are measured by a chromogenic Bethesda assay using bovine reagents.

Median age of the patients was 7.7 (range 0.3–15.3) years. Median time on emicizumab was 13.1 (range 2.7–36.6) months. A summary of laboratory assays used and results for our patients who are on emicizumab prophylaxis are detailed (Table). Full blood counts, renal function and liver functions were all in normal ranges with median creatinine level 40 (range7–73) µmol/L, ALT median 12 (range 5–29) IU/L and aPTP median 19 (range 15–23) seconds. Emicizumab levels were in normal ranges (40–60 µg/ml) in all patients as shown in (Table). Only, two patients had their emicizumab levels lower than normal in more than one occasion despite full compliance. First patient’s levels range was (14–20) µg/ml; moreover, he required additional FVIII treatment on three occasions. Anti-drug antibodies (ADA) were requested and anti-FX anti-emicizumab antibodies were found to be positive at low levels. The second patient’s levels range was (25–30) µg/ml with no bleeding events; therefore, ADA was not done. All inhibitors levels were <0.4 Bethesda unit (Buil/ml except in five patients who had inhibitors prior to starting emicizumab (range 0.7–922)) Bu/ml. It worth mentioning that one patient with inhibitors on follow-up after starting treatment had inhibitors levels normalized to <0.4 Bu/ml. On the other hand, one patient had recurrence of previously tolerated inhibitors after starting emicizumab (range 0.5–1.6) Bu/ml and this reflects the significance of continuous assessment of inhibitors levels.

Our results highlights the importance of laboratory monitoring of patients on emicizumab prophylaxis. We recommend that reliable laboratory assessment should be well established prior to initiation of emicizumab treatment.

Abstract Table: Table.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Assay</th>
<th>Results of our cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emicizumab levels</td>
<td>CSA with bovine sources reagents calibrated with r² diagnostics calibrators</td>
<td>Median after loading doses 52 µg/ml</td>
</tr>
<tr>
<td>Inhibitor levels</td>
<td>Chromogenic Bethesda assay with bovine FIXα and FX</td>
<td>Median after 1 month 54 µg/ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Median after 2 months 52µg/ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Median after 3 months 47 µg/ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Median every 3 months (48, 47.5, 52 and 50) µg/ml</td>
</tr>
</tbody>
</table>

Table . (Continued)

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**Normal ranges (40–60 µg/ml)**

Disclosure of Interest: None Declared

BSH2021-OR-036

Primary analysis of ZUMA-5: A phase 2 study of axicabtagene cileucel in patients with relapsed/refractory indolent non-hodgkin lymphoma

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Abstract Content: Axicabtagene cileucel (axi-cel) autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy is approved
for the treatment of relapsed/refractory (R/R) large B-cell lymphoma. Here, we present the primary analysis of ZUMA-5, a Phase 2, multicenter, single-arm study of axi-cel in patients with R/R indolent non-Hodgkin lymphoma (iNHL).

Adults with follicular lymphoma (FL; Grades 1-3a) or marginal zone lymphoma (MZL; nodal or extranodal) had R/R disease after ≥2 lines of therapy (must include an anti-CD20 mAb plus an alkylating agent) and ECOG 0-1. Patients underwent leukapheresis followed by conditioning therapy and a single infusion of axi-cel at ≥2 × 10^6 CAR T cells/kg. The primary endpoint was objective response rate (ORR) by central review (per Lugano classification; Cheson, et al. J Clin Oncol. 2014), analysed when ≥80 treated patients with FL had ≥12 months of follow-up. Secondary endpoints included complete response (CR) rate, duration of response (DOR), progression-free survival (PFS), overall survival (OS), safety, and levels of CAR T cells in blood.

As of 3/12/2020, 146 patients with iNHL (124 FL; 22 MZL) received axi-cel; 84 patients with FL had ≥12 months of follow-up. The median age was 61 years (range, 34-79); 57% of patients were male. Thirty-eight percent of patients had ECOG 1; 86% had stage III/IV disease; 47% had ≥3 FLIP1, and 49% had high tumor bulk (GELF). Patients had a median of 3 prior lines of therapy; 64% had ≥3 prior lines; 55% progressed <2 years after first chemotherapy, and 68% had refractory disease. Axi-cel was successfully manufactured for all enrolled patients.

With a median follow-up of 17.5 months, the ORR was 92% in efficacy-evaluable patients with iNHL (n = 104), with a 76% CR rate. In patients with FL (n = 84), the ORR was 94% (80% CR rate); in those with MZL (n = 20), the ORR was 85% (60% CR rate). ORR was comparable across key risk groups. As of the data cut-off date, 62% of all treated patients had ongoing responses (64% for FL). Twelve-month estimated rates of DOR, PFS, and OS were 72%, 74%, and 93%, respectively.

Grade ≥3 adverse events (AEs) occurred in 86% of patients with iNHL (85% in FL; 95% in MZL). Grade ≥3 cytokine release syndrome (CRS; per Lee, et al. Blood. 2014) occurred in 7% of patients with iNHL (6% in FL; 9% in MZL). Grade ≥3 neurologic events (NEs; per CTC AE v4.03) occurred in 19% of patients with iNHL (15% in FL; 41% in MZL). Most CRS (118/119) and NEs (81/87) of any grade resolved by data cut-off. Grade 3 AEs occurred in 3 patients; multisystem organ failure in the context of CRS (related to axi-cel), aortic dissection, and coxidiodidymosis infection (both unrelated to axi-cel).

The median peak CAR T-cell level was 38 cells/µL (range, 0–1415), and the AUC0–28 was 448 cells/µL×days (range, 6–19,900). Median time to peak was 9 days. In efficacy-evaluable patients with FL, median peak CAR T-cell levels were numerically greater in those with ongoing response at 12 months than in those who relapsed (P = 0.057). In all treated patients with FL, CAR T-cell peak was associated with Grade ≥3 CRS (P = 0.031) and NEs (P = 0.005).

Axi-cel had considerable and durable clinical benefit in patients with iNHL, with high ORR and CR rates. Axi-cel had a manageable safety profile, with lower rates of Grade ≥3 NEs observed in patients with FL than MZL and those previously reported in aggressive NHL (Locke, et al. Lancet Oncol. 2019).

Disclosure of Interest: C. A. Jacobson, MD Conflict with: Consultancy or advisory role for Kitex, a Gilead Company, Novartis, Celgene, BMS, Precision Biosciences, Nkarta, and Lonza; Speakers' bureau participation for AXIS and Clinical Care Options; and Travel support from Kitex, a Gilead Company, Novartis, BMS, Celgene, Precision Biosciences, Nkarta, and Lonza. J. C. Chavez, MD Conflict with: Consultancy or advisory role for MorphoSys, Bayer, Karyopharm, Kite, a Gilead Company, Novartis, Celgene/Juno, and AbbVie; Conflict with: Research funding from Merck, Conflict with: Speakers' Bureau with MorphoSys, AstraZeneca, BeGenie, Genentech, Kite, a Gilead Company, and Epizyme., A. R. Sehgal, MD Conflict with: Research funding from Gilead Sciences, Merck, and Bristol-Myers Squibb. B. M. Williams, MD Conflict with: Consulting or advisory role with Celgene, Kyowa Kirin, and Guidepoint Global; Conflict with: Research funding from Incyte, Dova, Merck, and Seattle Genetics., J. Munoz, MD, MS, FACP Conflict with: Consultancy or advisory role for Pharmacyclics, Bayer, Kite, a Gilead Company, Pfizer, Janssen, Juno/Celgene, BMS, Kyowa, Alexion, Fouskite, Innoven, Seattle Genetics, and Beigene, Conflict with: Research funding from Bayer, Kite, a Gilead Company, Juno/Celgene/BMS, Merck, Portola, Incyte, Genentech, Pharmacyclics, Seattle Genetics, Janssen, and Millennium; Conflict with: Honoraria from Kyowa and Seattle Genetics; Speakers' bureau participation for Kite, a Gilead Company, Kyowa, Bayer, Pharmacyclics/Janssen, Seattle Genetics, Acrobat/Aurobindo, Beigene, Verastem, AstraZeneca, Juno/Celgene/BMS, Genentech/Roche, and AbbVie; G. Salles, MD, PhD Conflict with: Consulting or advisory role for Abb-Vie, Autolus, BMS/Celgene, Debioipharm, Genmab, Kite, a Gilead Company, Epizyme, Janssen, Karyopharm, Pharmacyclics, Novartis, and Roche. Conflict with: Honoraria from BMS/Celgene/Kite, a Gilead Company, Epizyme, Janssen, MorphoSys, Novartis, and Roche, P. N. Mundt, MD Conflict with: Honoraria from Kite, a Gilead Company, and Incyte; Speakers' bureau participation for Kite, a Gilead Company, and Incyte. C. Casulo, MD: None Declared, D. G. Maloney, MD, PhD Conflict with: Consultancy or advisory role for A2 Bio-therapeutics, Conflict with: Research funding from Kite, a Gilead Company, Juno Therapeutics, and Celgene, Conflict with: Stock or other ownership in A2 Biotherapeutics; Honoraria from BioLine RX, Juno Therapeutics, Celgene, Kite, a Gilead Company, Gilead Sciences, Novartis, and Pharmacyclics; and Patents, royalties, or other intellectual property from Juno Therapeutics. S. De Vos, MD, PhD Conflict with: Consultancy or advisory role for Bayer and Verastem. R. Reshef, MD Conflict with: Consultancy or advisory role for Magenta, Atara, Celgene and Gilead., Conflict with: Research funding from Gilead, BMS, Takeda, Incyte, Pharmacyclics, Immatics, Shire, Bluebird, Atara and Kidasis, Conflict with: Honoraria from Gilead and Novartis; Expert testimony provided for Monsanto; and Travel support from Gilead. L. A. Leslie, MD Conflict with: Consulting or advisory role with TG Therapeutics, AbbVie; RCYC, Kite, a Gilead Company, Celgene, BMS, and ADC Therapeutics., Conflict with: Honoraria from Kite, a Gilead Company, AstraZeneca, Seattle Genetics, Epizyme, Karyopharm, Celgene, BMS, PCYC, and BeGenie; Speakers' bureau with Kite, a Gilead Company, Celgene, BMS, BeGenie, PCYC, Janssen, AstraZeneca, Seattle Genetics, Karyopharm, and Epizyme., I. Yakoub-Agha, MD, PhD Conflict with: Honoraria from Kite, a Gilead Company, Novartis, and Celgene. O. O. Olulowo, MD, MPH, MBBS Conflict with: Consultancy or advisory role for Kite, a Gilead Company, Pfizer, Spectrum Pharmaceuticals, Legend and Bayer. H. C. H. Fung, MD Conflict with: Personal fees from Janssen Oncology, Takeda, Incyte, Amgen, Celgene/BMS, Pfizer, Sanofi, AbbVie, Karyopharm, AstraZeneca and Kite, a Gilead Company, J. Rosenblatt, MD Conflict with: Consulting or advisory role with Synergys and BioGraph 55, Conflict with: Research funding from BioGraph 55 and Synergys. Conflict with: Leadership with Synergys; Stock or other ownership with Incyte and ISK; J. M. Rossi, MS Conflict with: Employment with Kite, a Gilead Company. L. Goyal, PhD Conflict with: Employment with Kite, a Gilead Company. V. Plaks, LLB, PhD Conflict with: Employment with Kite, a Gilead Company. Y. Yang, MS Conflict with: Employment with Kite, a Gilead Company. J. Lee, BS Conflict with: Employment with Kite, a Gilead Company; stock or other ownership in Gilead Sciences. W. Godfrey, MS, MD Conflict with: Previous employment with Kite, a Gilead Company; stock or other ownership in Kite, a Gilead Company.
Interim analysis of ZUMA-12: a phase 2 study of axicabtagene ciloleucel as first-line therapy in patients with high-risk large B-cell lymphoma

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Interim analysis of ZUMA-12: a phase 2 study of axicabtagene ciloleucel as first-line therapy in patients with high-risk large B-cell lymphoma

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Abstract Content: Patients with high-risk large B-cell lymphoma (LBCL) have poor outcomes with R-CHOP (Blood. 2016;128[suppl, abstr]:106), highlighting an unmet treatment need. Axicabtagene ciloleucel (axi-cel), an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, was approved for use in adults with relapsed/refractory LBCL after ≥2 prior systemic therapies based on the ZUMA-1 study. Here, we present the interim analysis of ZUMA-12, a Phase 2, open-label, multicenter, single-arm study of axi-cel as part of first-line therapy in patients with high-risk LBCL.

Adult patients (aged ≥18 years) met 2 criteria for high-risk LBCL: (1) double/triple-hit lymphoma by fluorescence in situ hybridization per investigator or LBCL with International Prognostic Index (IPI) score of ≥3 and (2) positive interim positron emission tomography (PET) per Lugano Classification (Deauville score [DS] of 4 or 5) after 2 cycles of an anti-CD20 and anthracycline–containing regimen. Patients underwent leukapheresis (≥2 weeks after prior systemic therapy) and then received conditioning chemotherapy with fludarabine and cyclophosphamide for 3 days and a single axi-cel infusion (2×10^6 CAR T cells/kg). The primary endpoint was complete response (CR) rate per investigator. Key secondary endpoints were objective response rate (ORR), adverse events (AEs), and CAR T-cell levels in blood.

As of 8/25/2020, 32 patients received axi-cel; 19 patients had ≥6 months of follow-up at the data cut-off date. The median age was 61 years; 50%/50% of patients had DS 4/5, 53% had double/triple-hit status, and 72% had IPI score of ≥3. Of 27 response-evaluable patients (centrally confirmed high-risk LBCL who received axi-cel and had ≥1 month of follow-up), the ORR was 85% (74% CR rate); 70% of patients had ongoing responses at the data cut-off date. Of 32 patients treated (safety analysis set), the ORR was 88% (78% CR rate); 75% of patients had ongoing responses at the data cut-off date.

Of 32 safety-evaluable patients, Grade ≥3 AEs occurred in 81% of patients, with the most common being neutrophil count decreased (44%), white blood cell count decreased (44%), and anaemia (25%). Grade ≥3 cytokine release syndrome (CRS) and neurologic events (NEs) occurred in 9% and 25% of patients, respectively. No Grade 4 or 5 CRS occurred and no Grade 5 NEs occurred. The median time to onset for any grade CRS and NEs was 4 days (range, 1–10) and 9 days (range, 2–44), respectively. One Grade 5 AE occurred due to COVID-19.

Despite similar assessment schedule and methodology, median peak CAR T-cell levels were greater in ZUMA-12 versus ZUMA-1 Phase 2 Cohort 1 (46 cells/µL [range, 10–555] vs 32 cells/µL [range, 1–1514]). Median CAR T-cell expansion (as measured by area under the curve in the first 28 days) was also greater in ZUMA-12 (587 cells/µL×day [range, 147–4261]) than in ZUMA-1 (357 cells/µL×day [range, 5–11,500]). The median time to peak levels of CAR T cells in blood was 8 days after infusion. Pharmacokinetic profiles were similar in patients with double/triple-hit lymphoma and IPI score of ≥3.

ZUMA-12 is the first study in which CAR T-cell therapy was evaluated as first-line therapy in high-risk LBCL, which notably was defined by both histology and/or IPI and dynamic risk assessment (PET). Axi-cel demonstrated substantial clinical benefit and a manageable safety profile. The study results also provide new insights into the pharmacology of CAR T-cell therapy for patients exposed to fewer prior therapies.

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Pirtobrutinib (LOXO-305), a next generation highly selective non-covalent Bruton’s Tyrosine Kinase inhibitor in previously treated chronic lymphocytic leukemia/small lymphocytic lymphoma: Results from the Phase 1/2 BRUIN study
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Abstract Content: Despite the marked efficacy of covalent BTK inhibitors (BTKi) in CLL/SLL, the development of resistance and discontinuation for adverse events can lead to treatment failure. Moreover, pharmacological liabilities of these agents such as low oral bioavailability or short half-life can lead to suboptimal BTK target coverage and ultimately result in acquired resistance in some patients (pts). To address these limitations, pirtobrutinib (LOXO-305), a highly selective, non-covalent BTKi that inhibits both WT and C481-mutated BTK with equal low nM potency was developed. We report the safety and efficacy of pirtobrutinib in previously treated CLL/SLL.

BRUIN is a multicenter phase 1/2 trial (NCT03740529) enrolling pts with advanced B-cell malignancies who have received ≥2 prior therapies. Oral pirtobrutinib was dose escalated in a standard 3+3 design in 28-day cycles. The primary endpoint was MTD/RP2D identification. Efficacy evaluable pts included all dosed pts who underwent their first response evaluation or discontinued therapy. Safety was assessed in all pts (n = 323). Response was assessed according to the iwCLL 2018 criteria, including PR with lymphocytosis (PR-L).

As of 27 September 2020, 323 pts with B-cell malignancies (170 CLL/SLL, 61 MCL, 26 WM, and 66 other B-cell lymphomas) were treated on 7 dose levels (25–300 mg QD). Among the 170 CLL/SLL pts, the median age was 69 (range 36–84) years. Median number of prior lines of therapies was 3 (range 1–11), 86% of CLL/SLL pts had received a prior BTKi, and 67% an anti-CD20 antibody, chemotherapy, and BTKi; 21% had received a PI3K inhibitor and 34% venetoclax. At enrollment, high risk features such as 17p deletion were present in 25% (20/81), TP53 mutation in 30% (27/91), and unmutated IGHV in 88% (71/81). Pirtobrutinib demonstrated high oral exposures, with doses ≥100mg QD exceeding the BTK IC90 for the entirety of the dosing interval. No DLTs occurred. Consistent with pirtobrutinib’s selectivity, the only treatment-emergent adverse events regardless of attribution or grade seen in ≥10% of pts (n = 323) were fatigue (20%), diarrhea (17%) and contusion (13%). Responses were observed at the first dose level of 25mg QD. A RP2D of 200mg QD was selected for future studies. At the efficacy cut-off date, 150 CLL/SLL pts remained on therapy and 139 were efficacy evaluable (121 BTKi-treated). Median follow-up was 6 months (range 0.6–18.7) for efficacy evaluable pts. The ORR was 63% with 69 PRRs, 19 PR-Ls, 45 SDs, 1 PD, and 5 discontinued prior to first response assessment. An additional 37 pts were ongoing and awaiting initial radiologic assessment. Responses deepened over time; among pts with at least 10 months of follow-up (n = 29), the ORR was 86%. ORR was not influenced by the reason for prior BTKi discontinuation (i.e., progression vs. intolerance), or other classes of prior therapy received (including a covalent BTK and a BCL2 inhibitor). Of the 88 responding pts, all except 5 remain on therapy (4 progressed, and 1
achieved a PR and electively discontinued). The longest followed responding pt continues on treatment for 17.8± months.

Pirtobrutinib demonstrated promising efficacy in CLL/SLL pts following multiple prior lines of therapy including a covalent BTKi and a BCL2 inhibitor. Importantly, the activity of pirtobrutinib was not restricted to pts with BTK C481 mutations. Pirtobrutinib was well tolerated and exhibited a wide therapeutic index.


**BSH2021-OR-039**

**ECHELON-2 (NCT01777152), a randomized, double-blind, phase 3 study of brentuximab vedotin plus cyclophosphamide doxorubicin and prednisone versus cyclophosphamide, doxorubicin, vincristine and prednisone in previously untreated patients with CD30-positive peripheral T-cell lymphoma: 5-year results**

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**Abstract Content:** ECHELON-2, a phase 3, randomised, double-blind, double-dummy, placebo-controlled, active-comparator, multi-centre study, established the superiority of frontline brentuximab vedotin plus cyclophosphamide, doxorubicin and prednisone (A+CHP) versus cyclophosphamide, doxorubicin, vincristine and prednisone
(CHOP) for patients (pts) with previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL) (Horwitz, Lancet 2019). At the primary analysis, risk of progression-free survival (PFS) per blinded independent central review (primary endpoint) and overall survival (OS) events favoured A+CHP over CHOP. A+CHP was the first treatment regimen to increase OS compared with CHOP in this population. We report the 5-year data from ECHELON-2.

Adults with untreated CD30-positive PTCL (aiming to recruit 75±5% of pts with sALCL) were randomised 1:1 to receive 6–8 cycles of A+CHP or CHOP. Pts were stratified by histological subtype and international prognostic index (IPI) score. We report PFS per investigator (INV) and the following key secondary endpoints: OS, PFS in sALCL, complete remission (CR) and objective response rates (ORR) in re-treated pts. Brentuximab vedotin-based subsequent therapies were allowed.

Of 452 pts enrolled, most had sALCL (n = 316 [70%]; 218 [48%] anaplastic lymphoma kinase [ALK]-negative and 98 pts [22%] ALK-positive) and most had advanced disease (27% Stage III, 53% Stage IV; 78% IPI ≥2). At data cut-off, median follow-up was 47.6 months for PFS and 66.8 months for OS. Hazard ratios (HRs) for PFS per INV (0.70 [95% confidence interval (CI): 0.53–0.91], P = 0.0077) and OS (0.72 [95% CI: 0.53–0.99], P = 0.0424) favoured A+CHP over CHOP. Median PFS was 62.3 months (95% CI: 42.0–not evaluable) and 23.8 months (95% CI: 13.6–60.8) for A+CHP and CHOP, respectively. Estimated 5-year PFS was 51.4% (95% CI: 42.8–59.4%) with A+CHP vs. 43.0% (95% CI: 35.8–50.0) with CHOP. Median OS was not reached in either arm. Estimated 5-year OS was 70.1% (95% CI: 63.3–75.9) for A+CHP vs. 61.0% (95% CI: 54.0–67.3) for CHOP. PFS in prespecified subgroups was generally consistent with overall PFS. In pts with sALCL, the HR for PFS (0.55 [95% CI: 0.39–0.79]) also favoured A+CHP over CHOP, with an estimated 5-year PFS of 60.6% (95% CI: 49.5–69.9) for A+CHP vs. 48.4% (95% CI: 39.6–56.7) for CHOP. A total of 29 pts (13%) in the A+CHP arm (sALCL [n = 19], PTCL not otherwise specified [n = 5], angioimmunoblastic T-cell lymphoma [n = 5]) and 54 pts (24%) in the CHOP arm received subsequent systemic therapy with brentuximab vedotin. In the A+CHP arm, median time to retreatment was 15.0 months (range, 3–64); 17 pts (ORR: 59%) had CR (n = 11) or partial remission (n = 6) after retreatment with brentuximab vedotin monotherapy (n = 25) or brentuximab vedotin-containing regimen (n = 4). Treatment-emergent peripheral neuropathy (PN) occurred in the A+CHP (n = 117) and CHOP arms (n = 124), of which, 72% and 78% had resolved or improved in the A+CHP and CHOP arms, respectively. In pts with ongoing events at last follow-up (A+CHP [n = 47] vs. CHOP [n = 42]) PN was grade 1, 2 and 3 in 70% vs. 71%, 28% vs. 26% and 2% vs. 2%, respectively.

At 5 years’ follow-up, frontline A+CHP continued to provide clinically meaningful improvements in PFS and OS versus CHOP, including ongoing remission in 59% of re-treated pts with sALCL, with a manageable safety profile, including continued resolution or improvement of PN.

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on an entity’s Board of Directors or advisory committees for AbbVie, Amgen, Astellas, Janssen, and Astex, A. Hüttmann Conflict with: Consultancy for Lead Discovery Center GmbH; membership on an entity’s Board of Directors or advisory committees for Takeda, Conflict with: research funding from Seagen Inc.; travel, accommodations, expenses (paid by any for-profit health care company) from Celgene, Takeda, and Gilead; and travel expenses from Roche; Conflict with: employment with University Hospital Essen, University of Duisburg-Essen, Essen, Germany, K. J. Savage Conflict with: consultancy for Servier, BMS, Merck, Seagen Inc., and AbbVie; membership on an entity’s Board of Directors or advisory committees for BMS, Conflict with: research funding from Seagen and AbbVie, Conflict with: Honoraria from Verastem, Merck, BMS, Seagen Inc., AbbVie, and Takeda, S. Yuen: None Declared, P. L. Zinzani Conflict with: Consultancy for Janssen, MSD, Eusapharma, Sanofi, Verastem and EUSA Pharma; membership on an entity’s Board of Directors or advisory committees for Portola, Sandoz, Janssen-Cilag, Celttrion, Kyowa Kirin, Immune Design, BMS, Merck, ADC Therapeutics, Kirin Kyowa, Gilead, Servier, Verastem, MSD, and EUSA Pharma; speakers bureau for Portola, Eusapharma, Sandoz, Janssen-Cilag, Celttrion, Kyowa Kirin, BMS, Merck, ADC Therapeutics, Kirin Kyowa, Gilead, Servier, Verastem, EUSA Pharma, Janssen, MSD, AbbVie, Takeda, Incyte, Roche, TG Therapeutics Inc., and Immune Design, Conflict with: research funding from Portola, Conflict with: Honoraria from Verastem, EUSA Pharma, BMS, Merck, ADC Therapeutics, Kirin Kyowa, Gilead, Servier, Janssen, AbbVie, Takeda, Incyte, Roche, and TG Therapeutics Inc., H. Miao Conflict with: employment with Millennium Pharmaceuticals, Inc., Cambridge, MA, USA, a wholly owned subsidiary of Takeda Pharmaceuticals Limited, Conflict with: Current equity holder in publicly traded company with Takeda, V. Bunn Conflict with: Research funding from Seagen Inc., Conflict with: employment with Millennium Pharmaceuticals, Inc., Cambridge, MA, USA, a wholly owned subsidiary of Takeda Pharmaceuticals Limited, K. Fenton Conflict with: employment and current equity holder in publicly traded company with Seagen, Inc., M. A. Fanale Conflict with: employment and current equity holder in publicly traded company with Seagen, Inc., M. Puhlmann Conflict with: employment and current equity holder in publicly traded company with Seagen, Inc., L. Trümper Conflict with: Consultancy for Janssen, Takeda Europe, and Nordic Nanovector, Conflict with: research funding from Takeda Europe, Mundipharma, Roche, and Seagen

Abstract Content: In the treatment of advanced Hodgkin lymphoma, it is increasingly common practice to modify escalated BEACOPP (eBPP) by removing oral procarbazine and replacing it with intravenous dacarbazine (250 mg/m2 D2-3) to reduce haematopoietic stem cell and gonadal toxicity. However, published data of the escalated BEACOPPDac (eBPDAC) regimen are very limited. This is a retrospective study of 147 patients from 16 centres in the UK, Ireland and France who were treated with eBPDAC as the first line for advanced stage Hodgkin lymphoma. Outcomes were compared with 58 matched patients treated with eBP at 4 UK centres. Most patients were treated as per HD15 or HD18 protocol. 28 patients in Paris and two in Truro followed the AHL2011 protocol with 2 courses of eBPDAC given upfront and if iPET2 negative were desescalated to 4 cycles of ABVD. From 2009, 205 patients were treated first line with either eBP (n = 58) or eBPDAC (n = 147) with median follow-up 51.3 months and 22.9 months respectively. Patients were well matched with no significant differences in age (median: 23 y vs. 27 y), sex, stage (stage 3A: 81% vs. 83%) and international prognostic score (IPS3: 74% vs. 65%). 51% of eBPDAC patients received only 4 cycles (vs. 12% of eBP patients; P < 0.001) reflecting publication of HD18 trial data. In total, 74% patients achieved iPET2 Deauville score ≤ 3 and 90% patients achieved PET negative remission by end of treatment. 77% of eBPDAC patients achieved iPET2 Deauville ≤ 3 which was statistically similar to the eBP cohort (67%; P = 0.181) and matched the 76% iPET D2/3 reported in HD18. Of 205 patients, 202 are alive and 197 continue in first remission. Two eBP patients have relapsed at 13 and 41 months and the latter died of refractory disease. One eBPDAC patient had primary refractory disease, and three have
relapsed at 2, 7 and 24 months. One 56-year-old eBPĐac patient with high IPS died with bowel perforation during cycle 1 and one 34-year-old with alcoholic liver disease died 8 months after treatment while still in remission.

Toxicity was compared over the first 4 cycles. Mean day 8 (D8) ALT was similar between the two regimens. Mean D8 neutrophil count was lower in eBPĐac than eBPP patients (1.81 vs. 2.45; P = 0.067; G-CSF given day 9); however, it increased to 5.61 in eBPĐac patients given G-CSF from day 4. There is a trend toward fewer non-elective days of inpatient care for eBPĐac compared with eBPP (mean: 3.74 vs. 5.83; P = 0.118), and eBPĐac patients received fewer red cell transfusions compared with eBPP patients (mean 1.93 units vs. 4.16 units; P < 0.001). Women aged < 35, who completed ≥4 cycles of eBPĐac/eBPP had a similar rate of return of menstrual cycles (eBPP: 22/25; eBPĐac: 29/29), although eBPĐac patients appeared to restart menstruation earlier post chemotherapy (mean: 4.48 months vs. 9.12 months, P = 0.0026). However, this could also reflect the higher mean chemotherapy cycle number completed by the eBPP women (5.86 vs. 4.60; P < 0.001). The use of Goserelin to suppress ovulation varied between centres.

Accepting the limitations of a retrospective study, we suggest that substituting dacarbazine for procarbazine is unlikely to compromise the efficacy of eBPP and may have some toxicity benefits. Despite a predominance of high risk advanced stage patients, with nearly 2 years median follow-up we have observed only 2 deaths and 4 progression events from 147 patients treated with eBPĐac, suggesting this regimen is highly efficacious for the treatment of Hodgkin lymphoma.

Abstract Table:

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>N = 58</th>
<th>N = 147</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (range)</td>
<td>23 (16-54)</td>
<td>27 (16-62)</td>
<td>U=4665, P = 0.293</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>29 (50%)</td>
<td>88 (60%)</td>
<td>Fisher, P = 0.213</td>
</tr>
<tr>
<td>Stage 2B/2X/2XB</td>
<td>11 (19%)</td>
<td>25 (17%)</td>
<td>Fisher, P = 0.879</td>
</tr>
<tr>
<td>IPS 0-2</td>
<td>9 (16%)</td>
<td>27 (18%)</td>
<td>Fisher, P = 0.474</td>
</tr>
<tr>
<td>3-4</td>
<td>15 (26%)</td>
<td>51 (35%)</td>
<td></td>
</tr>
<tr>
<td>5-7</td>
<td>32 (55%)</td>
<td>72 (49%)</td>
<td></td>
</tr>
<tr>
<td>IPS ≥3</td>
<td>43 (74%)</td>
<td>96 (65%)</td>
<td></td>
</tr>
<tr>
<td>Treatment Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cycle number 1</td>
<td>0</td>
<td>2 (1%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>28 (20%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>7 (12%)</td>
<td>73 (51%)</td>
<td>Fisher, (4 vs. 6)</td>
</tr>
<tr>
<td>5</td>
<td>5 (9%)</td>
<td>2 (1%)</td>
<td>P = 3.93E-10</td>
</tr>
<tr>
<td>6</td>
<td>45 (78%)</td>
<td>39 (27%)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1 (2%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>On treatment</td>
<td>10 (21%)</td>
<td>39 (27%)</td>
<td>Fisher, P = 0.181</td>
</tr>
<tr>
<td>iPET Deauville score 1-2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>22 (46%)</td>
<td>72 (50%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>16 (33%)</td>
<td>32 (22%)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>1 (1%)</td>
<td></td>
</tr>
<tr>
<td>≤5</td>
<td>32 (67%)</td>
<td>111 (77%)</td>
<td></td>
</tr>
<tr>
<td>No iPET</td>
<td>10</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Mean day 8 ALT (cycles 1-4) [SD]</td>
<td>40.2 ±32.7</td>
<td>46.5 ±31.5</td>
<td>t(96)=1.17, P = 0.244</td>
</tr>
<tr>
<td>Mean day 8 neutrophils (cycles 1-4) [SD]</td>
<td>2.45 ±1.45</td>
<td>1.81 ±1.09</td>
<td>t(87)=2.77, P = 0.0067</td>
</tr>
<tr>
<td>Mean no. days non-elective admission (cycles 1-4) [SD]</td>
<td>5.83 ±7.40</td>
<td>3.74 ±5.47</td>
<td>U=2762, P = 0.118</td>
</tr>
<tr>
<td>Mean no. of red cell units transfused (cycles 1-4) [SD]</td>
<td>4.16 ±4.12</td>
<td>1.93 ±2.89</td>
<td>U=1996, P = 2.52E-5</td>
</tr>
<tr>
<td>Median follow-up from diagnosis in months (range)</td>
<td>51.3 (5.0-127)</td>
<td>22.9 (0.89-47.0)</td>
<td>U=1053, P = 2.2E-16</td>
</tr>
<tr>
<td>Mean no. of months for return of menstrual period post-chemotherapy [SD]</td>
<td>9.12 ±5.73</td>
<td>4.48 ±2.06</td>
<td>t(24)=5.55, P = 0.0016</td>
</tr>
<tr>
<td>Mean no. of cycles completed by women &lt;35 years of age [SD]</td>
<td>5.86 ±0.35</td>
<td>4.60 ±0.93</td>
<td>U=113, P = 5.20E-6</td>
</tr>
</tbody>
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Transplantation, gene & cellular immunotherapies

One year follow-up of ZUMA-2, the multicenter, registration study of KTE-X19 in patients with relapsed/refractory mantle cell lymphoma

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Abstract Content: KTE-X19, an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, is currently being evaluated in patients (pts) with relapsed/refractory mantle cell lymphoma (R/R MCL) who received 1–5 prior therapies (including a Bruton tyrosine kinase inhibitor) in the Phase 2, registrational, multicenter ZUMA-2 study. In the primary analysis of ZUMA-2 (N = 60), the objective response rate (ORR) was 93% (67% complete response [CR] rate), with a median follow-up of 12.3 months (N Engl J Med. 2020;382:1331). Here, we present results for all pts with ≥1 year of follow-up.

Eligible pts with R/R MCL underwent leukapheresis and conditioning chemotherapy followed by a single infusion of KTE-X19 (2×10^6 CAR T cells/kg; N Engl J Med. 2020;382:1331). The primary endpoint was ORR (CR + partial response) as assessed by an Independent Review Committee according to the Lugano Classification (J Clin Oncol. 2014;32:3059). Efficacy data are reported for the 60 treated pts with ≥1 year of follow-up; safety data are presented for all 68 treated pts.

As of December 31, 2019, the median follow-up was 17.5 months (range, 12.3–37.6). The ORR was 92% (95% CI, 81.6–97.2), with a CR rate of 67% (95% CI, 53.3–78.3). Of all efficacy-evaluable pts, 48% had ongoing responses at the data cut-off. Medians were not reached for duration of response, progression-free survival (PFS), or overall survival; 15-month estimates (95% CI) were 58.6% (42.5–71.7), 59.2% (44.6–71.2), or 76.0% (62.8–85.1), respectively. Median PFS was not reached in pts who achieved a CR (15-month rate, 75.1% [95% CI, 56.8–86.5]). 3.1 months (95% CI, 2.3–5.2) in pts who achieved a partial response, and 1.1 months (95% CI, 0.9–3.0) in nonresponders. The first 28 pts treated had a median follow-up of 32.3 months (range, 30.6–37.6); 39.3% of these pts remain in remission with no further therapy.

Common Grade ≥3 adverse events were neutropenia (85%), thrombocytopenia (53%), anemia (53%), and infections (34%). Grade ≥3 cytopenias were reported in 60% of pts ≥30 days post-infusion. Grade ≥3 cytokine release syndrome (CRS; per Blood 2014;124:188) occurred in 15% of pts; 59% received tocilizumab for management of CRS. Grade ≥3 neurologic events (NEs) were reported in 31% of pts, and 38% received steroids for NE management. There were no Grade 5 CRS events or NEs, and no new Grade 5 events occurred with additional follow-up.

Median (range) peak CAR T-cell levels (cells/µL) and median (range) area under the curve (Days 0–28; cells/µL) were 98.9 (0.2–2565.8) and 1394.9 (3.8–27,700) in pts with ongoing responses at 12 months, 202.6 (1.6–2589.5) and 2312.3 (19.0–27,200) in pts who relapsed by 12 months, and 0.4 (0.2–95.9) and 5.3 (1.8–1089.1) in nonresponders. Of the 57 efficacy-evaluable pts with data available, 84% had B cells detectable by flow cytometry at baseline. Of those in ongoing responses at 12 months, B cells were detectable in 10/26 pts (38%) at 3 months, and 10/18 (56%) at 12 months; gene-marked CAR T cells were no longer detectable at 12 months in 5/28 evaluable pts (17%).

The ZUMA-2 study continues to demonstrate substantial and durable clinical benefit of KTE-X19 therapy, with most pts achieving durable CR. Safety remained manageable, with no new safety signals reported. Although early CAR T-cell expansion was higher in pts who achieved an objective response, those who later relapsed showed elevated CAR T-cell levels, pointing to alternate mechanisms of secondary treatment failure in MCL.

Disclosure of Interest: M. L. Wang, MD Conflict with: Consultancy or advisory role with Pharmacycics, Celgene, Janssen, AstraZeneca, MoreHealth, Pulse Biosciences, Nobel Insights, Guidepoint Global, Kite, a Gilead Company, Juno, Loxo Oncology, InnoCare, Oncentral, VelosBio, Conflict with: Research funding from Janssen, AstraZeneca, Acerta Pharma, Pharmacycics, Juno Therapeutics, Celgene, Kite, a Gilead Company, Loxo Oncology, Oncentral, honoraria from Pharmacycics, Janssen, AstraZeneca, OML, Targeted Oncology, OncLive, Davo Oncology, Beijing Medical Award Foundation, and Lu Daopei Medical Group, Conflict with: Travel, accommodations, and expenses from Janssen, Pharmacycics, Celgene, OMIM, Kite, a Gilead Company, AstraZeneca, J. Munoz, MD, MS, FACP Conflict with: Consultancy or advisory role for Pharmacycics, Bayer, Kite, a Gilead Company, Pfizer, Janssen, Juno/Celgene, Bristol-Myers Squibb, Kyowa, Alexion, FosunKite, Innocent, Seattle Genetics, and BeiGene, Conflict with: Research funding from Bayer, Kite, a Gilead Company, Juno/Celgene/Bristol-Myers Squibb, Merck, Portola, Incyte, Genentech, Pharmacycics, Seattle Genetics, Janssen, and Millennium, Conflict with: Honoraria from Kyowa and Seattle Genetics; Speakers’ bureau participation for Kite, a Gilead Company, Kyowa, Bayer, Pharmacycics/Janssen, Seattle Genetics, Acerotech/Aurobindo, BeIGene, Verastem, AstraZeneca, Juno/Celgene/Bristol-Myers Squibb, Genentech/Roche, and AbbVie, A. Goy, MD, MS Conflict with: Consultancy or advisory role for AstraZeneca, Celgene, Gilead Sciences, Kite, a Gilead Company, and Xcenda, Conflict with: Research funding from Acer, AstraZeneca, Celgene, Constellation, Genentech-Hoffmann La Roche, Infinity, and Infinity Verastem, Conflict with: Employment with
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BSH2021-OR-042 Pharmacological profile and clinical outcomes of KTE-X19 by prior bruton tyrosine kinase inhibitor exposure or mantle cell lymphoma morphology in patients with relapsed/ refractory mantle cell lymphoma in the ZUMA-2 trial

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Abstract Content: ZUMA-2 is a Phase 2 study evaluating KTE-X19, an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, in patients (pts) with relapsed/refractory mantle cell
lymphoma (R/R MCL) after 1–5 prior therapies, including a Bruton tyrosine kinase inhibitor (BTKi). In the primary analysis of ZUMA-2 (N = 60), the objective response rate (ORR) with KTE-X19 treatment (median follow-up, 12.3 mo) was 93% (67% complete response [CR] rate; N Engl J Med. 2020;382:1331). Here, we present ZUMA-2 results by MCL morphology and prior BTKi exposure (ibrutinib [Ibr] and/or acalabrutinib [Acala]), accompanied by basic product attribute characterization.

Product attributes and CAR T-cell levels in blood were assessed using methods previously described (Mol Ther. 2017;25:285). Clinical outcomes are reported in the 60 efficacy-evaluable pts; safety, product attributes, and pharmacology data are reported for all 68 pts treated with KTE-X19 (2 × 10^6 cells/kg; data cut-off, 7/24/2019).

For pts with classical (n = 40), blastoid (n = 17), or pleomorphic (n = 4) MCL, median (range) CD4/CD8 ratios in manufactured KTE-X19 products were 0.7 (0.04–2.8), 0.6 (0.2–1.1), or 0.7 (0.5–2.0), respectively. Product T-cell phenotypes (median [range]) included less differentiated CCR7+ T cells (classical, 40.0% [2.6–88.8%]; blastoid, 35.3% [14.3–73.4%]; pleomorphic, 80.8% [57.3–88.8%]) and CCR7−/effecter + effecter memory T cells (classical, 59.9% [11.1–97.4%]; blastoid, 64.8% [26.6–85.7%]; pleomorphic, 19.2% [11.1–42.7%]). Median (range) interferon (IFN)-γ levels (pg/mL) by coculture in pts with classical, blastoid, or pleomorphic MCL were 6309.5 (424.2–20,000), 12510.0 (2709.0–18,000), and 7887.5 (424.0–12,000), respectively. In pts with classical, blastoid, or pleomorphic MCL, median (range) peak CAR T-cell levels (cells/µL) were 77.6 (0.2–2241.6), 35.0 (0.2–2589.5), or 144.9 (39.2–431.3), respectively. ORR/CR rates were as follows: classical, 93%/65%; blastoid, 88%/53%; and pleomorphic, 100%/75%. The 12-mo survival rates in pts with classical, blastoid, or pleomorphic MCL were 86.7%, 67.9%, or 100%, respectively. Grade ≥3 cytokine release syndrome (CRS)/neurologic events (NEs) occurred as follows: classical, 15%/38%; blastoid, 6%/8%; and pleomorphic, 25%/50%.

Overall, 88% of pts had BTKi-refractory disease. For pts who received prior Ibr (n = 52), Acala (n = 10), or both (n = 6), median (range) CD4/CD8 ratios in manufactured KTE-X19 products were 0.7 (0.04–3.7), 0.6 (0.3–1.2), or 1.0 (0.7–1.9), respectively. Product T-cell phenotypes (median [range]) included less differentiated CCR7+ T cells (Ibr, 39.3% [2.6–86.4%]; Acala, 42.7% [16.3–88.8%]; both, 49.5% [14.3–83.0%]). CCR7−/effecter + effecter memory T cells (Ibr, 66.7% [13.7–97.4%]; Acala, 57.3% [11.1–83.8%]; both, 50.6% [17.0–85.7%]). Median (range) IFN-γ levels (pg/mL) by coculture in pts with prior Ibr, Acala, or both was 6496.0 (424.0–20,000), 5972.5 (2502.0–18,000), or 7985.5 (2709.0–12,000), respectively. For pts with prior Ibr, Acala, or both, median (range) peak CAR T-cell levels (cells/µL) were 95.9 (0.4–2589.5), 13.7 (0.2–182.4), or 115.9 (17.2–1753.6), respectively. Overall, ORR rates were as follows: Ibr, 94%/65%; Acala, 80%/40%; and both, 100%/100%. The 12-mo survival rates in pts with prior Ibr, Acala, or both were 81%, 80%, or 100%, respectively. Grade ≥3 CRS/NEs occurred as follows: Ibr, 17%/31%; Acala, 10%/10%; and both, 0%/67%.

All subgroups drew clinical benefit from KTE-X19 treatment despite some pharmacological differences.

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What factors affect allogeneic bone marrow transplant decisions in acute leukaemia patients? Does unconscious bias play a role?

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Abstract Content: Haematopoietic stem cell transplantation (HSCT) is potentially curative for acute leukaemia and its usage should be based on a patient’s disease risk, their estimated transplant-related mortality (age and co-morbidities) and personal values. However, previous studies have revealed demographic disparities in its use, disproportionately affecting survival of under-served communities. In this study we examined whether receipt of HSCT in acute leukaemia patients was influenced by socio-demographic factors.

We used the patient record and team meeting minutes to retrospectively identify a population of 260 patients with acute myeloid leukaemia (AML) and acute lymphoid leukaemia (ALL), aged 21 to 79, presenting to the haematology unit at St Bartholomew’s Hospital in London between 2018 and 2019.

The relationships between transplantation and age, gender, ethnicity, and index of multiple deprivation (IMD) decile ranking were assessed using chi-squared analysis. IMD deciles were assigned using the UK Office of National Statistics 2019 data and patient postcodes. The IMD incorporates weighted data on income, employment, education, disability, crime and barriers to services.

A measure of baseline disease risk was calculated for each patient using their presenting cytogenetics and white cell count (WCC), and their co-morbidities were used to calculate a HCT-co-morbidity index (HCT-CI) score (high, intermediate or low for both scores).

Multivariate logistic regression was then used to examine relationships between transplantation and these factors.

Overall 112 patients (43%) received HSCT, whilst 148 (57%) did not. Age, HCT-CI group, baseline disease risk, and IMD decile ranking were significantly correlated with transplantation receipt on chi squared analysis ($P < 0.05$), whilst ethnicity and gender were not, regardless of whether we compared each ethnic group separately; White versus non-White; or White-British versus all others.

In multivariate analysis, factors independently associated with higher odds of HSCT were: higher baseline disease risk (OR 1.98, 95% CI 1.32–2.97, $P < 0.05$), decreased age (OR 1.05, 95% CI 1.03–1.07, $P < 0.05$), and lower IMD decile ranking (OR 1.24, 95%CI 1.11–1.38, $P < 0.05$). Patients living in more deprived areas had lower odds of receiving transplant.

Gender, HCT-CI and ethnicity were not significantly associated with differing odds of HSCT on regression analysis, regardless of ethnic sub-groupings.

Thirteen of 260 patients did not have a recorded risk score; four had no co-morbidity data and two had no postcode data. As these were <5% of patients, these ‘empty’ points were filled by frequency imputation.

The association between socio-economic status and reduced likelihood of transplantation is significant. This could be due to lower donor availability, although this seems unlikely given the lack of association between ethnicity and transplantation. A second possibility is that more patients refuse the offer of a transplant. A third possibility, potentially concerning, is of unconscious bias: physicians, of generally high socio-economic status, being more likely to offer transplant to people of a similar one. Interventions could include unconscious bias training and the inclusion of a lay-member on the leukaemia MDT to advocate for patients at risk of being excluded from transplant options on this basis. Other components of the IMD could also be contributing, including language, education and mental health.

Disclosure of Interest: None Declared
ALL, AML, MDS & bone marrow failure

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NGS cannot replace standard fragment analysis for the detection of FLT3-ITD

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Abstract Content: NGS is increasingly used to provide a full molecular profile for acute myeloid leukaemia (AML) patients at diagnosis. The growing number of genes that need to be screened to provide full diagnosis, risk stratification, and identify any appropriate targeted therapeutic interventions, mean conventional analysis methods may be insufficient. Commercial AML panels are available, but many laboratories use “in-house” panels; all cover the most common AML mutated genes, but the number of genes and the regions covered vary. Detection of internal tandem duplication (ITD) mutations within fms-like tyrosine kinase 3 (FLT3) and accurate determination of the allelic ratio (AR) is an important variable in determining patient risk and disease management strategy. FLT3-ITD mutations are reported to range from 3 to greater than 400 bp in length. The insertion point is varied with a majority occurring within exon 14, insertion of the ITD within the tyrosine kinase domain of exon 15 is reported to reduce RFS and OS compared to other insertion sites. The conventional assay for FLT3-ITD detection is PCR followed fragment size analysis. This assay allows the size of ITD insertion and the allelic ratio to be calculated but does not give information on the insertion point or sequence inserted. To gain the most prognostic insight information on ITD size, mutation burden and insertion point would be of value. For this reason, widely available short-read sequencing technologies have been mooted as a potential analysis method.

In the >1500 patients with FLT3-ITDs identified in the Cardiff Trial lab insertions ranged from 3 to 246 bp with the majority of insertions being between 21 and 30 bp in size. However, 5% of patients had an ITD of 102 bp or larger. Longer ITDs may cause issues and not be mapped to the reference genome resulting in the ITD not being called. Bioinformatics tools such as PINDEL, Genomon ITDetector, ITD seek have been developed to improve detection of insertions in NGS.

To investigate the ability of bioinformatic tools to detect larger FLT3-ITDs we performed targeted NGS using the Thunderbolt Myeloid panel (including FLT3) for library preparation followed by sequencing on an Illumina MiSeq on 16 patient samples with a range of ITD sizes up to 246 bp, one sample with a 6-bp deletion, and several samples with multiple ITDs. Following sequencing, the fastq files were mapped against the human hg19 reference genome using bwa-mem, generating BAM files for further explorations and analysis. Data were manually visualised using IGV before analysis using PINDEL and Genomon ITDetector, two tools optimised for the detection of insertions and ITDs.

Neither tool was able to detect all FLT3-ITDs. The 6-bp deletion was not identified by either. Genomon ITDetector did identify one 111bp ITD but no other ITDs longer than 69 bp were detected by either tool. The use of NGS alone would therefore result in ITDs being missed in patients with longer insertions. As it has been shown that patients with longer ITDs have an inferior prognosis it is crucial that they are able to receive the appropriate TKI therapy. Patients identified as FLT3-ITD now qualify for addition of midostaurin to intensive chemotherapy following diagnosis, and for gilteritinib at point of relapse following NICE approvals of both these agents. In summary, although NGS can be used for identification of other mutations, the standard PCR and fragment analysis should still be run to ensure the detection of all FLT3-ITDs.

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BSH2021-PO-002

Shedding smart light on the effectiveness of chemotherapy; using Raman spectroscopy and machine learning to differentiate the effects of Cytarabine toxicity and crosstalk of leukaemic and bone marrow stromal cells.

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Abstract Content: Mesenchymal stromal cells (MSC) protect leukaemic cells from drug-induced toxicity within the bone marrow niche, with increasing evidence of leukaemic impact on supportive stroma. The nucleoside analogue, cytarabine (ara-C), is a front-line agent for acute myeloid leukaemia (AML); yet over a third of patients do not show continued response to ara-C-based regimens. DNA damage by agents such as ara-C can persist in bone marrow-MSC, which remain of host-origin post-allogeneic stem cell transplant, affecting functionality and compounding poor clinical outcomes, including bone marrow failure and secondary malignancies. There is a clinical need for rapid evaluation of AML cell chemosensitivity, in order to avoid unnecessary toxicity from patient exposure to ineffective agents, with current methods for testing genotoxicity or chemosensitivity proving time-consuming and costly. Raman spectroscopy enables probing for chemical changes within cells, correlated to cell health, and may provide an alternative rapid approach to assess treated cell toxicity. This study aimed to develop a novel method, combining AML-MSC coculture, Raman spectroscopy and machine learning for the differentiation of cell types and drug handling responses, to evaluate toxicity and better understand chemoresistance mechanisms.

AML cells (HL-60/K562) and MSC (HS-5) were mono-cultured or co-cultured in a developed model, allowing bidirectional crosstalk, prior to treatment with physiological dose ara-C (25 μM, equivalent to 100–200 mg/m²) for 1 or 48 h. Genotoxicity modulation by AML-MSC co-culture was assessed in ara-C-treated cells by micromass cell culture, Raman spectroscopy and machine learning for the differentiation of cell types and drug handling responses, to evaluate toxicity and better understand chemoresistance mechanisms.

AML cells (HL-60/K562) and MSC (HS-5) were mono-cultured or co-cultured in a developed model, allowing bidirectional crosstalk, prior to treatment with physiological dose ara-C (25 μM, equivalent to 100–200 mg/m²) for 1 or 48 h. Genotoxicity modulation by AML-MSC co-culture was assessed in ara-C-treated cells by micromass cell culture, Raman spectroscopy and machine learning for the differentiation of cell types and drug handling responses, to evaluate toxicity and better understand chemoresistance mechanisms.
Genotoxicity was significantly decreased in HL-60 ($P = 0.0007$) and K562 ($P = 0.003$) following co-culture with HS-5, while significantly increased in HS-5 following co-culture with HL-60 ($P = 0.0214$) and K562 ($P = 0.0002$). Monocultured cells were successfully identified by Raman spectroscopy using a leave-one-out fivefold cross-validation paradigm and a radial basis function support vector machine with moderate accuracy of 0.77 ($/\pm/ 0.34$). HL-60 were reliably characterised (1.0), while HS-5 (0.8) and K562 (0.5) had lower identification accuracy. Identification of the difference between untreated and ara-C-treated K562 cells showed moderate accuracy of 0.72 ($/\pm/ 0.08$). Principle component analysis showed some clustering, however, with variance between different cell types.

This study shows the potential for use of confocal Raman microscopy as a method for delineation of chemotherapeutic and crosstalk effects in AML cells and MSC within the context of the tumour microenvironment. Rapid identification of chemosensitive and chemoresistant patients may aid clinicians in selecting appropriate treatment strategies. Interpretation of Raman spectra may also provide mechanistic information linked to cellular chemical changes occurring in co-culture and following drug exposure, elucidating chemoresistance mechanisms in the leukaemic microenvironment.

**Disclosure of Interest:** None Declared

**BSH2021-PO-003**

**Expression of CD47 and CALR in myeloproliferative neoplasms: potential new therapeutical targets**

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**Abstract Content:** Myeloproliferative neoplasms (MPN) are myeloid malignancies characterized by overproduction of mature blood cells, hyperplastic bone marrow and tendency to evolve into acute myeloid leukaemia. In solid tumours, calreticulin (CALR) overexpression produces a pro-phagocytic signal and is counteracted by concomitant expression of anti-phagocytic CD47, reflecting an apoptosis versus survival mechanism. Increases of both CALR and CD47 on the cell membrane have been observed in response to chemotherapy; however, their role in myeloid malignancies is poorly understood.

**Aims:** To investigate the expression and cellular localisation of CALR and CD47 in untreated and treated patients with essential thrombocythaemia (ET), polycythaemia vera (PV) myelofibrosis (MF), in comparison with healthy controls.

**Methods:** Mononuclear cells were collected by Ficoll separation, from peripheral blood of 30 MPN (8 PV, 16 ET, 6 MF); 18 MPN patients received cyto-reductive therapies (Hydroxyurea, Anagrelide orRuxolitinib); and 4 controls. Cells were fractionised into 4 compartments: membrane, cytoplasm, cytosol and nucleus. Proteins were extracted using TRIzol, with CALR and CD47 protein expression analysed by western blotting.

**Results:** Total CALR and CD47 protein expression increased in MPN samples compared with controls (CALR- 7.9 vs. 5.1; CD47- 2.7 vs. 2.2 fold, respectively). CD47 showed higher expression of its overall protein on MPN cell membranes when compared with CALR (22% vs. 13.9%). We observed a significant reduction of CALR expression in all MPN subtypes when patients were treated with cyto-reductive agents (ET- untreated 43.3% vs. treated 2%, PV- 3.6% vs. 2.2%, ET- 21% vs. 11%). Interestingly we have observed a significant increase in CD47 cell membrane expression after treatment in MF and PV (CD47 in MF-untreated 11.8% vs. treated 34.3%, PV-11.4% vs. 35.9%), suggesting an anti-phagocytic effect induced by cytotoxic drugs. In ET cell membranes, however, CD47 expression is reduced after cyto-reductive treatment (22% vs. 16.6%), suggesting instead a prophagocytic effect.

**Summary/Conclusion:** CD47, but not CALR, is overexpressed on the membrane of patients with MPN, suggesting a role for CD47 as a strong antiphagocytic signal responsible for immune survival in MPN. We observed a significant difference in CD47 expression across different MPN subtypes with a significant increase in CD47 expression in PV and MF but not ET. The use of anti-CD47 antibodies could represent a new strategy to enhance the treatment response in particular in PV and MF.

**Disclosure of Interest:** None Declared
LYMPHOMA, CLL and MYELOMA

BSH2021-004

HIV status does not impact on the outcome of patients with Burkitt lymphoma: a UK analysis

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1Oxford University Hospitals NHS Foundation Trust, Oxford, 2University College London Hospitals NHS Foundation Trust, 3National Centre for HIV malignancy, Chelsea and Westminster Hospital, London, 4Cambridge University Hospitals NHS Foundation Trust, Cambridge, 5Nottingham University Hospitals, Nottingham, 6King’s College Hospital, London, 7Division of Cancer Sciences, University of Manchester, 8St. Bartholomew’s and The Royal London NHS Trust, London, United Kingdom

Abstract Content: Burkitt lymphoma (BL) is a rare, aggressive, B-cell non-Hodgkin lymphoma, with a predilection for the bone marrow (BM) and the central nervous system (CNS). There are approximately 250 new cases per year in the UK.

We retrospectively reviewed the patient, disease and treatment characteristics of 254 adult patients with newly diagnosed sporadic and HIV-associated BL at eight UK centres between 2008 and 2020. Median age at diagnosis was 47 years (24% aged ≥ 60 years), with a predominance of men (75%). 48% patients had ECOG performance status (PS) 2–4. 84% presented with advanced stage disease. 15% and 40% had BM involvement, CNS involvement, respectively. Of the 254 patients, 113 (44%) were HIV positive. These patients were younger (median age 44 vs. 50 years, 10% aged ≥60 years vs. 35%), had poorer PS (66% ECOG 2-4 vs. 32%), and were more likely to present with advanced stage disease (91% vs. 78%), BM involvement (49% vs. 33%) and LDH x10 upper limit of normal (ULN) (26% vs. 14%) compared to HIV negative patients (Table 1).

With a median follow-up of 34 months, median progression-free survival (PFS) was not reached. Complete remission (CR) rate was 68%. The 2- and 5-year PFS were 67% [95% CI 60%-72%] and 64% [95% CI 58%-70%], respectively. 11% patients relapsed, all but one within 12 months (median time to relapse 6 months), and 11% had refractory disease. Age ≥60 years, ECOG PS ≥2, advanced stage, LDH ≥5x ULN, involvement of the CNS, BM and ≥1 extranodal site were associated with worse PFS on univariable analysis. Patients with HIV infection had similar 2- and 5-year PFS, CR and relapse rates compared to HIV-negative patients (2-year PFS 70% [95% CI 62%-77%] HIV negative, 62% [95% CI 53% >71%] HIV positive), despite more often presenting with adverse clinical features (poor PS, advanced stage). More HIV-positive patients, however, were refractory to initial therapy (16% vs. 6%) (Table 1).

There is growing interest in the use of the lower intensity infusional regimen DA-EPOCH-R, to reduce treatment-related morbidity and mortality, with several recent studies demonstrating its efficacy in BL. Only 8% of this cohort was treated with DA-EPOCH-R, while 85% were treated with CODOX-M/IVAC+/-R. The DA-EPOCH-R treated patients were older, and fewer were HIV positive, compared to those treated with CODOX-M/IVAC+/-R (median age 66 vs. 44 years, 71% vs. 15% aged ≥60 years), but the two groups were otherwise similar in clinical features, such as ECOG PS, stage, LDH, BM, CNS, and extranodal involvement. There was no difference in survival (2-year PFS 70% CODOX-M/IVAC+/-R, 66% DA-EPOCH-R), CR (72% CODOX-M/IVAC+/-R, 76% DA-EPOCH-R) and relapse rate (12% CODOX-M/IVAC+/-R, 10% DA-EPOCH-R)

Abstract Table:

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<td>LDH &gt;10x ULN, N (%)</td>
<td>44 (17)</td>
<td>16 (14)</td>
<td>28 (26)</td>
</tr>
<tr>
<td>First-line regimen, N (%)</td>
<td></td>
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<tr>
<td>CODOX-M/IVAC+/-R</td>
<td>216 (85)</td>
<td>111 (79)</td>
<td>105 (93)</td>
</tr>
<tr>
<td>DA-EPOCH-R</td>
<td>21 (8)</td>
<td>17 (12)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>R-CHOP and related</td>
<td>10 (4)</td>
<td>10 (7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Supportive care</td>
<td>7 (3)</td>
<td>3 (2)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Median follow-up (months)</td>
<td>34</td>
<td>35</td>
<td>26</td>
</tr>
<tr>
<td>PFS at 2 years (95% CI)</td>
<td>67% (60–72)</td>
<td>70% (62–77)</td>
<td>62% (53–71)</td>
</tr>
<tr>
<td>CR rate, N (%)</td>
<td>173 (68)</td>
<td>98 (70)</td>
<td>75 (66)</td>
</tr>
<tr>
<td>Relapse rate, N (%)</td>
<td>29 (11)</td>
<td>14 (10)</td>
<td>15 (13)</td>
</tr>
<tr>
<td>Refractory rate, N (%)</td>
<td>27 (11)</td>
<td>9 (6)</td>
<td>18 (16)</td>
</tr>
</tbody>
</table>

P-value – Fisher’s exact test comparing HIV-positive and HIV-negative subsets

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British Journal of Haematology, 2021, 193, (Suppl. 1), 46–76
MOGA is effective in patients with blood involvement (ORR < 0.0001) (< 15% CD4+CD26+ CD7− cells by flow cytometry). VORI at each blood classification level (B1 or B2) with 13.07 and 3.30 months for MOGA and VORI, respectively (P < 0.0001) (Table 1). Drug-related treatment-emergent adverse events (TEAEs) were similar in patients regardless of blood involvement and were lower for MOGA than VORI at each blood classification level (Table 1).

Conclusion: MOGA is effective in patients with blood involvement (B1 and B2), often showing a greater clinical benefit in patients in the B1 and B2 groups than those in the B0 group. Drug safety is similar between patients irrespective of level of blood involvement.

Funding: This study was supported by Kyowa Kirin.

Abstract Table:

Table 1. Investigator-assessed PFS, ORR and TTNT in the intent-to-treat set, and TEAEs by blood classification in safety analysis set.

<table>
<thead>
<tr>
<th>Blood Classification</th>
<th>PFS, median months (n)</th>
<th>ORR, % (n)</th>
<th>TTNT, median months (n)</th>
<th>Drug-related TEAEs (≥Grade 3), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VORI (N = 186)</td>
<td>MOGA (N = 186)</td>
<td></td>
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<tr>
<td>B0</td>
<td>4.37 (62)</td>
<td>4.7 (64)</td>
<td></td>
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<tr>
<td>P-value</td>
<td>0.9480</td>
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<tr>
<td>B1</td>
<td>2.53 (31)</td>
<td>8.63 (31)</td>
<td></td>
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<tr>
<td>P-value</td>
<td>0.0142</td>
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<td></td>
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<tr>
<td>B2</td>
<td>3.30 (93)</td>
<td>11.17 (91)</td>
<td></td>
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</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
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<tr>
<td>ORR, % (n)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>B0</td>
<td>6.5 (62)</td>
<td>15.6 (64)</td>
<td></td>
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<tr>
<td>P-value</td>
<td>0.0549</td>
<td></td>
<td></td>
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<tr>
<td>B1</td>
<td>6.5 (31)</td>
<td>25.8 (31)</td>
<td></td>
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<tr>
<td>P-value</td>
<td>0.2758</td>
<td></td>
<td></td>
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<tr>
<td>B2</td>
<td>3.2 (93)</td>
<td>37.4 (91)</td>
<td></td>
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<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
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<tr>
<td>TTNT, median months (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B0</td>
<td>4.13 (49)</td>
<td>6.77 (46)</td>
<td></td>
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<tr>
<td>P-value</td>
<td>0.0992</td>
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<td></td>
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<tr>
<td>B1 and B2</td>
<td>3.30 (107)</td>
<td>13.07 (70)</td>
<td></td>
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<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
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</table>

MOGA, mogamulizumab; TEAE, treatment-emergent adverse event; VORI, vorinostat.

BSH2021-PO-005
Efficacy and safety of mogamulizumab by patient blood classification
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Abstract Content: Introduction and Objectives: Cutaneous T-cell lymphomas (CTCLs) are rare, serious and potentially life-threatening forms of non-Hodgkin lymphoma that primarily present in skin. Mycosis fungoides (MF) and Sézary syndrome (SS) are the classic subtypes and together account for around two-thirds of all CTCLs. Initial methods of disease staging in MF and SS built upon the tumour-node-metastasis (TNM) classification using disease-specific findings. Blood classification (B0–2) was added to staging in 2007 based upon the recognition of blood involvement as a prognostic factor; increasing blood tumour burden has previously been linked with worsening of overall survival (OS) and disease-specific survival (DSS), and an increased risk of disease progression (RDP) (Agar 2010, Am Soc J Clin Oncol), although this is a subject of debate and further study. Patients with B1 disease have previously been shown to have a median survival of just 3.2 years, similar to B2 for which it was 3.1 years (Agar 2010, Am Soc J Clin Oncol). The addition of blood classification allows for more specific disease staging which may inform clinical management strategy, whilst also contributing to a better understanding of prognostic factors and treatment response in MF and SS. This post hoc analysis from the MAVORIC trial examined the efficacy and safety of mogamulizumab (MOGA) compared with vorinostat (VORI), stratified by patient blood classification.

Materials & Methods: MAVORIC (NCT01728805) was an open-label, phase 3 study where patients were randomized 1:1 to receive either intravenous MOGA 1.0 mg/kg weekly for the first 28 days, then on days 1 and 15 of subsequent cycles, or oral VORI 400 mg once daily. VORI patients who experienced disease progression or intolerable toxicity could cross over to MOGA. The primary end-point was investigator-assessed progression-free survival (PFS).

Results: In MAVORIC, investigator-assessed PFS was significantly longer for MOGA than VORI overall at 7.7 months and 3.1 months, respectively (P < 0.0001). When data were stratified by blood classification, PFS was found to be significantly superior for MOGA as compared to VORI in patients with both B1 and B2 disease (Table 1). Overall response rate (ORR) was also significantly greater for MOGA than VORI in MAVORIC at 28.0% and 4.8%, respectively (P < 0.0001), and was found in this analysis to be significantly greater for MOGA than VORI in those patients with B2 disease (Table 1). ORR for B1 was not significant, but showed a trend (25.8% vs. 6.5% for MOGA and VORI, respectively). Time-to-next-treatment (TTNT) was not significant for patients without blood involvement (B0), but was significantly greater for MOGA in patients with blood involvement (B1 or B2) with 13.07 and 3.30 months for MOGA and VORI, respectively (P < 0.0001) (Table 1). Drug-related treatment-emergent adverse events (TEAEs) were similar in patients regardless of blood involvement and were lower for MOGA than VORI at each blood classification level (Table 1).

Conclusion: MOGA is effective in patients with blood involvement (B1 and B2), often showing a greater clinical benefit in patients in the B1 and B2 groups than those in the B0 group. Drug safety is similar between patients irrespective of level of blood involvement.

Disclosure of Interest: None Declared
BSH2021-PO-006
Isolated 'drenching night' sweats – a critical review of 2 Week Wait primary care referral to Birmingham haematology clinics

Birmingham Heartlands, Good Hope and Solihull Hospitals, University Hospitals Birmingham

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Abstract Content: Drenching night sweats have been identified as a potential symptom of Non-Hodgkin’s and Hodgkin lymphoma. Night sweats are included in NICE guidance 2005 ‘Suspected Cancer: Recognition and Referral guidance’ referral trigger to haematology-oncology clinic. Whilst referral with night sweats should be in context of lymphadenopathy or splenomegaly, these are frequently made without co-existent parameters. Clinician decision to limit investigation can be difficult and may correlate with confidence of the practitioner.

We report data from all referrals to haematology from primary care to a large Haematology service via the 2-week wait (2WW) pathway over a 2-year period between 2018 and 2020. This retrospective audit critically evaluates predictive value of sweats for malignancy, resource allocation and outcome. Only 2WW referrals with sweats as the principal reason for referral and no clear pre-assessment probability of haematological malignancy were evaluated.

Of a total 1110 2WW referrals, 16% (184) were referred solely for ‘night sweats’. Referral pattern was consistent throughout the assessment period. 28 patients were not assessed in clinic (screened and returned to refer, non-attendance or patient cancellation) giving a total of 156 evaluable patients. 25% (38) had significant concomitant symptoms (minor weight loss, lethargy, pruritus etc.) and many were polysymptomatic. 31.4% (49) were taking at least one drug (e.g. psychotropic, antidepressant and adjunct therapy for chronic pain) known to induce hyperhidrosis. 70% (109) of referrals triggered radiological investigation; 62% (96) underwent CT, MRI or PET imaging.

None (0%) of the scans demonstrated haematological malignancy. Retrospective review has confirmed that none of those discharged without imaging have since re-presented with diagnosis of lymphoma following a period of follow-up (median 13 months). One scan (1%) detected incidental renal tumour.

Of 156 patients investigated, three underwent bone marrow biopsy and cytogenetics for monocytosis. These patients had confirmed CMML.

Of 40% of patients discharged at initial appointment no patients had been diagnosed with haematological malignancy at analysis.

Resource implications are considered; 2WW referrals for sweats account for 1 in 6 of all referrals and initial clinical evaluation required over 46 hours of clinic time per annum, equating to 56.5 hours of clinician time. Follow-up visits arranged for over half consume further clinic resource.

These data confirm the very poor predictive value of ‘drenching night’ sweats as an isolated symptom and this cohort have a negligible incidence of lymphoma. The inclusion of the parameter on a tick box form for 2WW primary care referral leads to inappropriate referral patterns.

There may also be associated harm in attributing potential significance to this symptom: 2WW referrals to cancer centres generate significant patient anxiety, and patients may be exposed to the risks of irradiation and scans which have low value.

BSH2021-PO-007
Clinical characteristics and molecular insights into pathogenesis of peripheral T-cell lymphoma: a SEER population-based study of 11,463 patients and biological analysis

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Abstract Content: PTCL are a rarely heterogeneous group of aggressive malignancies with dismal outcomes and limited treatment options. There is no upfront standard chemotherapy and optimal target due to the elusive pathogenesis of T cells. Uncovering the molecular mechanisms of T cell transformation to elucidate the peculiar clinicopathological features of PTCL will lead to the characterization of novel antitumor therapies. Hence, we obtained a large population of PTCL from SEER database to understand different clinical features of each entity and search for gene expression profiling from GEO datasets to explore the molecular pathogenesis of T cells.

In all, 16082 patients were identified of peripheral T-cell lymphoma, and 11463 eligible patients with the most common three subtypes of PTCL were analyzed, of whom 6008 (37.36%) were Peripheral T-cell lymphoma, Not Otherwise Specified (PTCL-NOS), 3578 (22.25%) were Anaplastic large cell lymphoma (ALCL) and 1877 (11.67%) were Angioimmunoblastic T-cell Lymphoma (AITL). We showed clinical characteristics and survival prognosis of PTCL by univariate and multivariate analysis, finally we found PTCL-NOS and AITL are inferior compared to ALCL. Next, we explored the gene expression profiling to identify the pathogenesis of PTCL and the molecular features of each subtype. We also analyzed the DEGs of each entity of PTCL and functional enrichment of DEGs showed the possible oncogenic pathways: PI3K-Akt signaling pathway, focal adhesion, complement and coagulation cascades, and hematopoietic cell lineage. We further conducted comparison among PTCL to understand the signaling pathway contributed to poor survival, thereby providing optional treatment for refractory PTCL. TCR signaling and PD-1 checkpoint pathway were activated in PTCL-NOS and AITL. Finally, we drew hub genes and its predicted functions in PTCL, and then we continued to find biomarkers related to survival, thereby offering potential targets for new treatment regimes. The common hub genes of PTCL were C3, GNG12, GNB4, CXCL13, CCL19, ADRA2A, CSAR1, GPSM2, NPY1R, PNOC, which were associated with positive regulation of leukocyte chemotaxis, positive regulation of MAP kinase activity, positive regulation of ERK1 and ERK2 cascade, Ras signaling pathway and PI3K-Akt signaling pathway. Intriguingly, we also found other important participants might
Acalabrutinib-related cardiac toxicities in patients with chronic lymphocytic leukaemia: a meta-analysis of randomised controlled trials

Thura Win Htut, Myat Min Han, Kyaw Zin Thein

Division of Hematology and Medical Oncology, Oregon Health and Science University/Knight Cancer Institute, Division of Hematology and Medical Oncology, Oregon Health and Science University/Knight Cancer Institute, Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, Texas, United States

Abstract Content: Chronic lymphocytic leukaemia (CLL) is the most common adult leukaemia, Acalabrutinib, a second generation and more selective Bruton’s tyrosine kinase inhibitor, was developed to potentiate efficacy while minimizing ibrutinib-associated side effects. We undertook a systematic review and meta-analysis of randomised controlled trials to determine the risks of acalabrutinib-related cardiac toxicities in patients with chronic lymphocytic leukaemia.

A comprehensive literature search was performed through MEDLINE, EMBASE databases and meeting abstracts up to 31 July 2020. Phase III RCTs utilizing acalabrutinib in patients with CLL were incorporated in the analysis. The Mantel–Haenszel (MH) method was used to estimate the pooled risk ratio (RR), and risk difference (RD) with 95% confidence interval (CI) for cardiac events, AF and hypertension. Heterogeneity was assessed with I² and Cochran’s Q statistic.

A total of 833 patients with CLL from two phase III RCTs [(n = 526) in ELEVATE TN, and (n = 307) in ASCEND] were eligible. Studies compared acalabrutinib + obinutuzumab versus acalabrutinib monotherapy versus obinutuzumab + chlorambucil in ELEVATE TN trial and acalabrutinib versus investigator’s choice chemotherapy (idelalisib + rituximab or bendamustine + rituximab) in ASCEND trial. Acalabrutinib was administered to 357 patients with treatment-naïve CLL in ELEVATE TN study and to 154 patients with relapsed or refractory CLL in the ASCEND study.

The I² statistic for heterogeneity was low, suggesting homogeneity among RCT and the fixed effects model was applied. The pooled RR and RD were calculated for any-grade and high-grade adverse effects in each subset of cardiac events, AF, and hypertension in both acalabrutinib and control groups. Any-grade cardiac events were reported in 13.7% of participants in acalabrutinib arm compared to 7.8% in the control arm with the RR of 1.75 (95% CI: 1.13–2.73; P = 0.01) and RD of 0.06 (95% CI: 0.02–0.10; P = 0.007). High-grade cardiac events were noted in 4.3% of patients treated with acalabrutinib and 3.1% of patients treated with non-acalabrutinib based regimens. The pooled RR was not significant at 1.43 (95% CI: 0.65–3.16; P = 0.37).

The incidence of any-grade AF was 4.1% in the acalabrutinib group compared to 1.9% in the control arm. There was a considerable trend towards statistical significance in the pooled RR (RR 2.56; 95%CI: 0.99–6.64; P = 0.05). High-grade AF was observed in 0.6% in the study group versus 0.6% in the control group and the RR was 1.10 (95% CI: 0.21–5.79; P = 0.91). Any-grade hypertension was reported in 5.1% of participants in acalabrutinib arm compared to 3.4% in the control arm. The pooled RR was observed at 1.40 (95% CI: 0.69–2.87; P = 0.35). Similarly, 2.3% of patients treated with acalabrutinib arm and 1.9% of patients treated with non-acalabrutinib-based regimens experienced high-grade hypertension and the RR was not significant at 1.13 (95% CI: 0.44–2.89; P = 0.80).

Our meta-analysis depicted that patients on acalabrutinib containing groups experienced higher risk of any-grade cardiac events with the RR of 1.75 and there was a considerable trend towards statistical significance in the risk of any-grade AF. There was no significant increase in the risk of all grades of hypertension and high-grade cardiac events or AF in the acalabrutinib group. Future prospective studies are necessary to determine the potential risk factors to develop cardiac toxicities in patients with CLL who received acalabrutinib.

Disclosure of Interest: None Declared

Abstract Table:

Table 1. Characteristics of the studies included in the meta-analysis

<table>
<thead>
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<th>Study</th>
<th>Author (Year)</th>
<th>Study type</th>
<th>Study phase</th>
<th>Type of cancer</th>
<th>Line of treatment</th>
<th>Number of patients and Treatment rendered</th>
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<tr>
<td>ELEVATE-TN</td>
<td>Sharman (2020)</td>
<td>Randomized, multicenter,</td>
<td>Phase 3</td>
<td>Treatment-naïve chronic lymphocytic</td>
<td>First line</td>
<td>178 Acalabrutinib</td>
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<tr>
<td></td>
<td></td>
<td>open-label study</td>
<td></td>
<td>leukaemia</td>
<td></td>
<td>+ Obinutuzumab</td>
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<tr>
<td>ASCEND</td>
<td>Ghia (2020)</td>
<td>Randomized, multicenter,</td>
<td>Phase 3</td>
<td>Relapsed or refractory chronic</td>
<td>Second line</td>
<td>154 Acalabrutinib</td>
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<tr>
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Mechanisms of acquired resistance in B-cell malignancies treated with the selective BTK inhibitor (BTKi), tirabrutinib

Ross Jackson1,2, Harriet Walter1, Sandrine Jayne1, Ryoho Kozaki2, Juliane Juergensmeier3, Chris Fegan4, Martin Dyer5

1 The Ernest and Helen Scott Haematological Research Institute, University of Leicester, Leicester, United Kingdom, 2 Ono Pharmaceutical Co. Ltd, Osaka, Japan, 3 Gilead Sciences, Inc, Foster City, United States, 4 University Hospital of Wales, Cardiff, 5 University of Leicester, Leicester, United Kingdom

Abstract Content: Acquired resistance to the non-selective covalent BTKi ibrutinib is often mediated either by mutation of BTKC481 or the downstream kinase PLCG2. Here, we investigated the causes of resistance in chronic lymphocytic leukaemia (CLL) patients receiving the selective BTKi tirabrutinib as part of phase I/II trial (NCT02457958), and in cell line models of activated B-cell like diffuse large B-cell lymphoma (ABC-DLBCL).

Sequential samples were used to identify mutational profiles by whole exome sequencing (WES) and changes in gene expression by global mRNA sequencing (RNA-Seq). Only one patient acquired the BTKC481S mutation. 4 patients developed other, previously reported BTK ATP binding and gatekeeper mutations (L582W and T474I) (Maddock et al, 2015), suggesting different mutational patterns following tirabrutinib resistance. 4 patients did not exhibit BTK or PLCG2 mutations (at a depth of 100X coverage). Global mRNA sequencing revealed shared gene expression changes between patients following relapse, particularly in chemokine receptor signalling (CCL3, CXCL2, CXCL8, CXCL10, CXCL12, and CXCL13). Analysis of altered pathways, inferred by gene set enrichment analysis, did not show a significant enrichment of BCR or NFkB signalling gene sets.

To further characterise mechanisms of resistance, an acquired resistance cell line model of ABC-DLBCL was generated. WES studies from the resistant cell line showed a PLCG2R55W mutation but no BTK mutation. Comparative immunophenotypic and RNA-Seq analyses in parental and resistant cell line showed, a 2.1 and 2.8 log2 fold increase in expression of surface immunoglobulin and BCR positive regulator CD19 respectively, and concomitant downregulation of negative regulators CD5 and CD22 by log2 fold -12.5 and -1.7, respectively, indicating a highly activated BCR signalling pathway. CD5 was down-regulated at the transcriptional level but all other changes were non-transcriptional.

Upregulation of BCR signalling was accompanied by increased phosphorylation of BCR proteins CD19, SYK, BLNK, ERK, and AKT. This was in the absence of changes to total protein (except in the case of SYK which showed mRNA and protein upregulation). Identical effects were observed with acute tirabrutinib treatment in parental cell lines, suggesting a rapid pathway reactivation mediating resistance acutely.

Pathway analysis of RNASeq showed an enrichment of BCR signalling and NFkB pathway gene sets and marked decrease in gene sets associated with oxidative phosphorylation (OXPHOS). Metabolic analysis by Seahorse confirmed a 50% decrease in the amount of OXPHOS in tirabrutinib-resistant cells. In addition, chemokine receptor signalling genes (CCL3, CCL4, CXCL13, and CXCL10) were significantly differentially expressed, similar to the observations from CLL cases.

Ibrutinib inhibits migration of CLL cells towards chemokines such as CXCL12 and 15 and prevents secretion of BCR-dependent chemokines CCL3 and CCL4, suggesting that treatment inhibits homing and retention of malignant cells in their survival niches (de Gorter et al 2007, Ponader 2012), thus suggesting resistance may be mediated via alterations of cell migration and localisation (although the roles in DLBCL cell line models remain unclear).

Overall, these data show that resistance to tirabrutinib is mediated by rapid and profound changes in gene expression as well as non-transcriptional mechanisms affecting BCR and chemokine receptor signalling as well as metabolic changes.

Disclosure of Interest: R. Jackson: None Declared, H. Walter: None Declared, S. Jayne: None Declared, R. Kozaki: None Declared, J. Juergensmeier: None Declared, C. Fegan: None Declared, M. Dyer Conflict with: Funding from Gilead Sciences

Impact of COVID-19 on peripheral blood stem cell mobilisation for myeloma patients – A single centre experience at University College London Hospitals

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1 Haematology, University College London Hospitals NHS Foundation Trust, 2 Haematology, Cancer Institute, University College London, 3 Cancer Research UK and UCL Cancer Trials Centre, University College London, 4 Wolfson Cellular Therapy Unit, NIHR/UCLH Clinical Research Facility, University College London Hospitals NHS Foundation Trust, London, United Kingdom

Abstract Content: Due to the COVID-19 pandemic, NICE issued rapid guidance that advised using granulocyte colony stimulating factor (G-CSF) only (G-only) mobilisation rather than cyclophosphamide and G-CSF (cyclo-G) for multiple myeloma (MM) patients considered transplant eligible. This guidance aimed to reduce hospital visits and potential exposure to COVID-19. Cyclo-G is known to improve CD34+ yield but is associated with a prolonged collection process and risks of febrile neutropenia. After a short-term suspension in peripheral blood stem cell harvest (PBSCH) at our centre during the March 2020 lockdown, we followed NICE guidance upon PBSCH resumption in June 2020. We retrospectively compared the efficacy, toxicity and resource utilisation between G-only (n = 39; June–November 2020) and cyclo-G (n = 39; November 2019–March 2020) mobilisation strategies in MM patients. The minimum CD34+ target is ≥2 × 10^6/kg though a ≥4 × 10^6 CD34+/kg target is used to support 2 autografts, with plerixafor given either pre-emptively or as rescue treatment. CFU-GM doses of ≥20 × 10^6/kg permits transplantation locally when CD34+ thresholds are not met.

All cyclo-G patients had newly diagnosed MM (NDMM); 38 G-only patients had NDMM and 1 had 1st relapse MM after a 6-year remission. More G-only patients received lenalidomide, with 10/39 (25.7%) switched from a bortezomib-based doublet/triplet to a lenalidomide-based, oral regimen to reduce hospital attendances for parenteral therapy. Treatment changes within the cyclo-G cohort occurred due to toxicity, high-risk MM or need for salvage induction (2/39 [5.6%]). 51.2% G-only and 74.7% cyclo-G patients achieved ≥VGPR (P = 0.03); ≥40% had <5% bone marrow infiltration close to PBSCH mobilisation in both groups. All cyclo-G PBSCH achieved ≥2 × 10^6 CD34+/kg; 36/39 (92.3%) of G-only patients reached this minimum target, but 2 of the 3 with ≤2 × 10^6 CD34+/kg had enough CFU-GM for 1 autograft. Median CD34+ count was 3.3 × 10^6/kg with G-only versus 7.2 × 10^6/kg with cyclo-G (P < 0.001). The difference remained statistically significant after adjusting for disease response, plasma cell bone marrow infiltration, treatment duration and pre-PBSCH treatment-free period (95% CI —64% to -31%, P < 0.001). Cyclo-G always yielded ≥4 × 10^6 CD34+/kg PBSCs when required versus 9/13 (60%) with G-only. Also, 19/39 G-only patients (vs. 4/39 cyclo-G patients) needed ≥2 apheresis days with 5 having a central venous catheter (CVC) in situ, consequently needing an
overnight admission. Plerixafor was used in 7 G-only patients, given pre-emptively in 6/36 (17%) (vs. 1/39 [3%] with cycle-G) due to low peripheral blood CD34+ counts on the expected day of harvest. There was no febrile neutropenia in our small cycle-G cohort and our limited series was unable to identify poor mobilisers.

Our data imply that G-only prime led to higher plerixafor use, increased mobilisation failure, less likelihood to achieve PBSC targets and increased apheresis days which occasionally results in hospital admission to manage indwelling CVCs. Given the 40% failure rate in achieving ≥4 × 10^6 CD34+/kg with G-only prime, cyclo-G mobilisation should be considered in patients needing ≥4 × 10^6 CD34+/kg, alongside others predicted to mobilise poorly (extended lenalidomide treatment ≥6 cycles), previous PBSC failure and use of pelvic radiotherapy. We suggest that current national guidance adapts to allow for cyclo-G prime whenever it outweighs the risk of additional chemotherapy exposure.

Abstract Table: Summary of PBSCH Data

<table>
<thead>
<tr>
<th>G-only</th>
<th>Cyclo-G</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (years; range)</td>
<td>60 (29–72)</td>
<td>60 (38–73)</td>
</tr>
<tr>
<td>Male (n; %)</td>
<td>24 (61.5)</td>
<td>20 (51.3)</td>
</tr>
<tr>
<td>Female (n; %)</td>
<td>15 (38.5)</td>
<td>19 (48.7)</td>
</tr>
<tr>
<td>Disease Characteristics: ISS stage (n; %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISS-I</td>
<td>9 (23.1)</td>
<td>13 (33.3)</td>
</tr>
<tr>
<td>ISS-II</td>
<td>15 (38.5)</td>
<td>20 (51.3)</td>
</tr>
<tr>
<td>ISS-III</td>
<td>7 (17.9)</td>
<td>4 (10.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (20.5)</td>
<td>10 (25.6)</td>
</tr>
<tr>
<td>Disease response at PBSC mobilisation (n; %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR/sCR</td>
<td>10 (25.6)</td>
<td>7 (18)</td>
</tr>
<tr>
<td>VGPR</td>
<td>10 (25.6)</td>
<td>22 (56.4)</td>
</tr>
<tr>
<td>&lt;VGPR</td>
<td>19 (48.7)</td>
<td>10 (25.6)</td>
</tr>
<tr>
<td>Median treatment-free period pre-PBSCH (days; range)</td>
<td>35 (5–226)</td>
<td>38 (5–331)</td>
</tr>
</tbody>
</table>

Stem Cell Collection Outcomes

<table>
<thead>
<tr>
<th>G-only</th>
<th>Cyclo-G</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of CD34+/kg (10^6/kg median; range)</td>
<td>3.3 (0–11.2)</td>
<td>7.2 (2.3–28.3)</td>
</tr>
<tr>
<td>Number of GM CFC (10^6/kg median; range)</td>
<td>114.7</td>
<td>142</td>
</tr>
<tr>
<td>Duration of PBSCH (days median; range)</td>
<td>2 (1–3)</td>
<td>1 (1–3)</td>
</tr>
<tr>
<td>Plerixafor use (n; %)</td>
<td>7 (17.9)</td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Successful PBSCH (n; %)</td>
<td>36 (92.3)</td>
<td>39 (100)</td>
</tr>
<tr>
<td>Target Yield ≥2 × 10^6 CD34+/kg (n)</td>
<td>24</td>
<td>36</td>
</tr>
<tr>
<td>Achieved (n; %)</td>
<td>21 (87.5)</td>
<td>36 (100)</td>
</tr>
<tr>
<td>Not achieved (n; %)</td>
<td>3 (12.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Target Yield ≥4 × 10^6 CD34+/kg (n)</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>Achieved (n; %)</td>
<td>9 (60)</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Not achieved (n; %)</td>
<td>6 (40)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

1Of the 6 patients who had ≤4 × 10^6 CD34+/kg collected; 3 had sufficient cells to allow for 2 autografts based on an adequate GM CFC dose. PBSCH, peripheral blood stem cell harvest; ISS, International Staging System; CR, Complete Response; sCR, Stringent Complete Response; VGPR, Very Good Partial Response; GM CFC, granulocyte/macrophage colony-forming cells.

Disclosure of Interest: None Declared

BSH2021-PO-011

Recovery of ocular events with longer-term follow-up in the DREAMM-2 study of single-agent belantamab mafodotin in patients with relapsed or refractory multiple myeloma

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1Emory University, Winship Cancer Institute, 2Emory Eye Center, Emory University, Atlanta, 3University of Maryland School of Medicine, 4Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, 5University of Wisconsin, Carbone Cancer Center, Madison, 6Huntsman Cancer Institute, University of Utah, 7Moran Eye Center, University of Utah, Salt Lake City, United States, 8University College London Hospitals, NHS Foundation Trust, 9NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, United Kingdom, 10GlaxoSmithKline, Upper Providence, 11Massachusetts Eye and Ear, Harvard Medical School, Boston, 12University of Chicago Medical Center, Chicago, United States

Abstract Content: Belantamab mafodotin (belama; GS2857916) is a B-cell maturation antigen–targeting, antibody–drug conjugate (ADC) containing monomethyl auristatin F (MMAF). In DREAMM-2 (NCT03525678), single-agent belama demonstrated deep and durable responses with a manageable safety profile in heavily pre-treated relapsed/refractory multiple myeloma patients (Lonal ASCO 2020, Poster 436). Similar to other MMAF-containing ADCs, ocular events were common (Farooq et al. Ophthalm Ther 2020), including keratopathy (microcyst-like epithelial changes [MECs]: an eye exam finding with/without symptoms), best-corrected visual acuity (BCVA) changes, and symptoms (blurred vision, dry eye).

In DREAMM-2, eye exams (corneal exam and BCVA change from baseline: Snellen visual acuity [VA]) were conducted at baseline and prior to each dose in patients receiving belama (2.5 or 3.4 mg/kg every 3 weeks). Corneal events were graded per the Keratopathy and Visual Acuity (KVA) scale that combines corneal exam findings and BCVA changes from baseline. Events were managed using dose delay/modification guided by KVA grade. Patients were followed until recovery (Grade 1 exam findings/no exam findings, and ≤1-line decline in VA vs. baseline). A change to a BCVA ≤20/50 in the better-seeing eye constituted a clinically meaningful VA decrease. Recovery was defined as BCVA improvement to >20/50. We report ocular event outcomes for patients receiving belama 2.5 mg/kg (the approved dose) from a 13-month follow-up post hoc analysis.

Overall, 72% (68/95) of patients had a treatment-related eye exam finding of keratopathy (MECs). Fewer patients (56% [53/95]) had symptoms and/or a ≥2-line BCVA decline (better-seeing eye). Treatment discontinuations due to ocular events were rare (3% [3/95] total; 1% [1/95] each due to keratopathy [MECs], blurred vision, and reduced BCVA [Farooq Ophthalm Ther 2020]).

In patients with keratopathy (MEC) events Grade ≥2, 48% (29/60) had ≥1 event. The first event recovered in 77% (46/60). At last follow-up, 48% (29/60) recovered from their most recent event. In patients with unrecovered events, 45% (14/31) are receiving treatment or in follow-up. Of the remaining 55% (17/31), 9 died, 4 withdrew, and 4 were lost to follow-up. 84% (37/44) of patients with Grade 3/4 events were improving or had recovered.

Seventeen patients (18%) had a clinically meaningful BCVA decline, with no reports of complete permanent vision loss. Of these, 76% (13/17) had 1 event and 24% (4/17) had 2 events (none had ≥2
events). 82% (14/17) recovered from their first event and 82% (14/17) had recovery at last follow-up. Of the patients with unrecovered events, 1 patient is receiving treatment and 2 patients are no longer in follow-up (1 died due to disease progression; 1 withdrew).

Though keratopathy (MECs) were frequently observed, most patients did not experience a clinically meaningful BCVA decline, and events rarely led to treatment discontinuation. The first keratopathy (MEC) event or clinically meaningful BCVA decline recovered in most patients with events. Patients are being followed for recovery, and it is anticipated these events will recover over time.

**Funding:** GSK (205678); drug linker technology licensed from Seagen, Inc.; mAb produced using POTELLIGENT Technology licensed from BioWa.

**Encore statement:** Previously presented as Poster 3224 at the American Society of Hematology Annual Meeting, 5–8 December 2020; submitted with permission and on behalf of the original authors.

Transplantation, Gene & Cellular Immunotherapies

BSH2021-PO-012
Adrenal insufficiency following prolonged exogenous steroid treatment for graft versus host disease
Henry Simons¹, Ann Tivey¹², Ahmad Abdullah¹, John Murray¹, Claire Higham¹
¹The Christie NHS Foundation Trust, ²The University of Manchester, Manchester, United Kingdom

Abstract Content: Nearly half of all patients who have undergone allogeneic stem-cell transplantation will develop graft versus host disease (GvHD) necessitating long term use of exogenous steroids. Patients taking prolonged courses greater than 5 mg prednisolone daily (or equivalent) are at risk of adrenal insufficiency (AI) due to hypothalamic-pituitary axis suppression. A recent National Patient Safety Alert highlighted omission of steroids in patients with AI risks adrenal crisis or death. No guidelines exist for assessing adrenal function when exogenous steroids are stopped at completion of GvHD treatment.

Between January 2018 and January 2020 all patients at a tertiary haematology centre completing long term steroid therapy for GvHD underwent a short synacthen test (SST). 250 micrograms of SynACTHen was administered intramuscularly. Serum cortisol was measured at 0, 30 and 60 minutes (Roche Immunoassay). Oral steroids were held prior to testing (48 hours for prednisolone, 18 hours for hydrocortisone) with the exception of two patients taking budesonide. 30 minute cortisol >440 nmol/l was considered an adequate response or ‘pass’ (local threshold), Time 0 cortisol <150 nmol/l was considered a low baseline. Data was extracted from electronic patient records for demographic, laboratory and clinical features. The relationship between time from GvHD diagnosis (a surrogate for steroid exposure) to SST and baseline/30 minute cortisol was assessed using Pearson’s correlation coefficient. Institutional approval for audit purposes was obtained.

Thirty patients, median age 51 years (range 18–72) were included. 27% (8/30) of patients failed at least one SST indicating AI. These patients were all advised to continue physiological steroid replacement. Six patients had low baseline cortisol (<150), of which three passed the SST. In these, three patients steroids were not continued although one was advised to take supplemental hydrocortisone should they become unwell. Four patients had two SSTs during the audit period. One passed an initial SST but resumed steroids for GvHD and failed a subsequent SST. One failed an initial SST but following weaning passed an SST 9 months later and was able to stop steroids. No correlation was observed between time from GvHD diagnosis and baseline cortisol (r = −0.03, P = 0.89) or SST result (r = −0.10, P = 0.60). Descriptive analysis of demographic, clinical and laboratory features did not suggest any predictive factors for SST result (table 1). Both patients who continued budesonide passed the SST.

One in four patients in our cohort had AI at cessation of steroids. Identifying these patients, ensuring physiological steroid replacement and patient education is critical to prevent morbidity and mortality from AI. There were no identified factors predictive of inadequate SST response. In line with national guidance all patients receiving steroid therapy for GvHD should receive steroid emergency cards and education. Patients identified to have AI at steroid cessation need endocrinology referral for long term monitoring. As highlighted, it is possible for patients who fail an initial SST to subsequently successfully weaned. At this centre SSTs are now performed routinely at cessation of steroid therapy with support for testing and follow-up from an endocrinology service. Given the high incidence of AI in our cohort and lack of predictive factors, we recommend SSTs be considered for all patients receiving prolonged steroids for GvHD.

Abstract Table:

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 30)</th>
<th>Passed (22)</th>
<th>Failed (8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>14 (47%)</td>
<td>12 (55%)</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>Median Age (years)</td>
<td>51</td>
<td>50</td>
<td>51</td>
</tr>
<tr>
<td>Mean systolic BP (mmHg)</td>
<td>125</td>
<td>124</td>
<td>128</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.3</td>
<td>26.3</td>
<td>26.3</td>
</tr>
<tr>
<td>Unexplained weight loss</td>
<td>6 (20%)</td>
<td>4 (13%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Hyponatraemia</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hyperkalaemia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

BSH2021-PO-013
Impact of SARS-CoV-2 (COVID 19 infection) & MDS in the UK: results of a patient survey to document shielding uptake and patient experience following changes to consultation practice.
Pramila Krishnamurthy¹, John Chadwick², Sophie Wintrich², Janet Hayden³, Michelle Kenyon³, Austin KULASEKARARAJ³, Dominic Culligan³, David Bowen³, Sally Killick³ and UK NCRI MDS subgroup
¹Haematology, King’s College Hospital, London, ²Blackpool Teaching Hospitals, Blackpool, ³UK MDS Patient Support Group, King’s College Hospital, London, ³Aberdeen Royal Infirmary, Aberdeen, ³Leeds Teaching Hospitals, Leeds, ³University Hospitals Dorset, Royal Bournemouth Hospital, Bournemouth, United Kingdom

Abstract Content: From March 2020 patients with myelodysplastic syndrome (MDS) in the UK were categorised as clinically extremely vulnerable due to predicted high mortality risk from SARS-CoV-2 coronavirus infection and advised to shield (isolate stringently from others)¹. Changes to management were advised, including stratification of consultation type (remote vs. face-to-face) according to disease severity, to assist patients to shield².

To assess the impact of these changes on the MDS community, we devised a 120-question survey, available to complete online/via hard copy by patients/caregivers. The survey went live in September 2020; by December 2020, 339 responses were received, of which 291 were sufficiently complete for analysis.

Table 1 outlines our findings. 56% of responders were male (44% female); median age range was 61-80 years. Patients had MDS (n = 239, 82%), AML (n = 23, 8%), CMML (n = 14, 5%) or another bone marrow failure disorder (n = 15, 5%). Median time since diagnosis was 2–5 years. Patients were distributed amongst the Revised International Prognostic Scoring System (IPSS-R) categories; very low/low (93, 39%), intermediate (65, 27%) or high/very high risk (34, 14%) IPSS-R; with 43 (18%) unaware of their category. There were 283 replies regarding current treatment; 105 (37%) were on watch and wait, 178 (63%) had received treatment (growth factors/ transfusions/chemotherapy/allogeneic stem cell transplantation).
A total of 234 (80%) respondents had been informed to shield by letter/text; 253 (87%) stated they understood the rationale. Those unaware of their IPSS-R group were least likely to have received a text/letter advising shielding compared with those who knew their IPSS-R group or patients with AML/CMML/other diagnoses (66% vs. 80% vs. 95%, \( P < 0.05 \)). Patients within this group were also proportionately more likely to respond “don’t know” when asked their risk of contracting COVID-19 compared with those who knew their IPSS-R risk/had another diagnosis (32% vs. 9% vs. 4%; \( P < 0.05 \)).

A total of 265 (91%) patients reported 351 haematology consults during this period (in person, \( n = 112 \); telephone, \( n = 225 \); video, \( n = 14 \)). Patients more frequently reported high levels of satisfaction (score \( \geq 7/10 \)) with face-to-face (94/112, 84%) consultation than with remote (153/239, 64%, \( P < 0.05 \)). Patients with low/very low risk MDS IPSS-R category reported highest disparity in satisfaction between consultation type: 93% for face-to-face vs. 58% for remote, respectively (\( P < 0.05 \)).

Conclusion: We observed that 20% of respondents had not received a text/letter advising shielding; 13% of respondents were uncertain why shielding was needed. The 18% of patients unaware of their IPSS-R risk were more often unclear about their susceptibility to SARS-CoV-2. These observations hint at insufficient education of some patients about MDS and its risks, as previously noted. Reasons for shielding list omission could include deficiencies in disease coding or failed recognition by healthcare providers that all such patients needed to shield. Improved patient education and communication of diagnoses may help overcome these issues. Remote consultation was unsatisfactory in 36%, particularly low-risk MDS patients, whom clinicians may consider most amenable to remote review due to disease stability. Our findings support virtual consultation for MDS patients, but a greater understanding of barriers to patient satisfaction, through further detailed discussion with patient/caregiver representatives is needed.

Abstract Table:

Table 1. Summary of responses to the UK MDS COVID-19 questionnaire (total 291 suitable for analysis)

<table>
<thead>
<tr>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age range</td>
</tr>
<tr>
<td>21–40</td>
</tr>
<tr>
<td>41–60</td>
</tr>
<tr>
<td>61–80</td>
</tr>
<tr>
<td>81 or older</td>
</tr>
<tr>
<td>Respondent</td>
</tr>
<tr>
<td>Caregiver</td>
</tr>
<tr>
<td>Patient</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>Myelodysplastic syndrome (MDS)</td>
</tr>
<tr>
<td>Chronic myelomonocytic leukaemia (CMML)</td>
</tr>
<tr>
<td>Acute Myeloid Leukaemia (AML)</td>
</tr>
<tr>
<td>Other bone marrow failure (BMF) disorder*</td>
</tr>
<tr>
<td>Time since diagnosis</td>
</tr>
<tr>
<td>&lt;1 year</td>
</tr>
<tr>
<td>2–5 years</td>
</tr>
<tr>
<td>6–10 years</td>
</tr>
<tr>
<td>&gt;10 years</td>
</tr>
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</table>

Table . (Continued)

<table>
<thead>
<tr>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treating centre</td>
</tr>
<tr>
<td>MDS Centre of Excellency</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Knowledge of IPSS-R risk group</td>
</tr>
<tr>
<td>Very low/low</td>
</tr>
<tr>
<td>Intermediate</td>
</tr>
<tr>
<td>High/very high</td>
</tr>
<tr>
<td>Don’t know what this is/never been told</td>
</tr>
<tr>
<td>Awaiting results?</td>
</tr>
<tr>
<td>Watch and Wait</td>
</tr>
<tr>
<td>Active treatment</td>
</tr>
<tr>
<td>Awaiting Results</td>
</tr>
<tr>
<td>Received a letter/text advising shielding</td>
</tr>
<tr>
<td>Understood the need for shielding</td>
</tr>
<tr>
<td>Adequately able to access information about shielding</td>
</tr>
<tr>
<td>Shielding breakdown</td>
</tr>
<tr>
<td>IPSS-R risk known</td>
</tr>
<tr>
<td>( n = 192 )</td>
</tr>
<tr>
<td>IPSS-R risk unknown/awaited</td>
</tr>
<tr>
<td>( n = 47 )</td>
</tr>
<tr>
<td>AML/CMML/Other BMF</td>
</tr>
<tr>
<td>( n = 52 )</td>
</tr>
<tr>
<td>Perceived risk of contracting COVID-19 infection</td>
</tr>
<tr>
<td>“Low/medium/high”</td>
</tr>
<tr>
<td>“Don’t know”</td>
</tr>
<tr>
<td>Distribution of responses within subgroups: IPSS-R risk known</td>
</tr>
<tr>
<td>( n = 192 )</td>
</tr>
<tr>
<td>IPSS-R risk unknown/awaited</td>
</tr>
<tr>
<td>( n = 47 )</td>
</tr>
<tr>
<td>AML/CMML/Other BMF</td>
</tr>
<tr>
<td>( n = 52 )</td>
</tr>
<tr>
<td>Types of consultations during survey period (episodes)</td>
</tr>
<tr>
<td>Face-to-face</td>
</tr>
<tr>
<td>Telephone</td>
</tr>
<tr>
<td>Video</td>
</tr>
<tr>
<td>Satisfaction with consultation type</td>
</tr>
<tr>
<td>Face-to-face</td>
</tr>
<tr>
<td>Very low/low risk</td>
</tr>
<tr>
<td>Intermediate risk</td>
</tr>
<tr>
<td>High/very high risk</td>
</tr>
<tr>
<td>Risk unknown</td>
</tr>
<tr>
<td>AML/CMML</td>
</tr>
<tr>
<td>Other BMF</td>
</tr>
</tbody>
</table>
| Telephone/video                                      | Satisfied/total number of episodes:
| Very low/low risk                                     | 46/79 (58%) |
| Intermediate risk                                     | 33/48 (69%) |
| High/very high risk                                   | 20/29 (64%) |
| Risk unknown                                          | 21/38 (55%) |
| AML/CMML                                             | 27/34 (79%) |
| Other BMF                                             | 6/13 (46%) |
Patients self-classified as “Other bone marrow failure disorders” later specified as MDS ($n = 8$), MDS/myeloproliferative overlap syndrome ($n = 3$), blood disorder ($n = 3$), clonal cytopenia of uncertain significance ($n = 1$).

MDS Centres of Excellence. Haematology units within the UK where members of the UK MDS Forum are based.

Treatment included growth factor or transfusion support, iron chelation, immunosuppression and chemotherapy.

scored out of 10 (poor $= 1$, average $= 5$, excellent $= 10$) – consults scoring $\geq 7$ were assessed as satisfactory.


Disclosure of Interest: P. Krishnamurthy: None Declared, J. Chadwick: None Declared, S. Wintrich: None Declared, J. Hayden: None Declared, M. Kenyon: None Declared, A. KULASEKARARAJ: None Declared, D. Culligan: None Declared, D. Bowen: None Declared, S. Killick Conflict with: Jazz, Novartis, BMS, Takeda.
General Haematology Including ITP and Myeloproliferative Disorders

BSH2021-PO-014
Avapritinib induces responses in patients with advanced systemic mastocytosis, regardless of prior midostaurin therapy
Deepti Radia1,2, Mark W. Drummond2, Jason Gotlib1, Tracy I. George1, Albert T. Querry5, Elliot Winton6, Hui-Min Lin1, Brenton G. Mar2, Michael W. Deininger9, Daniel J. DeAngelo2
1Guy’s & St Thomas’ NHS Foundation Trust, London, 2Beatton Cancer Centre, Glasgow, United Kingdom, 3Stanford Cancer Institute/Stanford University School of Medicine, Stanford, 4ARUP Laboratories, University of Utah, Salt Lake City, 5University of Michigan, Ann Arbor, 6Winship Cancer Institute of Emory University, Atlanta, 7Blueprint Medicines Corporation, Cambridge, 8The University of Utah, Huntsman Cancer Institute, Salt Lake City, 9Dana-Farber Cancer Institute, Boston, United States

Abstract Content: Systemic mastocytosis (SM) is a rare, clonal mast cell (MC) neoplasm driven by KIT D816V mutation in ~95% of patients. Advanced SM (AdvSM) has a poor prognosis with limited and sub-optimal treatment options. EXPLORER is a phase 1, two-part (dose escalation and dose expansion phases) study of avapritinib, a selective, potent KIT D816V inhibitor, in patients with AdvSM. Primary objectives were to determine the maximum tolerated dose (MTD), recommended phase 2 dose, and safety. Secondary objective was efficacy, per centrally reviewed overall response rate (ORR) by modified International Working Group (IWG)-Myeloproliferative Neoplasms Research and Treatment and European Competence Network on Mastocytosis criteria and defined as complete remission (CR) + CR with partial recovery of peripheral blood counts (CRh) + partial remission (PR) + clinical improvement (CI) lasting ≥12 weeks. Patient-reported outcomes were studied in the dose expansion phase using the AdvSM-Symptom Assessment Form (AdvSM-SAF). As of 30 August 2019, 80 patients were enrolled: seven aggressive SM (ASM), 44 SM with associated hematologic neoplasm (SM-AHN), 11 MC leukaemia (MCL), and 16 indolent SM or smoldering SM. One patient had a non-SM diagnosis, and one had diagnosis pending central adjudication. In the dose escalation phase, 32 patients were enrolled and received doses from 30 to 400 mg orally once daily (QD); MTD was not reached. Forty-eight patients were enrolled in two dose expansion cohorts: 200 mg and 300 mg QD. Of 62 enrolled AdvSM patients, 48 were ORR-evaluable and 14 were not evaluable (insufficient follow-up, n = 5; no evaluable IWG organ-damage, n = 9). Patients receiving 200 mg and 300 mg had similar efficacy and time to response. Centrally reviewed ORR and best responses in all evaluable patients, by AdvSM subtype and by prior midostaurin exposure, are shown in the table. Median duration of response and overall survival were not reached. AdvSM-SAF scores were significantly improved by cycle 3 (P = 0.0037) and sustained at cycle 11 (P = 0.015). All patients exhibited ≥50% reduction in serum tryptase, marrow MC aggregates were eliminated in 85% of patients and in 92%, KIT D816V allele fraction decreased by ≥50%, reaching <1% in 68% of patients. Most frequent adverse events (AEs; all grades, grade ≥3) were peri-orbital oedema (71%, 4%), anaemia (55%, 29%), diarrhoea (41%, 1%), fatigue (40%, 9%), peripheral oedema (40%, 0%), nausea (39%, 4%), thrombocytopenia (39%, 26%), vomiting (34%, 4%), and cognitive effects (34%, 4%). The presence of grade 3 thrombocytopenia (platelets <50 x 10^9/L) at baseline was associated with non-traumatic intracranial bleeding (ICB). Among patients with platelets <50 x 10^9/L at baseline, 44% (4/9) had an ICB event, while in patients with platelets ≥50 x 10^9/L at baseline, 3% (2/71) had ICB events and treatment-emergent grade 3 thrombocytopenia. In total, 12 (15%) patients discontinued treatment due to clinical progression and 6 (8%) due to treatment-related AEs. The optimal phase 2 starting dose of avapritinib was determined as 200 mg QD. At this dose, avapritinib induced rapid, deep, and durable reductions in measures of MC burden, which were associated with significant reduction in disease-related symptoms, regardless of prior midostaurin exposure or AdvSM subtype. The phase 2 PATHFINDER trial for patients with AdvSM will provide further data to characterise the safety and efficacy of avapritinib.

Disclosure of Interest: D. Radia Conflict with: Clinical Advisory Board/Study steering group member (EXPLORER); Blueprint Medicines Corporation; Educational events and advisory board: Novartis, M. W. Drummond Conflict with: Research support: Blueprint Medicines Corporation; Educational events and advisory board: Novartis, J. Gotlib Conflict with: Dr. Gotlib is the Chair of the Response Adjudication Committee, received research funding, served on advisory boards, and received honoraria and funding to cover travel expenses from Blueprint Medicines Corporation. Dr. Gotlib has received research funding, is the co-chair of the Study Steering Committee and has honoraria for these roles and serves on Advisory boards for Deciphera. For Explorer: Dr. Gotlib is the Chair of the Response Adjudication Committee; has received funding for administration of the trial; served on advisory boards and has received honoraria. Dr. Gotlib has

Abstract Table: Best overall response

<table>
<thead>
<tr>
<th>Outcome</th>
<th>All (n = 48)</th>
<th>ASM (n = 3)</th>
<th>SM-AHN (n = 35)</th>
<th>MCL (n = 10)</th>
<th>All (n = 15)</th>
<th>No prior mido (n = 33)</th>
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<tbody>
<tr>
<td>ORR, %</td>
<td>77 (63–88)</td>
<td>100</td>
<td>77</td>
<td>70</td>
<td>60</td>
<td>85</td>
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<tr>
<td>CR, n (%)</td>
<td>4 (8)</td>
<td>0</td>
<td>2 (6)</td>
<td>2 (20)</td>
<td>0</td>
<td>4 (12)</td>
</tr>
<tr>
<td>CRh, n (%)</td>
<td>9 (19)</td>
<td>2 (67)</td>
<td>7 (20)</td>
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<td>0</td>
<td>9 (27)</td>
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<td>PR, n (%)</td>
<td>20 (42)</td>
<td>1 (33)</td>
<td>16 (46)</td>
<td>3 (30)</td>
<td>8 (53)</td>
<td>12 (36)</td>
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<tr>
<td>CI, n (%)</td>
<td>4 (8)</td>
<td>0</td>
<td>2 (6)</td>
<td>2 (20)</td>
<td>1 (7)</td>
<td>3 (9)</td>
</tr>
</tbody>
</table>

*95% confidence interval. Mido, midostaurin.

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also received funding to cover travel expenses, T. I. George Conflict with: Dr. George has received no funding for this research. ARUP Laboratories, owned by the University of Utah, has received funding from Blueprint Medicines Corporation. Dr. George received consulting fees from Blueprint Medicines Corporation. Dr. George is a consultant for Deciphera but has received no financial compensation for the past 12 months, A. T. Querry: None Declared, E. Winton Conflict with: Research support: Blueprint Medicines Corporation. Dr. Winton has also received research support from Samus Therapeutics and Incyte Corporation, H.-M. Lin Conflict with: Employee and shareholder of Blueprint Medicines Corporation, B. G. Mar Conflict with: Employee and shareholder of Blueprint Medicines Corporation, M. W. Deininger Conflict with: Dr. Deininger has received honorarium fees from Blueprint Medicines Corporation, Incyte, Medscape, Sangamo, and Takeda, and received consultancy fees from Blueprint Medicines Corporation, DisperSol Fusion Pharma, Novartis, Sangamo; received research funding from Blueprint Medicines Corporation, Incyte, Leukemia & Lymphoma Society, Novartis, Pfizer, SPARC, Takeda; is part of a study management committee for Blueprint Medicines Corporation, Takeda and is a case author for Medscape, D. J. DeAngelo Conflict with: Dr. Daniel DeAngelo has served as a consultant for Amgen, Autolys, Agios, Blueprint Medicines Corporation, Forty-Seven, Incyte, Jazz, Novartis, Pfizer, Shire, and Takeda. Dr. Daniel DeAngelo has received research funding from AbbVie, Glycometrics, Novartis, and Blueprint Medicines Corporation.

BSH2021-PO-015

CPI-0610, a bromodomain and extraterminal domain protein (bet) inhibitor, as monotherapy in advanced myelofibrosis patients refractory/intolerant to jak inhibitor: update from phase 2 manifest study

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Abstract Content: CPI-0610, a first-in-class, oral, small-molecule inhibitor of bromodomain and extraterminal domain (BET) proteins, potentially promotes disease-modifying activity through altered gene regulation of key oncogenic, fibrotic, and inflammatory factors and may transform the standard of care in myelofibrosis (MF). Many MF patients (pts) have suboptimal responses or are resistant to the JAK inhibitor (JAKi) ruxolitinib (rux) or develop anemia and transfusion dependence (TD). Here we present results from MANIFEST Arm 1, a global, open-label Phase 2 study of CPI-0610 monotherapy in advanced MF pts refractory/intolerant to JAKi. Pts are stratified as transfusion-dependent (TD, defined as ≥2U RBCs/no over 12 weeks) and non-transfusion-dependent (non-TD). Eligibility: MF pts intolerant/resistant/refractory/lost response to or ineligible for JAKi; DIPSS ≥Int-2; platelets ≥75 x 10^9/L; ≥2 symptoms measurable (score ≥1) per MFSAF v4.0; TD per IWG-MRT criteria in TD cohort or spleen volume of ≥450 cc by CT/MRI in non-TD cohort. 1° endpoints-TD cohort: TD to TI (transfusion independence: no transfusion for 12 weeks); non-TD cohort: SVR35 (≥35% spleen volume reduction) at week 24. 2° endpoints: TSS50 (≥50% total symptom score reduction) at wk 24, safety and PK.

As of 29 September 2020, 27 pts were treated in non-TD cohort (median: 51 weeks, range: 2, 147). Mean age 68 yo, male: 52%; DIPSS ≥Int-2: 74%; hemoglobin (Hgb) <10 g/dl: 63%; primary MF:70%; 52% with high molecular risk and 63% with JAK2 mutations. Median number of prior lines of therapies: 2 (range: 1–5). At wk 24, 30% (7/23) pts achieved SVR35 (median % change: −29%, range: −70%, 14%), 48% (10/21) pts achieved TSS50 (median % change: −56%, range: −100%, 25%). 50% (10/20) pts achieved absolute of ≥1.5 g/dl increase in Hgb levels without transfusions with notable hemoglobin improvement observed in patients who started treatment with baseline hemoglobin <10 g/dl.

In TD cohort, 19 pts were treated (median: 32 weeks, range: 5, 78). Baseline characteristics: mean age 71 yo (SD: 8), 63% male, 94% with DIPSS ≥Int-2, 95% with Hgb <10 g/dl, 58% with primary MF, 58% with high-molecular-risk and 68% with JAK2 mutations. Median number of prior lines of therapies: 2 (range: 1–6). 21% (3/14) of TD pts converted to TI at week 24, median spleen volume change = −11% (range: −35%, 90%); 8% (1/13) pts achieved SVR35, 8% (1/13) pts achieved TSS50 (median % change: −22%, range: −70%, 30%) at 24 weeks.

A total of 46 pts were evaluable for safety. Median exposure was 49 weeks. The most common hematological treatment-emergent adverse events (TEAEs) of any grade were thrombocytopenia (30%, ≥Gr3: 15%) and anemia (15%, ≥Gr3: 13%). The most common (≥20%) non-hematological TEAEs were nausea (39%, no ≥Gr3), diarrhea (37%, ≥Gr3: 4%), dysgeusia and asthenic conditions (30% each, no ≥Gr3), respiratory tract infections (28%, ≥Gr3: 2%), cough (26% each, no ≥Gr3), and constipation and weight decreased (22% each, ≥Gr3: 2% each). 9 pts discontinued treatment because of TEAEs. There were no Gr5 TEAEs.

CPI-0610 monotherapy is generally well-tolerated and provides clinical benefits in MF pts refractory/intolerant to rux. SVR35 and symptomatic improvement were observed. Half of non-TD pts demonstrated ≥1.5 g/dl increase in Hgb. Conversion to TI was observed in the TD cohort.

Disclosure of Interest: M. Drummond Conflict with: Novartis, Pfizer, Bristol Myers Squibb, Gilead, Jazz, Takeda, Astellas, Conflict with: Novartis, Blueprint Medicine Corporation, M. Talpaz Conflict with: Constellation Pharmaceuticals, BMS, IMAGO, Conflict with: Takeda, Novartis, R. Rampal Conflict with: Incyte, Celgene, Promodior, CITE Biopharma, Jazz Pharmaceuticals, Blueprint, Stemline, Galeto, Abbvie, Pharmassentia, Conflict with: Incyte, Stemline, Constellation, S. Verstovsek Conflict with: Incyte, Celgene, Novartis, Sierra Oncology, Conflict with: Incyte, Roche, NS Pharma, Celgene, Gilead, Promodior, CITE, Genentech, Blueprint Medicines Corp, Novartis, Sierra Oncology, PharmEssentia, AstraZeneca, Italfarma, Protagonist Therapeutics, J.-J. Kiladjian: None Declared, A. Vannucchi Conflict with: Novartis, Incyte, Blueprint, Celgene/BMS, AbbVie, M. Kremysnaskaya Conflict with: Protagonist Therapeutics, Bristol...
Secondary haemophagocytic lymphohistiocytosis in hospitalised COVID-19 patients is infrequent and does not lead to increased mortality

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Abstract Content: Mortality from SARS-CoV-2 infection causing COVID-19 in hospitalised patients in the United Kingdom has been reported to be 25.7%. Early reports have suggested that a subgroup of individuals suffer a hyperinflammatory state (HI) with high mortality which is associated with high levels of IL-6 and CRP of which secondary haemophagocytic lymphohistiocytosis (sHLH) is the most severe manifestation. To facilitate diagnosis of sHLH the HScore has been developed because of evidence that early recognition and intervention is beneficial. We set out to determine the prevalence of sHLH-like hyperinflammation by HScore in COVID-19. To account for inevitable missing data in COVID patients due to isolation precautions leading to lack of bone marrow biopsy and palpation findings, we calculated the maximum possible HScore of the recorded parameters (%HScore) - see Table.

The cohort was 567 COVID-19 patients who tested positive for SARS-CoV-2 viral RNA and were admitted to University Hospital Southampton. Investigation parameters were normalised to the date of SARS-CoV-2 viral RNA laboratory confirmation and outcome data tabulated from day -1 to day 21. %HScore in COVID-19 patients measured in the first 5 days of illness (day -1 to 4 after laboratory virus confirmation) was a strong predictor of the %HScore during the whole admission (r = 0.8499, P < 0.0001). The overall prevalence of individuals with an 85% probability of sHLH in our COVID-19 cohort was 1.59% (9 of 567) on admission and only rose to 4.05% (23 of 567) if calculated at any time during the whole disease course. Age conferred a strong negative correlation on %HScore across the cohort (Spearman r = −0.305, −0.38 to −0.226, P < 0.0001). Strikingly, the median %HScore was significantly lower (P < 0.0001) in the older age group: >75 years median %HScore 7.724 (0.0 to 18.16) vs. <75 years median %HScore 18.31 (7.72 to 28.57), %HScores were higher in younger patients (p<0.0001) and did not reliably predict outcome at any cut-off value (AUROC 0.533, P = 0.211; OR 0.99, 0.98 to 1.00). Even in the small cohort (n = 23) with %HScores suggestive of sHLH, there was no excess mortality compared with the whole cohort.

This is the largest dataset assessing sHLH frequency in COVID-19 patients to date (n = 567). These findings show that sHLH-type HI is not prevalent in COVID-19, and surprisingly does not predict outcome. Why %HScore (and most HScore parameters) decline with age in the context of COVID-19 is not clear but may predominantly reflect immunosenescence in this mainly elderly cohort of patients. We suggest that waning immunity with age may actually be protective against sHLH-type responses in COVID-19 patients. However, several studies have shown the benefit of anti-HI therapy in COVID-19 patients; Dexamethasone in oxygen dependent and Tocilizumab in ITU patients. Our study demonstrates the need for novel algorithms to predict HI in COVID-19 as well as randomised controlled trials targeted at this patient group.

Abstract Table:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HScore points (criteria)</th>
<th>%HScore points (criteria)</th>
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<tbody>
<tr>
<td>Temperature (°C)</td>
<td>0 (&lt;38.4), 33 (38.4-39.4), 49 (&gt;39.4)</td>
<td>0 (&lt;38.4), 33 (38.4-39.4), 49 (&gt;39.4)</td>
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<tr>
<td>No. of cytopenias*</td>
<td>0 (1 lineage), 24 (2 lineages), or 34 (3 lineages)</td>
<td>0 (1 lineage), 24 (2 lineages), or 34 (3 lineages)</td>
</tr>
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<td>Ferritin (mg/L)</td>
<td>0 (&lt;2,000), 35 (2,000-6,000), or 50 (&gt;6,000)</td>
<td>0 (&lt;2,000), 35 (2,000-6,000), or 50 (&gt;6,000)</td>
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<tr>
<td>Triglyceride (mmol/L)</td>
<td>0 (&lt;1.5), 44 (1.5-4), or 64 (&gt;4)</td>
<td>0 (&lt;1.5), 44 (1.5-4), or 64 (&gt;4)</td>
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<tr>
<td>Fibrinogen (g/L)</td>
<td>0 (&gt;2.5) or 30 (&lt;2.5)</td>
<td>0 (&gt;2.5) or 30 (&lt;2.5)</td>
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The V617F-positive SET2 cell line had
EZH2, V617F-positive HEL cell line. EGR1
<–<EGR1, WT1 KDM2B and
MPL <–WT1 Immune thrombocytopenia purpura (ITP)
<–WT1 (Suppl. 1), 46–76 were identified as being
enriched and these six polycomb associated genes
were also significantly downregulated in the ruxolitinib sensitive gene
list. Furthermore, the polycomb complex associated genes EZH2,
SUZ12, JARID2, MTF2, RNF2 and KDM2B were identified as being
significantly enriched.

A machine learning approach using random forest methodology was
developed, trained and tested using the transcriptomic datasets,
GSE103327 and GSE34482, of PMF or ET/PV with normal compar-
ators using EGR1, WT1 and these six polycomb associated genes
as variables. This approach could accurately distinguish PMF from
normal and ET/PV from normal (OBB estimate of error 1.75% and
1.92%) but could not accurately distinguish between ET and PV in
the second dataset.

Conclusions: This bioinformatic approach links ruxolitinib sensitive
genes in MPN cell line models to the accurate prediction of MPN
disease from transcriptomic datasets and highlights a potential role of
WT1, EGR1 and the polycomb complex in the pathogenesis in
MPN and in the ruxolitinib response.

Disclosure of Interest: G. Greenfield: None Declared, J. Blayney:
None Declared, M. F. McMullin Conflict with: advisory board work
and received speaker fees from Novartis, K. Mills: None Declared

Table 1. (Continued)

<table>
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<th>Parameter</th>
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<tr>
<td>AST/ALT (IU/L)</td>
<td>0 (&lt;30) or 19 (≥30)</td>
<td>0 (&lt;30) or 19 (≥30)</td>
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<td>Hemophagocytosis **</td>
<td>0 (no) or 35 (yes)</td>
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<td>Immunosuppression</td>
<td>0 (no) or 18 (yes)</td>
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<tr>
<td>Splenomegaly</td>
<td>(either), or 38 (both)</td>
<td>–</td>
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</table>

*haemoglobin <92 g/L and/or WBC ≤5 x 10⁹/L and/or platelets ≤110
x 10⁹/L; **features on bone marrow aspirate;
AST, Aspartate Transaminase; ALT, Alanine aminotransferase; IU,
International Units

BSH2021-PO-017
A Machine Learning Approach to Predicting MPN Patients
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Abstract Content: Introduction: The myeloproliferative neoplasms
(MPN) comprise a complex, heterogeneous group of clonal disorders
of the myeloid stem and progenitor cells. Overlapping clinicopatho-
logical features of polycythaemia vera (PV), essential thrombo-
ocythaemia (ET) and primary myelofibrosis (PMF) include
morphological similarities, a tendency to thrombus formation and a
tendency to leukaemic progression. Constitutive activation of the
JAK/STAT pathway via activating mutations in JAK2, CALR or MPL
links the patients genetically. Ruxolitinib is a JAK1/2 inhibitor
approved for use in PMF and PV with specific clinical benefits but
limited disease-modifying activity. Previous work has demonstrated
the epigenetic modifying of ruxolitinib on the histone modification
landscape of MPN cell line models and patient samples. Understanding
the complex control of transcription and the modifying effect of
JAK inhibition in MPN models may help develop further treatment
options in this group.

Methods and Results: We have undertaken RNA sequencing follow-
ning ruxolitinib treatment of the JAK2 V617F-positive HEL cell line.
In addition we identified two RNA sequencing datasets, GSE91062
and GSE69827, in which the JAK2 V617F-positive SET2 cell line had
been analysed following treatment with ruxolitinib at one and two
time points, respectively. Differential expression analysis, using
dgeR, identified 53 genes that were consistently downregulated (log
FC <0.5 and FDR <0.05) in all 4 datasets. All datasets were normal-
ised and combined for the 15851 common transcripts present. The
combined dataset was subject to a rank product analysis in R,
with 99 genes identified as significantly downregulated. The 99 rux-
olitinib sensitive gene list was enriched for KEGG pathways including
JAK/STAT signalling, MAPK pathways and TNF signalling. Analysis
for transcription factor binding motifs within 10 kbp up and down-
stream of transcriptional start sites highlighted STAT3 as having the
highest enrichment. Further interrogation of the dataset for enriched
transcriptional factor binding motifs with Enrichr was used to anal-
yse published CHIP sequencing transcription factor binding
experimental data available from the ChEA dataset. The transcription
factors WT1 and EGR1 were identified as significantly enriched and
were also significantly downregulated in the ruxolitinib sensitive gene
list. Further, the polycomb complex associated genes EZH2,
SUZ12, JARID2, MTF2, RNF2 and KDM2B were identified as being
significantly enriched.

A machine learning approach using random forest methodology was
developed, trained and tested using the transcriptomic datasets,
GSE103327 and GSE34482, of PMF or ET/PV with normal compar-
ators using EGR1, WT1 and these six polycomb associated genes
as variables. This approach could accurately distinguish PMF from
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1.92%) but could not accurately distinguish between ET and PV in
the second dataset.

Conclusions: This bioinformatic approach links ruxolitinib sensitive
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WT1, EGR1 and the polycomb complex in the pathogenesis in
MPN and in the ruxolitinib response.

Disclosure of Interest: G. Greenfield: None Declared, J. Blayney:
None Declared, M. F. McMullin Conflict with: advisory board work
and received speaker fees from Novartis, K. Mills: None Declared

BSH2021-PO-018
ITP and its management in the UK during the COVID-19 pandemic: interim results of a national audit
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Abstract Content: Immune thrombocytopenia purpura (ITP)
demonstrates significant heterogeneity in its presentation and
response to treatment, and management is thus tailored to each
patient. International consensus guidelines were published in 2019,
but there are potential concerns with standard first-line agents in the
context of the SARS-CoV-2 pandemic. These concerns include ster-
oids and immunosuppressants increasing the risk of COVID-19 dis-
ease, and thrombopoietin receptor agonists (TPO-RAs) increasing the
risks of thrombosis or hepatotoxicity in patients hospitalised with
severe COVID-19. In the absence of clear evidence, guidelines were
issued to provide a pragmatic response to these concerns.

With the support of contributors from the UK ITP Forum and
HaemStar, we are collecting data to record ITP practice across the
UK since the start of the SARS-CoV-2 pandemic. Here, we present
our interim analysis of 121 patients.

Since May 2020 to the current date, nineteen different Trusts
across all four nations of the UK have participated in the audit. Each
contributing Centre registers with their local Audit Department, and
is then provided with an online form to submit anonymised data
pertaining to patients treated for ITP since 01-March-2020. Addi-
tional questions related to COVID-19 vaccination status were added
in February 2021. In order to incentivise uptake, prizes have been
introduced for the biggest contributors.

The key parameters collected are highlighted in the Abstract
Table.

The real-world implications of the guidelines were assessed within
the audit. Success rate of first-line therapy, as determined by no need
for second-line therapy, was 63% (27/43) for 1 mg/kg Prednisolone;
60% (3/5) for 20 mg Prednisolone; 53% (10/19) for intermediate-
dose Prednisolone; 16% (3/19) for IVig; and 85% (11/13) for TPO-
RA. Platelet counts rose from a median of 7 to a post-therapy peak
of 170 (IQR 86 to 270). In 72/120 patients, platelets rose to > 30
within 7 days of treatment; 22/120 reached this threshold between 8
and 14 days; and 13/120 required at least 15 days. 12 patients had not seen a platelet count of > 30 during their follow-up period. At the time of submission of each case: none had died; 42 had suffered bleeding complications during the course of their ITP episode, of which 17 were major; and 5 had suffered thrombotic episodes (of which one patient was on both TXA and a TPO-RA, while neither agent was used in the other thrombotic events). “Guidance” was specifically referenced as justification for a first-line therapy choice in 38 of 120 contributors.

To our knowledge, this is the first UK-wide audit of ITP practice – irrespective of the SARS-CoV-2 pandemic. We conclude that there exists a significant variety in choice of first-line therapy for ITP, which presumably reflects the nature of the condition and the freedom with which clinicians can practise. There is excellent compliance with triggers for initiation of treatment for ITP, and relatively good compliance with choice of first-line agents and timing of steroid wean as compared to available guidance documents. We aim to receive further contributions to provide a more accurate representation of up-to-date ITP practice in the UK.

We would like to thank the UK ITP Forum, HaemStar and the Oxford Centre for Haematology for their support, and we are indebted to our many contributors, without whom this audit simply would not exist: we are very grateful for their hard work!

Abstract Table:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result</th>
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<tbody>
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<td>Mean age in years</td>
<td>58</td>
</tr>
<tr>
<td>Percentage women</td>
<td>52</td>
</tr>
<tr>
<td>Treatment commenced</td>
<td>120/121</td>
</tr>
<tr>
<td>Median Platelet count pre-treatment (IQR)</td>
<td>7 (3–12)</td>
</tr>
<tr>
<td>Indication for treatment</td>
<td></td>
</tr>
<tr>
<td>Bleeding symptoms</td>
<td>44</td>
</tr>
<tr>
<td>Platelet count &lt; 10</td>
<td>42</td>
</tr>
<tr>
<td>Platelet count &lt; 20</td>
<td>9</td>
</tr>
<tr>
<td>Platelet count &lt; 50</td>
<td>16</td>
</tr>
<tr>
<td>With need for anticoag/procedure</td>
<td></td>
</tr>
<tr>
<td>First-line therapy used</td>
<td></td>
</tr>
<tr>
<td>Prednisolone @ 1 mg/kg</td>
<td>43</td>
</tr>
<tr>
<td>Prednisolone @ 20 mg</td>
<td>5</td>
</tr>
<tr>
<td>Intermediate-dose Prednisolone</td>
<td>19</td>
</tr>
<tr>
<td>Where 20 mg &lt; Dose ≤ 0.5 mg/kg</td>
<td></td>
</tr>
<tr>
<td>IVIg @ 1 g/kg</td>
<td>19</td>
</tr>
<tr>
<td>TPO-RA</td>
<td>13</td>
</tr>
<tr>
<td>Other</td>
<td>21</td>
</tr>
<tr>
<td>e.g. Dexamethasone 20 mg or 40 mg; combinations</td>
<td></td>
</tr>
<tr>
<td>Time to start steroid wean</td>
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</tr>
<tr>
<td>0–7 days</td>
<td>33/90</td>
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<tr>
<td>8–14 days</td>
<td>35/90</td>
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<tr>
<td>15 days or more</td>
<td>22/90</td>
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<tr>
<td>Use of tranexamic acid (TXA)</td>
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<tr>
<td>For bleeding symptoms</td>
<td>43/120</td>
</tr>
<tr>
<td>For platelet count alone</td>
<td>32</td>
</tr>
<tr>
<td>For platelet count alone</td>
<td>5</td>
</tr>
</tbody>
</table>

Concordance with consensus guidelines

Provan, 2019 = 1; Neunert, 2019 = 2; Pavord, 2020 = 3

Prednisolone at 1 mg/kg (capped at 80 mg) is the pre-COVID-19 International consensus advice. The reduced dose of 20 mg Prednisolone has been advocated in context of COVID-19 in non-bleeding patients. An intermediate dose is not advocated in any major guidance document, but was used as frequently as IVIg, another accepted first-line option. TPO-RA is a suggested first-line in COVID, though funding implications have reduced availability until recently.

Where the international guidance recommends commencing after a maximum of 3 weeks (or 2 if no response), and the COVID-19 recommendations suggest 2 weeks prior to wean.

TXA is recommended for use by international consensus in the case of bleeding or ongoing high risk thereof. Owing to the prothrombotic nature of COVID-19, caution is necessary in active infections.

Disclosure of Interest: None Declared
Red Cell Disorder

BSH2021-PO-019

Fostamatinib treatment of warm antibody autoimmune hemolytic anemia: a global, randomized, double-blind, placebo-controlled, phase 3 study
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Abstract Content: Warm antibody autoimmune hemolytic anemia (wAIHA) is a rare disorder that can have serious complications. In this disorder, autoantibodies bind to antigens on red blood cells leading to phagocytosis and destruction of the cells. This is mediated by Fcγ receptors on macrophages through a spleen tyrosine kinase (SYK)-dependent pathway. Fostamatinib is a potent, oral SYK inhibitor approved for the treatment of chronic immune thrombocytopenia. Fostamatinib prevents platelet destruction by inhibition of platelet phagocytosis mediated through Fcγ receptor and SYK in macrophages. Fostamatinib was evaluated for wAIHA in an open-label, multicenter, phase 2 study (NCT02612538). This study demonstrated markedly improved hemoglobin levels in 11 of 25 patients (44%) after fostamatinib treatment. Adverse events (AEs) were consistent with the safety database (>4000 patients across multiple diseases). Based on this phase 2 study, a randomized, double-blind, placebo-controlled, global phase 3 study (NCT03764618) was initiated in wAIHA patients to investigate the safety and efficacy of fostamatinib.

The phase 3 study began enrolling patients at 103 sites in 22 countries (North America, Europe and Australia) in 2020 with a goal of enrolling approximately 90 patients. This is the first phase 3 study to evaluate a SYK inhibitor for the treatment of wAIHA.

Inclusion criteria include: age ≥18; documented diagnosis of primary or secondary wAIHA; failure of ≥1 prior wAIHA treatment; haemoglobin below normal or total bilirubin above normal or lactate dehydrogenase above normal; and baseline hemoglobin ≥9 g/dl or, if hemoglobin ≥9 g/dl and ≤10 g/dl, subject must be on permitted wAIHA treatment AND have anemia symptoms.

Exclusion criteria include: other forms of AIHA; uncontrolled or poorly controlled hypertension; neutrophil count <1,000/μl; platelet count <30,000/μl (unless patient has Evans syndrome); and transaminase levels >1.5 x normal.

Randomization of eligible patients will be 1:1 to fostamatinib or placebo for 24 weeks. Randomized patients will be stratified by concomitant steroid use and baseline anemia severity. Fostamatinib is started at 100 mg BID and increased to 150 mg BID at Week 4, if tolerated. The dose may be reduced for AEs. Patients may continue selected concurrent wAIHA therapies (maximum of 2) throughout the study. A steroid taper will be allowed in patients with a hemoglobin response. Rescue therapy will also be allowed. Patients who complete the study can rollover to an open-label extension.

Efficacy endpoints will include hemoglobin response, (≥10 g/dl with a ≥2 g/dl increase from baseline without rescue therapy); duration of hemoglobin response; and the need for rescue therapy. Safety endpoints will be the recording of AEs. Patients will be evaluated in the clinic at two-week intervals.

Using the Cochran–Mantel–Haenszel test at a two-sided significance level of 0.05, to detect a difference in response between the active and placebo groups with 80% power would require 90 subjects randomized 1:1. The response rate will be compared between groups using a chi-square test adjusted for randomization stratification factors.

As of 11 January 2021, 62 sites are open to screening (subject to local COVID-19 regulations), and 64 patients have been randomized. Disclosure of Interest: None Declared

BSH2021-PO-020

Results of the Pegasus Phase 3 Randomized Trial Demonstrating Superiority of the C3 Inhibitor, Pegcetacoplan, Compared to Eculizumab in Patients with Paroxysmal Nocturnal Hemoglobinuria
Morag Griffin1,*, Peter Hillmen1, Jeffrey Szer2, Ilene C. Weitz2, Alexander Roth3, Britta Höchsmann4, Jens Panse5, Kensuke Usuki6, Jean-Jacques Kiladjian7, Carlos M. De Castro8, Hisakazu Nishimori9, Lisa Tan10, Mohamed Hamdani11, Pascal Deschatelle12, Cedric Francois13, Federico Grossi14, Antonio Risitano14,15, Regis Peffault De Latour15,16
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Abstract Content: Paroxysmal nocturnal haemoglobinuria (PNH) is a rare, acquired, haematologic disease characterised by complement-mediated haemolysis including intravascular haemolysis (IVH) mediated by the membrane attack complex and extravascular haemolysis (EVH) mediated by C3 opsonisation. Standard of care treatments for PNH include the C5 inhibitors eculizumab (ECU) and ravulizumab, which have been shown to reduce IVH. However, despite prior ECU treatment, nearly 70% of patients remain anaemic and 36% require ≥1 transfusion per year due to C3-mediated EVH. The PEGASUS trial (NCT03500549) is a phase 3 randomised open-label active-comparator controlled study of the efficacy and safety of pegcetacoplan, a C3 inhibitor, compared to ECU.

Eighty patients ≥18 years of age with a confirmed PNH diagnosis and haemoglobin (Hb) levels <10.5 g/dl despite stable ECU for ≥3
months were enrolled in the trial. Patients completed a 4-week run-in period with both ECU and pegcetacoplan before 1:1 randomisation to pegcetacoplan (n = 41; 1080 mg subcutaneously twice weekly) or ECU monotherapy (n = 39; continued dosing regimen). The primary endpoint was the change from baseline (CBF) in Hb levels from the start of run-in period to Week 16. Key secondary endpoints included Hb normalisation in the absence of transfusions (defined as Hb levels of at least the lower limit of normal), transfusion avoidance, absolute reticulocyte count (ARC), lactate dehydrogenase (LDH), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score, and adverse events (AEs). Post hoc analyses included Hb stabilisation in the absence of transfusions (defined as avoidance of a >1 g/dl decrease from baseline).

Pegcetacoplan demonstrated superiority to ECU in Hb levels CBF at Week 16 with an adjusted treatment difference of 3.8 g/dl (P < 0.0001). The least-squares mean (LSM [standard error {SE}]) changes were 2.4 (0.4) g/dl for pegcetacoplan and −1.5 (0.7) g/dl for ECU-treated patients (Table). At Week 16 a greater proportion of pegcetacoplan-treated patients achieved ≥2 g/dl improvement in Hb (61% vs. 0%), Hb normalisation (34% vs. 0%), and Hb stabilisation in the absence of transfusions (85% vs. 15%) compared to ECU-treated patients. Pegcetacoplan demonstrated non-inferiority compared to ECU in transfusion avoidance (85% vs. 15%) and in ARC, with LSM changes of −136.0 (6.5) × 10⁴ cells/L for pegcetacoplan and 28.0 (11.9) × 10⁴ cells/L for ECU. LSM changes in LDH were −15.0 (42.7) U/L for pegcetacoplan treatment and −10.0 (71.0) U/L for ECU treatment. LSM changes in FACIT-Fatigue score increased with pegcetacoplan (9.2 [1.6]) and decreased with eculizumab (−2.7 [2.8]). Nearly 88% of pegcetacoplan and 87% of ECU-treated patients reported AEs, while 17% and 15% reported serious AEs, respectively. Most AEs were mild and included injection site reactions (pegcetacoplan: 37%; ECU: 3%), diarrhoea (pegcetacoplan: 22%; ECU: 3%) and infections (pegcetacoplan: 29%; ECU: 26%). By Week 16 breakthrough haemolysis was reported in 10% of pegcetacoplan-treated patients and 23% of ECU-treated patients, leading to pegcetacoplan discontinuation in 3 patients.

In this phase 3 trial pegcetacoplan demonstrated superiority to ECU in Hb levels and improved clinical outcomes at Week 16 for most patients. The safety profile of pegcetacoplan was comparable to ECU. The study results suggest pegcetacoplan can prevent both IVH and EVH and represents a new therapeutic option for PNH patients.

Disclosure of Interest: M. Griffin Conflict with: Biocryst (Membership on an entity’s Board of Directors or advisory committees); Alexion Pharmaceuticals (Honoraria), P. Hillmen Conflict with: Alexion, Apellis, AbbVie, AstraZeneca, Janssen, and Roche (consultancy and speakers bureau), Conflict with: Apellis, AbbVie, Alexion, Gilead, Janssen, Pharmacycils, and Roche (grants and research support), J. Szer Conflict with: Apellis (consultancy), Alexion (consultancy, honoraria, membership on an entity’s board of directors or advisory committees, speakers bureau), Conflict with: Takeda (honoraria, speakers bureau), Pfizer (honoraria, speakers bureau), Novartis (consultancy, honoraria, speakers bureau), Prevail Therapeutics (honoraria, membership on an entity’s board of directors or advisory committee), I. C. Weitz Conflict with: Alexion (Consultancy, Honoria, Speakers Bureau), Apellis (Consultancy, Honoraria), A. Roth Conflict with: Alexion (research funding, consultancy and honoraria), Apellis (consultancy and honoraria), Biocryst (consultancy and honoraria), Novartis (consultancy and honoraria), Roche

Abstract Table: Table. Primary and Secondary Endpoints at Baseline and Week 16

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<tr>
<th></th>
<th>Pegcetacoplan</th>
<th>ECU</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Week 16</td>
</tr>
<tr>
<td>Hb level, g/dl; NRR, 12.0–18.0 g/dl</td>
<td>n = 41</td>
<td>n = 37</td>
</tr>
<tr>
<td>Mean (SD)×</td>
<td>8.7 (1.1)</td>
<td>11.5 (2.0)</td>
</tr>
<tr>
<td>Range</td>
<td>6.0–10.8</td>
<td>6.7–15.6</td>
</tr>
<tr>
<td>Patients with Hb normalisation, n (%)b</td>
<td>N/A</td>
<td>14 (34)</td>
</tr>
<tr>
<td>Transfusion</td>
<td>N/A</td>
<td>n = 41</td>
</tr>
<tr>
<td>PRBCs transfused, units/patient, mean (SD)</td>
<td>n = 41</td>
<td>0.6 (2.0)</td>
</tr>
<tr>
<td>ARC, ×10⁴ cells/L; NRR, 30–120×10⁴ cells/L</td>
<td>n = 41</td>
<td>n = 35</td>
</tr>
<tr>
<td>Mean (SD)×</td>
<td>218.0 (75.0)</td>
<td>77.0 (26.6)</td>
</tr>
<tr>
<td>Range</td>
<td>100–420</td>
<td>30–150</td>
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<tr>
<td>Patients with ARC normalisation, n (%)b</td>
<td>N/A</td>
<td>32 (78)</td>
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<tr>
<td>LDH, U/L; NRR, 113–226 U/L</td>
<td>n = 41</td>
<td>n = 36</td>
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<tr>
<td>Mean (SD)×</td>
<td>257.0 (97.6)</td>
<td>189.0 (78.1)</td>
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<td>Range</td>
<td>119–584</td>
<td>86–550</td>
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<tr>
<td>Patients with LDH normalisation, n (%)b</td>
<td>N/A</td>
<td>29 (71)</td>
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<tr>
<td>FACIT-Fatigue Score; population norm (43.6)</td>
<td>n = 41</td>
<td>n = 36</td>
</tr>
<tr>
<td>Mean (SD)×</td>
<td>32.2 (11.4)</td>
<td>41.8 (9.6)</td>
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<tr>
<td>Patients with score improvement ≥3, n (%)b</td>
<td>N/A</td>
<td>30 (73)</td>
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<tr>
<td>Clone size: % PNH Type II + III cells</td>
<td>n = 41</td>
<td>n = 32</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>66.8 (26.5)</td>
<td>93.9 (6.4)</td>
</tr>
<tr>
<td>C3 loading: % C3d-positive PNH Type II + III cells</td>
<td>n = 41</td>
<td>n = 32</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>17.7 (13.5)</td>
<td>0.2 (0.3)</td>
</tr>
</tbody>
</table>

ARC, absolute reticulocyte count; ECU, eculizumab; FACIT, Functional Assessment of Chronic Illness Therapy; Hb, haemoglobin, LDH, lactate dehydrogenase; N/A, not applicable; NRR, normal reference range; PNH, Paroxysmal Nocturnal Haemoglobinuria; PRBC, packed red blood cell; SD, standard deviation.

×Observed values differ from the least-squares means described in the text. In the absence of transfusions, based on patients with available data at Week 16.
BSH2021-PO-021
Assessment of the Longitudinal Effects of Luspatercept on Iron Overload and Iron Chelation Therapy Usage in Adults With β-thalassaemia Enrolled in the Phase 3 BELIEVE Study

Olivier Hermine1,2,*, Maria Domenica Cappellini3, Ali T. Taher4, Thomas D. Coates5,6, Vip Viprakasit7, Ersi Voskaridou5, Ashutosh Lal3, Hong Keng Liew10, Silverio Perrotta11, Abderrahim Khelifi12, Antonis Kattamis13, Jeevan K. Shetty14, George Zhang15, Yu Olivia Tian15, Dimana Miteva16, Tatiana Zinger14, Derek Tang15, Jay T. Backstrom16, John B. Porter17

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Abstract Content: Luspatercept is approved by the FDA and EMA for treatment of anaemia in adult patients (pts) with β-thalassaemia who require regular red blood cell (RBC) transfusions. The phase 3 BELIEVE study is evaluating the efficacy and safety of luspatercept in adult pts with β-thalassaemia requiring regular RBC transfusions (NCT02604435). The effect of long-term luspatercept use on iron loading and iron chelation therapy (ICT) use in the BELIEVE trial is assessed here.

Eligible pts were adults with β-thalassaemia or haemoglobin (Hb) E/β-thalassaemia requiring regular RBC transfusions of 6–20 RBC units in the 24 weeks prior to randomization (with no transfusion-free period >35 days). 336 pts were randomised 2:1 to luspatercept 1.0 mg/kg (titrated up to 1.25 mg/kg; n = 224) or placebo (PBO; n = 112) subcutaneously every 3 weeks for ≥48 weeks. Pts were evaluated for risk of iron overload-related complications by stratification into categories based on serum ferritin (SF) level (<1,000 µg/L, 1,000 to <2,500 µg/L, ≥2,500 µg/L), liver iron concentration (LIC; ≤3 mg/g dry weight [dw], >3 mg/g dw), and myocardial iron (by T2* MRI; ≤20 ms, >20 ms). Long-term changes in SF and ICT use were assessed in pts remaining on treatment up to data cutoff (1 July 2019) or study discontinuation, whichever was earliest.

Mean baseline SF, LIC, and myocardial T2* for luspatercept versus PBO arms were 2,097 vs. 1,845 µg/L, 12.0 vs. 10.1 mg/g dw, and 33.5 vs. 34.8 ms, respectively. ICT use was reported by 97.3% of all pts at baseline. 67.9% of pts initially randomised to luspatercept were still receiving treatment at the end of 2 years as of 1 July 2019; 92 (82.1%) PBO pts crossed over to luspatercept after study unblinding. 24 of 141 (17.0%) pts luspatercept-treated pts with baseline mean SF ≥1,000 µg/L achieved post-baseline mean SF <1,000 µg/L when assessed over weeks 1–24, vs. 3 (5.0%) PBO-treated pts. During
weeks 73–96, 26/56 (46.4%) luspatercept pts with baseline mean SF ≥1,000 μg/L achieved post-baseline mean SF <1,000 μg/L (Table). 5/120 (4.2%) and 13/134 (9.7%) luspatercept pts, respectively, shifted from LIC ≥3 mg/g dw at baseline to ≤3 mg/g dw, vs. 4/61 (6.6%) and 4/68 (5.9%) PBO pts at weeks 24 and 48, respectively. At Wk 96, 15/105 (14.3%) of luspatercept pts shifted from LIC >3 mg/g dw at baseline to ≤3 mg/g dw. 6/30 (20.0%) pts receiving luspatercept shifted from myocardial iron T2* ≤20 ms at baseline to >20 ms at Wk 48 (vs. 1/11 [9.1%] PBO pts); at Wk 96, 6/24 (25.0%) luspatercept-treated pts shifted from ≤20 ms to >20 ms.

During the first 12 weeks, mean daily deferasirox dose in luspatercept pts was 1,477.08 mg (mean change from baseline +131.80 mg) in PBO pts. After the first 48 weeks, the proportion of pts receiving ≥1 ICT gradually declined in luspatercept responders (pts achieving ≥33% reduction in transfusion burden from baseline during weeks 13–24) and non-responders. Luspatercept responders and non-responders also experienced a gradual decrease in mean daily dose of deferasirox over time.

A higher proportion of luspatercept-treated pts shifted to lower SF, LIC, and myocardial iron levels during the first 48 weeks versus PBO, indicative of lower risk of iron overload complications.

In pts receiving long-term luspatercept treatment, an increased proportion had SF levels <1,000 μg/L and decreasing overall ICT use and deferasirox dosage.

This abstract was previously published (Hermine et al., Blood 2020;136(S1):47-48).

**Abstract Table:**

<table>
<thead>
<tr>
<th>Table. Decrease in SF category by pts in the BELIEVE trial.</th>
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<td><strong>Wks 1–24</strong></td>
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<td><strong>Wks 25–48</strong></td>
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<td><strong>Wks 49–72</strong></td>
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<tr>
<td><strong>Wks 73–96</strong></td>
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</tbody>
</table>

*Placebo patients evaluated up to Week 48.

PBO, placebo; pt, patient; SF, serum ferritin; wk, week.

**Disclosure of Interest:** O. Hermine Conflict with: Roche (consultancy); Celgene BMS (consultancy, research funding); AB Science (consultancy, current equity holder in publicly-traded company, honoraria, patents & royalties, research funding); Alexion, Novartis (research funding), M. D. Cappellini Conflict with: BMS (honoraria); Genzyme/Sanoﬁ (honoraria, membership on an entity’s board of directors or advisory committees); CRISPR Therapeutics, Novartis, Vifor Pharma (membership on an entity’s board of directors or advisory committees); CRISPR Therapeutics, Novartis, Vifor Pharma (consultancy, current equity holder in publicly-traded company, honoraria, membership on an entity’s board of directors or advisory committees); CRISPR Therapeutics, Novartis, Vifor Pharma (consultancy, current equity holder in publicly-traded company, honoraria, membership on an entity’s board of directors or advisory committees); apo pharma, Vifor Pharma (consultancy, honoraria, speakers bureau); Agios pharma (consultancy, honoraria), V. Viprakasit Conflict with: BMS, Novartis (consultancy, honoraria, research funding, speakers bureau); Agios Pharmaceuticals, Ionis Pharmaceuticals, La Jolla Pharmaceuticals, Protagonist Therapeutics, Vifor Pharma (consultancy, research funding), E. Voksiariou Conflict with: ACCELERON Company, AddressMEDICA Company. BMS, GENESIS Company (consultancy, research funding); NOVARTIS Company, PROTAGONIST Company (research funding), A. Lal Conflict with: bluebird bio, Inc, Insight Magnetics, La Jolla Pharmaceutical Company, Novartis, Terumo Corporation (research funding); Celgene, BMS, Protagonist (membership on an entity’s board of directors or advisory committees, research funding); Agios Pharmaceuticals, Chiesi USA (consultancy), H. K. Liew: None Declared, S. Perrotta Conflict with: Novartis (honoraria, research funding); Celgene, BMS (honoraria); Acceleron Pharma (research funding), A. Kheif: None Declared, A. Kattamis Conflict with: Novartis (consultancy, honoraria, membership on an entity’s board of directors or advisory committees, research funding, speakers bureau); Genesis Pharma SA, Ionis, Vertex, Vifor (membership on an entity’s board of directors or advisory committees); Apo-pharma/Chiesi (honoraria, speakers bureau); Celgene/BMS (honoraria, membership on an entity’s board of directors or advisory committees, speakers bureau); Agios (consultancy), J. K. Shetty Conflict with: BMS (current employment, current equity holder in publicly-traded company), G. Zhang Conflict with: BMS (current employment), Y. O. Tian Conflict with: BMS (current employment), D. Miteva Conflict with: BMS (current employment), T. Zinger Conflict with: Celgene International, A Bristol-Myers Squibb Company (current employment), D. Tang Conflict with: BMS (current employment, current equity holder in publicly-traded company), J. T. Backstrom Conflict with: Acceleron Pharma (current employment, current equity holder in publicly-traded company); BMS (current employment, current equity holder in publicly-traded company), J. B. Porter Conflict with: Agios Pharmaceuticals, bluebird bio, Inc., BMS (consultancy, honoraria); La Jolla Pharmaceuticals, Protagonist Therapeutics, Silence Therapeutics, Vifor Pharmaceuticals (honoraria)
A Retrospective Analysis From Patients Treated in The MEDALIST Study: Safety and Efficacy Of Luspatercept Treatment In Patients With Myelodysplastic Syndrome/Myeloproliferative Neoplasm With Ring Sideroblasts And Thrombocytosis


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Abstract Content: Luspatercept is FDA approved for treatment of anaemia in patients (pts) with lower-risk (LR) myelodysplastic syndromes (MDS) with ring sideroblasts (RS) or MDS/myeloproliferative neoplasm with RS and thrombocytosis (MDS/MPN-RS-T) after erythroid-stimulating agent (ESA) failure. We assessed the benefits of luspatercept in pts with MDS/MPN-RS-T enrolled in the phase 3 MEDALIST study evaluating the safety and efficacy of luspatercept in pts with LR-MDS requiring regular red blood cell (RBC) transfusions (NCT02631070).

Eligible pts were ≥18 years; had IPSS-R-defined LR-MDS with RS; were refractory, intolerant, or unlikely to respond to ESAs (serum erythropoietin ≥200 U/L); required regular RBC transfusions. Pts were randomised 2:1 to luspatercept 1.0 mg/kg (up to 1.75 mg/kg) or placebo (PBO) subcutaneously every 3 weeks. Primary endpoint was achievement of RBC transfusion independence (RBC-TI) ≥ 8 weeks (Wks 1–24).

23/229 (10.0%) pts with MDS/MPN-RS-T (WHO 2016) were identified by retrospective analysis in the MEDALIST trial; 14 received luspatercept and 9 PBO (Table). 52.2% of pts were male; median age was 69 years. No pts received lenalidomide previously. In the luspatercept arm, 9/14 (64.3%) pts achieved RBC-TI ≥ 8 weeks during Weeks 1–24, versus 2/9 pts (22.2%) in the PBO arm (odds ratio 11.3; 95% confidence interval [CI] 1.19, 106.12; P = 0.028). Luspatercept-treated pts were significantly more likely to achieve clinical benefit (i.e. RBC-TI ≥ 8 weeks and/or modified hematological improvement-erythroid [mHI-E] per IWG 2006 criteria ≥ 4 units/8 weeks reduction in RBC transfusion in pts with ≥ 4 units/8 weeks baseline [BL] RBC transfusion burden [TB]; haemoglobin [Hb] increase ≥ 1.5 g/dl in Weks 1–24 in pts with < 4 units/8 weeks BL RBC TB), versus pts receiving PBO (78.6% vs. 33.3%; P = 0.034).

Median time from start of clinical benefit to end of treatment was 94.6 weeks (range 8.0–150.0) with luspatercept versus 23.9 weeks (range 23.7–57.9) with PBO. In Weeks 1–24, 10 luspatercept pts achieved mHI-E (6 were high TB [HTB; i.e. BL TB ≥ 4 units/8 weeks] and 4 were low TB [LTB; i.e. BL TB < 4 units/8 weeks]) versus 1 PBO pt (1/5 HTB). RBC-TI ≥ 8 weeks was achieved by 4/8 HTB pts on luspatercept (vs. 0/5 PBO) and 5/6 LTB pts (vs. 2/4 PBO). Luspatercept pts had a mean Hb increase of ≥ 1.7 after 24 weeks vs. +0.9 g/dl in PBO pts (least squares mean difference [LSMD] +0.85 g/dl; 95% CI −1.13, +2.82). Greater reductions from BL in mean serum ferritin levels were observed with luspatercept (−121.8 µg/L) versus PBO (−9.19 µg/L) over Weeks 9–24 (LSMD −90.1%; 95% CI −758.4, 578.2). Luspatercept-treated pts had median platelet counts of 467.5 × 109/L and median leukocyte counts of 6.5 × 109/L post 24 weeks of treatment, versus PBO pts who had counts of 514.0 × 109/L and 6.2 × 109/L, respectively. Incidence of specific treatment-emergent adverse events (≥ 1 pt) were: arthralgia (1/14 [7.1%] luspatercept vs. 0/9 PBO), diarrhoea (6/14 [42.9%] vs. 1/9 [11.1%]), dizziness (7/14 [50.0%] vs. 0/9), dyspnoea (3/14 [21.4%] vs. 0/9), fatigue (1/14 [7.1%] vs. 1/9 [11.1%]), nausea (6/14 [42.9%] vs. 2/9 [22.2%]), and hypotension (3/14 [21.4%] vs. 0/9, 1/14 [7.1%] luspatercept-pts experienced ≥ 1 thromboembolic event (transient ischaemic attack) and 1/9 [11.1%] PBO-pts progressed to acute myeloid leukaemia.

Luspatercept demonstrated clinical efficacy with a generally well-tolerated safety profile in this pt population with limited treatment options.

This abstract was previously published (Komrokji et al., Blood 2020;136(S1):13-15).

Disclosure of Interest: R. S. Komrokji Conflict with: BMS; Novartis; Incyte; Jazz; AbbVie; Agios; Acceleron; Geron, Conflict with: Agios, BMS, JAZZ (honoraria, speakers bureau); AbbVie, Acceleron, Geron, Incyte, Novartis (honoraria). U. Platzecker Conflict with: Janssen, Novartis (consultancy, honoraria, research funding); AbbVie, Celgene/BMS, Geron, Takeda (consultancy, honoraria); Amgen (honoraria, research funding). P. Fenaux Conflict with: Abbvie, BMS, Jazz, Novartis (honoraria, research funding), G. Garcia-Manero Conflict with: AbbVie (honoraria, research funding); Acceleron Pharmaceuticals (consultancy, honoraria); Amphivena, H3 Biomedicine, Merck, Novartis, Onconova (research funding); Astex Pharmaceuticals, Celgene, Helsinn Therapeutics (consultancy, honoraria, research funding); Bristol-Myers Squibb, Genentech (consultancy, research funding); Jazz Pharmaceuticals (consultancy, research funding); G. J. Mufti Conflict with: AbbVie,Novartis (consultancy); BMS, Novartis (research funding), V. Santini Conflict with: Janssen (research funding); BMS, J&J, Novartis (honoraria); Acceleron, BMS, Menarini, Novartis (consultancy); Pfizer, Takeda (membership on an entity’s board of directors or advisory committees), M. Diez-Campelo Conflict with: BMS, Novartis, Takeda (consultancy, membership on an entity’s board of directors or advisory committees, research funding, speakers bureau), C. Finelli Conflict with: BMS (membership on an entity’s board of directors or advisory committees, research funding, speakers bureau); Novartis (membership on an entity’s board of directors or advisory committees, speakers bureau); Janssen (membership on an entity’s board of directors or advisory committees), J. G. Jurcic Conflict with: AbbVie, BMS, Daiichi-Sankyo (consultancy, research funding); Novartis (consultancy); Arog Pharmaceuticals, Astellas, Forma Therapeutics, Genentech, Kura Oncology, PTC Therapeutics, Syros
Abstract Table:
Table. Baseline disease characteristics of MEDALIST trial pts with MDS/MPN-RS-T

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Luspatercept (N = 14)</th>
<th>PBO (N = 9)</th>
<th>Total (N = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since original diagnosis of MDS, median (range), months</td>
<td>49.9 (10.0–108.0)</td>
<td>44.1 (9.2–152.1)</td>
<td>47.3 (9.2–152.1)</td>
</tr>
<tr>
<td>IPSS-R risk category, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very low</td>
<td>0 (0.0)</td>
<td>1 (11.1)</td>
<td>1 (4.3)</td>
</tr>
<tr>
<td>Low</td>
<td>12 (85.7)</td>
<td>8 (88.9)</td>
<td>20 (87.0)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>2 (14.3)</td>
<td>0 (0.0)</td>
<td>2 (8.7)</td>
</tr>
<tr>
<td>Mutated SF3B1, n (%)</td>
<td>13 (92.9)</td>
<td>8 (88.9)</td>
<td>21 (91.3)</td>
</tr>
<tr>
<td>RBC TB, median (range), units/8 weeks over period of 16 weeks</td>
<td>4.0 (2.5–8.0)</td>
<td>4.0 (2.0–11.5)</td>
<td>4.0 (2.0–11.5)</td>
</tr>
<tr>
<td>RBC TB category over period of 16 weeks, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4 units/8 weeks</td>
<td>6 (42.9)</td>
<td>4 (44.4)</td>
<td>10 (43.5)</td>
</tr>
<tr>
<td>4 to &lt;6 units/8 weeks</td>
<td>6 (42.9)</td>
<td>3 (33.3)</td>
<td>9 (39.1)</td>
</tr>
<tr>
<td>≥6 units/8 weeks</td>
<td>2 (14.3)</td>
<td>2 (22.2)</td>
<td>4 (17.4)</td>
</tr>
<tr>
<td>Pretransfusion Hb level, median (range), g/dL</td>
<td>7.5 (7.0–8.6)</td>
<td>8.1 (7.6–9.0)</td>
<td>7.7 (7.0–9.0)</td>
</tr>
<tr>
<td>Serum erythropoietin level, median (range), U/L</td>
<td>71.9 (29.2–368.8)</td>
<td>54.0 (38.2–138.1)</td>
<td>59.9 (29.2–368.8)</td>
</tr>
<tr>
<td>Serum erythropoietin level category, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;200 U/L</td>
<td>9 (64.3)</td>
<td>9 (100.0)</td>
<td>18 (78.3)</td>
</tr>
<tr>
<td>≥200 U/L</td>
<td>5 (35.7)</td>
<td>0 (0.0)</td>
<td>5 (21.7)</td>
</tr>
<tr>
<td>Previous iron chelation therapy, n (%)</td>
<td>3 (21.4)</td>
<td>3 (33.3)</td>
<td>6 (26.1)</td>
</tr>
<tr>
<td>Received ESA previously, n (%)</td>
<td>13 (92.9)</td>
<td>8 (88.9)</td>
<td>21 (91.3)</td>
</tr>
<tr>
<td>Reasons for ESA discontinuation, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractory</td>
<td>12 (85.7)</td>
<td>8 (88.9)</td>
<td>20 (87.0)</td>
</tr>
<tr>
<td>Intolerant</td>
<td>1 (7.1)</td>
<td>0</td>
<td>1 (4.3)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (7.1)</td>
<td>1 (11.1)</td>
<td>2 (8.7)</td>
</tr>
<tr>
<td>Platelet count, median (range), 10^9/L</td>
<td>462.5 (360.0–892.0)</td>
<td>447.0 (327.0–689.0)</td>
<td>447.0 (327.0–892.0)</td>
</tr>
<tr>
<td>Leucocyte count, median (range), 10^9/L</td>
<td>4.8 (2.5–12.4)</td>
<td>7.5 (3.2–12.9)</td>
<td>5.1 (2.5–12.9)</td>
</tr>
</tbody>
</table>

ESA, erythropoietin-stimulating agent; Hb, haemoglobin; IPSS-R, Revised International Prognostics Scoring System; MDS, myelodysplastic syndromes; MPN-RS-T, myeloproliferative neoplasm with ring sideroblasts and thrombocytosis; PBO, placebo; pt, patient; RBC, red blood cell; SF3B1, splicing factor 3B subunit 1; TB, transfusion burden; WHO, World Health Organization; wk, week.

*The baseline erythropoietin level was defined as the highest erythropoietin value within 35 days before the first dose; †Baseline value is defined as the last value measured on or before the date and time of the first dose.

Pharmaceuticals (research funding), P. L. Greenberg Conflict with: Aprea, BMS, H3 Biotech, Notable Labs (research funding), M. A. Sekeres Conflict with: BMS, Pfizer, Takeda/Millennium (consultancy, membership on an entity’s board of directors or advisory committees), A. M. Zeidan Conflict with: Abbvie, Boehringer-Ingelheim, Celgene/BMS, Incyte, Novartis, Pfizer, Takeda, Trovagene (consultancy, honoraria, research funding); Acceleron, Agios, Astellas, BeyondSpring, Cardinal Health, Daiichi Sankyo, Epizyme, Ionis, Jazz, Otsuka, Seattle Genetics, Taiho (consultancy, honoraria); Cardiff Oncology (consultancy, honoraria, other); CCITLA, Leukemia and Lymphoma Society (other); ADC Therapeutics, Aprea, Astex, MedImmune/AstraZeneca (research funding), A. E. DeZern Conflict with: Celgene (consultancy, honoraria); Astex (research funding); Abbvie, MEI (consultancy), M. R. Savona Conflict with: Astex, Incyte, Sune-sis, Takeda, TG Therapeutics (consultancy, research funding); Abb-Vie, BMS, Gilead, Ryu (consultancy); Karyopharm (consultancy, current equity holder in publicly-traded company); Boehringer Ingelheim (Patents & Royalties), J. K. Shetty Conflict with: BMS (current employment, current equity holder in publicly-traded company), R. Ito Conflict with: BMS (current employment, current equity holder in publicly-traded company), G. Zhang Conflict with: BMS (current employment), X. Ha Conflict with: BMS (current employment), D. Sinsimer Conflict with: BMS (ended employment in the past 24 months, current equity holder in publicly-traded company), J. T. Backstrom Conflict with: Acceleron Pharma (current employment, current equity holder in publicly-raded company); BMS (current equity holder in publicly-traded company), A. Verma Conflict with: stellexis (current equity holder in private company); BMS (consultancy, research funding), Acceleron (consultancy, honoraria); Jansen, Medpacto (research funding)

BSH2021-PO-023
Haematological Indices and Haemoglobin High Pressure Liquid Chromatography for diagnosis of Haemoglobinopathies in a Secondary care centre in North-East India

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1Pathology, Baptist Christian hospital, 2Pediatrics, Baptist Christian hospital, 3Medicine, Baptist Christian hospital, Tezpur, India

Abstract Content: Introduction: This study was performed in a secondary care center in Sonitpur District, Assam, to study the usefulness of hematological indices and hemoglobin High-Pressure Liquid Chromatography (HPLC) for characterization of hemoglobinopathies and to quantify the prevalence and types of anemia in a resource poor setting of North-East India. Methods: Data of 9936 hemoglobin estimations and 708 peripheral blood smear examinations performed over a year were retrieved. Complete blood count for 170 patients was performed by XS 800i Five-Part Sysmex Cell Counter whereas hemoglobin (Hb) HPLC was outsourced. Serum iron estimation was done for 100 samples by dry chemistry and serum ferritin assay was done for 100 samples by dry chemistry and serum ferritin assay was
Abstract Table: Table 1: Results of analysis of SCD patient database according to eligibility criteria for crizanlizumab and voxelotor as described in the SUSTAIN and HOPE trials. 1,2 (no. = number, p.a. = per annum)

<table>
<thead>
<tr>
<th>Category and Number</th>
<th>Age in years (range)</th>
<th>Sex</th>
<th>Iron</th>
<th>MCH</th>
<th>Hb gm/dl (range)</th>
<th>HCT % (range)</th>
<th>MCV fl (range)</th>
<th>MCH pg (range)</th>
<th>RDW CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n = 53)</td>
<td>13.8 (0.25–30)</td>
<td>M/F</td>
<td>N/L</td>
<td>II/ND</td>
<td>27.2 (1.4-10)</td>
<td>7.1 (2.3–14.8)</td>
<td>63.2 (47.6–113)</td>
<td>18.2 (9.8–28.3)</td>
<td>23 (14.9–43.4)</td>
</tr>
<tr>
<td>HbEE (n = 31)</td>
<td>15.3 (0.8–52)</td>
<td>19/12</td>
<td>18/60/6</td>
<td>27.9 (17.6–39.4)</td>
<td>9.2 (5–12.8)</td>
<td>56.7 (44.9–81.2)</td>
<td>18.7 (14.5–25.4)</td>
<td>22.2 (15.9–39.9)</td>
<td></td>
</tr>
<tr>
<td>HBAEE (n = 25)</td>
<td>10.8 (0.5–32)</td>
<td>12/13</td>
<td>10/7/1</td>
<td>29.9 (13.8–54.2)</td>
<td>9.3 (4.1–15.1)</td>
<td>66.3 (56.7–97.8)</td>
<td>20.4 (16.2–26.9)</td>
<td>19.2 (14.3–38.1)</td>
<td></td>
</tr>
<tr>
<td>β thal trait</td>
<td>21.7 (3–48)</td>
<td>3/8</td>
<td>6/1/0/4</td>
<td>24.5 (10.3–48.5)</td>
<td>9 (2.9–13.4)</td>
<td>64.1 (52.3–83.6)</td>
<td>19.7 (16.8–25)</td>
<td>20.1 (19.6–29.7)</td>
<td></td>
</tr>
<tr>
<td>(n = 11)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β thal major</td>
<td>7 (1.8–9)</td>
<td>0/4</td>
<td>1/0/3/0</td>
<td>2.44 (0.82–3.61)</td>
<td>4.8 (1.5–6.9)</td>
<td>15.8 (5.1–21.3)</td>
<td>64.1 (50.9–70.7)</td>
<td>19.3 (18–21)</td>
<td>35.7 (31.3–41.6)</td>
</tr>
<tr>
<td>(n = 4)</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>HbSS (n = 8)</td>
<td>19.3 (4–38)</td>
<td>5/2</td>
<td>1/0/6</td>
<td>2.46 (1.6–3.86)</td>
<td>6.3 (3.3–9)</td>
<td>20.7 (11.8–30.4)</td>
<td>79 (65–103)</td>
<td>26.7 (21.7–30.4)</td>
<td>21 (16.9–32.5)</td>
</tr>
<tr>
<td>HbAS (n = 12)</td>
<td>24.9 (1.75–42)</td>
<td>7/5</td>
<td>2/2/1/7</td>
<td>2.46 (1.59–5.61)</td>
<td>10 (2.9–14.9)</td>
<td>31.6 (23.3–46.2)</td>
<td>77.4 (56.4–95.3)</td>
<td>23.9 (17.1–29.1)</td>
<td>19.3 (13.1–40.8)</td>
</tr>
<tr>
<td>Compd hetero</td>
<td>9.9 (0.8–30)</td>
<td>8/6</td>
<td>6/1/4/4</td>
<td>3.0 (0.9–5.2)</td>
<td>6.2 (2.1–10.9)</td>
<td>19.7 (7.5–29.6)</td>
<td>67.1 (47.4–83.4)</td>
<td>21.5 (16.2–27.2)</td>
<td>25.4 (17.5–36.7)</td>
</tr>
<tr>
<td>(n = 15) 1*pt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inconclusive</td>
<td>7.7 (0.2–27)</td>
<td>8/3</td>
<td>5/2/0/4</td>
<td>2.46 (0.82–361)</td>
<td>6.8 (2.2–10.4)</td>
<td>23.3 (9.1–32.8)</td>
<td>66.7 (43.2–93.8)</td>
<td>19.3 (13.1–28.8)</td>
<td>22.1 (14.5–30.7)</td>
</tr>
</tbody>
</table>

Ineligibility due to anemia was present in 79.6% of samples. Microcytic hypochromic anemia was present in 52% patients. Mean age of was 15.4 years (3 months–56 years) with a slight female preponderance. Erythrocytosis was observed in 18.8% of samples. Microcytosis with low MCH was observed in 143 (84.1%) and 153 (90%) samples, respectively. On the basis of HB HPLC patients were categorized as: no abnormality in 53 (31.2%), hemoglobin E disease 31 (18.2%), hemoglobin E trait 25 (14.7%), ß-thalassemia minor 11 (6.5%), ß-thalassemia major 4 (2.4%), compound hemoglobinopathy 15 (8.8%), sickle cell trait 12 (7%) and sickle cell disease 8 (4.7%), and inconclusive in 11 (6.5%) patients. Serum iron was low in 39 (34.5%), normal in 65 (57.5%), and high in 9 (8%) of the 113 subjects tested. Conclusions: Prevalence of anemia and hemoglobin E abnormality was high with unexpected severe anemia in some heterozygotes for HbE, HbS, and β-thalassemia. Hemoglobin HPLC was useful in arriving at a presumptive diagnosis and must be used as a frontline investigation even in resource-poor settings.

Disclosure of Interest: M. Mishra: None Declared, B. Sangma Conflict with: Medical officer, D. George: None Declared, L. John: None Declared, K. George Conflict with: Consultant

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Eligibility for emerging therapies in sickle cell disease

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Abstract Content: Management of patients with sickle cell disease (SCD) in the UK relies largely on transfusion therapy and hydroxy-carbamide alongside supportive care. New therapies to improve morbidity and mortality are needed. Two new therapies undergoing NICE technology appraisal are crizanlizumab and voxelotor. Crizanlizumab, a p-selectin inhibitor, has been shown to reduce the frequency of vaso-occlusive crisis in patients aged 16 or over in a randomised, placebo-controlled phase 2 trial (SUSTAIN). Voxelotor is an HbS polymerisation inhibitor and showed increased haemoglobin levels with reduced markers of haemolysis in a phase 3 trial (HOPE). Both were approved by the FDA in November 2019.

The eligibility criteria used in the SUSTAIN and HOPE trials have been compared against the Bristol Haematology and Oncology Centre and Oxford University Hospitals SCD cohorts to identify those patients who would be eligible for these emerging therapies. The patient databases were cross-referenced with electronic notes to identify eligibility data. Vaso-occlusive crises (VOC) were determined by calls to the haemoglobinopathy team or helpline, attendance at the Acute Haematology Unit or admission. Electronic blood results were checked to ensure haemoglobin fell within the specified ranges. Results of analysis of SCD patient database according to eligibility criteria for crizanlizumab and voxelotor as described in the SUSTAIN and HOPE trials are shown in Table 1. Results show that, out of 158 patients with eligible sickle cell disorders, only 7 (4.4%) were eligible for both therapies. 8 (5.1%) were eligible for voxelotor only, and 2 (1.3%) were only eligible for crizanlizumab. Patients with tested by direct chemiluminescence for 13 patients. The number of hospital visits, hospitalization duration, blood transfusions, demographic profile, and unusual features in some patients was recorded.

Results: Anemia was present in 79.6% of samples. Microcytic hypochromic anemia was present in 52% patients. Mean age of was 15.4 years (3 months–56 years) with a slight female preponderance. Erythrocytosis was observed in 18.8% of samples. Microcytosis with low MCH was observed in 143 (84.1%) and 153 (90%) samples, respectively. On the basis of HB HPLC patients were categorized as: no abnormality in 53 (31.2%), hemoglobin E disease 31 (18.2%), hemoglobin E trait 25 (14.7%), ß-thalassemia minor 11 (6.5%), ß-thalassemia major 4 (2.4%), compound hemoglobinopathy 15 (8.8%), sickle cell trait 12 (7%) and sickle cell disease 8 (4.7%), and inconclusive in 11 (6.5%) patients. Serum iron was low in 39 (34.5%), normal in 65 (57.5%), and high in 9 (8%) of the 113 subjects tested.

Conclusions: Prevalence of anemia and hemoglobin E abnormality was high with unexpected severe anemia in some heterozygotes for HbE, HbS, and ß-thalassemia. Hemoglobin HPLC was useful in arriving at a presumptive diagnosis and must be used as a frontline investigation even in resource-poor settings.

Disclosure of Interest: M. Mishra: None Declared, B. Sangma Conflict with: Medical officer, D. George: None Declared, L. John: None Declared, K. George Conflict with: Consultant

Abstract Table: Table 1: Results of analysis of SCD patient database according to eligibility criteria for crizanlizumab and voxelotor as described in the SUSTAIN and HOPE trials. 1,2 (no. = number, p.a. = per annum)
no VOC in 12 months were ineligible for either therapy \( (n = 75, 47.5\%) \) and just under half of these patients had a baseline haemoglobin over the range of eligibility for voxelotor \( (n = 37, 23.4\%) \). 5 patients with a single VOC in 12 months had an Hb out of range for voxelotor \( (3.2\%) \). Regular transfusion therapy was the second most common exclusion \( (n = 29, 18.3\%) \). Age over 65 excluded 8 \( (5.1\%) \) of our patients, and 6 \( (3.8\%) \) had significant comorbidity that rendered them ineligible. 15 \( (9.5\%) \) of our patients had moved out of area so estimates of VOC per year are likely to be inaccurate. Other reasons for exclusion included titration of hydroxycarbamide and family planning.

Though new therapies are being developed for prevention of VOC in SCD, few patients in our cohort are eligible for these. Incidence of severe VOC may be underestimated as patients self-manage at home, particularly in the current COVID-19 pandemic. This should be kept under review and closer liaison with patients about their VOC may help identify eligible patients. Strict adherence to eligibility based on that of clinical trials is likely to result in very few patients benefitting from these new therapies.

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**Education and Professional**

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**COVID-19 VTE Champions: a supportive quality improvement programme that optimised thromboprophylaxis in patients with COVID-19**

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**Abstract Content**: COVID-19 is associated with an increased risk of venous thromboembolism (VTE). During the start of the pandemic, admission rates rapidly increased, there was a redeployment of healthcare professionals, and changes in thromboprophylaxis guidelines for patients with COVID-19. Medical teams were under a great deal of pressure. There was an urgent need to support all healthcare professionals as well as to ensure the optimal use of thromboprophylaxis.

The aim was to coordinate a hospital-wide quality improvement programme to both improve thromboprophylaxis use and to support medical teams.

A quality improvement programme called ‘COVID-19 VTE champions’ was developed to ensure both the comprehensive assessment and treatment of VTE risk, as well as to support healthcare professionals. Junior doctors, within a large UK-based teaching hospital, were contacted in March 2020 and asked to volunteer to take part in the programme. At least two VTE champions were assigned to each ward caring for patients with COVID-19. Support was provided to all medical wards with peer-to-peer teaching. An audit was performed to assess the use of new COVID-19 specific thromboprophylactic guidelines. A survey of VTE champions was performed in January 2021 to assess the success of the programme.

Thirty junior doctors volunteered and were recruited to the VTE champions programme. Weekly virtual meetings were arranged to educate the VTE champions about new thromboprophylaxis guidelines, arrange the audit and to coordinate peer support. VTE champions provided both ‘on-the-job’ teaching to the other healthcare professionals working with them, and more traditional tutorials to their peers. This focussed on the need for optimisation of thromboprophylaxis and the new guidelines being implemented for medical patients with COVID-19. The group audited the VTE thromboprophylaxis assessments performed on all medical in-patients each week, to identify areas within the hospital where further teaching or support was needed. A comprehensive audit of all patients admitted between the 1st April 2020 and 15th May 2020 was also performed to assess the impact of the new thromboprophylaxis guidelines. A total of 569 cases (179 COVID-19 positive, 390 COVID-19 negative) were assessed. Most patients with COVID-19 (86%) received thromboprophylaxis in accordance with the new guidelines.

VTE champions were given the opportunity to present their data locally, regionally and nationally. Multiple conference abstracts have been written and a manuscript has been submitted for publication. All VTE champions were surveyed following implementation of this programme. The majority of the VTE champions (75%) felt 'very supported' whilst participating, 100% enjoyed the project ('a little'-a lot'), 100% felt more confident performing quality improvement projects in the future and 100% felt it helped meet curriculum requirements/contributed to their portfolio.

The VTE champions programme was successful in coordinating a hospital-wide audit, leading to effective implementation of new thromboprophylaxis guidelines during the COVID-19 pandemic. Peer-to-peer supportive teaching and a coordinated approach, increases interest and success in quality improvement projects, leading to improved patient outcomes. This is an effective way to implement clinical change quickly, efficiently and in a supportive way.

**Disclosure of Interest**: None Declared

**BSH2021-PO-026**

**The development of an ambulatory community service for post-HSCT patients to promote shielding during the SARS-CoV-2 pandemic**

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**Abstract Content**: Introduction: In the spring of 2020 as the SARS-CoV-2 pandemic escalated, health care systems came under increasing pressure to minimise the exposure of the virus to vulnerable and immunocompromised patients. Telemedicine suddenly became part of our daily practice as the haematopoietic stem cell transplant (HSCT) patients were urged to remain isolated whilst innovative changes in health care practice to protect patients were encouraged. Svahn et al (2002) as part of a large case-controlled study suggest that visiting patients post-HSCT in the community rather than patients attending for regular hospital visits decreases HSCT infection-related complications. Thus, in response to the SARS-CoV-2 pandemic, the Bristol BMT team developed and implemented a post-HSCT ambulatory community service.

**Method**: The community visits to the post-HSCT patients at the hospital apartments are undertaken by 2 people; either a BMT associate specialist and BMT advanced clinical practitioner or BMT clinical nurse specialist. These combinations allow for continuity of care but also provide a robust service provision during the SARS-CoV-2 pandemic. Clinical governance was paramount in the development of this service; an MDT written standard operating procedure was reviewed at both the local COVID-19 pandemic response meeting and the BMT quality governance meeting. The service remains time efficient as this is simply a rearrangement in current service provision which protects the most vulnerable patients.

As part of the visit, we undertake a comprehensive holistic review including medicines review and optimisation, psychology support and clinical examination if indicated. Patients’ weight, bloods tests including routine haematology and biochemistry, BMT PCR and immunosuppression level monitoring are taken. We are able to monitor chimerisms at appropriate time points and undertake all central line care. At each consultation we have online access to the patients’ electronic medical notes, so we can access and update their clinical data.

**Results**: The service started on 6 April and continues to run successfully. Data collected since 6 April shows the BMT service has undertaken over 600 individual visits for 41 patients; both post-allograft patients and CAR T cell patients. To date, none of the patients receiving community care have developed SARS-CoV-2.

A patient satisfaction survey was undertaken surveying 15 patients seen during the first wave of the pandemic. Of 15 surveys distributed...
there was an 86.7% return rate. The patients surveyed reported feeling comfortable allowing their apartments, they felt safe and able to discuss all their concerns during the review. All of them, when given the choice of location of consultations opted for the apartments rather than the hospital setting. 100% of respondents reported the service as ‘excellent’.

Conclusion: Throughout the literature, there are many excellent services which have been developed to give patients choice over where they receive their oncology out-patient care (Robottom 2013, de Lord 2015, Gunter et al 2012). Such services report that the delivery of home based, holistic, patient-centred care has benefitted patients whilst reflecting national standards designed to enhance the quality of care. We strongly believe that this service development also reflects patient choice in the delivery of effective, patient-centred post-HSCT care whilst promoting shielding during the SARS-CoV-2 pandemic.

Disclosure of Interest: None Declared

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Use of machine learning-enabled scenario-based teaching in Haematology and Biomedical Science, as a replacement and supplement to traditional tools and in-person teaching during COVID-19

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Abstract Content: One of the biggest challenges during the COVID-19 pandemic has been maintaining student engagement and providing the best learning experience with limited face-to-face (FTF) contact. Whilst multiple tools are available to provide some interactivity in online learning, such as quiz software and virtual laboratories, there are limited options for continuous learning, or decision-making, such as interpretation of case studies or scenarios.

Alongside traditional teaching forms such as lectures (albeit online), we utilised a machine learning-enabled scenario-based tool (Resimion) with BSc (Hons) Biomedical Science students (n = 150 second- and n = 52 third-year), to replace activities which would normally have been laboratory-based or FTF tutorials. With this tool, students see and understand the impact of decisions they make, based on text and other media. Decision-making is tracked, and continuous engagement monitored, as well as formative and summative feedback provided.

Our data shows considerably increased student engagement when using tools such as Resimion. Third-year haematology students were provided with an optional post-lecture Resimion case study and an alternative online quiz, with uptake of 75% and 12% respectively.

In 53% of cases, students took a given scenario more than once, obtaining a better outcome in 76% of additional attempts. Further, using peer reminders, where students are reminded to attempt the scenario and the percentage of their cohort who have already engaged is indicated, engagement increased by 14%.

Whilst student engagement remains a major goal of institutions, student outcome is the primary endpoint. Resimion optimises reminder communications so that learning occurs at the student’s personal optimal time (OT) of the day and week, to maximise outcomes. Using Re-enforcement Learning (a machine learning discipline), Resimion uses Markov Decision Processes to determine OT based on i) individual historic OT, ii) best outcome OT, and iii) cohort OT. It took 3 scenarios to determine the best OT, achieving a 9% increase in our students selecting the optimal scenario path and therefore the best outcome.

A considerable issue highlighted in the past year has been digital poverty and access for some students to resources. We did not experience this issue in this study, due to access via a standard web browser or through the app on any mobile device. Further, 1.2% of scenarios run within our cohort would have been unable to do so without the inbuilt accessibility features.

Student feedback using this approach was very positive, with requests to increase use within teaching in every module that used it. Competitive, real-time scenarios in live online tutorials were particularly popular. This produced cohort cohesion and peer-learning in times where students tend to otherwise feel very isolated.

Scenario-based learning is an effective tool to complement or replace existing teaching and assessment methods. Of note are laboratory practicals and clinical case studies, where learners undertake logical decision-making, choosing most appropriate tests to reach the correct diagnosis. Detailed feedback is provided to the learner and lecturer, enabling modification of current and future sessions to address poor understanding. Based on a wealth of literature confirming retention of 90% of active learning, versus 10% of passive learning, scenario-based teaching is a valuable addition to our toolbox of methods for haematology and biomedicine.

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Laboratory Haematology and Transfusion

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One step at a time: delivering a safe laboratory service for transfusion
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Abstract Content: Risk management improves quality and safety of healthcare services by identifying the circumstances that put patients at risk of harm and then acting to prevent or control those risks. Incident reporting and investigations play an important part in helping identify risks. Effective risk identification practices include both reactive and proactive approaches. A systems-based approach provides more efficient and safer systems, and human factors and ergonomics can complement this by identifying how people work within these systems.

The Serious Hazards of Transfusion (SHOT) haemovigilance scheme collects and analyses data regarding serious adverse events and serious adverse reactions of blood components transfused in the United Kingdom. Incidents attributed to errors within the laboratory are further categorised into the step where the error primary occurred; sample receipt and registration (SRR), testing, component selection (CS) and component labelling, availability and handling and storage (CL, A, H&S). Transfusion laboratories are integral to patient management and staff must have diverse knowledge and skills to provide effective transfusion support for patients. Errors may occur at any of these steps and have the potential to cause patient harm. Analysis of errors in safety critical steps helps improve processes.

Laboratory errors reported to SHOT from January 2015–December 2019 were retrospectively analysed to determine at which step in the laboratory process errors occurred.

Laboratory errors accounted for 2267/7115 (31.9%) of all reports. The proportion of laboratory errors remained stable over this period, with an average of 31.9% (±5.0%). Most errors occurred at the CL, A, H&S step, 964/2267 (42.5%), followed by testing 504/2267 (22.2%), SRR 464/2267 (20.5%) and CS 259/2267 (11.4%). The highest proportion of CL, A, H&S errors occurred in 2018, accounting for 271/530 (51.1%) of all laboratory errors reported.

CL, A, H&S is the terminal step within complex laboratory processes and is the last chance for the laboratory to detect and rectify errors in component selection or labelling. In 2019, SHOT launched the ‘Component exit check’ to encourage laboratory staff to take a ‘stop moment’ and review components before release. However, this step encompasses several processes, it is possible that if these steps (labelling the component, its availability and the physical storage of the component) were considered separately, different results would be seen.

Data from SHOT has repeatedly identified that a high proportion of laboratory transfusion errors occur at these critical stages. Transfusion errors adversely impact patient safety and every effort must be made to reduce these errors. Staff need to be vigilant and work towards getting it right first time at every step of the transfusion process. However, with certain steps being more prone to errors, it is vital that risk management approaches take this into consideration.

CL, A, H&S and testing are the safety critical steps which must be closely considered when designing laboratory layout, time allocation and staff resources, to ensure safe patient care is delivered. Staff should not be distracted, and they should have the appropriate resources to provide a safe service. Learning from previous incidents should be shared, and staff should be encouraged to engage in brainstorming, effective change management and safety walkabouts for proactive risk identification approaches.

Disclosure of Interest: None Declared
Joint Health Outcomes in Patients with Hemophilia A Receiving Antihemophilic Factor (Recombiant) in a Real-world Setting: Results of a 6-year Interim Analysis of the AHEAD International Study

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Abstract Content: The antihemophilic factor (recombinant) (rAHF) hemophilia A outcome database (AHEAD) study evaluates long-term effectiveness and safety outcomes in patients with hemophilia A receiving rAHF in routine clinical practice. This 6-year interim analysis assessed age-stratified joint health in AHEAD study patients receiving either prophylactic (PRO) or on-demand (OD) rAHF.

AHEAD is an international, non-interventional, prospective, multicenter study (NCT02078427, started in 2011) including patients with moderate (factor VIII activity 1-5%) or severe (factor VIII < 1%) hemophilia A. Ethics committee approval and patients’ informed consent were obtained. The primary objective for AHEAD is to describe joint health outcomes. In this analysis, joint health was assessed using the pain (score 0–3), bleeding (score 0–3), and physical exam (score 0–12) Gilbert scale parameters; higher scores for each category represent worsening conditions. Here we report results of the 6-year interim descriptive analysis in patients aged 2 to <12, 12 to <18, and ≥18 years with available Gilbert score data (data cutoff: 15 July 2019).

At year 1, Gilbert score data from 52 children (2 to <12 years; all PRO), 19 adolescents (12 to <18 years; all PRO), and 116 adults (≥18 years; PRO, n = 86; OD, n = 30) were available for analysis. In PRO children, average Gilbert scores remained consistently low throughout the observation period (Table 1); scores were lower in children and adolescents than in adults. Among adults aged ≥18 years, means and medians for average Gilbert scores were consistently lower in patients receiving rAHF PRO versus OD; this may represent a clinically meaningful difference. No new safety signals were observed for this 6-year interim analysis versus previous analyses.

These real-world data in patients with moderate and severe hemophilia A support early initiation of PRO rAHF as a treatment strategy to preserve joint health.

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Does apixaban pretreatment alter alteplase-induced thrombolysis: An in vitro study?
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Abstract Content: Non-vitamin K antagonist oral anticoagulants (novel oral anticoagulants [NOACs]) are frequently used for secondary prevention of thrombotic events in patients with atrial fibrillation and previous stroke. Apixaban is a NOAC, which directly inhibits both free and clot-bound coagulation factor FXa, preventing prothrombin cleavage to active thrombin. With increasing number of patients treated with apixaban, there is increasing number of patients on apixaban who have stroke recurrence. However, it is unclear if such patients could receive intravenous thrombolysis, which is the first-line treatment for acute ischemic stroke. Therefore, the aim of this study was to investigate the interaction between apixaban pretreatment and alteplase-induced thrombolysis using combination of two in vitro thrombolytic models.

Red blood cell (RBC) dominant clots, with and without apixaban, were prepared from the blood of healthy human donors and subsequently exposed to alteplase treatment. All blood donors had agreed to donate blood samples on the premise of signed informed consent for the collection of blood. Static and flow models, which were optimized to determine the suitably measurable effect of alteplase in highly repeatable manner, were used. The static model consisted of plastic tubes filled with medium, in which the clots were individually incubated; the flow model comprised of silicone chips with bifurcation to enable permanent circulation in the system, thus maintaining the hydromechanical forces involved in the clot removal. Each system was maintained at 37°C for 60 minutes (static model) or 180 minutes (flow model). Apixaban and alteplase were used at clinically relevant concentrations, ie. 250 ng/ml and 1.3 mg/L, respectively. Clot lysis in the static model was determined by clot mass loss and spectrophotometric determination of RBC release. Clot lysis in the flow model was determined by measuring recanalization time, clot length and spectrophotometric determination of RBC release. In the static model, clots without apixaban; compared to those with apixaban had alteplase-induced mass loss 54±8% vs. 53±8%, P = 1.00; RBC release 0.14±0.04 vs. 0.12±0.04, P = 0.14, respectively. Very similar results were obtained if plasma was used instead of physiological buffered saline as the incubation medium. In the flow model, plasma was used as incubation medium; clot lysis without apixaban compared to those with apixaban was as follows: recanalization time 107.46 min vs. 127.31 min, P = 1.00; recanalization frequency 90±22% vs. 90±22%, P = 1.00; clot volume reduction 32±15% vs. 34±10%, P = 1.00; RBC release 0.029±0.007 vs. 0.022±0.0079, P = 0.16, respectively.

Apixaban at clinically relevant concentration did not alter the level of alteplase-induced thrombolysis and recanalization in both the in vitro static and flow models. Our data support current clinical practice, that thrombolysis remains contraindicated in stroke treatment for patients who have been treated with anticoagulants because such combination is likely to increase bleeding risk but does not offer benefit in terms of improving recanalization rates.

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Point of care testing to monitor vitamin K antagonist international normalised ratio (INR) control in patients with antiphospholipid syndrome during the COVID-19 pandemic
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Abstract Content: Patients with persistent antiphospholipid antibodies (APA) are at risk of thrombotic complications. Current guidelines for management of antiphospholipid syndrome (APS) recommend patients with unprovoked thrombosis have lifelong anticoagulation to prevent recurrence. This has been mainly with vitamin K antagonists (VKAs) such as warfarin. Warfarin has an unpredictable anticoagulant effect and requires regular monitoring to maintain adequate dosing. Although point of care testing (POCT) is widely used to monitor INR, its use for APS patients has been discouraged over concerns of an interaction between APA and POCT testing reagents falsely influencing results. The COVID-19 pandemic has highlighted the many benefits of POCT to self-monitor INRs. Minimising hospital visits reduces strain on pressurised NHS services, and prioritises patient safety by limiting spread of the virus.

The aim of this study was to review the reliability of POCT INR monitoring of anticoagulation in patients with APS during the COVID-19 pandemic.

36 patients with APS (6 male and 30 female, age range 27–79 years old) using POCT were included. Paired POCT INR and venous INRs monitored using CoaguChek XS devices at Guy’s and St Thomas’ Hospital from July 2018 to February 2021 were compared. The six-month time in therapeutic range (TTR) was compared to both control cohorts; 72 patients with APS (25 male & 47 female, age range 44–82 years old) using venous INR monitoring only, and 30 non-APS patients with similar thrombotic indications (17 male & 13 female, age range 20–91 years old) also using POCT.

87.2% of paired POCT and venous samples (n = 94) had an acceptable INR variation (≤±5.5 difference) in the APS POCT cohort and a high correlation between POCT and venous testing (r = 0.9) excluding any INR results ≥4.8. This decreased to 79.1% when paired results with POCT between 4.8–8.0 were included and showed a similar high correlation (r = 0.87). Bland-Altman analysis of all APS POCT paired samples (n = 115) showed high concordance. Mean six-month TTR for APS patients using POCT was 57.1% (±24.8); compared to both 59.2% (±23.2) in the venous testing APS cohort (P = 0.66) and 80.0% (±18.9) in non-APS patients using POCT (P = 0.0002).

Results from this study showed high concordance between paired POCT and venous testing INR results, supporting POCT as a valid method for monitoring warfarin therapy in patients with APS. Additionally, six-month TTRs were comparable between APS patients using POCT and those using venous monitoring only. With the rise in telemedicine accelerated by the COVID-19 pandemic, these results may encourage the future remote management of APS and active patient involvement in their care, although this requires further study.

Disclosure of Interest: None Declared
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Quality of life and its predictors among adult patients with haemophilic arthropathy

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Abstract Content: Recurrent hemarthrosis that begin in childhood lead to progressive joint deterioration. Patients with haemophilia have chronic pain, functional disability and a reduced perception of health-related quality of life.

The objective was to analyse the perceived quality of life of adult patients with haemophilic arthropathy and its relationship with pain, joint condition, kinesiophobia and catastrophism.

Eighty-three adult patients with haemophilia were included in this multicentre, cross-sectional, descriptive study. Perceived quality of life (36-Item Short Form Health Survey), perceived usual and maximum pain (visual analogue scale), joint condition (Haemophilia Joint Health Score), kinesiophobia (Tampa Scale of Kinesiophobia) and catastrophism (Pain Catastrophizing Scale) were assessed. Sociodemographic, clinical and therapeutic variables and drug consumption for pain control were collected. Descriptive statistics used means and standard deviations. The correlation of quality of life with the dependent variables was calculated with the Pearson correlation test. The differences in quality of life as a function of the binomial variables were calculated with Student’s t-test for independent samples.

Physical component of quality of life perceived by patients with hemophilia is lower than Spanish population (30.51 vs. 48.85). Regarding the mental component, patients with hemophilia showed higher values (56.07 vs. 49.97). Catastrophism correlated (P < 0.05) with all items of quality of life questionnaire. Kinesiophobia correlated (P < 0.05) with all items of quality of life except to role-emotional (r = −0.18; P > 0.05). Habitual and maximal joint pain correlated with all items except to role-emotional (r = −0.19 and r = −0.09, respectively) and mental component score (r = −0.16 and r = −0.07, respectively). Catastrophism and weekly drug intake were inversely correlated with quality of life. Age was positively correlated with perceived quality of life. There were differences in quality of life as a function of the severity of haemophilia and the intake of drugs for pain control.

The perceived quality of life of adult patients with haemophilia is worse than that of the Spanish population. Pain, kinesiophobia, catastrophism, haemophilia severity and the intake of pain-control medication influence the quality of life of these patients.

Disclosure of Interest: None Declared
ALL, AML, MDS & bone marrow failure

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Anthracycline-induced cardiomyopathy in paediatric acute myeloid leukaemia-A single centre age-stratified retrospective analysis and the early impact of dexrazoxane
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Abstract Content: As survival rates for paediatric acute myeloid leukaemia (AML) have improved over recent decades, the risk of anthracycline-induced cardiomyopathy has become an increasing concern for the treating clinician and can have detrimental effects on the quality of life of survivors. Despite this, data regarding the frequency of cardiotoxicity amongst this population is rare in the United Kingdom and various risk factors have been associated, including age less than 4 years. Dexrazoxane has been shown as an efficacious agent in the prevention of anthracycline-induced cardiotoxicity, however, in 2011 its use in the paediatric population was contraindicated by the EMA due to lack of efficacy in this cohort and concerns about its side effect profile. Subsequent analysis has resulted in its acceptance as a cardioprotective agent in the treatment of paediatric malignancies.

We conducted a retrospective analysis of all patients who had been diagnosed with AML at BCH over the 5-year period between January 2016 and January 2021. Our aim was to assess the frequency of anthracycline-induced cardiotoxicity in the paediatric AML population, the effect of age, and the impact that dexrazoxane has had since its routine incorporation into anthracycline-containing treatment protocols. The patient cohort was obtained from the departmental database and clinical information and echo reports were obtained from hospital online record systems, PEPR and Heart-Suite.

40 patients received a diagnosis of AML at BCH over the 5-year study period, 2 patients were excluded as they died prior to treatment, leaving 38 patients for analysis with a mean age of 6 years 10 months. 3 patients had relapsed disease, the remaining 35 were primary presentations and 17 patients were aged under 4 years, with 5 patients having Down Syndrome. Mean left ventricular ejection fraction (LVEF) prior to 1st course of treatment was 67% (65% in those aged over 4 years and 69% in the younger cohort), decreasing to 61% post 1st course anthracycline-containing treatment and 59% at the end of treatment (see table 1). 6 patients (16%) experienced a significant reduction in cardiac function secondary to anthracycline chemotherapy, with 1 patient now on a palliative pathway due to dilated cardiomyopathy despite her AML being in remission. 4 of these patients are under long-term cardiology follow up and the remaining patient died of transplant complications. Out of the 5 patients who received dexrazoxane prior to their anthracycline therapy, no deterioration in cardiac function was observed, and all these patients count recovered prior to their day 35 bone marrow assessments.

Our data highlights the significant impact that anthracycline-induced cardiac toxicity can have on paediatric AML patients, particularly those aged under 4 years, and the promising benefit that dexrazoxane may have in addressing this longstanding problem.

Abstract Table:
Table 1 Age-stratified impact of anthracycline chemotherapy on cardiac function at different stages in AML treatment

<table>
<thead>
<tr>
<th>Parameter (mean)</th>
<th>Pre #1</th>
<th>Post #1</th>
<th>End of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction</td>
<td>Overall</td>
<td>67%</td>
<td>61%</td>
</tr>
<tr>
<td></td>
<td>&gt;4 years</td>
<td>65%</td>
<td>61%</td>
</tr>
<tr>
<td></td>
<td>&lt;4 years</td>
<td>69%</td>
<td>62%</td>
</tr>
<tr>
<td>Fractional shortening</td>
<td>Overall</td>
<td>35%</td>
<td>Incomplete data</td>
</tr>
<tr>
<td></td>
<td>&gt;4 year</td>
<td>35%</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>&lt;4 years</td>
<td>35%</td>
<td>Incomplete data</td>
</tr>
</tbody>
</table>

* 1 patient now palliative due to dilated cardiomyopathy.

Disclosure of Interest: None Declared

BSH2021-PO-034
A regional experience of NGS Myeloid panels in Myeloid Haematological malignancies
Sebastian Francis1, Ferkhanda Zareen1,*, Catherine Turner1, Jack Neeson1
1Haematology, Sheffield Teaching Hospitals NHS Foundation Trust, SHEFFIELD, United Kingdom

Abstract Content: Next generation sequencing (NGS) myeloid panels have revolutionised the diagnosis of myeloid malignancies. It has become an important diagnostic tool alongside the bone marrow biopsy and karyotype. The European Leukaemia Network (ELN) has incorporated molecular abnormalities to risk stratify Acute Myeloid Leukaemia (AML) and various risk scores in Myelodysplasia (MF) and Chronic Myelomonocytic Leukaemia (CMML) also incorporate molecular mutations. NGS is generally indicated in patients under the age of 70 with blood cancers including AML, Myelodysplastic Syndrome (MDS), MF, CMML and Myeloproliferative Neoplasms (MPN). NGS testing can be requested inappropriately for several reasons such as having no impact on clinical management and those receiving unnecessary repeat tests without disease progression. We assessed the financial impact on clinical management and those receiving unnecessary NGS test results processed between 13/3/2018-16/4/2020 were collected alongside patient demographics, clinical test request details, diagnoses and bone marrow (BM) biopsy results (BM taken at closest time-point to NGS test request) using the Haematono-Oncology Diagnostic Service (HODS) computer system. Patient groups were subdivided by haematological diagnosis (AML/MDS/MF/MPN/CMML)/‘normal’ BM and ‘other’ haematological diagnosis. The financial cost of unnecessary NGS testing from five UK hospital haematology departments over a two-year period.

NGS test results processed between 13/3/2018-16/4/2020 were collected alongside patient demographics, clinical test request details, diagnoses and bone marrow (BM) biopsy results (BM taken at closest time-point to NGS test request) using the Haematono-Oncology Diagnostic Service (HODS) computer system. Patient groups were subdivided by haematological diagnosis (AML/MDS/MF/MPN/CMML)/‘normal’ BM and ‘other’ haematological diagnosis. The financial cost of unnecessary NGS testing from five UK hospital haematology departments over a two-year period.

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doi: 10.1111/bjh.17492
based on age, test repetition, diagnoses and disease progression. The reasons for unneeded tests were documented.

Of 431 NGS tests recorded, diagnoses included AML (N = 92), MDS (N = 83), MF (N = 49), MPN (N = 52), CMML (N = 50), ‘normal’ BM (N = 99) and ‘other haematological diagnosis’ (N = 26). Patients had an average age of 61 years. 235/431 (54.5%) had MDS and over half of all tests considered unnecessary. Education regarding NGS requesting is needed particularly in ensuring preliminary checks for common causes of pancytopenia have been completed before requesting more in-depth tests. NGS myeloid panels are not required if the BM appearances are within normal limits. The NGS myeloid panel can identify patients with the TP53 mutation who have poor outcomes post allograft.

Disclosure of Interest: None Declared

**BSH2021-PO-035**

**Response of Immunosuppressive Therapy in patients of Acquired Aplastic Anemia: Real world experience from a developing country**

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Abstract Content: **Introduction:** Acquired Aplastic Anemia is a rare bone marrow failure syndrome characterized by pancytopenia with a hypoplastic bone marrow. The underlying cause of Aplastic Anemia is unknown; however, a number of patients cannot undergo HSCT either due to lack of suitable donor or unfit to receive HSCT. Immunosuppressive therapy (IST) can lead to hematologic improvement in Acquired AA.1

**Objective:** To determine the response of IST in patients of Acquired AA

**Materials and Methods:** We conducted a retrospective single centre study at AFBMTC / NIBMTC for patients of acquired AA. Study duration was January 2002 to December 2019. Inclusion criteria included diagnosed cases of acquired AA receiving IST for at least 12 weeks, both genders and all age groups. Exclusion criteria included patients not completing 12 weeks of IST due to death, side effects or non-compliance. IST included Cyclosporin (CsA) alone, CsA + Androgens, CsA + Rabbit Anti Thymocyte Globulin (aATG), CsA + Anti lymphocyte Globulin (ALG). Primary outcome measure was response to IST; secondary outcome measure was overall survival (OS).

**Results:** A total of 511 patients received IST. Out of which 371 (72.5%) were males and 140 (27.5%) were females. Median age was 23 years (range 2-97 years). We had 116 (22.7%) patients with NSSA, 278 (54.40%) with SAA, and 117 (22.89%) with VSAA. In study cohort, 155 (30.2%) patients responded to the IST, out of which 63 (12.3%) patients achieved complete response (CR) while 92 (17.9%) patients achieved partial response (PR). The ORR according to disease severity was best seen in NSAA group 50.4% followed by SAA group (28.7%) and VSAA group (13.7%). There is a significant association between disease severity and response rate (P < 0.001). The ORR of CsA alone in NSAA, SAA and VSAA was 52.60%, 28.10% and 10% respectively whereas ORR of CsA + androgen in NSAA, SAA and VSAA was recorded to be 18.10%, 18.10% and 0% respectively. The ORR of CsA + ATG in NSAA, SAA and VSAA was 50%, 35.10% and 22.50% respectively whereas ORR of CsA + ALG in NSAA, SAA and VSAA was 100%, 43.70% and 33.30% respectively.

OS was 38% at a median follow up of 36 months. There was a significant difference in the survival distributions of different treatment modalities (P = 0.016). Median survival time 60 months (CsA), 9 months (CsA+ androgens) and 39 months (CsA+ ATG/ ALG). The percentage of patients surviving in the group receiving CSA alone was 45%, which is significantly higher than the group receiving CSA with androgen (P = 0.005) in which 33% patients survived at the end of the study. The percentage of patients surviving at the end of the study in the group receiving CSA+ATG/ALG was 36%. The survival rates of patients differ significantly according to disease severity (P < 0.001). Survival rate at the end of the study was 62% in NSAA group. Since more than 50% patients survived till the end of the study, median is not reported. Median survival time was 47 months (SAA) and 10 months (VSAA). 43% patients with SAA and 18% with VSAA survived by the end of the study.

**Conclusion:** In developing countries with limited availability of hATG, use of ratATG with CsA is not superior to CsA alone. CsA alone results in adequate responses in patients with NSAA.

**Reference**

1. Hoffbrand AV, Higgs DR, Keeling DM, Metha AB. Postgraduate Haematology

**Table:**

<table>
<thead>
<tr>
<th>Response outcome according to disease severity (n (%))</th>
<th>NSAA</th>
<th>SAA</th>
<th>VSAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responded</td>
<td>59 (50.4%)</td>
<td>80 (28.7%)</td>
<td>16 (13.7%)</td>
</tr>
<tr>
<td>Not responded (NR)</td>
<td>42 (36.2%)</td>
<td>168 (60.4%)</td>
<td>86 (73.5%)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

**BSH2021-PO-036**

**Prognostic significance of BAALC expression in cytogenetically normal acute myeloid leukemia**

Anita Chopra1, Deepak Verma1, Rajive Kumar2, Jay Singh3, Shadab Ali4, Sameer Bakshi5, Atul Sharma6, Jayanth Kumar Palanchamy7, Surender Kumar Sharawat8

1Laboratory Oncology, Dr. BRAIRCH, AIIMS, New Delhi, India, 2Mahavir Cancer Sansthan, Patna, Bihar, India, 3Department of Pulmonary Medicine, AIIMS, New Delhi, India, 4Medical Oncology, Dr. BRAIRCH, AIIMS, New Delhi, India, 5Department of Biochemistry, AIIMS, New Delhi, India

**Abstract Table:**

<table>
<thead>
<tr>
<th>Response to treatments n (%)</th>
<th>NSAA</th>
<th>SAA</th>
<th>VSAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responded</td>
<td>155 (30.2%)</td>
<td>63 (12.3%)</td>
<td>92 (17.9%)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared
Abstract Content: Title: Prognostic significance of BAALC expression in cytogenetically normal acute myeloid leukemia

Acute myeloid leukemia (AML), a cytogenetically and molecularly heterogeneous disease, constitutes approximately 35% of adult leukemia. Karyotype at the time of diagnosis provides the most important prognostic information in adults with AML. However, 40 to 50% of patients do not have clonal chromosomal aberrations. This karyotypically normal group, CN-AML, less well understood biologically and clinically, has been shown to have mutations and altered gene expression that predict prognosis. Brain and acute leukemia, cytoplasmic (BAALC) has been identified as a leukemia-associated gene and has been shown to be highly expressed in CD34-positive hematopoietic cells. The aim of this study was to investigate the prognostic relevance of BAALC expression in CN-AML adult patients.

In this prospective study, 149 CN-AML adult patients were recruited. We determined the expression of BAALC gene at diagnosis and examined its impact on patient survival.

BAALC gene was overexpressed in 60 (40.27%) CN-AML patients. We did not find any association between BAALC expression and age at diagnosis (P = 0.37), gender (P = 0.16), total leucocyte count at diagnosis (P = 0.12) (Table 1). The BAALC overexpression was associated with NPM1 wild type status (<0.001). However, it was not associated with FLT3-ITD (P = 0.198) and CEBPA mutations (P = 0.85) (Table 1). On survival analysis, we found a significant association between BAALC expression and overall survival (OS) (P = 0.017). However, we did not find any association between its expression and event free survival (P = 0.49). On further analysis of FLT3-ITD/NPM1 double negative CN-AML patients, we found BAALC overexpression still predicted poor OS (P = 0.02).

We conclude that BAALC expression is associated with poor OS. The testing of its expression can be used to risk stratify CN-AML patients, particularly, FLT3-ITD/NPM1 double negative patients in routine clinical practice.

Abstract Table

Table 1. Correlation of BAALC expression with patient characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>BAALC low</th>
<th>BAALC high</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td></td>
<td></td>
<td>0.37</td>
</tr>
<tr>
<td>Median</td>
<td>57</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>18–75</td>
<td>18–74</td>
<td></td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
<td>0.16</td>
</tr>
<tr>
<td>Male</td>
<td>53 (59.6%)</td>
<td>43 (71.7%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>36 (40.4%)</td>
<td>17 (28.3%)</td>
<td></td>
</tr>
<tr>
<td>TLC &lt;50,000/µl</td>
<td></td>
<td></td>
<td>0.122</td>
</tr>
<tr>
<td>TLC ≥50,000/µl</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NPM1 mutation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wild type</td>
<td>41 (60.3%)</td>
<td>39 (90.7%)</td>
<td></td>
</tr>
<tr>
<td>Mutated</td>
<td>27 (39.7%)</td>
<td>4 (9.3%)</td>
<td></td>
</tr>
<tr>
<td>FLT3-ITD</td>
<td></td>
<td></td>
<td>0.198</td>
</tr>
<tr>
<td>Absent</td>
<td>59 (86.8%)</td>
<td>41 (95.3%)</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>9 (13.2%)</td>
<td>2 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>CEBPA mutation</td>
<td></td>
<td></td>
<td>0.85</td>
</tr>
<tr>
<td>Wild type</td>
<td>55 (84.6%)</td>
<td>41 (95.3%)</td>
<td></td>
</tr>
<tr>
<td>Monoallelic</td>
<td>5 (7.7%)</td>
<td>3 (7.3%)</td>
<td></td>
</tr>
<tr>
<td>Biallelic</td>
<td>5 (7.7%)</td>
<td>2 (4.9%)</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared


BSH2021-PO-037
The molecular landscape of acute myeloid leukaemia in Northern Ireland
Graeme Greenfield1*, Adam Waterworth3, Naomi Anderson4, Julie Mcgimpsey2, Andrew Hindley2, Claire Arnold2, Damian Finnegan2, Mark Catherwood2, Mary Frances McMullin4
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Abstract Content: Introduction: Acute myeloid leukaemia (AML) is a serious neoplastic disorder of the myeloid stem and progenitor cells resulting in a characteristic bone marrow infiltrate of blast cells and resulting bone marrow failure. Heterogeneity within the disease has long been recognised with distinctive morphological variation and a wide range of cytogenetic abnormalities detectable. The more recent introduction of next generation sequencing (NGS) panels into standard clinical practice in the diagnosis and work up of AML has provided additional insight into the genetic complexity of the disorder, providing additional prognostic information and potential personalised treatment options.

We undertook a retrospective review of myeloid NGS panel results to determine the mutational and genetic landscape of AML in Northern Ireland where all patients are referred through a central laboratory

Methods and Results: Fifty-eight patients with acute myeloid leukaemia and recent myeloid NGS panels were identified from the regional laboratory database between February 2018 and June 2020. 2 patients were excluded due to incomplete data. 42 samples were obtained at diagnosis of disease and 14 samples at disease relapse/progression. In total, 138 pathogenic mutations were identified across 29 genes in all patients (range 0-8). 5 patients had no mutations identified by the panel with cytogenetic abnormalities present in 4 of these individuals. There were 9 instances of multiple mutations detected within the same gene in the same individual. The most frequently mutated genes were DNMT3A (23%) of patients, RUNX1 (21%), SRSF2 (14%), IDH2 (14%), FLT3 (14%), TET2 (13%) and NPM1 (13%). FLT3-internal tandem duplication analysis was available in 49 patients and detected in 14 patients.

Cytogenetic results were available for 95% of analysed patients with failed cytogenetic analysis occurring in 5%. These results were grouped as favourable, intermediate or adverse against the European Leukaemia Net 2017 classification with normal cytogenetics and complex cytogenetics included as additional groups. Chi-square test was used to determine significance of associations between cytogenetic grouping and individual mutations. There was a trend towards higher number of mutations in the normal cytogenetics group with an average of 3 mutations per individual (p value 0.08). TP53 mutations were identified at a significantly higher rate in the complex cytogenetic group (P value <0.001). Combining the complex group with the remaining adverse patients resulted in a loss of this significance. NPM1 and RUNX1 mutations were identified in the normal cytogenetic group at a significantly higher rate (p value 0.03 and 0.02) while patients having no mutations were significantly more frequent in the intermediate group (P value 0.04). These associations are shown in Table 1.

Conclusions: This study highlights the complex and heterogeneous genetic landscape in the AML patients in Northern Ireland with a number of significant associations between individual gene mutations and cytogenetic risk profiles identified.
Cytogenetic and mutational profile analysis of CD56-positive Acute Myeloid Leukaemia: A single centre experience

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Abstract Content: Background: Acute Myeloid Leukaemia (AML) is a heterogeneous disease characterised by genetic and phenotypic alterations. CD56 antigen expression in AML generally carries an unfavourable outcome and is associated with complex cytogenetic aberrations.

Aim: To analyse genetic and karyotype profile of patients with CD56-positive AML.

Methods: All transplant-eligible patients with CD56-positive AML were extracted from Systemic Anti-Cancer Treatment database, from January 2019 till January 2021. The median age of the patients was 50 (range 27 - 73 years) with a male to female ratio of 1.1:1.0. Conventional and molecular karyotype analytical methods were used in samples from patients, along with analysis of myeloid gene panel. Interphase and metaphase chromosomes from cultured bone marrow samples were analysed by FISH, using probes specific for AML-associated chromosomal abnormalities, such as KMT2A (MLL) (11q23), RUNX1-RUNX1T1 t(8;21) or CBFB-MYH11 inv (16)/t(16;16) rearrangements and deletions of 5q31 or 7q31, or monosomy of chromosomes 5 or 7, along with PML-RARA. NPM1 exon 12 insertion was analysed by qPCR melt curve analysis. Semi-quantitative assessment of FLT3-TKD and FLT-ITD allelic ratio was performed by restriction digestion of PCR products using EcoRV. Molecular karyotyping was performed using the Affymetrix Chromosome Analysis Suite software with minimum analytical resolution for CNV detection of 5 Mb and for LOH detection of 10 Mb genome-wide. Balanced chromosomal rearrangements, nucleotide variants, low level clonality (<15%) for any chromosome imbalances, and low level clonality (<20%) for LOH and constitutional (inherited or de novo) losses or gains were not validated to be detected with this method [CB4]. To obtain the myeloid gene panel for variant analysis, multiplex PCR, using custom Ion Ampliscope™, and the Ion PGM System were used to amplify and sequence 253 clinically-relevant regions within 21 myeloid genes, and analysed by Torrent Suite Software and Ion Reporter Software (Thermo Fisher Scientific Inc) for variant calling.

Results: A total of 13 patients were identified over a period of 2 years. All patients had either CD56-positive monoblasts or myeloblasts. A total of 6 patients (45%) had pre-existing haematological conditions; 4 patients (30%) had pre-existing MDS (RAEB-2) and 2 patients (15%) had a pre-existing myeloproliferative disorder (1 Essential thrombocytopenia and 1 Polycythaemia rubra vera). 5 patients (38%) had complex karyotype on conventional karyotyping and 2 (15%) patients had one additional chromosomal translocation, 6 patients (45%) had normal karyotype. Deletion of 5q was seen in 2 out of 13 patients (15%). Isolated NPM1 mutation was seen in 2 (15%) patients. FLT3-ITD was seen in 1 patient with no patients with FLT3 TKD mutation. ASXL1 mutations were seen in 4 patients and Tet2 mutations were detected in 3 patients. SRS2 and TP53 mutations were each seen in 1 patient (7.5%). Only one (16%) patient from the patients with complex cytogenetics had clinically pathogenic variant (AXSL1) on myeloid gene panel.

Summary/Conclusion: CD56-positive AML patients exhibit heterogeneous clinical, chromosomal and genetic phenotype. Surrogate markers using existing investigations can be modelled based on clinical outcome to predict and risk stratify.

Disclosure of Interest: None Declared

Use of Non-funded Drugs in advanced haematological malignancies

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Abstract Content: New drugs and treatments not funded by NHS are used in advanced haematological malignancies however data on efficacy and impact on quality of life is scarce. Most studies in solid tumours suggest that targeted or novel treatments used towards the end of life have little impact on prolonging quantity or quality of life. The aim of this study was to evaluate the impact of treatments not funded by the NHS in a single centre setting with a large haematological practice. Patients aged 16 years and above, treated for advanced haematological malignancies between January 2017 and January 2020 were included. Data was collected retrospectively from the electronic patient and pharmacy records. Date of last follow up was 16th of February 2021. Conventional disease-specific criteria were used to assess response to treatment. Days spent in hospital was used as a surrogate for quality of life and treatment toxicity was graded as per the common toxicity criteria version 5. Twenty-three patients with a median age of 55 years (range 24 to 81 years) were included. Twelve (52%) were male. The two most common diagnoses were AML (n = 13, 56%) and lymphoma (n = 6, 26%). Twenty-two patients (95%) had relapsed or refractory disease. The median number of prior therapies was 3 (range 0–10).

Two patients who received non-funded drug upfront had a diagnosis of systemic mastocytosis. The drugs used included decitabine (n = 4), venetoclax either on its own or in combination with azacitidine, decitabine or cytarabine (n = 7), Lenalidomide (n = 6), Midostaurin (n = 3), Brutinib (n = 1), Mylotarg (n = 1) and Interferon (n = 1). Majority of these drugs were provided through compassionate access schemes from the pharmaceutical company or the hospital trust paid for the treatment in 3 cases. Patients received a median of 2 cycles of the non-funded drug (range 1-5). Seventeen (73%) patients did not receive any subsequent treatment. Five patients (22%) achieved a complete remission with a median remission duration of 11.5 months (range 7 months to 3.4 years). Characteristics of patients who achieved remission are listed in Table 1. Median overall survival was 225 days (range 30 to 1351 days). The median time spent in hospital from starting treatment was 10 days

Table: Cytogenetic and mutation associated identified with odds ratio, confidence intervals and P value calculated by Chi-square test.

<table>
<thead>
<tr>
<th>Cytogenetic Group</th>
<th>Mutation</th>
<th>Odds Ratio</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate</td>
<td>Nil</td>
<td>6.15</td>
<td>0.9-41.8</td>
<td>0.04</td>
</tr>
<tr>
<td>Normal</td>
<td>NPM1</td>
<td>9.47</td>
<td>1.1-85.0</td>
<td>0.03</td>
</tr>
<tr>
<td>Normal</td>
<td>RUNX1</td>
<td>5.25</td>
<td>1.2-22.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Complex</td>
<td>TP53</td>
<td>36.75</td>
<td>3.8-359.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Disclosue of Interest: None Declared

Introduction

In patients with febrile neutropenia. Despite observed benefits (P < 0.017) there was an < 0.01) of tumor-associated residues (PSL lectin) < 0.01) in the N-glycoprotein structures is conclusive (range 0–139 days). These admissions were mainly for neutropenic sepsis and symptom management. Eleven patients (47%) experienced grade 3/4 haematological toxicity and thirteen patients (56%) experienced grade 3/4 non-haematological toxicity including sepsis, nausea and bleeding. Eight patients died within 90 days of starting treatment. There were no treatment-related deaths.

Based on these results, non-funded pharmaceutical treatments in our cohort of relapsed/refractory haematological malignancies provided only limited durable responses in majority of patients with more than half of the patients experiencing grade 3/4 toxicity and hospital admissions. This data highlights the challenge of appropriate patient selection, who may benefit from these novel treatments. Any potential benefit needs to be weighed up against the toxicity of treatment, impact on quality of life and the true cost to the hospital and healthcare service. A patient-centred approach is key.

Disclosure of Interest: None Declared

BSH2021-PO-040
Carbohydrate components of glycoconjugates of blast cell membranes in B-cell acute lymphoblastic leukemia in adults
Olha Shalay1,*, Vira Barilka1, Olena Zotova1, Volodymyr Lohinsky1
1State institution “Institute of Blood Pathology and Transfusion Medicine of NAMS of Ukraine”, Lviv, Ukraine

Abstract Content: Introduction: It is of interest to study the glycoprotein structures of the cell membrane (glycocone) using lectins, probes of the cell surface. Glycosyl residues are structural and functional elements of most antigens and receptors of the cell membrane, intracellular proteins. They play an important role in the processes of intercellular interaction, in particular with the cells of the microenvironment and vascular endothelium, in the metastasis and spread of tumors. The study of cell glycoconjugates in the process of malignant transformation can be used as additional diagnostic markers.

Materials and methods: Carbohydrate determinants of cell membrane were studied in 10 patients with B-cell acute lymphoblastic leukemia (ALL) and in 15 healthy controls using a panel of 12 lectins with main carbohydrate specificity.

Findings: In the B-cell ALL patient group compared with the control group in the conclusive part of cases (pF = 0.017) there was an increase in the expression level (p < 0.01) of tumor-associated Thomsen-Friedenreich antigen, characteristic of O-glycans type III chains in the membrane of young lymphocytes (receptor for Galβ→ 3 GalNAcb in N-glycan type I and II chains. In a conclusive number of cases (pF = 0.020) the level of positive cells, containing Manx residues (PSL lectin) in the core of N-glycans, decreases significantly (P < 0.001). Blast cells membrane contains fewer GlcNAcb residues (P < 0.01) in the N-glycans of the branched polycetylglucosamine type, as evidenced by the reduced percentage of cells that interact with WGA lectin. There is a reduced number of cells that contain N-glycans of type II 4-antenna chains and interact with polyspecific PHA-L lectin (P < 0.001).

There are changes in the level of expression of H-antigen, which is absent in mature lymphocytes of healthy individuals. There is a conclusive increase in frequency of positive cases (pF = 0.017) and the percentage of cells where the expression (P < 0.01) of glycans with terminal Fuc increases (LAL lectin). No significant differences in sialylation of normal and blast cells were observed (SNL lectin).

Conclusion: It was found that the general feature of glycosyl phenotype in B-cell ALL is the increase in O-glycans carbohydrate determinants expression (T, F antigens) with decrease in poly-antennae N-glycans sequences with complex-type chains (I and II) and hybrid-type chains and increase in fucosylation (H antigen).

Disclosure of Interest: None Declared

BSH2021-PO-041
An audit of fever-2-needle time in haematology patients during COVID-19.
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Abstract Content: Neutropenic sepsis is a medical emergency, with mortality rates ranging from 2-21% and a linear relationship between mortality and each hour delay in antibiotic administration [1,2,3]. NICE guidance and our Trust guidelines reflect these data, recommending rapid administration of antimicrobials - within 1 hour of clinical trigger [4].

Following an audit showing poor compliance with early antibiotic administration with a target fever-2-needle (F2N) time of less than 1 hour, a Patient Group Directive (PGD) was implemented in 2017, allowing initiation of antibiotics by trained nurses, prior to medical review, in patients with febrile neutropenia. Despite observed benefits to practice, the PGD was suspended due to COVID-19 pandemic restrictions (on staffing). We have re-audited F2N time of febrile neutropenia during the COVID-19 pandemic.

Data were collected over a 12-week period, recording the time elapsed between first fever ≥ 38°C and administration of antibiotics in haematology inpatients at St Bartholomew’s Hospital. Neutropenic (neutrophil count ≤ 0.5 × 10⁹/L) and non-neutropenic
patients were included. Variables included antibiotic choice, investigations performed and positive findings.

A total of 23 patients were included (60% had acute leukaemia). 91.4% were receiving chemotherapy/stem cell transplant. 61% of subjects were neutropenic, with neutrophil count at time of fever ranging from 0 to 42 × 10^9/L (median, 0.1). Of these neutrophenic patients, 92.9% were prescribed antibiotics in accordance with guidelines: combination tazocin and amikacin in the absence of beta-lactam allergy. All non-neutropenic patients were prescribed co-amoxiclav, with 1 patient also receiving amikacin. F2N time ranged from 11 to 201 minutes (median, 60 minutes) for the ‘first’ antibiotic and 19 to 377 minutes (median, 84 minutes) for the ‘second’. Overall, 41.2% of patients received both antibiotics (where appropriate) within 1 hour. Septic screen investigations: peripheral and PICC line blood cultures were performed in 78% and 100% of patients. These yielded 14% and 10% positive findings, respectively. 73% of patients had urine cultures with 11% positive findings, and 87% had chest x-rays, of which 22% had significant findings.

Compared to previous audits, there has been a significant deterioration in F2N time during this 12-week period in the COVID-19 pandemic. The suboptimal results of F2N time are of concern given the known association of increasing mortality with delays in antibiotic initiation. The PGD to enable nurse-led administration of antibiotics in patients with febrile neutropenia has been re-introduced and a re-audit of F2N time is ongoing.

References


Disclosure of Interest: None Declared

BSH2021-PO-042

Ensembl variant effect predictor results and other phenotypes reported on the clinically pathogenic variants identified on patients with CD56-positive Acute Myeloid Leukaemia

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Abstract Content: Background: The CD56 antigen is an isoform of neural adhesion molecule (NCAM) and has been reported in several haemopoietic disorders, including Acute Myeloid leukaemia (AML). Its increased expression on AML cells has been associated with adverse prognosis and unfavourable outcomes along with complex cytogenetic aberration and mutation profiles.

Aim: The aim of this study was to identify pathogenic genetic variants present in CD56-positive AML patients, utilising available Next Generation Sequencing (NGS) datasets. The Ensembl Variant Effect Predictor (VEP) was used to further identify and understand the clinical spectrum of disease entities and phenotypes associated with such variants, to better understand the mutational burden of such at-risk patients.

Methods: NGS data of 11 transplant-eligible patients with known diagnosis of AML or high-risk myelodysplasia, were obtained from Systemic Anti-Cancer Treatment (SACT) database from January 2019 until January 2021. These patients were selected based on their upregulated CD56 expression on myeloblasts and monoblasts.

A myeloid gene panel was obtained by amplification of 231 clinically relevant regions of 21 myeloid genes using a custom Ion AmpliseqTM and the Ion PGM System. The Torrent Suite Software and Ion Reporter Software (Thermo Fisher Scientific Inc), which can detect variants with up to 5% mutant allele frequency, were then used for variant calling. Structural variations including large insertion/deletions (>50 bp) were, however, not analysed.

Overall, the variant calling of the NGS panels reported variants with likely or possible clinical relevance. The assay is intended for detection of somatic mutations by database search, and rare germline variants were not excluded without investigations of paired normal DNA. These assays also did not automatically filter out variants outside of the targeted sequenced regions. Variants reported for all cases were then processed and analysed through VEP.

Results: Of all 5 variants called from the subset of eleven AML patients, 38% were nonsense and frameshift variants; 44% of which were found within the coding sequences of myeloid genes. 11% of all variants were associated with significant gain-of-function stop codon changes. Additionally, 9% of variants were reported to be within gene regulatory regions, while 4% where those affecting downstream gene function.

Phenotypic correlations of these identified variants were then matched through a literature search on ClinVar and orphaned evidence, showing reported associations with AML as expected. Interestingly, the variants were also reported to be pathogenic in several conditions predisposing to AML including various stages of myelodysplastic syndromes including refractory anaemia, chronic myelomonocytic leukaemia, dyskeratosis congenita, and acquired idiopathic sideroblastic anaemia. In addition to these, some variants were also found to be associated with myeloproliferative disorders including essential thrombocythaemia, aggressive systemic mastocytosis, polycythaemia rubra vera and primary myelofibrosis.

Conclusion: Our analysis identified a correlation between a diverse range of clinical phenotypes and genetic variants found in high-risk AML patients. Larger sample sizes should be analysed using COLOC and MOLOC bioinformatics pipelines to better elucidate the significance of these mutations in AML aetiology as well as in potential increased predisposition to AML.

Abstract Table: Reference

https://www.ensembl.org/info/docs/tools/vep/index.html

Disclosure of Interest: None Declared

BSH2021-PO-043

Real-life efficacy of fixed-dose hypomethylating agents in older patients with acute myeloid leukemia: a single center experience

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Abstract Content: Abstract

Background: Prognosis of elderly patients with acute myeloid leukemia (AML) is dismal. Hypomethylating agents (HMAs) are recommended treatments for these patients due to their acceptable toxicity
profiles and favorable efficacy. However, their high cost precludes their general use, especially in developing countries. Therefore, the fixed-dose HMAs approach was adopted in Thailand in order to reduce the expense.

**Aims:** This study aimed to investigate the clinical outcome of various treatment protocols including intensive chemotherapy, fixed-dose HMAs, and palliative treatment in Thai AML patients aged over 60 years. Fixed-dose HMAs included 5-azacitidine given at 100 mg per day for 7 days and decitabine given at 20 mg per day for 5 days.

**Patients and Methods:** We conducted a 10-year retrospective, single-center study in elderly AML patients diagnosed between January 1, 2010, and December 31, 2020. The inclusion criteria were (1) patients aged above 60 years; and (2) patients with newly diagnosed AML. The exclusion criteria were acute promyelocytic leukemia with NPM1 abnormalities have been observed. Our study confirms the poor outcome of AML in elderly patients, especially in patients receiving palliative strategy. The fixed-dose regimen of HMAs is the treatment of choice for these patients which is non-inferiority to intensive therapy.

**Disclosure of Interest:** None Declared

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**BSH2021-PO-044**

**Myeloid sarcoma: a single centre experience**

Christopher Mullen*, Sarah Beverstock, Wael Al-Qsous, Huw Roddie, Victoria Campbell

**Abstract Content:** Myeloid sarcoma (MS) is a rare extramedullary tumour of myeloblasts. It may develop de novo, concurrently with acute myeloid leukaemia (AML), myeloproliferative neoplasms (MPNs) or myelodysplasia (MDS) or rarely as the presenting feature of AML, or a sign of disease relapse. It may affect any part of the body. The use of AML regimes is accepted. Prognosis is generally poor.

We describe the experience of a BSH level three unit through a limited case series. As expected, anatomical sites differed: breast, testis, lymph nodes, femur and uterine cervix; 2 cases had AML on staging BM investigation, both had normal full blood count at presentation. 1 had antecedent MPN, confirmed on staging BM, the others presented with de novo disease. Median age at diagnosis was 41 years (range 23–61 years); all were suitable for intensive chemotherapy, 4 were treated within NCRI trial (AML 17 and AML 19), 1 received Vyxeos due to associated cytogenetic abnormalities. Following induction 3 cases achieved complete remission (CR), 1 CRi. Despite 80% initially demonstrating disease response outcomes were varied. 2 patients died of refractory disease (1 progressed through second induction having attained CRi), 1 relapsed 30 months after completion of intensive therapy with AML requiring allogeneic transplant, 2 patients remain in remission >5 years post treatment.

In terms of molecular associations, NPM1 mutations are seen in 15-28% of cases of MS, typically with monoblastic or myelomonocytic morphology, normal karyotype and absence of CD34 expression. It is unclear whether NPM1 mutations carry the same favourable prognosis in MS as in AML if negative after 2 cycles of induction chemotherapy. MS is also seen in association with FLT3-ITD, detected in 15% of MS cases. Again, the prognostic significance is unclear. FLT3 inhibitors are not routinely used in the management of MS (although one case report described the use of sorafenib in FLT3-ITD mutated MS who relapsed post allogeneic stem cell transplant) but this would clearly be an interest in a patient harbouring FLT3-ITD mutations. DNMT3A and IDH2 abnormalities have been respectively observed in 7-27% and 7-11% of MS cases. The prognostic implications are currently unclear; however the possibility of IDH2 inhibitors as a therapeutic strategy is attractive.

There is some literature data to support that patients with isolated MS may have better prognosis than those who present with AML. Our patients have MS involving a number of different anatomical sites. A large retrospective study of MS patients in the United States grouped anatomical sites into 3 prognostic groups – good, intermediate and poor. Lymph nodes and connective tissue/bone MS was noted to have a poor overall survival, consistent with the patients diagnosed with MS at these sites in our group. Reproductive organ MS is associated with a good overall survival and breast MS intermediate.

As MS is a rare disease entity, multi-centre studies are needed to share experiences, better elucidate the biology of the disease and develop risk-adjusted treatments.

**Disclosure of Interest:** None Declared

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**BSH2021-PO-045**

**Spontaneous regression of acute myeloid leukaemia following SARS-CoV-2 infection**

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**Abstract Content:** Here, we report a Coley’s toxin-like phenomenon in acute myeloid leukaemia (AML) complicated by SARS-CoV-2 infection before induction chemotherapy. A 67-year-old gentleman presented with malaise and bruising: FBC confirmed severe thrombocytopenia, with AML blast forms on bone marrow aspirate. Karyotyping revealed 45,X,-Y,t(8;21)(q22;q22.1), encoding the RUNX1-RUNX1T1 fusion gene. At day 13 post-diagnosis he contracted SARS-CoV-2 pneumonia, managed with supportive transfusion, oxygen, dexamethasone, remdesivir and piperacillin-tazobactam. From day 21 post-infection, his thrombocytopenia resolved, with concomitant reduction in circulating blasts via the surrogate index of the automated monocyte differential. Since the 1950s, approximately 50 cases of spontaneous AML regression following febrile illness have been reported (median duration 7.1 months), attributed, at least in part, to modulation, by cytokine storms, of the soluble microenvironment. Balanced translocations predominate known cases, with a predominance of core-binding protein leukaemias. Spontaneous regression of peripheral AML during SARS-CoV-2, or any PCR-proven viral infection, is a novel observation, updating Coley’s observations of twinned immune hyperactivation and tumour regression to the context of Covid-19 disease.

**Disclosure of Interest:** None Declared
BSH2021-PO-046
All-trans retinoic acid induced myocarditis as a feature of differentiation syndrome: a case report and literature review
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Abstract Content: Acute promyelocytic leukaemia (APL) is a distinct subtype of acute myeloid leukaemia defined by the translocation t(15;17)(q22;q21). All-trans retinoic acid (ATRA) is a cornerstone of treatment for APL. However, ATRA use is associated with a spectrum of severe complications known as differentiation syndrome (DS). With the exception of pericardial effusion, cardiac involvement is extremely rare after ATRA exposure. We present a patient who developed myocarditis as an unusual complication after ATRA treatment.

A 23-year-old female presented with one week history of generalised headache, emesis, and ecchymosis. Lab findings revealed leukocytosis (44.5 × 10⁹/mm³), normocytic anaemia (11.3 g/dl), thrombocytopenia (38 000/mm³), hypofibrinogenaemia (fibrinogen 64 mg/dl), elevated d-dimer (48 293 ng/ml), and coagulopathy (prothrombin time international normalised ratio 2.0) consistent with disseminated intravascular coagulation. Peripheral blood smear demonstrated 82% blasts with Auer rods, consistent with acute promyelocytic leukaemia (APL) and later confirmed on bone marrow aspirate and biopsy. PCR for PML-RARA fusion gene was positive. Karyotype was 46,XX,del(9)(q13q22),t(15;17)(q22;q11). On confirmation of the diagnosis, the patient was initiated on ATRA and idarubicin. One day following the first administration of ATRA, the patient began to complain of dyspnea on exertion and chest pain. She developed transient hypoxia (SpO₂ 90%) and sinus tachycardia.

Troponin I was elevated to 2849 pg/ml, but there were no electrocardiographic changes suggestive of ischemia. Computerised tomography of the chest demonstrated new bilateral interstitial infiltrates and small pleural effusions. Blood and bronchoalveolar lavage microbiology cultures were negative. Echocardiogram was negative for any valvular dysfunction, systolic dysfunction, or wall motion abnormalities. However, cardiac magnetic resonance imaging (MRI) demonstrated delayed focal subependymal enhancement suggestive of myocarditis. The patient was immediately started on intravenous dexamethasone 10 mg every 12 hours for treatment of both DS and myocarditis, and demonstrated resolution of symptoms as well as normalisation of cardiac enzymes. She was advised to continue a prolonged prednisone tapering regimen for treatment of both DS and myocarditis, and demonstrated resolution of symptoms as well as normalisation of cardiac enzymes. She was advised to continue a prolonged prednisone tapering regimen after completion of dexamethasone for 14 days. Three months after her diagnosis, follow-up echocardiogram demonstrated normal function with a complete resolution of symptoms.

DS is a heterogeneous condition whose pathogenesis and diagnostic criteria remain yet to be clearly defined. This patient meets criteria for possible differentiation syndrome given the presence of dyspnea with interstitial pulmonary infiltrates, as well as a small pericardial effusion, after ATRA induction. Review of existing literature identified 11 other cases of ATRA-induced myocarditis, of which only 2 reported concurrent DS-defining symptoms. All cases demonstrated onset of symptoms within 1 month of ATRA induction. Due to the scarcity of available reports, cardiac complications are an under-recognised sequela of ATRA use. We postulate that myocarditis although rare, is likely to be a constituent of the amalgam of pathologies involved in DS. Cardiac MRI may be a more accurate non-invasive diagnostic test to confirm myopericarditis after ATRA induction.

Disclosure of Interest: None Declared

BSH2021-PO-047
FLT3-ITD negative relapse following FLT3 inhibition
Christopher Mullen*, Victoria Campbell

Abstract Content: The treatment landscape for AML is rapidly evolving. Together with developing diagnostics treatment decisions are becoming increasingly complex and less standardised. We present a case with targetable abnormalities, treatment rationale and clinical outcome.

A 69 year old female with core binding factor acute myeloid leukaemia (AML): 47,XX,+8,t(8;21)(q22;q22),add(17)(q215), FLT3-ITD+ and NPM1 wild type. Treatment was intensive with daunorubicin/cytarabine (DA) and midostaurin. Gemtuzumab (GO) was precluded as blasts were CD33 negative. Morphological and cytogenetic remission was achieved after cycle 1. Response was consolidated with 1 cycle of DA and 2 cycles of intermediate dose cytarabine (IDAC) all with midostaurin. End of treatment assessment confirmed ongoing remission with complete count recovery. She proceeded to midostaurin maintenance, stopped at six months due to toxicity. Two months after discontinuation bloods showed new cytopenias (neutrophils 0.56 × 10⁹/L, platelets 63 × 10⁹/L). Bone marrow examination confirmed relapse with 17% blasts and recurrence of t(8;21)(q22;q22.1); RUNXI-RUNX1T1 though additional cytogenetic abnormalities were not present. Molecular analysis was negative for all variants including FLT3-ITD. She developed treatment resistant infection precluding further therapy; she died of progressive leukaemia.

FMS-like tyrosine kinase 3 (FLT3) is a proto-oncogene involved in proliferation, differentiation and survival of haematopoietic cells. The FLT3-ITD mutation is associated with a poorer clinical outcome. The allelic ratio holds prognostic significance with a significantly shorter time to relapse in those with a high allelic burden (>0.5). FLT3-ITD may be utilised as a parameter in the detection of minimal residual disease (MRD), however it is recognised that FLT3 status may change (either acquisition or loss of FLT3-ITD) during treatment. Paired analysis of FLT3-ITD mutation status in initial and relapse samples from patients with AML has shown loss of FLT3-ITD status is associated with a longer period to relapse, whilst those who acquire FLT3-ITD have a much diminished time to relapse (15.4 vs 6.3 months). The incidence of loss of FLT3-ITD at relapse varies across reports (5.9–25.0%). Most patients with a FLT3-ITD mutation at diagnosis however will not only retain the FLT3-ITD mutation but often with a higher allelic burden; there is evidence that relapsed AML may be more dependent on FLT3 signalling.

These observations suggest there is value in repeat FLT3-ITD mutation testing throughout the patient journey to guide the most appropriate therapy; supported by both the NCCN and ELN 2017 guidelines. It will be interesting to see how the incidence of FLT3 negative relapse changes with the use of FLT3 inhibitors in clinical practice. The anti-CD33 immunoconjugate gemtuzumab has been shown to reduce the risk of relapse, as well as conferring a survival benefit in those with favourable cytogenetics. The investigators of the ALFA-0701 trial suggested that patients with FLT3-ITD had a greater survival benefit from gemtuzumab than those who were wild type, although this was not corroborated in a meta-analysis.

This case highlights the complexity of AML and the need for genetic results to tailor treatment, though licensing and toxicities must be considered. Clinical trials to determine optimal therapy and markers of disease are vital to ensure continued improvement in treatment options and patient outcomes.

Disclosure of Interest: None Declared
A case of thrombotic stroke in a newly diagnosed APML
Mohammed Hatata*, Durgadevi Moratuwagama

Abstract: Acute Promyelocytic Leukemia (APML) is a rare subtype of Leukemia that has first been recognized in the late 1950s. Coagulopathies with associated bleeding tendencies have always posed serious and sometimes fatal risks to patients especially in the early phase of the disease. Thrombotic events, however, proved to be less common and possibly under-reported. We describe a case of a 40 years old male who suffered a thrombotic stroke 4 days following diagnosis of APML.

Case: A 40 years old male who was previously fit and well presented to the local A&E with two weeks history of feeling generally unwell and having very high temperatures. Systemic examination was unremarkable, but his full blood count revealed profound pancytopenia with Hb 79 g/L, WCC 2.2 \times 10^9/L, Neutrophil 0.2 \times 10^9/L and Platelets 40 \times 10^9/L. The coagulation screen was also deranged with Prothrombin time 16.1 seconds and Clauss fibrinogen level 0.9 g/L. His blood film showed evidence of circulating Promyelocytes.

Immunophenotyping of the peripheral blood reported Myeloid blast population detected making up approximately 36% of the total nucleated cell count. Immunophenotyping of the bone marrow reported Myeloid blast population detected making up approximately 75% of the total nucleated cell count. Fluorescence in situ hybridization (FISH) genetic testing reported an abnormal signal pattern consistent with the presence of a PML-RARA gene rearrangement, thus establishing a diagnosis of WHO classification: Acute promyelocytic leukaemia with t(15;17)(q24;q21)PML-RARA. ATRA was commenced promptly.

On the 4th day following presentation, the patient had an episode of transient slurring of speech and mouth deviation. At that point his platelets count was 50,000 and clotting profile was starting to normalize. He had a CT scan which didn’t show any evidence of bleeding or other acute findings. Later, an MRI of his brain revealed a left external capsule area of restricted diffusion. Appearances likely indicating an acute infarction. A repeat MRI 6 weeks later confirmed the presence of an established infarct. The patient was not left with any neurological deficits as a result of the thrombotic stroke, and once his platelets normalized, he was commenced on an antiplatelet.

Discussion: Early mortality in APML due to haemorrhages remains a major cause of induction failure. On the other hand, thrombotic phenomena are largely underreported and poorly understood. They are less common compared to bleeding and presence is based mainly on individual case reports. Potential explanations include mere coincidence (genetic predisposition; prolonged bed rest; immobility), causation by APL (release of prothrombogenic particles: TF, inflammatory cytokines, and expression of adhesion molecules on the surface of tumour cells), higher expression of tissue factor in APL, causation by ATRA or as part of the differentiation syndrome.

Conclusion: Greater awareness should be attained as towards the risks of thromboembolic events in APML cases, especially in the early periods of the disease. Management remains centred on treating the underlying cause and offering standard treatments as per established guidelines.

Disclosure of Interest: None Declared
Education and professional

BSH2021-PO-049
Diagnostic yield and safety of splenic core biopsy – A single Centre experience
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Abstract Content: Objective: To assess the diagnostic yield and safety of percutaneous image-guided splenic biopsies in patients at a District General Hospital over 10 years.

Methods and results: Data from all image-guided splenic biopsies performed at a single institution over 10 years were reviewed retrospectively. Twenty-three patients underwent splenic biopsy as a day case procedure (14 male and 9 female patients; mean age 68.5; age range, 38–92 years). Over 50% [n = 12, 52.1%] of these cases were performed in the last 2 years. The mean platelet count was 178 × 10^9/L (range 27 × 10^9/L to 558 × 10^9/L). Only one patient received a prophyllactic platelet transfusion. All biopsies were performed under ultrasonographic guidance. 18-gauge needles were used in 19 cases, 16-gauge in 3 cases and 20-gauge in 1 case. The mean number of core biopsy samples obtained were 3 (range 1–5 cores). 4 patients subsequently had elective splenectomy.

 Adequate tissue was achieved in 22 of 23 cases. The single case with insufficient tissue had the biopsy performed using a 20-gauge needle and was later confirmed to have low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy. Haematological malignancy was confirmed in 11 cases and was suspected in a further 2 cases. These 2 patients later underwent splenectomy which confirmed the initial suspicion of Diffuse Large B Cell Lymphoma (DLBCL) and low grade B cell lymphoma respectively. Of the 11 confirmed cases with haematological malignancy, DLBCL (7 cases) was the most frequent diagnosis and the remaining included 2 cases of low grade B cell lymphoma on splenectomy.}

Conclusions: This small case series demonstrates that ultrasound guided splenic biopsy using an 18-gauge needle is a minimally invasive procedure with a low complication rates and a high diagnostic yield. These findings would support the suggestion that splenic biopsies performed by an experienced operator can play a greater diagnostic role in clinical practice and can thus avoid the need for a more invasive procedure like splenectomy.

Disclosure of Interest: None Declared

BSH2021-PO-050
Patient feedback on Lymphoma services during the COVID pandemic
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Abstract Content: During the COVID pandemic Lymphoma and Haematology services across the nation have been forced to make drastic changes to reduce the risk of exposure to the COVID-19 virus. In Cardiff, the impact on outpatient services has been enormous, routine face to face outpatient clinics were cancelled, swapped to telephone consultations and clinic and treatments still running, were moved out of the hospital into lower risk sites. The unprecedented change to services were all done at speed but without any consultation with patients themselves.

Throughout the last year three patient feedback audits were carried out to gather retrospective insights into how patients themselves felt about these enforced changes and what they wanted for the future of our outpatient Lymphoma service.

The three audits consisted of; A telephone audit for people on surveillance in the low grade lymphoma clinic; a postal audit of curative follow up lymphomas who had their appointments postponed; and a telephone audit early on in the pandemic of random patients from various lymphoma clinics or those having day unit treatment. A total of 143 people fed back in the three audits (51, 42, and 51 respectively).

Overall, the majority of patients were satisfied with the change from face to face consultations to telephone consultations (87%) “I don’t want to enter the hospital in light of the current pandemic”. However a third of people wished to return to face to face when safe to do so.

Of those not happy with the changes from a face to face clinic, their comments included; “I felt adrift by phone”; “I am worried that I have not had my lumps felt by a professional”; “as I am only seen once a year, I would prefer it face to face”.

Of the low-grade lymphoma patients, only two of the 51 patients audited said they felt they had had their treatment delayed because of the telephone consultations, but equally two said that they held back from letting us know about symptoms as they have been reluctant to start treatment during the pandemic.

Phlebotomy was previously carried out in clinics, had to be moved out to the community. Only three out of 51 patients audited felt they had difficulties getting their bloods done in the community (50% had bloods done in their GPs, 30% continued to attend the hospital for the drop-in service, 20% had appointments booked into to various local hospitals).

For the future, 82% would like to be given the choice of having a telephone, video, or face to face appointment. Video consultations were not available at the time of the audit but 26% expressed interest to have them introduced.

For those patients having to change location for face-to-face appointments or treatments, 57% felt confident that the area was safe but 43% felt the main hospital was safer than the main hospital, however there was comment about not being happy to travel further during the pandemic and someone commented that it had become frightening to visit the main hospital with all the warning posters and staff in PPE. 91% of patients were
satisfied with the initial COVID safety measures put in place, of staff PPE, social distancing and mask wearing.

Overall, the enforced changes to the lymphoma outpatient service in Cardiff have been acceptable, with the majority of patients appearing to be satisfied and feel safe. Continuing to get feedback and improve the service under difficult circumstances is paramount to prevent any future delays in people accessing timely review and treatments.

Disclosure of Interest: None Declared

**BSH2021-PO-051**

**A Clinical Audit of Discharge Plans for Haematology Oncology Inpatients at Queen Elizabeth Hospital, Birmingham; Implementing the Safe Discharge Guideline**

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**Abstract Content:** Discharge planning anticipates the support a patient might require upon discharge and is the process by which hospital teams liaise with outpatient services to effectively manage the patient in the community 1. Haematology Oncology (Haem-Onc) inpatients require careful co-ordinated planning with the haematology day unit to enable monitoring of blood counts for anticipated cytopenias, blood transfusions, G-CSF administration and line care 2. The Queen Elizabeth Hospital (QEH) has documented a high incidence of Haem-Onc discharges and admissions and an audit was performed to assess the quality of discharge letters and the accuracy of outpatient follow up plans. Local standards were created based on an agreed consensus from haematology consultants, pharmacists and day unit staff for common haematological malignancies and chemotherapy regimens depending on their intensity (Table 1). 100 Haem-Onc patient discharges were reviewed from QEH between 03/09/2020 to 12/12/2020. The majority of discharge letters were completed by junior medical staff with a junior speciality doctor writing 31% of all discharge letters. Details of chemotherapy type should have been included in 72% of discharge letters however 30% (n = 21) of these did not state the type administered. Out of 100 patients, 42 patients required early clinic review and of those, 21% did not have an early clinic date documented however most patients (61%) did have a routine clinic appointment date documented on their discharge letter. The majority of patients (92%) had a repeat day unit blood test booked in appropriately depending on their reason for admission and treatment regime. 16 patients required an inpatient systemic anti-cancer therapy (SACT) referral and all but one had this requested. All patients that required intrathecal chemotherapy as an outpatient had an appropriate referral put in and the majority (4 out of 5) patients who required an outpatient bone marrow biopsy, had a request put in place. Not all audit standards were met upon review of 100 discharge letters (Table 1), highlighting the need for further education for medical staff completing discharge letters. We therefore created of an easy-to-read guideline called the Safe Discharge Guideline (SDG). It provides a step-by-step guide on how to arrange follow up for patients depending on their chemotherapy regime and also offers examples. We also incorporated the SDG into a teaching session with all new junior medical staff rotating to the Haem-Onc wards. Following the dissemination of the guideline and an educational session, a re-audit was performed to assess if there had been an improvement in the quality of discharge follow up plans. The results of the re-audit showed an improvement in the written information provided in the discharge letter and also the outpatient follow up plans (Table 1).

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<thead>
<tr>
<th>Audit Standards</th>
<th>Audit Result</th>
<th>Re-audit Results</th>
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<td>99% SAME</td>
</tr>
<tr>
<td>100% of discharges should include the reason for admission</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>100% of discharges should include the details of chemotherapy</td>
<td>71%</td>
<td>100%</td>
</tr>
<tr>
<td>100% of patients should have appropriate day unit blood test booked depending on their regime</td>
<td>92%</td>
<td>95% IMPROVEMENT</td>
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<tr>
<td>100% of patients should have an appropriate and timely clinic follow up</td>
<td>79%</td>
<td>100%</td>
</tr>
<tr>
<td>100% of patients that require further inpatient chemotherapy should have it booked on discharge via PICs</td>
<td>44%</td>
<td>50% IMPROVEMENT</td>
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<tr>
<td>100% of patients that require further outpatient chemotherapy should have it booked on discharge via PICs</td>
<td>92%</td>
<td>100%</td>
</tr>
<tr>
<td>100% of patients that require an intrathecal chemotherapy or bone marrow biopsies as an outpatient, should have it booked via PICs</td>
<td>80%</td>
<td>100%</td>
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Disclosure of Interest: None Declared

**BSH2021-PO-052**

**Impact of the Covid-19 pandemic on haematology research trials at the Christie Hospital**

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**Abstract Content:** Covid-19 has spread across the globe causing a devastating number of deaths and impacting on every aspect of life as never before. The NHS Constitution recognises the important role of the NHS to “conduct and use of research to improve the current and future health and care of the population” [1]. The pandemic demonstrated the ability of the NHS to make meaningful contributions to key clinical research relating to the management of COVID-19 but placed unprecedented challenges on other areas of clinical research.

The Christie Hospital is one of the largest dedicated cancer treatment centres in Europe. As well as providing expert cancer care, it is a tertiary research centre with an internationally recognised expertise in cancer research. We looked at the impact of COVID-19 haematological cancer research activity at The Christie. Clinical trial activity records were reviewed for the 6-month time periods before (Sept. – Feb. 2019-20), during (Mar. – Aug. 2020) and after (Sept. – Feb. 2020-21) the first UK lockdown. Effects on the opening of and recruitment to clinical trials were analysed. In addition, adaptations made to the delivery of clinical research, were considered.

The lockdown brought about a dramatic decline in patient recruitment, from 7 to 2 patients/month. This reflects a decision to almost totally halt recruitment to allow research staff to be deployed and protocols to be implemented to minimise the risk to research patients from COVID-19 infection whilst on the hospital site. Following this, a cautious recovery period began in which clinical trial recruitment resumed, whilst maintaining COVID-19 safety measures, allowing recruitment recovery to near pre-lockdown levels; 6 patients/month.

A delayed effect on new trial opening was observed. In the pre-lockdown 6-month period, 9 new trials were opened, with 8 opened during lockdown. This fell to 6 trials in the following 6-months. The delayed effect was likely due to the length of the setup process, with much work already having occurred before the lockdown allowing ongoing new trial opening. However, new trial set up has been slow to recover, impacted by ongoing pressures on service departments (e.g., radiology) preventing timely reviews as part of the set-up process.

Documented deviations from trial protocol were agreed with sponsors and seen as necessary to conduct clinical haematological research safely within the setting of a pandemic. Examples documented include switching from face-to-face to remote consultations and omitting or relocating some trial related investigations. A potential impact on data quality was accepted and deviations were recorded to allow review of this impact at a later date. Other key changes included the expediting of a move to allow remote, anonymised, supervised, electronic record access for trial monitoring visits, and specialised courier delivery of trial medication, where appropriate.

As a dedicated tertiary cancer hospital, there was organisational motivation to try to safely resume clinical research activity following the first lockdown. The consequences of halting clinical haematological research on future developments within the field is difficult to quantify but potentially serious. It is essential that clinical cancer research learns to adapt to the ‘new normal’ in the COVID era.


Disclosure of Interest: None Declared

Abstract Table: TRIAL ACTIVITY

<table>
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<tr>
<th>September to February 2019/2020</th>
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<th>September to February 2020/2021</th>
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<tr>
<td></td>
<td>Consented</td>
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<tr>
<td>Patient enrolment</td>
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<td>New trials opening</td>
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BSH2021-PO-053

The oncontrol powered bone marrow device: an audit of 100 patients in Oxford

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Abstract Content: Introduction: The OnControl system is a battery-powered bone marrow biopsy system designed to enable faster and improved biopsy samples, and to be less painful than manual techniques. The device was CE-marked in 2005 and reviewed by NICE in 2015. Despite this, the majority of UK hospital trusts still use manual needles (MN). The Oxford Technology Advisory Group approved the use of the OnControl powered device (PD) for a 100-patient audit, 15th June - 29th of July 2020.

Methods: Six key indicators were used to assess outcomes: 1) patient satisfaction, assessed by qualitative patient questionnaires; 2) aspirate and trephine sample quality, assessed by biopsy reports, and recorded as adequate or inadequate; 3) adverse events, defined as patient contact to report a problem following a biopsy; 4) repeat biopsies, defined as a repeat procedure due to sample inadequacy only; 5) duration of biopsy, as time per patient, and as time per bone marrow list and 6) operator satisfaction, assessed by registrar feedback from those with experience of both needle types. The secondary aim was to evaluate cost savings. All patients gave their consent at the time of the biopsy. On-site training was provided by Teleflex and the trial was approved by the Oxford Technology Advisory Group.

Results: The overall patient experience was: better than expected (40% vs. 32%) for PD vs. MN, respectively. The modal pain score (on a scale where 0=no pain and 10=unimaginable pain) was 1 vs. 3, and the percentage requiring Entonox was 35% vs 47% for the PD vs MN respectively. The number of inadequate aspirate samples improved (14% vs. 39%) for PD vs. MN. The percentage of inadequate trephine samples was improved (13% vs. 31%, PD vs MN).

Two adverse events occurred with the MN: one with pain, which resolved with simple analgesia, the second a fracture of the right iliac spine, treated with antibiotics and analgesia and discharged after a 9-day inpatient stay. With the PD there were two adverse events: persistent pain, 7 days after a biopsy which resolved with simple analgesia, and a superficial infection at the biopsy site treated with oral antibiotics. A total of nine patients (N=9/67=13.4%) required a repeat bone biopsy with the MN. No patients have required a repeat biopsy with the PD system to date. The average time per patient was 58 mins vs. 1 hour 5 mins for the PD vs MN respectively. This is a saving of 7 mins per patient. This would allow an extra 6.72 patients to be booked per month. The majority of registrars found the PD easy to use (N=5/6, 83%) and (N=5/6, 83%) would be happy to use the PD again. Oxford Trust purchase MN from Mana-Tech at a combined cost of £22,90. This means an additional cost of £38,40 per patient with the PD. Although more expensive per se, the PD results in an annual cost-
savings of £50 864 (based on a recall rate of 13%, and a reduced time per procedure of 7 mins).

**Conclusion:** this audit of 100 bone marrow procedures with the OnControl device suggests improved patient experience, reduced need for Entonox, better quality samples and the majority of registrars would be happy to use the PD again. Two patients reported adverse events. None of these was serious, and no patients required admission. The time saving, combined with a reduced recall rate suggests an overall cost saving, despite initial higher purchasing costs. The PD has been adopted in Oxford. We hope that this audit will encourage other trusts to do the same.

**Disclosure of Interest:** None Declared.

**BSH2021-PO-054**

**Should we replace telephone with video consultation to improve patient experience? - The Queen Elizabeth Hospital experience**

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**Abstract Content:** The COVID-19 pandemic has mandated rapid adoption of a new approach to outpatient appointments for our Haematology patients, the majority of whom are classed as vulnerable and have been required to isolate for prolonged periods following government guidelines. Within a short space of time remote consultation by telephone replaced the traditional face-to-face outpatient consultation for the majority of our patients. There has been appetite in other departments locally and regionally to consider implementation of video consultation as a replacement for telephone consultation and we were asked as a department to consider implementation to enhance patient experience. We were concerned that adoption of video consultation would create barriers for some, and questioned whether our patients would perceive a benefit of video, compared to telephone consultation.

We identified and contacted by telephone 36 consecutive patients who had participated in a general haematology telephone consultation during the final two weeks of June 2020. We designed a survey to assess patient satisfaction of the telephone consultation; access to hardware necessary to participate in video consultation; relevant experience of using video calling / conferencing and their preference when offered further remote consultations. Of the 29 patients who consented to be surveyed, 28 were satisfied with the process and quality of their telephone consultation (97%). We found that 6 patients (21%) did not have access to necessary hardware to participate in video consultation and although the rest had the hardware to participate; only 15 patients (52%) had any prior experience of using video calling / conferencing and would feel confident to use similar software. We asked our patients about their level of preference for video consultation in the future. We found that only 5 patients (17%) would prefer to have a video consultation, with the level of preference falling further to only 2 patients (7%) should the software required to participate not be available to install remotely on a home device.

Our results show that our patients have a high level of satisfaction using the telephone as a method of remote consultation. We demonstrate a low level of perceived preference for video consultation and highlight both the high level of unfamiliarity using video calling / conferencing software and inability for a significant proportion to access the necessary hardware to participate in video consultation at all.

We conclude as a department, that changing to video consultation from telephone consultation as a standard means of remote consultation will not increase patient satisfaction and will focus our attention and resource allocation on other areas of practice to improve our patient’s experiences.

**Disclosure of Interest:** None Declared.

**BSH2021-PO-055**

**The impact of the COVID-19 pandemic on the diagnosis of myeloid malignancies: a single institution experience**

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1Haematology Department, Aneurin Bevan University Health Board (ABUHB), Newport, United Kingdom

**Abstract Content:** Introduction: Since the emergence of COVID-19, steps taken to reduce the spread of the virus have significantly disrupted the provision of routine healthcare. Referrals from non-primary care sources to all cancer services at ABUHB, serving a population of 600,000, have reduced by 27% during the pandemic. Cancer care has been significantly impacted causing potential delays in diagnosis and treatment. The diagnosis and management of myeloid malignancies (MM) is suspected to reflect these changes.

**Aim:** To evaluate the impact of the COVID-19 pandemic on the diagnosis rate and management of patients with MM at ABUHB.

**Method:** We retrospectively analysed our local database of patients with MM in ABUHB. We compared the number and characteristics of patients diagnosed in 2019/2020, and examined changes in relation to phases of the pandemic over 4 month consecutive periods in 2020. Diagnoses had to fulfil the WHO revised 4th edition criteria. We also quantified the numbers of patients with chronic myeloid leukaemia (CML) who were offered a trial of Treatment-Free Remission (TFR).

**Results:** A total of 200 patients were diagnosed with MM over the study period. Almost twice as many MM diagnoses were made in 2019 compared to 2020 (131 (65.5%) vs 69 (34.5%)), consistent across all diagnostic sub-groups. Over the study period, 98 patients with Philadelphia-negative myeloproliferative neoplasms (MPN) were diagnosed. An MPN diagnosis was made far more frequently in 2019 (69 (70.4%) vs 29 (29.6%)). MPN patients showed a younger median age in 2019 (62 years (range 32-92 years) vs 69.5 years (range 52-87 years)). For CML, 11 patients (68.8%) were diagnosed in 2019 while only 5 (31.2%) were diagnosed in 2020. The difference in diagnoses made was least for patients with acute myeloid leukaemia/myelodysplastic syndrome (AML/MDS). Out of a total of 86 patients diagnosed, 51 patients (59.3%) were diagnosed in 2019.

We observed a marked reduction in diagnoses made after April 2020 coinciding with pandemic restrictions. Considering all diagnoses made in 2020, 37 patients (53.6%) were diagnosed with a MM during January to April, whilst only 15 patients (21.7%) and 17 patients (24.7%) were diagnosed between May to August, and September to December, respectively.

Four patients were offered TFR in 2019. The single patient who was offered TFR in 2020 was pre-COVID-19. No patient was offered TFR from February 2020.

In contrast, only 6 patients with a new or established MM diagnosis had evidence of COVID-19 infection (2 patients with essential thrombocythaemia, 1 patient with polycythaemia vera, 2 patients with AML, one patient with MDS). No deaths due to COVID-19 were recorded.

**Conclusion:** Our data shows a marked reduction in the rate of diagnosis of MM since the start of the COVID-19 pandemic. Remarkably, only a few patients developed COVID-19 infection, perhaps a testament to the enhanced level of protection given to cancer patients. The pandemic has clearly had a significant impact on not just the rate of diagnosis, but also on treatment and follow-up.
Introduction

A study in 2009 demonstrated there were a number of preventable serious incidents occurring in hospitals around the UK. These were termed Never Events (NE). In 2015, as a way to mitigate these serious incidents, the National Patient Safety Agency (NPSA) released a report, recommending the creation and implementation of National Safety Standards for Invasive Procedures (NatSSIPs), which at a local level would be named Local Safety Standards for Invasive Procedures (LocSSIPs). In 2017, University Hospitals Birmingham (UHB) NHS Foundation Trust set up a LocSSIP steering committee, with the commitment to create and implement LocSSIPs across the trust.

Aims/Objectives: Our aim was to create and develop LocSSIPs within the haematology department and audit its implementation.

Methods: The project plan was divided into 4 phases: scoping, development, implementation and maintenance and monitoring. We identified a LocSSIP ‘champion’ within haematology and identified key procedures which would require LocSSIPs. Our safety standards were framed on NPSA guidance and standards of the WHO checklist but tailored for procedures within haematology. Following implementation, compliance was audited.

Results: The LocSSIP checklist was successfully developed and approved for implementation. Pre-procedure and sign-out sections were created to allow safety checks before and after the procedures whilst allowing for efficiency and effective use. All questions were tailored to haematology such as bone marrow biopsies, lumbar punctures, and line insertions. Additionally, key safety questions for conscious sedation were created in line with local Trust and NICE guidance. Compliance of haematology LocSSIPs was 93.5% involving 31 procedures.

Informal feedback overall mentioned that staff members felt safer using LocSSIPs. Standardisation further facilitated patient safety following redeployment of staff due to the pandemic and recent merger of Trusts.

Discussion/Conclusion: We have successfully demonstrated implementation and compliance of a LocSSIP in haematology. As with every quality improvement project, the work is longitudinal and the troubleshooting process is still ongoing. Continuous auditing and monitoring of their use is required as well as the long term effects on serious incidents.

Disclosure of Interest: None Declared

Abstract Table: Table 1. Performance comparison of various Deep learning models for blood cell classification.

<table>
<thead>
<tr>
<th>Models</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>F1-score</th>
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<tbody>
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Disclosure of Interest: None Declared

BSH2021-PO-058
Audit of uptake and user satisfaction of Attend Anywhere video consultations in Haematology outpatients QHB
Mariyam Eman Iqbal1*, Ifran Khan1, Harry Hambleton1, Ahmad Aldalaq1, Humayun Ahmad1, Aurangzeb Razzak1, Donna Beal1
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Abstract Content: Introduction: Telemedicine clinics have historically been unpopular due to a range of clinical barriers. In March 2020 WHO declared COVID-19 as a global pandemic. This was a paradigm shift in the world of clinical medicine and initiated a rapid transition into virtual clinics as a strategy to minimise face to face (FiF) visits and limit viral spread.

At Queen’s Hospital Burton, Haematology patients are among the most vulnerable given the immunosuppressive effects of their conditions and treatments. Our outpatient work involves assessment of patients receiving chemotherapy which can be associated with fatal complications. It was felt that telephone consultations may be suboptimal for these assessments, and with the unclear duration of the pandemic, there has been an initiative to recruit more patients to video clinics. The ‘Attend Anywhere’ (AA) video consultation system

Disclosure of Interest: None Declared

BSH2021-PO-057
Local safety standards for invasive procedures (LocSSIPs) in haematology
Zeba Ahmed1,*, Rushmi Purmessur3, Karen Sheldon2, Justin King1, Maria Stewart1, Richard Steyn1, Tim Graham1 and LocSSIPs Steering Committee UHB
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Abstract Content: Introduction: A study in 2009 demonstrated there were a number of preventable serious incidents occurring in

Disclosure of Interest: None Declared
was implemented in June. This drastically reduced the need for FtF visits to reduce infection risks.

**Objective:** The primary objective of this audit was to evaluate the uptake of AA over time. We also used the data to assess whether particular patient groups were more likely to engage in video consultations. A concurrent survey was organised in order to assess patient satisfaction with AA.

**Method:** A quantitative analysis of data from a consultant-led clinic was obtained from June to December 2020. The clinic letters were examined for patient demographics and to assess the type of consultation undertaken. A separate mixed-method survey of 29 patients was conducted as a part of our audit.

**Results:** The results revealed a trend towards video consultations over telephone consultations during the period of time analysed, although the volume of patients undertaking telephone consultations remained higher overall. Despite the proportion of AA consultations being higher in the lower age groups, it remained popular in older age groups.

The patient survey showed a high rate of patient satisfaction. A lot of the patients considered AA to be an excellent alternative to FtF and cited other significant benefits in saving time, reducing effort and minimising risk. Video consultations also felt more personal than over the phone and patients felt all their concerns were addressed with high standards of patient care.

**Conclusion:** The audit showed that AA consultations are popular with patients in all demographics. They are felt to be safer than telephone consultations. As many appointments are still conducted via telephone, there is further work to be done to encourage more patients onto AA.

A number of barriers to AA were noted. There were initially difficulties with staff accessing the software. There were a number of cases where patients either had no computer access, or struggled with the software. Improving communication and information booklets helped to overcome this. The older ages may have had higher representation if they had easier access to a computer, or if the software had been more straightforward. It is felt that a dedicated mobile application may provide a more user-friendly system for patients.

Whilst the added value of physical examination is missing in AA consultations, especially in new clinic patients, this has been a novel solution to challenges the pandemic has brought. It has helped to ensure continuity and safety in patient care.

**Disclosure of Interest:** None Declared

**BSH2021-PO-059**

**Haematology teams handover: improving communication, improving patient safety**

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**Abstract Content:** Introduction: The Royal College of Physicians recommend that standardisation of handover is vital to improving efficiency and patient safety [1,2]. At the Queen Elizabeth Hospital (QEH) Birmingham, the non-resident haematology on call specialist registrar (SpR) completes a 24-hour shift from 08.30 to 08.30 and is not on site to provide a face-to-face handover. In addition, there is a resident Twilight SpR from 13:00 to 22:00. Previously, 100% of haematology registrars felt that there should be a more formal process of handover. This has led to the implementation of a Microsoft Teams handover system called the Haematology Team Handover (HTH).

**HTH Design:** A Microsoft Team was created using the video conference platform which included haematology middle grade doctors working at QEH. The Morning Team Handover began at 08:30 every day excluding Sunday with the aim of facilitating handover from the overnight SpR to each ward team. A secondary aim was to prepare for anticipated admissions and review staffing levels. The Afternoon Team Handover began at 16:30 Monday to Friday with the addition of the Twilight SpR. A chair was assigned for each meeting and this was usually a senior SpR. The role of the chair was to lead the handover, ensure each team representative was present to receive and give handover for both meetings, review staffing levels and highlight elective admissions. The structure of the handover meetings was also placed in each doctor’s office on the haematology wards and a daily reminder was sent to each middle grade doctor to attend the meeting.

**Implementation:** The pilot phase of the HTH commenced on 16/12/2020 to 12/01/2021 and in this time period, 30 Morning Team Handovers and 20 Afternoon Team Handovers took place. We collected 15 days of data which focused on the following parameters: Timely start of Handover, attendance, themes of discussion (sick patients, admissions, staffing issues) and duration of meeting. From our data collection, we found that the handover started on time 81% of the time and there was at least one attending haematology consultant present 68% of the time. There were 2 instances of the overnight registrar not attending the handover, however a verbal handover was given. Sick patients were discussed 100% of the time and 90% of discussions also focused on anticipated admissions. Staffing issues were discussed on 23% of occasions to highlight rota gaps or redistribution of staff and on average, the handover lasted 13 minutes (range 5–29 min).

**Conclusion:** The Handover system was quickly established and although it was in a pilot phase, the majority of haematology registrars embraced the new handover system and felt it had integrated well into their working day. A survey of those who used HTH found that 100% of middle grades and consultants felt it improved patient safety.

**References:**

**Disclosure of Interest:** None Declared

**BSH2021-PO-060**

**Educational preferences in Maternal Haematology- A needs assessment**

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**Abstract Content:** Women with haematological disorders have unique needs during the perinatal period, where the intersection of the haematological disease and pregnancy can mutually impact each other, resulting in significant morbidity and even mortality. Haematologists, Internal Medicine (IM) physicians and Obstetricians are increasingly faced with the complex care of these women. There are limited data on the learning needs of these physicians to optimize the care of these patients. The objective of this study was to identify the educational needs of physicians caring for women with haematologic disease in pregnancy to direct the development of educational activities.
We conducted a cross-sectional study using a self-administered electronic questionnaire sent to Haematologists, Obstetricians, Maternal-Fetal Medicine (MFM) Specialists and IM Specialists across Canada. The study was approved by the Research Ethics Board of Sinai Health System in Toronto, Ontario.

The survey was administered electronically in English in collaboration with the Canadian Haematology Society and Canadian MFM program directors, using an online survey-distributing website, Survey Monkey™. The survey was administered from December 2019 to March 2020. Physicians were asked to rate prior education relating to relevant haematologic conditions in the context of pregnancy, the need for additional education and preferences for future learning.

Ninety-seven participants responded to the invitation, and 82 (85%) completed the survey. Fifteen (16%) incomplete surveys (completion of less than 25% of the questionnaire) were excluded from analysis. Respondents included 17 (20.7%) MFM specialists, 21 (26%) Obstetricians, 34 (42%) haematologists and five (6%) IM physicians. Half of respondents had < 5 years of practice (53%). Most respondents were female (70%).

Only 38% of respondents described the quality of their prior educational experiences as ‘very useful’ or ‘extremely useful’. Approximately half of the respondents rated their knowledge of Maternal Haematology as intermediate, 25% as beginner and 25% as advanced. Four percent of respondents described their knowledge level as ‘expert’.

All respondents in Obstetrics and MFM (100%) considered knowledge of how to diagnose venous thromboembolism during pregnancy as ‘important’. Amongst Haematology and IM physicians, anticoagulation (97%) and management of women with bleeding disorders in pregnancy (97%) were important topics.

Three-quarters of the respondents preferred a blended learning program, which would include a combination of face-to-face teaching and technology-enhanced learning activities. Respondents predominantly (76%) agreed that learning collaboratively with other specialties in a combined Maternal Haematology program would be helpful.

This multidisciplinary survey suggests that an interdisciplinary learning program involving collaboration across relevant subspecialties would be preferred by participants for the teaching and learning of Maternal Haematology. A program involving blended (in-person and technology-enhanced) learning modalities was viewed favourably by participants, and should aim to incorporate various topics identified as relevant. Future studies should assess the effect of a blended education program on learning and patient care.

Disclosure of Interest: None Declared

BSH2021-PO-061
Primary EBV driven secondary HLH successfully treated with Anakinra- a case report
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1Haematology, Colchester hospital, Colchester, United Kingdom

Abstract Content: Background: Haemophagocytic lymphohistocytosis (HLH) is a severe, life-threatening syndrome characterised by hyperinflammation and macrophage activation. Viral infections such as Epstein-Barr virus (EBV) are a well-recognised trigger of HLH but the treatment of such cases is not well-defined. We present a case of primary EBV driven HLH that was successfully treated with the interleukin-1 inhibitor anakinra in addition to rituximab and high-dose steroids.

Case: A 22-year-old female with no past medical history developed a mononucleosis-like illness lasting five days characterised by fevers, sore throat and neck swelling. Two weeks following this she presented with fevers, night sweats, fatigue and right upper quadrant pain. She was diagnosed with HLH based on high fevers with hyperferritaeemia, hypertriglyceridaemia, pancytopenia, abnormal liver function tests and hepatosplenomegaly. Extensive investigation revealed an EBV viral load of 23,000,000 copies/ml with nil other obvious triggers. A diagnosis of primary-driven EBV HLH was made. She was treated with the interleukin-1 inhibitor anakinra, methylprednisolone and IVIG and a single dose of rituximab.

Following the commencement of treatment, the patient made a dramatic improvement. Her EBV viral load reduced to 660 within nine days and her blood counts and liver function returned to normal. She was discharged from hospital on day sixteen. She continued the anakinra for 5 weeks at a weaning dose and completed a 12-week weaning dose of steroids. She has returned to her studies and has no lasting complications from her illness.

Discussion: This case highlights the potential of primary EBV infection to cause fulminant HLH. The prompt diagnosis and treatment of HLH using anakinra and rituximab in addition to conventional HLH treatment was safe, and associated with a dramatic clinical improvement. The use of anakinra has been documented in other cases of HLH but none, to our knowledge, of primary EBV-driven HLH with no underlying haematological or rheumatological condition.

Disclosure of Interest: None Declared

BSH2021-PO-062
Educational videos on haematology practical procedures: A UK first in online high-quality open access resources
Angharad Everden1,*, David Tucker1
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Abstract Content: High quality peer-reviewed online educational resources for specialist medical training are of vital importance in the digital era, particularly during the social distance constraints of the current pandemic. Performance of practical procedures to a high standard by the Haematology trainee is an essential part of Haematology training and is paramount for the delivery of excellent clinical care. To date, high quality online resources demonstrating standard techniques for haematological procedures are limited and access is often restricted by subscriptions. We identified this as an area of unmet need in the delivery of Haematology specialist training as well as for other specialists and healthcare professionals learning to perform practical procedures. We present the first open-access resource of quality-assured, demonstration videos for haematological procedures within the UK.

A series of videos was conceived, designed and produced, for the demonstration of bone marrow sampling and skin punch biopsy. The subject of bone marrow sampling was selected because of its universal requirement in haematological training. Skin punch biopsy was identified as particularly important given the relative novelty of this procedure within Haematology and its recent requirement for samples alongside bone marrow biopsy for patients eligible for the National Whole Genome Sequencing program. Evidence-based protocols for standardised technique were designed and peer-reviewed by a regional multi-disciplinary team, including consultant Haematologists and biomedical scientists. Patient safety, consent and confidentiality together with information governance were maintained through strict adherence to local Trust policy and with permission from the local National Health Service (NHS) Trust. The procedures were explained and demonstrated on models and subsequently on volunteer patients by senior clinicians. Video was captured and edited using Apple iMovie™ software. After approval by the Trust information governance lead, the videos have
Disclosure of Interest: None Declared

BSH2021-PO-063
Assessment of anti A and anti B IgM titre levels among aphaeresis platelet donors at national blood centre
Achana Obris*

Abstract Content: Assessment of Anti A and anti B IgM Titre Levels Among Aphaeresis Platelet Donors at National Blood Centre

(From 01st January 2019 to 31st December 2019)

Background: Prophylactic and therapeutic transfusions of platelets are effective in patients with qualitative and quantitative platelet defects. Platelet concentrates are derived from whole blood donations and apheresis donations. Even though the evidence suggests that the transfusion of ABO identical platelets is the component of choice such strategy could not be implemented due to unequal distribution of blood groups and the short life span of the platelets. Aphaeresic platelets contain substantial amount of plasma. Unavoidable group switching in platelet transfusions lead to increased risk of haemolysis due to high titre anti A and anti B IgM antibodies. Before implementation of a policy to use ABO non identical platelets such events should be minimized. Assessment of anti A/B titres is an effective method to identify high risk donors who are capable of causing haemolytic transfusion reactions.

Objective: To study the prevalence of anti A and anti B IgM titres in aphaeresis platelet donors at the National Blood Centre.

Materials and Methods: A descriptive prospective study was conducted among aphaeresis platelet donors who donated at the National Blood Centre during the period of one year from 01st of January to 31st December 2019. EDTA samples of these 301 donors with group O, A and B were collected and anti A and/or anti B IgM titer levels were tested with the saline tube method. Critical titer was considered as 128. These data were entered in a computerized database and analyzed with SPSS and Microsoft excel.

Results: Among the 301 donors, there were 100 group O aphaeresis platelet donors. From that 27% of them had a titer of anti A IgM above the critical level. Titrer levels ranged from 4 to 1024. Both median and mode of the titer were 64. Anti B titer of the group O donors ranged from 4 to 256 with a 32 titer of median and mode. Only 12% of them had a titer above the critical level. There were 110 group B aphaeresis donors whose anti A IgM titer levels ranged from 2 to 256. Median and mode of the titer were 32. High titer anti B was detected above the critical level. Titre levels ranged from 4 to 1024. Both median and mode of the titer were 32. High titer anti B was detected above the critical level. There were more than 39 years while most prevalent age group was 32-38 years. Almost 99% of them were males and majority of them were Sinhalese (96.68%). Tamils (1.61%) and Muslims (1.61%) represented a minority.

Conclusion: In Sri Lankan population considerable number of aphaeresis platelet donors present with a high titre anti A and/or anti B. Implementation of a policy on testing anti A and/or anti B in platelet aphaeresis donors should be warranted before using ABO non identical platelets in order to prevent passive haemolytic transfusion reactions.

Disclosure of Interest: None Declared

Abstract Content: CART QUOL is a study that has recently opened in the University Hospital of Wales Cardiff and was designed and set up by the Chief Investigator Emma Williams. Emma is a nurse and has been working within haematology since 2009. The study will be used to inform a dissertation project though will be done within her capacity of a research manager of the Clinical Research Group. CART therapy and regenerative medicine are a research theme of specialist interest within the South Wales Bone Marrow Transplant programme and a joint initiative between them and Wales Blood Service to establish a translational research platform in which to bring novel therapies to clinical practice.

As we have become more focused on establishing outcomes in a patient centred way, this project aligns to values based healthcare with its aim to collect real world data and experiences.

The aim of this study is to build on previous published data looking at the quality of life of patients who undergo CART therapy and follows on from a study published by Mariarz et al in BJH 2019.

Two quality of life tools will be used, one FACTLYM as used within the Mariarz study, specifically for Lymphoma patients and and EQ5DL tool which is widely established in clinical trials and recommended by health assessment bodies (EQ5DL 2019). The CART team looked at the tools used in the previous study and decided that the EQ5DL was easier to navigate and the terminology was easier for our patients to understand.

This study will align with Standard of care visits and patients will be consented after their initial CART counselling visit and prior to the infusion of cells. The rest of the quality of life forms will be collected at day 30, 3, 6, 9, 12 and 18 months. Our CART service aims to treat 12-15 patients per year with CART therapy and it has been estimated that accrual into the trial would be 8-10 patients per year.

There is an invisibility of nursing research due to a number of factors Seidlecki (2016) and this abstract aims to highlight the need for projects such as this despite Covid being an added obstacle. The REC authority and all involved with this study could see its relevance, moreso at this difficult time due to heightened anxieties of patients.

Emma has progressed from research nurse to research manager to PI and most recently CI and hopes this work will encourage others to take a lead on nursing projects which will in turn add breadth to the research portfolio.

This project was initially designed as a pilot study and for a single centre however it has potential to become a multi centred study and...
Education and professional
grow and benefit the haematology community and our patients further. The author is also keen to share her experiences of the R&D process and REC submission and how projects can be turned around quite quickly as this one if thought through and collaboration has been made between all parties.

Disclosure of Interest: None Declared

BSH2021-PO-065
Building resilience in face of change fatigue
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Abstract Content: Changes happen all the time within healthcare and being able to work flexibly is an integral part of our roles. Changes to services, ways of working, physical environment, staffing, our own work / life balance each require a period of adjustment, which has a cognitive, physical and psychological impact. Building resilience (defined as a process, not a personal trait) helps to increase our capacity to work flexibly and handle the effects of changes.

If changes occur more frequently, without the appropriate pause for embedding the new practices, that resilience can decrease and result in change fatigue. This has the potential to happen at any time in our lives, however it is clear that the amount and pace of change has been far greater for all those working within healthcare over the past year.

This presentation aims to build on the panel discussion about staff burnout, also being presented at this conference. We plan to focus on increasing awareness of the impact of multiple changes (both organisational and more general), strategies to build resilience and collate a variety of different sources of staff wellbeing offerings in order to provide delegates with a simple resource list to draw on.

Disclosure of Interest: None Declared

Abstract Table:

<table>
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<tr>
<th>N</th>
<th>Sex, age</th>
<th>Diagnosis, year of onset</th>
<th>Previous therapy</th>
<th>Rituximab therapy regimen</th>
<th>Pre-treatment condition</th>
<th>Start of treatment with Rituximab</th>
<th>Result of the first course</th>
<th>Response duration (months)</th>
<th>Current status</th>
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<td>1</td>
<td>F,72</td>
<td>Lewis-Sumner syndrome (NADASAM), 2001</td>
<td>Steroids, plasmapheresis</td>
<td>Course of 375 mg/m²-4 weekly infusions. 4 courses every 6 months.</td>
<td>Moving and standing with walkers only</td>
<td>08.2016</td>
<td>Walking without support after the first month</td>
<td>40</td>
<td>Worsening since 08.2020</td>
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<tr>
<td>2</td>
<td>F,48</td>
<td>Demyelinating polyneuropathy associated with monoclonal IgM, anti-myelin associated glycoprotein antibodies, 2010</td>
<td>Steroids, plasmapheresis, azathioprine</td>
<td></td>
<td></td>
<td>08.2017</td>
<td>Walking without support after the first month</td>
<td>49</td>
<td>Stable improving</td>
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<tr>
<td>3</td>
<td>M,58</td>
<td>Demyelinating polyneuropathy associated with monoclonal IgG, 2013</td>
<td></td>
<td>Walking on the stairs with support only</td>
<td>04.2019</td>
<td>Walking on the stairs without support after the 5 months</td>
<td>17</td>
<td>Stable improving</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F,69</td>
<td>Chronic inflammatory demyelinating polyneuropathy, 2019</td>
<td>Prednisolone 1000 mg - 2 biweekly infusions</td>
<td>Walking with trekking poles only</td>
<td>09.2020</td>
<td>Non available (in-bed after traumatic lumbar vertebral fracture)</td>
<td>NA</td>
<td>In-bed</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F,59</td>
<td>Motor multifocal polyneuropathy, 2011</td>
<td>IV immunoglobulin 1000 mg/m²-2 biweekly infusions</td>
<td>Walking with trekking poles only</td>
<td>12.2019</td>
<td>No response</td>
<td>–</td>
<td>–</td>
<td></td>
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</tbody>
</table>
Liaison haematology: starting to quantify the hidden patient need

Frances Seymour1*, Samuel Harrison2, Shereef Elmoamly3, Charles Percy4, Will Lester4, Suzy Morton4, Isabelle Craner5, Holly Baker4, Gillian C. Lowe, Hayder Hussein

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Abstract Content: Liaison haematology is an essential component of many haematologists’ job roles. It involves providing clinical advice to a broad spectrum of clinical specialities in primary and secondary care, regarding a wide range of conditions. Haematology trainees routinely provide the first point of contact for referrals in many centres, and training for this has historically been experiential, and variable between training rotations. We attempted to evaluate the service provided in liaison haematology in a large tertiary teaching hospital with a retrospective review, and prospective study, to identify patterns of referrals. We found that an average of 18 contacts were made with the liaison team per day, with questions regarding cytopenias, thrombosis/anticoagulation queries and suspected malignancy being the most common. We hope to use this data to enhance the service, by tailoring training provided to trainee haematologists undertaking this role, and producing supporting materials and guidelines for referring teams to improve consistency. It will also be used to better quantify the demand for the service for the purposes of job and departmental planning.

Disclosure of Interest: None Declared
General Haematology including ITP and Myeloproliferative Disorders

BSH2021-PO-068

CPI-0610, a bromodomain and extracellular domain protein (bet) inhibitor, in combination with ruxolitinib, in jak-inhibitor-naive myelofibrosis patients: update of manifest phase 2 study

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Abstract Content: CPI-0610, a first-in-class, oral, small-molecule inhibitor of bromodomain and extraternal domain (BET) proteins, potentially promotes disease-modifying activity through altered gene regulation of key oncogenic, fibrotic, and inflammatory factors and may transform the standard of care in myelofibrosis (MF). CPI-0610 in combination with ruxolitinib (CPI-0610 +rux) is currently being studied in JAK-inhibitor (JAKi) treatment-naïve MF patients (pts) in Arm 3 of MANIFEST, a global, open-label, phase 2 study. Approximately one third of JAKi naïve MF patients treated with rux (35%; 106 of 301) or fedratinib (37%; 35 of 96) achieved a spleen volume reduction ≥ 35% (SVR35) at 6–12 months. CPI-0610, a potential disease-modifying therapeutic agent with a novel mechanism of action may improve the outcome in MF pts. Here we report the safety and efficacy data from Arm 3 of the ongoing MANIFEST study. Eligibility: JAKi-treatment-naïve MF pts with DIPSS score ≥Int-2; platelet ≥100 × 10^9/L; spleen volume ≥ 450 cc by CT/MRI; ≥2 symptoms measurable (score ≥3) or a total symptom score (TSS) of ≥10 using the MFSAF v4.0. Primary endpoint: SVR35 response (≥35% reduction in spleen volume) at week 24; key secondary endpoint: TSS50 response (≥50% reduction in TSS) at wk 24; other endpoints: safety, PK; changes in proinflammatory cytokines and bone marrow morphology/fibrosis.

As of 29 September 2020, 78 pts treated, 66 pts ongoing. Baseline characteristics: mean age: 67 years old; 72% male; primary MF: 54% pts; DIPSS ≥Int-2: 76% pts; IPSS ≥Int-2: 83%; 65% pts anemic (Hgb <10 g/dl); median platelet: 294 × 10^9/L (range: 100, 1849); median spleen volume: 1719 cc (range: 451, 4782); median TSS: 16 (range: 0, 38); high-molecular-risk mutations: 55% pts, and JAK2 mutation: 72%. At week 24, 67% (42/63) pts achieved SVR35 (median % change from baseline: −50%; range: −84.4%, 23.7%) and 57% (34/60) pts achieved TSS50 (median % change from baseline: −59%; range: −100%, 225%). Additionally, 33% (16/48) of pts had at least one grade improvement in bone marrow fibrosis. 78 pts were evaluable for safety. Median exposure was 40 wks. The most common hematological treatment-emergent adverse events (TEAEs) of any grade were anemia (33%, ≥Gr3: 30%) and thrombocytopenia (32%, ≥Gr3: 8%). These cytopenias were generally manageable with dose modifications. The most common non-hematological TEAEs (≥15%) were diarrhea (30%, no ≥Gr3), dysgeusia (19%, no ≥Gr3), asthenic conditions (19%, no ≥Gr3), musculoskeletal pain (19%, no ≥Gr3), respiratory tract infections (18%, ≥Gr3: 1%), nausea (17%, no ≥Gr3), abdominal pain (17%, no ≥Gr3), and dizziness (17%, no ≥Gr3).

CPI-0610 + rux combination is generally well-tolerated in JAKi-treatment-naïve MF pts. The encouraging clinical data demonstrate the potential for the combination treatment to provide enhanced efficacy as evidenced by higher SVR35 and TSS50 rates at wk 24 compared with historical data from pivotal phase 3 studies. Overall, the data suggest that the addition of CPI-0610 to rux is potentially synergistic in JAKi-naïve MF pts. A phase 3, randomized, double blind, active-control study to further evaluate this combination is initiated.

Disclosure of Interest: A. Mead Conflict with: Novartis, Celgene/BMS, AbbVie, CTI, Gilead, Conflict with: Novartis, Celgene/BMS, Conflict with: Novartis, Celgene/BMS, J. Mascarenhas Conflict with: Celgene, Predule, Galecto, Promedior, Geron, Constellation Pharmaceuticals, Incyte, Conflict with: Incyte, Kartos, Roche, Promedior, Merck, Merus, Arog, CTI, Janssen, PharmaEssentia, M. Talpaz Conflict with: Constellation Pharmaceuticals, BMS, IMAGO, Conflict with: Takeda, Novartis, A. Patriarca: None Declared, T. Devos: None Declared, F. Palandri Conflict with: Novartis, F. Passamonti: None Declared, R. Rampal Conflict with: Incyte, Celgene, Promedior, CTI Biopharma, Jazz Pharmaceuticals, Blueprint, Stemline, Galecto, Abb-Vie, PharmaEssentia, Conflict with: Incyte, Stemline, Constellation, M. Kremyanskaya Conflict with: Protagonist Therapeutics, Bristol Myers Squibb, Astex Pharmaceuticals, Conflict with: Protagonist Therapeutics, Constellation Pharmaceuticals, Incyte Corporation, J. Scandura Conflict with: AbbVie, T. Somerville Conflict with: Novartis, Conflict with: Imago Bioscience, M. Wondergem: None Declared, N. Granacher: None Declared, R. Hoffman Conflict with: Dompe, V. Gupta Conflict with: Novartis, Sierra Oncology, Bristol Myers Squibb, Pfizer, Conflict with: Novartis, Incyte, Conflict with: Novartis, BMS, Incyte, K. Luptakova Conflict with: Constellation Pharmaceuticals, J. Wang Conflict with: Constellation Pharmaceuticals, Conflict with: Constellation Pharmaceuticals, G. Colak Conflict with: Constellation Pharmaceuticals, J. Shao Conflict with: Constellation Pharmaceuticals, S. Bobba Conflict with: Constellation Pharmaceuticals, P. Trojer Conflict with: Constellation Pharmaceuticals, S. Verstovsek Conflict with: Incyte, Celgene, Novartis, Sierra Oncology, Conflict with: Incyte, Roche, NS Pharma, Celgene, Gilead, Promedior, CTI, Genentech, Blueprint Medicines Corp, Novartis, Sierra Oncology, PharmaEssentia, AstraZeneca, Italfarma, Protagonist Therapeutics, C. Harrison Conflict with: Celgene, Novartis, Conflict with: Celgene, CTI, Gilead, Incyte, Jansen, Novartis, Shire, AOP Orphan Pharmaceuticals, Promedior, Roche, Sierra Oncology
Advanced systemic mastocytosis with clonal emergence of acute myeloid leukaemia while receiving the KIT D816V inhibitor avapritinib: successfully managed by allogeneic haematopoietic cell transplantation.

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1Haematology, Guy’s and St Thomas’ Hospital, London, United Kingdom, 2Blueprint Medicines, Cambridge, United States, 3Haematology research department, Guy’s and St Thomas’ Hospital, London, 4Haematology, The Royal Marsden NHS Foundation trust, Sutton, 5Haematology, The Royal Bournemouth Hospital, Bournemouth, 6Haematology, Southampton General Hospital, Southampton, United Kingdom

Abstract Content: Advanced systemic mastocytosis (AdvSM) is a rare, life-limiting mast cell (MC) neoplasm driven by the KIT D816V mutation in 90-95% of patients. Patients with mast cell leukaemia (MCL) or with co-mutations in SRSF2, ASXL1 and/or RUNX1 have a poor prognosis 60–70% of AdvSM patients have an associated haematological neoplasm (AHN) and are therapeutically challenging. Avapritinib a selective tyrosine kinase inhibitor against KIT D816V, has shown potent activity and durable responses amongst these patients in the Phase 1 EXPLORER study (NCT02561988).

Abstract Table:
Table 1: Summary of patients’ diagnostics and response to treatments. PRCA = Pure red cell aplasia; ND = not detected

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Case 1</th>
<th>Case 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>45</td>
<td>64</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>AdvSM-AHN (MDS/MPN-U)</td>
<td>MCL-AHN (CMML-0)</td>
</tr>
<tr>
<td>Baseline Tryptase (µg/L)</td>
<td>962</td>
<td>606</td>
</tr>
<tr>
<td>Baseline BM MC bulk (%)</td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td>Baseline MGP</td>
<td>GATA2; DNMT3A; TET2 [AC/AC/A]; TET2 [G-G/A]</td>
<td>ATRX; SRSF2; GATA2 [GTTGC&gt;GTTGC/G frameshift]; ASXL1(A&gt;A/AGG frameshift)</td>
</tr>
<tr>
<td>Baseline C-KIT D816V allele burden (%)</td>
<td>11.9</td>
<td>44</td>
</tr>
<tr>
<td>Avapritinib daily dose (mg)</td>
<td>60 start, escalated to 100</td>
<td>200 start, reduced to 100</td>
</tr>
<tr>
<td>No. of cycles on avapritinib</td>
<td>43</td>
<td>27</td>
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<tr>
<td>Best Tryptase response (µg/L)</td>
<td>9.7</td>
<td>11</td>
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<tr>
<td>SM response (modified IWG-MRT -ECNM criteria)</td>
<td>CR</td>
<td>CR</td>
</tr>
<tr>
<td>Tryptase at time of AML diagnosis (ug/L)</td>
<td>13</td>
<td>137</td>
</tr>
<tr>
<td>Baseline AML bulk (%)</td>
<td>80</td>
<td>25-30</td>
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<tr>
<td>MGP at AML diagnosis</td>
<td>TP53; SRSF2; TET2 [L1514P]; NPM1</td>
<td>GATA2 [G135]; ASXL1 [A&gt;A/AG frameshift]</td>
</tr>
<tr>
<td>- Screening</td>
<td>15.52 33.32 34.03 ND 45.8 ND 47.1 ND</td>
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<tr>
<td>- C3D1</td>
<td>1.2 24.7 22.3 ND – – – –</td>
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<td>- C7D1</td>
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<td>- C11D1</td>
<td>ND 38.4 35.9 ND 39.7 34.9 38.6 7.9</td>
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<td>- C18 D1</td>
<td>ND 36.9 36.6 ND 24 35.4 23.6 19.7</td>
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<td>- C24D1</td>
<td>ND 42.3 39.8 ND 2.5 31.4 2.7 38.9</td>
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<td>- C42D1</td>
<td>ND 42.7 41.8 ND – – – –</td>
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<tr>
<td>AML treatment</td>
<td>FLAG-Ida x2</td>
<td>CPX-351 x2</td>
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<tr>
<td>Best AML response</td>
<td>Morphological CR</td>
<td>Morphological PR</td>
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<tr>
<td>Allo-HCT</td>
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<td>- Donor</td>
<td>Fludarabine/Busulfan</td>
<td>Fludarabine/Melphalan/Campath</td>
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<td>- Conditioning</td>
<td>O+ve/A-ve</td>
<td>A+ve/B+ve</td>
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<td>- ABO group (Recipient/Donor)</td>
<td>–/–</td>
<td>+/+</td>
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<td>- CMV status</td>
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<td>D+11</td>
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<td>- Day of neutrophil engraftment</td>
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<tr>
<td>- D+100&lt; complications</td>
<td>PRCA due to ABO mismatch</td>
<td>None – DLI</td>
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<tr>
<td>- D+100&gt; complications</td>
<td>Ciclosporin/MMF</td>
<td>Ciclosporin/short course MTX</td>
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<td>- Immunosuppression</td>
<td>100% whole blood+100</td>
<td>100% whole blood</td>
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<tr>
<td>- PB Chimerism D100</td>
<td>CR</td>
<td>CR</td>
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<tr>
<td>- Response post HCT</td>
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</table>
We report 2 patients with AdvSM on avapritinib in the EXPLORER study who developed Acute Myeloid Leukaemia (AML) having a complete remission (CR) of SM. We review responses to avapritinib as per the modified IWG-MRT-ECNM criteria and describe clonal dynamics as detected by a targeted myeloid gene panel (MGP).

**Case 1**: Female 45 years with ASM-AHN (MDS/MPN-U): ECOG 1, urticaria pigmentosa, weight loss, splenomegaly, anaemia, tryptase 962 µg/l, 50% bone marrow (BM) MC burden & GI infiltration. In addition to KIT D816V, GATA2, TET2 and DNMT3A mutations were detected at enrolment. Treated with avapritinib 60 mg increased to 100 mg OD. She had a marked clinical response within 6 months; ECOG 0, skin rash resolution, normal spleen & morphological remission of SM with CR achieved by 18 months. Noted a rash at C42; biopsy showed blastic plasmacytoid dendritic cells & BM confirmed AML. Acquisition of new pathogenetic mutations TP53, SRSF2, TET2 and NPM1 were identified. Underwent salvage therapy with FLAG-Ida x 2 complicated by aspergillosis and achieved CR post #2. She proceeded to reduced intensity unrelated donor allogeneic haematopoietic cell transplant (allo-HCT). At present she is 8 months post allo-HCT, complicated by veno-occlusive disease and red cell aplasia due to donor ABO incompatibility, and remains in CR re: AML with 100% donor chimerism.

**Case 2**: Male 64 years with MCL-AHN (CMML-0): ECOC 2 with weight loss, splenomegaly, anaemia, thrombocytopenia, tryptase 606 µg/l and 40% BM MC burden. Marked clinical response with avapritinib 100 mg OD on study; at 6 months normal spleen, SM morphological CR, ECOC 0 and SM CR at 12 months. AML diagnosed on routine trial C24 BM. In contrast to case 1, multiple mutations were detected at baseline MGP including ATRX, SRSF2, GATA2 and ASXL1. Notably, at diagnosis of AML, GATA2 and ASXL1 variant allelic frequency (VAF) increased as KIT D816V VAF decreased. Following CPX-351 x 2, achieved a partial morphological response complicated by invasive fungal infection. At present he is 15 months following unrelated donor allo-HCT, remains clinically well in CR re: AML with 100% donor chimerism.

**In conclusion** we present 2 cases of AdvSM patients successfully treated to SM CR with avapritinib on the EXPLORER study. Emergence of AML in these cases likely represents expansion of low-level clones and acquisition of new clones within the BM AHN ‘niche’ while the SM component is in CR. Both patients were clinically asymptomatic with normal blood counts at time of AML diagnosis, highlighting the importance of regular MRD monitoring to detect early signs of AHN progression. Avapritinib is the first investigational treatment to achieve CR in AdvSM patients, making allo-HCT a potentially curative treatment option, with improved outcomes for patients with AHN who have a suitable donor.


**Abstract Content**: CPI-0610, a first-in-class, oral, small-molecule inhibitor of bromodomain and extraterrestrial domain protein (BET) proteins, potentially promotes disease-modifying activity through altered gene regulation of key oncogenic, fibrotic, and inflammatory factors and may transform the standard of care in myelofibrosis (MF). The majority of MF patients (pts) show suboptimal responses to ruxolitinib. In addition, ≥Gr3 anemia (45.2%) and thrombocytopenia (12.9%) are AEs associated with rux treatment. CPI-0610 may act synergistically in combination with rux in advanced MF. Here we present results from Arm 2 of the ongoing Phase 2 MANIFEST study, investigating CPI-0610 as “add-on” to rux in advanced MF pts with suboptimal response to rux.

Pts are stratified as transfusion dependent (TD, defined as ≥2U RBCs/month over 12 weeks), and non-transfusion dependent (non-TD). Eligibility: MF pts having a suboptimal or lost response to rux; DIPSS ≥Int-2; platelets ≥5 x 10^11/L; ≥2 symptoms measurable (score ≥1) per MSFAF v4.0; RBC TD (TD cohort) or spleen volume of ≥450 cc by CT/MRI (non-TD cohort). Pts treated with rux for ≥6 months and on a stable dose for ≥8 weeks prior to enrollment. Rux dose escalation is not allowed during the study. Primary endpoints: TD cohort: TD to TI (transfusion independence) [defined as no transfusion for 12 weeks per IWG-MRT criteria]; non-TD cohort: SVR35 response (≥35% spleen volume reduction) at week 24. Secondary endpoints: TSS50 response (≥50% total symptom score reduction) per MSFAF v4.0 at wk 24, safety and PK.

As of 29 Sep 2020, 52 pts were treated in the TD cohort (median treatment duration 30 weeks, range: 1, 166 weeks). Mean age 70 years, 67% male, 94% with hemoglobin (Hgb) <10 g/dL, 100% with DIPSS ≥Int-2, 79% with primary MF, 56% with high-molecular-risk and 52% with JAK2 mutations. 36% (13/36) of TD pts converted to TI. At wk 24, 21% (7/33) pts achieved SVR35 (median % change from baseline: BSH2021-PO-070 CPI-0610, bromodomain and extraterrestrial domain protein (BET) inhibitor, as “add-on” to ruxolitinib, in advanced myelofibrosis patients with suboptimal response: update of MANIFEST phase 2 study

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−19%, range: −54%, 48%), and 46% (15/33) pts achieved TSS30 (median % change from baseline: −8%, range: −100%, 24%).

In non-TD cohort, 26 pts were treated (median treatment duration 51 weeks, range: 2, 111 weeks). Mean age 63 years (SD: 7), 50% male, 73% with DIPSS ≥Int-2, 54% with primary MF, 77% with high-molecular-risk and 81% with JAK2 mutations. At week 24, 29% (6/21) pts achieved SVR35 (median % change from baseline: −17%, range: −90%, 16%), and 38% (8/21) pts achieved TSS30 (median % change from baseline: −45%, range: −100%, 22%).

78 pts were evaluable for safety across the TD and non-TD cohorts. Median exposure was 45 weeks. The most common hematological treatment-emergent adverse events (TEAEs) of any grade were thrombocytopenia (45%, ≥Gr3: 23%) and anemia (14%, ≥Gr3: 10%). The most common (≥20%) non-hematological TEAEs were diarrhea (51%, ≥Gr3: 4%), respiratory tract infections (35%, ≥Gr3: 5%), asthenic conditions (33%, ≥Gr3: 4%), nausea (33%, ≥Gr3: 3%), cough (24%, no ≥Gr3) and dysgeusia (22%, no ≥Gr3). 9 pts (12%) discontinued treatment due to TEAEs.

Early clinical data indicate that CPI-0610 as “add-on” to ruxolitinib is generally well tolerated. The combination therapy provided clinical benefits in most pts as assessed by SVR, and symptomatic responses. In addition, conversion to TI was also observed in TD patients.

Disclosure of Interest: T. Somervaille Conflict with: Novartis, Conflict with: Imago Bioscience, S. Verstovsek Conflict with: Incyte, Celgene, Novartis, Sierra Oncology, Conflict with: Incyte, Roche, NS Pharma, Celgene, Gilead, Promedior, CTI, Genentech, Blueprint Medicines Corp, Novartis, Sierra Oncology, PharmaEssentia, AstraZeneca, Italfarma, Protagonist Therapeutics, J. Macarenahas Conflict with: Celgene, Prelude, Galecto, Promedior, Geron, Constellation Pharmaceuticals, Incyte, Conflict with: Incyte, Kartos, Roche, Promedior, Merck, Merus, Arog, CTI, Janssen, PharmaEssentia, M. Kremyanskaya Conflict with: Protagonist Therapeutics, Bristol Myers Squibb, Astex Pharmaceuticals, Conflict with: Protagonist Therapeutics, Constellation Pharmaceuticals, Incyte Corporation, R. Hoffman Conflict with: Dompe, R. Rampal Conflict with: Incyte, Celgene, Promedior, CTI Biopharma, Jazz Pharmaceuticals, Blueprint, Stemline, Galecto, Abbvie, PharmaEssentia, Conflict with: Incyte, Stemline, Constellation, V. Gupta Conflict with: Novartis, Sierra Oncology, Bristol Myers Squibb, Pfizer, Conflict with: Novartis, Incyte, Conflict with: Novartis, BMS, Incyte, M. Talpaz Conflict with: Constellation Pharmaceuticals, BMS, IMAGO, Conflict with: Takeda, Novartis, N. Grancher: None Declared, R. Leber Conflict with: Otsuka Pharmaceutical, Pfizer, Novartis, Abbvie, BMS/Celgene, A. Patriarca: None Declared, J. Lambert Conflict with: Constellation Pharmaceuticals, J. Christo Conflict with: Constellation Pharmaceuticals, J. Wang Conflict with: Constellation Pharmaceuticals, G. Colak Conflict with: Constellation Pharmaceuticals, J. Shao Conflict with: Constellation Pharmaceuticals, S. Bobba Conflict with: Constellation Pharmaceuticals, P. Trojer Conflict with: Constellation Pharmaceuticals, C. Harrison Conflict with: Celgene, Novartis, Conflict with: Celgene, CTI, Gilead, Incyte, Janssen, Novartis, Shire, AOP Orphan Pharmaceuticals, Promedior, Roche, Sierra Oncology.

BSH2021-PO-071
An interesting case highlighting the need to test for JAK2 fusions
Christopher Mullen*, Herimela Degefa, Neill Storrar, Anthony Bench, Victoria Campbell

Abstract Content: A 66-year-old male referred with an incidental leucocytosis (HB 140 g/L, WCC 47.5 × 10⁹/L, neutrophils 30.4 × 10⁹/L, eosinophils 2.9 × 10⁹/L, monocytes 0.63 × 10⁹/L and platelets 123 × 10⁹/L). He had minimal past medical history. He had no constitutional, infective or inflammatory symptoms. Clinical examination was normal. Clinical biochemistry was unremarkable, inflammatory indices were normal. Blood film showed no dysplasia. Peripheral blood molecular testing was negative for JAK2 V617F and KIT D816V mutations and BCR-ABL1, and FIP1L1-PDGFRA fusions. Bone marrow aspirate and trephine were markedly hypercellular with myeloid expansion but minimal dysplasia; basophilis, eosinophils and mast cells were prominent. Myeloblasts were not increased. There was no evidence of fibrosis. Immunophenotyping demonstrated 1% CD34 positive cells. Karyotyping revealed a normal male karyotype. Fluorescence in situ hybridisation (FISH) demonstrated a normal pattern with FIP1L1-CHIC2-PDGFRA, FGFR1 and PDGFRB probe systems. Next generation sequencing revealed a likely pathogenic variant within TET2 (c.5618T>G; p.(Ile1873Thr)) and a BCR-JAK2 fusion joining BCR exon 1 to JAK2 exon 19. FISH did not detect an obvious gross structural change of BCR. The final diagnosis was myeloproliferative neoplasm (Unclassifiable) with associated BCR-JAK2 fusion, it could also be considered a variant of ‘Myeloid neoplasms with PCM1-JAK2’, a provisional entity of the World Health Organisation classifications. The patient was initially treated with hydroxyureabamide pending approval for ruxolitinib whilst being worked up for allogeneic stem cell transplant.

Myeloproliferative neoplasms (MPNs) are clonal haematopoietic stem cell disorders characterised by expansion of the myeloid lineages. Many are associated with abnormalities in genes encoding tyrosine kinases such as JAK2. The gain-of-function Val617Phe mutation is the most frequent genetic aberration within JAK2. Fusions involving JAK2 are much rarer than mutations and can be associated with a range of haematological disorders including leukaemia, lymphoma, MPN and myelodysplastic/myeloproliferative neoplasms (MDS/MPN). Several JAK2 fusion partners have been identified, with BCR, PCM1 and ETV6 being the most common. The BCR-JAK2 fusion gene has only been identified in a few cases worldwide with three clinical phenotypes: a myeloproliferative neoplasm (as in our case), acute lymphoblastic leukaemia and acute myeloid leukaemia. The JAK1/JAK2 inhibitor ruxolitinib was developed following the identification of abnormal JAK/STAT signalling in MPNs; it is licensed for use in disease-related splanchnomegaly or symptomatic myelofibrosis, primary or secondary. JAK2 fusions are thought to be associated with a more aggressive clinical course than other chronic myeloid malignancies, and as such allogeneic stem cell transplant is considered the most appropriate treatment where possible, with ruxolitinib being utilised as a bridge to transplant, by improving remission rate prior to the transplantation.

Given the distinct clinical and pathological characteristics, as illustrated in this case, we believe testing for a JAK2 fusions should be considered in otherwise unclassifiable myeloid / lymphoid neoplasms, especially those with eosinophilia.

Disclosure of Interest: None Declared.
**BSH2021-PO-072**

**A Longitudinal Population Level Analysis of Healthcare Resource Utilization and Morbidities in Idiopathic Multicentric Castleman Disease Patients.**

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**Abstract Content:** Human herpesvirus-8 (HHV8)-negative/idiopathic multicentric Castleman disease (iMCD) is a heterogeneous group of diseases characterized by a proinflammatory hypercytokinemic state with a wide range of systemic manifestations, ranging from generalized lymphadenopathy to death in severe cases. Limited data has shown an increased prevalence of organ dysfunction and cancers in iMCD patients either as a result of underlying disease pathophysiology or treatment received. The objective of this study was to assess the healthcare resource utilization and patterns of iMCD-related morbidities for iMCD patients in a real-world setting.

We performed a retrospective analysis of administrative claims data for more than 30 million United States patients continuously enrolled over a 3-year study period from January 1, 2017 to December 31, 2019. Patients were identified as having iMCD if they had an ICD-10 diagnosis code for Castleman disease (D47.Z2) and 2 diagnostic codes corresponding to the minor criteria from the international evidence-based consensus diagnostic criteria for iMCD. Exclusion criteria included history of HIV, HHV-8, lymphoma, myeloma, lupus, or rheumatoid arthritis within 1 year of diagnosis of Castleman disease. Index diagnosis date (IDD) was defined as the first time a patient received a diagnosis for Castleman disease using the new ICD-10 code (D47.Z2) or the general code for lymphadenopathy (785.6) in ICD-9 that included Castleman disease, whichever was diagnosed first between 2006 and 2019. Included patients were followed for up to 5 years from IDD and evaluated for post-diagnosis hospitalizations, emergency room (ER) visits, hematologic malignancies, non-hematologic malignancies, thromboses, and organ dysfunction.

We identified 199 iMCD patients, 111 women (55.8%) and 88 men (44.2%), with a mean age of 50.6 years (range: 6–90). The average post-diagnosis follow-up was 3.2 years after IDD (range: 0.3–14.1). The annual prevalence of hospitalizations, ER visits and iMCD-related morbidities in patients following iMCD diagnosis are presented in Table 1. Within the first year of iMCD diagnosis, 59.8% of patients required inpatient hospitalization and 54.3% had at least one ER visit. Among the patients who remained enrolled after the first year, an average of 25.9% were hospitalized and 36.5% visited the ER during each subsequent year. The annual rate of hospitalizations and ER visits for the entire database of over 30 million patients was 9.0% and 20.6%, respectively. The annual prevalence of iMCD-related morbidities in this cohort was 18.0% for non-hematologic malignancies, 6.3% for hematologic malignancies (including lymphomas and myelomas from second year of follow-up onwards), 5.9% for thromboses, 6.3% for renal failure, and 5.2% for respiratory failure.

Using a large, nationally representative health claims database, we identified a cohort of iMCD patients and found a high rate of hospitalizations and ER visits in the first 5 years following diagnosis. The annual prevalence of iMCD-related organ failure was approximately 5–6%, primarily involving renal and respiratory systems. This study provides further evidence to support the previously reported increase in frequency of subsequent hematologic and non-hematologic malignancies in iMCD patients.

**Abstract Table:**

Table 1. Annual prevalence of hospitalizations, emergency room visits and iMCD-related morbidities in patients following iMCD diagnosis

<table>
<thead>
<tr>
<th>Years following initial iMCD diagnosis</th>
<th>Total remaining enrolled iMCD patients (n)</th>
<th>Annual percentage of iMCD patients with inpatient hospitalizations (n)</th>
<th>Annual percentage of iMCD patients with emergency room visits (n)</th>
<th>Annual prevalence of iMCD-related comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hematologic malignancies</td>
</tr>
<tr>
<td>1</td>
<td>199</td>
<td>59.8% (119)</td>
<td>54.3% (108)</td>
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<td>25.4% (43)</td>
<td>33.7% (57)</td>
<td>5.9% (10)</td>
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<td>3</td>
<td>110</td>
<td>24.5% (27)</td>
<td>28.2% (31)</td>
<td>5.5% (6)</td>
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<tr>
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<td>33.3% (27)</td>
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<td>55</td>
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</tbody>
</table>
BSH2021-PO-073
Long-term Safety of Fostamatinib, an Oral Spleen Tyrosine Kinase Inhibitor, in Treating Immune Thrombocytopenia and Rheumatoid Arthritis
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Abstract Content: Fostamatinib, an oral spleen tyrosine kinase inhibitor has been shown to be efficacious for the treatment of immune thrombocytopenia (ITP). Spleen tyrosine kinase couples immune cell receptors to intracellular signaling pathways. Data on the long-term safety of fostamatinib (doses up to 150 mg BID) were collected in >4000 patients with ITP, rheumatoid arthritis (RA), and other autoimmune, allergic and neoplastic disorders. Fostamatinib was consistently safe and well-tolerated across the different patient populations. Safety analysis of fostamatinib in the ITP and RA studies is summarized below.

Safety data on fostamatinib in ITP were pooled from two randomized, double-blind, placebo-controlled, phase 3 studies and a long-term, open-label, extension study for this analysis. These studies had a starting dose of 200 mg/day, which increased to 300 mg/day after 4 weeks in 88% of patients. Thirteen phase 2/3 studies on fostamatinib in RA were pooled based on dosing regimens of 100–150 mg/day (n = 1232) or 200–300 mg/day (n = 2205).

For ITP, the data set contained 146 patients (60% female; median age 53 years). Fostamatinib treatment continued a mean duration of 19 months (range ~1–62 months) reflecting 229 patient exposure years. Adverse events (AEs) were reported in 87% of patients. Mild to moderately severe AEs were seen in 63% of patients. For 58 patients that received fostamatinib for over one year, the incidence of diarrhea, hypertension, and elevations in alanine aminotransferase and aspartate aminotransferase were compared in 3-month increments to assess any cumulative effects of fostamatinib. A decreasing frequency of these AEs was observed during the second, third, and fourth quarters of fostamatinib treatment compared to first quarter. The use of rescue therapy was decreased quarterly, and median platelet counts increased during each quarter in this population of patients. Only 0.7% of all patients had potential thrombocytopenia (ITP). Spleen tyrosine kinase couples immune cell receptors to intracellular signaling pathways. Data on the long-term safety of fostamatinib (doses up to 150 mg BID) were collected in >4000 patients with ITP, rheumatoid arthritis (RA), and other autoimmune, allergic and neoplastic disorders. Fostamatinib was consistently safe and well-tolerated across the different patient populations. Safety analysis of fostamatinib in the ITP and RA studies is summarized below.

For RA, the pooled data set included 3437 patients treated with fostamatinib (83% female; median age 54 years). Fostamatinib treatment lasted a mean duration of 18 months (range ~1–81 months) corresponding to 5134 patient exposure years. Overall, AEs were reported in 86% of RA patients. Mild to moderate AEs were seen in 73% of patients. In placebo-controlled studies, 2414 RA patients received fostamatinib and 1169 received placebo. Despite a greater exposure to fostamatinib vs placebo (823 vs. 367 exposure years), only 26% more AEs were observed with fostamatinib than placebo (68% vs 54%).

The most common AEs (not disease-related) for ITP and RA, respectively, were diarrhea (36% and 24%), hypertension (22% and 19%) and nausea (19% and 8%). Additionally, epistaxis (19% and 0.5%), petechiae (15% and 0.3%), contusion (12% and 2%), and fatigue (10% and 2%) were associated with ITP but uncommon with RA. One-third of the RA patients were on lower doses (100–150 mg/day) than those generally given in the ITP trials (200–300 mg/day), suggesting some of the observed AEs may be dose-related.

Over 4000 patients have been treated with fostamatinib across several disease populations with up to 81 months of continuous treatment. The safety profile has been consistent and manageable, with no new safety signals and no cumulative toxicity with long-term treatment.

Disclosure of Interest: None Declared

BSH2021-PO-074
Manifest-2, a global, phase 3, randomized, double-blind, active-control study of cpi 0610 and ruxolitinib vs. placebo and ruxolitinib in jaki-treatment-naive myelofibrosis patients
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Abstract Content: The bromodomain and extramterminal domain (BET) family of proteins bind to chromatin to regulate the transcription of target genes involved in multiple pro-fibrotic pathways and is a potential novel therapeutic target for reducing fibrosis in myelofibrosis (MF). CPI-0610, a first-in-class, oral, small-molecule inhibitor of bromodomain and extraternal domain (BET) proteins, potentially promotes disease-modifying activity through altered gene regulation of key oncogenic, fibrotic, and inflammatory factors and may transform the standard of care in myelofibrosis (MF). Janus kinase 1/2 inhibitors (JAKi) are currently approved for treatment of MF, including ruxolitinib (rux) and fedratinib. Approximately one third of JAKi naïve MF patients treated with rux (35%; 106 of 301) or fedratinib (37%; 35 of 96) achieved a spleen volume reduction ≥35% (SVR35) at 6–12 months. CPI-0610, a potential disease-modifying therapeutic agent with a novel mechanism of action may improve the outcome in MF pts. Blocking BET activity with CPI-0610 altered megakaryocyte differentiation and decreased cytokine production in preclinical studies. In addition, synergistic therapeutic effect of BETi and JAKi combination was observed in preclinical MF models. Clinical activity of CPI-0610 in combination with rux in JAKi naïve MF patients observed in the phase 2 MANIFEST study was higher (SVR35 at wk 24: 67%) than that observed with rux alone in historical phase 3 trials (Mascarenhas, ASH 2020).

MANIFEST-2 is designed as a global, phase 3, 1:1 randomized, double-blind, active-control study of CPI-0610 + rux vs. placebo + rux in JAKi treatment-naïve patients with primary MF, post-polycythaemia-vera MF, or post-essential-thrombocythemia MF. Key eligibility criteria: DIPSS score ≥Int-1; platelet ≥100 × 10^9/L; spleen volume ≥450 cc by CT/MRI; ≥2 symptoms measurable (score ≥2) or a total symptom score (TSS) of ≥10 using the MFSAF v4.0; peripheral blast count <3%, ECOG ≤2. Approximately 310 patients (155 in each arm) will be enrolled in the study. Patient randomization will be stratified by DIPSS risk category (Intermediate-1 vs. Intermediate-2 vs. High), platelet count (> 200 × 10^9/L vs. 100 – 200 × 10^9/L), and spleen volume (≥ 1800 cm^3 vs. < 1800 cm^3). Double-blind treatment (CPI-0610 or matching placebo) will be administered once daily (QD) for 14 consecutive days followed by a 7-day break, which is considered 1 cycle of treatment (1 cycle = 21 days). Rux will be administered twice daily (BID) for all 21 days within each cycle. Primary endpoint: SVR35 response (≥35% reduction in spleen volume) at wk 24; key secondary endpoint: TSS0 response (≥50% reduction in TSS) at wk 24; other secondary endpoints: safety, PK, PD, changes in bone marrow fibrosis and myeloid differentiation during treatment, duration of SVR35 response, duration of TSS50...
The study has highlighted the presence of increased Alpha-2-macroglobulin (A2M).

**Disclosure of Interest:** A. Mead Conflict with: Novartis, Abbvie, Celgene/BMS, CTI, Gilead, Conflict with: Novartis, Celgene/BMS, J. Marcaenhans Conflict with: Celgene, Prelude, Galecto, Promedior, Geron, Constellation Pharmaceuticals, Incyte. Conflict with: Incyte, Kartos, Roche, Promedior, Merck, Merus, Arog, CTI, Janssen, PharmaEssentia, A. Gerds Conflict with: PharmaEssentia, Constellation Pharmaceuticals, BMS, K. Luptakova Conflict with: Constellation Pharmaceuticals, J. Christo Conflict with: Constellation Pharmaceuticals, J. Wang Conflict with: Constellation Pharmaceuticals, G. Colak Conflict with: Constellation Pharmaceuticals, J. Shao Conflict with: Constellation Pharmaceuticals, S. Bobba Conflict with: Constellation Pharmaceuticals, P. Trojer Conflict with: Constellation Pharmaceuticals, J. Humphrey Conflict with: Constellation Pharmaceuticals, S. Verstovsek Conflict with: Incyte, Celgene, Novartis, Sierra Oncology, Conflict with: Incyte, Roche, NS Pharma, Celgene, Gilead, Promedior, CTI, Genentech, Blueprint Medicines Corp, Novartis, Sierra Oncology, PharmaEssentia, AstraZeneca, Italfarma, Protagonist Therapeutics, C. Harrison Conflict with: Celgene, Novartis, , Conflict with: Celgene, CTI, Gilead, Incyte, Janssen, Novartis, Shire, AOP Orphan Pharmaceuticals, Promedior, Roche, Sierra Oncology

**BSH2021-PO-075**

**Abnormal serum protein electrophoretic pattern of patients with severe SARS-CoV-2 infection in the Intensive Care Unit reveals very high levels of dimeric form of alpha-2-macroglobulin**

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**Abstract Content:** Background: Alpha-2-macroglobulin (A2M) belongs to a group of large glycoproteins important in proteinase inactivation, cytokine and growth factor modulation, and misfolded protein stabilisation. It can bind to both activators and inhibitors of the coagulation and fibrinolytic pathways as A2M can indiscriminately bind to a range of host proteinases.

**Aim:** To identify whether patients with severe SARS-CoV-2 infection in the Intensive Care Unit (ICU) present with abnormal serum protein electrophoresis profiles and pinpoint specific protein types that are abnormally increased or decreased.

**Method:** We conducted a retrospective observational study, looking at all the serum electrophoretic samples of patients with SARS-CoV-2 infection, who had inpatient hospital admission at Ipswich site of East Suffolk and North Essex NHS Foundation Trust (ESNEFT). The samples were read and compared against a validated standardised clinical electrophoresis serum protein profile panel provided by Helena Biosciences, based on mass-spectrometry validation.

**Results:** A total of nine patients with severe SARS-CoV-2 infection who needed ICU treatment, both in the first and second wave of COVID-19 pandemic, showed an abnormal electrophoretic pattern with broadening of the A2M peak. Notably, these findings were not observed in non-infected patients and in paucisymptomatic COVID-19 patients.

The analysis of the broadened A2M peak identified in our ICU-treated subset of patients was characterised by a marked anodal shift. Interestingly, these features are associated with functional changes of A2M binding to serum proteinases, or dissociation of A2M to a dimeric form, typically seen in inflammatory states. A2M usually exists as tetramer of two non-covalently associated dimers in serum.

When bound to proteinases, A2M becomes activated, acquiring a more compact structure with increased electrophoretic mobility, and shifting towards the anode in protein electrophoresis. Furthermore, A2M has been shown to dissociate into a dimeric form that can also shift towards the anode when exposed to endogenous oxidants produced during inflammation (1). Studies of neonatal cord plasma have confirmed that A2M can play an important role in inhibiting thrombin when levels of antithrombin III (ATIII) are naturally lower, with this effect being lost when levels of ATIII were artificially increased to adult levels (2). Beheiri et al hypothesised that A2M increased the risk of thrombosis via inhibition of activated protein C, looking at children with venous thromboembolic diseases or ischaemic stroke, who had elevated A2M 12-18 months after the events. This finding supports the hypothesis that A2M acts as a pro-coagulant instead of an anticoagulant (3). Given the role of A2M in thrombosis as discussed above, we hypothesise that A2M plays an important causative role in thromboembolic events seen in more severe forms of COVID-19.

**Conclusion:** The study has highlighted the presence of increased dimeric form of A2M in patients with severe COVID-19 requiring ICU treatment. Mass spectrometry evaluation is needed for confirming this specific alteration, opening the case for having this test run as a routine in severely affected patients. We finally hypothesise that this notable A2M serum protein profile shift may explain, at least in part, the pro-thrombotic state seen in patients with severe COVID-19 infection.

**Reference**


**Disclosure of Interest:** None Declared

**BSH2021-PO-076**

**Hypophosphatemia following ferric carboxymaltose (FCM) infusions and its associated factors**

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1Haematology and Transfusion Medicine, Oxford University Hospitals NHSFT, Oxford, United Kingdom, 2National Blood Transfusion Service, 3Epidemiology unit, Ministry of Health, Colombo, Sri Lanka

**Abstract Content:** Iron deficiency is present in around 30% of adults and causes a multitude of symptoms and signs, the most prevalent being fatigue; but also increase risks of infections, reduced cardiac function, impaired cognition and poorer surgical outcomes. Due to the significant health burden of iron deficiency, The Oxford Iron
Deficiency Management Service (IDMS) was established in 2019, to care for adults with this condition, in a community setting.

Intravenous iron therapy plays a significant role in management, when oral iron therapy is inadequate, not tolerable or not efficient, such as with the functional iron deficiency seen in inflammatory conditions. Ferric Carboxymaltose (FCM) is one of the most convenient intravenous iron preparations that are widely used. However it can result in a fall in phosphate levels through its action on fibroblast growth factor 23 (FGF23), a protein which participates in vitamin D regulation. Hypophosphatemia after intravenous FCM infusion is a documented side effect that has drawn much attention in the recent past.

The objectives of our study were to assess the prevalence of hypophosphatemia among adults treated with FCM and to describe the association of phosphate drop with nine selected factors: age, gender, ethnicity, initial haemoglobin, serum ferritin, adjusted calcium level, alkaline phosphate (ALP), percent transferrin saturation (TSAT %) and Vitamin D level among patients in the IDMS database.

This retrospective study was carried out amongst patients receiving FCM infusions during a 6-month period from July to December 2020. All new referrals that were given FCM were included in the analysis. Pre and Post FCM phosphate levels and day 1 (immediately prior to FCM administration) haemoglobin, ferritin, adjusted calcium level, alkaline phosphatase (ALP) level, percent transferrin saturation (TSAT %) and Vitamin D levels were extracted from the Electronic Patient Recording system. Post FCM blood investigations were done after the completion of the first full FCM dose. The first post infusion phosphate level was taken for analysis. The prevalence of mild (0.6–0.7 mmol/L), moderate (0.3–0.6 mmol/L), severe (<0.3 mmol/L) hypophosphatemia were described. The associations of the phosphate drop were analysed with the Mann-Whitney U test and Chi Square test. The significance level was regarded as 5%.

Altogether there were 149 new recipients of FCM infusions. The median (IQR) age was 68 (47.5–78) years with a male: female ratio of 2:3. A drop in serum phosphate compared to the pre-FCM phosphate level was seen in 93 patients (75.6%), with 52.3% falling below the normal range; mild, moderate and severe hypophosphatemia was seen in 21 (14.1%), 35 (23.5%) and 6 (4.0%) participants. There was no statistically significant association between the phosphate drop and any of the nine factors explored for its associations: age (P = 0.328), sex (P = 0.244), ethnicity (exact P = 0.687), day 1 haemoglobin (P = 0.504), day 1 ferritin (P = 0.391), day 1 TSAT P = 0.642, day 1 alkaline phosphate (P = 0.495), day 1 adjusted-calcium (P = 375) and day 1 vitamin D (P = 0.473).

In conclusion, the majority of patients had a fall in serum phosphate levels following FCM, leading to moderate or severe hypophosphatemia in 27.5% of cases. The clinical significance is not yet clear but many patients experienced unwanted side effects and required phosphate support. There are case reports of osteomalacia.

Disclosure of Interest: None Declared

BSH2021-PO-077
A survey of healthcare professionals in the United Kingdom to describe current pathways and management practices in chronic myeloid leukaemia: the ADAPT CML survey
Mhairi Copland¹, Katherine Gibson², Nicholas C. P Cross³, Brian Huntly⁴, Jennifer Billot⁵, Jacqueline Ryan⁶, Adam Mead⁶
¹Paul O’Gorman Leukaemia Research Centre, University of Glasgow, Gartnavel General Hospital, Glasgow, ²Novartis Pharmaceuticals UK, London, ³Faculty of Medicine, University of Southampton, Southampton, ⁴Department of Haematology, Wellcome Trust-MRC Cambridge Stem Cell Institute, University of Cambridge, Cambridge, ⁵OPEN VIE, The Weighbridge Brewery Courtyard, High Street, Marlow, ⁶MRC Weatherall Institute of Molecular Medicine, NIHR Oxford Biomedical Research Centre Haematology Theme, Radcliffe Department of Medicine, University of Oxford, Oxford, United Kingdom

Table 1. Factors influencing choice of tyrosine kinase inhibitor by line of treatment

<table>
<thead>
<tr>
<th>Factors that play a part in decision-making process when selecting a TKI for a patient with CML-CP¹</th>
<th>Line of treatment, N (% [n = 46])</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2L (after 1L intolerance)</td>
</tr>
<tr>
<td>Efficacy</td>
<td>31 (67%)</td>
</tr>
<tr>
<td>Safety profile</td>
<td>32 (70%)</td>
</tr>
<tr>
<td>Tolerability</td>
<td>35 (76%)</td>
</tr>
<tr>
<td>Quality of life</td>
<td>22 (48%)</td>
</tr>
<tr>
<td>Dosing regimen</td>
<td>16 (35%)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>45 (98%)</td>
</tr>
<tr>
<td>Age</td>
<td>33 (72%)</td>
</tr>
<tr>
<td>CML progression risk score</td>
<td>28 (61%)</td>
</tr>
<tr>
<td>CV risk score</td>
<td>31 (67%)</td>
</tr>
<tr>
<td>Patient choice</td>
<td>19 (41%)</td>
</tr>
<tr>
<td>Cost</td>
<td>14 (30%)</td>
</tr>
<tr>
<td>Guidelines</td>
<td>27 (59%)</td>
</tr>
<tr>
<td>Aiming for TFR</td>
<td>24 (52%)</td>
</tr>
<tr>
<td>Standard local management choice</td>
<td>16 (35%)</td>
</tr>
<tr>
<td>Physician experience</td>
<td>13 (28%)</td>
</tr>
<tr>
<td>Mutational profiling/screening</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

¹not mutually exclusive
Novartis, J. Billot Conflict with: None declared, J. Ryan Conflict with: Employed by Novartis Pharmaceuticals UK, A. Mead Conflict with: Novartis, Conflict with: Participated in advisory boards for Novartis, Bristol-Myers Squibb (BMS) and Pfizer

BSH2021-PO-078
Real-world survival among patients with intermediate- to high-risk myelofibrosis in the United States: impact of ruxolitinib approval
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Abstract Content: Ruxolitinib (RUX; Janus kinase [JAK] 1/2 inhibitor) was approved by the US Food and Drug Administration in November 2011 for the treatment of adult patients (pts) with intermediate- or high-risk myelofibrosis (MF) based on phase 3 COMFORT data, and has demonstrated significantly improved overall survival (OS). The aim of this real-world analysis was to assess the OS of pts newly diagnosed with intermediate- to high-risk MF before RUX approval, and for those who were RUX-unexposed vs -exposed post-approval.

Medicare Fee-for-Service claims database (Parts A/B/D; January 2010–December 2017) data were used to identify pts aged ≥65 years (intermediate-1 or higher risk MF due to age) with ≥1 inpatient claim or ≥2 outpatient claims with a documented MF diagnosis. The index date was the date of the first qualifying MF claim, ≥12 months of pre-index continuous medical and pharmacy enrollment was required. Pts with evidence of an MF diagnosis ≤12 months pre-index were excluded. Pts with a diagnosis of myelodysplastic syndrome, hemato logic malignancies (leukemias, multiple myeloma, and lymphomas), or solid tumors either ≤12 months before, on, or any time after index were also excluded in a stepwise manner. The study sample was classified into 3 groups: MF diagnosis pre-approval (index year 2010–2011; no post-index exposure to RUX); MF diagnosis post-approval and unexposed to RUX (index year 2012–2017); and MF diagnosis post-approval and exposed to RUX (index year 2012–2017). One-year survival rate and mortality risk were estimated using Kaplan-Meier and Cox proportional hazards regression analyses, adjusting for baseline demographic and clinical characteristics. OS was measured from index until death or end of follow-up. Pts without a death date were censored at disenrollment or the end of the study period, whichever occurred first.

Among eligible pts with an MF diagnosis (N = 1677), median age was 78 years, 39.8% were male, and 84.1% were white. The analysis included 278 pts diagnosed pre-approval (all RUX-unexposed) and 1399 diagnosed post-approval (RUX-unexposed, n = 1127; RUX-exposed, n = 272). Median follow-up for the pre- and post-approval groups was 12.5 and 11.3 months (RUX-unexposed, 10.2 months; RUX-exposed, 14.0 months), respectively. In the pre-approval group, 119 pts (42.8%) had a valid death date vs 436 (31.2%) in the post-approval group (RUX-unexposed, n = 382 [33.9%]; RUX exposed, n = 54 [19.9%]). One-year survival rate (95% CI) was 55.6% (49.4%–61.3%) for the pre-approval group, 72.5% (69.5%–75.2%) for the post-approval RUX-unexposed group, and 82.3% (76.7%–86.7%) for the post-approval RUX-exposed group. Mortality risk was lowest among RUX-exposed pts (adjusted hazard ratio [aHR], 0.36; 95% CI, 0.26–0.50; P < 0.0001 vs the pre-approval group). Pts in the post-approval group unexposed to RUX also had a lower risk of mortality, although less pronounced than RUX-exposed pts.
compared with the pre-approval group (aHR, 0.67; 95% CI, 0.56–0.80; P < 0.0001).

In this real-world study of US pts diagnosed with intermediate- or high-risk MF, 1-year survival was improved in pts diagnosed post vs pre-RUX approval. In the post-approval time frame, the 1-year survival rate was greater for those who received RUX than for those who did not. These findings complement the survival benefit results demonstrated in the CONFORT studies using real-world data.


**BSSH2021-PO-079**

**Outcomes of haematology patients requiring admission to ICU: experience from a UK tertiary centre**


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**Abstract Content:** Patients with haematological diagnoses are at high risk of clinical deterioration. Unfortunately, outcomes after escalation to intensive care units (ICUs) can be poor and this may prevent timely escalation of suitable patients. We present a single centre study of haematology patients admitted to ICU over a 17-month period compared with historical data from 10 years earlier.

Patients were identified retrospectively from ICU medical records at Nottingham City Hospital. 140 consecutive admissions were identified between April 2016 and August 2018. Our historical cohort comprised 114 admissions between April 2006 and August 2008. The same time of year was chosen to negate any seasonal effects. Statistical analysis was performed using SPSS. T-tests were used for parametric data; Mann-Whitney tests for non-parametric data and Fisher’s exact test for categorical data.

**Abstract Table:**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of admissions</th>
<th>Number Surviving to discharge (%)</th>
<th>Number Surviving to 6 months (%)</th>
<th>Median age in yrs (range)</th>
<th>Mean Apache II (CI)</th>
<th>Percentage post SCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML/MDS</td>
<td>50</td>
<td>12 (36%)</td>
<td>12 (23%)</td>
<td>66 (23–83)</td>
<td>23 (22–26)</td>
<td>Allo 48%</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>52</td>
<td>26 (50%)</td>
<td>20 (39%)</td>
<td>60 (18–84)</td>
<td>23 (21–25)</td>
<td>Allo 46% Auto 10%</td>
</tr>
<tr>
<td>Myeloma</td>
<td>10</td>
<td>7 (70%)</td>
<td>7 (70%)</td>
<td>65 (50–83)</td>
<td>19 (16–22)</td>
<td>Allo 20%</td>
</tr>
<tr>
<td>ALL</td>
<td>11</td>
<td>7 (64%)</td>
<td>5 (46%)</td>
<td>39 (18–72)</td>
<td>20 (17–24)</td>
<td>Allo 55%</td>
</tr>
<tr>
<td>Other Malignant</td>
<td>9</td>
<td>2 (22%)</td>
<td>2 (22%)</td>
<td>65 (50–79)</td>
<td>27 (20–35)</td>
<td>Allo 67%</td>
</tr>
<tr>
<td>Non-malignant</td>
<td>8</td>
<td>8 (100%)</td>
<td>8 (100%)</td>
<td>30 (18–58)</td>
<td>9 (5–13)</td>
<td>N/A</td>
</tr>
<tr>
<td>Overall current cohort</td>
<td>140</td>
<td>67 (48%)</td>
<td>53 (38%)</td>
<td>62 (18–84)</td>
<td>23 (22–24)</td>
<td>Allo 47% Auto 4%</td>
</tr>
<tr>
<td>Historical Cohort</td>
<td>105</td>
<td>43 (41%)</td>
<td>38 (36%)</td>
<td>60 (17–84)</td>
<td>26 (25–27)</td>
<td>Allo 29% Auto 9%</td>
</tr>
</tbody>
</table>

Overall survival to discharge was 48% with 38% survival to 6 months. Haematological diagnosis had a significant effect on survival at both time points (P = 0.01 6 months, P < 0.01 at discharge), being worst for AML and highest for non-malignant patients (table 1). This in part represents haematological prognosis; the cause of death was disease in 41% of AML patients. Only four patients were admitted following autograft with 2/4 surviving till discharge and 1/4 at 6 months. 62 patients were admitted post allograft with 42% survival to discharge and 27% at 6 months. Survival for transplant patients was not significantly different from patients with another malignant diagnosis. There was also no impact of age on survival with patients in the oldest quartile having equivalent survival to the youngest at both time points. The presence of GVHD or neutropenia on admission also had no impact on survival. 23 patients had grade III/IV GVHD of which 10/24 survived to discharge and 7/24 to 6 months.

The most common reasons for ICU admission were sepsis (43%) or respiratory failure (32%). 27% of patients required mechanical ventilation, 46% inotropes and 12% renal replacement therapy. Mechanical ventilation was associated with worse survival to discharge at 34% v 54% (P = 0.04), although this was not seen at 6 months. The median APACHE II (acute physiology and chronic health evaluation II) score, a validated tool for predicting ICU mortality, was lower in those alive at discharge (24 v 20, P < 0.01) and 6 months (23 < 21, P = 0.03). Median ICU length of stay was 2.4 days.

Data from 10 years prior showed a survival to ICU discharge of 45% with 33% of patients alive at 6 months, broadly equivalent to current data. Median age was 60 versus 62. The total number of admissions increased from 105 to 140, a 33% increase over an equivalent period, reflecting an increase in the number of patients being treated intensively and increased transplant activity.

Our data reveals a substantial proportion of patients achieve long term survival after ICU admission, despite potential deterioration due to both the underlying disease as well as the cause of the critical illness. Unfortunately, despite advances in ICU care we are yet to demonstrate evidence of improved overall survival compared with historical data. Whilst scoring systems may be useful, they are imperfect for predicting outcomes. Similarly, there are no singular patient factors indicative of a poor prognosis. Therefore, joint working between haematologists and intensivists is essential to select the patients most likely to benefit from escalation of care.

**Disclosure of Interest:** None Declared
BSH2021-PO-080
ITP treatment-associated osteoporosis risk assessment in a Haematology cohort
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Abstract Content: Introduction: A Good Practice Paper (Quinten et al, BSH 2019) looked at the need for haematologists to consider stratifying osteoporotic fracture risk and considering commencement of bisphosphonate in patients with ITP starting high dose steroids. Glucocorticoid use is a risk factor for fragility fractures (particularly vertebral). Fracture risk increases by 30-50% with the use of long-term steroids. Glucocorticoids cause the most rapid reduction in Bone Mineral Density (BMD) within the first 3-6 months of use. Beyond 6 months there is ongoing loss of BMD but at a slower rate. A Quality Improvement Project was constructed to review practice within a haematology service in SEHSCT.

Methodology: A Data Capture Tool was constructed. Parameters included age, gender, previous/current bisphosphonate use, concurrent initiation of bisphosphonate with high dose steroid in high risk patients. Stratification parameters from Good Practice describe high risk patients as; male/female >70 years old or male >50 years old/postmenopausal woman with previous fragility fractures. Calculation of FRAX algorithm is recommended for assessing osteoporotic fracture risk in patients with “intermediate” risk i.e. 40-69 year old with clinical risk factor(s) +/- BMD. A retrospective FRAX score was calculated for all patients > 40 years old to determine osteoporotic risk. Patient aged <40 years did not have a FRAX score calculated in line with the Good Practice Paper recommendations. Clinical risk parameters collated in FRAX score calculation included age, gender, weight, height, previous fracture, parental hip fracture, current smoking, steroid use, rheumatoid arthritis, pre-existing conditions strongly associated with secondary osteoporosis, alcohol >3 units/day and bone mineral density (BMD) scan. Where required, patients were contacted directly to ascertain results for certain parameters to ensure an accurate FRAX score calculation.

Results: Thirteen patients with new diagnosis/relapsed ITP commencing high dose Prednisolone were audited. High risk patients due to age >70 years account for 46% (6/13) of cohort. The intermediate risk group of patients between 40-69 years accounts for 38% (5/13); they were identified through retrospective FRAX score +/- DEXA scan. One patient within the intermediate risk group was upgraded to high risk based on FRAX score. This shows there is a need in performing a FRAX score in patients aged 40-69 year with a clinical risk factor. The majority (86% [6/7]) of high risk patients did not commence bisphosphonate therapy.

Conclusion: The review of practice within a haematology service against the BSH Good Practice Paper showed a failure to commence bisphosphonate therapy in high risk patients. Findings also revealed a potential for intermediate risk patients to be stratified as high risk depending on FRAX scores. These revelations have led to the implementation of an ITP clinical pathway to prompt haematologists to stratify risk and prescribe bisphosphonate. A collaborative approach between the haematologist, pharmacist and GP was considered in the construction of the pathway.

Disclosure of Interest: None Declared

BSH2021-PO-081
Patient preferences and experiences regarding thrombopoietin-receptor agonists for immune thrombocytopenia in the United Kingdom (TRAPEze UK study)
Vickie McDonald¹*, Adrian Newland², Mervyn Morgan³, Koo Wilson⁴, Jameel Nazir⁵, Peter Maguire⁶, Emma Goldman⁷, Tammy Wynne⁸
¹Department of Haematology, The Royal London Hospital, Barts Health NHS Trust, ²Academic Haematology Unit, Blizard Institute, Barts & The London School of Medicine & Dentistry, Queen Mary Institute of London, London, ³ITP Support Association, Bohnhurst, United Kingdom, ⁴Swedish Orphan Biovitrum AB, Stockholm, Sweden, ⁵Wickenstons Ltd, Abingdon, United Kingdom

Abstract Content: Thrombopoietin-receptor agonists (TPO-RAs) are a standard second-line therapy option for patients with immune thrombocytopenia (ITP) who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). While it has been reported that TPO-RA characteristics may influence patient choice, there is limited evidence that quantifies the differential impact of these characteristics on preference. The TRAPEze (Thrombopoietin-Receptor Agonist Patient experience survey) study aims to identify patients’ perceptions and preferences regarding the specific attributes of TPO-RAs, as well as investigate how these therapies are used in the ITP population. Presented here are the complete UK cohort findings from this ongoing multinational study. The study was fielded in the UK via an online survey and patients were recruited through the UK-based ITP Support Association. The main element of the survey consisted of eliciting patient preference through a discrete choice experiment, based on TPO-RA product attributes (method of administration, frequency of dosing, drug and food interactions, monitoring requirements, platelet response and potential side effects). The study also collated data regarding patient demographics, disease characteristics, work and productivity, healthcare resource utilisation and wider social impact via a patient burden survey. Current and prior treatments, including reasons for discontinuing and overall satisfaction with TPO-RAs, were also explored with open and closed questions. The UK cohort consisted of 31 ITP patients (21-83 years old, mean age 58 years), of which 65% were female. Patients’ preference towards TPO-RAs were more likely to be driven by method of administration (odds ratio (OR) 5.64; 95% confidence intervals (CI) 3.15–10.11) and drug and food interactions (OR 3.23; 95% CI 1.85–6.84). 48% of patients were currently or most recently on eltrombopag, of which 93% were satisfied with this therapy’s mode of action. 52% of patients were currently or most recently on romiplostim, 81% of which reported satisfaction with this mode of administration. In this cohort, 50% and 19% reported making changes to their daily routine and diet, respectively, to take their treatment, but 100% of patients reported consistent adherence to their treatment. The most common symptoms of ITP that patients experienced were fatigue (87%), bruising (77%), petechiae (71%), anxiety surrounding their platelet count (48%) and unexplained nosebleeds (26%). 43% of patients ranked fatigue as the most negatively impactful symptom on quality of life. 76% of patients reported that their TPO-RA was effective at treating their ITP symptoms, but only 21% reported an increase in their energy levels. In conclusion, ITP patients prefer oral tablets and treatments without food restrictions; attributes which are individual to eltrombopag and romiplostim, respectively. Despite the efficacy of both TPO-RAs in
treating ITP symptoms, fatigue is still a prominent symptom that impacts many aspects of patients’ quality of life. To date, this is the first reported use of discrete choice experiments to quantify patient preference towards TPO-RAs for the treatment of ITP.


BSH2021-PO-082
Are advisory letters an acceptable alternative to in-person outpatient clinic reviews? A retrospective analysis of referrals to a haematology outpatient clinic
Fiona Lynott1,*, Orla Gildea1, Brian Hennessy1
1Department of Haematology, University Hospital Waterford, Waterford, Ireland

Abstract Content: As of 29th October 2020, 7456 patients in Ireland are awaiting initial review in a consultant-led haematology clinic. (1) Undoubtedly, the Covid-19 pandemic will only serve to further increase waiting lists as day-to-day hospital activities are interrupted. (2) It is imperative that healthcare providers develop new and innovative means of managing outpatient waiting lists and ensuring that priority is given to those patients who need to be reviewed in this specialist clinic.

The aim of this study was to retrospectively analyse referrals to the outpatient haematology clinic of University Hospital Waterford (UHW), identifying referrals that were dealt with by means of an advisory letter and assessing, six years on, how many of this cohort subsequently attended haematology outpatient clinics in UHW. UHW is a tertiary referral centre and the designated cancer centre for the south-east of Ireland.

Data pertaining to referral letters received from February to December 2014 inclusive was gathered from a departmental database and records of patient letters. The linked data systems IPMS, T-PRO and LabWebEnquiry systems were used to gather data relating to attendance at clinics.

From February to December 2014 a total of 281 referral letters for haematology outpatient review were received. The majority of these, 76.9% (n = 216), were from general practitioners, with 23.1% (n = 65) from hospital sources. All referrals were reviewed and triaged by a consultant haematologist. Over half of referrals resulted in appointments (n = 157), with the remaining 124 referrals being dealt with by means of an advisory letter. These advisory letters were composed by a consultant haematologist and offered advice regarding potential causes for the issue at hand, further work-up required (if any) and detailed potential situations in future when in-person haematology review may be warranted.

The most common issues that were dealt with by advisory letters were leucocytosis (n = 23), leucopenia (n = 17) and hyperferritinaemia (n = 17). Of the 124 referrals that were dealt with by advisory letter, 21 of these patients were ultimately reviewed in the haematology outpatient clinic in UHW during the following 6 years. Sixteen of these were discharged from the clinic, 3 have ongoing haematology input (for reasons unrelated to their original referral) and 2 patients have since died (from haematological issues unrelated to their original reason for referral).

This review demonstrates that, when appropriately employed, a consultant-led referral triage and advisory letters service may offer a safe and effective alternative to in-person reviews for patients with a number of commonly occurring haematological issues. Whilst international data is somewhat limited in the area, reviews from Canada and the UK have reached similar conclusions. (3) (4)

Disclosure of Interest: None Declared

BSH2021-PO-083
Utility of urinary prostaglandin & N methyl histamine measurements across mast cell disorders (Mastocytosis, Hereditary Alpha Tryptasemia and Mast cell activation syndromes)
Bethan Myers*, Pavel Chudakov1
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Abstract Content: Introduction: Mast cell disorders (MCDs) are a heterogeneous group of conditions comprising Systemic or cutaneous Mastocytosis, (CM, SM) monoclonal mast cell activation syndrome (MMCAS), non-clonal mast cell activation syndrome (MCAS) and the recently described hereditary alpha tryptasemia (HxT).

Baseline serum tryptase is a stable measure usually raised in SM, MMCAS and HxT but nearly always low/normal in MCAS. Abnormalities in urinary prostaglandins DM, D2 and F2 α, and/or N methyl histamine levels are an alternative way to demonstrate biochemical abnormalities of mast cell function. Prostaglandins are present in the preformed granules within mast cells and are activated either by antigen cross-linking IgE or non-IgE mechanisms on the cell surface, degranulating with contents released into the circulation. Prostaglandins D2 (PGD2) was initially found in the urine of patients with systemic mastocytosis. PGD2 is unstable with a short half-life (1-30 minutes). It is readily broken down into various metabolites, a major metabolite being 1-beta-PGF2alpha (PGF2α).

It is recommended that prostaglandin levels are measured on a 24 hour urine sample when investigating mast cell activation syndrome

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Median no. symptom gps</th>
<th>%triple pos (PGD,D2,F2α)</th>
<th>% double pos (PGD,D2,F2α)</th>
<th>% single pos (PGD,D2,F2α)</th>
<th>Negative %pos NMH (PGD,D2,F2α)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SM</td>
<td>3</td>
<td>17%</td>
<td>33%</td>
<td>33%</td>
<td>17%</td>
</tr>
<tr>
<td>MMCAS</td>
<td>4</td>
<td>50%</td>
<td>50%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>MCAS</td>
<td>4</td>
<td>4%</td>
<td>26%</td>
<td>54%</td>
<td>16%</td>
</tr>
<tr>
<td>HxT</td>
<td>3</td>
<td>0%</td>
<td>33%</td>
<td>33%</td>
<td>0%</td>
</tr>
<tr>
<td>CM</td>
<td>2</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>
(MCAS) as symptom flares and the short half-life of mast cell mediators can lead to a normal result in spot urine samples. Some patients with MCAS may not have raised mast cell mediator levels (tryptase, urine methylhistamine and prostaglandins) unless they are symptomatic. If there is good clinical history but negative results, it is recommended that the tests are repeated on a spot urine sample when the patient is symptomatic. F2 alpha remains elevated in clonal mast cell disorders where it is produced by an increased mast cell mass or in non-clonal mast cell activation disorders where it is produced by chronically active mast cells. Care to ensure sample is kept chilled throughout is important to avoid degradation of samples.

Methods: Data from our local data base of MCDs was used to access information on 94 patients with one of the mast cell diagnoses, whose results for urinary tests were available. 6 had SM, 1 CM, 2 MMCAS, 75 MCAS and 10 HxT.

Results: table 1 summarises the percentage of positive results for the urinary tests and median number of symptoms in each group.

Discussions & Conclusions: The results demonstrate strongest positivity in the SM group, lack of positive results in CM, and intermediate positive results in HxT and MCAS groups. This demonstrates that urine tests established for SM are also applicable to HxT and MCAS as long as careful attention is given to keeping samples chilled throughout.

Disclosure of Interest: None Declared

BSH2021-PO-084

The course of cutaneous mastocytosis in a prospective group of 163 children according to parent electronic survey

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Abstract Content: Background: Mastocytosis occurs due to clonal mast cell proliferation and may have different clinical course. As the disease only rarely occurs in pediatric population there are very few clinical observations describing its symptoms, prognosis and therapy response in pediatric cohorts.

Aim: Characterization of gender, symptoms, prognosis and therapy in children with mastocytosis using data obtained by electronic parent survey.

Methods: The study data was collected from November 2014 till August 2020 from parents referring for consultation via “Vkontakte” social network. All parents completed two surveys. The first one was performed right after the referral, the second one was performed from May 2020 to August 2020. The data on age at symptoms onset, symptoms, rash distribution and clinical course was obtained and analyzed.

Results: The data on 163 children was obtained. The median age was 6 (0.5–22) years. The median time of onset was 2 (0–120) months, interquartile range –1.5 months. At the end of survey the median observation time was 61.5 (2–276) months. Symptoms of mastocytosis observed in 123 (75.4%) children. The second survey was conducted in 139 (85.2%) pts. At the time of survey symptoms progression was seen in 4 (2.9%) patients, while in one of them – fatal transformation to mast cell leukemia with expression of CD30. The main results are presented in table.

Conclusion: The onset of diseases mostly occurs in the first year of life. Most frequent symptoms are itching and rash in response to various triggers. Antihistamine drugs led to symptoms mitigation. The clinical course is benign in most children.

Abstract Table:

<table>
<thead>
<tr>
<th>N (%)</th>
</tr>
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<tbody>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Boys</td>
</tr>
<tr>
<td>Girls</td>
</tr>
<tr>
<td>Variants of mastocytosis</td>
</tr>
<tr>
<td>Urticaria pigmentosa</td>
</tr>
<tr>
<td>Mastocytoma</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
<tr>
<td>Diagnosis verification</td>
</tr>
<tr>
<td>Clinical only</td>
</tr>
<tr>
<td>Skin biopsy</td>
</tr>
<tr>
<td>Main complains</td>
</tr>
<tr>
<td>Skin reaction triggered by various factors</td>
</tr>
<tr>
<td>Itching</td>
</tr>
<tr>
<td>Flushing</td>
</tr>
<tr>
<td>Main triggers</td>
</tr>
<tr>
<td>Variations of temperature</td>
</tr>
<tr>
<td>Emotions</td>
</tr>
<tr>
<td>Regular therapy</td>
</tr>
<tr>
<td>Antihistamines</td>
</tr>
<tr>
<td>Ketotifen</td>
</tr>
<tr>
<td>Follow-up</td>
</tr>
<tr>
<td>Improvement</td>
</tr>
<tr>
<td>Stabilization</td>
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<tr>
<td>Progression</td>
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</tbody>
</table>

Disclosure of Interest: None Declared

BSH2021-PO-085

Management of anaemia in medical oncology patients in a day unit setting.

Katrina Fordwor*, Sarah Jaafar, Eliz Flanagan, Sue Pavord

Abstract Content: Anaemia is a common finding in oncology patients and can result in patients experiencing significant fatigue, a reduction in overall quality of life and possible blood transfusion. Often the cause of anaemia is assumed to be the malignancy or chemotherapy without further investigation. In order to reduce unnecessary blood transfusions being given on the oncology day unit we determined what proportion of the anaemic patients had iron deficiency and could be managed with iron alone. A preliminary audit in 2017 identified that only 25% had their iron status checked, and of those, iron deficiency was found in 71%. Therefore we instituted a policy to check iron status at the point of referral for chemotherapy. Repeat audits in 2019 and 2020 were carried out to determine adherence to this policy, following increased efforts to educate relevant staff. We gathered data from the records of 300 patients; 250 consecutive patients from each of two time periods who were starting a new chemotherapy regimen between 1st October 2019 and 31st December 2019 and 1st March 2020 and 31st May 2020. The patients were identified using the electronic chemotherapy prescribing system and blood test results were gathered from the hospital electronic patient record. Thresholds of a haemoglobin (Hb) <120 g/L and a ferritin of <100 mcg/L and/or a transferrin saturation of <20% were used to define anaemia and iron deficiency respectively.

In the first time period, 80/250 patients (32%) were found to be anaemic. Of these, 45 (56%) had their iron status checked and in 32/45 (71%) iron deficiency was confirmed. Functional iron deficiency defined by ferritin >100 mcg/L was present in 14/32 (44%) and absolute iron deficiency in 18/32 (56%). Of the 32 patients who were iron deficient, only 5/32 (16%) were given intravenous iron and only 1/32 (3%) received a blood transfusion. In the second time period, 72/250 (29%) were anaemic. Of these 45 (62%) had their iron status checked, with 38/45 (84%) being iron deficient, this being
functional in 22/38 (58%) and absolute in 16/38 (42%), 15/38 (40%) were treated with an iron infusion. 7/38 (18%) had a blood transfusion. Of the patients who received an iron infusion and had a repeat Hb, 10/12 (80%) of them had a Hb increase of 1-3 g/L after a week.

Our study highlights the high prevalence (around 29-32%) of anaemia in medical oncology patients. Importantly, the majority of these are iron deficient (71-84% of those tested); absolute and functional ID being in approximately equal proportions. The use of IV iron improved between the two time periods but use of iron remains inadequate and avoidable blood transfusions are still given. Ongoing education is required to maintain improvements in practice.

Disclosure of Interest: None Declared

BSH2021-PO-086
The outcome following a COVID-19 diagnosis on haematology patients; data from the South East Scotland Cancer Network
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Abstract Content: Early in the COVID-19 pandemic, patients with underlying haematological malignancies were found to have inferior outcomes due to immune dysfunction from their underlying disease and immunosuppressive therapies, with mortality rates 34%.1 Collective experience regarding clinical course of COVID-19 in context of haematological disorders which are clinically, morphologically and genetically heterogeneous, needs to be shared.

We reviewed 40 patients diagnosed with COVID-19 within the Haematology South East Scotland Cancer Network from the beginning of lockdown, March 2020, to February 2021 (11-month time period). Data on demographics, diagnosis, treatment, co-morbidities and outcomes was collected retrospectively from trakcare notes.

Table 1 summarises mortality, ITU admissions and O2 therapy (high flow O2 60% venturi or above) by underlying haematological condition.

Overall mortality was 43%. Median age at death 72 years (range 49–90 years), with a mortality of 25% in <60 s, 47% 60–80 s and 56% >80 s, 25 men, 15 women (mortality 52% vs. 27%). Median time from diagnosis to death 12 days (range 3–39 days). Mortality also correlated with pre-infection performance status (PS) PS0 28%, PS1 44%, PS2 69%. 53% had no underlying co-morbidities with mortality 33% in this group. Median time from diagnosis to death 12 days (range 3–39 days). 93% were hospitalised, median stay 9 days (range 0–47 days). 13% required critical care admission - 2 for intubation, 3 for high flow nasal O2. Sadly, none of these patients survived (median age 66; range 49-70 years; 3 PS0, 1 PS1, 1 PS3).

All patients were on watch and wait (W+W) or had received treatment in preceding 6 months. There was no difference in mortality between intensive treatment (n = 15, mortality 40%), non-intensive (n = 18, mortality 44%), W+W (n = 5, mortality 40%) or no active treatment but treated within previous 6 months (n = 10, mortality 40%). 16% patients had rituximab within preceding 6 months, 43% mortality in this group. 100% (2) with previous alloengenic transplant died of COVID-19 and 33% (1) with autologous transplant.

15% patients were enrolled in RECOVERY trial (3 standard care, 1 lopinavir/ritonavir, 2 hydroxychloroquine), 8% to UK ISARIC4C trial. 25% patients received dexamethasone with 70% mortality, 8% received remdesivir with 33% mortality.

Consistent with other studies mortality was significantly higher (43%) in those with underlying haematological malignancy of any type compared with general Scottish population (3.5%) regardless of intensity of treatment or recent rituximab use. Mortality and severity of disease were increased in MDS, lymphoma, especially high grade, and CLL. History of autologous or alloengenic stem cell transplant increased mortality to 60%, higher than the 25% in European Bone Marrow Transplant registry though numbers were small within our cohort, supporting national guidance to consider deferring transplant where possible.

In summary, patients with haematological malignancies are extremely high risk of severe COVID-19 disease and mortality regardless of underlying co-morbidities or treatment received.

1Vijenthira A. et al, American Society Haematology, 2020

Abstract Table: Table 1

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mortality (%)</th>
<th>ITU (%)</th>
<th>O2 (%)</th>
<th>High flow O2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low grade lymphoma (N = 6)</td>
<td>20</td>
<td>17</td>
<td>50</td>
<td>33</td>
</tr>
<tr>
<td>High grade lymphoma (N = 7)</td>
<td>57</td>
<td>29</td>
<td>57</td>
<td>57</td>
</tr>
<tr>
<td>Chronic lymphocytic leukaemia (CLL) (N = 4)</td>
<td>50</td>
<td>0</td>
<td>75</td>
<td>50</td>
</tr>
<tr>
<td>Acute leukaemia (N = 8)</td>
<td>38</td>
<td>13</td>
<td>38</td>
<td>75</td>
</tr>
<tr>
<td>Myeloproliferative neoplasm (N = 4)</td>
<td>40</td>
<td>0</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>Myeloma, POEMS syndrome, amyloidosis (N = 6)</td>
<td>33</td>
<td>0</td>
<td>17</td>
<td>33</td>
</tr>
<tr>
<td>Myelodysplasia (MDS) (N = 5)</td>
<td>60</td>
<td>0</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Overall (N = 40)</td>
<td>43</td>
<td>13</td>
<td>58</td>
<td>40</td>
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</table>

Disclosure of Interest: None Declared

BSH2021-PO-087
A review of primary care electronic advice requests to a tertiary centre Haematology department.
Eamon Mahdi1, Rosie McDonald2,*, Ali Mahdi3, Steven Knapper4
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Abstract Content: Background: The provision for Haematology electronic advice provides flexible and swift specialist advice to primary care in the hope of reducing outpatient capacity pressures. Integration within patient records allows for prompt documentation for audit, evaluation and reference. However, considering the increasing demand on laboratories leading to the inevitable pick-up of incidental abnormalities and the ease of advice seeking, this has the potential to significantly increase workload.

Clinical correlation with the abnormality is a must and depending on the Haematologist’s experience, sub-specialism and threshold there may be a variability in the advice given within a department. There are no national guidelines that set specific limits for abnormal laboratory values relating to Haematology that require referral and the request of advice is at the discretion of the referrer. Local
guidance may be available but are often difficult to locate and may not answer a specific question.

**Aim:** To evaluate and analyse the electronic advice request (EAR) in patients with CPV, all hemogram parameters from primary care to a tertiary centre Haematology department, to help to refine the local guidelines and improve education.

**Methods:** Retrospective review of each EAR over a 20-month period from February 2019 (inception) to September 2020. The data was separated and tabulated into referral reason, laboratory and or clinical abnormality, further investigations requested, generated outpatient referrals and how many replies it took to close each case.

**Results:** In total there were 837 EARs generating approximately 42 referrals per month. Note, there is a separate system for outpatient Haematology referrals. Interestingly, 789 (94.3%) were dealt within one reply, 40 (4.8%) in two replies and 6 (0.7%) for three or more replies. The number of referrals generated to outpatient Haematology was 110 (13.1%) and the rest of the EARs were dealt with by reply only. Approximately 553 referrals (66.6%) may have been dealt with by a targeted guideline if one were available at the time.

A number of EARs contained multiple questions and thus there were a total of 902 identifiable queries. The most common request was the interpretation and significance of raised, polyclonal immunoglobulins and/or free light chains, in the absence of any feature to suggest a plasma cell dyscrasia or lymphoproliferative disorder, total number being 104 (11.5%). Also, the presence of a paraprotein of < 10 g/l with no other associated abnormal laboratory features totalled for 87.1% of the total paraprotein related queries. There were 78 (8.6%) queries regarding the presence of a paraprotein. Advice regarding the suitability of switching a patient from warfarin to a direct oral anticoagulant totalled 32 (3.5%) EARs and led to the writing of a specific flow-diagram.

The time taken to complete the EARs could not be inferred but through the data collection there was often missing information which likely led to increased time being spent on each request due to looking at patient records on another system.

**Conclusion:** Electronic advice provides reassurance, improves the requirement for refinement. Using the results acquired from this data can lead to structured, targeted guidelines, templates as well as frequently asked questions to ease the number of communications received but maintain available advice.

**Disclosure of Interest:** None Declared

**BSH2021-PO-088**

Features of the course of various clinical forms of polycythemia vera

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**Abstract Content:** **Background:** With the introduction of changes in the 2008 WHO classification in 2016, it became necessary to divide patients with polycythemia vera (PV) into 2 groups: with latent polycythemia vera (LPV) and with classic polycythemia vera (CPV). Due to the low levels of hemoglobin and hematocrit patients with LPV often remain out of sight, and it leads to a lack of adequate treatment and frequent thrombohemorrhagic complications.

**Aims:** to establish risk groups for thrombotic complications (TC) and to identify the incidence of TC in patients with LPV and CPV.

**Methods:** 193 patients with a diagnosis of PV were studied. The diagnosis of patients was established based on the WHO classification of 2008 and 2016. The analysis of laboratory data and clinical characteristics of patients was carried out. The risk groups of TC were determined using the Marchioli scale. The parameters in the groups were put in a variation range. For each range the arithmetic mean value (M), standard deviation from this value (m), minimum (min) and maximum (max) values were calculated.

**Results:** Out of 193 patients, 127 (65.8%) patients were with classical form, 66 patients (34.2%) were with latent form. The analysis of patients with PV revealed the following hemogram parameters (M ± m): hemoglobin-174 ± 2 g/l, erythrocytes-5.9 ± 0.1 x 1012/l, hematocrit-68.7 ± 1.2 %, leukocytes - 11.5 ± 0.5 x 109/l, platelets - 492 ± 24.1 x 109/l. Parameters of hemoglobin in CPV and LPV were compared (M ± m): hemoglobin-182.66 ± 2.1 g/l and 157.97 ± 2.2 g/l (P < 0.05), erythrocytes-6.18 ± 0.1 x 1012/l and 5.46 ± 0.1 x 1012/l (P < 0.05), hematocrit-71.85 ± 1.4% and 63.5 ± 1.8% (P < 0.05), leukocytes-11.92 ± 0.6 x 109/l and 10.79 ± 0.7 x 109/l (P > 0.05), platelets - 429.3 ± 34.7 x 109/l and 526.85 ± 30.9 ± 109/l (P > 0.05).

Out of 193 patients with PV, 69 patients were classified as low risk group, 35 as intermediate risk, 89 as high risk group for TC. In CPV, 56.34% of patients was classified as low risk, 38.03% of patients was classified as intermediate risk, 5.63% of patients was classified as high risk group of TC. In LPV-31.3% of patients was classified as low risk, 16.2 % as intermediate risk, 32.5% as high risk group of TC.

In 22 patients (11.3%), TC were observed. 14 of them were with LPV and 8 - with CPV.

**Summary/Conclusion:** In patients with CPV, all hemogram parameters, except the count of platelets, were higher than in LPV. Patients with LPV, in contrast to patients with CPV, had higher platelet counts. Despite low hemoglobin and hematocrit, patients with LPV were more likely to have TC than with CPV. This can be associated with a high count of platelets in LPV, as well as with untimely, inadequate treatment of these patients.

**Disclosure of Interest:** None Declared

**BSH2021-PO-089**

Preliminary gastrointestinal safety and tolerability of fedratinib from the phase IIIb FREEDOM trial in patients with intermediate- or high-risk myelofibrosis previously treated with ruxolitinib

Claire Harrison1,*, Vikas Gupta2, Abdulraheem Yacob3, Salman Fazal4, Carole Miller5, Srdan Verstovsek6, Ruben Mesa7, Giovanni Barosi8, Jean-Jacques Kiladjian9, Ryan Mattison10, Lindsay Rein10, Brandi Reeves13, Stephen Oh13, Vinod Parameswaran14, H. Joachim Deeg15, Shelonita Rose16, Vincent Chia17, Tianhua Wang18, Moshe Talpai12

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**Abstract Content:** **Introduction:** Fedratinib is a selective JAK2/FLT3 inhibitor shown to induce spleen responses and symptom improvement in patients with myelofibrosis. Gastrointestinal (GI) events including nausea, vomiting, and diarrhea, were the most common adverse events (AEs) in fedratinib clinical trials, and were most
frequent during early treatment. The JAK1/2 inhibitor, ruxolitinib, has demonstrated efficacy in patients with myelofibrosis; however, many patients discontinue ruxolitinib due to loss of response or drug-related cytopenias. The ongoing, single-arm, phase IIb FREEDOM study evaluates fedratinib in myelofibrosis patients previously treated with ruxolitinib. FREEDOM includes prospective mitigation strategies for managing GI events.

**Objective:** Review the frequency, severity, and mitigation of GI events during early fedratinib treatment in FREEDOM.

**Methods:** Eligible patients are aged ≥18 years, with intermediate- or high-risk myelofibrosis, ECOG-PS score 0–2, platelet count ≥50 × 10^9/L, and splenomegaly ≥450 cm^3 or palpable spleen ≥5 cm below LCM; and had previously received ruxolitinib for ≥3 months (or ≥28 days with intolerance). Patients receive fedratinib 400 mg/day in continuous 28-day cycles. Study design includes mitigation strategies (prophylaxis, symptomatic treatment, dosing modifications, dosing with food) for managing GI toxicities. AEs are evaluated in all treated patients.

**Results:** At data cutoff (26-Mar-2020), 22 patients had enrolled: 4 patients discontinued (none due to GI-related events). Median age was 68.5 years (range 49–80). All patients had received ≥3 months of prior ruxolitinib treatment; the most common reason for ruxolitinib discontinuation was relapse (27%). Median fedratinib treatment duration was 18.6 weeks (range 1.6–48); 10 patients (46%) received ≥6 fedratinib cycles. Diarrhea, vomiting, and nausea occurred in 32%, 18%, and 14% of patients, respectively; none of these events were grade 3–4 or required dose modification or discontinuation. 12 patients (55%) received ondansetron and 6 (27%) received loperamide.

**Conclusions:** Fedratinib was generally well-tolerated. In similar patients receiving fedratinib 400 mg/day (starting dose) in the phase II JAKARTA2 study, which did not prespecify mitigation for GI events, rates of diarrhea, nausea, and vomiting through end-of-cycle 6 ranged from 41% to 62%. Early data from the FREEDOM study suggest frequency and severity of GI events may be reduced via mitigation strategies. Study enrollment is ongoing.

This abstract was published in Clinical Lymphoma, Myeloma, & Leukemia, Vol 20, Supp 1, Gupta et al., Preliminary Gastrointestinal Safety and Tolerability of Fedratinib from the Phase IIb FREEDOM Trial in Patients with Intermediate- or High-Risk Myelofibrosis Previously Treated with Ruxolitinib, Page S331-2, Copyright SOHO (2020).

**Disclosure of Interest:** C. Harrison Conflict with: Celgene, Novartis, Conflict with: Celgene, CTI Biopharma Corp, Gilead, Incyte, Janssen, Novartis, Shire, AOP Orphan Pharmaceuticals, Promedior, Roche, Sierra Oncology, V. Gupta Conflict with: Novartis, Sierra Oncology, Pfizer, Conflict with: Novartis, Incyte, Conflict with: Bristol Myers Squibb, A. Yacob Conflict with: Agios, Incyte, Novartis, Conflict with: Dynavax, Ardevex, Hylapharm, Cara Therapeutics, S. Fazal Conflict with: Bristol Myers Squibb, Takeda, Agios, GlaxoSmithKline, Gilead, Novartis, Amgen, Stemline, Jazz, Conflict with: Celgene, Karoypharm, Incyte, Janssen, C. Miller: None Declared, S. Verstovsek Conflict with: Incyte, Roche, NS Pharma, Celgene, Gilead, Promedio, CTI Biopharma, Genentech, Blueprint Medicines, Novartis, Sierra Oncology, PharmaEssentia, AstraZeneca, Italfarma, Protagnost Therapeutics, R. Mesa Conflict with: Novartis, Sierra Oncology, La Jolla Pharmaceutical, Conflict with: Bristol Myers Squibb, Incyte, Abbvie, Samus Therapeutics, Genentech, Promedior, CTI Biopharma, G. Barosi Conflict with: Bristol Myers Squibb, J.-J. Kladjian Conflict with: Novartis, AOP Pharma, AbbVie, Bristol Myers Squibb, R. Matson: None Declared, L. Rein Conflict with: Celgene, Novartis, Blueprint Medicine, Clinical Care Options, B. Reeves Conflict with: Bristol Myers Squibb, Incyte, Takeda, S. Oh Conflict with: Incyte, Gilead, Novartis, Kartos, CTI Biopharma, Celgene/BMS, Disc Medicine, Blueprint Medicine, PharmaEssentia, Constellation, V. Parameswaran: None Declared, H. J. Deeg: None Declared, S. Rose Conflict with: Bristol Myers Squibb, V. Chia Conflict with: Bristol Myers Squibb, T. Wang Conflict with: Bristol Myers Squibb, M. Talpaz Conflict with: IMAGO, Conflict with: Takeda, Novartis, Conflict with: Bristol Myers Squibb, Constellation Pharmaceuticals

**BSH2021-PO-090**

**A Phase 1/2 Study of INCB000928 as Monotherapy or in Combination with Ruxolitinib in Patients with Anemia Due to Myelofibrosis (INCB 00928-104)**

Stephen Oh1,*, Jean-Jacques Kladjian1, Francesca Palandri2, Jason Gotlib3, Sanjay Mohan3, Haris Ali6, Ekatherine Asatiani1, Francis Seguy5, Feng Zhou8, Srdan Verstovsek9

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**Abstract Content:** Anemia represents a therapeutic challenge in patients with myelofibrosis (MF). ALK2 activation is associated with elevated hepcidin, which may contribute to anemia of chronic disease and anemia due to hematologic malignancies, and is associated with increased transfusion rate and reduced overall survival. This phase 1/2, open-label, multicenter, dose-escalation/dose-expansion study will evaluate the safety and tolerability of INCB000928, a potent, highly selective, ALK2 inhibitor, as monotherapy or combined with ruxolitinib in patients with anemia due to MF (INCB 00928-104; NCT04455841).

Patients with histologically confirmed primary or secondary MF presenting with symptomatic anemia or transfusion-dependence will receive oral INCB000928 either alone (treatment group [TG] A) or combined with ruxolitinib (TGB). In TGA, patients must have intermediate (INT)-2 or high-risk (per Dynamic International Prognostic Scoring System [DIPSS]) disease that is intolerant, resistant, refractory, or has lost response to prior JAK inhibitor therapy (≥12 weeks). In TGB, patients must have received stable ruxolitinib therapy for ≥12 consecutive weeks before first dose and have INT-1, INT-2, or high-risk disease. Eligibility also requires age ≥18 years, ECOG 0–1 (dose-escalation) or 0–2 (dose-expansion), life expectancy >6 months, no other hematologic malignancy, no prior stem cell transplantation, no major surgery within 28 days, and no prior disease-directed therapy within 6 half-lives or 28 days of first dose.

In Part 1 (dose escalation), TGA will receive INCB000928 monotherapy starting at 50 mg/day (28-day cycles). Dose-escalation will follow a Bayesian optimal-interval design to determine the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE). Dose increases not exceeding 2-fold will continue until Grade ≥2 treatment-related toxicity occurs. TGB will receive INCB000928 plus ruxolitinib; INCB000928 dose escalation will start 2 dose levels below the highest dose determined to be safe and tolerable in TGA. In Part 2 (dose expansion), the RDE in TGB will be evaluated in combination with ruxolitinib in ~25 patients; treatment will continue for ≤12 months, and may continue if clinically beneficial and no progression occurs.

Primary objective is to determine the safety and tolerability of INCB000928 as monotherapy or combined with ruxolitinib. Secondary objectives are to determine the efficacy of INCB000928 as monotherapy or combined with ruxolitinib (anemia response, duration of anemia response, mean change from baseline in hemoglobin,
and RBC transfusion rate through weeks 24 and 48; evaluate INCBO0928 pharmacokinetics; and evaluate effects of INCBO00928 as monotherapy or combined with ruxolitinib in hepatic lesions and other measures of iron homeostasis and erythropoiesis.


**BSH2021-PO-091**

*A phase 1 study of INCBO57643 monotherapy in patients with relapsed/refractory myelofibrosis (INCBO 57643-103)*

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**Abstract Content:** Many neoplasms including myelofibrosis (MF) are associated with activation of transcription factors that regulate oncogenic processes. These may respond to inhibition of bromodomain and extra-terminal domain (BET) protein. In the first-in-human study INCB 57643-101, the BET inhibitor INCBO57643, was generally safe and tolerable as monotherapy, and demonstrated preliminary efficacy in patients with MF as monotherapy or combined with the JAK inhibitor, ruxolitinib (Falchook G, et al. Blood. 2020). This phase 1, open-label, two-part dose confirmation and expansion study further evaluates the safety and tolerability of INCBO57643 monotherapy in patients with relapsed/refractory MF (INCBO 57643-103; NCT04279847).

Eligible patients must be aged ≥18 years with histologically confirmed primary or secondary MF (post-polycythemia vera, post-essential thrombocytopenia), have received ≥1 prior therapy including ruxolitinib, have no known clinically beneficial therapy available, have intermediate-2/high risk disease by Dynamic International Prognostic Scoring System, have ECOG PS 0–2, life expectancy ≥24 weeks, and willing to provide a bone marrow biopsy and/or aspirate at baseline (or archival sample obtained after most recent therapy). Exclusion criteria include prior BET inhibitor or anticancer treatment within specified intervals before first dose; concurrent anti-cancer therapy; allogeneic hematopoietic stem cell transplant (allo-HSCT) ≤6 months before enrollment; active graft versus host disease or immunosuppressive therapy after allo-HSCT ≤2 weeks before first-dose; significant and uncontrolled disease (e.g., gastrointestinal, cardiovascular); history of bleeding disorders, high risk of bleeding, or abnormal hematologic, hepatic, renal, coagulation, or metabolic laboratory values.

In part 1, ≥8 patients will receive oral INCB057643 4 mg once-daily continuously. Doses will be deemed tolerable if ≤2 patients experience dose-limiting toxicities (DLTs) and ≤2 patients discontinue due to treatment-related adverse events (TRAEs) during the DLT evaluation period. Part 2 will further characterize safety and tolerability as well as evaluate preliminary efficacy of INCB057643 in ≤9 patients. The starting dose will be 4 mg once-daily if tolerated in Part 1, and 2 mg once-daily if not. Treatment may continue if clinically beneficial and discontinuation criteria are not met.

The primary objective is to determine safety and tolerability of INCB057643 monotherapy. Secondary objectives are to evaluate anemia response by International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet Consensus Report (ELN), transfusion dependence, spleen volume, rate and duration of spleen response by IWG-MRT and ELN, and impact on quality of life. Patients will be assessed every 3 cycles and will receive follow-up for safety for 30–35 days after last dose.

**Disclosure of Interest:** P. Vachhani: None Declared, C. Lihou Conflict with: Employee and stock holder of Incyte Corporation, G. Zhou Conflict with: Employee and stock holder of Incyte Corporation, F. Zheng Conflict with: Employee and stock holder of Incyte Corporation

**BSH2021-PO-092**

*A randomized, double-blind, placebo-controlled phase 3 study of parsaclisib plus ruxolitinib in patients with myelofibrosis who have suboptimal response to ruxolitinib*

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**Abstract Content:** Ruxolitinib (JAK1/JAK2 inhibitor) is indicated for the treatment of adults with intermediate (INT) or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF, but a subset of patients may exhibit a suboptimal response due to possible persistent PI3K/AKT activation. Targeting PI3K/AKT signaling may therefore have clinically relevant effects on MF disease burden. This phase 3, randomized, double-blind, placebo-controlled study will determine the effect of add-on parsaclisib, a highly selective PI3Kα inhibitor, on signs and symptoms of MF in patients with suboptimal or declining response to stable ruxolitinib treatment (INCB 50465-304; NCT04551053).

Eligible patients are aged ≥18 years with a diagnosis of at least INT–1-risk category according to the Dynamic International Prognostic Scoring System (DIPSS; Passamonti. Blood. 2010; 115:1703-1708) primary or secondary (post-polycythemia vera or post-essential thrombocythemia) MF, have received ruxolitinib for ≥3 months with a stable dose (5–25 mg twice daily) for ≥8 weeks prior to receiving the first dose of study drug (Day 1), have evidence of suboptimal response to ruxolitinib (palpable spleen ≤5 cm below left subcostal margin, and total symptom score ≥10), and ECOG PS ≤2. Patients are excluded if they received prior therapy with any PI3K inhibitor, experimental or standard drug therapy for MF (except ruxolitinib) within 3 months of starting study drug, or have platelet count <50 × 10^9/L, recent history of inadequate bone marrow reserve, or inadequate liver or renal function at screening.

Approximately 212 patients on a stable dose of ruxolitinib will be randomized (1:1) to receive add-on parsaclisib 5 mg daily or
matching placebo beginning on Day 1, with stratification by platelet count ($\geq 100 \times 10^{9}/L$ or 50 to $<100 \times 10^{9}/L$) and DIPSS risk category (high, INT-2, or INT-1) at randomization. Treatment will continue as long as tolerated and discontinuation criteria are not met. When a patient has completed 24 weeks of treatment, he/she will be unblinded and if found to be randomized to ruxolitinib plus placebo with adequate hematology parameters, the patient will be able to crossover to receive ruxolitinib plus add-on parsaclisib.

The primary objective is to evaluate and compare the efficacy of add-on parsaclisib versus placebo on spleen volume at Week 24. Secondary objectives are to evaluate and compare the effect of add-on parsaclisib versus placebo on: patient-reported MF symptoms, overall survival, time to onset and duration of spleen volume response, and safety and tolerability. Sites are opening throughout the US, EU, China, and Japan.


B3H2021-PO-093
Long-term efficacy of first-line versus second-line pegylated interferon in the treatment of essential thrombocythaemia and polycythaemia vera - results of a single-centre retrospective audit

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Abstract Content: Pegylated interferon (PegIFN) is increasingly used in the treatment of myeloproliferative neoplasms (MPN), including essential thrombocythaemia (ET) and polycythaemia vera (PV). It is often favoured over hydroxycarbamide, particularly in younger patients with MPN, as its non-cytotoxic nature avoids the long-term concerns sometimes associated with hydroxycarbamide. However, there is relatively little data relating to the long-term efficacy and toxicity of PegIFN.

To further characterise the response to PegIFN, we conducted a retrospective audit of patients with ET or PV under follow-up in the University College London Hospitals MPN clinic. The hospital e-prescribing system was searched to identify ET and PV patients who have been treated with PegIFN within the past 10 years. Patients with less than 3 months follow-up on PegIFN were excluded. Efficacy and toxicity data for eligible patients were collected using the hospital’s electronic patient record (EPR). Clinicohaematological responses were assessed using the European LeukemiaNet response criteria and adverse effects were classified according to CTCAE v5.0 criteria.

Thirty-nine eligible patients were identified (25 ET, 14 PV), with an overall median age of 50 (range 28-90) years. Median follow-up was 48 (9-86) months. JAK2 V617F was identified in 19 (76%) ET and 12 (86%) PV patients. One PV patient had a novel JAK2 exon 13 mutation, four (16%) ET patients had a CALR mutation, and the remaining three (2 ET, 1 PV) patients had no identifiable mutations. 80% of ET and 71% of PV patients were identified as high risk using BSH criteria. PegIFN was used as first-line therapy in 36%, and as second-line in 64% of patients, following resistance or intolerance to primary therapy.

Of the ET patients, 17/25 (68%) achieved complete response (CR) and a further 7/25 (28%) achieved partial response (PR), as their best response. Of the PV patients, 13/14 (93%) achieved CR. The remaining ET and PV patients did not respond. Median time to response in ET was 3 months (IQR 3-7.5 months), and 9 months (IQR 3-24 months) in PV ($P = ns$). Six patients took more than 24 months to establish their best response. Importantly, the CR rates did not significantly differ between first- and second-line therapy (86% vs. 72%, $P = 0.702$). However, time to complete response was significantly more variable for second-line versus first-line therapy (SD 24.9 vs 5.8 months, $P = 0.005$). This difference persisted regardless of the indication for second-line therapy.

Six patients discontinued PegIFN because of resistance to PegIFN (n = 2), remitting disease (n = 2) or no longer requiring PegIFN (e.g. following childbirth) (n = 2). Adverse effects were reported in 29 (74%) patients. The most commonly reported adverse effects were fatigue/lethargy (28%), mood disturbances (18%), headache (15%), pruritus (15%), and injection site reactions (15%). All adverse events were CTCAE grade I/II, except for one case of a grade III pruritic maculopapular rash.

In conclusion, PegIFN is an effective cytoreductive agent which can induce a complete response in most patients, with good tolerability. Although it may take a long time to achieve complete response, this time is not influenced by PegIFN being used as a 1st line or 2nd line therapy.

Disclosure of Interest: None Declared

B3H2021-PO-094
PACIFICA: A Randomized, Controlled Phase 3 Study of Pacritinib Versus Physician’s Choice in Patients with Primary or Secondary Myelofibrosis and Severe Thrombocytopenia

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Abstract Content: Background: Myelofibrosis (MF) is a serious and life-threatening myeloproliferative neoplasm (MPN) caused by clonal proliferation of myeloid cells. Patients (pts) with MF and severe thrombocytopenia (platelet counts <50 x 109/L) are generally older and have more advanced disease with increased risk of bleeding, higher rates of anemia, higher rates of complex or unfavorable cytogenetics and shortened overall survival (~15 months) compared to MF pts with higher platelet counts. Currently approved JAK inhibitors, ruxolitinib (RUX) and fedratinib (FED), were not studied in the high-risk thrombocytopenic population, and neither drug has a recommended starting dose for the treatment of pts with severe thrombocytopenia. RUX often requires dose reductions for pts with platelet counts <100 x 109/L due to drug-induced thrombocytopenia. Such dose reductions impair efficacy compared to higher doses. European Leukemia Net (ELN) recommendations and National Comprehensive Cancer Network (NCCN) guidelines suggest enrollment in clinical trials for pts with severe thrombocytopenia due to limited therapeutic options. Pacritinib (PAC) is an oral JAK2/IRAK1 inhibitor with demonstrated clinical activity in pts with MF in prior phase 3 studies (PERSIST-1, PERSIST-2) and a phase 2 dose-finding study (PAC203), including in pts with severe thrombocytopenia. The
PACIFICa trial (NCT03165734) is designed to evaluate the efficacy and safety of PAC 200 mg twice daily (BID) vs physician’s choice (P/C) therapy in pts with MF and severe thrombocytopenia.

**Study Design and Methods:** PACIFICa is a multinational, multicenter, randomized, controlled phase 3 trial of PAC vs P/C in adult pts with primary or secondary MF who are not candidates for stem cell transplant, with DIPSS intermediate- or high-risk disease, ECOG PS 0–2, and platelet counts <50 × 10^9/L who have had limited prior JAK2 inhibitor treatment or are JAK2 inhibitor-naïve. Additional exclusion criteria include recent cardiac or hemorrhagic events, left ventricular ejection fraction <50%, QTc >450 msec, or use of medications that increase the risk of hemorrhage or QT prolongation.Pts in the PAC arm receive continuous PAC 200 mg BID. Pts in the P/C arm receive one of the following agents as selected prior to randomization: low-dose ruxolitinib, danazol, corticosteroids, or hydroxyurea. The primary objective is to compare the efficacy of PAC vs P/C as assessed by the proportion of pts achieving a ≥35% spleen volume reduction (SVR) from baseline to week 24. Secondary objectives include comparisons of the proportion of pts achieving a ≥50% reduction in total symptom score (TSS) at week 24, overall survival, safety, and proportion of pts who self-assess as ‘very much improved’ or ‘much improved’ as measured by the Patient Global Impression of Change (PGIC). Tertiary endpoints include leukemia-free survival, alternative SVR analyses, hematologic improvement (transfusion independence and improvement in hemoglobin and platelet levels), fatigue improvement as measured by the PROMIS v.1.0 - Fatigue - Short form 7a, and changes in biomarkers and gene expression. The study will enrol approximately 348 pts in a 2:1 ratio (PAC to P/C). The primary analysis (for SVR) will be based on approximately 168 pts; the secondary analyses (including for TSS) will be based on the full sample size. PACIFICa is currently enrolling, with approximately 140 sites worldwide (US, Australia, Europe, Canada, Middle East, Asia, Russia).

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**Pre-operative anaemia pathway for elective orthopaedic surgery at Manchester University Foundation Trust (MFT)**

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**Abstract Content:** Pre-operative anaemia is a common, modifiable and independent risk factor for morbidity post-surgery. International consensus guidelines therefore recommend treating anaemia prior to elective surgery. At Manchester University Foundation Trust (MFT), the pre-operative anaemia pathway was introduced in 2017 to identify and correct pre-operative anaemia in patients listed to undergo elective arthroplasty.

The aim of this retrospective analysis was to evaluate the performance and impact of this service using data from 208 patients who underwent surgery between August 2017–March 2020. Where available, details surrounding diagnosis, treatment and follow-up were obtained from electronic records. 62.5% of patients were female, 37.5% male with a median age of 72.6 years.

The service performed at 100% efficacy in reviewing patients with pre-operative anaemia, the prevalence of which was 65.9% as per World Health Organisation (WHO) thresholds. 82.6% of patients demonstrated a normocytic anaemia at listing vs 13.8% microcytic. There was a high prevalence of iron deficiency: 68.4% of patients demonstrated Iron saturations of <20%, 14.7% demonstrated Ferritin levels <30 μg/L. 47.7% of patients were treated with oral/IV iron pre-operatively. 40.4% of cases did not have a correctable component. 8.8% received only B12/folate supplementation and 2.2% received pre-operative blood transfusion. In the female cohort, there was a significant improvement in mean haemoglobin (Hb g/L) to 117.92 vs 111.63 pre-op (P < 0.0001). Mean Hb for those that received intervention was higher than the total mean at 120.93 (P < 0.0001) reaching the normal WHO threshold, compared with non-correctable cases where Hb remained the same from listing to pre-op (111.63 vs 111.17, P = 0.7463). Similarly, for anaemic males, intervention for anaemia demonstrated a significant rise in Hb from 119.99 to 125.38 (P = 0.0117), compared with non-correctable cases where Hb remained the same (P = 0.4887). In the post-operative period, there was a reduction in mean Hb to 98.97 for anaemic females and 103.27 for males (P < 0.0001) at day 0/1 post-op. The greatest reduction was seen within 1 month of surgery with a mean Hb nadir of 98.04 (females) and 99.97 (males) yet remaining above transfusion thresholds.

For anaemic females, by 60-89 days and likewise 90-180 days there was no significant difference from pre-op Hb with mean Hb of 118 and 115.52 respectively (P = 0.6026 and P = 0.4155), thus demonstrating that recovery to pre-surgery levels occurs from 2 months post-op. There was no difference between pre-intervention levels and Hb at 90-180 days (111.47 at listing vs 114.53, P = 0.1775). At 90-180 days, males also showed recovery to original pre-intervention Hb (mean 113.6 vs 118.53, P = 0.2615) but not to optimised pre-operative levels. Mean Hb levels were predictably lower at 90-180 days in anaemic compared to non-anaemic patients: for females 115.52 vs 128.17 (P = 0.0218) and males 113.6 vs 136.42 (P < 0.0001).

Despite intervention pre-operatively, many patients remain anaemic 3-6 months post-op, although there appears to be meaningful Hb recovery in the months following surgery to pre-intervention levels. Based on available data from 208 patients, the anaemia service has demonstrated a significant therapeutic role, although the lack of routine anaemia follow-up post-operatively is detrimental. More emphasis on follow-up and guidelines for management of post-operative anaemia is required to enhance long-term benefit.

**Disclosure of Interest:** None Declared

**BSH2021-PO-096**

**A Two-Part Phase 2 Study of Itacitinib Immediate Release in Patients with Primary or Secondary Myelofibrosis Who Have Received Prior Ruxolitinib and/or Fedratinib**

**Monotherapy**

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Abstract Content: Ruxolitinib (JAK1/JAK2 inhibitor) and fedratinib (JAK2/FLT3 inhibitor) are indicated in the US for myelofibrosis (MF); however, some patients fail to achieve adequate/sustained response to initial JAK-inhibitor therapy. Itacitinib is a potent JAK inhibitor selective for JAK1 over JAK2 when administered as a once-daily sustained-release (SR) formulation. This SR formulation improved MF-related symptoms but had less effect with respect to spleen volume reduction. When dosed as a twice-daily (BID) immediate release (IR) formulation, itacitinib may offer increased JAK2 inhibition (in addition to JAK1 inhibition) to better address the JAK2-mediated myeloproliferative features of MF. This open-label phase 2 study is designed to determine a tolerable and safe dose of itacitinib IR that results in clinically significant reductions in symptoms and spleen volume in patients with MF who have previously received ruxolitinib and/or fedratinib monotherapy (INCB 39110-213; NCT046292508).

Eligible patients are ≥18 years, diagnosed with at least INT-1 risk (Dynamic International Prognostic Scoring System [Passamonti. Blood. 2010; 115:1703-1708]) primary or secondary (post-polycythemia vera or post-essential thrombocythemia) MF and have received ruxolitinib and/or fedratinib monotherapy. Patients must also have palpable splenomegaly and platelets ≥50 × 10^9/L at screening. Exclusion criteria include receipt of a JAK inhibitor other than ruxolitinib or fedratinib, ≥10% myeloid blasts in peripheral blood or bone marrow, or inability to taper ruxolitinib/fedratinib over 14 days without use of other agents.

Two itacitinib IR dose levels (DLa) will be evaluated in part 1 following a Bayesian optimal interval design algorithm: 3–9 patients will be enrolled at DLa (300 mg BID) and observed for 28 days for dose-limiting toxicity before enrollment at DLa (600 mg BID). Part 2 will enroll 55 patients at the recommended phase 2 dose (RP2D) determined in part 1. Patients may remain on treatment until week 48 if they are receiving clinical benefit and have not met study withdrawal criteria. A safety follow-up will occur 30 days after treatment completion.

Primary objectives (Table): part 1 - evaluate safety and tolerability of itacitinib IR and select the RP2D; part 2 - evaluate efficacy of itacitinib IR at the RP2D based on spleen volume reduction at week 24. Secondary objectives (part 2 only): evaluate safety and tolerability of itacitinib IR; evaluate efficacy of itacitinib IR with respect to MF symptom improvement at week 24 in patients with baseline total symptom score ≥10, quality-of-life improvement, and patient global impression of change. Sites are opening in the US and EU.


BSH2021-PO-097

A phase 3, randomized, double-blind, placebo-controlled study of ruxolitinib plus parsaclisib in patients with JAK- and PI3K-inhibitor treatment-naïve myelofibrosis

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Abstract Content: Ruxolitinib (JAK1/JAK2 inhibitor) significantly improves outcomes in patients with myelofibrosis (MF); however, a subset of patients may experience a suboptimal response. Recent phase 2 data showed that addition of PI3K inhibitor parsaclisib to ruxolitinib monotherapy resulted in additional alleviation of MF symptoms and splenomegaly in patients with MF (Yacoub. EHAA2020. S216). This phase 3, randomized, double-blind study (INCB 50465-313; NCT04551066), evaluates the combination of ruxolitinib and parsaclisib in patients with MF who are naïve to Janus kinase (JAK) and PI3K inhibitor therapies.

Eligible patients are ≥18 years with a diagnosis of primary MF, post-polycythemia vera MF, or post-essential thrombocythemia MF, have a Dynamic International Prognostic Scoring System (DIPSS; Passamonti. Blood. 2010;115:1703-1708) risk category of at least Intermediate (INT)-1, palpable spleen ≥5 cm below left subcostal margin; total symptom score ≥10 at screening, ECOG PS 0–2, and life expectancy ≥24 weeks. Patients will be excluded if they previously received therapy with any JAK inhibitor, any PI3K inhibitor, any experimental or standard drug therapy for MF ≤3 months of first study dose and/or lack of recovery from all toxicities related to previous therapies to grade ≤1, have recent history of inadequate bone marrow reserve (eg, platelet count <50 × 10^9/L) or have inadequate liver or renal function at screening.

Approximately 440 patients will be randomized (1:1) to ruxolitinib plus parsaclisib 5 mg QD or ruxolitinib plus matching placebo, with stratification at randomization by DIPSS risk category (high vs INT-2 vs INT-1) and platelet count (≥100 × 10^9/L vs 50 to <100 × 10^9/L inclusive). Treatment will begin on Day 1, with starting ruxolitinib dose level determined by baseline platelet count, and will continue as long as treatment is tolerated and discontinuation criteria are not met. When the last enrolled patient has completed 24 weeks of treatment, the study will be unblinded and patients randomized to ruxolitinib plus placebo who have adequate hematology parameters will be able to crossover to receive parsaclisib together with continued ruxolitinib.

The primary objective is the evaluation and comparison of spleen volume at Week 24 for patients who received ruxolitinib plus parsaclisib versus ruxolitinib plus placebo. Secondary objectives include evaluation and comparison of patient-reported MF symptoms, overall survival, time to onset and duration of response in spleen volume, and safety and tolerability for ruxolitinib plus parsaclisib versus ruxolitinib plus placebo. Sites are opening across the US, Canada, EU, and Asia.

Disclosure of Interest: A. Yacoub: None Declared, S. Erickson-Viitanen Conflict with: Employee and stock holder of Incyte Corporation, F. Zhou Conflict with: Employee and stock holder of Incyte
Impact of JAK2V617F Mutation on Coagulation Function Tests and Inflammatory Markers in Sudanese Patients with Essential Thrombocythemia

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Abstract Content: Background: Essential Thrombocythemia (ET) is characterized by a clonal expansion of megakaryocyte, marked thrombocytosis, genomic instability, dysregulated signaling pathways, overproduction of inflammatory markers, and tendency to develop thrombosis, hemorrhage, and myeloblastic or leukemic transformation with a consequent heavy burden of morbidity and mortality.

Objective: To investigate the impact of JAK2V617F mutation on coagulation function tests (platelets count, activated partial thromboplastin time (APTT), prothrombin time (PT), plasma fibrinogen level and D-dimer) and inflammatory markers (leukocytes count and pro-inflammatory IL-6) in Sudanese ET patients.

Methods: This cross-sectional study was conducted in hematology clinic of Radiation and Isotope Center at Khartoum (RICK) between 2017-2020. A total of 88 patients (54 females, 34 males; mean age 48 ±13 years) diagnosed with ET according to the 2016 WHO, and 50 healthy individuals as controls were included in this study. Demographic characteristics, clinical information, cardiovascular complications collected using designed interview based questionnaire. JAK2V617F mutation analysis performed using amplification refractory mutation system-polymerase chain reaction (ARM5-PCR) technique. Platelets count and leukocytes count were evaluated using the Sysmx analyzer. APTT and PT were measured using clot based assay, plasma fibrinogen level was measured using Clauss method and D-dimer was measured using sandwich immunodetection method. IL-6 was measured by enzyme-linked immunosorbent assay (ELISA)

Results: In total, 41% (36/88) ET patients were positive for the JAK2V617F mutation, of whom 28 patients (32% of total) were heterozygous and 8 patients (9%) were homozygous. JAK2V617F mutation was associated with significantly higher fibrinogen levels (P = 0.031) and higher leukocytes count (P = 0.029), while no associations were observed with regard to platelets count, APTT and PT (P > 0.05). IL-6 levels were significantly higher in ET patients compared to control subjects (P = 0.000), while it is not significant difference between JAK2 wild-type and JAK2V617F patients (P > 0.05). Moreover, JAK2V617F homozygosity associated with significantly higher fibrinogen levels (P = 0.048), higher D-dimer level (P = 0.022) and higher leukocytes count (P = 0.048), while platelets count, APTT, PT and IL-6 levels were not significant different between JAK2V617F homozygous and JAK2V617F heterozygous patients (P > 0.05). The correlation analysis displayed that IL-6 in ET had a significant positive correlation with fibrinogen level (P = 0.319, r = 0.002) and leukocytes count (P = 0.718, r = 0.000).

Conclusions: This data indicated that JAK2V617F mutation, in particular JAK2V617F homozygosity, associated with hypercoagulable status, leukocytosis and relatively inflammatory conditions. Such associations may possibly the contributors to the poor prognostic
outcome such as thrombosis, bleeding and short survival in ET patients with JAK2V617F mutation.

Keywords: Essential thrombocythemia; Hypercoagulability; Inflammation; JAK2V617F; Leukocytosis; Pro-inflammatory IL-6.

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BSH2021-PO-100

Experience with Pegasys in patients with myeloproliferative neoplasm

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Abstract Content: Pegylated interferon alfa-2a (Pegasys) in our patients with MPN across Oxford University Hospital and Royal Berkshire Hospital. The aim of this study was to review tolerability of Pegasys and to assess haematological response in patients with MPN.

We reviewed 41 patients receiving Pegasys by accessing patient electronic records. Patient characteristics include: median age 50 (age range 18–83), 19 male, 37 Caucasians and 4 Southeast Asians. Underlying diagnosis include: Polycythemia Rubra Vera (PRV)(16), Essential Thrombocythemia (ET)(23) and Primary Myelofibrosis (PMF)(2). Treatment duration was between 3 to 60 months. Treatment response was assessed as per ELN and IWG-MRT criteria: complete response (CR) and partial response (PR). Adverse effects were graded according to Common Terminology Criteria for Adverse Events (CTCAE).

A large proportion of patients were JAK2 positive (68%) with PRV being the largest contributor (16) followed by ET (12) and MF (2). The remaining ET patients were CALR mutated (7) and triple negative (4). 25 patients had high risk disease: 14 in ET, 10 in PRV and 1 in MF. 15 patients were started on Pegasys as first line treatment, 8 patients were previously on venesection, 12 patients on previous cytoreductive therapy (hydroxycarbamide/anagrelide) and 6 other patients were on interferon alfa which were discontinued. Common causes for starting pegasys include young age, poor disease control, side effects while on hydroxycarbamide/anagrelide and discontinuation of interferon alfa.

In ET, 17 (74%) patients attained CR and 4 (17%) patients attained PR. In PRV 9 (56%) patients had CR and PR seen in 5 (31%) patients. 2 patients with MF attained CR (100%). Average time for attainment of CR in patients with ET was 9 to 12 months, in PRV 12 to 18 months and 12 months in MF. One patient lost CR at 5 years and required venesection, this was a patient with high risk JAK2 mutated PRV. There were no disease transformations or thrombotic complications seen while on Pegasys. Common haematological toxicities include neutropenia (4) and anaemia (2). Non haematological toxicities include grade 1-2 hepatotoxicity (11), Grade 1-3 fatigue (4), grade 1-2 arthralgia/myalgia(9) and grade 2-3 rash (2). Only one elderly patient discontinued treatment due to grade 3 rash. 92% of patients (38) were started on a dose of 45 mcg weekly. Average maintenance dose to maintain CR/PR is about 45 to 135 mcg. We also note that patients who were switched to Pegasis from interferon alfa maintained their CR.

In conclusion, we find that Pegasis is well tolerated and is valuable in inducing haematological remission. Gradual dose titration, careful patient selection and efficient management of side effects can increase efficacy and tolerability of Pegasis. Patients with high risk disease may need combination treatment with JAK2 inhibitors such as Ruxolitinib, this however needs further clinical trials for evaluation.

Disclosure of Interest: None Declared

BSH2021-PO-101

Management of postpartum anaemia

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Abstract Content: Anaemia following childbirth is associated with fatigue and increased risk of postnatal depression, both of which have been shown to improve following iron supplementation. The risk of sepsis and poor wound healing may also be increased. We conducted an audit to assess compliance with national guidelines for the identification and management of postpartum anaemia.

The electronic patient records of the first 150 pregnant women who had dating scans in February 2020 were examined to determine whether they had an indication for a haemoglobin (Hb) check within 48 hours of delivery; uncorrected anaemia antenatally <105 g/dl, estimated blood loss >500 ml or the presence of symptoms of anaemia; and in what proportion of these Hb was checked. For those women with postnatal anaemia (Hb <100 g/dl), an assessment was made as to whether oral or intravenous (IV) iron or blood transfusion was an appropriate treatment, and which treatment was given. Oral iron was indicated if Hb <100 g/dl and the patient was haemodynamically stable with only mild or no symptoms; IV iron was indicated if the patient was intolerant of oral iron or had severe symptoms. Blood transfusion was indicated if there was continued bleeding or risk of further bleeding, haemodynamic instability or significant symptoms requiring urgent correction. Oral iron prescriptions were audited against the 2019 BSH recommendation of 40-80 mg of elemental iron daily or alternate days for at least three months.

Data was available for 138 of the 150 records analysed. 60/138 (43%) of women had an indication for an Hb check within 48 hours of delivery and of those 87% had their Hb checked. A total of 61/138 (44%) women had their Hb checked within this timeframe; 52/61 (85%) of these were indicated and 9/61 (15%) had an Hb check with no obvious indication. 8/60 (13%) of women did not have an Hb check despite having an indication. 32/138 (23%) of women were found to have postnatal anaemia. In 25/32 (78%) of these women oral iron was the appropriate treatment. 4/32 (13%) had an indication for IV iron and 2/32 (6%) had indication for blood transfusion. For 2/32 (6%) the most appropriate treatment could not be determined from the documentation.

Of the women in whom oral iron therapy was indicated 20/25 (80%) received oral iron and 3/25 (12%) were not treated. 7/32 (22%) women were treated with IV iron. In 4/7 (57%) this was appropriate, in 1/7 (14%) documentation did not allow an assessment of appropriateness to be made, and 2/7 (29%) could have been treated with oral iron.

There was considerable heterogeneity of oral iron prescriptions, with only 1/20 (5%) for OD therapy, 17/20 (85%) were prescribed BD therapy, and in 2/20 (10%) the frequency was unclear. 6/20 (30%) of prescriptions were for a duration of 14 days, 4/20 (20%) for 28 days, and 1/20 (5%) for 30 days. 9/20 (45%) did not have a duration documented.
These results show good (87%) adherence to guidelines in identifying women with postnatal anaemia, however in some (12%) no treatment was given and in others (29%) oral iron was underused. In those treated with oral iron only 5% were in line with BSH guidelines.

Dissemination of results and ongoing education is required to improve practice, particularly in the prescribing of oral iron.

Disclosure of Interest: None Declared

BSH2021-PO-102
Treatment free remission in Tunisian patients with chronic myeloid leukemia
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Abstract Content: Treatment free remission (TFR) is an opportunity for chronic myeloid leukemia (CML) patients with sustained deep molecular responses. Tyrosine Kinase Inhibitor (TKI) discontinuation in chronic phase CML is being implemented in clinical routine. In this study we characterize the outcome of Tunisian patients with CML who discontinued TKI therapy.

Patients with CML who discontinued their TKI outside clinical trials were enrolled. Information collected included reasons for discontinuation, duration of TKI treatment before discontinuation, molecular response (MR) status at TKI discontinuation and treatment-free remission (TFR) duration.

17 patients with CML who discontinued their TKI were identified. The median treatment duration before discontinuation was 117 months. Reasons for interruption were adverse events (n = 1); pregnancy (n = 3) and deep molecular response (n = 13) mainly with MR3/4 (n = 8; 61.5%), 6(35.3%) patients lost major molecular response (MMR) and re-initiated TKI treatment at a median 4 months (1–21) after stopping TKI. All relapsed patients promptly resumed TKI therapy and regained at least major molecular response. TFR was maintained in 11 (64.7%) patients with a median follow up of 23 months (3–124).

Despite lack of recommendations in national guidelines at the time; our results suggest that TKI discontinuation is safe outside clinical trials and particularly effective in CML patients who are in sustained deep molecular response with longer TKI treatment duration.

Disclosure of Interest: None Declared

BSH2021-PO-103
Efficacy and Safety of Pegylated Interferon in Myeloproliferative Neoplasms – A Regional Experience
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Abstract Content: Introduction: Hydroxycarbamide (HU) has traditionally been the first-line cytoreductive therapy for high risk patients with Philadelphia negative myeloproliferative neoplasms, but the optimal method of cytoreduction is unclear in younger patients with ET/PV. The advent of longer acting pegylated IFN-a-2a (PEG) has made the use of interferon far more tolerable for patients with fewer side-effects. However, there is a scarcity of longer-term outcome data.

Thus, we report on the experience of a cohort of MPN patients treated with PEG in the four major haematology centres in the province of Munster, Ireland.

Methods: This is a multi-centre retrospective analysis. Patient inclusion criteria in the study consisted of any patient with a diagnosis of either PV or ET based on WHO 2016 criteria who were treated with pegylated interferon. Patients treated with PEG first-line, as well as patients previously treated with other agents, were included in this study. Data was collected retrospectively via chart review. Haematological response was defined per standard ELN criteria.

Results: 30 patients fulfilled the inclusion criteria. All patients were Caucasian with a median age at diagnosis of 44.4 (range 22-82) and consisted of 20 females and 10 males. The median age starting PEG was 49.3. The median duration of follow up was 18 months with 8 patients on therapy for over 4 years.

For 46.6% patients, PEG was the first cytoreductive therapy utilised. Five patients were transitioned to PEG due to HU or anagrelide resistance, others were intolerant of prior therapies.

Of the 20 patients who have been on PEG for over a year, 75% have achieved a complete response by ELN criteria. The overall response rate (CR and PR) for our cohort was 86.6% based on ELN criteria. Of the five patients who were resistant to hydrea or anagrelide, 60% achieved CR after one year on PEG.

43.3% had PEG as primary therapy. Median time to CR was 4.5 months and only one patient on therapy for over a year failed to achieve CR. Adverse effects necessitated permanent cessation of therapy in two cases. One was stopped due to respiratory toxicity and one due to drug induced lupus, which resolved after PEG cessation. Other notable adverse effects included hepatic dysfunction, cytopoenias and fatigue.

We report on the outcome of one patient who conceived and completed pregnancy whilst on PEG without evidence of placental insufficiency.

No patient had an arterial or venous thrombotic event whilst on PEG. The median dose in the patients in CR was low, at 90 mcg/week.

Conclusion: In this cohort of MPN patients with a young median age but a wide age range, PEG was well tolerated with acceptable times to response and low rates of discontinuation. This is a retrospective study, and thus we have not been able to formally assess the impact of PEG on quality of life.

The outcomes of IFN in our patient cohort echoes clinical efficacy seen in other studies. The tolerability, absence of leukaemogenic effect and lack of known teratogenicity make this an attractive option for cytoreduction in the young MPN patient cohort.

Disclosure of Interest: None Declared

BSH2021-PO-104
A case of polycythaemia vera treated with ropeginterferon-2b during pregnancy
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Abstract Content: Polycythaemia Vera (PV), a myeloproliferative neoplasm (MPN), is usually diagnosed in patients ≥60 years. However, 15-20% of PV patients are less than 40 years of age at diagnosis. MPN patients have increased risk for pregnancy-related complications (miscarriage, thrombosis, haemorrhage, intrauterine growth restriction, pre-eclampsia and stillbirths). Hence the importance of a correct management during this time, including the
employment of aspirin, low molecular weight heparin (LMWH), venesection and cytoreductive therapy when needed.

When cytoreduction is necessary, in PV patients wishing to conceive, interferon alfa is the choice. The development of pegylated formulations, including ropeginterferon alfa-2b (Besremi®), has resulted in improved tolerability and easier administration.

We present the case of a 32-year-old woman with diagnosis of PV followed up at Guy’s Hospital who was on ropeginterferon alfa-2b during pregnancy, with adequate control and no complications. In December 2018, at the age of 29, she presented with numbness and intermittent parasthesia in the right side of her face and body. She had had previous history of skin rash and bilateral conjunctival congestion. She had no history of thrombotic events. Neurological causes of her hyperviscosity syndrome were ruled out. Her leucocyte count was 25.2 × 10⁹/L (neutrophils 22.2 × 10⁹/L), with haemoglobin of 175 g/L, haematocrit (Hct) of 0.57, platelets 926 × 10⁹/L, and platelets 859 × 10⁹/L. Abdominal ultrasound scan showed splenomegaly (16 cm). JAK2 V617F mutation was detected and PV, with bone marrow features of pannmyelosis, no immature precursors and grade 1 fibrosis, was diagnosed according to WHO criteria. She had several venesections and started aspirin 150 mg/day. Due to myeloproliferative features, treatment with peginterferon alfa-2a (Pegasys®), 90 mcg weekly, was added, with later increases up to 225 mcg weekly.

As she had no major response to peginterferon alfa-2a, with persistent high leucocyte and platelet counts (leukocytes 23.8 × 10⁹/L, neutrophils 21.2 × 10⁹/L, Hb 175 g/L, HCT 0.57, platelets 859 × 10⁹/L), the patient underwent local follow up with no special symptoms or signs of abnormal fetal development. Ultrasound scan in the third trimester demonstrated stability in spleen size.

The baby was delivered on 14th December 2020, at 38 weeks of gestation, with a weight of 2.8 kg. The patient’s most recent blood control in January 2021, after delivery, showed a leucocyte count of 19.1 × 10⁹/L (neutrophils 15.7 × 10⁹/L), haemoglobin of 119 g/L, Hct of 0.42 and platelet count of 855 × 10⁹/L.

To our knowledge, this is the first case in which ropeginterferon alfa-2b is used in a pregnant PV patient and also the first reported case where a patient with inadequate disease control with peginterferon alfa-2a attained sufficient response with ropeginterferon alfa-2b.

An informed consent has been obtained from the patient to write this abstract.

**Disclosure of Interest**: I. Sanchez: None Declared, C. Woodley: None Declared, G. Durgam: None Declared, N. Curto-Garcia: None Declared, J. O’Sullivan: None Declared, S. E. Robinson: None Declared, S. Ali: None Declared, D. McIlrnan: None Declared, C. Harrison Conflict with: C. Harrison has received advisory board and speaker fees from AOP pharma.

**BSH2021-PO-105**

A Diagnostic conundrum: coombs-negative, steroid refractory hemolytic anemia with reduced reticulocyte index despite a functioning marrow

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**Abstract Content**: We present a unique, diagnostically challenging case of a 28-year-old man with a past medical history of hypothyroidism who presented with a severe hemolytic anemia. On admission, his hemoglobin was 3.8 (g/dl), with hyperbilirubinemia and elevated lactate dehydrogenase indicative of acute hemolysis. The patient had risk factors for autoimmune disease, but he was persistently coombs-negative and refractory to steroids. Further work-up revealed a reduced reticulocyte index and an intramedullary process was pursued. However, his marrow demonstrated an appropriate erythrophasia on biopsy and positron emission tomography-computed tomography was negative for malignancy. Work-up for immune, malignant, infectious, and medication-based etiologies of hemolysis were largely unrevealing. Meanwhile, he required twenty units of packed red blood cell transfusions over the span of 10 days. Multiple hematologists were at a loss as to the etiology of this severe coombs-negative hemolytic anemia.

Ultimately, a diagnosis was reached on hospital day 10 with the utilization of a super coombs test. Unlike the direct antibody testing of the traditional coombs, the super coombs detects immunoglobulins by flow cytometry. The patient’s test resulted positive for IgG on the surface of red blood cells, thus diagnosing a warm autoimmune hemolytic anemia (AIHA). Subsequently, the patient became transfusion-independent with intravenous immunoglobulin for 5 consecutive days and weekly infusions of rituximab, 10 weeks following discharge his hemoglobin recovered to a normal range.

Still, a simple autoimmune hemolytic anemia does not explain the reduced reticulocyte index that obscured the case. Following discharge, the patient’s anti-intrinsic factor antibody resulted positive, providing a previously unknown diagnosis of pernicious anemia. In rare instances, simultaneous, co-dominant pernicious anemia and AIHA may alter the erythroid lineage such that the ample reticulum of typical young erythroid cells is lost prior to exiting the marrow. The erythroid cells released systemically are functional, but are not reticulocytes. This altered cell
Generic tyrosine kinase inhibitors (TKI) have significant ameliorated the financial burden imposed by long-term TKI use. Numerous retrospective observational studies attest to bioequivalence in terms of efficacy, pharmacokinetics and adverse effects profile. Moreover, we report a case of dramatic constitutional upset following a switch from Glivec to generic imatinib, which resolved rapidly upon resumption of the branded product. A 73 year-old woman presented in September 2010 with a myeloproliferative disorder manifesting as extreme thrombocytosis resistant to hydroxyurea and therapy and requiring therapeutic apheresis. Her past medical history was significant for a T3N1M0 mid-rectal polyploid adenocarcinoma, requiring abdominoperineal resection with colostomy formation in 2007; in addition to CKD3, type 2 diabetes mellitus, essential hypertension, COPD and ischaemic heart disease. Cytogenetics revealed the presence of the Philadelphia chromosome (p210), consistent with a diagnosis of CML-CP. The patient was commenced on imatinib mesylate 400 mg (Glivec, Novartis) in June 2011, achieving major molecular remission. Glivec maintained a molecular remission and was well-tolerated with minimal reported adverse effects for a five-year period. In March 2017, the patient was switched to generic imatinib mesylate (manufactured by Sandoz). Two months later, the patient reported an isolated episode of petechial bruising, followed by insidious onset of fatigue and severe diarrhoea, with the development of intractable muscle cramps by August 2017. By February 2018, she had developed a progressive, severe macrocytic anaemia, with ongoing lethargy, arthralgia, muscle cramps and diarrhoea. Subsequently the patient’s imatinib dose was reduced to 300 mg, but with minimal effect on tolerability. Ultimately, in January 2019, the patient had lost over 20 kg in weight – weighing 41 kg from 67 kg prior to the switch to generic imatinib – and continued to discharge diarrhoeal stool from her colostomy. Extensive investigation revealed no obvious cause for her deterioration. A CT chest, abdomen and pelvis demonstrated no evidence of occult malignancy; upper GI endoscopy revealed only minor reflux oesophagitis, with no pathology noted on colonoscopy. The patient demonstrated no features of decompensated heart failure to account for her stark decline, albeit with echocardiography demonstrating a severe dilated left ventricle. Throughout this period both her total white cell count and BCR-ABL/ABL ratio remained stable.

A non-formulary request for reversion to branded Glivec was accepted on a trial basis in March 2019, to establish whether switching to this formulation alleviated her symptoms. Rapid resolution of her diarrhoea and muscle cramps occurred, with progressive weight gain. Poor tolerance of generic imatinib formulations has been noted in a number of patients attending our service. No gross difference in excipients disclosed at the level of summaries of product characteristics (SmPC) offers an obvious explanation for this phenomenon. Arguably by recognising rare cases of severe intolerance to generic TKI formulations, unnecessary switches to more advanced lines of therapy may be avoided and protracted periods of undesirable effects minimized.

Disclosure of Interest: None Declared

BSH2021-PO-106
Dramatic constitutional deterioration following switch to generic imatinib: a case report and one centre’s experience
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Abstract Content: Generic tyrosine kinase inhibitors (TKI) have significantly ameliorated the financial burden imposed by long-term TKI use. Numerous retrospective observational studies attest to bioequivalence in terms of efficacy, pharmacokinetics and adverse effects profile. Here, we report a case of dramatic constitutional upset following a switch from Glivec to generic imatinib, which resolved rapidly upon resumption of the branded product.

A 73 year-old woman presented in September 2010 with a myeloproliferative disorder manifesting as extreme thrombocytosis resistant to hydroxyurea and therapy and requiring therapeutic apheresis. Her past medical history was significant for a T3N1M0 mid-rectal polyploid adenocarcinoma, requiring abdominoperineal resection with colostomy formation in 2007; in addition to CKD3, type 2 diabetes mellitus, essential hypertension, COPD and ischaemic heart disease. Cytogenetics revealed the presence of the Philadelphia chromosome (p210), consistent with a diagnosis of CML-CP. The patient was commenced on imatinib mesylate 400 mg (Glivec, Novartis) in June 2011, achieving major molecular remission. Glivec maintained a molecular remission and was well-tolerated with minimal reported adverse effects for a five-year period.

In March 2017, the patient was switched to generic imatinib mesylate (manufactured by Sandoz). Two months later, the patient reported an isolated episode of petechial bruising, followed by insidious onset of fatigue and severe diarrhoea, with the development of intractable muscle cramps by August 2017. By February 2018, she had developed a progressive, severe macrocytic anaemia, with ongoing lethargy, arthralgia, muscle cramps and diarrhoea. Subsequently the patient’s imatinib dose was reduced to 300 mg, but with minimal effect on tolerability. Ultimately, in January 2019, the patient had lost over 20 kg in weight – weighing 41 kg from 67 kg prior to the switch to generic imatinib – and continued to discharge diarrhoeal stool from her colostomy. Extensive investigation revealed no obvious cause for her deterioration. A CT chest, abdomen and pelvis demonstrated no evidence of occult malignancy; upper GI endoscopy revealed only minor reflux oesophagitis, with no pathology noted on colonoscopy. The patient demonstrated no features of decompensated heart failure to account for her stark decline, albeit with echocardiography demonstrating a severe dilated left ventricle. Throughout this period both her total white cell count and BCR-ABL/ABL ratio remained stable.

A non-formulary request for reversion to branded Glivec was accepted on a trial basis in March 2019, to establish whether switching to this formulation alleviated her symptoms. Rapid resolution of her diarrhoea and muscle cramps occurred, with progressive weight gain. Poor tolerance of generic imatinib formulations has been noted in a number of patients attending our service. No gross difference in excipients disclosed at the level of summaries of product characteristics (SmPC) offers an obvious explanation for this phenomenon. Arguably by recognising rare cases of severe intolerance to generic TKI formulations, unnecessary switches to more advanced lines of therapy may be avoided and protracted periods of undesirable effects minimized.

Disclosure of Interest: None Declared

BSH2021-PO-107
Effect of metformin-induced serum vitamin B12 deficiency on haematological parameters in type 2 diabetes patients
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Abstract Content: Although studies have shown metformin-induced serum vitamin B12 deficiency to affect red blood cell indices in type 2 diabetes mellitus (T2DM) patients, it remains unclear whether folate deficiency is a confounding factor for this observation. Moreover, limited data is available on the effect of metformin-induced vitamin B12 deficiency on other haematological parameters. This study therefore investigated the effect of metformin on serum vitamin B12, folate and haematological parameters in T2DM patients.

We conducted a case-control study involving 80 type 2 diabetes on metformin (T2DM+M) patients, 76 type 2 diabetes mellitus not on metformin (T2DM-M) patients and 56 non diabetes mellitus (DM) healthy subjects were recruit attending the Endocrinology clinics at the University of Nigeria Teaching Hospital (UNTH) Ituku-Ozalla, Enugu Nigeria. Demographic information was obtained and serum vitamin B12, serum folate and haematological parameters were assayed.

The prevalence of serum vitamin B12 deficiency was 27.5% (22/80) in, T2DM+M subjects, 10.53% (8/76) T2DM-M subjects and the difference was significant. Therefore, vitamin B12 deficiency was associated with metformin use (χ2=13.803, P = 0.001). Folate deficiency was not observed. Haemoglobin, reticulocytes and monocyte were significantly (P < 0.05) lower in T2DM-M subjects. Moreover, WBC and neutrophil were significantly (P < 0.05) higher in T2DM-M+ subjects. Two way ANOVA showed that both metformin use and serum vitamin B12 deficiency interacted to increase Hb, RBC and haematocrit and decrease platelets, PCT and PDW levels in vitamin B12 deficient T2DM-M+ subjects. Also, anaemia was more prevalent in T2DM-M+ subjects than T2DM-M subjects and hypersegmented neutrophil and oval macrocytes were observed only in T2DM-M+ subjects. Serum vitamin B12 levels negatively associated with reticulocyte while a positive association was observed with monocytes.

Metformin use in T2DM subjects was associated with vitamin B12 deficiency and metformin-induced vitamin B12 deficiency affected some haematological parameters. Folate deficiency was not observed and therefore, the effect of metformin-induced vitamin B12 on haematological parameters was not subjected to folate deficiency as a confounding variable.

Disclosure of Interest: None Declared
Immune Thrombocytopenia (ITP) in pregnancy

A 69-year-old male was admitted directly to hospital with bilateral ureteric obstruction following referral by his General Practitioner to the Urology team with suspected renal colic. Deterioration in his renal function was noted (eGFR 18 ml/min/1.73 m² at referral, from 59 ml/min/1.73 m² three months previously).

Unenhanced CT of the urinary tract demonstrated multiple calculi within both kidneys and ureters causing bilateral hydronephrosis. The calculi were of relatively low density, measuring <300 Hounsfield Units on CT, consistent with uric acid calculi. There was no previous history of gout.

Laboratory investigations demonstrated leucocytosis, anaemia, elevated creatinine and extreme hyperuricaemia (Table 1). A full blood count performed two years previously had been normal. Blood film examination showed a leucocytosis comprised primarily of neutrophils and myelocytes, with a prominent basophilia, in keeping with chronic myeloid leukaemia (CML) in chronic phase. This was confirmed by bone marrow aspirate and demonstration of the presence of BCR-ABL1 rearrangement in 93% of cells examined by fluorescent in situ hybridisation.

The kidney injury was managed with insertion of bilateral nephrostomies to decompress the renal collecting systems, with the expectation that ureteric stent placement would be needed to allow passage of the larger stones.

Treatment for CML was started, with hydroxyureabamide 1 g daily until the white cell count was under 200 × 10⁹/l, when imatinib 400 mg daily was commenced. Rasburicase 0.2 mg/kg IV was given on the first day of hydroxyureabamide treatment for prevention of tumour lysis syndrome followed by allopurinol 100 mg daily. A further 3 mg dose of rasburicase was given when imatinib was started.

Repeat CT scan eleven days after the initial rasburicase dose was performed following the accidental removal of one of the nephrostomies when the patient was repositioned in bed. This showed resolution of the renal calculi bilaterally and ureteric calculi on the left. Residual non-obstructing small volume calculi were demonstrated in the right distal ureter and further tiny calculi within the dependent aspect of the urinary bladder. Following the CT scan, the remaining nephrostomy was also successfully removed. Serum creatinine and urate had normalised when rechecked on day 20 of his admission (Table 1).

Rasburicase is a recombinant urate oxidase, an enzyme which converts uric acid into the more soluble compound allantoin. It is licensed in the UK for the prevention and treatment of tumour lysis syndrome in patients receiving systemic anti-cancer therapy. The administration of rasburicase in this patient coincided with complete resolution of the acute kidney injury and clearance of presumed uric acid stones from the renal collecting system. This case builds on the anecdotal evidence for the use of rasburicase in the management of uric acid renal stones already reported in the literature.¹ ²

References

1. Dissolution of extensive urolithiasis: extending the utility of rasburicase can avoid the need for surgical intervention and renal replacement therapy. Resvani et al. Surg Case Rep. 2016 Feb 24;2016 (2)
in first trimester with good effect. None of the patients required emergency treatment at delivery. Eight patients with a platelet count above 70 had neuraxial anaesthesia without any complications. One patient required prednisolone 20 mg daily for 2 days to remove epidural catheter as platelet count dropped to 39. Of the 20 patients we reviewed, one patient had splenectomy prior to pregnancy and did not have a relapse in pregnancy, her baby was well with no thrombocytopenia. 13 patients had spontaneous vaginal delivery and 4 had caesarean section for obstetric reasons. Five of 20 babies were born with neonatal thrombocytopenia. One baby had platelet count of 89 at birth which further dropped to 39 a week later and recovered spontaneously 3 days later. This baby has a sibling previously affected with NT. None of the women reported any significant bleeding in the postpartum period. There were no deviations from the recommendations specified in the intrapartum care plan in any of the cases.

Overall the number of women needing antenatal treatment was higher than expected but all responded well to prednisolone 20 mg daily with no complications. The number of neonates with thrombocytopenia was also unexpectedly high (25%), but all were managed as advised and had no complications.

In conclusion, our study reassured us of the value of the documented intrapartum care plan and how advice was reliably followed. Disclosure of Interest: None Declared

BSH2021-PO-110
The treatment of chronic myeloid leukaemia with tyrosine kinase inhibitors - a single centre retrospective review
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Abstract Content: Chronic myeloid leukaemia (CML) treatment has been revolutionised by the identification of the Bcr-Abl1 fusion oncogene and the introduction of tyrosine kinase inhibitors (TKI) to target its activity. The European Leukaemia Net (ELN) sets targets to assess treatment response to TKIs for CML patients, including monitoring for Complete Haematological Response (CHR), Complete Cytogenetic Response (CCyR) and Major Molecular Response (MMR) at specified timepoints. Defined milestones guide physicians on disease response and identify if TKI dose adjustment or switch is required.

In this retrospective study, we evaluated our CML cohort’s response to TKI treatment and assessed whether milestones, as defined by ELN, are being met. Using our CML database, patients’ demographics, laboratory results and molecular/cytogenetic (peripheral blood & bone marrow) reports were analysed.

In total 49 CML patients were identified; 39 patients currently under active follow-up were included (20 female and 19 male). The remaining are followed-up elsewhere (n = 3) or have died (n = 7). Most patients were over 50 years old at diagnosis (n = 30, range 33–91 years). Eight (15.4%) patients were diagnosed within the previous 18 months. The majority of our cohort (85%, n = 33) received Imatinib as first-line treatment; 6 (15%) patients received a second-generation TKI upfront. For the Imatinib group, 100% achieved CHR (range 1–5 months) and, at 6 months, 50% (n = 2) had achieved CCyR; the remaining 2 achieved it >6 months (range 6-8 months). Seventy-five percent of this cohort (n = 3) achieved MMR within ≤12 months (range 8–12 months); 1 patient is awaiting 12-month transcript levels. Two patients received Nilotinib as first-line treatment; both achieved CHR (range 2-8 months), one achieved CCyR at 6 months and both patients achieved MMR. Collectively, 87% (n = 34) of our patients achieved CHR at ≤3 months, 41% (n = 16) achieved CCyR at ≤6 months and 43.6% (n = 17) achieved MMR at ≤12 months. Time limits aside, 100% achieved CHR, 89.7% achieved CCyR and 76.9% achieved MMR. Ten (25.6%) patients were switched to a second-line TKI due to loss of response (n = 7) or side-effects (n = 3). Three (7.7%) patients required a third TKI (nilotinib and 33.3% due to loss of MMR.

The findings of our review are in keeping with other real-world cohorts of CML patients treated with TKIs, with our overall CHR, CCyR and CMR meeting international standards. ELN milestones were met, although not always in a timely fashion, and our cohort required less drug switches due to side-effects than others. Second generation TKIs achieved a more rapid MMR than Imatinib; overall MMR rates between the two groups are comparable. Further research is needed into the timely achievement of milestones, particularly cytogenetic response. Disclosure of Interest: None Declared

BSH2021-PO-111
A bone marrow diagnosis: metastatic melanoma with no primary
Sarah Beverstock1, Christopher Mullen, Tamasin Doig, Victoria Campbell

Abstract Content: Melanoma, a highly aggressive tumour of melanocytes, can rarely metastasise to bone marrow (BM). In a minority, metastatic disease can be discovered in absence of a primary tumour, which may reflect tumour regression. We present a case of metastatic melanoma in the BM and myocardium without occult primary site.

A 77 year old male was admitted with a 2 month history of progressive, exertional dyspnoea, anorexia and weight loss of 28% total body mass. Past medical history included ischaemic heart disease, previous coronary artery bypass grafting (CABG) and hypertension. Transthoracic echocardiography revealed globally hypokinetic left ventricle (LV) with moderate LV systolic impairment, right ventricular hypertrophy, thickened inter-atrial septum, impaired longitudinal function and mild pulmonary impairment. Concerns were raised that this could represent myocardial amyloid or an infiltrative process. Full blood count was normal. Blood film showed nucleated red cells and neutrophil left shift. Protein electrophoresis, urinary Bence Jones and serum free light chains were normal. A CT 1 month previously showed no evidence of primary malignancy and no cardiac changes other than evidence of previous CABG. The bone marrow aspirate was hypercellular with a striking significant infiltrate of abnormal, large cells with bi- and occasionally multi-nucleate forms constituting >20% of all nucleated cells. Cytoplasmic blebbing was prominent. Trephine showed deposits of metastatic malignancy with sheats of medium-to-large sized cells; majority had pale staining cytoplasm but a minority were noted to be pigmented. Staining for Congo red and cytookeratin was negative, but positive for S100 and Melan-A confirming presence of metastatic melanoma.
The patient continued to deteriorate rapidly despite supportive measures and died 13 days after admission.

Diagnosis of antemortem cardiac metastasis is unusual and described in <10% melanoma. It is not infrequently identified at post mortem (PM); a study showed discordance between clinical manifestations and PM findings with up to 65% patients having cardiac involvement at PM whilst only 11% had clinically significant cardiac dysfunction. Findings on transthoracic echo depend on the area of metastatic deposition but majority involve the myocardium and ECHO findings are therefore often non-specific, meriting further investigation with cardiac MRI or CT. Interestingly, this patient did not have evidence of cardiac dysfunction on CT. Whilst unusual for patients to present with metastatic melanoma without a primary tumour this is observed in 5-15% cases. BM involvement is rare, occurring in approximately 5% of patients with disseminated disease but occult BM infiltration is seen in up to 45% at PM. In summary, the combination of cardiac and BM involvement by melanoma in the absence of a primary tumour is extremely unusual.

This unusual case report highlights the value of bone marrow examination in challenging cases.

Disclosure of Interest: None Declared

BSH2021-PO-112
The diagnosis, treatment and monitoring of patients with chronic myeloid leukaemia: the impact of ELN guidelines on clinical practice in a district general hospital
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Abstract Content: Department of Haematology, North West Anglia NHS Foundation Trust, Cambridge, UK

Tyrosine Kinase Inhibitors (TKI) have revolutionised the treatment and outcome of patients with Chronic Myeloid Leukaemia. This treatment, however, is associated with significant toxicity, in particular cardiovascular complications, and emergence of drug resistance. In order to optimise the TKI treatment pathway, European Leukaemia Net (ELN) published a Guidelines in 2013 (Baccaran et al, Blood, 2013; 122:872–84). But the recent UK TARGET CML study carried out in the United Kingdom has identified significant variations in compliance with the above guidelines (Milojkovic et al, Br Haematol. Br J Haematol. 192(1):62-74). Prompted by this report, we conducted an audit into the treatment pathway of all patients currently treated with a TKI in our hospital. Patient demographics, clinical features at presentation, diagnostics, clinical risk assessment, prognostic evaluation, treatment choice, frequency of response monitoring and interventions at treatment failures were analysed in a cohort of 51 (31 male and 20 female) patients. The age group of this patient population is 24-88 years (mean 59.4). Good clinical records documenting relevant clinical information are available in 40/51 (78.4%) cases. Cardiac co-morbidities are recorded in 21/51 (41.2%) patients. These include type II diabetes mellitus (11.7%), hypertension (11.7%), cardiac arrhythmias (5.8%), obesity (21.6%), ischaemic heart disease (5.8%) and hyperlipidaemia (1.9%). Relevant clinical signs are recorded in 86% of the cases but this information is missing in 14% of the notes studied. Splenomegaly and hepatomegaly were noted at presentation in 14 (27.4%) and 1 (1.9%) patients respectively. All patients (100%) had bone marrow evaluation and cytogenetics done at diagnosis but prognostic scores are recorded only in 10 (19.6%) cases. The first line TKI was imatinib in 44/51 (86.2%), dasatinib in 4/51 (7.8%) and nilotinib in 3/51 (5.8%). The selection of TKI was appropriate in 114 patients (100%) with known cardiac risk factor(s). A second generation TKI was selected on the basis of risk assessment in 3 patients. The reason for the selection of a second generation TKI in the other 4 cases was not recorded. 22/51 (43.1%) patients developed treatment failure at various time points. One patient opted for palliative care. Appropriate changes to treatment were made in 18/21 (85.7%) patients. However, there were delays in introducing changes to treatment in the remaining 3/21 cases (14.2%). Second line TKI treatment was dasatinib in 10 (47.6%), nilotinib in 6 (28.6%) and imatinib in 5 (23.8%) patients. The choice of second generation TKI was based on cardiovascular risk assessment in 18/21 (85.6%). Tyrosine Kinase Domain mutation analysis was carried out prior to changing TKI in 6/21 (28.6%). The test was not performed in 15/21 (71.4%) cases. The results of the current audit were compared with the previous audit conducted in 2011, prior to the introduction of ELN Guidelines. Although the comparison shows significant improvements in the CML diagnosis, clinical risk assessment, disease monitoring and drug selection at treatment failure, it is concluded that there is still room for further improvements, in particular, in areas of prognostic evaluation, risk-adapted drug choice and TKI mutation analysis at treatment failures.

Disclosure of Interest: None Declared

BSH2021-PO-113
Does obstructive sleep apnoea really cause polycythaemia?
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Abstract Content: Introduction: True polycythaemia is uncommon – at a rate of 0.3% for both men and women in the general population. Individuals with clonally-driven polycythaemia have higher rates of cardiovascular and all-cause mortality and morbidity. However, the majority of erythrocytosis referred to haematology are secondary phenomena. Chronic hypoxaemia causes a secondary rise in haematocrit and conditions in which patients are recurrently hypoxic will be at higher risk of secondary polycythaemia. ‘A guideline for the Diagnosis and Management of Polycythaemia Vera’ published in 2018 in the British Journal of Haematology (BJH) cite obstructive sleep apnoea (OSA) as a potential cause and suggest onward referral to investigate, if suspected. However anecdotal, it seemed very few patients truly had both diagnoses. Additionally, of those that had an erythrocytosis and fit the criteria for initiating treatment of OSA, it was unclear if treatment of their OSA normalised their haematological indices. We reviewed the haematocrit (Hct) of patients with confirmed OSA and aimed to find out if those with a raised haematocrit had a haematological response once the gold standard treatment for OSA - continuous positive airway pressure (CPAP) was commenced.

Methods: Overnight polysomnography data taken prior to commencing CPAP were released from the Sleep Studies department at the Northern General Hospital for 244 patients. All patients commenced overnight CPAP between June 2017 and May 2018. All had confirmed OSA and had been referred from hospitals in South Yorkshire. Their personal demographic data were taken from their electronic patient records and blood results from ICE, allowing a baseline full blood count to be taken up to a year prior to commencing CPAP. Severity of OSA was graded using Apnoea Hypopnoea Index and was taken from their baseline polysomnography report. Patients without a prior FBC were excluded from the results.

Results: 69 (34%) patients were female, 132 (66%) male. 43 were excluded. 93 (46%) had severe sleep apnoea, 75 (37%) moderate, 27 (13%) mild and 6 could not be graded. 41 (20%) had a baseline haematocrit above the local laboratory reference range. 4 (2%)...
patients fulfilled strict criteria of erythrocytosis (Hct>0.52 for males and >4.8 for females). Of these 4 patients (3 with moderate OSA and one severe), only 2 had repeat FBC testing and these patients continued to have a Hct above the reference range (but below the criteria for erythrocytosis – 0.47 and 0.48).

**Conclusions:** OSA does not cause clinically significant polycythaemia and the severity of OSA does not correlate with the degree of haematocrit elevation. In those whose haematocrit was elevated, commencement of CPAP decreased but did not normalise it. These patients had other risk factors - including diuretic use and diabetes - to account for an elevated haematocrit. The effect of intermittent nocturnal hypoxemia probably results in non-sustained EPO secretion.

Whilst this was a small sample of patients, it is part of a growing body of evidence; we propose referral for investigation of OSA should not be part of the investigative pathway for a new diagnosis of polycythaemia.

**Disclosure of Interest:** None Declared

**BSH2021-PO-114**

**A rare case of posterior reversible encephalopathy syndrome in Acute Intermittent Porphyria leading to seizures and cardiac arrest**

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**Abstract Content:** Acute intermittent porphyria is a rare autosomal dominant disorder characterised by partial deficiency of porphobilinogen deaminase leading to accumulation of porphyrin precursors in the body. Typical flares including abdominal pain, constipation, nausea and vomiting as well as behavioural changes. We present a rare case of a 27-year-old lady with AIP who suffered a cardiac arrest after having a seizure due to posterior reversible encephalopathy syndrome. She was initially admitted with a flare of her AIP with severe abdominal pain, behavioural changes and vomiting and was being treated with a haem arginate infusion, as well as opioids and anti-emetics. After having a seizure, she was treated for hypoglycaemia with IV dextrose and potential opioid toxicity with naloxone. She spontaneously recovered but then suffered another seizure 30 minutes later. A CT scan of the head showed a small occipital infarct. However, a stroke review confirmed that the stroke was too small to have explained her seizures. Subsequent MRI confirmed posterior reversible encephalopathy syndrome which is a clinico-radiological syndrome typically consisting of headaches, seizures, altered mental status and visual loss. It is characterised by white matter vasogenic oedema affecting the posterior occipital and parietal lobes of the brain mainly. The management of PRES is largely supportive and includes treating the seizures with anti-epileptics and blood pressure regulation. This patient’s PRES resolved over the next week as confirmed by subsequent MRI scan imaging.

**Disclosure of Interest:** None Declared
Laboratory Haematology and Transfusion

BSH2021-PO-115
The effect of an ambulatory care pathway on management of anaemia in a district general hospital
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Abstract Content: The burden of iron deficiency anaemia (IDA) is reflected by the rising number of emergency admissions related to IDA and reports of the monumental cost of managing the condition as an inpatient. The National Health Service spends approximately £55 million per annum on IDA-related non-elective admissions, many of which could be preventable and managed in the community or ambulatory care setting.

In 2018, a retrospective data collection was performed to assess the overall management of 50 newly diagnosed cases of anaemia presenting to a district general hospital between May – July 2018. This data was compared to quality standards issued by the British Society of Gastroenterology and recommendations on blood transfusion as advised by the National Institute for Health and Care Excellence. An ambulatory anaemia pathway was created and implemented in 2018 with the aim of streamlining investigations for anaemia and establishing criteria for urgent referral and safe ambulation. A further 77 cases of anaemia presenting to secondary care between November and February 2019-2020 were assessed against the same quality standards used in the initial data collection and results compared.

74% cases with anaemia were appropriately investigated in 2019/2020 compared to 48% in 2018. Only 18% of the cohort with IDA had a urine dip performed and documented and 27% patients in this group did not have a coeliac screen in 2019/2020. Many patients received blood transfusions above haemoglobin thresholds recommended by NICE, however a modest increase of 17% patients in 2019/2020 had a haemoglobin review between units. Iron replacement in IDA improved from 59% to 73% in 2019/2020, respectively. In 2019/2020 there was a 25% increase in the number of patients with a confirmed malignancy that were referred appropriately under a two-week wait compared to 2018. The proportion of patients that were clinically appropriate and subsequently ambulated was 75% and 73% in 2018 and 2019/20, respectively.

Although overall management of anaemia improved after the ambulatory anaemia pathway was implemented, basic investigations such as a urine dipstick and coeliac screen were not performed in several cases. Treatment of IDA was superior in 2019/2020, as there was an improvement in iron replacement and fewer patients were transfused multiple units of blood without review between units. A greater number of patients who were subsequently diagnosed with a malignancy had appropriate urgent follow-up in 2019/2020 compared to 2018. There was a marginal decline in the number of patients who were clinically appropriate for ambulatory care and were discharged, however these decisions are often complicated by complex medical and social factors.

As a result of national bed shortages following the COVID-19 pandemic, the requirement to reduce non-elective admissions and preserve blood products has never been more pressing. Therefore, it is proposed that the ambulatory anaemia pathway could help reduce non-elective admissions for anaemia by encouraging safe ambulation, avoid unnecessary blood transfusions and provide appropriate follow-up. It would be prudent to assess the impact of COVID-19 on hospital admissions with anaemia and determine whether ambulated patients demonstrate clinical improvement or require subsequent admissions for their symptoms of anaemia.

Disclosure of Interest: None Declared

BSH2021-PO-116
Evaluation of a new reticulated platelet parameter using an ADVIA 2120i
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Abstract Content: A new reticulated platelet (RP) parameter has been developed and introduced with the latest v6.10.9 software upgrade on the ADVIA 2120i and 2120i haematology systems (Siemens Healthcare Laboratory Diagnostics, Tarrytown, NY).

The classical use described for reticulated platelet measurements is to assist with differentiating the cause of thrombocytopenia. In reduced-production states such as acute leukaemia, aplastic anaemia, and bone marrow infiltration the RP count is typically low. Conversely, in increased-consumption states such as disseminated intravascular coagulation (DIC), immune thrombocytopenia (ITP) and thrombotic thrombocytopenic purpura (TTP) the RP count is raised.

Studies have shown that immature platelets come in a variety of sizes, and so automated approaches that rely upon volume alone may not be the best approach. The ADVIA 2120i & 2120i reticulated platelet count can enumerate platelets that are RNA positive using the nucleic acid dye oxazine 750, regardless of size, using a combination of absorption and refractive index measurements.

The aim of this study was to establish a reference range for the new parameter and evaluate the clinical utility of the percentage of reticulated platelets (%RP) to differentiate a reduced production from an increased destruction cause of thrombocytopenia using an ADVIA 2120i.

Three-hundred and sixty samples sent for a routine full blood count with a platelet count within our stated reference range (150 - 450 x10^9/L) and with no known underlying pathology were used to determine a reference range for %RP. In addition, %RP measurements were recorded for forty-two patients with platelet counts below 100 x10^9/L with clinically confirmed aplastic anaemia (n = 27) and ITP (n = 15). Analyzer quality control and maintenance tasks were performed according to the manufacturer’s instructions.

The normal range for %RP was determined to be 0.38% to 5.81% with a mean of 2.06%. %RP measured in those patients with aplastic anaemia ranged from 0% to 6.13% with a mean of 1.11%. %RP measured in those patients with ITP ranged from 0.84% to 19% with a mean of 8.27%.

Statistical analysis showed a highly significant difference in %RP values between aplastic anaemia and ITP (P < 0.001). Receiver operating characteristic (ROC) curve analysis and the Youden’s Index showed the optimum cut-offs for %RP to be ≤1.03% in aplastic anaemia (sensitivity 81.5%, specificity 78.3%) and ≥5.77% in ITP (sensitivity 80%, specificity 97.5%).

Our study showed that %RP values tended to be much lower in aplastic anaemia than ITP when the platelet count was below 100 x10^9/L. Rapid automated measurement of the percentage of
reticulated platelets using an ADVIA 2120i, when combined with other clinical and laboratory parameters, is a useful and cost-effective tool for differentiating causes of thrombocytopenia.

Disclosure of Interest: None Declared

BSH2021-PO-117
Knowledge and attitude towards blood donation and prevalence of hepatitis B and C among secondary school teachers in Calabar, Nigeria
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Abstract Content: Blood for transfusion or biopharmaceutical medication is obtained through blood donation. It is an indispensable component of health that contributes to saving lives since blood/blood products are unique. Major source of safe blood is voluntary non-renumerated blood donors. Considering the role of teachers in the education of young people in the populace, this study aims to provide information on knowledge and attitude towards blood donation and the prevalence of Hepatitis B and C among secondary school teachers in Calabar, Nigeria. With ethical approval and informed consent, a total of 200 apparently healthy teachers were recruited from two secondary schools. Structured questionnaires were administered and blood was collected and screened for the presence of hepatitis B and C using standard strip method. Data obtained were analyzed using Chi-square test and P < 0.05 was considered statistically significant. The study subjects comprised of males (49.5%) and females (50.5%) with 38% being within the ages of 27–37 years. Majority (67.5%) had attained tertiary level of education while the remaining 32.5% had secondary education. Ninety five percent of participants think voluntary blood donation is good with 100% affirming that it is important yet only 10% had actually donated blood; eight percent had received blood transfusion previously. A good number (87% and 65%) were willing to donate for a family member and in case of emergency. Eighty-four and half percent of respondents think that blood donation is beneficial, 78% think there is lack of awareness while 70% would advise others to donate blood voluntarily. Of the 200 participants, 66% believe blood donation to be a civic duty yet 82% and 85.5% respectively were of the opinion that blood donors should be paid or given gifts; indeed 83% agreed they would donate if paid. None of the respondents were against blood donation however 13% believed it poses a risk of collapse or death to the donor. The prevalence of Hepatitis B and C was observed to be 10% and 4% respectively among the study population. This study has shown that secondary school teachers have good knowledge of blood donation, agree that it is important but are not willing to donate without remuneration. Lack of voluntary non-remunerated donation leads to shortage of safe blood for transfusion and will promote commercial donation with associated risks. There is need for regular awareness campaigns and blood drive among the populace.

Key words: Knowledge, Attitude; Blood donation, Secondary school teachers

Disclosure of Interest: None Declared

BSH2021-PO-118
An audit of blood transfusions on an inpatient haematology unit in an English teaching hospital: what percentage of transfusions are given overnight and what factors contribute to this?
Amanda Adams

Abstract Content: Patients with a haematological condition commonly require transfusion of blood products during the course of their disease and treatment. Current hospital policy states that blood transfusions should be completed by 22:00, unless there is a clear clinical indication for the transfusion to be given overnight. This is in line with national recommendations, as transfusing at night has been widely identified in the literature as carrying a higher risk to patients than administering blood products during the day. Anecdotal evidence suggested that many of the transfusions administered in the inpatient haematology wards in the Trust were being given overnight. It was therefore decided to investigate this by carrying out a clinical audit of current practice to ascertain the percentage of transfusions occurring after 22:00, and explore where delays are occurring in the transfusion process which could explain why transfusions are being given overnight.

A descriptive, cross-sectional, retrospective study was carried out, analysing data from all red cell transfusions administered on the inpatient haematology wards of a large NHS Trust hospital during October 2019. Data was collected on the times of each stage of the transfusion process, and the intervals between stages were calculated. 201 red cell transfusions were analysed and 57.21% of these took place between 22:00 and 08:00. Delays were found at all stages of the transfusion process but the greatest delays were seen in the interval between blood becoming available in blood bank and the transfusion commencing, with a mean delay of 7 hours 21 minutes between these two points. Despite 80.71% of units of blood being available before 18:00, only 42.79% were collected between 08:00 and 18:00, and only 23.88% of transfusions were commenced within this time period.

Possible factors delaying the availability of blood components included late phlebotomy, late request for blood component, need to repeat the Group and Screen sample and identification of atypical antibodies. Suggested factors delaying the collection of blood components and commencement of transfusion included nursing staff numbers and workload, the practice of waiting for several units to be available before collecting from blood bank, and patient-related factors such as multiple intravenous therapies resulting in limited line time, patients becoming unwell, and patients leaving the ward for investigations.

A much higher percentage of transfusions occurring overnight were found in this study than in other similar studies. The greatest delays were in collecting the product from blood bank and in commencing the transfusion after storage in the satellite fridge, suggesting factors affecting these intervals should be the focus for further study and improvement interventions. Recommended interventions were commencing regular collections of blood components from blood bank, medical staff to clearly document whether transfusions are appropriate to be given overnight, and education of nursing staff on the risks of overnight transfusion. Further research into causes of delays in collecting blood components and commencing transfusion was also recommended.

Disclosure of Interest: None Declared
Abstract Content: Background and aims: Monitoring of ABO isoagglutinins titer is important in management of ABO incompatible transplant recipients. While automation has the advantage of objectivity, ease of use and reproducibility with well-defined end points of agglutination reaction, little is known about the utility of these methods for the purpose of antibody titration. Aim of the present study was to compare results obtained by manual conventional tube technique (CTT) with results obtained by semi-automated, column agglutination technique (CAT) and fully automated hemagglutination/solid phase red cell adherence (HA/SPRCA).

Materials and methods: This was a prospective, observational study conducted from October 2019 to March 2020. All consecutive A, B and O group donors who consented to participate were included in the study. All samples were consecutively tested by CTT, CAT and HA/SPRCA for anti-A and anti-B, IgG and IgM titer.

Results: A total of 300 (100 each from A, B and O blood groups) donors were included in the study. IgG titer were higher than IgM titer in most group O individuals. This difference was more evident with use of CAT. Anti-A IgG and IgM titer results were higher for group O individuals as compared to group B individuals. Similarly, anti-B IgG and IgM titer results were higher for group O individuals as compared to group A individuals. Correlation between CTT and CAT was found to be strong whereas correlation between CTT and HA/SPRCA was found to be variable for anti-A and anti-B, IgG and IgM titer. When measured by CTT and CAT, median anti-A and anti-B titer results for group O individuals were similar. Anti-A and anti-B median titer results obtained by CTT and CAT for group A and B individuals were also similar.

Conclusion: Semi-automated method (CAT) shows higher ability in detecting ABO isoagglutinins than manual method (CTT) and automated method (HA/SPRCA). However, higher sensitivity also leads to false positivity which increases cost of management of an ABO incompatible transplant recipient. The results from the present study make it evident that these methods cannot be used interchangeably. Despite longer testing times and cumbersome nature, the authors continue to perform titer evaluation by age old manual method (CTT).

Abstract Table:

<table>
<thead>
<tr>
<th>Method</th>
<th>Blood group</th>
<th>Antibody</th>
<th>IgM&gt; IgG (%)</th>
<th>IgM</th>
<th>IgM=IgG (%)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>A</td>
<td>Anti-B</td>
<td>46</td>
<td>10</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>Anti-A</td>
<td>36</td>
<td>15</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>O</td>
<td>Anti-B</td>
<td>14</td>
<td>68</td>
<td>18</td>
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<tr>
<td></td>
<td>Anti-A</td>
<td>15</td>
<td>68</td>
<td>17</td>
<td></td>
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<td>A</td>
<td>Anti-B</td>
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<td>5</td>
<td>54</td>
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<tr>
<td></td>
<td>B</td>
<td>Anti-A</td>
<td>38</td>
<td>5</td>
<td>57</td>
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<tr>
<td></td>
<td>O</td>
<td>Anti-B</td>
<td>2</td>
<td>91</td>
<td>7</td>
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<tr>
<td></td>
<td>Anti-A</td>
<td>7</td>
<td>84</td>
<td>9</td>
<td></td>
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<tr>
<td>HA/SPRCA</td>
<td>A</td>
<td>Anti-B</td>
<td>77</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>Anti-A</td>
<td>85</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>O</td>
<td>Anti-B</td>
<td>15</td>
<td>71</td>
<td>14</td>
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<tr>
<td></td>
<td>Anti-A</td>
<td>19</td>
<td>67</td>
<td>14</td>
<td></td>
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</tbody>
</table>

Disclosure of Interest: None Declared
Abstract Table:
Table 1: Haematological findings of COVID-19 negative pregnant women, COVID-19 negative pregnant women who went on to develop COVID-19 as well as COVID-19 positive non-pregnant women

<table>
<thead>
<tr>
<th>Pregnancy status</th>
<th>Pregnant throughout pregnancy (group A)</th>
<th>Pregnant at start of pregnancy (group B)</th>
<th>Became positive during pregnancy (group C)</th>
<th>P-value (A vs B vs C)</th>
<th>Post-hoc analysis</th>
<th>Not pregnant at time of infection Positive (group D)</th>
<th>P-value (C vs D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>124 (118–132)</td>
<td>123 (114–129)</td>
<td>111.1 (105–123)</td>
<td>0.0001*</td>
<td>1&gt;2</td>
<td>34.875(1.53)</td>
<td>0.1188</td>
</tr>
<tr>
<td>MCV</td>
<td>–</td>
<td>–</td>
<td>85 (81.4–87.3)</td>
<td>–</td>
<td>–</td>
<td>84.2 (77.2–87.5)</td>
<td>0.6342</td>
</tr>
<tr>
<td>WBCs</td>
<td>8.3 (7–9.9)</td>
<td>9.0 (7.5–10.5)</td>
<td>9.8 (8.4–12.6)</td>
<td>0.001*</td>
<td>1&gt;2</td>
<td>243.92 (203–376)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Neu</td>
<td>5.455 (4.58–6.84)</td>
<td>6.25 (5.19–7.56)</td>
<td>7.42 (5.7–10.1)</td>
<td>0.001*</td>
<td>1&gt;2</td>
<td>84.2 (77.2–87.5)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Lymph</td>
<td>1.92(1.54–2.35)</td>
<td>2.02 (1.77–2.3)</td>
<td>1.63 (1.25–2.03)</td>
<td>0.0349*</td>
<td>1&gt;2</td>
<td>5.8 (4.7–6.9)</td>
<td>0.1492</td>
</tr>
<tr>
<td>Mono</td>
<td>0.52 (0.44–0.65)</td>
<td>0.56 (0.47–0.68)</td>
<td>0.68 (0.5–0.8)</td>
<td>0.0001*</td>
<td>1&gt;2</td>
<td>3.53(2.82–5.01)</td>
<td>0.0003*</td>
</tr>
<tr>
<td>Eos</td>
<td>0.1 (0.05–0.15)</td>
<td>0.1 (0.06–0.22)</td>
<td>0.04 (0.01–0.09)</td>
<td>0.004*</td>
<td>1&gt;2</td>
<td>1.40 (0.93–1.77)</td>
<td>0.3660</td>
</tr>
<tr>
<td>Baso/Lymph</td>
<td>0.03 (0.02–0.04)</td>
<td>0.03 (0.02–0.04)</td>
<td>0.03 (0.02–0.03)</td>
<td>0.861</td>
<td>–</td>
<td>0.33(0.24–0.51)</td>
<td>0.0126*</td>
</tr>
<tr>
<td>INR</td>
<td>–</td>
<td>–</td>
<td>0.95 (0.90–0.98)</td>
<td>–</td>
<td>1&gt;2</td>
<td>1.11(1.06–1.20)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>PLT</td>
<td>252.5 (226–311)</td>
<td>285 (236–329)</td>
<td>252 (209–303)</td>
<td>.0314*</td>
<td>1&gt;2</td>
<td>122.00 (113–129)</td>
<td>0.7283</td>
</tr>
<tr>
<td>Urea/Alb</td>
<td>–</td>
<td>–</td>
<td>0.081 (0.06–0.106)</td>
<td>–</td>
<td>–</td>
<td>0.083 (0.073–0.1023)</td>
<td>0.7298</td>
</tr>
</tbody>
</table>

Non-normally distributed continuous variables are presented as medians (interquartile ranges, IQR). Continuous variables were analysed using a Kruskal-Wallis test with a post hoc Dunn’s multiple comparison test or a Mann-Whitney U test where appropriate. The use of - denotes no data available.

Disclosure of Interest: None Declared

BSH2021-PO-121
Impact of the SARS-CoV-2 (COVID-19) virus pandemic on Blood Transfusion laboratory activity, including pre-transfusion testing and blood component utilisation: A Single-centre Experience
Prabal Mittal1,*, Anna M.Y. Li1, Jenny Li1, Seble Tekle1, Stephanie Mellin1, Ann-Marie Ellis1, Anushka Natarajan1, Misbah Malvernkar1, Mallika Sekhar1, Samah Alimam1
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Abstract Content: The SARS-CoV-2 (COVID-19) viral pandemic has challenged the resourcefulness of hospital services, in the face of rapidly shifting clinical demands and workforce pressures. This applies equally to the Hospital Blood Transfusion service.

In this retrospective single centre study, we reviewed Transfusion laboratory activity during a six week period in the “first wave” of infections (23rd March - 4th May 2020), and used an equivalent date period in 2019 as a historical control. Our aims were to compare overall workload trends and look for specific patterns in the COVID-19 cohort.

We extracted Group and Screen (G&S) results, coupled with patients’ respective COVID-19 swab results and usage data for blood components, from the laboratory results system. Antibody panel reports were divided into: 1) specific antibody identified and 2) non-specific reaction. Exclusions included pan-reactive samples and those with incomplete antibody screens or panel reports.

As outlined in table 1, our data confirms blood component usage in 2020 was lower compared to 2019.

Within the 2020 cohort, COVID-19 patients with a G&S were more likely to proceed to red cell transfusion than non-COVID-19 patients (52.3% vs 13.5%; P < 0.01 by Fisher’s Exact Test, two tailed). Transfused COVID-19 patients tended to receive a greater number of red cell units (mean: 3.6 vs 2.8). The ratio of red cell units transfused to number of G&S samples was higher in the COVID-19 group (0.81 vs 0.3:1).

Of the 982 COVID-19 patients admitted in this period, 109 (11.1%) received blood component transfusion, with 92 (9.3%) receiving red cells. Main indications for red cell transfusion were symptomatic anaemia (47.6%), anaemia in setting of renal dialysis (30.4%) and gastrointestinal bleeding (9.7%). As reported elsewhere, we also saw lower usage of Platelets, plasma and cryoprecipitate in COVID-19 patients (0.5%, 0.2%, 0.1% respectively).

Comparing total pre-transfusion testing activity in the first wave to the control period, our analysis shows a 44% drop in G&S

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British Journal of Haematology, 2021, 193, (Suppl. 1), 77–232
The existing blood ordering schedule is out-of-date and 0.02). Specific panel antibodies were more 2

Excessive bloods are being taken on patients =

4

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out of 92 patients who had an extended antibody  

Introduction:  

129

173 orthopaedic procedures were done over this period. 109

Pre-operative bloods were being  

3

cost approximately 176) and non-COVID-19 patients (8.6%). There was a trend towards a

activity of the transfusion lab shifted during the pandemic. Whilst total blood component usage fell, G&S samples from COVID-19 patients generated proportionately more transfusion work and manual testing. The increase in pre-transfusion non-specific reactions are a signal that COVID-19 infection might be contributory. Further investigation is merited and could include a trial of modified laboratory methods to eliminate non-significant reactions.

Abstract Table:

Component Usage 2020 2019 % Reduction
Red cells 880 1015 13.3%
Platelets 35 72 50%
FFP 106 204 48%
Cryoprecipitate 12 50 76%
Albumin (20%) 684 971 29.6%
2020 Data: COVID Non-COVID Total
G&S processed Samples: 395 2011 2406
Patients: 176 1448 1624
Positive Antibody screen
Positive Patients: 17 (9.6%) 75 (5.2%) 92
Specific panel antibody detected: 13 (7.4%) 41 (2.8%) 54
Non-specific antibody detected in panel: 4 (2.3%) 23 (1.6%) 27
Red cells transfused Total units: 330 550 880
Patients : 92 (52.2%) 195 (13.4%) 287 (17.8%)

Indication for red cell transfusion in COVID-19 patients:
Symptomatic anaemia 43 (47.6%)
Anaemia and renal dialysis 28 (30.4%)
GI bleeding 9 (9.7%)
Haematuria 4 (4.3%)
Preop 3 (3.3%)
Bleeding (Grade 2 or less) 2 (2.2%)
Massive haemorrhage 2 (2.2%)
Thalassaemia 1 (1.1%)

BSH2021-PO-122
Rationalising pre-operative trauma bloods can lead to significant cost savings
David Keohane1,*, Shafagh Khodadadi2, Meghan O'Brien3, John F. Quinlan1, Victoria McMullan4
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Abstract Content: Introduction: Pre-operative bloods were being done on nearly all trauma patients who were admitted to our institute for surgery. Routine bloods included a full blood count (FBC), renal profile, coagulation screen and a group and hold, or group and cross match. These bloods were done regardless of factors such as injury sustained, patient age or co-morbidities. There are significant costs associated with taking and processing these bloods – particularly a group and hold or cross match. The aim of our research was to examine how much money could be saved by rationalising the pre-operative blood schedule.

Methods: All of the orthopaedic theatre books in our institute were reviewed for a five-week period in late 2020. All of the pre-operative bloods for each of these patients were identified using the online blood system. The laboratory provided information on which patients required post-operative transfusions. Costs were associated with each blood test based on an estimate of the time and materials it took to take the blood sample and process it.

Results: 173 orthopaedic procedures were done over this period. 109 (63%) procedures had a group and screen or crossmatch pre-operatively. 15 (8.6%) procedures required post-operative blood transfusions. A full set of bloods (FBC, renal profile, coagulation screen and group and cross-match) cost approximately €51.23 to take and process.

Discussion: The existing blood ordering schedule is out-of-date and does not take into account the patient or the injury they have sustained. We proposed a new pre-operative blood schedule for trauma patients whereby only hip fractures, pelvic fractures and polytrauma patients get routine pre-operative FBC, renal profile, coagulation and a group and hold or crossmatch. All patients over 45 years old get routine FBC, renal profile and coagulation. No other bloods are done as routine unless clinically indicated e.g. if the admission haemoglobin is low on a patient over 45 years old, then they get a group and screen or crossmatch. When these rules were retrospectively applied to our 173 cases, we identified an excess of 69 group and screens or crossmatches, and an excessive amount of FBCs, renal profiles and coagulation screens. This equated to a cost of €2,496 over five weeks. If this figure is extrapolated up to one year, it could lead to potential annual savings of €25,960.

Conclusion: Excessive bloods are being taken on patients – particularly group and screens or crossmatches. The pre-operative blood schedule should include reference to patient age and injury. A pragmatic pre-operative blood schedule could potentially lead to significant actual cost savings. This approach should be applied to all surgical disciplines.

Disclosure of Interest: None Declared

Disclosure of Interest: None Declared
Knowledge, attitudes and practices surrounding voluntary non-remunerated blood donation among medical and non-medical students at The University of the West Indies in Trinidad and Tobago

Kenneth S. Charles1 and Tamia Thompson1, Michael Timson3, Malika Tripathi1, Bernice Turner1, Sanjana Vedula1, Akilah Wade1, Sydney Williams1, Marvellous Wuddina1, Marsh Yook See2, Kenneth S Charles2

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Abstract Content: Knowledge, attitudes and practices surrounding voluntary non-remunerated blood donation among medical and non-medical students at The University of the West Indies in Trinidad and Tobago.

The World Health Organisation (WHO) recommends collection from exclusively voluntary non-remunerated blood donors for safety, adequacy and equity. More than 80% of blood donors in Trinidad and Tobago are family replacement donors. Young persons (age 18 – 25) constitute only 7% blood donors. The University of the West Indies is the main tertiary education institution in Trinidad and Tobago. The main campus is located in St. Augustine and the Faculty of Medical Sciences at the nearby Eric Williams Medical Sciences Complex. A UW1 initiative based on research, education and donor-friendly settings resulted in the establishment of a successful VNRD programme at the Eric Williams Medical Sciences in 2015. In 2018, the Ministry of Health announced its intention to use this programme as a model for transitioning to exclusive VNRD collection nationally. This study was done to compare blood donation knowledge, attitudes and practice among medical students with those in non-medical students on the main campus to make recommendations for increasing voluntary non-remunerated blood donation in this valuable potential donor group. Ethical approval was granted by The University of the West Indies’ Campus Research Ethics Committee, St. Augustine. A validated questionnaire consisting of 26 close-ended questions (with 6 Likert scale questions) was distributed online via Google Forms to non-medical students on the UW1 St. Augustine campus and medical students at the Eric Williams Medical Sciences Complex. Students were classified by faculty of study and sociodemographic variables. Index scores were calculated for knowledge, attitude and practice. SPSS version 21 was used for statistical analysis, chi square for strength of associations and logistic regression for inferential statistics. A P value of < 0.001 was taken as statistically significant. Out of 544 eligible responses, 273 were from medical and 271 from non-medical students. Medical students had significantly higher mean scores and percentage good scores in all domains (75.5 vs 35.1, 68.1 vs 41.7 and 59.8 vs 41.9, P < 0.001 for all). However, only 22.8% of medical students and 20.5% of non-medical students (P = 0.371) had previously donated blood. The main deterrents to blood donation were fear of needles, losing blood or contracting disease (29.7%), feeling unfit to donate (29.5%), lack of time (18.7%) and seeing no reason to donate (14.2%). As many as 96.7% preferred social media as the method for receiving blood donor information. Dissemination of blood donor information including eligibility criteria, national need and details of the UW1 VNRD programme by social media is needed to increase voluntary non-remunerated blood donation among medical and non-medical students of the UW1.

Disclosure of Interest: None Declared

BSH2021-PO-124
Single centre review of granulocyte use
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Abstract Content: Granulocyte infusions (GI) have been used for prophylaxis against or in the treatment of life-threatening infections in immunocompromised patients for over 50 years. However, the lack of consensus in the evidence to support their efficacy has resulted in variability in their use. NHS Blood and Transfusion (NHSBT) provide hospitals across England with pooled granulocytes and in rare instances leucocytes.

We performed a retrospective case note review audit of the use of granulocytes at University College London Hospitals (UCLH) between April 2019 and October 2020. Our aim was to evaluate adherence to the NHSBT guideline INF276/4, establish recipient patient characteristics and outcomes, and identify reasons for wastage.

There were 23 treatment episodes for 19 patients; 10 females and 9 males, median age was 42 years (range of 17-69 years). Four patients had two separate clinical episodes requiring G1. 303 granulocyte units (157 doses) and 20 leucocyte units (2 doses) were ordered in total. The majority (9/19 (47%)) of patients had acute myeloid leukaemia. GI requests were predominantly for the treatment of active severe life-threatening soft tissue, gastrointestinal and respiratory infections (see table for further details).

Across UCLH, there was good adherence (20/23 (87%)) to the NHSBT indications for use of GI. Complications were documented in 25/283 (9%) infusions. The most commonly reported adverse event was pyrexia in 21/283 (7%) infusions. Three patients discontinued treatment due to adverse events (2/3 because of pyrexia and 1/3 due to formation of allo-antibody). At 28 days post initiation of GI 16/23 (70%) patients were alive.

There were 16 units wasted. Reasons for wastage included failure to inform the lab of discontinuation of treatment (10/16 (63%)), expiry of GI due to poor venous access (2/16 (13%)), unfilled blood status form (1/16 (6%)) and the late arrival of GI on the ward (1/16 (6%)). 2/16 (13%) units were wasted due to an acute clinical change resulting in contraindication for use. Two leucocyte doses (20 units) were wasted due to ineffectiveness in administering the product. Interestingly, we found 11 granulocyte units continued to be given in patients with neutrophil recovery (neutrophils >0.5x10^9). The total cost of wasted units was £21,303.72.

In conclusion, there was good local adherence to the NHSBT guideline INF276/4 on the use of GI at UCLH. We identified a significant proportion of potentially avoidable wastage and have recommended the following measures:
1. Regular education of the haematology clinical team on the use of GI and the NHSBT guidance.
2. Clinical team to work closely with the transfusion lab and inform the lab of treatment discontinuation decisions in a timely manner.
3. A transfusion practitioner to act as a granulocyte champion who will be responsible for weekly reviews of the standing orders for GI and review wasted units.
4. A re-audit to be performed in 6 months.
Abstract Table: Disease and Infection Profile of GI Recipients

<table>
<thead>
<tr>
<th>Underlying Disease/Treatment Modality</th>
<th>No of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Myeloid Leukaemia</td>
<td>9</td>
</tr>
<tr>
<td>Allogeneic Stem Cell Transplant</td>
<td>4</td>
</tr>
<tr>
<td>Myelodysplastic Syndrome</td>
<td>2</td>
</tr>
<tr>
<td>Chimeric Antigen Receptor T-Cell Therapy</td>
<td>2</td>
</tr>
<tr>
<td>Burkitt’s Lymphoma</td>
<td>1</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukaemia with Richter’s Transformation</td>
<td>1</td>
</tr>
<tr>
<td>Infections by Organ System</td>
<td>No of Infections</td>
</tr>
<tr>
<td>Skin</td>
<td>10</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>8</td>
</tr>
<tr>
<td>Respiratory</td>
<td>8</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>4</td>
</tr>
<tr>
<td>Pericoronitis</td>
<td>1</td>
</tr>
<tr>
<td>Infective Organism Identified</td>
<td>No of organisms</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>6</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>5</td>
</tr>
<tr>
<td>Other gram negative organisms</td>
<td>3</td>
</tr>
<tr>
<td>(Escherichia coli, Serratia marcescens &amp; Enterobacter cloacae)</td>
<td></td>
</tr>
<tr>
<td>Other gram positive organisms</td>
<td>3</td>
</tr>
<tr>
<td>(Staphylococcus epidermidis, Staphylococcus haemolyticus &amp; Enterococcus faecalis)</td>
<td></td>
</tr>
<tr>
<td>Fungal (Rhizopus microsporus)</td>
<td>1</td>
</tr>
<tr>
<td>No organism identified at the point of initiation of granulocyte infu-</td>
<td></td>
</tr>
<tr>
<td>Disclosure of Interest: None Declared</td>
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</table>

BSH2021-PO-126
RhD cell-free fetal DNA screening results in reduction of anti-D use at Guy’s and St Thomas’ Hospital
Charelene Furtado1, Emma Abbott2, Angela Ugen2, Ursula Wood3, Rosie O’Dea4, Dharsnana Jeyapalan5, Susan Robinson6, Gavin Ling1
1Haematology, Guy’s and St Thomas’ Hospital NHS Foundation Trust, 2Antenatal, Guy’s and St Thomas’ Hospital NHS Foundation Trust, London, United Kingdom

Abstract Content: Cell-free fetal DNA (cffDNA) screening is a non-invasive antenatal test which has use in a wide variety of diagnostic applications such as Down’s syndrome or fetal sexing to ascertain risks of certain genetic diseases. Guy’s and St Thomas’ NHS Foundation Trust (GSTT) antenatal and transfusion service introduced cffDNA testing to the anti-D pathway for all D negative pregnant women to determine the RhD genotype of the fetus. The testing was rolled out in January 2020 and is in line with British Society for Haematology (BSH) guidance and the National Institute for Health and Care Excellence (NICE) recommendations.

At GSTT, 3957 women were booked for maternity care between March and August 2020. Of these, 344 women were identified as D negative and requiring routine antenatal anti-D prophylaxis. Mean number of booking visits were 57 D negative women a month (from March-August 2020). Tests were performed by NHS Blood and Transplant (NHSBt) with an expected false predicted D negative rate at 0.08%.

Of these 344 women, 55 women (16%) were not tested due to a variety of reasons such as transfer of care, miscarriages, poor sample labelling and non-attendance. 3 women declined the test. The remainder of women screened (286) showed 92 predicted to be carrying a D negative fetus and therefore did not receive antenatal anti-D prophylaxis.

GSTT being in the centre of London, sees a varied ethnicity of women booking and the incidence of D negative women was 9% of all expectant mothers between March and August 2020. Of these, 32% had D negative predicted fetuses. This is in line with national data where approximately 15% of the Caucasian population are D negative and 38-40% of these women will carry RhD negative babies. Approximately 15 D negative women a month were predicted to carry a D negative fetus resulting in a 30% reduction in attendance at the hospital’s anti-D clinics. Cord blood samples were taken immediately after delivery in all women who consented to testing revealing no false predicted D negative born babies in this cohort.

As this service is relatively new to the Trust, at present there are no significant cost changes. However, the screening test (currently £22.50) and the anti-D clinic appointments (each appointment is approximately £9.06 for 20 minutes of a band 6’s time) could in future be reduced and lead to potential cost savings. The screening programme does demonstrate an increase in the safety of these women as 92 women who had a predicted D negative fetus(es) did not need to unnecessarily attend an additional Anti-D appointment and receive a minimum of at least one prophylactic Anti-D for the duration of their pregnancy.

Implementation of this updated pathway has successfully resulted in the reduction of unnecessary anti-D use, as well as streamlining care for D negative women with D negative predicted fetuses.

Disclosure of Interest: None Declared

BSH2021-PO-127
A survey of resident surgeons’ knowledge concerning transfusion medicine in Khartoum, Sudan
Ahmed Sayedahmed1, Ali Altaib2, Salma Jamal3
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Abstract Content: Abstract: Blood transfusion is considered as an effective and life-saving management in many circumstances. Knowledge about transfusion medicine may have a positive impact on the transfusion process and eventually on patient care. The aim of this study was to assess the knowledge of resident surgeons regarding transfusion medicine and determine whether additional training is needed.

This is a cross-sectional hospital-based study; it was conducted on resident surgeons at Omdurman Teaching Hospital, Bahry Teaching Hospital and Umbada Teaching Hospital, Sudan in 2020. We have used a pre-tested self-administered questionnaire, and it was contain questions about demographic characteristics and knowledge about transfusion medicine, education, training and experience regarding blood transfusion.

A number of 128 resident surgeons were responded to our study. The mean total knowledge score toward transfusion medicine was 14.3 ± 3.1 (11-17) out of 25. About 45.1% of the participants have identified the correct required criteria for blood transfusion, and 57.2% of them knew the indications of the use of Fresh Frozen Plasma (FFP). The mean score of knowledge was higher among resident surgeons who indicated that they had received special training regarding blood transfusion (P = 0.02). About 89% of the participants stated that they had received insufficient training and 96.2%
believed that they require additional training about the blood transfusion.

We have found that there are uncertainties among resident surgeons regarding blood transfusion. Therefore, we suggest to organize a special transfusion medicine courses and training programs to the surgical residents.

**Keywords:** Blood transfusion, training, knowledge, medical education, surgeons, transfusion medicine

**Disclosure of Interest:** None Declared

**BSH2021-PO-128**

**An audit of allocation of Paedipacks to polytransfused neonates in a tertiary neonatal unit**

Frederick Soole1,*,1, Pascal Winter*, Angela Maddison2, Julia Lancut*, Catherine Booth1

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**Abstract Content:** Most neonatal transfusions are carried out in low birth weight preterm infants treated on neonatal intensive care units. They are usually repeated small-volume ‘top-up’ red cell transfusions. Up to 60% of preterm babies weighing less than 1500 g at birth are transfused at least once.

Although neonatal components have additional safeguards above those of adult units, to further reduce the risk of transfusion-transmitted infection it is recommended to minimise donor exposure by allocating single donor units split into ‘paedipacks’. One donation is divided into 6 small packs that can be used for sequential transfusions. Our centre has a large tertiary neonatal unit and local policy is to reserve 4 paedipacks for the extremely premature neonates most likely to require multiple transfusions.

We carried out an audit to evaluate how many transfusions were received by polytransfused neonates, and to how many donors they were exposed. The aim was to assess and strengthen clinical and laboratory processes with regards to paedipack allocation.

We identified 48 neonates who received more than one transfusion over a 6-month period. The mean number of transfusions was 5.45 and mean number of donor exposures was 3.85. The mode number of transfusions was 2. By comparison, over the same time frame there were 26 babies who received one transfusion only.

12 of the polytransfused babies (25%) were exposed to one donor only. One of these received 4 transfusions; the remaining 11 received only 2 transfusions. 7 received all of their transfusions on the same day (suggesting a large volume transfusion or surgical procedure).

12 other neonates received 4 transfusions or fewer but were exposed to 2 donors or more. Of these, 8 could potentially have been exposed to one donor only. The remaining 4 were transfused over a period exceeding the normal shelf life of packed red cells so would have been exposed to more than one donor anyway.

Half of our population (24 neonates) received 5 transfusions or more. This flags up the fact that there should be a system in place to recognise these babies and allocate them another set of paedipacks from a single donor once the first allocation of 4 units is used.

Our data show that neonates requiring several blood transfusions on the neonatal intensive care unit at our hospital have been unnecessarily exposed to multiple blood donors. This indicates that the pathway for allocating 4 paedipacks to the most vulnerable neonates is not being followed. Most babies who are transfused in the neonatal period will receive more than one unit, and should be considered for single donor paedipack allocation. On the other hand, because the mode number of transfusions was 2, robust pathways must be implemented to de-reserve paedipacks which are not required and issue them to other patients. We have developed a new process focused on strengthening communication between the laboratory and the clinical teams, which we hope will improve transfusion care for this patient group and minimise wastage of this precious component.

**Disclosure of Interest:** None Declared

**BSH2021-PO-129**

**Can haematological markers of COVID-19 positive patients at presentation to hospital predict subsequent Intensive Treatment Unit (ITU) admission and mortality?**

Usama (Sami) Hussain1, Elen Roblin*,3, Pranay Balijepalli1, Ali Rismani1

1University College London, London, London, United Kingdom

**Abstract Content:** Background and Aims: On 11th of March 2020, the World Health Organisation declared a pandemic caused by the SARS-CoV-2, a novel coronavirus, first identified in China. Also known as COVID-19, this virus has been responsible for sharply increased admissions to ITU and mortality. Often the virus presents with a very similar disease prodrome, primarily consisting of a dry cough, pyrexia and anosmia, making it hard to identify patients early that are at greatest risk of subsequent deterioration.

This exposes a crucial need for predictive tools of disease severity as it enables strategic management of health resources; an area of significant interest for the modern NHS. Doctors have numerous tools to monitor patients, one of which is tracking blood indices. Our aim is to find, if any, haematological, inflammatory or clotting parameters that can predict adverse health outcomes in COVID-19 patients. Current literature notes an association between: Decreased haemoglobin (Hb) and lymphocytes; elevated neutrophil/lymphocyte ratio (NLR); raised C-reactive protein (CRP), fibrinogen and ferritin with increased disease severity [1, 2, 3].

**Methods:** This is a retrospective single-centre observational study of 368 patients who presented to a central London district general hospital and tested positive between 10th March 2020 and 20th April 2020. We excluded all under 18-year-olds. To take a proxy of disease severity, we stratified the patients into four groups: discharged from Emergency Department (ED), admitted for ward-level care, admitted to ITU (at any point during said admission) or deceased. The blood test data used was from viral swab date, or as close to as possible. CRP, ferritin, activated partial thromboplastin time (APTT) and derived fibrinogen. The data was then analysed using Microsoft Excel and GraphPad Prism 8.

**Results:** Of the 368 patients, 48 were discharged from ED, 194 were admitted for ward-care, 36 were admitted to ITU and 90 deceased. Patients deceased or admitted to ITU were more likely to have abnormal neutrophils (P < 0.001), lymphocytes (P < 0.001), APTT (P < 0.001), WCC (P < 0.01), fibrinogen (P < 0.01), Hb (P < 0.05), CRP (P < 0.05) and ferritin (P < 0.05) at presentation. This finding was in keeping with the literature noted above [1,2,3,4,5]. On logistic regression analysis, abnormal APTT was the strongest predictor associated with ITU admission and mortality (P < 0.01).

**Conclusions:** Although blood test data is just one of many patient parameters to consider in COVID-19, our team found abnormal APTT as a novel predictor of COVID-19 disease severity. We believe the usefulness of APTT as a predictive marker is amplified in patients with other minimal risk factors. Hence, we recommend APTT be considered a part of the medical toolkit when caring for COVID-19 positive patients.

Abstract Table:

Table 1. Mean scores for variables

<table>
<thead>
<tr>
<th></th>
<th>Deceased (n = 90†)</th>
<th>ITU (n = 36†)</th>
<th>Ward (n = 194†)</th>
<th>Discharged (n = 48†)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>118.4 ± 24.1</td>
<td>129.4 ± 21.1</td>
<td>123.9 ± 20.9</td>
<td>130.2 ± 19.0</td>
</tr>
<tr>
<td>WCC</td>
<td>11.83 ± 32.9</td>
<td>9.714 ± 4.62</td>
<td>7.870 ± 6.66</td>
<td>6.550 ± 2.08</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>4.404 ± 32.8</td>
<td>0.8528 ± 0.40</td>
<td>1.560 ± 5.39</td>
<td>1.267 ± 0.55</td>
</tr>
<tr>
<td>Neut/Lymph*</td>
<td>10.11 ± 12.1</td>
<td>12.44 ± 8.77</td>
<td>6.778 ± 7.71</td>
<td>4.786 ± 3.33</td>
</tr>
<tr>
<td>Platelets</td>
<td>225.0 ± 115 (n = 89)</td>
<td>227.7 ± 81.8</td>
<td>216.4 ± 84.0 (n = 192)</td>
<td>222.8 ± 86.1 (n = 47)</td>
</tr>
<tr>
<td>Platelet/Lymph*</td>
<td>316.5 ± 312 (n = 89)</td>
<td>323.1 ± 200</td>
<td>249.9 ± 220 (n = 192)</td>
<td>198.3 ± 106 (n = 47)</td>
</tr>
<tr>
<td>CRP*</td>
<td>136.3 ± 103 (n = 89)</td>
<td>204.2 ± 121 (n = 35)</td>
<td>96.22 ± 88.3 (n = 191)</td>
<td>61.38 ± 56.5 (n = 45)</td>
</tr>
<tr>
<td>Ferritin</td>
<td>1362 ± 229 (n = 18)</td>
<td>1732 ± 122 (n = 30)</td>
<td>1001 ± 140 (n = 62)</td>
<td>1214 ± 134 (n = 12)</td>
</tr>
<tr>
<td>APTT</td>
<td>39.37 ± 16.9 (n = 58)</td>
<td>21.59 ± 18.1</td>
<td>11.97 ± 17.2 (n = 154)</td>
<td>7.371 ± 12.9 (n = 34)</td>
</tr>
<tr>
<td>DF</td>
<td>512.0 ± 121 (n = 35)</td>
<td>598.0 ± 142 (n = 23)</td>
<td>501.6 ± 163 (n = 122)</td>
<td>503.4 ± 162 (n = 27)</td>
</tr>
</tbody>
</table>

APTT, Activated partial thromboplastin time; CRP, C-reactive protein; DF, Derived fibrinogen; Hb, Haemoglobin; ITU, Intensive treatment unit; WCC, White cell count.
†Where differences in number of patients occurred, this is shown in brackets; * data was log-transformed for statistical analysis.


Disclosure of Interest: None Declared

BSH2021-PO-130

Diagnosis and management of a patient with probable alloantibody towards the universal Kell antigen (Ku)
Susudu Jayanetti1,†, Bandulatha Samarajeewa² and National Blood Center, National Blood Transfusion Service, Sri Lanka

1National Blood Transfusion Service, National Blood Centre, Colombo, Sri Lanka

Abstract Content: The presence of rare clinically significant alloantibodies complicates the management of transfusion recipients. Some rare alloantibodies can be formed against the Kell blood group system and these antibodies can cause haemolytic transfusion reactions (HTR) as well as haemolytic disease of fetus and newborn (HDFN).

A 41 year old unmarried female of South Indian origin with fibroid uterus, who was on warfarin therapy presented with heavy menstrual bleeding. She had a severe episode of menorrhagia 8 months ago, which required several red cell transfusions. She possess a well-functioning mitral valve prosthesis following mitral valve replacement performed at 17 years of age, but had residual trivial aortic regurgitation. While on warfarin, she had an ischemic stroke at the age of 37 years attributed to poor INR regulation. There’s no family history of any hematological or neuromuscular disorders. She was pale, but haemodynamically stable. No significant muscle atrophy noted. She had an intentional tremor, but no choreiform movements. Her haemoglobin was 6.4 g/dl and the red cell indices, blood picture and low serum ferritin of 6.01 ng/ml were suggestive of iron deficiency anaemia. Furthermore some acanthocytes were seen in blood film.

Her blood sample was assessed at Immuno-Haematology Reference Laboratory as the antibody screening was positive during red blood cell (RBC) compatibility testing. Her blood group’s O Rh D Positive and the direct antiglobulin test was negative. The antibody identification revealed a panreactive antibody in the low ionic strength saline medium at indirect antiglobulin phase (IAT). The extended phenotype was Rh(Rh), Jk(a+b+), Fy(a+b+), MMSs, Le(a+b+), P1 neg and both Kell and Cellano negative. The serum when tested with Kell positive, Cellano negative selected cell was reactive. All the crossmatches with E, c, Kell, K+ negative donor cells were positive 37°C IAT. Considered a rare antibody to Kell antigen system as both Kell and Cellano phenotypes were negative and Anti Ku (K5) was a possibility. Antibody screening cells were treated with 0.2 M DTT (dithiothreitol) to gain Kell null (K0) RBCs and the serum did not react with DTT treated red cells. The patient’s antibody screening was negative eight months ago prior to red cell transfusions, hence an alloantibody’s produced, probably Anti Ku antibody. McLeod phenotype was excluded and molecular typing’s essential in excluding Anti Ku like antibody in K(neg) phenotype.

Anti Ku can cause both HTR and HDFN and only compatible blood type is K0 phenotype. As K0 Phenotype is extremely rare, performed family tracing to find a compatible blood donor, but was unsuccessful. Autologous transfusion’s an alternative, however this patient was not a suitable candidate due to her medical status. Considering patient’s age and fertility wishes, myomectomy was the preferred surgical option, but the risk of bleeding’s higher than hysterectomy. Since the provision of compatible blood was complicated, an urgent surgery was not decided. She was provided multi-disciplinary care and managed with drug and hormonal treatment while managing anaemia with intravenous iron, erythropoietin and haematinsics.

This case provides valuable information on significance of antibody screening and identification in compatibility testing with relevant immuno-haematological investigations and the importance of Patient Blood Management in individuals with rare blood group phenotypes possessing rare alloantibodies.

Disclosure of Interest: None Declared

BSH2021-PO-131

Avoidable ‘Out-of-Hours’ Red Cell Transfusions: A Retrospective Audit at a District General Hospital
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Abstract Content: Blood transfusions are complex multistep procedures with potential for error at every stage. Out of hours, the risk of harm to patients is increased due to reduced levels of laboratory,
Aim: To examine whether the Mean platelet volume (MPV) can be used as an indicator of active inflammatory bowel disease (IBD).

Abstract Content: Aim: To examine whether the Mean platelet volume (MPV) can be used as an indicator of active inflammatory bowel disease (IBD).

Methods and Materials: A descriptive cross-sectional study was conducted on hundred patients with inflammatory bowel disease (61 Ulcerative colitis, 29 Crohn’s disease) of both genders (female:male: 67:33). Disease activity was assessed with clinical activity indices. Samples were taken for Full blood count (FBC), Erythrocyte Sedimentation rate (ESR) and C-reactive protein (CRP) from all participants. The correlation between the mean platelet volume and clinical disease activity index scores were examined. The cutoff point of Mean platelet volume to differentiate active disease was obtained from ROC curve analyses.

Results: MPV was negatively correlated with disease activity index scores of Ulcerative colitis and Crohn’s disease; simple clinical colitis activity index (SCCAI) and Crohn’s disease activity index (CDAI), respectively (MPV vs SCCAI; r = (-0.590), P < 0.001 and MPV vs CDAI; r = (-0.674), P < 0.001). MPV predicted IBD activity best as compared to ESR, CRP, WBC, platelet count and absolute neutrophil count. In this study MPV was inversely correlated with all tested covariates in the total IBD group and two subgroups (UC and CD) except the platelet count in CD group.

Conclusion: Mean platelet volume is a low-cost sensitive, indicator to assess IBD activity.

Abstract Table: Table 5. Receiver operating characteristic (ROC) curve analysis of MPV and other inflammatory markers in the diagnosis of active and inactive IBD.

<table>
<thead>
<tr>
<th>Marker</th>
<th>Cut off value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>AUC</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPV (fl)</td>
<td>7.05</td>
<td>80.4</td>
<td>88.9</td>
<td>0.885</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>7.15</td>
<td>82.6</td>
<td>85.2</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.25</td>
<td>84.8</td>
<td>83.3</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>23.0</td>
<td>84.8</td>
<td>72.2</td>
<td>0.866</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>24.5</td>
<td>80.4</td>
<td>75.9</td>
<td>78</td>
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<td></td>
<td>25.5</td>
<td>80.4</td>
<td>77.8</td>
<td>79</td>
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<tr>
<td>ESR (mm/hr)</td>
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<td>87.0</td>
<td>74.3</td>
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<tr>
<td></td>
<td>34.5</td>
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<td>37.5</td>
<td>82.6</td>
<td>77.8</td>
<td>80</td>
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<tr>
<td>WBC x10³/cummm</td>
<td>8850</td>
<td>82.6</td>
<td>64.8</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8950</td>
<td>80.4</td>
<td>66.7</td>
<td>73</td>
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<td>9050</td>
<td>80.4</td>
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<tr>
<td>ANC</td>
<td>5865</td>
<td>82.6</td>
<td>75.9</td>
<td>0.820</td>
<td>79</td>
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<td></td>
<td>5897.5</td>
<td>80.4</td>
<td>75.9</td>
<td>78</td>
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<td></td>
<td>5950.5</td>
<td>80.4</td>
<td>77.8</td>
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<tr>
<td>PLT x10³/</td>
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<td>82.6</td>
<td>46.3</td>
<td>0.835</td>
<td>63</td>
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<td>cumm</td>
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<td>48.1</td>
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<td></td>
<td>263.0</td>
<td>80.4</td>
<td>50.0</td>
<td>64</td>
<td></td>
</tr>
</tbody>
</table>

AUC – area under the curve

Disclosure of Interest: None Declared

BSH2021-PO-133
Daire Quinn1*, Jennifer Laird2
1West of Scotland Transfusion Centre, 2West of Scotland Transfusion Centre, Gartnavel General Hospital, Glasgow, United Kingdom

Abstract Content: Infection remains a significant cause of morbidity and mortality in patients with absolute or functional neutropenia. A large proportion of these patients have neutropenia secondary to chemotherapy/myeloablative conditioning, while others will have neutropenia in the context of the underlying disease process.

Despite the relatively long history of the use of granulocyte transfusion in neutropenic patients there remains a paucity of compelling data in the form of randomised controlled trials with the majority of policies based upon anecdotal evidence and non-randomised trials.
The current SNBTS guidance on the use of granulocyte transfusion states that granulocyte therapy may be suitable for patients who meet the following criteria:

- Receiving active treatment in an attempt to achieve disease remission
- Proven or highly probable fungal or bacterial infection that is unresponsive to appropriate antimicrobial therapy with evidence of progressive tissue or organ involvement
- Neutrophil count recovery is expected in the near future and/or definitive therapy with curative intent is planned

13 requests for concessory release of granulocytes were approved during the year 2020. Of these, one was for research purposes, three episodes were for one patient and two for another patient. In total nine patients had concessory release of granulocytes approved.

One of the nine patients was not transfused granulocytes due to count recovery with associated clinical improvement.

All patients had positive blood cultures or sputum samples. Two patients had no clear source of infection identified on imaging, of these one patient had an obvious SSTI of the perianal area. Two patients had probable infective changes on chest imaging, two patients had definite lung abscesses on CT, one patient had a bowel perforation proven on CT.

Only a small number of patients are given granulocyte transfusions through SNBTS each year.

The patients requiring granulocyte transfusion are generally systemically very unwell having had multiple lines of antimicrobials and prolonged periods of profound neutropenia which predisposes to significant bacterial and fungal infection.

Eventually seven of the eight patients who were treated with granulocyte transfusions unfortunately died having succumbed to multi-organ dysfunction secondary to sepsis in the context of either progressive disease or failure to regenerate counts.

One patient treated with granulocyte transfusion had resolution of a severe SSTI. The clinical records indicate that improvement was temporally related to initiation of granulocyte transfusion.

Overall, adherence to SNBTS guidance on indications for use of granulocyte transfusion was good (at over 85%).

There was anecdotal evidence of clinical improvement in one patient following granulocyte transfusion, however, overall outcomes for patients requiring treatment was dismal with all patients dying within weeks of commencing this therapy.

However, this is likely to be multi-factorial and may reflect the fact that the patients receiving this treatment are heavily pre-treated and that treatment is instituted late in the course of their infective episode.

Further studies are required to provide evidence for the role of granulocyte transfusion in the management of these patients and it is hoped that the report from the PorGrES International observational survey of granulocyte transfusion will provide additional insight into specific therapeutic effects of this treatment.

Disclosure of Interest: D. Quinn: None Declared, J. Laird Conflict with: None declared

BSH2021-PO-134
Investigation of ABO-incompatible RBC transfusions in a tertiary care hospital in Tunis
Sonia Mahjoub1*, Rahma Cherni1, Aya chakroun1, Hela Baccouche1, Neila Ben romdhane1
1Hôpital La rabta, Tunis, Tunisia

Abstract Content: Background and objectives: Hemovigilance was implemented in Tunisia in 2007, and covers all procedures for the surveillance, evaluation and prevention of transfusion incidents. ABO-incompatible red blood cell (RBC) transfusions are a serious risk in transfusion medicine. Identification of factors leading to this hazard is important to improve transfusion safety. The aim of this retrospective study was to assess the incidence and main causes of all ABO-incompatible RBC transfusions, detected by a Tunisian hemovigilance center.

Material and methods: All consecutive ABO-incompatible transfusions occurring from January 2009 to December 2019 at the Rabta Hospital in Tunis, Tunisia were analyzed.

Results: A total of 137,842 RBC units were transfused, and fourteen patients erroneously received 14 ABO-incompatible RBC concentrates. The mean age of patient was 49.5 year (15-84 year). The majority of these accidents occur during on-call hours. The most frequent error was the incorrect bedside testing (n = 6). Five cases of discrepancies were discovered, most of them were due to phlebotomy errors. There were no fatal mistransfusions. Three patients had no or only mild reactions.

Conclusion: Misidentification at the bedside and incorrect bedside testing persists as the main cause of ABO-incompatible transfusion. These findings emphasize the need of further training to limit these accidents.

Disclosure of Interest: None Declared

BSH2021-PO-135
Sachintha Abeyrathna*

Abstract Content: Among all the components transfused, the most administered blood product to sick neonates is packed red blood cells (PRBCs). Better understanding on the patterns of neonatal transfusions and the clinical outcome of transfusions among the neonatal population is important in improving neonatal care by minimizing the unnecessary transfusions and thereby reducing the adverse effects of transfusion. Our aim was to determine the appropriate use of packed red cells, as per the BCSH (British committee for Standards in hematology) guidelines and to determine the clinical outcome of transfusions in neonatal setting. A total of 3206 neonates were admitted during the study period and 276 neonates were enrolled for the study. Out of 276 neonates, one hundred fifty-one (54.8%) were males and most (n = 207, 74.9%) were delivered preterm. The mean (SD) APGAR at 1st minute was 6.91±1.6, while it was 8.63±2.4 at the 5th minute among 208 neonates.

Out of all neonates who received at least one blood or blood component transfusion (n = 276) majority (n = 193, 60.9%) was not transfused with PRBCs. Out of 83 neonates who received RCC (red cell concentrate) 20.3% (n = 56) received 1-2 transfusions and 9.8% (n = 27) received >2 transfusions. One hundred eighty-six RCC transfusions were given to 83 neonates and indications for red cell transfusion was assessed according to BCSH guidelines and majority (n = 128, 68.8%) of red cell transfusions were in accordance with BCSH guidelines. Majority of out of guideline transfusions were given to extreme premature neonates (n = 26, 44.8%) The transfusions volume of 15-ml/kg group received a mean (SD) volume of 14.1 ± 3.4 ml of blood per transfusion, whereas those in the 20-ml/kg group received 17.4 ± 3.3 ml of blood per transfusion. Mean value of Hb (Hemoglobin) and HCT (Hematocrit) is always higher in post-transfusion compared to the pretransfusion values. Following transfusion, there was an increase in Hb (mean 2.8 +/- 1.6 g/dl (SD)) and HCT (9.0% +/- 4.7%) (P < 0.05). Further, when considering the clinical improvement with each transfusion in multiple
transfused neonates, in first transfusion to 8th there is significant increment ($P < 0.05$) of Hb level. There is significant increment of HCT in first to fifth transfusions ($P < 0.05$) and 9th transfusion ($P = 0.013$). There is significant improvement in tachycardia in 2nd to 5th transfusion of RCC ($P < 0.05$) and similarly in the 8th transfusion ($P = 0.013$).

In conclusion, although most of the findings are keeping with the literature and in par with the guidelines there are a considerable proportion of transfusions that are not in accordance with the guidelines. It is important to firmly evaluate on this proportion of transfusions. Although, some of the transfusions are justifiable some of the transfusions can be avoided. Clinical outcome of transfusions is appropriate according to the study, but this can be further increased by appropriate component usage and use of alternative therapies other than blood products.

Disclosure of Interest: None Declared

**BSH2021-PO-136**

Determinants of voluntary blood donation among female students in a tertiary institution in Nigeria

Mutiat Kehinde Ogunfemi$^{1,2}$, Hannah Oluwayemisi Olawumi$^{1,2}$, Khadijah Olaian Omokanye$^{1}$, Akeem Olasunkunmi Shittu$^{1}$

$^{1}$Haematology and Blood transfusion, University of Ilorin Teaching Hospital, $^{2}$Haematology and Blood transfusion, University of Ilorin, Ilorin, Nigeria

**Abstract Content:** Female blood donors, majority of which are voluntary non-remunerated blood donors, constitute a negligible number of the donor pool especially in Sub-Sahara Africa (SSA). Several factors have been shown to affect donation from potential female donors. The aim of this study was to assess the determinants of voluntary blood donation among female students.

This was a questionnaire based study using a semi-structured format among female respondents in a tertiary institution in North central, Nigeria. Knowledge, attitude and practice of blood donation were enquired. Those with score below the mean were said to have poor knowledge and those who score 50% and below were said to have poor attitude towards blood donation. Factors motivating and inhibiting blood donation were also enquired.

A total of four hundred female respondents were recruited for this study with a mean age of 19.9±1.8 years. More than half were in their first year in school 236(59.0%) and majority was single, 391 (97.8%). Most of the respondents (89.0%) had a poor knowledge of voluntary blood donation. Only twenty seven (6.8%) of the respondents had ever donated blood. Respondents (8.1%) who are aware of voluntary blood donation were likely to practice blood donation and this was shown to be statistically significant ($X^2=3.878, P = 0.049$). Predictors of voluntary non-remunerated blood donation using binary logistic regression (multivariate analysis) showed that students who were in vocational and technical school had 3.6 times increase in the odds of practice of VNRBD as compared with those in science school and this was statistically significant ($P \text{ value}= 0.014$) (OR: 3.647; 95% CI: 1.298–10.251).

Knowledge, attitude and practice of voluntary blood donation is poor among female respondents in this study. The school a respondent is, within the institution was found to be a significant determinant of voluntary blood donation.

**Disclosure of Interest:** None Declared

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**BSH2021-PO-137**

To improve efficiency of haematology junior doctor working by reducing ad hoc G&S sample requests-A Quality Improvement Project

Maira Hafeez$^{1}$, Mohammad Fahad $^{1}$

$^{1}$Leicester university hospital, Leicester, United Kingdom

**Abstract Content:** Blood Transfusions is one of the most common interventions happening on the Haematology wards. If there is no valid G&S (Group and Save) sample present on the day of transfusion then this leads to a delay in the intervention and also an additional job is created for the junior doctor on the ward to bleed the patient which leads to inefficient time management of the junior doctors. Hence this change was introduced to improve time management of doctors that will help manage work load on doctors which will ultimately help in better patient care.

The change introduced was Introduction of scheduled venepuncture for G&S sampling during regular phlebotomy rounds in the mornings twice a week for the identified patients, for this the request forms were filled pre-emptively by the junior doctors. PDSA (Plan Do Study Act) cycle was adopted.

Data source used for identifying the audit population was ICE Reporting system. Audit population was Appox 300 patients over 11 weeks (all inpatient on hematology during data cycles) and data collection method used was retrospective.

Time period being used to identify the population was 24/02/20 to 03/03/20 (cycle 1), 04/03/20 to 19/04/20 (cycle 2) and 27/04/20 to 24/05/20 (cycle 3).

More measures were identified as the project progressed in order to consider process and balancing these were taken into...
Abstract Table:

<table>
<thead>
<tr>
<th>QI Measures</th>
<th>Source of standard</th>
<th>Target (n)</th>
<th>Pre Intervention</th>
<th>Post Intervention</th>
<th>2nd Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Outcome measure: Number of ad hoc G&amp;S samples carried out</td>
<td>None</td>
<td>0</td>
<td>12</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2a Process Measure: Number of phlebotomy G&amp;S sample</td>
<td>None</td>
<td>N/A</td>
<td>Not Recorded</td>
<td>Not Recorded</td>
<td>20</td>
</tr>
<tr>
<td>2b Process Measure: number of out of hours transfusions (surrogate marker of efficiency; OOH defined as not within 0600-2000)</td>
<td>None</td>
<td>N/A</td>
<td>Not Recorded</td>
<td>Not Recorded</td>
<td>15</td>
</tr>
<tr>
<td>Balance Measure: phlebotomy workload (number of forms as surrogate measure)</td>
<td>None</td>
<td>N/A</td>
<td>Not Recorded</td>
<td>Not Recorded</td>
<td>39</td>
</tr>
</tbody>
</table>

consideration. This data was collected for the first time in the 3rd Cycle.

3rd cycle showed findings: Out of hours transfusion is a surrogate marker for efficiency as repeated samples mean blood bank provision of transfusion is later in the day. Early morning transfusion is common practice on haematology and is deemed safe. We therefore defined out of hours transfusion as outside of the hours of 0600-2000 (based on perceived safety implications). Having excluded platelet transfusions (which do not rely on a valid G&S sample), there were 15 transfusions during this time.

Post intervention Significant Reduction in number of ad hoc G&S sampling (67%) was seen. This project had very positive feedback given that it was quite relevant to the speciality and it addressed a core issue impacting the time management of junior doctors on the ward. Phlebotomy team support was vital for the success of this project. Out of Hour red cell transfusions should be noted but cannot be foreseen and are therefore outside the scope of the improvement project. It is not anticipated that this project will negate the need for this entirely, but it is an ongoing measure that could be monitored moving forwards.

Going forward, plans are in place to continue educating junior doctors in the beginning of each rotation regarding the project and regular G&S request form filling for the phlebotomy round. Also a poster regarding the project is being displayed in Junior Doctors office as a reminder.

Disclosure of Interest: None Declared

BSH2021-PO-138
Abnormal haematological parameters in COVID – 19 positive patents. A single centre study from the United Kingdom.

Deborah Abrams*, Oliver Firth, Diana Lobo, Vita Ceidiene, Aida Rajic, Federica Masieri, Robert Banthorpe, Joanne King, Sanjana Bade, Akshaye Pratipati, Andrew Hodson, Mahesh Prahladan

1Haematology, East Suffolk and North Essex NHS Foundation Trust, Ipswich, 2Haematology, Addenbrooke’s Hospital, Cambridge University Hospitals Foundation NHS Trust, Cambridge, 3Biotechnology Unit, Directorate of Life Science, School of Engineering, Arts, Science and Technology, 4Biotechnology Unit, Directorate of Life Science, School of Engineering, Arts, Science and Technology, University of Suffolk, Ipswich, 5Masters in Genomics programme, University of Cambridge, Cambridge, United Kingdom

Abstract Content: The current COVID - 19 global pandemic, caused by the novel coronavirus, SARS-CoV-2, is ongoing through a second wave in many countries and has resulted in an unprecedented mortality and morbidity. The typical clinical presentation includes flu-like symptoms, such as fever, cough and asthma, and also COVID-19 specific anosmia; however, the symptom spectrum spreads from being asymptomatic, to a severe acute respiratory distress syndrome, to multiple organ failure.

Aim: The aim of this study is to evaluate the abnormalities seen in the full blood count parameters of patients with positive qPCR test for SARS-CoV-2 infections.

Method: This was a retrospective analysis of all full blood count parameters from patients who tested positive for SARS-CoV-2 following a qPCR test, and were admitted to hospital with symptoms in the first wave of COVID-19, from March 2020 to June 2020. 12 different parameters were assessed for any abnormalities, including: haemoglobin (Hb), white blood cell count (WCC), neutrophil, lymphocytes, eosinophils, basophils, platelets, Mean Cell Volume (MCV), Mean Cell Haemoglobin (MCH), haematocrit (HCT), and red blood cell distribution width (RDW).

Inclusion criteria for the study were: admission to hospital, positive qPCR test, no known malignancy or HIV, and no current immunosuppressive or chemo-therapy. The full blood count parameters from all patients admitted with suspected SARS-CoV-2 infection were extracted from the analyser. Only the patients with positive qPCR test were selected for the study.

Results: Samples from a total of 278 patients (162 male and 116 female) were analysed. The median age of patients was 76 (range from 1 year to 99 years). Abnormal WBC count with a predominant leucocytosis was seen in 27% of patients. 1.4% patients had abnormal RBC, while 41% had abnormal Hb, with 18% of patients with Hb <100 gm/l. HCT was abnormal in 60% of patients. Furthermore, abnormal neutrophil and lymphocyte counts were detected in 43% and 54% patients respectively. Lymphopenia and thrombocytopenia were seen in 52% and 13% of patients respectively. No evidence of reduced total white cell count was seen. Abnormal monocytosis were seen in 15% of patients. There was no striking eosinophilia, but rather a decrease in circulating eosinophils in 82% of patients. Overall, the changes were more pronounced in HCT, lymphocyte and eosinophil counts.

Conclusion: Significant abnormalities in full blood count parameters seen in COVID-19 patients could possibly help to elucidate the pathogenesis of SARS-CoV-2 infection along with other biomedical parameters. These abnormal parameters can be modelled to a risk stratifying algorithm to predict the severity of the COVID-19 infection in a hospital setting.

Disclosure of Interest: None Declared
BSH2021-PO-139
Temporal Trends in the Prevalence of Hepatitis B, Hepatitis C and Human Immuno-Deficiency virus in Blood Donors of Pakistan
Sajeel Saeed1, Ansar Ullah1
1Medical Student, Rawalpindi Medical University, Rawalpindi, Pakistan

Abstract Content: A Transfusion transmitted infection (TTI) is a virus, parasite, or other potential pathogens that can be transmitted in donated blood through a transfusion to a recipient. Hepatitis B, hepatitis C, Human Immuno-deficiency virus are common examples of TTIs. The aim of this study was to determine the temporal trends in the prevalence of HBV, HCV and HIV in blood donors of Pakistan over the last 14 years. A retrospective study was carried out in the blood donors who donated their blood at Pakistan Institute of Medical Sciences (PIMS) Islamabad. Blood samples were screened for HBV, HCV and HIV over a period of 14 years from 2005 to 2018. Blood donors were selected according to the WHO criteria for blood donation. A total of 312320 individuals donated blood between 2005 and 2018 out of which 311476 (99.7%) were males and only 991(0.3%) were females. The number of annual blood donations increased from 7829 in 2005 to 30731 in 2018. The total number of donors found positive for HBV, HCV and HIV was 5752, 8951 and 124 respectively. Along the study period a slight increase in HBV prevalence of 1.225% in 2005, to 1.451% in 2018 was observed. Meanwhile, the prevalence of HCV decreased from 2.25% to 1.474%. While an alarming increase was observed in the prevalence of HIV. Its prevalence was 0% in 2005, 0.006% in 2006 and reached 0.065% in 2018. The study has shown that HCV is the most prevalent transfusion-transmitted infection found in Pakistan blood donors. HBV has the lowest prevalence but has shown the highest increase over the course of the last 14 years i.e., by a factor of 11. A net decrease was observed in the prevalence of HBV while HCV showed an increased prevalence. The results show that there is a need to take safety measures to control the increasing prevalence of TTIs in the Pakistani population.

Abstract Table: Table 1 showing the temporal trends of HBV, HCV, HIV from 2005 to 2018.

<table>
<thead>
<tr>
<th>Years</th>
<th>Donors</th>
<th>HBV prevalence %</th>
<th>HCV prevalence %</th>
<th>HIV prevalence %</th>
</tr>
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Chi Square for trend P: <0.001 <0.001 <0.001

Disclosure of Interest: None Declared

BSH2021-PO-140
A retrospective analysis of the association of iron deficiency status and its effect on severity in patients with dengue fever in a tertiary care hospital in sri lanka
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1Haematology, Sri Jayewardenepura General Hospital, 2Community medicine, Ministry of health, COLOMBO, Sri Lanka

Abstract Content: Dengue fever is a major public health problem in Sri Lanka with high incidence, morbidity and cost of treatment. Iron deficiency prevalence varies from 15% to 36% among children and women in Sri Lanka.

Reticulocyte haemoglobin (CHr) level can be used to diagnose iron deficiency anemia (IDA), especially in cases where there is an ongoing infective or inflammatory processes. According to a research conducted at Sri Jayewardenepura General Hospital CHr value less than 26 pg was diagnostic of iron deficiency.

The aim of this study was to determine any association between dengue fever and severity of dengue infection with iron deficiency. If proven, iron treatment could reduce the incidence, morbidity and economic burden of dengue fever.

The objectives of this study was to analyze the association between iron deficiency and dengue infection among adult patients and to determine any association between iron deficiency and severity of dengue fever.

This was a retrospective analytical study conducted from October 2020 to February 2021 at SJGH. Sample size (273) was calculated using the formula by Charan & Biswas. Information from records of adult patients with positive dengue NS1 antigen were obtained. Analysis done using chi square test. Control sample of 273 to match the test group in number were randomly selected from patients with no consideration of their iron status who were negative for dengue and who did not have other factors which could influence their CHr. The control sample was included to compare the prevalence of iron deficiency in the two groups of patients, with and without dengue infection respectively.

Of the test sample (273), patients with and without iron deficiency were 81 (29.7%) and 192 (70.3%) respectively. Out of the 273 patients in the aged matched control group, 115 (42.1%) had iron deficiency, while 158 (57.9%) had normal iron status. There was a higher prevalence of iron deficiency in the control group as opposed to the test group. Among dengue fever patients 122 (44.7%) had iron deficiency, while 158 (57.9%) had normal iron status. The CHr value less than 26 pg was diagnostic of iron deficiency in the two groups of patients, with and without dengue infection respectively.

Mean CHr was 26.6 pg in the patients’ group while 25.97 pg in the control group. Iron deficiency was not significantly high in both groups and the CHr value indicates a reduced prevalence of iron deficiency in the test group indicating no increase of dengue fever noted among patients with iron deficiency. Statistically significant difference was not observed between severity of infection & iron deficiency status as P value was >0.05 (0.651).

In conclusion there was no association between iron deficiency and dengue fever. Therefore, the hypothesis that dengue infection can be more prevalent in patients with iron deficiency was not proven in our study. Iron status had no association with the severity of the dengue infection as well.

Key Words: Dengue Infection, Iron deficiency, Reticulocyte Haemoglobin (CHr)

Disclosure of Interest: None Declared
Usage of Therapeutic plasma Exchange (TPE) in leptospirosis associated severe pulmonary haemorrhagic syndrome

Sandun Gunawardene

Abstract Content: Usage of Therapeutic plasma Exchange in leptospirosis associated severe pulmonary haemorrhagic syndrome

Gunawardene S.M.P.1

The emergence of leptospirosis-associated severe pulmonary hemorrhagic syndrome (SPHS) with high case fatality has been reported from Sri Lanka in many other countries. The purpose of this study was to describe the outcome and complications of therapeutic plasma exchange in managing leptospirosis associated severe pulmonary haemorrhagic syndrome (SPHS).

This study was conducted at National hospital of Colombo, Sri Lanka from February 2019 to February 2020. All confirmed cases of leptospirosis who presented during this period and were admitted to medical units and medical ICU referred to the blood bank were included in this study. SPHS was defined as a patient presenting: haemoptysis, arterial hypoxemia (Acute Lung Injury Score < 2.5), haemoglobin drop (10% from the previous value), or diffused alveolar shadow in chest radiograph, without alternative explanation other than leptospirosis.

Of the 25 confirmed cases of leptospirosis 84 % had acute kidney injury (AKI) whilst SPHS was seen in 68%. Patients typically developed SPHS mostly on days 4 and 5. The case fatality rate of this study sample was 25%, Among SPHS patients 95% received therapeutic plasma exchange (TPE). The survival rate was higher (75%) when the TPE was performed within the first 48 h of detecting SPHS compared to patients in whom the procedure was done after 48 h. for all replacement fluid used was FFP with 1-1.5 volume exchanges. Leptospirosis patients with SPHS who did not receive TPE, 90% died of MODS.

During the study period, SPHS was common and the mortality rate was higher in the study area. TPE beneficial in treating them how ever treatment modalities tested need further evaluation and confirmation.

Disclosure of Interest: None Declared

Case Report: Therapeutic Plasma Exchange in Acute Liver Injury Following Paracetamol Over Dose

E. A. P. M. Premaratne, Janaki Dissanayake

Abstract Content: Introduction: Acute liver failure is an uncommon clinical manifestation of sudden and severe hepatic injury. Paracetamol poisoning is one of the most common causes of acute liver failure in Sri Lanka.

Case 1: A 37 year old person presented to the local hospital with a history of found unconscious at home. According to the history given by the family members, patient has consumed around 80 tablets of paracetamol (PCM). The dose of PCM was equal to 667 mg/Kg which was well above the toxic level. Following admission to the local hospital patient was given IV NAC infusion for 2 days and due to the poor response to IV NAC patient was transferred to our tertiary care center. On admission patients GCS was 3 and electrolytically intubated the patient at ETU then patient was transferred to the ICU. AST > 1000 IU/l, ALT >2000 IU/l with SBR of 200 mg/dl and patient had metabolic acidosis, INR > 2. Hb was > 9 g/dl throughout. As the response to IV NAC was poor he was referred for Therapeutic Plasma Exchange (TPE). Daily 1.5 volumes 3 cycles of TPE performed with FFP substitution. By the end of 3 cycles patients GCS was improved and he was extubated. Patient was discharged from ICU and while on ward stay he was referred to a consult psychiatrist and follow up arranged. After 2 weeks of admission patient was discharged from the hospital.

Case 2: A 32 year old lady presented to the local hospital with history of ingestion of 60 tablets of PCM and kerosene oil (volume uncertain). Paracetamol dose was 545 mg/Kg again the dose was well above the toxic dose. She was presented to the local hospital within one hour but gastric lavage was not performed due to ingestion of kerosene oil. As liver enzymes were high patient was referred to the GE unit. Both AST and ALT were > 200 IU/l, SBR also >60 mg/dl, patient was treated with IV NAC infusion. Patient was referred for TPE on the following day of admission. Three cycles of 1.5 volumes TPE with FFP replacement performed and patient’s biochemical parameters improved. As patient’s creatinine level was rising hemodialysis also was performed. She recovered completely and discharged from hospital after the psychiatric referral.

Discussion: Paracetamol poisoning is a common presentation to Emergency department among all drug-over dose cases. Toxicity due to paracetamol poisoning is caused by accumulation of the harmful intermediate metabolite N-acetyl-p-benzoquinone imine (NAPQI). The first line treatment of paracetamol toxicity is NAC, which supplements endogenous glutathione stores and promotes conjugation of NAPQI to a non-toxic metabolite. Despite the availability and efficacy of this NAC still there can be cases in which response may be poor to early initiation of NAC therapy leading to acute liver injury. One reason for this can be in the case of a large ingestion (paracetamol dose >500 mg/kg total body weight), here in these two cases also the dose of paracetamol was well above this level. In such cases one of the alternative treatment modality is TPE to remove toxic substances thereby accelerating the recovery of liver injury or as a bridging therapy until the liver transplant.

Here in two cases we report both patients recovered fully with combine therapy of NAC and TPE 3 cycles. These cases demonstrate the role of TPE in selected patient with Acute Liver Injury (ALI) following paracetamol poisoning. We suggest Randomised trials will be needed to assess the efficacy of TPE in ALI due to paracetamol toxicity.

Disclosure of Interest: None Declared

G-6-6 PD Deficiency in Crete, Greece during the last five years

Maria C. Maisi1, Evangelia Illaki1, Galatia Gourniezaki1, Georgios Tsioulou2, Emmanouela Maisi2, Konstantinos Giannakoudakis3, Eirini Kalokiri1, Anna Koziri1

Abstract Content: Purpose: Report of G-6-6 PD deficiency in adults examined in our hospital during the years 2014-2018.

Theory: G-6-6 PD deficiency is the most common enzyme deficiency which affects 400 million people worldwide. It is a hereditary, gender-related red-blood cell disorder which causes neonatal hyperbilirubinemia and chronic hemolytic anemia. Exposure to oxidant factors such as drugs, food and infections may cause hemolytic crisis. Crete is one of the regions with high G-6-6 PD deficiency frequency. Crete is one of the regions with high G-6-6 PD deficiency frequency. Material-Method: G-6-6 PD activity was measured quantitatively in 571 adults of which 290 male and 281 female. Whole blood samples were analysed by Dialab company reagents. The method is based on the oxidation of G-6-6D to 6-phosphogluconic acid and the reduction of NADP to NADPH in the presence of G-6-6 PD enzyme according to the reaction G-6-6P+NADP→G-6-6G+NADPH2. NADPH2 formation grade is directly proportional to the enzyme activity and it is measured by spectrophotometric method. G-6-6D efficiency values are 6-
17.2 U/gHb, partial deficiency values 2.5-6.5 U/gHb while total deficiency values are < 2.5 U/gHb.

**Results-Conclusion:** Out of 571 patients examined, 533 (93.35%) were found to have normal enzyme activity, 14 patients (2.45%) partial deficiency and 24 patients (4.20%) total enzyme deficiency. In total G-6-PD deficiency was reported in 38 people 6.65%, percentage which is a bit higher than that of an older study in 2000 in Crete that was 5.38%. In addition higher deficiency frequency in men (60.5%) than in women (39.5%) was confirmed due to gender related heredity in men.

### Abstract Table:

<table>
<thead>
<tr>
<th>G-6-PD</th>
<th>Patients</th>
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<td>Normal enzyme activity</td>
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<td>Partial deficiency</td>
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**Disclosure of Interest:** None Declared
Lymphoma, CLL and Myeloma

BSH2021-PO-144
Acalabrutinib (Acala) vs Idelalisib plus Rituximab (IdR) or Bendamustine plus Rituximab (BR) in Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia (CLL): ASCEND Final Results

Abraham Jacob1, Paolo Ghia2, Andrzež Plušeč3, Malgorzata Wach4, Daniel Lysak4, Tomas Kozak5, Martin Simkovic6, Polina Kaplanska7, Iryna Kraychkova8, Arpad Illes9, Javier De La Serna10, Sean Dolan11, Philip Campbell12, Gerardo Musuraca13, Eric Joseph Avery14, Jae Hoon Lee15, Denise Wang16, Priti Patel17, Cheng Seok Quah18, Wojciech Jurczak19
1Royal Wolverhampton Hospital NHS Trust, Wolverhampton, United Kingdom, 2Università Vita-Salute San Raffaele and IRCSS Ospedale San Raffaele, Milan, Italy, 3Department of Hematological Oncology, Oncology Specialist Hospital, Brzozow, 4Department of Hematology and Bone Marrow Transplantation, Medical University of Lublin, Lublin, Poland, 5Fakultní Nemocnice Plzen, Plzen, 6Fakultní Nemocnice Královské Vinohrady, Prague, 7University Hospital Hradec Kralove, Charles University, Hradec Kralove, Czech Republic, 8City Clinical Hospital No. 4 DCC, Dnipro, 9National Cancer Institute, Kiev, Ukraine, 10University of Debrecen, Faculty of Medicine, Department of Hematology, Debrecen, Hungary, 11Hospital Universitario 12 de Octubre, Madrid, Spain, 12Saint John Regional Hospital, University of New Brunswick, Saint John, NB, Canada, 13Barrow Health University Hospital Geelong, Geelong, VIC, Australia, 14Istituto Scientifico Romagnolo per lo Studio e la cura dei Tumori, Meldola, Italy, 15Nebraska Hematology Oncology, Lincoln, NE, United States, 16Cachon University Gil Medical Center, Incheon, Korea, Republic Of, 17Acerta Pharma, San Francisco, CA, 18Acerta Pharma, South San Francisco, CA, 19Acerta Pharma, South San Francisco, United States, 20Maria Skłodowska-Curie National Institute of Oncology, Krakow, Poland

Abstract Content: Background: Acala is a second-generation, highly selective, covalent Bruton tyrosine kinase inhibitor approved for patients (pts) with CLL including those with R/R CLL. The efficacy and safety of acala alone vs IdR or BR were shown in R/R CLL pts in a preplanned interim analysis of ASCEND. Here, we present the final results of this trial.

Methods: In this randomised, multicentre, phase 3, open-label study (NCT02970318), R/R CLL pts were randomised 1:1 to receive oral acala 100 mg twice daily until progressive disease or unacceptable toxicity; or investigator’s (INV) choice of IdR (Id: 150 mg orally twice daily until progression or toxicity, R: 375 x1 then 500 mg/m² intravenously [IV] for 8 total cycles) or BR (R: 70 mg/m² IV and R: 375 x1 then 500 mg/m² IV for 6 total cycles) both, until progressive disease or unacceptable toxicity. Progression-free survival (PFS), overall survival (OS), overall response rate (ORR), and safety were assessed.

Results: 310 pts (acala, n = 155; IdR, n = 119; BR, n = 36) were enrolled (median age: 67 years; del(17p) n = 49 (15.8%); del(11q) n = 83 (26.8%); unmutated IgHV n = 243 (78.4%); complex karyotype with ≥3 abnormalities n = 96 (31%); Rai stage 3/4 n = 129, (41.6%)). At a median follow-up of 22.0 months, acala significantly prolonged INV-assessed PFS vs IdR/BR (median: not reached vs 16.8 months; hazard ratio: 0.27, P < 0.0001); 18-month PFS rates were 82% for acala and 48% for IdR/BR. 18-month OS rate was 88% for both treatment regimens. ORR was 80% with acala vs 84% with IdR/BR (ORR + partial response with lymphocytosis 92% vs 88%, respectively). Common adverse events (AEs) are listed in the Table below. AEs led to drug discontinuation in any cohort

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<th>Common AEs2, n (%)</th>
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<td>Pyrexia</td>
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<td>11 (9)</td>
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<tr>
<td>Fatigue</td>
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<td>21 (14)</td>
<td>10 (9)</td>
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<tr>
<td>Nausea</td>
<td>Any Grade</td>
<td>17 (11)</td>
<td>16 (14)</td>
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<tr>
<td>Infusion-related reaction</td>
<td>Any Grade</td>
<td>11 (7)</td>
<td>9 (8)</td>
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Abstract Table: Table. Most common AEs in ≥15% (Any grade) or ≥25% (grade ≥3) of patients in any cohort

BSH2021-PO-145
Pirtobrutinib (LOXO-305), a next generation highly selective non-covalent Bruton’s Tyrosine Kinase inhibitor in previously treated mantle cell lymphoma and other non-Hodgkin lymphomas: Results from the phase 1/2 BRUIN study
Toby Eyre1,3, Nirav N. Shah2, Alvaro Alencar3, James N. Gerson4, Manish R. Patel5, Bita Fakhri6, Wojciech Jurczak7, Xuan Tari8, Katharine Lewis9, Timothy Peskoe9, Catherine C. Coombs10, Ian Flinn11, David Lewis12, Steven Le Gouill13, M. Lia Palomba14, Jennifer Woyach15, John M. Pagel16, Nicole Lamanna17, Jonathon B. Cohen18, Minal A. Barve19, Paolo Ghia20, Ming Yin21, Binoj Nair21, Donald E. Tsai21, Nora C. Ku21, Anthony R. Mato24, Chan Y. Cheah25, Michael L. Wang22
1Oxford University Hospitals NHS Foundation Trust, Churchill Cancer Centre, Oxford, United Kingdom, 2Medical College of Wisconsin, Brookfield, 3University of Miami Miller School of Medicine, Miami, 4Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, 5Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, 6University of California San Francisco, San Francisco, United States, 7Marie Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland, 8Linear Clinical Research and Sir Charles Gardiner Hospital, Perth, Australia, 9Medical College of Wisconsin, Milwaukee, 10University of North Carolina at Chapel Hill, Chapel Hill, 11Sarah Cannon Research Institute, Nashville, United States, 12University Hospitals Plymouth NHS, Plymouth, United Kingdom, 13Service d’hématologie clinique du CHU de Nantes, INSERM CRCINA Nantes-Angers, NoCT Université de Nantes, Nantes, France, 14Memorial Sloan Kettering Cancer Center, New York, 15The Ohio State University Comprehensive Cancer Center, Columbus, 16Swedish Cancer Institute, Seattle, 17Herbert Irving Comprehensive Cancer Center, Columbia University, New York, 18Winship Cancer Institute, Emory University, Atlanta, 19Mary Crowley Cancer Research, Dallas, United States, 20Université Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milan, Italy, 21Loyo Oncology at Lilly, Stamford, 22MD Anderson Cancer Center, Houston, United States

Abstract Content: Despite the marked efficacy of covalent BTK inhibitors (BTKi) in MCL, WM, and MZL, the development of resistance and discontinuation for adverse events can lead to treatment failure. Moreover, pharmacological liabilities of these agents such as low oral bioavailability or short half-life, can lead to suboptimal BTK target coverage and ultimately result in acquired resistance in some patients (pts). To address these limitations, pirtobrutinib (LOXO-305), a highly selective, non-covalent BTKi that inhibits both WT and C481-mutated BTK with equal low nM potency was developed. Here we report the safety and efficacy of pirtobrutinib in previously treated MCL and other NHLs.

BRUIN is a multicenter phase 1/2 trial (NCT03740529) enrolling pts with advanced B-cell malignancies who have received ≥2 prior therapies. Oral pirtobrutinib was dose escalated in a standard 3+3 design in 28-day cycles. The primary endpoint was MTD/RP2D identification. Efficacy evaluable pts included all dosed pts who underwent their first response evaluation or discontinued therapy. Safety was assessed in all pts (n = 323). Response was assessed according to Lugano Classification or iwWM.

As of 27 September 2020, 323 pts with B-cell malignancies (170 CLL/ SLL, 61 MCL, 26 WM, and 66 other B-cell lymphomas) were treated on 7 dose levels (25-300 mg QD). Median age was 69 (range 50–87) years for MCL pts, 68 (42–84) for WM pts, and 68 (27–86) for other NHLs pts. Median number of prior lines of therapy was 3 (range, 1-8) for MCL, 3 (2–11) for WM, and 4 (2–10) for other NHLs. 93% of MCL, 70% of WM and 36% other NHL pts had received a prior BTKi.
Pirtobrutinib demonstrated high oral exposures, with doses ≥100 mg QD exceeding the BTK IC50 for the entirety of the dosing interval. No DLTs occurred. Consistent with pirtobrutinib’s selectivity, the only treatment emergent adverse events regardless of attribution or grade in ≥10% of pts (n = 323) were fatigue (20%), diarrhea (17%) and contusion (13%). Grade 3 atrial fibrillation/flutter was not observed; 1 pt had grade 3 hemorrhage in the setting of mechanical trauma. Responses were observed at the first dose level of 25 mg QD. A RP2D of 200 mg QD was selected. At the efficacy cutoff date, 35 (57%) MCL pts, 18 (69%) WM pts and 34 (52%) other NHL pts remained on therapy. Among the 52 efficacy-evaluable prior BTKi treated MCL pts, the ORR was 52% with 13 CR, 14 PR and 9 SD. Median follow up was 6 months (range 0.7-18.3+) for MCL. Responses in MCL were observed in 9/14 pts (64%) with prior autologous or allogeneic transplant, and 2 of 2 with prior CAR-T cell therapy. Among the 19 efficacy-evaluable pts with WM, the ORR was 68% (9 PR, 4 MR, 3 SD), and 69% in prior BTKi treated pts. 10 of 13 WM responders were ongoing (follow-up time from initial response: 0.8-9.2 months). For the 55 efficacy-evaluable other NHL pts, best response was as follows: DLBCL - 24% ORR (4 CR, 2 PR, 2 SD, 12 PD, 5 NE), FL - 50% ORR (2 CR, 2 PR, 1 IR, 3 PD), MZZL - 22% ORR (2 PR, 7 SD), Richter’s transformation - 75% ORR (6 PR, 1 SD, 1 NE) and Other (2 B-PLL, 3 Low grade transformation) - 1 SD, 2 PD, 2 NE.

Pirtobrutinib demonstrated promising efficacy in MCL pts following multiple prior lines of therapy, including a covalent BTKi. Pirtobrutinib also showed efficacy in previously treated other NHLs. Pirtobrutinib was well tolerated and exhibited a wide therapeutic index.

**Disclosure of Interest:** T. Eyer Conflict with: Gilead, Conflict with: Roche, Loxo Oncology, Gilead, AbbVie, Jansen, BeiGene, AstraZeneca, and Kite, N. N. Shah Conflict with: Loxo Oncology, Celgene, Miltenyi Biotech, Incyte, Kite, Verastem, A. Alencar Conflict with: Loxo Oncology, Conflict with: Karyopharm, Kit, Amgen, Celgene, Spectrum Pharmaceuticals, J. N. Gerson Conflict with: Loxo Oncology, Conflict with: AbbVie, Pharmacycics, Genentech, M. R. Patel Conflict with: Janssen, Conflict with: Gilead, Olalekan O. Oluwolowo, MBBS, MPH, Yi Lin, MD, PhD, Ira Braunschweig, MD, Brian T. Hill, MD, PhD, John M. Timmerman, MD, Abhinav Deol, MD, Patrick M. Reagan, MD, Patrick Stiff, MD, Ian W. Flinn, MD, PhD, Umar Farooq, MD, Andre H. Goy, MD, Peter A. McSweeney, MB, ChB, Javier Munoz, MD, MS, FACQ, Tanya Siddiqi, MD, John M. Rossi, MD, Adrián A. Bot, MD, PhD, Lianqing Zheng, PhD, Ruben Veze, MD, PhD, Zahid Bashir, MBBS, MS, Jenny J. Kim, MD, MS, Rong Chu, PhD, Satvaa S. Neelapu, MD

**BSH2021-PO-146**

Long-term survival and gradual recovery of B cells in patients with refractory large B-cell lymphoma treated with axicabtagene ciloleucel

Caron A. Jacobson, MD, MMSc,1 Fredrick L. Locke, MD,2 Armin Gobadi, MD,3 David B. Miklos, MD, PhD,6 Lazaros J. Lekakis, MD,5 Olalekan O. Oluwolowo, MBBS, MPH, Yi Lin, MD, PhD,3 Ira Braunschweig, MD,4 Brian T. Hill, MD, PhD,9 John M. Timmerman, MD10, Abhinav Deol, MD10, Patrick M. Reagan, MD10, Patrick Stiff, MD10, Ian W. Flinn, MD, PhD14, Umar Farooq, MD10, Andre H. Goy, MD10, Peter A. McSweeney, MB, ChB11, Javier Munoz, MD, MS, FACQ, Tanya Siddiqi, MD,12 John M. Rossi, MD12, Adrián A. Bot, MD, PhD12, Lianqing Zheng, PhD12, Ruben Veze, MD, PhD12, Zahid Bashir, MBBS, MS12, Jenny J. Kim, MD, MS12, Rong Chu, PhD12, Satvaa S. Neelapu, MD12

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**Abstract Content:** Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved for the treatment of patients (pts) with relapsed/refractory large B-
cell lymphoma (LBCL) with ≥2 prior systemic therapies. ZUMA-1 is the multicenter, single-arm, registrational Phase 1/2 study of axi-cel in pts with refractory LBCL. In a 2-y analysis of ZUMA-1 (median follow-up, 27.1 mo; N = 101), axi-cel demonstrated objective response, complete response (CR), and ongoing response rates of 83%, 58%, and 39%, respectively (Locke et al. *Lancet Oncol.* 2019; 20:31). Here, we present additional survival findings with ≥4 y of follow-up and recovery of normal, polyclonal B cells from ongoing responders in ZUMA-1. Eligible pts with refractory LBCL underwent leukapheresis followed by conditioning chemotherapy (fludarabine and cyclophosphamide) and infusion of 2 × 10^6 anti-CD19 CAR T cells/kg (Neelapu et al. *N Engl J Med.* 2017;377:2541; NCT02348216). The primary endpoint was objective response rate (ORR), and the first response assessment was 4 wk post infusion. Response assessments were performed per protocol up to 24 mo or disease progression, whichever occurred first. For pts in ongoing response beyond Month 24, response assessments continued per institutional standard of care (SOC). In pts with ongoing responses and evaluable samples, blood levels of CAR T cells were quantified using polymerase chain reaction, and B cells were characterized using flow cytometry.

Of 111 pts enrolled, 101 received axi-cel. Among pts who received axi-cel, the median time from axi-cel infusion to both objective response and CR was 1.0 mo (range, 1–12 mo; Locke et al. *Lancet Oncol.* 2019; 20:31). Among the entire enrolled intent-to-treat population (N = 111), median manufacturing time was 17 d (range, 14–51 d; n = 110 as manufacturing was not feasible for 1 pt). Additionally, among the 111 pts, the median time from enrollment/leukapheresis to objective response and CR was 1.7 mo (range, 0.7–12.9 mo) and 1.9 mo (range, 0.7–13.3 mo), respectively. Responses have been durable, and with a median follow-up of 51.1 mo, median overall survival (OS) was 25.8 mo, and 4-y OS rate was 44%. No axi-cel–related secondary malignancies have been reported.

Blood samples from 21 pts in ongoing response (per institutional SOC) at ≥3 y were available for analysis of CAR T cells and evaluation of B-cell recovery. All evaluable pts (n = 21) had detectable B cells in blood at 3 y post axi-cel. Notably, 91% of pts in ongoing response at ≥3-y follow-up showed recovery of polyclonal B cells, measured by presence of both kappa and lambda light chains on nonmalignant CD19+CD20+ B cells (median kappa/lambda ratio = 1.6), and more prominent naive B-cell immunophenotypes. Also, 14/21 pts (67%) had detectable CAR gene-marked cells and polyclonal B cells in blood at 3 y.

Axi-cel produced rapid responses and long-term disease control in pts with refractory LBCL. Most responses occurred by the first assessment, and the brief time elapsed between enrollment and response supports both the speed and success of manufacturing. Furthermore, axi-cel–treated pts with ongoing responses at ≥3 y showed evidence of restoration of a polyclonal B-cell compartment and clearance of functional CAR T cells, a critical component of the long-term safety of CD19-directed CAR T-cell therapies. **Disclosure of Interest:** C. A. Jacobson, MD, MMSc Conflict with: Research funding from Pfizer, Conflict with: Honoraria from and consultancy or advisory role for Kite, a Gilead Company, Celgene, Novartis, Pfizer, Humanigen, Precision Biosciences, Nkarta, Lonza, and AbbVie; Speakers’ bureau participation for Axis and Clinical Care Options; Travel support from Kite, a Gilead Company, Celgene, Novartis, Pfizer, Humanigen, Precision Biosciences, and Lonza, F. L. 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**Abstract Content:** Based on historical data, most relapses in classical Hodgkin lymphoma (cHL) occur within 5 years of treatment (Raddford et al, BMJ 1997). In the ECHELON-1 study, treatment with brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine (A+AVD) significantly improved modified progression-free survival (PFS) per independent review facility in patients (pts) with newly diagnosed Stage III/IV cHL compared with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) (Connors et al, NEJM 2018). Durable PFS per investigator (INV) benefits with A+AVD vs ABVD in the intent-to-treat (ITT) population, and across most key pt subgroups, were seen after 3 and 4 years’ follow-up (Straus et al, Blood 2020; Bartlett et al, Blood 2019), improvements were seen, irrespective of interim positron emission tomography (PET) scan status, disease stage and baseline disease risk factor score. We report updated efficacy and safety results after 5-years’ follow-up.

Pts with previously untreated Stage III or IV cHL were randomised 1:1 to receive up to 6 cycles of A+AVD (n = 670) or ABVD (n = 670) intravenously on days 1 and 15 of a 28-day cycle. Patients were required to have an interim PET scan after cycle 2 (PET2). Analyses were performed after extended follow-up (cutoff date 18 September, 2020) to assess PFS per INV. Resolution and
improvement (improvement by ≥ 1 grade from worst grade as of the latest assessment) of peripheral neuropathy (PN) in pts with ongoing symptoms at the end of treatment (EoT) were monitored throughout the extended follow-up period. The rate of secondary malignancies, and the incidence and outcomes of pregnancies among pts and their partners were also assessed.

After a median follow-up of 60.9 months (95% confidence interval [CI] 55.2–56.7), estimated 5-year PFS per INV rates were 82.2% (95% CI 79.0–85.0) for A+AVD and 75.3% (95% CI 71.7–78.5) for ABVD. PFS per INV favoured A+AVD over ABVD (hazard ratio [HR] 0.681; 95% CI 0.534–0.867; P = 0.002) (Table). Estimated 5-year PFS with A+AVD vs ABVD in the ITT population was 84.9% vs 78.9% in PET2-negative pts (HR 0.663; 95% CI 0.502–0.876; P = 0.004) and 60.6% vs 45.9% in PET2-positive pts (HR 0.702; 95% CI 0.393–1.255; P = 0.229).

In the A+AVD and ABVD arms, 85% and 86% of pts with treatment-emergent PN had complete resolution or improvement of symptoms. Median time to complete resolution of PN events ongoing at EoT was 34 weeks (range 0–262) in the A+AVD arm and 16 weeks (range 0–267) in the ABVD arm; median time to improvement was 49 weeks (range 8–270) and 12 weeks (range 2–70), respectively. In the A+AVD arm, 29% of pts had ongoing PN with a maximum severity of grade 1 (17%), grade 2 (9%), grade 3 (3%) and grade 4 (<1%). In the ABVD arm, PN was ongoing in 21% of pts; maximum severity was grade 1 (14%), 2 (6%) or 3 (1%). In total, 131 pregnancies were reported; the proportion of ongoing pregnancies or live births in female pts was similar in both arms (85% and 74% in the A+AVD and ABVD arms, respectively).

At 60.9 months’ median follow-up, sustained PFS benefit was observed with A+AVD vs ABVD, which was independent of disease stage and PET2 status. In addition, treatment adaptation by interim PET2 status is not required for A+AVD and bleomycin is avoided. The durable and robust treatment benefit with A+AVD is coupled with a manageable safety profile; these results suggest that A+AVD is an attractive treatment option for all pts with previously untreated Stage III or IV cHL.

### Abstract Table: Table: PFS per INV at 60.9 months by PET2 status and age in the ITT population

<table>
<thead>
<tr>
<th>Group</th>
<th>A+AVD</th>
<th>ABVD</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All pts</td>
<td>n = 664</td>
<td>n = 670</td>
<td>0.681 (0.543–0.867)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>82.2 (79.0–85.0)</td>
<td>75.3 (71.7–78.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PET2-negative</td>
<td>n = 588</td>
<td>n = 578</td>
<td>0.663 (0.502–0.876)</td>
<td>0.004</td>
</tr>
<tr>
<td>PET2-positive</td>
<td>n = 47</td>
<td>n = 58</td>
<td>0.702 (0.393–1.255)</td>
<td>0.229</td>
</tr>
<tr>
<td>Pts aged &lt;60 years</td>
<td>n = 580</td>
<td>n = 568</td>
<td>0.665 (0.505–0.876)</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>60.3 (45.0–73.1)</td>
<td>45.9 (32.7–58.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pts aged ≥60 years</td>
<td>n = 521</td>
<td>n = 493</td>
<td>0.675 (0.492–0.927)</td>
<td>0.14</td>
</tr>
<tr>
<td>PET2-negative</td>
<td>n = 62</td>
<td>n = 50</td>
<td>0.702 (0.370–1.331)</td>
<td>0.274</td>
</tr>
<tr>
<td>PET2-positive</td>
<td>n = 42</td>
<td>n = 50</td>
<td>0.820 (0.494–1.362)</td>
<td>0.370</td>
</tr>
<tr>
<td></td>
<td>63.1 (46.4–75.9)</td>
<td>49.3 (34.7–62.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pts aged &lt;60 years</td>
<td>n = 67</td>
<td>n = 57</td>
<td>0.720 (0.401–1.292)</td>
<td>0.268</td>
</tr>
<tr>
<td></td>
<td>67.1 (59.0–81.3)</td>
<td>54.9 (35.3–74.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pts aged ≥60 years</td>
<td>n = 5</td>
<td>n = 8</td>
<td>0.923 (0.229–3.715)</td>
<td>0.910</td>
</tr>
<tr>
<td></td>
<td>40.0 (5.2–75.3)</td>
<td>25.0 (3.7–55.8)</td>
<td></td>
<td></td>
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</tbody>
</table>

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Prophylactic corticosteroid use with axicabtagene ciloleucel in patients with relapsed/refractory large B-cell lymphoma

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**Abstract Content:** In Cohorts 1+2 (C1+2; N = 101) of ZUMA-1, the pivotal Phase I/II study of axicabtagene ciloleucel (axi-cel) in patients with refractory large B-cell lymphoma (LBCL), rates of Grade ≥3 cytokine release syndrome (CRS) and neurologic events (NEs) were 13% and 28%, respectively, at the 6-month primary analysis (N Engl J Med. 2017;377:2531), and the objective response rate (ORR) was 82% (54% complete response [CR] rate). With a median follow-up (FU) of 51.1 months, median overall survival (OS) was 25.8 months, and the 4-year OS rate was 44% (Jacobson et al. ASH 2020. #1187). In safety management Cohort 4 (C4; N = 41), with its earlier corticosteroid use than C1+2, rates of Grade ≥3 CRS and NEs were 2% and 17%, respectively, and the ORR was 73% (51% CR; Topp et al. ASH 2019. #243). In Cohort 6 (C6), the effect of prophylactic corticosteroid use on CRS and NEs was evaluated. Presented here are results of the primary analysis of C6, alongside those of C4 and C1+2 for context.

Eligible patients were leukapheresed, could receive optional bridging chemotherapy (in C4 and C6 but not C1+2), and received conditioning chemotherapy before axi-cel (target dose, 2x10^6 chimeric antigen receptor [CAR] T cells/kg). Patients in C6 received dexamethasone 10 mg orally on Days 0 (before axi-cel), 1, and 2 and earlier intervention with corticosteroids and tocilizumab. Primary endpoints were incidence and severity of CRS and NEs.

As of 6/16/20, 40 C6 patients had received axi-cel, with median F/U of 8.9 months. The median age was 64 years (50% aged ≥65 years); 58% of patients were male; 55% had Eastern Cooperative Oncology Group performance status of 1; 65% had disease stage III/IV, and 53% received bridging chemotherapy. C6 patients had median tumor burden (by sum of product diameters post-bridging, if given, but before conditioning) lower than C1+2 and C4 (C6, 1184 mm^2; C1+2, 3723 mm^2; and C4, 2100 mm^2). Median baseline LDH was similar in C6 and C4 but was lower in C1+2 (C4, 236 U/L; C4, 262 U/L; and C1+2, 356 U/L).

Among patients who received corticosteroids, median cumulative corticosteroid use (cortisone-equivalent dose) in C6 (1252 mg [n = 40]) was greater than that in C4 (939 mg [n = 30]) but less than that in C1+2 (6388 mg [n = 24]). In C6, there was no Grade ≥3 CRS; 13% of patients had Grade ≥3 NEs, and there were no Grade 5 CRS or NEs. Onset of CRS appeared to be delayed in C6 (median 5 vs 2 days in C4 and C1+2), and 68% of patients had no NEs or CRS within 72 hours of axi-cel. ORR was 99% (80% CR), and 63% of patients had ongoing responses at the data cutoff date.

Median peak CAR T-cell levels trended higher in C6 than in C1+2 and C4 (C6, 64 cells/µL; C1+2, 42 cells/µL; and C4, 53 cells/µL), which was corroborated by median CAR area under the curve in blood (C6, 526 cells/µL×day; C1+2, 462 cells/µL×day; and C4, 511 cells/µL×day). Median peak serum levels of biomarkers associated with CAR T-cell treatment-related adverse events (eg, C-reactive protein, interferon-γ, granulocyte-macrophage colony-stimulating factor, and interleukin-2) were lower in C6 vs C4 and C1+2.

Prophylactic corticosteroid use appears to reduce the rate of severe CRS and NEs and delay onset of CRS, without affecting median peak CAR T-cell levels or responses. Differences in cohort sizes and baseline characteristics should be considered when comparing cohorts. Longer F/U is required to determine the impact on duration of response and survival.

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Retreatment with axicabtagene ciloleucel in patients with relapsed/refractory Indolent non-Hodgkin lymphoma in ZUMA-5

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Abstract Content: The clinical efficacy of retreatment with axicabtagene ciloleucel (axi-cel) anti-CD19 chimeric antigen receptor (CAR) T-cell therapy in indolent non-Hodgkin lymphoma (iNHL) is unknown. Here, we report outcomes of patients with relapsed/refractory (R/R) iNHL retreated with axi-cel in the primary analysis of ZUMA-5.

Eligible adults with follicular lymphoma (FL) or marginal zone lymphoma (MZL) had R/R disease after ≥2 lines of therapy. Patients were eligible for retreatment if they progressed after a complete response (CR) or partial response (PR) at 3 months and had no evidence of CD19 loss or Grade 4 cytokine release syndrome (CRS) or neurologic events (NEs) with first treatment. At both first treatment and retreatment, patients received conditioning chemotherapy followed by axi-cel (2×10^6 CAR T cells/kg).

As of 12/3/2020, 11 patients with iNHL (9 FL; 2 MZL) were retreated with axi-cel. Before first treatment, 82% of patients had stage 3–4 disease, 91% had ≥2 FLIPI, and 91% had high tumor bulk (GELF). The median prior lines of therapy was 4 (range, 2–7); 60% of patients progressed <2 years after initial chemoimmunotherapy
(POD24), and 82% had refractory disease. Retreated patients had significantly higher tumor burden (median sum of product diameters (SPD)) before first treatment than nonretreated patients (3981 vs 2303 mm²; \( P = 0.014 \)).

After first treatment, 10 patients achieved a CR, and 1 patient achieved a PR. The first median DOIR was 8.3 months. CRS occurred in 7 patients (4 Grade 1; 3 Grade 2), and NEs occurred in 4 patients (3 Grade 1; 1 Grade 2). Among patients with FL, those who received retreatment \( (n = 9) \) had lower median peak CAR T-cell levels at first treatment versus those who did not receive retreatment \( (n = 115) \): 13.2 vs 41.9 cells/µl; \( P = 0.024 \); median peak CAR T-cell levels were also lower when normalized to SPD (0.003 vs 0.023 cells/µL/mm²; \( P = 0.006 \)). Similar trends were observed in patients with MZL.

All 11 patients with iNHLL also responded to axi-cel retreatment, with 10 patients achieving a CR and 1 achieving a PR. With a median follow-up of 2.3 months, responses were ongoing for 9 patients (82%) at the data cutoff date. Comparable instances of CRS and NEs were observed with retreatment as with first treatment; CRS occurred with retreatment in 8 patients (6 Grade 1; 2 Grade 2), and NEs occurred in 4 patients (3 Grade 1; 1 Grade 2). No patient experienced Grade ≥3 CRS or NEs with retreatment. Median peak levels of cytokines typically associated with severe CRS and NEs were numerically similar at retreatment and first treatment (IL-6, 5.4 vs 5.5 pg/ml; IL-2, 1.8 vs 0.9 pg/ml; IFN-γ, 62.9 vs 64.2 pg/ml).

At retreatment, SPD was lower than that before first treatment (674 vs 3981 mm²; \( P = 0.004 \)). Median levels of cytokines typically associated with tumor burden appeared lower before retreatment than before first treatment in patients with FL (TNFa, 1.4 vs 5.3 pg/ml; IL-2Rα, 1.6 vs 19.4 ng/ml). Median peak CAR T-cell levels were similar for patients with FL at retreatment as at first treatment (9.0 vs 13.2 CAR-positive cells/µL blood) and remained similar when normalized to SPD (0.006 vs 0.003 cells/µL × mm²).

With a limited sample, axi-cel retreatment exhibited a high response rate in patients with R/R iNHLL. Safety profiles and CAR T-cell expansion were similar at retreatment and first treatment, and SPD was lower before retreatment vs first treatment. Confirmatory analyses with more patients and longer follow-up are needed.

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L. Goyal, PhD Conflict with: Employment with Kite, a Gilead Company; stock or other ownership in Gilead; J. Chou, PhD Conflict with: Employment with Kite, a Gilead Company; stock or other ownership in Kite, a Gilead Company, and Five Prime Therapeutics; travel support from Kite, a Gilead Company; V. Plaks, LLB, PhD Conflict with: Employment with Kite, a Gilead Company; M. P. Avanzi, MD, PhD Conflict with: Previous employment with Kite, a Gilead Company; stock or other ownership in Kite, a Gilead Company and Gilead; patents, royalties and other intellectual property from MSKCC, NYBC, and travel support from Gilead.

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Transcriptional suppression of WEEl and PARP1 genes improve sensitivity to Rituximab: a novel promising targets to overcome drug resistance in diffuse large B-cell lymphoma

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**Abstract Content:** Diffuse Large B-Cell Lymphoma (DLBCL) is the commonest and most aggressive type of lymphoma worldwide. Currently, more than 40% of DLBCL patients are relapsed on the standard therapy which is composed of chemotherapy (CHOP) and Rituximab (anti-CD20). Up to date, the exact mechanism of resistance is not fully understood. Although, new anti-cancer drugs have been discovered in the last years, it is still unclear whether these drugs can improve the patient’s response without antagonizing the efficacy of anti-CD20. Therefore, a persistent need to overcome the resistance to Rituximab in DLBCL become mandatory. In the current study, we aimed to access the biological effects of the dual transcriptional suppression of WEEl and PARP1 genes in Rituximab resistant DLBCL cell lines. The study was conducted on three phases: [1]: 

**Bioinformatics analysis:** An Integrative bioinformatics analysis was conducted to screen the differentially expressed genes (DEGs) linked to Rituximab resistance in DLBCL and the biological significance of these genes was examined. Furthermore, a weighted gene co-expression network analysis was construct, from which we identified the co-expressed genes “WEEl and PARP1” that have crucial determines of Rituximab resistance. [2]: 

**Transcriptional suppression:** We perform an in-vitro transcriptional suppression of two genes (WEEl and PARP1) in Rituximab resistant and sensitive DLBCL cell lines, using siRNAs. [3]: The biological effect of suppression was tested by the following assays: (1): the cell cytotoxicity was evaluated by cell proliferation assay (MTT), (2): the cell apoptosis was detected by Flow cytometry using Annexin V and Propidium iodide staining, (3):
the WEE1 and PARP1 proteins expression was detected in transfected cells using immunofluorescence technology. (4): gene expression analysis for WEE1 and PARP1 genes was measured by qPCR. We demonstrated that transcriptional suppression of WEE1 and PARP1 genes induce apoptosis and enhance anti-apoptotic dependency in DLBCL. In addition, treatment of cell lines with si_WEE1 and si_PARP1 induce a significant reduction in cell viability from as detected for Annexin V/PI staining by flow cytometry. Moreover, increase sensitivity of DLBCL cells to Rituximab was observed in WEE1 and PARP1 suppressed cells, and the co-suppression of both genes was more effective than suppression of single gene. Finally, marked reduction for protein and gene expression were detected in suppressed cells as proved by IF and qPCR. In conclusion, dual suppression of WEE1 and PARP1 genes in combination with Rituximab can be used as an approach to enhance sensitivity and overcome resistance to Rituximab in DLBCL.

Keywords: Rituximab, WEE1, PARP1, Lymphoma, drug resistance.

Disclosure of Interest: None Declared

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CheckMate 436: primary efficacy and safety analysis of the PHASE 2 Study Evaluating Nivolumab Combined With Brentuximab Vedotin for Relapsed/Refractory Mediastinal Gray Zone Lymphoma

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Abstract Content: Mediastinal gray zone lymphoma (MGZL) is a rare form of non-Hodgkin lymphoma (NHL) with intermediate features between classical Hodgkin lymphoma (cHL) and primary mediastinal B-cell lymphoma (PMBL); shared features include tumor CD30 expression, 9p24.1 chromosomal alterations, and programmed death 1 (PD-1) ligand expression. Compared with PMBL, MGZL patients (pts) with MGZL have inferior survival outcomes. Nivolumab is a fully human IgG4 PD-1 immune checkpoint inhibitor antibody commonly used in combination with brentuximab vedotin (BV), an anti-CD30 antibody–drug conjugate. The ongoing CheckMate 436 study (NCT02581631) includes pts with relapsed/refractory (R/R) NHL subtypes with CD30 expression (DLBCL, PTCL, CTCL, PMBL, MGZL); nivolumab + BV treatment demonstrated a high objective response rate (ORR; 73%) and complete response (CR) rate (37%) in pts with PMBL. This analysis evaluated the efficacy and safety of nivolumab + BV in the MGZL cohort of the open-label, phase 1/2 CheckMate 436 study.

The expansion cohort of the study enrolled adult (≥18 years old) pts with ECOG performance status of 0 or 1, who had confirmed R/R MGZL after autologous hematopoietic cell transplantation (auto-HCT) or, if ineligible for auto-HCT, after ≥2 multi-agent chemotherapy regimens. Pts received 240 mg nivolumab (day 8 of cycle 1, then day 1 of later cycles) and 1.8 mg/kg BV (cycle day 1) every 3 weeks until disease progression or unacceptable toxicity. Primary endpoints were investigator-assessed ORR (Lugano 2014 criteria) and safety.

Among 10 treated, evaluable pts, median age (range) was 35 (25–72) years; 6 pts (60%) were male. Pts had a median of 2 prior lines of systemic therapy and none had received prior auto-HCT. At 8 months after the last pt received the first treatment (database lock), all pts had discontinued treatment; 5 due to disease progression, 3 due to maximum clinical benefit, 1 due to alopecia (alo)-HCT, and 1 due to auto-HCT. Pts received a median of 7 doses each of nivolumab and BV. ORR was 70% (80% CI, 45–88%), with 5 pts (50%) achieving CR. Time to CR was 1.2–4.8 months; duration of CR was 1.5–3.2 months before pts were censored for subsequent therapy. Pts who achieved CR were bridged to HCT (4 allo-, 1 auto-) and censored (all were alive at database lock). Eight of 9 (89%) pts who were evaluable for response had ≥25% tumor reduction. At a median follow-up of 12.4 (range, 0.1–25.5) months, the 6-month overall survival rate was 80.0% (95% CI, 40.9–94.6). Duration of response and progression-free survival could not be estimated due to censoring of pts who received subsequent therapies. Nine pts (90%) experienced treatment-related adverse events (TRAEs); the most common were neutropenia (n = 3; 1 grade 1, 1 grade 2, and 1 pt experienced 4 grade 1/2 events and 1 grade 3 event) and paresthesia (n = 3; all grade 1). Three pts had grade 3–4 TRAEs. Infusion-related reaction occurred in 1 pt (grade 1). One pt had an immunemediated AE (grade 2 maculopapular rash; resolved without systemic steroids). One pt had a serious drug-related AE (grade 3 febrile neutropenia). All 3 deaths were caused by disease progression.

In pts with R/R MGZL, nivolumab + BV demonstrated a high investigator-assessed ORR of 70%, with a 50% CR rate and a tolerable safety profile, similar to findings in PMBL. The regimen represents a potential option for bridging to HCT based on the rapid and frequent responses and favorable safety profile compared with standard chemotherapy.

Disclosure of Interest: A. Santoro Conflict with: Arqule, Sanofi, Conflict with: Advisory Board: Bristol Myers Squibb, Servier, Gilead, Pfizer, Eisai, Bayer, MSD; Speaker’s Bureau: Takeda, Bristol Myers Squibb, Roche, AbbVie, Amgen, Celgene, Servier, Gilead, AstraZeneca, Pfizer, Arqule, Lilly, Sandoz, Eisai, Novartis, Bayer, MSD, A. Moskowitz Conflict with: Miragen, Seattle Genetics, Merck, Bristol Myers Squibb, and Incyte, Conflict with: Honoraria: Immunib Therauteics L.P., Merck, and Seattle Genetics, S. Ferrari: None Declared, C. Carlo-Stella Conflict with: Boehringer Ingelheim and Sanofi , Conflict with: ADC Therapeutics and Rhizene Pharmaceuticals, Conflict with: Membership on an entity’s Board of Directors or Advisory Committees - Servier, Novartis, Genenta Science srl, ADC Therapeuticals, F. Hoffmann-La Roche, Karyopharm, Jazz Pharmaceuticals,Honoraria - Bristol-Myers Squibb, Merck Sharp & Dohme, Janssen Oncology, AstraZeneca, G. Collins Conflict with: Roche, Takeda, Gilead, BeiGene, Incyte, Daiichi Sankyo, Conflict with: Bristol Myers Squibb, MSD, Cellerton, Pfizer, Amgen, M. Fanale Conflict with: Employee and equity holder – Seattle Genetics, S. Francis Conflict with: Employment and equity ownership – Bristol Myers Squibb, M. Sacchi Conflict with: Employee - Bristol Myers Squibb, K. Savage Conflict with: Merck, Bristol Myers Squibb, Seattle Genetics, Gilead, AstraZeneca, AbbVie, Servier, Conflict with: Roche, Bristol Myers Squibb, Conflict with: Other: BeiGene (steering committee); Merck, Bristol Myers Squibb, Seattle Genetics, Gilead, AstraZeneca, AbbVie (honoraria), Kyowa

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The risks of hematological toxicities and bleeding with acalabrutinib in the treatment of chronic lymphocytic leukaemia

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Abstract Content: More selective second-generation Bruton's tyrosine kinase inhibitors (BTKi) including acalabrutinib were developed to potentiate efficacy and minimize toxicity associated with first-generation BTKi in the treatment of high risk or TP53 mutated chronic lymphocytic leukaemia (CLL). We undertook a systematic review and meta-analysis of randomized controlled trials (RCT) to determine the risks of haematological toxicities and bleeding in patients with CLL treated with acalabrutinib.

A comprehensive literature search was performed through MEDLINE, Embase databases and meeting abstracts up to 31st July 2020. Phase III RCTs utilizing acalabrutinib in patients with CLL were incorporated in the analysis. Mantel-Haenszel (MH) method was used to estimate the pooled risk ratio (RR), and risk difference (RD) with 95% confidence interval (CI) for anaemia, thrombocytopenia and bleeding. Heterogeneity was assessed with I2 and Cochran’s Q statistic.

The characteristic features of included studies were summarised in Table 1. A total of 833 patients with CLL from two phase III RCTs ([n = 526] in ELEVATE TN, and [n = 307] in ASCEND) were eligible. Acalabrutinib was administered to 357 patients with treatment-naïve CLL in ELEVATE TN study and to 154 patients with relapsed or refractory CLL in the ASCEND study. The I2 statistic in our meta-analysis was low, suggesting homogeneity among RCTs.

Any-grade anaemia occurred in 13.5% of participants in acalabrutinib arm compared to 10.5% in the control arm with the RR of 1.27 (95% CI: 0.87–1.87; P = 0.22). Similarly, 7.8% of patients treated with acalabrutinib-based regimen and 7.1% of patients treated with non-acalabrutinib based regimens reported high grade anaemia and the RR was not statistically significant at 1.17 (95% CI: 0.72–1.91; P = 0.52). The pooled RR observed for neutropenia were statistically significant as follows: any-grade neutropenia 0.46 (95% CI: 0.37–0.57; P < 0.00001); and high-grade neutropenia 0.45 (95% CI: 0.36–0.57; P < 0.00001). Any-grade neutropenia and high-grade neutropenia were reported in 20.5% and 18.4% in acalabrutinib groups compared to 43.8% and 39.7% in control groups, respectively. Any-grade thrombocytopenia occurred in 10.3% of participants in acalabrutinib arm compared to 13.9% in the control arm with RR of 0.75 (95% CI: 0.51–1.09; P = 0.13). 5.1% of patients treated with acalabrutinib arm and 9.3% of patients treated with non-acalabrutinib based regimen reported high-grade thrombocytopenia and the pooled RR was statistically significant at 0.51(95% CI: 0.30–0.84; P = 0.009). 36.4% of patients treated with acalabrutinib reported any-grade bleeding compared to 9.6% in the control group with RR of 3.50 (95% CI: 2.45–5.00; P < 0.00001) and RD of 0.25 (95% CI: 0.20–0.30; P < 0.00001). However, major bleeding occurred in only 1.7% of patients in the acalabrutinib group and 1.2% in the control group and the pooled RR for major bleeding was not statistically significant at 1.53 (95% CI: 0.45–5.15; P = 0.49).

Our meta-analysis demonstrated that patients on acalabrutinib monotherapy or combination regimens experienced higher incidence of any grade of bleeding, but lower incidence of all grades of neutropenia and high-grade thrombocytopenia compared to non-acalabrutinib based therapy. However, there were no statistically significant differences in the risks of major bleeding between the two groups. Careful consideration of bleeding risks should be given with acalabrutinib in patients on antithrombotic treatment.

Disclosure of Interest: None Declared

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Extrapolating progression free survival curves in chronic lymphocytic leukaemia (CLL) using peripheral blood minimal residual disease (MRD) measurements from venetoclax trials

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Abstract Content: Sequential MRD measurements in the peripheral blood in relapsed/refractory CLL were modelled and analysed for two venetoclax monotherapy trials (M13982 & M14032) and the Murano trial for the combination treatment regimen of venetoclax plus rituximab.

To understand the dynamics of changing MRD peripheral blood levels during and after treatment, predict the shape of PFS curves beyond their current timescale as a means of potentially shortening the duration of future clinical trials, and model the rate of fall of MRD to potentially tailor treatment.

Mathematical modelling techniques were used to examine the way that blood MRD levels fall initially with treatment, and either stay at levels below the MRD sensitivity range, or begin to rise, ultimately leading to progression. The slope of disease regrowth was extrapolated back to the start of treatment (y-intercept) to identify an estimate of the upper limit of pre-treatment resistant disease (i.e. the applied model assumes that resistance does not evolve during treatment). At a population level, the parameters obtained by examining

Abstract Table: Table 1 Characteristics of the studies included in the meta-analysis

<table>
<thead>
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<th>Study</th>
<th>Author (Year)</th>
<th>Study type</th>
<th>Study phase</th>
<th>Type of cancer</th>
<th>Line of treatment</th>
<th>Number of patients and Treatment rendered</th>
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<td>ELEVATE-TN</td>
<td>Sharman</td>
<td>Randomized, multicenter, open-label study</td>
<td>Phase III</td>
<td>Treatment-naïve chronic lymphocytic leukaemia</td>
<td>First line</td>
<td>178 Acalabrutinib + Obinutuzumab</td>
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<td></td>
<td>(2020)</td>
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<td></td>
<td></td>
<td></td>
<td>179 Acalabrutinib</td>
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<td></td>
<td></td>
<td></td>
<td>169 Obinutuzumab + Chlorambucil</td>
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<tr>
<td>ASCEND</td>
<td>Ghia (2020)</td>
<td>Randomized, multicenter, open-label study</td>
<td>Phase III</td>
<td>Relapsed or refractory chronic lymphocytic leukaemia</td>
<td>Second line onwards</td>
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<td>35 Bendamustine + Rituximab</td>
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</table>
Lymphoma, CLL and Myeloma

the distribution both of regrowth rates and of this initially resistant disease were then input to a previously developed mathematical model to generate the relevant PFS curve and project it forward in time.

The MRD levels in the peripheral blood fall with different degrees of rapidity, following which they rise in a pattern found to be clearly consistent with exponential regrowth in all 3 trials. Re-growth rates were consistent across trials and were clearly log-normally distributed. In the Murano trial, looking at the 145 out of 389 patients who had 3 or more rising MRD levels, the mean log doubling time of regrowth rates came to 51 days (SD = 31) in this population.

Back-extrapolating the MRD levels to calculate levels of (resistant) cells at the start of treatment showed a clear correlation between these levels and the regrowth rates for all 3 trials. It can be inferred that patients with more rapidly growing disease had lower levels of what was assumed to be resistant disease at the start of treatment. The rate of fall of MRD was also modelled and showed a correlation both with subsequent PFS ($\chi^2=21.1$ stratifying by arm, $P < 0.0001$) and with the back-extrapolated $y$-intercept ($r = 0.43$, $P < 0.001$). It appears that patients with more rapidly growing disease have a more rapid decline on venetoclax, and their disease is reduced to lower levels such that it takes longer for the disease to progress, as well as potentially increasing the proportion of patients where the disease is reduced to such a low level that progression is very long, or possibly even prevented completely.

The Murano venetoclax plus rituximab PFS curve is predicted to gradually fall to a plateau. This was corroborated independently by fitting this model to a combination of the Murano data and another set of older combination chemotherapy data with much longer follow-up, which provides a kind of anchor to fix the general shape of the curve.

MRD modelling enables PFS curves to be effectively extrapolated beyond their current timescale, with the potential to shorten the duration of future clinical trials.

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**BSH2021-PO-154**

A Phase 1 study Of CC-92480, a novel CELMoD agent, in patients with relapsed/refractory multiple myeloma: pharmacodynamic effects of dose and schedule

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**Abstract Content:** CC-92480-MM-001 is a phase 1 study (NCT03374085) investigating the effects of a broad range of doses and schedules of CC-92480, an oral novel cereblon (CRBN) E3 ligase modulator (CELMoD) agent, in heavily pre-treated pts with RRMM. CC-92480 co-opts CRBN to enable rapid degradation of the transcription factors Ikaros and Aiolos, leading to apoptosis of myeloma cells and immune-stimulatory effects. The pharmacodynamic (PD) effects of CC-92480 are presented here.

An adaptive Bayesian dose-escalation design was used to evaluate several dosing schedules. Continuous schedules included 10 days (d) on + 4 d off × 2, and 21 d on + 7 d off in a 28-d cycle; intensive schedules included 3 d on + 11 d off × 2, and 7 d + 7 d off × 2. For characterization of PD changes, an intensive biomarker sampling programme was included. For biomarker analysis, peripheral blood (PB) and bone marrow (BM) aspirates (BMA) were obtained from pts enrolled in part 1 of the dose-escalation study. Biomarker analyses included Ikaros and Aiolos levels in PB mononuclear cells by flow cytometry; CRBN, Ikaros, Aiolos, and ZFP91 expression by immunohistochemistry (IHC) in BMA; weekly levels of serum free light chain (sFLC) and soluble B-cell maturation antigen (sBCMA); and effects on immune cells in PB. CC-92480 plasma exposures were also collected.

Based on tolerability, efficacy, and PD effects, the CC-92480 recommended phase 2 dose (RP2D) was selected at 1.0 mg, 21/28 d. In BM plasma cells, degradation of Ikaros and Aiolos was evident at all dose levels independent of baseline CRBN staining intensity and prior treatment. CC-92480 at the RP2D induced rapid and sustained decreases in sFLC (median 94%) and sBCMA (median 78%) in Cycle 1. Ikaros and Aiolos degradation in PB T cells was dose-dependent.
BSH2021-PO-155


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Abstract Content: Systemic anaplastic large cell lymphoma (sALCL) is a T-cell lymphoma, historically associated with low cure rates

following relapse. Expression of the ALK protein is more common in younger patients and associated with improved survival outcomes. Following a pivotal phase II study (Pro et al) and European licence, the immuno-conjugate Brentuximab Vedotin (BV) became available in England via the Cancer Drugs Fund (CDF) in 2013. To date, no large-scale population-based studies have described outcomes following BV. Public Health England (PHE) collects information on all cancer diagnoses in England, and since April 2012 all delivered Systemic Anti-Cancer Therapy (SACT). We aimed to evaluate whether routinely collected PHE data can reliably assess outcomes of patients with lymphoma. Survival outcomes for BV mono-therapy in relapsed ALCL in all England was chosen as a pilot project to explore the value of PHE data due to the well-defined disease and SACT cohort.

Following NHS REC approval, we requested anonymised Office of Data Release (ODR) information on sALCL patients ≥18 years treated with BV mono-therapy between 1st Jan 2014-31st Dec 2019. We excluded primary cutaneous and breast-implant associated ALCL, patients in the ECHELON-2 trial and BV received in combination. We requested baseline demographics, ALK status, dates and number of BV cycles, and SACT data prior to and following BV, prior autologous/allogeneic stem cell transplantation (SCT). Kaplan-Meier survival methods were used to compare the primary outcome of all-cause mortality between groups defined on the basis of age, gender and ALK status (positive vs. negative) in univariate analyses.

173 patients were identified, of whom 46 were excluded. The final cohort comprised 127 patients with t/r ALCL with a median age of 60 years at initiation of BV and median follow up time of 10 months. 49 (38.6%) patients were ALK+ve and 78 (61.4%) ALK-ve. The median time from diagnosis to BV was nine months (range 1–143), 106 (83.5%) received BV second line, and 13 (10.2%) third or fourth line. 95 (74.8%) received CHOP first line. Based on SACT data 18 (14.2%) received SCT in first remission (16 auto, 2 allo). The median number of BV cycles received was five. Median 2-year overall survival (OS) was 46.6%. The majority (59) of deaths occurred within the first 18 months, followed by a survival plateau with only four subsequent deaths. There were 20 (15.7%) deaths prior to cycle 5, the timepoint where the CDF mandates response assessment. There was no difference in OS between ALK+ve and ALK-ve (P = 0.78), age <40 vs ≥40 years (P = 0.89), age <60 vs ≥60 (P = 0.96), between genders (P = 0.25) or prior SCT (P = 0.55). Two patients received SCT after BV, with both alive 18+ months post-transplant. Receiving BV second line therapy was associated with improved survival, with 2-year OS of 50.3% versus 29.7% for those third or fourth line (P = 0.03).

We confirm BV is a highly effective treatment for t/r sALCL with real world survival outcomes across sub-groups highly comparable with clinical trial data. Weaknesses of this study include lack of information on toxicity and data from double blind studies, although this data is now being collected. Analysis of routinely collected PHE data offers the opportunity to undertake high quality, nationwide population-based studies, to inform the efficacy of high-cost drugs such as BV in routine clinical practice.

Disclosure of Interest: None Declared

BSH2021-PO-156
Parathyroid hormone levels and prognosis in multiple myeloma?
George Vassiliou*, Joanna Su Ling Tung**
*Department of Haematology, Cambridge University Hospitals Trust, Cambridge, United Kingdom

Abstract Content: Based on anecdotal reports of raised serum parathyroid hormone (PTH) levels in some patients with multiple myeloma, we set out to investigate if this is a common finding and to establish if parathyroid hormone levels act as predictors of outcome in multiple myeloma.

- Patients with newly diagnosed multiple myeloma at Cambridge University Hospitals between 2015 and 2021 were identified from electronic records (EPIC). Blood parameters including paraprotein, PTH, beta-2 microglobulin (ß2M), albumin and others, recorded near the time of diagnosis were collected. We use the International Staging System (ISS), defined as, ISS stage I: ß2M <3.5 mg/L and albumin ≥35 g/dl, ISS stage II: neither I or III, ISS stage III: ß2M ≥3.5 mg/L and our novel ‘ISS+PTH’ score, calculated from a sum of: ß2M <3.5 mg/l (0), ≥3.5 mg/l (1); PTH <10 pmol/l (0), ≥10 pmol/l (1); albumin <35 g/dl (0), ≥35 g/dl (0). We use Pearson correlation and Kaplan-Meier survival analyses to investigate factors that correlate with PTH levels and assess their impact on prognosis.

We identified 1066 patients with multiple myeloma (640 men/426 women). Median age at diagnosis was 70 years and median survival was 832 days. Of these, 182 had PTH levels assayed at diagnosis. Median serum PTH level was 4.77 pmol/l (range 0-103.3 pmol/l) and 35 patients had PTH >10 pmol/l. Median survival for those with PTH >10 pmol/l was 859 days, compared to those with PTH <10 pmol/l, with a median survival of 1495 days (P <0.029). PTH level significantly correlated with creatinine and other parameters (Table 1A). To understand if PTH levels can enhance the predictive power of the International Staging System (ISS), we compared the performance of the ISS score to a modified score including PTH as a variable, applied to participants for whom all relevant tests were available. We noted that ß2M and albumin levels correlated significantly to each other (r = −0.37), raising the possibility that additional variables could be used to refine prognosis. Therefore, we tested if PTH could be added to ISS and re-stratified patients into 4 categories (Table 1B). Upon incorporation of PTH, we found that distribution across the classes was similar, but the worse prognostic group fared significantly worse (Table 1B). As noted by the mean survival differences between ISS and ISS+PTH, we observed better separation of the categories on survival curves by the latter. Of note, 17 patients with a very high PTH (>15 pmol/l) had a significantly poorer mean survival of 368 days and high median values for albumin (28.5 g/L), ß2M (12.2 mg/L), creatinine (258 µmol/L) and Corrected Calcium (2.35 mmol/L).

Collectively, our findings show that PTH levels correlate with other parameters and do not significantly improve the prognostic ability of the ISS score overall, but do identify a group with particularly poor prognosis. PTH has a very short half-life of 5 minutes, as it is rapidly cleared by the liver and kidney, so the correlation with creatinine and urea may allude to renal failure being at least partially responsible for PTH accumulation. In addition, our findings show that PTH levels in multiple myeloma are often inappropriately elevated in relation to the prevailing calcium level, a factor that can contribute to the cytokine-driven myeloma bone disease. Therefore, we next investigate the impact of inappropriately raised PTH on myeloma bone disease per se and any clinical/therapeutic implications this may have on patient management.

Abstract Table: Table 1: Comparison of ISS and ISS-PTH prognostic scores

<table>
<thead>
<tr>
<th>(A) Significant Correlations to PTH</th>
<th>Unsignificant Correlations to PTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>0.520**</td>
</tr>
<tr>
<td>Urea</td>
<td>0.439**</td>
</tr>
<tr>
<td>Potassium</td>
<td>0.326**</td>
</tr>
<tr>
<td>ß2M and serum</td>
<td>0.192*</td>
</tr>
<tr>
<td>Lambda free light chain</td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>-0.185*</td>
</tr>
</tbody>
</table>

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Adjusted calcium  
Paraprotein  
(B)  
Kappa/Lambda ratio  
Survival  
Mean survival (days)

<table>
<thead>
<tr>
<th>Score (ISS)</th>
<th>Number of patients</th>
<th>Mean survival (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>67 (23.8%)</td>
<td>1651</td>
</tr>
<tr>
<td>II</td>
<td>192 (68.3%)</td>
<td>1360</td>
</tr>
<tr>
<td>III</td>
<td>22 (7.8%)</td>
<td>1152</td>
</tr>
</tbody>
</table>

Total score (ISS+PTH)  
1 50 (27.6%) 1480  
2 65 (35.9%) 1712  
3 54 (29.8%) 1108  
4 12 (6.6%) 823

A. Correlations to PTH, * significant. B. Numbers per class and mean survival for patients classified using the ISS and ISS+PTH scores.

Disclosure of Interest: None Declared

BSH2021-PO-157
The clinical outcome of haemato-oncology patients who tested positive for the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a single centre experience

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Abstract Content: Background: The emergence of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had a significant impact on the management of haematological malignancies. Local and national guidelines had to be implemented rapidly to ensure the safety of patients. I present a single centre experience on the impact of SARS-CoV-2 infection in the management of blood cancer patients.

Aim: To assess the clinical outcome of patients with the diagnosis of haematological malignancy who tested positive for the SARS-CoV-2 virus.

Methods: A prospectively maintained database of adult haematology oncology patients who tested positive for SARS-CoV-2 was created at the start of the COVID-19 pandemic. All reported patients had a positive SARS-CoV-2 PCR nasal swab.

Results: 41 patients with an underlying haematological malignancy tested positive for SARS-CoV-2 between 27/03/20 and 03/01/21 at University Hospital of Wales, Cardiff. Mean age at diagnosis was 62 years old (range 18-90) and 75.6% were males. 60.9% (25/41) patients had a diagnosis of lymphoid malignancy, the commonest reported diagnosis was chronic lymphocytic leukaemia in 22% (9/41). Half of the patients (51%) were receiving chemotherapy or chemo-immunotherapy, 24.3% were awaiting to start treatment, 9.8% post-treatment and 7.3% were either managed with observation or palliation. 46.3% (19/41) had other risk factors, the commonest was hypertension in 17% (7/41) followed by Hypogammaglobulinaemia in 14.6% (6/41), 80% (33/41) required hospital admission with an average hospital stay of 12.9 days (range 1-45). 46.3% (19/41) presented with symptoms of fever and/or shortness of breath, this was followed by cough in 39% (16/41). 19.5 % (8/41) patients required invasive ventilation and 4.8% (2/41) had Continuous positive airway pressure (CPAP). Unfortunately, all 10 patients who required escalation of care died. 19.3% received Dexamethasone, 7.3% Remdesivir and 2.4% received either Anakinra or Tocilizumab. 39% (16/41) died within 28 days following the diagnosis of COVID which was considered the main cause or a major contributing factor, 51% (21/41) recovered and 9.7% were deemed to have a false positive result following further investigations and discussions with virologists. Complications reported in our cohort included multi-organ venous thrombosis, Ischemic bowel, upper limb deep vein thrombosis, right atrial thrombus, acute left middle cerebral artery infarction and invasive pulmonary fungal infection each reported in 1 patient. 15 patients had their treatment delayed or interrupted following COVID-19 diagnosis. 11 patients had serial SARS-CoV-2 PCR testing before starting treatment. Average time for patient test negative was 22.1 days (range 7-40) and the average time to start treatment was 27.8 days (range 7-50).

Summary: The true burden of SARS-CoV-2 infection in haematology patients is likely to be underestimated. Patients with mild or no symptoms are likely to go undetected. Despite this, our database demonstrated the significant morbidity and mortality associated with SARS-CoV-2 infection. There was a significant delay in initiating treatment following COVID-19 infection. Although 4 patients were deemed to have a false positive PCR swab, this resulted in delays starting treatment including 2 patients who were admitted for stem cell transplant procedures. Ongoing data collection remains vital to guide further management.

Disclosure of Interest: None Declared

BSH2021-PO-158
Atypical infections with BCRi: real world data in chronic lymphocytic leukaemia patients from a London tertiary referral centre

Hanna Renshaw*, Satyen Gohil, Amit Nathwani, Parag Jasani

Abstract Content: Patients with chronic lymphocytic leukaemia (CLL) are at risk of developing infections due to the immune dysfunction inherent to the disease and the immunosuppressive effects of its treatment. More atypical infections were seen, in addition to bacterial infections, with the introduction of fludarabine based chemotherapy replacing the conventional alkylator regimens. Now with the newer molecular targeted therapies changing the therapeutic landscape of the disease, we have seen higher rates of atypical infections, such as Aspergillus, pneumocystis pneumonia (PCP) and cytomegalovirus (CMV), adding to the morbidity and mortality of the disease. Current European Medicine Agency guidance is that PCP prophylaxis and CMV monitoring is carried out for patients taking Idelalisib but not routinely for patients on ibrutinib. Anti-fungal prophylaxis is not routinely prescribed and care must be taken due to potential CYP3A4 interactions.

We conducted a retrospective evaluation of all patients who have received Ibrutinib, Idelalisib or Venetoclax for CLL in our tertiary referral centre. All patients were followed up at our centre throughout treatment. Baseline patient characteristics were collected as were all lines of therapy received. All opportunistic infections occurring during molecular treatment were recorded, including PCP, invasive and disseminated fungal infections, toxoplasmosis, viral disseminated infections and localised zoster reactivation. Infection diagnosis was determined based on treating physicians’ documentation and confirmatory or radiological testing. Concurrent steroid or other immunosuppressive use was collected and multiple infections occurring in the same patient were considered separately unless caused by the same agent.

A total of 117 patients were analysed. 73% (85) were male and the median age at diagnosis was 59 years (39-86 years). The median lines of treatment received were 2 (range 1-10), 7.7% (9) of patients had received all three molecular agents, ibrutinib, idelalisib and venetoclax. 12.8% (15) had received venetoclax and ibrutinib. 4.3% (5) had received venetoclax and idelalisib. 7.7% (9) had received...
In response to the COVID-19 pandemic, modifications to treatment regimens and delivery of care for clinically vulnerable multiple myeloma (MM) patients have been rapidly implemented alongside shielding restrictions, to minimise risks of exposure to and severe sequelae of COVID-19 infection. Several haematological advisory bodies have produced guidance for clinicians treating MM throughout this time, however one aspect which has received little attention is the psychological impact on patients.

Patients with MM are at risk of both atypical and typical infections, and with the use of haematopoietic cell transplantation (HCT) and immunomodulatory agents (IMiDs) such as thalidomide and lenalidomide, the incidence of infections has increased. While ibrutinib is known to increase the risk of infection, there is a paucity of published data around the rate, type and delay of infections with the addition of an IMiD to the use of ibrutinib. We aimed to determine the infection rate, type and delay of infections in patients receiving ibrutinib and IMiDs.

Material and Methods: We retrospectively reviewed all adult patients receiving ibrutinib for first line or relapsed/refractory multiple myeloma and/or chronic lymphocytic leukaemia (CLL) at two tertiary referral haematology centres in the UK and Canada from January 2016 to May 2020. Details were collected on patient characteristics, treatment regimens, IMiDs prescribed and, for patients with COVID-19, details of infection.

Results: 91 patients were treated with ibrutinib and IMiDs. 41 patients were treated for MM and 50 for CLL. 15 (16%) patients had a COVID-19 infection, of whom 8 (26.7%) were MM and 7 (14%) were CLL. 13 patients (14%) received IMiDs in addition to ibrutinib.

Ibrutinib and idelalisib. 1.7% (2) had received only venetoclax, 10.2% had received only idelalisib and 55.6% (65) had received only ibrutinib.

4.3% (5/117) of patients had atypical infections recorded whilst receiving molecular therapy, with an incidence of 2 per 100 patient years. There were no atypical infections in patients receiving first line treatment and median time to infection was 13 months on therapy (4-32 months). None of them were taking any other forms of immunosuppression and 44% of patients had an IgG <6.0 g/l (29/65).

60% (3/5) of infections were PCP and 66.7% (2/3) of these occurred whilst taking ibrutinib. 66.7% (2/3) of patients had been prescribed prophylaxis although there was no documentation confirming they had been taking this. 40% (2/5) of infections were fungal and no cases of CMV reactivation was recorded on these agents.

Our rates of atypical infection reflect previously published data and remain relatively low. We would strongly recommend PCP prophylaxis in all patients receiving treatment for relapsed CLL. We would also recommend the documentation of compliance with prophylaxis at each clinic visit. Frontline treatment for CLL may not need PCP prophylaxis, however more data is needed to clarify risk prior to a universal recommendation.

Abstract Table:

<table>
<thead>
<tr>
<th>Atypical Infection</th>
<th>Disease Relapse</th>
<th>BCRi Duration on BCRi (months)</th>
<th>Prescribed PCP prophylaxis (N/Y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>PCP</td>
<td>3rd</td>
<td>Ibrutinib</td>
</tr>
<tr>
<td>Patient 2</td>
<td>PCP</td>
<td>4th</td>
<td>Ibrutinib</td>
</tr>
<tr>
<td>Patient 3</td>
<td>PCP</td>
<td>1st</td>
<td>Venetoclax</td>
</tr>
<tr>
<td>Patient 4</td>
<td>Fungal chest infection</td>
<td>2nd</td>
<td>Ibrutinib</td>
</tr>
<tr>
<td>Patient 5</td>
<td>Fungal sinus infection</td>
<td>4th</td>
<td>Ibrutinib</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

BSH2021-PO-160
Patient preferences, treatment satisfaction and quality of life in newly diagnosed and relapsed/refractory multiple myeloma patients receiving injectable-containing or fully oral therapies: the EASEMENT study
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Abstract Content: As multiple myeloma (MM) therapies advance, understanding patients’, caregivers’ and physicians’ perspectives on, and satisfaction with, available treatment options, and the impact of these options on quality of life (QoL), is important.

EASEMENT is a real-world, observational, cross-sectional study conducted in the UK, Canada and Italy using retrospective chart reviews and surveys. The primary objectives were to describe patient and caregiver QoL, patient preference for oral or injectable therapies (single discrete-choice question) and patient satisfaction (Treatment Satisfaction Questionnaire for Medication-9 items [TSQM-9]; questionnaire consisting of 32 questions covering a wide variety of topics including shielding, treatment adaptations and coping with their condition was sent to MM patients at any disease stage from MGUS to 3rd+ relapse that were under the care of the Royal United Hospitals Bath (RUH) haematology team. We received 50 responses with 24 (48%) males and 26 (52%) females. The most common age range was between 66-75 (52%), and 45 (90%) participants were shielding with at least one other person. Responses to the questionnaire demonstrated that whilst full compliance with the government’s shielding advice was initially high (94%), 25 (50%) respondents reported a decrease in their level of compliance as the national lockdown continued with participants stating they had grown ‘bored’ and ‘frustrated’ over not being able to take advantage of their limited lifespan. 19 (38%) patients reported changes to their MM treatment regimens, however 65.7% did not feel these protective measures lessened their concern of COVID-19 infection. Furthermore, when asked which was more important: risk of being infected with COVID-19 or the progression of their MM, at the start of lockdown only 4 (8%) patients considered their MM to be the most important, however at the time of completing the questionnaire this had risen to 11 (22%). When asked if this lockdown period had changed their perception of MM, notable answers from patients stated they had been ‘cheated of time’ and were ‘unable tick off bucket list items’, due to the progressive nature of MM coupled with being advised to stay at home. Overall, patients’ wellbeing was more commonly affected in a negative way due to shielding, most frequently described as a frustrating and isolating experience. Our study outlined that an understanding of the psychological impact of shielding is essential when reviewing efficacy of policies and treatment guidelines. Due to the likelihood of further social restrictions being implemented over the coming months, coupled with evidence from the first wave of COVID-19 infections showing that withholding cancer treatment to cancer patients had an overall detrimental effect, it is necessary for the wellbeing of vulnerable MM patients that a continual assessment of their opinions on COVID-19 and progression of their disease is undertaken in order to limit some of the psychological burden exhibited by participants in our study.

Disclosure of Interest: None Declared

BSH2021-PO-159
The psychological impact of the COVID-19 pandemic on multiple myeloma patients
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1Medical School, University of Bristol, Bristol, 2Haematology Department, Royal United Hospitals, Bath, United Kingdom

Abstract Content: In response to the COVID-19 pandemic, modifications to treatment regimens and delivery of care for clinically vulnerable multiple myeloma (MM) patients have been rapidly implemented alongside shielding restrictions, to minimise risks of exposure to and severe sequelae of COVID-19 infection. Several haematological advisory bodies have produced guidance for clinicians treating MM throughout this time, however one aspect which has been sparsely addressed is the psychological ramifications of living with MM during this pandemic. This study explored how MM patients’ psychological wellbeing was affected by these precautionary changes and aimed to give shielding MM patients representation to express their opinions concerning changes in their mental wellbeing, concerns about treatment changes and balancing the risk of infection with COVID-19 against the progression of their MM. An online psychological assessment of their opinions on COVID-19 and progression of their disease is undertaken in order to limit some of the psychological burden exhibited by participants in our study.

Disclosure of Interest: None Declared
convenience, effectiveness and global satisfaction subscales; score range 0–100, indicating lower-to-higher satisfaction) by newly diagnosed MM (NDMM) or relapsed/refractory MM (RRMM) status and by investigator-classified treatment – injectable-containing (‘injectables’) versus fully oral (‘orals’). A secondary objective was to compare direct healthcare resource utilisation (HRU) between injectable and oral treatments. Descriptive/unadjusted data are presented.

399 patients were enrolled, including 192 NDMM and 206 RRMM patients (status missing for 1 patient). Median age was 71 years (interquartile range 64–76), 61% were male, 74% were retired, 24% had an Eastern Cooperative Oncology group performance status ≥2 and 51%/41% were/were not living with their caregiver (8% missing). At the time of study visit, among NDMM patients, 77% were receiving injectables and 23% orals (treatment regimens are summarised in the Table). 9% of NDMM patients preferred injectables and 34% orals (52% no preference, 5% missing). Among RRMM patients, 42% were receiving injectables and 58% orals (treatment regimens are summarised in the Table). 3% of RRMM patients preferred injectables and 55% orals (34% no preference, 7% missing).

There were no differences in treatment satisfaction between NDMM and RRMM patients. Results from the TSQM domains are reported for injectable versus orals, respectively; mean convenience score was significantly lower (74.7 vs 78.3; \(P = 0.0414\)); mean TSQM perception of effectiveness (72.4 vs 74.7; \(P = 0.3857\)) and global satisfaction (72.1 vs 74.2; \(P = 0.1948\)) scores did not differ. QoL dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) were not significantly different between NDMM and RRMM patients or between patients receiving injectables or orals. When patients were asked to rate their health on a visual analogue scale (range 0, worst imaginable health, to 100, best imaginable health, as perceived by patients), mean score was significantly higher in NDMM versus RRMM patients (68.0 vs 63.1, \(P = 0.0313\)), but similar between patients receiving injectables versus orals (65.0 vs 66.2, \(P = 0.9069\)). Preliminary HRU data suggest that the rate of outpatient visits related to MM and its complications was numerically higher among patients receiving injectables versus orals (2.6 vs 2.3 outpatient visits per patient during the last 6 months or since RR disease).

EASEMENT data indicate patients’ perceived greater convenience with orals versus injectables and that more patients prefer orals versus injectables. Patients receiving orals versus injectables required a numerically lower rate of outpatient visits. Orals are useful options for patients who cannot, or prefer not to, travel to clinics, especially in the context of the COVID-19 pandemic.

Abstract Table:

<table>
<thead>
<tr>
<th>Treatment regimens at index date</th>
<th>NDMM</th>
<th>RRMM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injectables (n = 148)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mAb-based</td>
<td>2%*</td>
<td>56%</td>
</tr>
<tr>
<td>mAb+PI</td>
<td>1%</td>
<td>21%</td>
</tr>
<tr>
<td>mAb+IMiD</td>
<td>1%</td>
<td>20%</td>
</tr>
<tr>
<td>mAb</td>
<td>1%</td>
<td>15%</td>
</tr>
<tr>
<td>PI</td>
<td>9%</td>
<td>14%</td>
</tr>
<tr>
<td>PI+ALK or PI+other</td>
<td>45%</td>
<td>13%</td>
</tr>
<tr>
<td>PI+IMiD</td>
<td>43%</td>
<td>13%</td>
</tr>
<tr>
<td>ALK</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Other†</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td>Orals</td>
<td>NDMM (n = 44)</td>
<td>RRMM (n = 120)</td>
</tr>
<tr>
<td>PI+IMiD</td>
<td>5%</td>
<td>30%</td>
</tr>
</tbody>
</table>

*Percentages do not sum due to rounding; †All PI→ALK; ‡One patient each with PI→stem cells–allogenic stem cell transplant (NDMM), IMiD (RRMM) and IMiD→ALK (RRMM), and data missing for 1 patient with RRMM; §All IMiD→ALK. ALK, alkylating agent; IMiD, immunomodulatory drug; mAb, monoclonal antibody; PI, proteasome inhibitor.


BSH2021-PO-161

The promoting individualised self-management and survivorship (PrISMS) clinic - a multidisciplinary remote monitoring clinic for a patient-centred approach in multiple myeloma

Catherine Lecat1, Marquita Camilleri1, Dunnya DeSilva1, Orla McCourt1, Sarah Worthington1, Alyse Hart2, Inayah Uddin1, Charlotte Roche3, Abigail Fisher4, Kwee Yong1

1University College London Cancer Institute, 2University College London Hospitals NHS Foundation Trust, 3University College London Institute of Epidemiology & Health Care, London, United Kingdom

Abstract Content: Introduction: Myeloma patients who have completed chemotherapy moved from an intensive period of interaction with healthcare professionals, to less frequent visits. At this time, they often struggle with disease burden, treatment side effects and age-related co-morbidities. Improved patient survival with novel therapies has resulted in increasing patient numbers in outpatient haematology clinics. Centralisation of services means that many patients travel long distances to maintain contact with their transplant centres because they value the access to new drugs and clinical trials, and expertise in management of transplant-related complications and relapse. Faced with growing numbers of patients in follow up with survivorship needs, a new patient-centred model of care is needed.

Method: The Promoting Individualised Self-Management and Survivorship (PrISMS) clinic was designed for myeloma patients who are off treatment and in plateau phase. This remote clinic is staffed by a doctor, a nurse specialist and a physiotherapist, a multidisciplinary team (MDT) approach to holistic management centred on patient needs and providing consistent individualised physical activity and lifestyle advice. Two weeks before the consultation, patients complete a questionnaire about their concerns, symptoms and ways in which they would like to improve their health. This allows the MDT to prepare appropriate advice for each patient, ensuring efficient use of consultations. Patients are also required to have a blood test either locally or at University College London Hospital before the clinic.
Results: From March 2019 to October 2020, 54 patients were enrolled into the pilot PrISMS clinic and 197 telephone or video consultations were held. The median call duration was 12 minutes. Most patients had their blood tests (89%) and questionnaires (84%) completed before the appointment. Patients needing closer monitoring or active treatment due to disease relapse (9/54) were referred immediately back to face-to-face clinics. 78% and 89% of patients received nurse specialist’s and physiotherapist’s advice respectively at any point in time, with 11 patients (20%) referred to local exercise programmes. Patients were signposted to survivorship tools such as online exercise videos and lifestyle mobile applications when appropriate. Patient feedback was positive, with 31 of the 36 surveyed patients (86%) agreed or strongly agreed that they felt more confident in self-managing myeloma after PrISMS consultations. 94% (34/36) agreed or strongly agreed that their concerns and symptoms were addressed, and 77% (28/36) gave an overall service rating of good or excellent. Thematic analysis of telephone feedback interviews with 22 participants revealed additional benefits of reduction in travel costs and time, substantially shorter clinic waiting times and reduction in associated psychological stress (Table 1).

Conclusion: This new patient-centred model of care has been demonstrated to be safe and feasible, with good patient satisfaction. We hope that this MDT approach will empower patients, improve their clinical experience, and build trust in their clinical teams, as well as reducing patients’ sense of isolation and vulnerability particularly in this time of COVID-19 crisis. Future work is needed to formally confirm its effects on patient reported outcome measures, safety and healthcare resource usage.

Abstract Table: Table 1: Examples of quotes from telephone interviews

| Pre-clinic blood test and questionnaire | "With the PrISMS process I get it (blood result) there and then and that’s actually really quite a big weight off my mind… So, in that respect it’s been super-helpful really, a big improvement.” |
| | "For my wife and I to come to London, we have to lay out £50. It is so much nicer to have blood tests done locally and an hour later I could be having a normal day.” |
| | "The crib (questionnaire) is a nice idea because it is a reminder. It makes you review what you wouldn’t otherwise do. And I don’t think I would have done if I had a face-to-face consultation.” |
| | "(The questionnaire) allows me to direct the doctors to talk about the things that I want to talk about. Sometimes when you have a phone interview, you don’t get to say the things you want to say, it gives the chance to set the agenda for the discussion.” |

Table 1. (Continued)

| Waiting and travel time | “It saves me, what, the best part of two hours travelling, there and back. But also because, the feeling that I got was the (PrISMS) consultations are much more likely to happen roughly at the right time, compared with face-to-face consultations, which could be an hour and a half later.” |
| | “People would sit around waiting, waiting for ages in hospital, for their clinic appointment, and it’s always running late. I’ve seen people in tears, because it is a very stressful thing.” |
| Remote clinic consultation | “I think it feels more personalised, and I think that’s just because you’re talking one to one on the telephone… And in the (face-to-face) clinic, sometimes people are popping in. I don’t know, you feel like in the (face-to-face) clinic there’s a bit more clock-watching going on because people are stressed and they’re having to deal with other situations other than just you.” |
| | “At the moment I am feeling pretty well, so I think that the phone one is absolutely fine. But I suspect that if I was struggling a bit, if I had a lot more symptoms, a lot more complications, I might feel that a face-to-face appointment would be better.” |
| | “The PrISMS clinic is a really good thing, because you can be interviewed in the comfort of your own home, and it takes away a lot of the tension of waiting around.” |
| | “I think it (PrISMS) was more inclusive which sounds a bit bizarre given it’s remote, but I think sometimes it’s easier to say things when you’re just on your own to somebody on the telephone.” |
| Holistic care | “(The physiotherapist) took off and put me on the programme with the Tottenham Hotspurs physio, which was extremely useful getting a bit more active, a bit more movement. And building up some muscle power. That was absolutely invaluable.” |
| | “I don’t even have to leave my home to get a more holistic service… and it was quite interactive with people chipping in and coming in and out of the conversation.” |
| | “I think the holistic nature of the consultations is much more beneficial. When you’re dealing with just a consultant on a one-to-one basis it’s, for me, a pretty narrow discussion.” |

Disclosure of Interest: None Declared
Thromboprophylaxis in patients with myeloma on ‘imid’ therapies - an audit of outcomes following introduction of direct oral anticoagulants.

Fatima Jamil*, Alexander Langridge, Meghan Acres

Abstract Content: There are around 24,000 people living with myeloma in the UK. It is a haematological malignancy arising from plasma cells and treated with various chemotherapies, some of which are associated with an increased incidence of venous thromboembolism (VTE). In particular, the immunomodulatory drugs are associated with a heightened thrombosis risk; Thalidomide, Lenalidomide, Pomalidomide and Carfilzomib. Our study examines whether the administration of direct oral anticoagulants (DOACs) as prophylaxis instead of traditional anti-platelet therapy (Aspirin) affects the incidence of thrombosis.

To carry out this project, 220 patients were identified at the Newcastle Upon Tyne Hospital Trust who received one of the subject therapies. We used electronic records to identify the therapy given, number of cycles received and the thromboprophylaxis used. Clinic letters and radiology reports were reviewed for identifying thrombotic episodes.

We found that Rivaroxaban as standard thromboprophylaxis instead of aspirin has not increased rate of thrombosis (4 thrombotic events recorded in 974 cycles of therapy (0.41%) vs 10 thrombotic events in 2109 cycles (0.47%) respectively and may have in fact decreased it in Lenalidomide-treated patients (5 events in 1740 (0.29%) vs 1 in 623 (0.16%)%). Thalidomide appears to have higher thrombosis incidence than Lenalidomide (7 thromboses episodes per 577 cycles of treatment (1.2%) vs 6 thrombotic events per 2363 cycles of treatment (0.25%) respectively. It was however noted that 11 of 22 patients had their thrombosis on first line treatment (usually within 6 months) and Thalidomide is used first line which could skew these results in particular.

In conclusion, rivaroxaban appears as effective and may well be more protective than traditional anti-platelet therapy in avoiding thrombotic events in patients treats with certain myeloma chemotherapy agents, especially Lenalidomide.

Disclosure of Interest: None Declared

Risk for infections with selinexor in patients with relapsed/refractory multiple myeloma: a systematic review of clinical trials

James Wu*, Haisam Abid, Muhammad Bilal Abid

Abstract Table:

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Clinical Trail Identifier</th>
<th>Study Phase</th>
<th>Treatment Arm</th>
<th>Control Arm</th>
<th>Number of Patients (n)</th>
<th>Median Age (Years)</th>
<th>Median Prior Lines of Therapy</th>
<th>Incidence of Severe Infection, n (%)</th>
<th>Severe Infection Types (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen et al. (2018)</td>
<td>NCT01607892</td>
<td>1</td>
<td>Sd or S</td>
<td>NA</td>
<td>84</td>
<td>62</td>
<td>6</td>
<td>6 (7.1%)</td>
<td>FN: 5, Sepsis: 1</td>
</tr>
<tr>
<td>STORM Part-1 (2018)</td>
<td>NCT02336815</td>
<td>2b</td>
<td>Sd</td>
<td>NA</td>
<td>79</td>
<td>63</td>
<td>7</td>
<td>15 (19.0%)</td>
<td>URTI: 1, Lung Infection: 1, FN: 1</td>
</tr>
<tr>
<td>STORM Part-2 (2019)</td>
<td>NCT02336815</td>
<td>2b</td>
<td>Sd</td>
<td>NA</td>
<td>123</td>
<td>65</td>
<td>7</td>
<td>16 (13.0%)</td>
<td>Pneumonia: 11, URTI: 2, Sepsis: 2, Bacteremia: 1, FN: 2</td>
</tr>
<tr>
<td>STOMP Arm-2 (2018)</td>
<td>NCT02343042</td>
<td>1b/2</td>
<td>SVd</td>
<td>NA</td>
<td>42</td>
<td>64</td>
<td>3</td>
<td>2 (4.8%)</td>
<td>Pneumonia: 2, Rhinovirus: 2</td>
</tr>
<tr>
<td>STOMP Arm-5 (2020)</td>
<td>NCT02343042</td>
<td>1b/2</td>
<td>SDd</td>
<td>NA</td>
<td>34</td>
<td>69</td>
<td>3</td>
<td>4 (11.8%)</td>
<td>Pneumonia: 1, URTE3, UTI: 2, Mastoid Osteomyelitis: 2</td>
</tr>
<tr>
<td>Jakubowiak et al. (2019)</td>
<td>NCT02199665</td>
<td>1</td>
<td>SKd</td>
<td>NA</td>
<td>21</td>
<td>64</td>
<td>4</td>
<td>8 (38.1%)</td>
<td>Pneumonia: 24, URTE: 5, LRTI: 4, UTI: 4, Gastroenteritis: 4, Septic Shock: 4, Influenza: 3, FN: 1</td>
</tr>
<tr>
<td>BOSTON (2020)</td>
<td>NCT03110562</td>
<td>3</td>
<td>SVd</td>
<td>Vd</td>
<td>Treatment: 195, Control: 207</td>
<td>1</td>
<td>66</td>
<td>49 (25.1%)</td>
<td>Treatment: 28 (13.5%)</td>
</tr>
</tbody>
</table>

S, Selinexor; V, Bortezomib; R, Lenalidomide; D, Daratumumab; K, Carfilzomib; d, dexamethasone; FN, febrile neutropenia; URTE, upper respiratory tract infection; UTI, urinary tract infection; LRTI, lower respiratory tract infection.

*BOSTON (2020) – Relative risk for severe infections (SVd vs Vd): 1.83, 95% CI 1.20—2.79, P = 0.005.
Abstract Content: One of the newest Food and Drug Administration approved treatments for relapsed/refractory multiple myeloma (RRMM) is selinexor (Xpovio; KPT-330), a first-in-class selective inhibitor of nuclear export that blocks the nuclear export protein exportin 1. While infections are frequently reported across all modalities of MM treatment, the incidence and risk of infections with selinexor is unknown. We conducted a systematic review of clinical trials to determine the incidence of severe infections associated with selinexor in RRMM patients.

A comprehensive electronic search was conducted in Medline, Scopus, Web of Science, and Cochrane databases to December 31, 2020 identifying all published full-text articles of clinical trials in patients with MM treated with Selinexor. Findings were organized in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis framework.

7 clinical trials with 578 patients with RRMM were included in the final description of infections (Table 1). For severe infections, Chen et al. reported 6 cases (7.1%), STORM Part-1 15 (19.0%), STORM Part-2 16 (13.0%), STOMP Arm-2 2 (4.8%), STOMP Arm-5 4 (11.8%), and Jakubowiak et al. 8 (38.1%). The BOSTON trial was the only study that included a control arm, allowing for relative risk (RR) analysis of infection. Compared to the bortezomib and dexamethasone group, the RR for severe infections was significantly higher in the selinexor, bortezomib, and dexamethasone group (RR: 1.83, 95% CI: 1.20–2.79, P = 0.005). Across 7 clinical trials included in the study, we found the overall incidence of severe infections with selinexor in RRMM patients to be 17.3% (100 total cases). Pneumonia (38 total cases) and upper respiratory tract infection (11 total cases) were the most commonly reported severe infections.

Although only one trial allowed for quantitative analysis, the RR for severe infections associated with selinexor was nearly twice as much as compared to the control arm. For a descriptive comparison across various treatment options for RRMM, severe infection incidence in randomized control trials range from 33.7% with pomalidomide, 7.2% with lenalidomide, 7% with thalidomide, 16.3% with bortezomib, 39.3% with carfilzomib, to 21.4–28.3% with daratumumab. As compared to some of the newer novel agents and monoclonal antibodies, the relatively lower incidence of severe infections could be explained by possible reduction in viral infections with selinexor, which account for significant morbidity and mortality in MM patients. In preclinical studies, selinexor has been shown to reduce the risk of viral infections by blocking virion export from the nucleus. Despite a lower incidence of severe infections as compared to other newer anti-myeloma agents, infection reporting across clinical trials of site/organ, pathogen/organism, diagnostic methods, and prophylactic and treatment strategies was inconsistent.

Our study synthesizes the currently available selinexor clinical trial data, establishes a severe infection incidence baseline, and identifies gaps in knowledge surrounding severe infection reporting and risk. Anti-cancer and anti-viral properties of selinexor hold potential for decreased infections, quality of life improvement, and improved outcomes in this heavily immunosuppressed cohort. Prospective studies and randomized trials with detailed documentation of infection subtypes are needed to better understand the infection risk associated with selinexor.

Disclosure of Interest: None Declared
Outcomes of patients with HGNHL treated with RCE at first line or relapse.

<table>
<thead>
<tr>
<th>RCE used</th>
<th>RCE used</th>
</tr>
</thead>
<tbody>
<tr>
<td>first line</td>
<td>at relapse</td>
</tr>
<tr>
<td>(n = 47)</td>
<td>(n = 27)</td>
</tr>
</tbody>
</table>

- Patients achieving CR, n (%) | 11 (23.4) | 7 (25.9) |
- Patients achieving VGPR, n (%) | 8 (17.0) | 6 (22.2) |
- Patients achieving PR, n (%) | 15 (31.9) | 2 (7.4) |
- Patients with SD, n (%) | 3 (6.4) | 0 |
- Patients with PD, n (%) | 3 (6.4) | 8 (29.6) |
- Patients who died during RCE, n (%) | 3 (6.4) | 1 (3.7) |
- Patients without radiological assessment of response, n (%) | 4 (8.51) | 3 (11.1) |

Overall response rate (%) | 72.3 | 55.5 |
Median overall survival in months (range) | 16 (0-103) | 22 (1-111) |

Disclosure of Interest: None Declared

BSH2021-PO-166
Identifying a subgroup of patients with asymptomatic myeloma who have a low risk of disease progression and long duration of stable disease
Philip Cannon*1, Gavin Preston2
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Abstract Content: Multiple myeloma is a malignancy of plasma cells. Symptomatic myeloma always requires treatment if possible, whilst it has been less clear whether asymptomatic myeloma, often referred to as smouldering myeloma, warrants treatment. Early meta-analysis showed treatment improved progression free survival (PFS) but made no difference in overall survival (OS). It also showed that the burden of active treatment with chemotherapy was high. More recent studies have shown promising results utilising some of the newer treatments of myeloma. However, few have shown definitive improvement in overall survival and those that do are not without other flaws. In an effort to guide whether to treat asymptomatic myeloma, two groups, the International Myeloma Working Group (IMWG) and the Mayo Clinic, have provided separate definitions of high-risk asymptomatic myeloma. Patients meeting the IMWG’s definition are recommended to be initiated on myeloma treatment. Patients that meet the Mayo Clinic’s definition should be followed up closely and considered for clinical trials. The aim of this project was to investigate asymptomatic myeloma in NHS Grampian in terms of PFS and OS to compare with the available literature to determine if a change in practice was needed. The impact of myeloma in terms of hospital admissions, complications and deaths was also examined as a secondary outcome.

Asymptomatic myeloma patients diagnosed from January 2006-August 2020 in NHS Grampian were identified using the myeloma multidisciplinary team meetings. The relevant information was obtained from hospital records, collated using Microsoft Excel and analysed using a mixture of Microsoft Excel and SPSS.

In total 86 applicable patients with asymptomatic myeloma were identified with a median of 32 months of follow up data, and a total of 311 patient years of observational data. Within this follow up, 41% of patients progressed to symptomatic myeloma, taking a median of 63 months to do so. Two of these patients required urgent admission due to end organ damage while a further two also required hospital admission due to their myeloma. Eleven patients who developed symptomatic disease subsequently required hospitalisation at least once due to their myeloma treatment. Patients had a median OS of 88 months. In total 26 patients died during the study timeframe, 17 of whose myeloma had progressed to being symptomatic. There were 15 patients identified that met the Mayo Clinic’s definition of high-risk disease and 8 patients that met the IMWG’s definition. Both groups had a median PFS of 12 months, the Mayo Clinic group had a median OS of 62 months and the IMWG group had a median OS of 49 months. Whereas the 68 low risk patients that did not meet either groups’ definition of high risk had a median PFS of 71 months and a median OS of 88 months. One Mayo Clinic high risk patient had an end organ damage event, as did a low-risk patient also.

These results indicate that the majority of asymptomatic myeloma patients are not deemed high risk by the IMWG or the Mayo Clinic, have excellent outcomes and are unlikely to benefit significantly from earlier myeloma therapy. A potential limitation of this study was the lack of cytogenetic and molecular data for risk stratification as this is likely to guide treatment in the future. We therefore suggest that studies in asymptomatic myeloma should be targeted at high risk groups identified by means such as the Mayo criteria rather than all patients.

Disclosure of Interest: P. Cannon: None Declared, G. Preston Conflict with: Received honoraria from Janssen, Takeda and Abbvie. Have attended meetings sponsored by Celgene.

BSH2021-PO-167
Service improvement and re-design during the COVID-19 Pandemic: sharing your Myeloma clinic experience
Mai Khalifa*1, Stuart Laidlaw1, Andrea Foster1, Yousef Ezaydi 1, Andrew Chantry1
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Abstract Content: During the COVID-19 pandemic, we witnessed rapid reform and redesign of National Health Service (NHS) services to cope with the unprecedented emergency. Practice changes were implemented at a rapid pace. In normal circumstances these would have taken months if not years to implement.

At Sheffield Teaching Hospitals, we took advantage of the rapidly changing environment during the pandemic to address the increased demand of our weekly Myeloma clinic. The new and multiple lines of Myeloma treatment have improved the long term survival of patients transforming it into a ‘long term’ illness. Discharge rates from Myeloma clinics are therefore much reduced, leading to steadily increasing numbers.

Pre COVID:
- 60-70 patients for 4-5 clinicians
- Mixture of new patients, active chemotherapy treatments, post stem cell transplant/ chemotherapy, smouldering Myeloma, Monoclonal Gammapathy of Undetermined Significance (MGUS) monitoring
- Very long waiting times for consultations, blood results and chemotherapy
- Not enough time to fully address concerns and provide holistic care
- Pressure on staff on days when others on annual leave

Post COVID:
- All patients changed to telephone consultation unless clinical urgency for face to face review
Lymphoma, CLL and Myeloma

- Clinic streamlined into 3 smaller clinics: MGUS clinic, smouldering myeloma clinic, chemotherapy + post treatment clinic.
- New appointment letters with clear instruction of pre appointment and appointment arrangements including blood test requirements
- Blood tests to be done a few days pre appointment at a newly set up drive through service (some patients use hospital phlebotomy or GP surgery)
- Home delivery of oral chemotherapy for all patients
- Long term plan of nurse specialist running the MGUS clinic, Physician associates (PA) running smouldering Myeloma clinic and pharmacist seeing some stable long term chemotherapy patients

Six months after running the new clinic set up, we interviewed 20 patients over the phone to explore patient experience. They were asked to rate different aspects of the service from 1-5 (5: Excellent 4: very good 3: good 2: fair 1: poor) (Table 1)
- 50% split of males and females, 75% were above the age of 60
- 60% on treatment, 40% monitoring patients
- 70% of patients when given the choice opted for telephone consultations and 30% to face consultations
- Long term stable patients on treatment or monitoring who opted for telephone consultations also preferred the option of having a face to face consultation if their condition were to change or if there were treatment related concerns.
- Pros of telephone consultations: convenient, less waiting times for consultations and blood results, no waiting for chemotherapy, no parking issues
- Cons of telephone consultations: lack of human contact, patients forgot to ask questions at the end of the phone call

We believe that the pandemic has taken us many steps forward in service improvement and brought about innovation. Virtual consultations have played a pivotal role in healthcare service and will probably continue to do so in the long run. A hybrid model of virtual and face to face consultation will shape the future of healthcare services. In Haematology it is very clear that we have a few patient groups that suit this model well and care can be provided safely and effectively. Drive through phlebotomy services and home chemotherapy delivery improve patient experience and satisfaction, which supports the model of ‘care closer to home’ that we should all be working towards.

Abstract Table: Table 1: Some of the parameters assessed

<table>
<thead>
<tr>
<th>Parameter Assessed</th>
<th>% of patients who rated the service ‘very good’ or ‘excellent’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information and instructions on the appointment letter</td>
<td>85%</td>
</tr>
<tr>
<td>Drive through phlebotomy service</td>
<td>90%</td>
</tr>
<tr>
<td>Overall rating of the consultation</td>
<td>80% (both patients on treatment and monitoring)</td>
</tr>
<tr>
<td>Information given about their treatment or condition</td>
<td>85%</td>
</tr>
<tr>
<td>Questions/ concerns addressed and appointment duration</td>
<td>95%</td>
</tr>
<tr>
<td>Home delivery of chemotherapy</td>
<td>100%</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

The first early access to medicines scheme in relapsed/refractory multiple myeloma
Sheetal Fermahan*,1 Peter John Davies1, Philip Woods1, Helen Spencer1, Sunil Navani1, Patrick De Barr1,2
1Sanofi Genzyme, 2Formerly of Sanofi, Reading, United Kingdom

Abstract Content: The Early Access to Medicines Scheme (EAMS) aims to provide patients with life-threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need. Here we present an overview of the first EAMS in Relapsed/Refractory Multiple Myeloma (RRMM), where eligible patients could access isatuximab in combination with pomalidomide and dexamethasone.

EAMS approval was granted on 02 December 2019, with the first patient enrolled in February 2020 and the last in June 2020 when marketing authorisation was received for isatuximab. Among other key inclusion/exclusion criteria, patients were able to access the scheme only if they had received 3 prior lines of therapy (including lenalidomide and a proteasome inhibitor) and had demonstrated disease progression on the last therapy. After closure of the scheme, data from the anonymised enrolment forms were extracted, and aggregated.

Of the 130 requests received, 111 adult patients were approved for enrolment onto the scheme. Across the UK 94 patient requests were from hospitals in England, 10 from Wales, 6 from Scotland and 1 from Northern Ireland. Many operational arrangements had to be in place with each site prior to approving any request. This was to ensure regulatory requirements were met for provision of core information documents, agreement to additional pharmacovigilance and completion of mandatory training on the unlicensed medicine. A total of 85 training sessions were delivered, involving approximately 300 healthcare professionals consisting of consultant haematologists, pharmacists, and nurses.

Baseline patient demographics showed 62% were male and 37% female, with one unknown record (<1%). 54 patients were aged less than 65 years, 44 aged 65–75 years and 13 patients over 75. The mean age was 66 years, with the youngest and oldest aged 33 and 83 years, respectively. The table below shows the patients’ treatment history at previous lines.

In this small population of patients with RRMM, a higher proportion of patients were male and aged under 65. The most frequently used combinations at 1L, 2L and 3L were CTD, VCD and IRD respectively, although much variability of treatment choices was noted. The high uptake in this EAMS reinforced the lack of optimal treatment options available for these difficult-to-treat patients. Furthermore, the scheme was active during emergence of COVID-19 and despite the pandemic, applications continued with an upward trajectory.

There is great value in an EAMS to bring earlier patient access to new therapies where there is an unmet need, such as in RRMM. Although resource-intensive, the success of the programme is greatly reliant on a robust internal operational process and good communication with external stakeholders.

Abstract Table:

<table>
<thead>
<tr>
<th>Line of therapy</th>
<th>Top 3 combinations administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>First line/induction (1L)</td>
<td>CTD VCD VTD</td>
</tr>
<tr>
<td>Autologous stem cell transplant</td>
<td>Yes = 70% No = 30%</td>
</tr>
<tr>
<td>Second line (2L)</td>
<td>VCD CTD RD</td>
</tr>
<tr>
<td>Third line (3L)</td>
<td>IRD RD RCD</td>
</tr>
</tbody>
</table>

CTD, cyclophosphamide, thalidomide, dexamethasone; VCD, bortezomib, cyclophosphamide, dexamethasone; VTD, bortezomib, thalidomide, dexamethasone; RD, lenalidomide, dexamethasone;
IRD, ixazomib, lenalidomide, dexamethasone; RCD, lenalidomide, cyclophosphamide, dexamethasone.

Disclosure of Interest: None Declared

BSH2021-PO-169
Teenage & young adult haematology patients have low antibody levels after standard chemotherapy which respond to post-treatment immunisation
Lucinda Eve Sanders*,1, Kaljit Bhuller2
1Teenage young adult and Paediatric Haematology, 2Teenage, young adult and Paediatric Haematology, Leicester Royal Infirmary, Leicester, United Kingdom

Abstract Content: In the UK, there is national childhood cancer guidance regarding immunisation after chemotherapy, but for adults recommendations are specific to transplant evaluation. We evaluated antibody levels in teenage and young adult (TYA) patients, aged 18-24 years at diagnosis who received standard chemotherapy for a haematology malignancy between April 2015 to March 2020. Patients who relapsed, received stem cell transplantation or had known immunodeficiency were excluded. We measured Tetanus, Haemophilus influenzae (HiB) and Pneumococcal serotypes 1, 3, 4, 6b, 9v, 14, 18c, 19a, 23f at a minimum of 6 months post end of treatment. Immunisation was recommended based on these levels and if performed, subsequent antibody response was measured.

39 patients were identified; the majority (29/39 (74%) had classical Hodgkin lymphoma. Antibody levels were tested at a mean of 26 months post treatment. Low antibody titres after therapy were detected in 39/39 (100%) for Pneumococcal serotypes, 23/39 (59%) for HiB and 5/39 (12%) for tetanus. Of those who received subsequent immunisation for Pneumococcus 13/16 had 7/9 serotypes respond and 1 patient had 5/9 serotypes respond with protective levels; for HiB and Tetanus all patients who received immunisation developed protective levels.

Our data demonstrated that all patients had low antibody levels after treatment with chemotherapy. The majority of patients who received post-treatment immunisation mounted an antibody response producing optimal protective IgG levels. Although immunisation appears logical to prevent infection there are limitations due to the variability of the host immune response. Checking antibody levels for specific pathogens pre-vaccination seems reasonable however antibody levels are only a surrogate marker of the immune response. Irrespective of measurable antibodies, there may be an effective primed T-cell response that if exposed will stimulate a rapid specific anamnestic B-cell response. We acknowledge this is a single centre evaluation and there is an absence of immunisation history prior to chemotherapy which may be relevant.

For adults in the UK, unless it is defined in a treatment protocol, there is no well-defined recommendation for revaccinating haematology patients. In the paediatric population there are published studies demonstrating a reduction in immunity to vaccine antigens such as HiB, Meningococcus C, Tetanus, Polio, Measles and Pneumococcal serotypes; protective antibody responses have been demonstrated to these antigens with revaccination. Currently the Children’s Cancer and Leukaemia Group recommend children treated with intensive chemotherapy are offered immunisation, typically 6 months post therapy.

In conclusion our data shows TYA patients who receive chemotherapy develop low antibody levels. The majority of patients were able to mount a protective antibody response to post-treatment immunisation, but the clinical implications of this are unclear. As infection is a well-known cause of morbidity and mortality, it is reasonable to consider implementation of vaccination schedule post chemotherapy for TYA patients.

Disclosure of Interest: L. E. Sanders: None Declared, K. Bhuller Conflict with: Consultant

BSH2021-PO-170
The impact of isatuximab treatment on monitoring monoclonal protein concentration in myeloma
Rachel D Wheeler*,1, Fenella Willis2, Yasmin Reyal3, Joanne E. Morris1, Sarah E. Linstead1
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Abstract Content: Isatuximab is an IgG kappa monoclonal chimeric antibody to CD38 that was approved for treatment of myeloma in 2020. Isatuximab is administered in doses that are high enough for it to be detected on serum protein electrophoresis. This is similar to another anti-CD38 monoclonal antibody therapy, daratumumab, which has been used to treat some myeloma patients since 2018. The fact that these monoclonal antibody therapies can be detected on protein electrophoresis means they have the potential to cause confusion when monitoring a patient’s monoclonal protein. It is important that laboratories are familiar with the migration patterns of these drugs.

We describe two patients with myeloma who have been treated with isatuximab. In both cases, isatuximab appeared as a small peak in the fast gamma region on capillary zone electrophoresis that was distinct from the patients’ monoclonal proteins. However, when attempting to confirm complete remission with immunofixation for one of the patients, isatuximab migrated in the mid-gamma region on gel electrophoresis, with similar electrophoretic mobility to the patient’s IgG kappa monoclonal protein. A single band of IgG kappa was detected and it was not possible to determine whether the patient’s monoclonal protein had truly disappeared. This issue will be resolved once a Hydrashift assay for isatuximab becomes available.

Laboratory staff need to be aware that isatuximab migrates differently on capillary zone electrophoresis compared to gel electrophoresis. This is different from daratumumab, which appears as a small peak in the slow gamma region on both capillary zone electrophoresis and protein electrophoresis. It is important for clinicians and laboratory staff to be extra vigilant when interpreting electrophoresis results for patients treated with isatuximab. As demonstrated here, isatuximab may prevent complete remission being confirmed by immunofixation, which is important for some treatment decisions and clinical trials, in which case a Hydrashift assay should be requested. We recommend establishing a mechanism by which the laboratory is alerted when a patient starts on isatuximab so that results can be interpreted appropriately.

Disclosure of Interest: None Declared

BSH2021-PO-171
Are there any variables and clinical significance in length of stay for patients with diffuse large B-cell lymphoma receiving high dose methotrexate prophylaxis for central nervous system relapse?
Maxine Rudkin*

Abstract Content: High dose Methotrexate (HDMTX) is used as Central nervous system (CNS) relapse prophylaxis for patients with...
diffuse large-B cell lymphoma (DLBCL) and requires careful patient selection administration of supportive therapies and careful patient monitoring.

Local data was analysed to identify opportunities to increase efficiency and cost effectiveness through reduced length of stay, reduction in toxicity and improve patient experience and wellbeing. Patient data was gathered retrospectively on 29 patients with DLBCL receiving HDMTX on 1 to 3 cycles with a combined total of 62 HDMTX treatments between May 2016 and December 2019. Information included HDMTX clearance times, impact of nephrotoxicity, timing of serum MTX levels, leucovorin escalation, urinary alkalisation and leucovorin discharge prescriptions. Logistical processes such as blood results pre chemotherapy, chemotherapy authorisation and preparation and admission times were also incorporated to assess the impact on patient’s length of stay.

Most patients were admitted after 5 pm, with 46% treatments commenced longer than 24 hours after admission and HDMTX was predominantly administered between midday and 5 pm despite guideline recommendations of administration between 8 am and midday. This has an impact on serum MTX levels as blood tests are usually carried at 8 am and therefore the median time of MTX levels was 42 hours 56 minutes which is approximately 5 hours prior to the criteria of 48 hours. This is significant because the level will be higher than it would be 5 hours later and this level is used to decide if MTX is cleared and leucovorin rescue escalation meaning that patients may be inaccurately deemed as 'not cleared' or have leucovorin escalated inappropriately.

Leucovorin was predominantly administered intravenously despite guidelines advocating a change to the oral route after two doses if the patient is not experiencing any nausea or vomiting. Leucovorin was usually prescribed as both Intravenous and oral route but was only administered orally on 11 occasions.

12(41%) patients experienced nephrotoxicity with acute kidney injury (AKI) 1 or 2 and there was no incidence of AKI 3, 4 or 5. Nephrotoxicity consistently impacted on MTX clearance and on average took an extra day longer to clear.

Recommendations include a review of logistical processes to provide timely administration of MTX; implementing afternoon admission of MTX started the following morning would also promote timely administration of MTX and reduce costs.

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12(41%) patients experienced nephrotoxicity with acute kidney injury (AKI) 1 or 2 and there was no incidence of AKI 3, 4 or 5. Nephrotoxicity consistently impacted on MTX clearance and on average took an extra day longer to clear.

Recommendations include a review of logistical processes to provide timely administration of MTX; implementing afternoon admission of MTX started the following morning would also promote more accurate MTX levels. Changing to oral administration of leucovorin after the second dose may reduce the risk of infection and burden on nursing time however, this may not be convenient for patients in terms of sleep disturbance and volume of oral tablets and requires further investigation. Utilising leucovorin discharge prescriptions may reduce inpatient stay by one night per eligible patient.

HDMTX incorporates many challenges and patients have significant variables that affect clearance and toxicity. There are aspects of clinical practice that could be enhanced for clinical and service improvement ultimately leading to reduced inpatient stay, cost reductions and improved clinical effectiveness.

**Disclosure of Interest:** None Declared

### BSH2021-PO-172

**Glioblastoma, IDH-wildtype - a new association with IgM paraproteinaemic neuropathy?**

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**Abstract Content:** Central Nervous System involvement in Waldenström’s Macroglobulinaemia (WM) as seen in Bing Neel syndrome is well recognised. We present three cases of classical IgM paraproteinaemic neuropathy who developed Glioblastoma Multiforme (GBM) in the course of their illness following treatment with chemoimmunotherapy (CIT). Haematological investigations revealed that the underlying diagnosis of the neuropathy was monoclonal gammapathy of clinical significance (MGCS) in 2 cases while the other case fulfilled WHO criteria for a diagnosis of WM. Due to the progressive symptomatic nature of their neuropathy, all patients were treated with CIT using a protocol similar to the Dimopoulos regimen shown to be effective in WM. CIT comprised 6 cycles of intravenous rituximab 375 mg/m², intravenous cyclophosphamide 750 mg/m², and oral prednisolone 50 mg/m² (days 1 to 5) every 21 days. All patients completed the full treatment protocol with good tolerance. GBM was diagnosed between 9 months and 6 years post treatment and all cases were negative for the isocitrate dehydrogenase-1 mutation (IDH1) typical of primary GBM.

Recognised risk factors for GBM include pre-morbid radiation therapy, an immune tumour local environment, as well as single

### Abstract Table:

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian male</td>
<td>Caucasian male</td>
<td>Caucasian male</td>
</tr>
<tr>
<td>56 years</td>
<td>56 years</td>
<td>65 years</td>
</tr>
<tr>
<td>Numbness in the feet ascending to mid-calf</td>
<td>Numbness in the feet and distal legs</td>
<td>Prominent sensory ataxia</td>
</tr>
<tr>
<td>Lymphoplasmacytic lymphoma (WM)</td>
<td>MGCS</td>
<td>MGCS</td>
</tr>
<tr>
<td>Absent</td>
<td>64500</td>
<td>20500</td>
</tr>
<tr>
<td>IgM Kappa 2.6 and 5</td>
<td>IgM Lambda 3.6</td>
<td>IgM Kappa 4.7</td>
</tr>
<tr>
<td>Generalised tonic-clonic seizure and behaviour change</td>
<td>Rapid cognitive decline and behaviour change</td>
<td>Rapid onset left sided facial drop and slurred speech</td>
</tr>
<tr>
<td>14 years</td>
<td>10 years</td>
<td>10 years</td>
</tr>
<tr>
<td>5 years</td>
<td>9 months</td>
<td>6 years</td>
</tr>
<tr>
<td>2 months</td>
<td>2 months</td>
<td>4 months</td>
</tr>
</tbody>
</table>
nucleotide polymorphisms (SNPs) and variations in IL-2RA (CD25) genes. Currently, there are no reports in the literature of GBM related to any form of chemotherapy or immunosuppressive therapy. None of the patients had unequivocal evidence of known predisposing factors for GBM. CIT has been shown to be an effective treatment in patients with IgM paraproteinaemic neuropathy evidenced by sustained clinical and serological improvement over time. The extensive use of this CIT and other similar regimens throughout haematological and rheumatological practice over a number of decades has produced no evidence to suggest a link with GBM. These cases highlight an apparent association between IgM paraproteinaemic neuropathy and GBM. Both disorders are very rare so it is highly unlikely that this is a random occurrence. The literature evidence at present suggests a link is more likely to be due to shared epidemiological risk factors, genetic predisposition or common pathophysiologic pathways. Therefore, although a direct causal link between use of immunosuppression and GBM is unlikely, we suggest clinicians be cautious about use of CIT in this specific patient group.

Disclosure of Interest: None Declared

BSH2021-PO-173
An automated pipeline to assess treatment response and treatment eligibility in myeloma
Tamir Sirkis*, 1, Angela Cooper2, Loretta Ngu3, Thomas Coats3
1Exeter University Medical School, 2Blood Sciences, 3Haematology, RD&E, Exeter, United Kingdom

Abstract Content: The International Myeloma Working Group Uniform Response Criteria (URC) is widely used to monitor treatment response in myeloma patients. Eligibility for NHS funded treatments is based on this and the National Cancer Drugs Fund (CDF) criteria. The application of these criteria is currently done manually by clinicians, which can be both arduous and error-prone. We have retrospectively validated an electronic myeloma pipeline that automatically calculates response to treatment, based on URC, as well as the eligibility for CDF treatments.

Difference between involved/uninvolved LC

Serum M-protein (pp), serum free light chain (SFLC) and chemotherapy treatment details were obtained for 27 patients treated at The Royal Devon & Exeter (RD&E) between 2015 and 2019. A calculator based on the URC criteria was designed using python and run on Anaconda’s Jupiter Notebook. Modifications were made to URC criteria as urine-M protein and serum immunofixation are not routinely performed at the RD&E beyond myeloma diagnosis (Table 1). A new response category, presumed progressive disease (pPD), was added to capture cases where treatment was changed before a second confirmatory sample could be taken. To ascertain eligibility for CDF treatments we created 2 scenarios: i) patient relapsed at the next time point and ii) treatment stopped but relapse did not occur for a further 6 months. The CDF criteria (version 1.173) for 15 myeloma treatments were converted into digital algorithms using open source software (esyN, www.esyn.org). The inputs to run these algorithms were generated based on the calculated responses to treatment. Patients were assumed to have responded to all treatments commenced before 2015 and have a Performance Score 0-2. Accuracy of the algorithm outputs was verified by 2 clinicians.

27 patients received a median of 3 treatments (range 1-8), 72 lines of therapy had a baseline pp and SFLC to be able to assess disease response. 620 disease responses were calculated (Table 1). Patients who had achieved at least a very good partial response (VGPR) (n = 12) had a median time to next treatment of 432 days, compared with 386 for a partial response (n = 16) and 224 for those

Disclosure of Interest: None Declared

Abstract Table: Table 1. Summary of responses in cohort of 27 patients treated with myeloma.

<table>
<thead>
<tr>
<th>Disease Type (and definition)</th>
<th>Response Category</th>
<th>Criteria for response (modified from IMWG URC)</th>
<th>No. confirmed response assessments (n = 620)</th>
<th>Best response by line of therapy (n = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurable disease Serum M-protein &gt;=10 g/L</td>
<td>sCR</td>
<td>Undetectable M-protein in serum and SFLC normal ratio</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>CR</td>
<td>Undetectable M-protein in serum but SFLC ratio not normal</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>VGPR</td>
<td>&gt;=90% reduction in serum M-protein</td>
<td>45</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>PR</td>
<td>&gt;50% but less than 90% reduction in serum M-protein</td>
<td>141</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>PD</td>
<td>&gt;=25% increase from baseline of serum M-protein and absolute increase of &gt;=5 g/L</td>
<td>92</td>
<td>0</td>
</tr>
<tr>
<td>Presumed PD (pPD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Presumed PD</td>
<td>One PD reading but not confirmed. Patient subsequently started new treatment</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Non-measurable disease Urine and serum pp not detectable serum p &lt; 10 g/L, abnormal k/l ratio and involved LC &gt;=100 mg/L ase</td>
<td>sCR</td>
<td>Undetectable M-protein in serum and SFLC normal ratio</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>CR</td>
<td>Detectable M-protein (&lt;10) in serum and SFLC normal ratio</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>VGPR</td>
<td>Difference between involved/uninvolved SFLC &gt;=90% reduction</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>PR</td>
<td>Difference between involved/uninvolved SFLC &gt;=50% reduction</td>
<td>35</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>PD</td>
<td>&gt;=25% increase from baseline and absolute increase of &gt;100 mg/L</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Presumed PD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Presumed PD</td>
<td>One PD reading but not confirmed. Patient subsequently started new treatment</td>
<td>124</td>
<td>15</td>
</tr>
</tbody>
</table>
who did not respond (n = 25). PD, or pPD, was detected by the calculator in 43/47 instances where new, non-maintenance, treatment was started. 'Missed' progressions were due to i) a blood test performed at another hospital, ii) a relapse from CR with hypercalcaemia but below the threshold for PD, iii) a light chain only relapse in a patient with measurable disease, and iv) an extra-medullary relapse.

Missed progressions were amended and treatment eligibility (TE) was calculated in the 2 relapse scenarios. TE algorithm was 99.7% accurate for CDF funded treatments. For 10 patient-drug combinations, TE was different depending on whether the relapse happened immediately, or 6 months after drug cessation. Isatuximab and ixazomib regimens were the most affected.

We show that it is possible to automate classifying treatment response and produce relevant patient and cohort level statistics. This information was successfully used to discern eligibility for future therapies. Further work is needed to incorporate imaging reports and other disease markers (e.g. hypercalcaemia), to detect non-biochemical disease progression. Care is also needed to detect likely disease progression occurring below the threshold of URC. This work shows the potential for automated processes to support and enhance clinical performance.

Confirmed responses according to a modified response criteria based on IMWG URC (amended to account for responses being assessed on serum protein electrophoresis and serum free light chains (SFLC) only) and including an additional category of 'presumed' progressive disease (pPD). With the exception of pPD, all responses confirmed on a second sample. Measurable and non-measurable disease established based on the disease parameters at commencement of a line of therapy, CR – complete response, sCR – stringent complete response, VGPR – very good partial response, PR – partial response, PD – progressive disease, k – kappa, I - lambda.

Disclosure of Interest: None Declared

**BSH2021-PO-174**

**Fracture risk in treatment of lymphoma: no longer a bone of contention**

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**Abstract Content:** Within malignant haematology practice we often treat an ageing population with high doses of corticosteroids which can lead to a loss of bone mineral density (BMD) with subsequent increased fracture risk and reduced relative survival. There is consensus guidance for formal risk assessment and risk modification before steroid treatment in immune thrombocytopenia (ITP) but less clear guidance in malignant haematology. A recent observational, retrospective study demonstrated a cumulative fracture incidence of 11.4% at 18 months follow up in patients with diffuse large B-cell lymphoma (DLBCL).

In our centre, data were retrospectively collected on patients over the age of 70 who were treated with steroid-containing regimens for lymphoma of any sub-type between April 2017 and April 2019. Electronic notes were reviewed to ascertain baseline characteristics and disease-related data; however, it is likely our study was not sufficiently powered to detect this. The fracture incidence of 12% is almost identical to that demonstrated in a recent large observational study (11.4%) which demonstrated independent risk factors for fracture on multivariate analysis including bone involvement of DLBCL, previous history of osteoporosis and pre-phase steroid use.

The strength of this study was the inclusion of all subtypes of lymphoma and retrospective specialist review of imaging to identify fractures which may have been asymptomatic and not necessarily included on initial reports. This allows a more accurate estimation of true fracture incidence. It may well be the case that these fractures will subsequently be symptomatic. Limitations are the relatively small sample size and retrospective nature of the study.

This study adds to a growing evidence base of fracture risk in this group and supports the need for individualised risk assessment and the consideration of preventative strategies. Prophylactic treatment options include lifestyle modification, vitamin-D and calcium supplementation and bisphosphonate therapy.

**Abstract Table: Table 2. Fracture events identified.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time since start of treatment to development of fracture (months)</th>
<th>Mode of imaging</th>
<th>Site of vertebral fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>PET-CT</td>
<td>T7, T10, L4</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>Plain CT</td>
<td>T6, T9</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>MRI</td>
<td>L5</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>Plain CT</td>
<td>L3, L4</td>
</tr>
<tr>
<td>5</td>
<td>21</td>
<td>Plain CT</td>
<td>T5, T12</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>PET-CT</td>
<td>L1</td>
</tr>
</tbody>
</table>

PET-CT, Positron emission tomography–computed tomography; CT, computed tomography; MRI, magnetic resonance imaging; T, thoracic; L, lumbar

Disclosure of Interest: None Declared

**BSH2021-PO-175**

**Has COVID-19 affected the presentation of patients with lymphoid malignancies?**

Sarah Beverstock*,1, Jennifer Clarke2, Vic Campbell1

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**Abstract Content:** The COVID-19 pandemic has had an immeasurable impact on the NHS. We hypothesised it would result in patients presenting later, with more advanced disease due to cancelled routine
Abstract Content: Daratumumab is an anti-CD38 monoclonal antibody approved as monotherapy by the National Institute for Health and Care Excellence (NICE) for the treatment of relapsed/refractory myeloma in patients who have had at least 3 lines of prior therapy including a proteasome inhibitor and an immunomodulatory agent (NICE TA510). The approval was in part based on the phase II SIRIUS study which demonstrated a response rate of 29.2% in 106 patients and median overall survival of 17.5 months (Lonial et al, 2016). Real world outcomes and tolerability often differ from trial data as patients can be frailier with increased comorbidities. This study reviews the baseline patient characteristics, response to and tolerability of daratumumab monotherapy prescribed within the NICE authorisation at 2 centres in Bristol.

Patients were identified from clinical records from the time of daratumumab approval in February 2018 to November 2020. Data were gathered from electronic clinical systems. Thirty-two patients were identified, 14 male and 18 female, with a median age of 72.5 years (range 50-85). All patients were performance status (PS) 0-2, 40% PS2, and 19% had a creatinine clearance <30 ml/min. Five patients (16%) had high risk cytogenetics at diagnosis as per RISS definition and 8 had gain of 1q alone or in addition to another high-risk change. There was variation in practice in delivery of the first dose of daratumumab, with one centre providing single dose IV administration as an inpatient and the other split dose administration on an outpatient basis. Both were well tolerated with a total of 7 adverse events reported, the majority of which were grade 1-2. There was one grade 4 tumour lysis syndrome. Fewer infusion related reactions were reported in the split dose group (1 event) versus the single dose (6 events). The overall response rate was 53% (12 PR and 5 VGPR by IMWG criteria (Durie 2006). Response was not assessable in 4 patients; due to death in the first cycle in 3 patients and in one patient due to ascetery disease. The median progression-free survival was 12 months, with a 12 month overall survival of 50%. The median number of cycles completed was 4.5.

Compared to the SIRIUS trial the patients in this study were older (72.5 vs 63.5), frailer (40% PS2 vs 8%) and had poorer baseline renal function (CrCl <30 ml/min 19% vs 4%). However, overall response was better in this cohort (53% vs 29.2%), as was the median PFS (6 months vs 3.7 months). Despite this 12 month overall survival was poorer (50% vs 64.8%). There was also a lower reported rate of adverse events (22% vs 42%) possibly due to increased event reporting within a clinical trial. However, it is notable that adverse events were particularly low in the split dose group of patients observed in this audit. These findings also appear favourable compared with other real-life retrospective studies, where response rates of 24-33% with a PFS of 1.9–4.6 months have been reported (Jullien et al 2019, Minarik et al 2017). While this study adds to the evidence that daratumumab is efficacious and well tolerated, a number of patients died during first cycle or were refractory. This indicates a need for new treatment combinations and a need to consider parallel planning with palliative care at the start of 4th line treatment. Ixazumab, pomalidomide and dexamethasone has recently been NICE approved in this setting so future study should compare the efficacy and tolerability of these 2 regimes.

Disclosure of Interest: None Declared

BSH2021-PO-176

Real world outcomes of fourth line daratumumab for relapsed/refractory myeloma in two UK centres

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Lymphoma, CLL and Myeloma
BSH2021-PO-177
Real world single-centre experience of daratumumab monotherapy in heavily pretreated relapsed/ refractory multiple myeloma
I Sanchez1,2, H P J Lam1, G Milner1, I El-Najjar1, S Sachchinananthan3, M Gleeson1, M Kazmi1, K Bailey1, R Benjamin1, H Cuthill1, L Yuen1, M Streetly1
1Haematology, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, 2Haematology, Hospital Universitario Principe de Asturias, Alcala de Henares, Spain, 3Haematological Medicine, Kings College Hospital, 4Pharmacy, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom

Abstract Content: Daratumumab, an anti-CD38 monoclonal antibody, was approved by NICE in January 2018 as 4th line monotherapy for relapsed/refractory multiple myeloma (RRMM) patients, whose previous therapies included a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD). In June 2020 subcutaneous (SC) daratumumab gained approval in Europe.

This is a retrospective study of 24 RRMM patients who started daratumumab monotherapy between 05/2018 and 09/2020 at Guy’s Hospital, London. We reviewed data from patient electronic report to assess eligibility criteria for this therapy, clinical characteristics, response rates and toxicity profile. Patients who completed ≥1 cycles were included in response analysis. Kaplan-Meier method was used for survival outcomes.

Median age at the start of daratumumab was 65 (range 47-91); 14 (58.3%) patients were female. Clinical characteristics are summarised in Table 1. All patients had previous exposure to a PI (bortezomib 100%, ixazomib 50%, carfilzomib 8.3%) and an IMiD (lenalidomide 100%, thalidomide 79.2%, pomalidomide 16.7%). Three (12.5%) were bortezomib-refractory, including 1 (4.2%) refractory to both VTD (bortezomib, thalidomide, dexamethasone) and IRd (ixazomib, lenalidomide, dexamethasone) therapies. Twelve (50%) patients had undergone autologous stem cell transplant. Six (25%) had been included in a clinical trial (with no anti-CD38).

All patients had progression before starting daratumumab, with extramedullary disease in 4 (16.7%) patients. Median treatment duration was 4.1 months (m) (0.7-22.7) and median number of cycles was 1 (range 1-23), 22 patients completed ≥1 cycles. Overall response rate (ORR) was 40.9% (9/22), with 18.2% (4/22) achieving very good partial response (VGPR). Median time to partial response (PR) was 2.3 m (2-3.6). Median progression-free survival (PFS) is 5.5 m; longer PFS is associated with completion of ≥1 cycle (median 6.5 m) and with deeper response (VGPR vs. PR or less, 15.3 vs. 3.8 m (P 0.014)). Median overall survival (OS) is 15.5 m.

Administration was SC in 4 (19%) patients and was converted from intravenous (IV) to SC in 4 (19%) others. First-dose infusion related reactions (IRR) occurred in 9 (37.5%) patients; 8/9 (88.9%) were associated with IV daratumumab, among which 3 were classified as grade ≥3 (including hypertension, fevers, desaturation and vomiting).

Common (≥15%) adverse events (AEs) were anaemia (95.8%), lymphopenia (83.3%), thrombocytopenia (75%), neutropenia (33.3%) and infections in 11 (45.8%) patients, the majority being non-severe respiratory infections (45.4%).

Grade ≥3 AEs were found in 13 (54.2%) patients: grade ≥3 thrombocytopenia in 5 (38.5%), anaemia in 7 (53.8%), lymphopenia in 7 (53.8%) and neutropenia in 1 (7.7%).

Grade ≥3 new infections after daratumumab start happened in 4/13 (30.8%) patients: sepsis related to Gram negative bacteriaemia leading to death, sepsis of unknown origin, pneumonia and urinary tract infection.

In summary, our experience with daratumumab monotherapy demonstrates encouraging response rates in heavily pretreated patients, similar to those reported in a pooled analysis of GEN501 and SIRIUS phase 1-2 trials. It also shows an acceptable safety profile, favouring SC administration.

Abstract Table:
Table 1. Clinical characteristics of the population.

<table>
<thead>
<tr>
<th>Characteristics (n = 24)</th>
<th>Overall data (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple myeloma type</td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>15/24 (62.5%)</td>
</tr>
<tr>
<td>IgA</td>
<td>4/24 (16.7%)</td>
</tr>
<tr>
<td>Bence-Jones</td>
<td>5/24 (20.8%)</td>
</tr>
<tr>
<td>ISS stage at diagnosis</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8/24 (33.3%)</td>
</tr>
<tr>
<td>II</td>
<td>4/24 (16.7%)</td>
</tr>
<tr>
<td>III</td>
<td>9/24 (37.5%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3/24 (12.5%)</td>
</tr>
<tr>
<td>ISS-R stage at diagnosis</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>6/24 (25%)</td>
</tr>
<tr>
<td>II</td>
<td>6/24 (25%)</td>
</tr>
<tr>
<td>III</td>
<td>3/24 (12.5%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>9/24 (37.5%)</td>
</tr>
<tr>
<td>Cytogenetics at diagnosis*</td>
<td></td>
</tr>
<tr>
<td>Non-high risk</td>
<td>10/24 (41.7%)</td>
</tr>
<tr>
<td>High risk</td>
<td>5/24 (20.8%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>9/24 (37.5%)</td>
</tr>
<tr>
<td>ECOG performance scale ≤2</td>
<td>19/24 (79.2%)</td>
</tr>
</tbody>
</table>


Disclosure of Interest: None Declared

BSH2021-PO-178
Incidence of fragility fracture risk factors and management of bone related complications in people treated for Lymphoma with glucocorticoid containing regimens, a single centre experience.
Charlotte Bloodworth1, Chandrachapa Gamage1, Zainab Shweejawey1, Agisilaos Zerdelis1, Lydia Boyle1, Nagah Elmusharaf1
1Haematology, UNIVERSITY HOSPITAL OF WALES, Cardiff, United Kingdom

Abstract Content: Background: Fragility fractures occur in up to 30–50% of adults receiving long term glucocorticoids. UK evidence-based guidelines for osteoporosis prevention include the management of patients receiving oral glucocorticoids with an anticipated duration of ≥3 months. However, people being treated for lymphoma receive high doses of steroid therapy but given intermittently so direct application of general guidance is limited. Nevertheless, bone related complications acknowledged as a late effect of Lymphoma treatment.

Grade ≥3 AEs were found in 13 (54.2%) patients: grade ≥3 thrombocytopenia in 5 (38.5%), anaemia in 7 (53.8%), lymphopenia in 7 (53.8%) and neutropenia in 1 (7.7%).

Grade ≥3 new infections after daratumumab start happened in 4/13 (30.8%) patients: sepsis related to Gram negative bacteriaemia leading to death, sepsis of unknown origin, pneumonia and urinary tract infection.

In summary, our experience with daratumumab monotherapy demonstrates encouraging response rates in heavily pretreated patients, similar to those reported in a pooled analysis of GEN501 and SIRIUS phase 1-2 trials. It also shows an acceptable safety profile, favouring SC administration.

Abstract Table:
Table 1. Clinical characteristics of the population.

<table>
<thead>
<tr>
<th>Characteristics (n = 24)</th>
<th>Overall data (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple myeloma type</td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>15/24 (62.5%)</td>
</tr>
<tr>
<td>IgA</td>
<td>4/24 (16.7%)</td>
</tr>
<tr>
<td>Bence-Jones</td>
<td>5/24 (20.8%)</td>
</tr>
<tr>
<td>ISS stage at diagnosis</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8/24 (33.3%)</td>
</tr>
<tr>
<td>II</td>
<td>4/24 (16.7%)</td>
</tr>
<tr>
<td>III</td>
<td>9/24 (37.5%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3/24 (12.5%)</td>
</tr>
<tr>
<td>ISS-R stage at diagnosis</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>6/24 (25%)</td>
</tr>
<tr>
<td>II</td>
<td>6/24 (25%)</td>
</tr>
<tr>
<td>III</td>
<td>3/24 (12.5%)</td>
</tr>
<tr>
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<td>9/24 (37.5%)</td>
</tr>
<tr>
<td>Cytogenetics at diagnosis*</td>
<td></td>
</tr>
<tr>
<td>Non-high risk</td>
<td>10/24 (41.7%)</td>
</tr>
<tr>
<td>High risk</td>
<td>5/24 (20.8%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>9/24 (37.5%)</td>
</tr>
<tr>
<td>ECOG performance scale ≤2</td>
<td>19/24 (79.2%)</td>
</tr>
</tbody>
</table>


Disclosure of Interest: None Declared
Aim: This aim of the audit was to identify the incidence of risk factors associated with bone complications in people being treated for lymphoma using steroids containing regimens and to identify frequency and management of these complications, with the aim of developing a local assessment and management pathway.

Methods: A prospectively maintained database of adult lymphoma patients treated at the University Hospital of Wales was reviewed between 2016 and 2020, only patients who received more than 3 cycles of R+/- CVP/CHOP or 2 cycles of R-GDP were included. Risk factors of osteoporosis and fractures were audited and patients with bone related symptoms were identified.

Results: 175 patients were identified, and their data analysed, characteristics and risk factors of osteoporosis are summarized in table 1. Given the population age, there were a small proportion already receiving Calcium and Vitamin D supplement 18/175 (10.3%) and 5/175 (2.9%) were receiving bisphosphonate therapy prior to receiving chemotherapy. The data showed that 32/175 (18.3%) patients reported symptoms of bone pains with radiological imaging showing 18/175 (10.3%) had evidence of degenerative bone disease, primarily in the vertebral spine, 9/175 (5.1%) had evidence of lymphoma in the bones, 5/175 (2.9%) had evidence of vertebral fractures and 2/175 (1.1%) lower limb fractures. Of the 12/175 (6.9%) who had bone density scan (DEXA) scans, 7/175 (4%) had evidence of osteoporosis, 2/175 (1.1%) Osteopenia. Audit of subsequent management demonstrated that 15/175 (8.6%) patients were started on Vitamin D during or after chemotherapy, 13/175 (7.4%) were started on Bisphosphonate therapy, 9/175 (5.1%) were referred to the bone density clinic, 6/175 (3.1%) to physiotherapy and 9/175(5.1%) were referred to the spinal team where 4/175 (2.4%) required surgical intervention, the others were managed conservatively or referred to the chronic pain clinic.

Conclusion: Without further evidence on the added risks of pulsed steroid treatment on fracture risk available, a local pathway for management and prevention of bone complications specifically for lymphoma patients is not possible. However, this audit demonstrated that a high proportion of people having lymphoma treatments in this single centre study do have several risk factors associated with bone complications. Therefore, routine review of these risk factors should be carried on every person having treatment for their lymphoma, as should advice be given to reduce risks, such as following a healthy diet, maintaining a normal body mass index, stopping smoking, limiting alcohol intake and engaging in low-impact weight-bearing exercises. Those with multiple risk factors (such as women aged over 70 years, with a history of previous fragility fractures) should be flagged for ongoing assessment and management through their General Practitioner where national recommended scoring and/or bone density scans can be considered.

Disclosure of Interest: None Declared

BSH2021-PO-179
Improved outcome in elderly patients with advanced stage Diffuse Large B-Cell Lymphoma if completion of intended 6 cycles of R-CHOP21: A single centre study of patients receiving first-line treatment for DLBCL
Annabel Hill1, Rebecca Oliver2, Linda Hollen3, Stephen Robinson4, Laura Percy5, Sanne Lugthart2,4
1Bristol Medical School, University of Bristol, 2Haematology Department, University Hospitals of Bristol and Weston NHS Foundation Trust, 3Centre for Academic Child Health, Bristol Medical School, 4Department of Cellular and Molecular Medicine, University of Bristol, Bristol, United Kingdom

Abstract Content: Diffuse large B-cell lymphoma (DLBCL) is the most common form of Non-Hodgkin lymphoma. It is primarily a disease of the elderly, with most patients being diagnosed in their 7th decade of life. Combination chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP21), is the established first-line treatment with good outcomes. Survival data from the UK NCRI randomised controlled study showed a CR rate and 2 year OS rate of 63% and 82% respectively. However, multiple further studies have shown poorer outcomes in older patient groups. We performed a real-world observational study of patients receiving R-CHOP21 for first line treatment for DLBCL within our University centre in Bristol. We compared outcomes with those seen in the UK NCRI trial, and particularly focused upon outcomes within patients aged ≥65 years.
Lymphoma, CLL and Myeloma

Abstract Table: Table 1. Outcomes, patient and treatment characteristics for patients with DLBCL treated with first line R-CHOP at University Hospitals Bristol (N = 119).

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Overall (N = 119)</th>
<th>Age at diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS months (median IQR)</td>
<td>26 (14-27)</td>
<td>29 (17-41)</td>
</tr>
<tr>
<td>EFS months (median IQR)</td>
<td>14 (5-30)</td>
<td>17 (6-36)</td>
</tr>
<tr>
<td>Treatment outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR (N %)</td>
<td>77 (68.8%)</td>
<td>29 (70.7%)</td>
</tr>
<tr>
<td>PR (N %)</td>
<td>26 (23.2%)</td>
<td>10 (24.4%)</td>
</tr>
<tr>
<td>PD (N %)</td>
<td>9 (8.0%)</td>
<td>2 (4.9%)</td>
</tr>
<tr>
<td>Patient characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age years (median IQR)</td>
<td>68 (54-74)</td>
<td>68 (56.8%)</td>
</tr>
<tr>
<td>Gender (N %) males</td>
<td>61 (51.3%)</td>
<td>36 (48.0%)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I (N %)</td>
<td>21 (18.6%)</td>
<td>21 (18.0%)</td>
</tr>
<tr>
<td>II (N %)</td>
<td>21 (18.6%)</td>
<td>7 (23.1%)</td>
</tr>
<tr>
<td>III (N %)</td>
<td>23 (20.3%)</td>
<td>8 (20.5%)</td>
</tr>
<tr>
<td>IV (N %)</td>
<td>48 (42.5%)</td>
<td>15 (38.4%)</td>
</tr>
<tr>
<td>Treatment characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cycles*</td>
<td>6 (3-6)</td>
<td>6 (3.5-6)</td>
</tr>
<tr>
<td>&gt;= median (6)</td>
<td>74 (62.2%)</td>
<td>29 (65.9%)</td>
</tr>
<tr>
<td>Delay (N %) yes</td>
<td>77 (64.7%)</td>
<td>29 (65.9%)</td>
</tr>
</tbody>
</table>

OS, Overall Survival; IQR, Interquartile Range; EFS, Event-Free Survival; CR, Complete Response; PR, Partial Response; PD, Progressive Disease.

*Number of cycles of R-CHOP21.

Adult patients with DLBCL receiving R-CHOP21 as first-line treatment between July 2014 and December 2019 were identified retrospectively using an electronic prescribing database. Case files were evaluated for Ann-Arbour stage, number of R-CHOP21 cycles received, treatment response and treatment delay. The overall survival (OS) and event free survival (EFS) were calculated. Patients with insufficient information in the notes were excluded. Two- and three-year OS and EFS were estimated using Kaplan Meier plots. Five prognostic factors were examined using survival analyses: age (<65 years, ≥65 years), sex (male/female), stage (I-II vs. III-IV), treatment delay (yes/no), number of cycles received (<6, ≥6).

In total, 142 patients were identified, of which 23 patients were excluded. The median age of remaining 119 patients was 68 years, with 63% of patients over 65 years of age. The largest group of patients had stage IV disease (42%). There was treatment delay for 65% of patients; median total treatment delay observed was 3 days. Patient and treatment characteristics (Table 1) were comparable to those in the NCRI trial.

Two thirds of the cohort showed a complete response (CR) (69%). Median OS was 26 months, and 2 and 3 year OS were 81% and 73% respectively. The OS was significantly lower in those aged ≥65 years (2-year OS 76% vs. 90%) and those that received <6 cycles (2-year OS 65% vs. 91%). Elderly patients with advanced stage DLBCL who were unable to complete an intended 6 cycles of R-CHOP21 (n = 13), were nearly 7 times more likely to die, compared to elderly patients with advanced stage DLBCL who completed 6 cycles of treatment (n = 35). Median EFS was 14 months, and 3 year EFS was 51% and 50% respectively. Elderly patients that received <6 cycles or those with stage III-IV disease were significantly more at risk to exhibit an event. Treatment delay did not influence treatment response, OS or EFS.

This retrospective study has demonstrated that outcomes of patients with DLBCL treated at University Hospitals of Bristol and Weston were comparable to those seen in the 2013 UK NCRI trial (CR 63%; 2-year OS 83%), despite an older patient cohort within the Bristol group. Subgroup analyses of patients aged over 65, demonstrated a worse OS; however, in elderly patients with stage III/IV disease, there was a trend towards an improved outcome if they completed at least 6 cycles of R-CHOP21. This data suggests that if we can support elderly patients to complete a full course of R-CHOP21, then we may be able to partially overcome the poorer OS seen in this group.

Disclosure of Interest: None Declared

BSH2021-PO-180

Case series: Transformed Follicular Lymphoma treated with Lenalidomide

N Lafferty, R Lown, N Sargent

25–35% of patients with Follicular lymphoma (FL) undergo high-grade transformation to Diffuse Large B-Cell Lymphoma (DLBCL).

Whilst transformed Follicular Lymphoma (tFL) has historically conferred a poor prognosis, fit patients may now be successfully treated using the modern immunochemotherapy regimens typically used in DLBCL; either alone or in combination with autologous stem cell transplant. However, in patients who are not fit for intensive treatment and/or have received these therapies previously, the optimal treatment strategy is less well defined. Lenalidomide is an immunomodulatory drug which is now licensed in the UK for treatment of relapsed or refractory FL when used in combination with Rituximab (‘R’). Both R and lenalidomide monotherapy have also been shown to produce responses in a minority of relapsed or refractory DLBCL patients. Some studies evaluating the efficacy of lenalidomide in DLBCL have included small sub-analyses of patients with tFL, indicating that responses may also be achieved in this
population, although, overall, there exists limited data on this patient group.

We conducted a retrospective analysis of the outcomes of patients who received lenalidomide for treatment of TFL between January 2014 and May 2019 at University Hospital Southampton, through the compassionate use scheme offered by Celgene.

Eleven patients were included in the analysis. Median age was 68 years (56–81) and ECOOG performance scores ranged from 0–2. Patients of all disease stages were represented. Histological classification, using the Hans algorithm, showed ten patients to be of GCB subtype, and one to be of non–GCB subtype. Median number of previous treatments was 5 (3–11), including autologous stem cell transplant in 5 patients, and allogeneic stem cell transplant (AlloSCT) in one patient.

Lenalidomide was given either as monotherapy (n=3) or in combination with other treatments. Treatments combined with lenalidomide were: dexamethasone (n=1), radiotherapy (n=2), and rituximab (n=5).

The median number of cycles of lenalidomide received was 8 (2–141). Treatment was stopped in seven patients, due to progressive disease (n=4), adverse effects (n=2), or completion of a planned treatment course (n=1), whilst the other four patients remained on treatment at the time of data collection.

Overall response rate was 45%, with four patients (36%) achieving a partial remission and one patient (9%) achieving a sustained complete remission of over 11 years. At 1 year, overall survival (OS) was 73%.

During their course of treatment, three patients (27%) developed neutropenia requiring GCSF support, two patients (18%) required admission for treatment of infections, and three patients (27%) developed second malignancies. The second malignancies observed were: basal cell carcinoma (n=2), myelodysplastic syndrome (n=1) and lung adenocarcinoma (n=1).

Overall, our experience adds to a growing body of evidence for the efficacy of lenalidomide in patients with TFL. We have also demonstrated the potential utility of lenalidomide in the setting of relapse post–AlloSCT. We observed a relatively high rate of second malignancies during treatment. Lenalidomide has previously been associated with an increased risk of second malignancies and patients starting treatment should be counselled regarding this.

Disclosure of Interest: None Declared

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**Table 1. Annual prevalence of hospitalizations, emergency room visits and iMCD-related morbidities in patients following iMCD diagnosis**

<table>
<thead>
<tr>
<th>Years following initial iMCD diagnosis</th>
<th>Total remaining iMCD patients</th>
<th>Annual percentage of iMCD patients with inpatient hospitalizations (n)</th>
<th>Annual percentage of iMCD patients with emergency room visits (n)</th>
<th>Hematologic malignancies</th>
<th>Non-hematologic malignancies</th>
<th>Thrombus</th>
<th>Renal failure</th>
<th>Respiratory failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>199</td>
<td>59.8% (119)</td>
<td>54.3% (108)</td>
<td>7.5% (15)</td>
<td>19.1% (38)</td>
<td>6.5% (13)</td>
<td>12.6% (25)</td>
<td>6.5% (13)</td>
</tr>
<tr>
<td>2</td>
<td>169</td>
<td>25.4% (43)</td>
<td>33.7% (57)</td>
<td>5.9% (10)</td>
<td>14.8% (25)</td>
<td>4.1% (7)</td>
<td>6.5% (11)</td>
<td>4.1% (7)</td>
</tr>
<tr>
<td>3</td>
<td>110</td>
<td>24.5% (27)</td>
<td>28.2% (31)</td>
<td>5.5% (6)</td>
<td>20.0% (22)</td>
<td>5.5% (6)</td>
<td>6.4% (7)</td>
<td>1.8% (2)</td>
</tr>
<tr>
<td>4</td>
<td>81</td>
<td>28.4% (23)</td>
<td>33.3% (27)</td>
<td>3.7% (3)</td>
<td>16.0% (13)</td>
<td>6.2% (5)</td>
<td>2.5% (2)</td>
<td>6.2% (5)</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>25.5% (14)</td>
<td>50.9% (28)</td>
<td>9.1% (5)</td>
<td>20.0% (11)</td>
<td>7.3% (4)</td>
<td>3.6% (2)</td>
<td>7.3% (4)</td>
</tr>
</tbody>
</table>

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**BSH2021-PO-181**

**Bone marrow biopsy in the staging of Hodgkin lymphoma - breaking the habit**

Michael Caruana Dingli1, Denise Gatt2, Nadia Shamala3,
Anthony Samuel3, David James Camilleri1, Mark Grech1,
Asterios Giotas1, Alex Gatt1

1Department of Haematology, 2Foundation Doctor, 3Department of Nuclear Imaging, Mater Dei Hospital Malta, Swieqi, Malta

Abstract Content: Introduction: In our institution, bone marrow biopsy (BMB) has been carried out as part of the staging of Hodgkin lymphoma. However, since the advent of positron emission tomography (PET), several international guidelines have dropped this painful procedure except in certain circumstances. We wanted to verify the usefulness or otherwise of BMB as part of the staging process.

Aims: To study the sensitivity and concordance rates between BMB and positron emission tomography (PET) for the detection of marrow involvement in cases of Hodgkin lymphoma.

Methods: All patients diagnosed with Hodgkin lymphoma in Malta between 2010-2020 were included in this study amounting to a total initial sample size of 173. The following information was documented, namely gender, subtype of Hodgkin lymphoma, Ann Arbor Stage, focal iliac crest positivity on PET, bone marrow involvement on trephine and the presence and type of skeletal involvement on the initial PET scan which was described as follows:

1. ‘Diffuse’ – most likely representing reactive finding
2. ‘Unifocal’ single focus of tracer uptake within bone - most likely disease
3. ‘Multifocal’ - multiple areas of bone tracer uptake- most likely disease

The initial stage according to the Ann Arbor Staging system was calculated based on the PET scan results. We then re-calculated the stage following trephine to see whether this resulted in the patient being upstaged.

Consideration was given to whether iliac crest involvement was present, as this is the usual site of bone marrow trephine, and thus may affect the likelihood of marrow involvement being picked up during this procedure.

Results: Of the initial 173 patients, 37 (21.4%) were excluded. 13 were excluded for not having undergone an initial PET scan, 12 for having no BMB, and 10 had neither an initial scan nor a BMB.

The majority (73%) were of the Nodular Sclerosis type and there was a slight male preponderance (55%). The Stage of disease...
PET scan appears to be much more sensitive than BMB. Responses to PET positivity to ascertain whether this is due to disease or not. The vast majority of cases in the staging process of Hodgkin lymphoma. No cases were upstaged by BMB as opposed to PET. Our results confirm that it is possible to phase out the use of BMB in the vast majority of cases in the staging process of Hodgkin lymphoma. Targeted BMB might be indicated in cases of unilocal bone marrow PET positivity to ascertain whether this is due to disease or not.

**Conclusion:** PET scan appears to be much more sensitive than BMB for the detection of marrow involvement in cases of Hodgkin lymphoma. No cases were upstaged by BMB as opposed to PET. Our results confirm that it is possible to phase out the use of BMB in the vast majority of cases in the staging process of Hodgkin lymphoma. Targeted BMB might be indicated in cases of unilocal bone marrow PET positivity to ascertain whether this is due to disease or not.

**Abstract Table:** Detection of Marrow Involvement by PET scans and Trephines

<table>
<thead>
<tr>
<th>Bone Marrow involvement on Trephine (n = 11)</th>
<th>No Marrow involvement on Trephine (n = 127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET Scan Negative (n = 104)</td>
<td></td>
</tr>
<tr>
<td>Diffuse Tracer Uptake</td>
<td>0</td>
</tr>
<tr>
<td>No Uptake</td>
<td>17 (12.3%)</td>
</tr>
<tr>
<td>PET Scan Positive (n = 34)</td>
<td></td>
</tr>
<tr>
<td>Unifocal uptake</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>Multifocal uptake</td>
<td>10 (7.2%)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Disclosure of Interest:** None Declared

**BSH2021-PO-183**

**Abstract Content:** A review of 2 week wait referrals to the lymphoma clinic over a 2 year period, including during the coronavirus pandemic. The number of referrals received, symptoms leading to referral and eventual diagnosis were recorded. In particular we were keen to establish whether the number of referrals received declined during the pandemic and if this therefore resulted in a drop in cancer diagnoses made. Between September 2018 and September 2020, 143 patients were referred by their GP via a 2 week wait pathway to the lymphoma clinic at University Hospital Southampton. The number of referrals received between March and September 2019 was 53 compared to 24 in the same time period in 2020. The first national lockdown in the UK came into effect on the 16th March 2020. Reassuringly however the number of cancer diagnoses made from these referrals remained very similar, 14 in 2019 and 13 in 2020 in the same time period. In total, over the 2 year period, 39 of the patients referred were diagnosed with cancer out of the 143 referrals. 32 of these were lymphoma, most commonly Chronic Lymphocytic Lymphoma and Diffuse Large B Cell Lymphoma. The majority of these diagnosed by ultrasound guided core biopsy or flow cytometry of peripheral blood. The criteria for a 2-week wait referral for suspected lymphoma is unexplained lymphadenopathy or splenomegaly. Consideration also to be given to associated symptoms such as fever, night sweats, weight loss, pruritus and alcohol induced lymph node pain. The majority of referrals (77%) were with lymphadenopathy. Overall a significant proportion of referrals resulted in a cancer diagnosis being made in the 2 year period reviewed, more than most other 2 week wait pathways. Therefore there is no indication to make the referral criteria more restricted. Whilst the number of referrals halved during the coronavirus pandemic, the number of cancer diagnoses remained very similar suggesting those who needed to be seen were still referred.

**Disclosure of Interest:** None Declared

**BSH2021-PO-183**

**Abstract Content:** Belantamab mafodotin (belama; GS2857916) is a B-cell maturation antigen (BCMA)-targeting antibody-drug conjugate. In the Phase II DREAMM-2 study, single-agent belama demonstrated deep and durable responses and a manageable safety profile in patients refractory and/or intolerant to ≥ 3 lines of therapy (LOT), including an anti-CD38 monoclonal antibody (mAb; e.g. daratumumab [DAR]) (Lonial et al. Lancet Oncol 2020). Responses were sustained at 13 months of follow-up with belama (2.5 mg/kg intravenously [IV] every 3 weeks [Q3W]); overall response rate (ORR) was 32% and median duration of response (DoR) was 11.0 months (Lonial et al. ASCO 2020 Poster 436).

**Disclosure of Interest:** None Declared
Triple combination regimens (e.g. DEX + bortezomib [BOR] + dexamethasone [DEX]; [D-Vd]) are a standard of care for patients with relapsed/refractory multiple myeloma (RRMM) and have demonstrated superior antimyeloma activity to monotherapy and dual combination regimens (e.g. BOR + DEX).

Preclinical data suggest synergistic antimyeloma activity of bel- maf and BOR (a proteasome inhibitor). Initial results from the ongoing Phase II/III DREAMM-6 study of belmaf + BOR + DEX (B-Vd) indicate an acceptable safety profile (Nooka et al. ASCO 2020 Oral 8502). The DREAMM-7 study (NCT04246047) will evaluate the efficacy and safety of B-Vd vs D-Vd in RRMM patients.

DREAMM-7 is an ongoing, randomised, open-label, global, multi-centre, Phase III, two-arm study in patients with measurable RRMM who had received ≥1 prior therapy with documented disease progression during or after their most recent therapy. Eligible patients are aged ≥18 years with Eastern Cooperative Oncology Group Performance Status 0–2, with adequate organ system function, and who provide informed consent. Patients intolerant/refractory to DAR or BOR or with prior exposure to anti-BCMA therapy will be excluded. Patients will be stratified by the Revised International Staging System, prior exposure to BOR, and number of prior LOT.

Approximately 478 patients will be randomised (1:1) to Arm A (B-Vd) or Arm B (D-Vd).

In Arm A, patients will receive belmaf 2.5 mg/kg (IV) Q3W on Day 1 of each cycle; BOR 1.3 mg/m² (subcutaneously) on Days 1, 4, 8, and 11 of Cycles 1–8 (21-day cycles); and DEX 20 mg (IV or orally) on the day of, and the day after, BOR treatment. In Arm B, patients will receive DAR 16 mg/kg (IV) in 21-day cycles: Cycles 1–3 Q1W, Cycles 4–8 Q3W, and from Cycle 9 onwards Q4W; DEX and BOR schedules will be the same as in Arm A. Treatment will continue in both arms until disease progression, death, unacceptable toxicity, withdrawal of consent, or study end.

The primary endpoint is progression-free survival (PFS; time from randomisation to the earliest date of documented disease progression or death [any cause]). The key secondary endpoint is minimal residual disease negativity rate, assessed by next-generation sequencing. Further secondary endpoints include complete response rate, ORR, DoR, PFS2 (PFS after initiation of new anticancer therapy), overall survival, and endpoints related to pharmacokinetics, antidrug antibody levels, safety, and health-related quality of life. As of August 2020, the study is enrolling.

Funding: GSK (Study 207503): drug linker technology licensed from Seagen, Inc.; mAb produced using POTTLEGEN Technology licensed from BioWa.

Encore statement: Previously presented as Poster 3247 at the American Society of Hematology Annual Meeting, 5–8 December 2020; submitted with permission and on behalf of the original authors.

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BSH2021-PO-184

Central nervous system aspergillosis complicating ibrutinib chemotherapy: a case series

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Abstract Content: Introduction: Ibrutinib is a small molecule Bruton’s tyrosine kinase (BTK) inhibitor which has revolutionised treatment of chronic lymphocytic leukaemia (CLL). BTK is involved in B-cell receptor signalling regulating normal B-cell activation, interactions and survival.

Ibrutinib use can predispose to invasive fungal infections (IFI), via dysregulation of the innate immune system.

We report three patients exhibiting central nervous system (CNS) aspergillosis as a complication of Ibrutinib therapy.

Case 1: A 73-year-old man diagnosed with TP53-deleted CLL commenced second-line ibrutinib after initial bendamustine therapy. Five months after starting ibrutinib, he presented with confusion and worsening mobility. Ring-enhancing lesions suggestive of cerebral abscesses were identified on CT and were aspirated. Aspirate confirmed Aspergillus fumigatus and he completed a three-month course of voriconazole. Despite successful treatment of IFI, his CLL progressed and alternative chemotherapy was no-longer suitable. He died six months after discharge from pneumonia.

Case 2: A 64-year-old woman with CLL diagnosed in 2020 commenced second-line ibrutinib after initial bendamustine therapy. Three weeks into cycle three of ibrutinib, at a time of clinical remission, she presented with a one week history of lethargy, confusion and ataxia without fever or lateralising neurological signs. MRI head demonstrated two large ring-enhancing lesions. In view of aspergillosis risk, empirical voriconazole was initiated. Aspergillus fumigatus was isolated following abscess drainage and voriconazole treatment continued with clinical improvement. She remains well three months after discharge and is planned to re-commence ibrutinib.

Case 3: A 61-year-old woman with a background of Crohn’s disease on long term prednisolone was diagnosed with TP53-mutated Lymphoma, CLL and Myeloma
CLL in 2005 and commenced ibrutinib in 2020. COVID-19 pneumonitis was diagnosed three months prior to presentation which was treated with dexamethasone (without IL-6 inhibition). In January 2021 she was admitted with a three-week history of worsening headache, visual field defect and pyrexia. MRI imaging indicated cerebral abscess. She underwent drainage and Aspergillus fumigatus was grown. She made good clinical progress with voriconazole, although her admission was complicated by Pneumocystis jirovecii pneumonia.

**Discussion:** CLL is a haematological malignancy with low incidence of IFI. Cerebral aspergillosis is uncommon, even amongst immunosuppressed individuals, however literature reports have indicated an association with ibrutinib.

The first two cases had no other clear predisposition for IFI and are likely attributable to ibrutinib. Case 3 had additional risk factors of long-term and acute steroid use. Onset of ibrutinib-induced CNS IFI can occur early in treatment without any other risk factor and presentations may be atypical, such as the absence of fever in Case 1, or with non-specific symptoms as in Case 2. Ring-enhancement on MRI was present in all three cases.

Increased awareness of the potential for IFI, particularly CNS infection, in patients taking ibrutinib is crucial with its increasing use. Clinical suspicion is needed for any patient treated with BTK inhibitors presenting with neurological symptoms or undifferentiated fever. Further research is required to determine if the incidence of invasive aspergillosis in ibrutinib recipients warrants routine antifungal prophylaxis.

**Disclosure of Interest:** None Declared

**BSH2021-PO-185**

**Experience in a large district general hospital of excision versus core needle lymph node biopsy over a five year period**

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**Abstract Content:** Some national guidance favour excision biopsies for the diagnosis of lymphomas while others are more permissive of core biopsies. Core biopsies are commonly used as the first line diagnostic procedure for practical purposes in current practice. We sought to investigate the experience of a large district general hospital in a 5 year period with both these diagnostic modalities. Data was collected from all lymph node biopsies carried out in the trust between January 2015 and March 2020. The data were then categorised by modality and diagnosis. Most of the haematological malignancies diagnosed were lymphomas. Non-diagnostic samples included those with insufficient or unsatisfactory tissue. Further subgroup analysis of non-diagnostic samples was carried out from electronic patient records. A total of 2499 biopsies were carried out - 41% were core needle biopsies and 59% were excision biopsies (see table). The commonest diagnosis for all biopsies regardless of modality were non-malignant (49%), haematological malignancy (24%), non-haematological malignancy (23%) and non-diagnostic (4%). They were significantly more (P < 0.001) non-diagnostic samples with core needle biopsies (8%) compared to excision biopsies (1%). Of the 92 patients who had an initial non-diagnostic biopsy, 70% went on to have a repeat biopsy. Of these, 59% were excision biopsies, 28% were core needle biopsies and 13% were by other modalities (EBUS, VATS etc). The remaining 30% did not have a repeat biopsy. For 89% of these patients, a decision was made for no further investigation, while 11% died before any other investigation could be undertaken. The average time taken from initial biopsy to repeat biopsy of any modality was 45 days (range 10-120 days). There was no statistically significant difference (P = 0.36) in the time taken for a repeat core needle biopsy (mean 38 days) in comparison to a repeat excision biopsy (mean 49 days). A small number of patients who had an initial non-diagnostic sample did not have a further biopsy arranged. This was either due to low clinical suspicion, no other suitable targets for biopsy or a decision to monitor via imaging. Should a repeat biopsy be required, excision biopsy was the preferred method. This was appropriate as it is the more accurate method and is in line with national guidance. Although there was no statistical difference in the time taken for a repeat core needle biopsy compared to a repeat excision biopsy, this was longer than expected (over 6 weeks). This area could explored to see if this can be improved. This analysis has shown that both core needle biopsies and excision biopsies are both accurate methods of acquiring histological diagnosis (both over 90% respectively). Excisions biopsies are more accurate, however consume more resources and carry more risk, while the reverse can be said for core biopsies. A personalised approach for every patient should be considered, with the most suitable diagnostic method selected after weighing up risks versus benefits of unique individual and disease factors. This approach will not only benefit patients while not compromising diagnostic accuracy, but will also help conserve healthcare resources - which is especially important during the current global COVID-19 pandemic.

**Abstract Table:**

<table>
<thead>
<tr>
<th>Outcomes of Patients Undergoing Biopsies by Modality and Diagnosis</th>
<th>INITIAL CORE NEEDLE BIOPSY</th>
<th>INITIAL EXCISION BIOPSY</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 1024 (%)</td>
<td>Haematological Malignancy</td>
<td>418 (41)</td>
</tr>
<tr>
<td>Non-Haematological Malignancy</td>
<td>272 (27)</td>
<td>Non-Haematological Malignancy</td>
</tr>
<tr>
<td>Non-Malignant</td>
<td>251 (24)</td>
<td>Non-Malignant</td>
</tr>
<tr>
<td>Non-Diagnostic</td>
<td>83 (8)</td>
<td>Non-Diagnostic</td>
</tr>
<tr>
<td>Repeat Biopsy by all modalities for initial non-diagnostic result</td>
<td>n = 64 (%)</td>
<td>Haematological Malignancy</td>
</tr>
<tr>
<td>Non-Haematological Malignancy</td>
<td>7 (10)</td>
<td>Non-Malignant</td>
</tr>
<tr>
<td>No Repeat Biopsy for initial non-diagnostic result</td>
<td>n = 28 (%)</td>
<td>No further investigations planned</td>
</tr>
<tr>
<td>Died prior to diagnosis</td>
<td>3 (11)</td>
<td></td>
</tr>
</tbody>
</table>

**Disclosure of Interest:** None Declared

**BSH2021-PO-186**

**Apixaban in the prevention of thromboembolism in patients with Multiple Myeloma receiving immunomodulatory medications. Real world experience - data from two centers in North Wales, United Kingdom**

Aswathi Balakrishnan*,1, Jesmin Hossain, Victoria Jones, Earnest Heartin, Durgadevi Moratuwagama

1Haematology, Glan Clwyd Hospital, Rhyl, United Kingdom

**Abstract Content:** The risk of venous thromboembolism (VTE) in patients with Multiple Myeloma is very high especially within the first 6 months. The reason for increased thrombogenicity is...
multifactorial including the disease process itself and the medications used for its treatment.

There was a part of the Myeloma XI trial that looked into the risk of thromboembolism in myeloma patients. It concluded that 12.4 percent of patients developed VTE out of which 87.6 percent of patients were already on thromboprophylaxis (aspirin, low molecular weight heparin (LMWH) and warfarin). There are large studies looking into the use of new oral anticoagulants (NOAC) as thromboprophylaxis in patients with cancer but myeloma patients are underrepresented in these studies. A handful of small studies have looked into the effectiveness of NOACs as thromboprophylaxis in patients with myeloma and the results look promising.

The aim of our study was to look into the effectiveness of NOACs specifically apixaban in the prevention of venous thromboembolism in patients with multiple myeloma on immunomodulatory medication (thalidomide, lenalidomide and pomalidomide) who were started on apixaban and a few patients who were switched from LMWH to apixaban.

We looked into the incidence of venous thromboembolism (deep vein thrombosis (DVT) and pulmonary embolism (PE)) in the first 104 patients, 75 patients from Glen Clwyd Hospital and 29 patients from Ysbyty Gwynedd (Bangor hospital) who were on immunomodulatory therapy and received apixaban as thromboprophylaxis. The dose of apixaban used was 2.5 mg twice a day. Data was collected from online patient records (Welsh clinical portal), pharmacy records and online clinic letters (EPRO).

There were 55 males and 49 females in the study. Our results showed that out of the 104 patients none of the patients had VTE while on apixaban thromboprophylaxis.

We conclude that apixaban appears to be effective in preventing VTE in patients with Multiple Myeloma on immunomodulatory therapy. In our study none of the patients developed venous thromboembolism while on apixaban, which is much less when compared to Myeloma XI trial data. This potentially indicates that apixaban might be superior to aspirin, LMWH and warfarin. Larger randomised studies are needed to validate the use of NOACs as an effective thromboprophylactic option in this group of patients.

Disclosure of Interest: None Declared

BSH2021-PO-187
Microsatellite aberrations dynamics in relapse and progression of follicular lymphoma
Sychevskaya Kseniia1, Sergey Kravchenko1, Bella Biderman1, Elena Nikulina1, Anna Misurina1, Natalya Risinskaya1, Andrey Sudarikov1
1National Research Center for Hematology, Moscow, Russian Federation

Abstract Content: Every tenth follicular lymphoma (FL) patient dies within two years after onset due to the resistant disease. Effective treatment protocols for this group are not elaborated. New drugs development depends on tumor progression pathogenesis understanding. So the study of tumor evolution in refractory FL is an urgent task.

Genetic aberrations that determine tumor resistance occur due to various changes in the original DNA structure. Normally DNA damage is eliminated by the repair mechanisms. The mismatch repair system (MMR) is one of the key elements in genetic homeostasis. It is known that the MMR deficiency leads to microsatellite instability (MSI).

The aim was to study microsatellite profile changes in refractory FL patients.

Four FL grade 1-2 patients, 7 FL patients grade 3A, and 10 patients with FL grade 3B and the transformation of FL into large-cell lymphoma were included. All patients gave their voluntary consent to participate in the study. The first and the second biopsies were performed in 12 patients at debut and relapse, in 6 patients – at debut and during progression on chemotherapy, and in 3 patients – at debut and after progression following “wait and watch” period.

Abstract Table:

<table>
<thead>
<tr>
<th>Patient</th>
<th>FL grade</th>
<th>Disease course</th>
<th>EMAST+/the first biopsy</th>
<th>EMAST+/the second biopsy</th>
<th>LOH+/the first biopsy</th>
<th>LOH+/the second biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>FL 3A</td>
<td>Relapse</td>
<td></td>
<td></td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>#2</td>
<td>FL grade 1-2</td>
<td>Relapse</td>
<td></td>
<td></td>
<td>Y*</td>
<td>Y*</td>
</tr>
<tr>
<td>#3</td>
<td>FL grade 1-2</td>
<td>Relapse</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>#4</td>
<td>FL 3B and transformation</td>
<td>Progression on therapy</td>
<td></td>
<td></td>
<td>Y</td>
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<tr>
<td>#5</td>
<td>FL 3A</td>
<td>Progression on therapy</td>
<td>Y</td>
<td></td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>#6</td>
<td>FL grade 1-2</td>
<td>Progression on therapy</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>#7</td>
<td>FL 3B and transformation</td>
<td>Progression on therapy</td>
<td></td>
<td></td>
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<td>Y</td>
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<tr>
<td>#8</td>
<td>FL 3B and transformation</td>
<td>Relapse</td>
<td></td>
<td></td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>#9</td>
<td>FL 3A</td>
<td>Relapse</td>
<td></td>
<td></td>
<td>Y</td>
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<tr>
<td>#10</td>
<td>FL 3B and transformation</td>
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<td></td>
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<tr>
<td>#11</td>
<td>FL 3B and transformation</td>
<td>Progression on &quot;wait and watch&quot;</td>
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<td></td>
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<td>#12</td>
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<tr>
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<td></td>
<td></td>
<td>Y</td>
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<tr>
<td>#15</td>
<td>FL 3A</td>
<td>Relapse</td>
<td></td>
<td></td>
<td>Y*</td>
<td>Y*</td>
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<tr>
<td>#16</td>
<td>FL 3B and transformation</td>
<td>Relapse</td>
<td></td>
<td></td>
<td>Y</td>
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<tr>
<td>#17</td>
<td>FL 3B and transformation</td>
<td>Progression on &quot;wait and watch&quot;</td>
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<td></td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>#18</td>
<td>FL 3B and transformation</td>
<td>Progression on therapy</td>
<td></td>
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<td>#19</td>
<td>FL 3B and transformation</td>
<td>Progression on &quot;wait and watch&quot;</td>
<td>Y</td>
<td></td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>#20</td>
<td>FL 3A</td>
<td>Progression on therapy</td>
<td></td>
<td></td>
<td>Y</td>
<td>Y*</td>
</tr>
<tr>
<td>#21</td>
<td>FL grade 1-2</td>
<td>Relapse</td>
<td></td>
<td></td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

Total: 5 (23.8%) 8 (38.1%) 9 (42.9%) 16 (76.2%)

*LOH loci are not identical
Lymphoma, CLL and Myeloma

MSI was studied using CorDIs Plus kit (Gordiz, Russia) in tumor tissue and in peripheral blood cells as a control sample. Amplification and fragment analysis were performed using thermal cycler DNA Engine (BioRad, USA) and genetic analyzer Nanofor-05 (Sintol, Russia) respectively.

The detected microsatellite aberrations were classified as follows: EMAST (elevated microsatellite alterations at selected tetranucleotide repeats) – the appearance of a new allele of tetranucleotide loci; LOH (loss of heterozygosity) – allelic imbalance. EMAST is considered to be a particular variant of MSI. The data are shown in Table 1.

There is a tendency of MSI degree increase during the disease course in the material of paired biopsies. For the LOH the differences between the debut and relapse/progression groups were statistically significant ($P = 0.02$, df=1, $\chi^2 = 4.8$). The association of the mutations dynamics with FL grade, disease clinical course was not traced. However, this negative result may only be a consequence of a limited sample size.

Mainly microsatellite profile was preserved from onset to relapse in the majority of patients with only a few new LOH and EMAST loci emerged during the course of the disease. However, in 3 cases, the LOH loci in the debut and relapse/progression were different. As mutational profile at debut is not totally inherited at relapse, we can assume tumor clones develop independently from the earlier tumor stem cell.

It is known that chemotherapy provokes the genetic aberrations occurrence. We are not able to deny the possibility of drugs mutagenic effect on microsatellites changes in patients in the cohort with disease treatment. However, in all patients with both biopsies performed before the therapy initiation, the new genetic events appearance indicates that tumor evolution may occur without cytotoxic pressure.

It should be noted, that the therapy failure in FL is often regarded by clinicians as a result of an inappropriate first-line regimen. However, our observations demonstrated that at least in some cases therapy resistance in FL could be due to some intrinsic tumor features and has no relation to the drugs administered. Therefore these features require further investigations that possibly could point to new therapeutic approaches.

Disclosure of Interest: None Declared

BSH2021-PO-188

Infectious complications related to the treatment of Chronic Lymphocytic Leukaemia: Comparison of risks associated with chemoimmunotherapy and ibritinib

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Abstract Content: Infectious complications in patients with Chronic Lymphocytic Leukaemia (CLL) is a major cause of increased morbidity and mortality. A variety of treatment options exist for the management CLL, and recent studies have highlighted the high risk of infection associated with novel therapies, such as ibritinib, with particular focus on opportunistic and fungal infections. Risk of infection is increased during the treatment of CLL, and it is well recognised that this risk persists for several months after cessation of some therapies, particularly bendamustine and fludarabine-based regimens where immune reconstitution can take over 12 months.

This retrospective analysis studies patients in NHS Grampian who have received treatment for CLL, with the aim of identifying if there is a difference between rate, severity, and types of infections between different treatment options.

Sixty-five patients, who had been treated for CLL between 01/01/2017 and 31/12/2019, were included in this study. Infections were defined as episodes of clinical infection in which patients were treated in hospital, or those that occurred in an outpatient setting where patients received antimicrobial therapy. This included fungal infections, viral infections and suspected Pneumocystis jiroveci pneumonia (PJP).

The median age of this population was 64 years (range: 46-86). 85.71% of the treatment episodes recorded were first-line treatments for CLL, with 11.69% being second-line and 2.60% third-line treatments. 53.85% of patients had 1 or more ‘serious’ co-morbidity; where a serious co-morbidity was defined as having the potential to independently increase the risk of infection.

This study found that patients suffered on average 1.04 infections for every year on treatment (or in the 6 months post-therapy). A wide variety of infections were identified, with the most common being respiratory infections, sepsis of unknown origin and fungal nail/skin infections.

In the vast majority (84.42%) of treatment episodes, patients were on prophylactic therapy. Consequently, only 2 cases of PJP and 1 case of herpes zoster virus (HZV) were found. Furthermore, the rate of infections (number of episodes per patient year) was comparable between those treated with ibritinib (0.99) and those prescribed chemoimmunotherapies (0.92). However, there were fewer inpatient infections in the ibritinib cohort (35.29%) when compared to the chemoimmunotherapy cohort (51.61%), indicating that perhaps there were fewer serious infections in those treated with ibritinib. Although limited by sample size and duration of study, this report suggests the use ibritinib may reduce the risk of infectious complications compared with conventional chemoimmunotherapy in CLL.

Furthermore, it suggests that current prophylactic regimens are effective against PJP and HZV infection. Nonetheless, there is still a considerable burden of infections for patients treated for CLL, and additional research into optimal prophylactic strategies, both during and after treatment, is required to improve overall outcomes.

Disclosure of Interest: K. Hutchinson: None Declared, G. Preston Conflict with: Honoraria from Jansen-Cilag and Abbvie

Abstract Table:

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Patients Treated</th>
<th>Total Infections</th>
<th>Inpatient Infections</th>
<th>Outpatient Infections</th>
<th>Patients with ≥1 Infections</th>
<th>Patient Years on Therapy</th>
<th>Infections per Patient Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrutinib</td>
<td>19</td>
<td>34</td>
<td>12</td>
<td>22</td>
<td>73.68%</td>
<td>34.34</td>
<td>0.99</td>
</tr>
<tr>
<td>Chemoimmunotherapy (Total)</td>
<td>38</td>
<td>31</td>
<td>16</td>
<td>15</td>
<td>50.00%</td>
<td>33.80</td>
<td>0.92</td>
</tr>
<tr>
<td>FCR</td>
<td>14</td>
<td>10</td>
<td>8</td>
<td>2</td>
<td>42.86%</td>
<td>12.92</td>
<td>0.77</td>
</tr>
<tr>
<td>R-Bendamustine</td>
<td>13</td>
<td>14</td>
<td>8</td>
<td>6</td>
<td>61.54%</td>
<td>10.30</td>
<td>1.36</td>
</tr>
<tr>
<td>Obinutuzumab &amp; Chlorambucil</td>
<td>11</td>
<td>7</td>
<td>0</td>
<td>7</td>
<td>45.45%</td>
<td>10.38</td>
<td>0.66</td>
</tr>
</tbody>
</table>
BSH2021-PO-189
DREAMM-8: A phase III study of the efficacy and safety of belantamab mafodotin with pomalidomide and dexamethasone vs pomalidomide plus bortezomib and dexamethasone in patients with relapsed/refractory multiple myeloma
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Abstract Content: Belantamab mafodotin (belmafa; GSK2857916) is a B-cell maturation antigen (BCMA)-targeting antibody-drug conjugate approved in the US and the EU. In the Phase II DREAMM-2 study, single-agent belamaf demonstrated deep and durable responses with a manageable safety profile in heavily pretreated patients with relapsed/refractory multiple myeloma (RRMM; Lonial et al. Lancet Oncol 2020 and Lonial et al. ASCO 2020 Poster 436).

Preclinical data suggest synergistic antymyeloma activity of belmafa in combination with pomalidomide/dexamethasone (Pd). Preliminary data from an ongoing Phase I/II study (NCT03715478) evaluating belamaf in combination with Pd (BPd) suggest an acceptable safety profile and early signs of clinical activity in patients with RRMM. The DREAMM-8 study (NCT04486423) will evaluate the efficacy and safety of BPd compared with bortezomib and Pd (PVd).

This is an ongoing Phase III, two-arm, randomised, open-label, multicentre study in patients with measurable RRMM who have received ≥1 prior line of therapy (including lenalidomide), with documented disease progression during/after their most recent line of treatment (LOT). Patients aged ≥18 years with Eastern Cooperative Oncology Group Performance Status 0–2, with adequate organ system function, and who provide informed consent will be eligible. Patients with prior exposure to BCMA-targeted therapies or pomalidomide and those intolerant/refractory to bortezomib will be excluded.

Approximately 450 patients will be randomised (1:1) to Arm A (BPd) or Arm B (PVd), stratified by number of prior lines of treatment, prior exposure to bortezomib, and International Staging System status. No more than 50% of participants with ≥2 prior LOT will be enrolled. In Arm A, patients receive belamaf 2.5 mg/kg (IV) Q4W on Day 1 in Cycle 1 (28-day cycle) followed by belamaf 1.9 mg/kg (IV) Q4W on Day 1 in Cycle 2 onwards (28-day cycles); pomalidomide 4 mg (orally [PO]) will be administered on Days 1–21 and dexamethasone 40 mg (PO) on Days 1, 8, 15, and 22 in all cycles (28-day cycles). In Arm B, pomalidomide 4 mg (PO) will be administered Q3W on Days 1–14 in all cycles (21-day cycles); bortezomib 1.3 mg/m² will be administered subcutaneously on Days 1, 4, 8, and 11 in Cycles 1–8 and Days 1 and 8 in Cycle 9+ (21-day cycles). Dexamethasone 20 mg (PO) will be administered on the day of and the day after bortezomib. The dose level of dexamethasone in each arm will be reduced by half in patients >75 years of age. Treatment in both arms will continue until progressive disease, unacceptable toxicity, withdrawal of consent, initiation of another anticancer therapy, or end of study or death.

The primary endpoint is progression-free survival (PFS; time from randomisation to the earliest date of documented disease progression or death [any cause]). Minimal residual disease negativity rate is a key secondary endpoint. Additional secondary endpoints include ORR, time to response, duration of response, time to progression, overall survival, PFS2 (PFS after initiation of new anticancer therapy), safety, health-related quality of life, and pharmacokinetic and pharmacodynamic parameters.

Funding: GSK (Study 207499); drug linker technology licensed from Seagen, Inc.; mAb produced using POTEIGILkENT Technology licensed from BioWa.

Encore statement: Previously presented as Poster 2302 at the American Society of Hematology Annual Meeting, 5–8 December 2020; submitted with permission and on behalf of the original authors.

Disclosure of Interest: S. Trudel Conflict with: consultant (Celgene, Amgen, and GSK), Conflict with: grant/research support (GSK, Celgene, Janssen, Amgen, and Genentech), Conflict with: honoraria (Celgene, Janssen, Takeda, Sanofi, Karyopharm, and Amgen Canada), R. Davis Conflict with: GSK (employee), Conflict with: GSK (stocks and shares), N. M. Lewis Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK), K. K. Bakshi Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK), B. Chopra Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK), R. Montes de Oca Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK), G. Ferron-Brady Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK), L. Eliason Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK), B. E. Kremer Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK), D. Stowell Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK), I. Gupta Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK), F. S. Wu Conflict with: industry (GSK employee), Conflict with: stock and shares (GSK)

BSH2021-PO-190
Impact of comorbidity on therapeutic intent and treatment outcomes in older adult patients with diffuse large B-cell lymphoma
Karen Valdés-Díaz1, Halbert Hernández-Negrín2, Leonel Valdés-Leiva3
1Arnoldo Milian Hospital, Santa Clara, Cuba

Abstract Content: Lymphomas with aggressive histology in the older adult patient are a challenge for treating physicians. Decision making and the establishment of a therapeutic strategy is often complex due to various factors such as the association of comorbidities. The present study aimed to determine the impact of comorbidity on therapeutic intent and treatment outcomes in older adult patients with diffuse large B-cell lymphoma (DLBCL). We retrospectively included all patients diagnosed with DLBCL older than 60 years treated at the Arnaldo Milian University Hospital, Cuba, between 2004-2020. Comorbidity was assessed using the Charlson Comorbidity index. Binary logistic regression models were used to determine the impact of comorbidity on therapeutic intention and response to treatment. Kaplan-Meier curves and Cox regression models were used for survival analysis. 88 patients were studied, of whom 59 (67%) received treatment with curative intent. The median age of patients treated with curative and palliative intent was 68 years (interquartile range between 61 and 73) and 75 years (interquartile range between 70 and 79), respectively. Comorbidity had no association with therapeutic intent, however, high comorbidity in those patients where treatment was administered with curative intent was significantly
associated with worse therapeutic response and incomplete treatment. (Table 1) Cox multivariate proportional hazards analysis identified that patients who were treated with curative intent and had high comorbidity had worse overall survival, independent of other prognostic factors that make up the International Prognostic Index [hazard ratio 7.45 with 95% confidence interval [2.55 to 21.86], P = 0.000]. Although comorbidity did not impact therapeutic intent, it did determine poor therapeutic outcomes. These results highlight the need for recognition and assessment of comorbidity when planning the treatment strategy for older adult patients with DLBCL in our setting.

Abstract Table: Table 1: Factors associated with therapeutic intention, treatment response and incomplete treatment.

<table>
<thead>
<tr>
<th>Model 1. Outcome: treatment with palliative intent.</th>
<th>Univariate OR</th>
<th>IC 95%</th>
<th>P</th>
<th>Multivariate OR</th>
<th>IC 95%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.19</td>
<td>1.09–1.30</td>
<td>0.000</td>
<td>1.16</td>
<td>1.06–1.27</td>
<td>0.001</td>
</tr>
<tr>
<td>ECOG ≥2</td>
<td>4.08</td>
<td>1.50–11.08</td>
<td>0.006</td>
<td>2.30</td>
<td>0.62–8.49</td>
<td>0.208</td>
</tr>
<tr>
<td>Ann Arbor (III/IV)</td>
<td>1.18</td>
<td>0.44–3.18</td>
<td>0.730</td>
<td>1.32</td>
<td>0.40–4.36</td>
<td>0.640</td>
</tr>
<tr>
<td>CCI ≥3</td>
<td>0.54</td>
<td>0.31–1.91</td>
<td>0.047</td>
<td>0.45</td>
<td>0.14–1.46</td>
<td>0.188</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 2. Outcome: Non-response or progression</th>
<th>Univariate OR</th>
<th>IC 95%</th>
<th>P</th>
<th>Multivariate OR</th>
<th>IC 95%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.01</td>
<td>0.92–1.11</td>
<td>0.766</td>
<td>1.06</td>
<td>0.94–1.21</td>
<td>0.293</td>
</tr>
<tr>
<td>ECOG ≥2</td>
<td>1.52</td>
<td>0.48–4.85</td>
<td>0.471</td>
<td>0.48</td>
<td>0.11–2.13</td>
<td>0.338</td>
</tr>
<tr>
<td>Ann Arbor (III/IV)</td>
<td>4.57</td>
<td>0.92–22.7</td>
<td>0.063</td>
<td>5.77</td>
<td>0.93–35.61</td>
<td>0.059</td>
</tr>
<tr>
<td>CCI ≥3</td>
<td>8.08</td>
<td>1.98–32.9</td>
<td>0.000</td>
<td>10.19</td>
<td>2.13–48.67</td>
<td>0.004</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 3. Dependent variable: incomplete treatment.</th>
<th>Univariate OR</th>
<th>IC 95%</th>
<th>P</th>
<th>Multivariate OR</th>
<th>IC 95%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.01</td>
<td>0.91–1.13</td>
<td>0.756</td>
<td>1.05</td>
<td>0.91–1.22</td>
<td>0.460</td>
</tr>
<tr>
<td>ECOG ≥2</td>
<td>1.45</td>
<td>0.37–5.67</td>
<td>0.593</td>
<td>0.52</td>
<td>0.10–2.63</td>
<td>0.434</td>
</tr>
<tr>
<td>Ann Arbor (III/IV)</td>
<td>2.12</td>
<td>0.40–11.14</td>
<td>0.373</td>
<td>2.08</td>
<td>0.31–13.7</td>
<td>0.445</td>
</tr>
<tr>
<td>CCI ≥3</td>
<td>13.84</td>
<td>1.66–115.59</td>
<td>0.001</td>
<td>16.89</td>
<td>1.81–157.0</td>
<td>0.013</td>
</tr>
</tbody>
</table>

OR: Odds Ratio; CI: Confidence Interval; CCI: Charlson Comorbidity Index; ECOG: Eastern Cooperative Oncology Group. *Only patients who underwent treatment with curative intent were included in this analysis.

Disclosure of Interest: None Declared

BSH2021-PO-191
Bisphosphonate use in multiple myeloma: an audit of compliance and cost analysis
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Abstract Content: Background: The international myeloma working group (IMWG) recommendations of 2013 advise the use of bisphosphonates (BP) in myeloma irrespective of lytic skeletal lesions. Bisphosphonate therapy can be discontinued after 2 years in patients achieving complete response (CR) or very good partial response (VGPR) or after 1 year in the absence of active bone disease and CR/VGPR.

Aims: Our aim is to audit our haematology day unit at our main hospital where virtually all myeloma patients in Malta are catered for. We aim to compare our practice with the recommended guidance with respect to duration of treatment; indications; dosage and method of administration as per product specifications. We also want to perform a cost analysis of our bisphosphonate therapy program for multiple myeloma.

Methods: Patients with a plasma cell dyscrasia attending our Haematology Day Care Unit from January 2016 and December 2020 for any form of care were retrospectively identified. Cases were reviewed through patient notes and electronic records noting down frequency, indication, infusion time and adequacy of dosage of bisphosphonates with respect to creatinine clearance and corrected calcium. The occurrence of atypical fractures and bisphosphonate induced osteonecrosis of the jaw (BONJ) at diagnosis and 5 for undocumented reasons. There were 4 (4.0%) instances of BONJ which necessitated interruption of treatment, 2 of whom, were eligible for potential bisphosphonate discontinuation as per IMWG guidance.

Out of all 1,453 bisphosphonate infusion episodes, 74 (5.1%) prescriptions went against product dosing literature according to renal function and 41 (36.9%) patients lacked documentation regarding pre-bisphosphonate dental assessment. BP therapy was not indicated in 4 (3.9%) patients, 1 with a solitary plasmacytoma and 3 patients with smoldering myeloma without evidence of osteopenia/osteoporosis, amounting to 113 (7.8%) doses. Thirty-five (35.4%) patients were eligible for bisphosphonate discontinuation; of whom 10 were in CR/VGPR, lacked baseline bone disease and had completed 1 year of bisphosphonate therapy and 25 were in VGPR/CR with baseline bone disease and had completed 2 years of BP. These amounted to a total of 350 doses (24%). An average of 4.7 doses per patient were potentially avoidable. Cost of potentially avoidable BP therapy based solely on drug expenditure, equates to 227 Euros/patient/year. This cost analysis excludes concomitant pre-medication; hydration; bed occupancy at day unit and staffing.

Conclusion: Our study demonstrates that there is room for better implementation of recommended guidance in our myeloma bisphosphonate therapy program.

Disclosure of Interest: None Declared

BSH2021-PO-192
The management of lymphoma and chronic lymphocytic leukaemia patients on long term intravenous immunoglobulin replacement therapy: a single centre experience
Bethany Webster1, Nagah Elmusharaf2,3
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Abstract Content: Background: Intravenous Immunoglobulin (IVIg) replacement therapy in patients with secondary hypogammaglobulinaemia, history of infections and low serum IgG levels leads to a significant reduction in clinically significant infections. However current practice is mainly driven by clinical experience and data from IVIg use in primary...
immunodeficiencies. The emergence of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had a significant impact on the management of haematology patients.

**Aim:** To review the management of lymphoma and chronic lymphocytic leukaemia (CLL) patients receiving IVIg at University Hospital of Wales, Cardiff.

**Methods:** An immunoglobulin link nurse was appointed to manage patients receiving IVIg. Serum Immunoglobulin levels were collected at different time points to help guide dosing and frequency of IVIg replacement.

**Results:** 41 patients with the diagnosis of lymphoproliferative disorder were receiving IVIg. Patients’ characteristics are listed in the table provided. During the first COVID-19 national lockdown, high risk patients (i.e. history of recurrent infections) were switched to Subcutaneous Immunoglobulin replacement (SCIg) (9/41), (3/41) patients had IVIg administered at home under the care of the immunology department. The rest of the patients had their IVIg infusions postponed and were provided with antibiotics prophylaxis. The majority of patients resumed IVIg infusions after an average of 12 weeks apart from 5 patients: 2 opted to stay on (SCIg), 2 had an average IgG level of 7.3 g/L and one patient opted to continue on prophylactic antibiotics. No infections were reported by any of the patients. The average trough IgG level before restarting IVIg was 4.8 g/L. Trough levels were monitored regularly, average trough IgG levels following 3 doses of IVIg infusions was 9.4 g/L. 10/41 patients had consistently high IgG levels above 10 g/L with no history of infections. As a result, 2/41 patients had their IVIg doses reduced and 8/41 patients had their dose interval changed. Unfortunately due to the significant increase in COVID-19 infections in Wales, further modifications to IVIg delivery had to be reintroduced including postponing IVIg infusions. Virology screen was performed in all patients, 2 patients had positive Hepatitis core antibodies detected, however further investigations revealed the likely passive transfer of antibodies. The majority of patients found (SCIg) to be poorly tolerated and opted to switch back to IVIg replacement.

**Conclusions:** The appointment of an IVIg link nurse helped to provide high quality care to patients receiving IVIg. Our data showed low IgG levels off treatment in the majority of patients indicating the need to continue IVIg replacement. The continuous monitoring of trough IgG levels showed most patients are having an adequate IVIg replacement with no breakthrough infections. It also allowed dose adjustments for patients with high IgG levels. This will likely have a positive impact on patients’ quality of life, nurses staffing levels and a favourable financial impact in the long term. The current department of health clinical guidelines on IVIg replacement recommend reasonable attempts should be made to reduce the dose, by increasing the dosing interval or by using reduced dose, or both. However, there are no available practical guidelines to assist in decision making.

**Abstract Table:**

<table>
<thead>
<tr>
<th>Total Numbers</th>
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<tbody>
<tr>
<td>N = 41</td>
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</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>Total Numbers</th>
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<tbody>
<tr>
<td>Male</td>
<td>17 (41.4%)</td>
</tr>
<tr>
<td>Female</td>
<td>24 (58.6%)</td>
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</table>

<table>
<thead>
<tr>
<th>Age (years old)</th>
<th>Total Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>41–50</td>
<td>3 (7.3%)</td>
</tr>
<tr>
<td>51–60</td>
<td>4 (9.8%)</td>
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<tr>
<td>61–70</td>
<td>10 (24.4%)</td>
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<tr>
<td>71–80</td>
<td>15 (36.6%)</td>
</tr>
<tr>
<td>81–90</td>
<td>9 (22%)</td>
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</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Total Numbers</th>
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</thead>
<tbody>
<tr>
<td>CLL</td>
<td>30 (73.2%)</td>
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**Table 1. (Continued)**

<table>
<thead>
<tr>
<th>Type of IVIg</th>
<th>Total Numbers</th>
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<tbody>
<tr>
<td>Privigen</td>
<td>32 (78%)</td>
</tr>
<tr>
<td>Octagam</td>
<td>7 (17.1%)</td>
</tr>
<tr>
<td>Gamunex</td>
<td>2 (4.9%)</td>
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<table>
<thead>
<tr>
<th>IVIg dose</th>
<th>Total Numbers</th>
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<tbody>
<tr>
<td>25 grams</td>
<td>3 (7.3%)</td>
</tr>
<tr>
<td>30 grams</td>
<td>33 (80.5%)</td>
</tr>
<tr>
<td>40 grams</td>
<td>4 (9.8%)</td>
</tr>
<tr>
<td>50 grams</td>
<td>1 (2.4%)</td>
</tr>
</tbody>
</table>

**Average number of years on IVIG**

<table>
<thead>
<tr>
<th>Patients requiring supportive medications due to history allergic reactions to IVIg</th>
<th>Date available for 29/41 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/41 (29.3%)</td>
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</table>

**Disclosures of Interest:** None Declared

**BSH2021-PO-193**

A retrospective single-centre cohort study of the efficacy and safety of daratumumab with bortezomib and dexamethasone therapy for previously treated multiple myeloma

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**Abstract Content:** Daratumumab, bortezomib and dexamethasone (Dvd) is a therapy that has demonstrated significant clinical activity in relapsed/ refractory multiple myeloma (RRMM). In April 2019, it was approved by NICE. In June 2020, subcutaneous (SC) daratumumab gained EMA approval.

This is a real-world retrospective study of 21 patients with RRMM who started Dvd treatment between April 2019 and November 2020 at Guy’s Hospital, London. Clinical characteristics, response rates and treatment emergent toxicity were reviewed using electronic records; response outcomes were assessed for patients who received ≥1 cycles.

The median age at the start of therapy was 61 (range 42–86), with 13 (61.9%) male patients. Clinical characteristics are shown in Table 1. Seventeen (81%) patients had 1 previous line of therapy: 5 (29.4%) VMP (bortezomib, melphalan, prednisone), 5 (29.4%) VTd (bortezomib, thalidomide, dexamethasone), 2 (11.8%) VCd
Lymphoma, CLL and Myeloma

(bortezomib, cyclophosphamide, dexamethasone), 1 (5.9%) CRd (bortezomib, lenalidomide, dexamethasone) and 4 (23.3%) a clinical trial. Four (19%) had 2 prior lines, including a clinical trial in all cases. Twelve (57.1%) had undergone autologous stem cell transplant.

Overall, 18/21 (85.7%) patients had been exposed to bortezomib: overall response rate (ORR) was 88.9% and 1/18 (5.6%) was bortezomib-refractory in 1st line. Median progression free survival (PFS) and median treatment-free interval were 44.8 and 36 months, respectively.

All patients had progression and 1 (4.8%) extramedullary disease prior to starting DvD. Median time on treatment was 9.6 months (0.2-18.2), with a median number of cycles of 12 (2-20). Six (28.6%) patients discontinued therapy: 4 (66.6%) due to progressive disease, 1 (16.7%) for patient’s choice and 1 (16.7%) died on treatment (due to SARS-CoV-2-related pneumonia).

At a median follow-up of 11 months (1.8-20.5), 20 (95.2%) patients have completed ≥1 cycles. ORR is 85%, with very good partial response (VGPR) in 7 (35%) patients; only 1 (4.8%) patient had no response. The patient who was bortezomib-refractory in 1st line has a partial response (PR) so far. Median time to PR in the population is 36 days (15-67). PFS and overall survival (OS) rates are 76% and 96% at 11 months.

Daratumumab administration was SC in 6 (28.6%) patients, and was switched from intravenous (IV) to SC during treatment in 8 (38.1%) patients. Six (28.6%) patients had a first-dose infusion related reaction (IRR) with daratumumab, in all cases being IV. In 2 (33.3%) cases it was grade ≥3 and infusion could be resumed (both consisting of hypotension).

Common (≥15%) AEs were: lymphopenia (81%), anaemia (71.4%), thrombocytopenia (61.9%), peripheral sensory neuropathy (38.1%) and infections (28.6%), most of them SARS-CoV2 related (50%).

Grade ≥3 AEs happened in 10 (47.6%) patients. Three (30%) developed thrombocytopenia, 1 (10%) anaemia, 3 (30%) neutropenia and 6 (60%) lymphopenia. Moreover, 3 (30%) patients had SARS-CoV2-related pneumonia (in one of them leading to death) and another one (10%) sepsis secondary to jaw infection.

Daratumumab combined with bortezomib and dexamethasone in RRM demonstrates encouraging outcome results in our centre, similar to those exposed in the analysis of the phase III CASTOR study. It is expected that as more patients are treated and with a longer follow-up, the survival rates will improve. There is an acceptable safety profile in our population, with no IRRs to the moment since the introduction of SC daratumumab.

Abstract Table: Table 1. Clinical characteristics of the population.

<table>
<thead>
<tr>
<th>Characteristics (n = 21)</th>
<th>Overall data (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM type</td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>16/21 (76.2%)</td>
</tr>
<tr>
<td>IgA</td>
<td>2/21 (9.5%)</td>
</tr>
<tr>
<td>Bence-Jones</td>
<td>2/21 (9.5%)</td>
</tr>
<tr>
<td>Non-secretory</td>
<td>1/21 (4.8%)</td>
</tr>
<tr>
<td>ISS stage at diagnosis</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>11/21 (52.4%)</td>
</tr>
<tr>
<td>II</td>
<td>6/21 (28.6%)</td>
</tr>
<tr>
<td>III</td>
<td>4/21 (19%)</td>
</tr>
<tr>
<td>ISS-R stage at diagnosis</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>6/21 (28.6%)</td>
</tr>
<tr>
<td>II</td>
<td>7/21 (33.3%)</td>
</tr>
<tr>
<td>III</td>
<td>2/21 (9.5%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>6/21 (28.6%)</td>
</tr>
<tr>
<td>Cytogenetics at diagnosis*</td>
<td></td>
</tr>
<tr>
<td>Non-high risk</td>
<td>15/21 (71.4%)</td>
</tr>
<tr>
<td>High risk</td>
<td>1/21 (4.8%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>5/21 (23.8%)</td>
</tr>
<tr>
<td>ECOG performance scale ≤2</td>
<td>21/21 (100%)</td>
</tr>
</tbody>
</table>

Abbreviations: MM, Multiple myeloma; ISS, International Staging System; ISS-R, Revised International Staging System; ECOG, Eastern Cooperative Oncology Group. *High risk cytogenetics at diagnosis: t(4;14), del(17/17p), t(14;16).

Disclosure of Interest: None Declared

BSH2021-PO-194

Long-term survival outcomes in Multiple Myeloma: A single centre experience

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Abstract Content:

Multiple myeloma (MM) remains an incurable disease of the malignant plasma cells. However, the introduction of novel therapies has significantly improved the outcomes of the patients in recent years.

The objectives of the study are to compare the survival outcomes of a single district general hospital to the national data and identify the clinical determinants that predict the survival outcome.

The retrospective cohort study included consecutive patients with new diagnosis of MM from 2009 to February 2020 and data was retrieved from clinical portal and patients’ physical notes. The definitions of outcome were standardised according to the International Myeloma Working Group (IMWG) guideline. Survival analysis was performed using Kaplan Meier curve and Cox regression analysis.

Of the 171 patients included, 55% (n = 94) were male and the mean age was 69.6 years. In autologous stem cell transplant (ASCT) eligible patients, 51% had ASCT. Survival rates at 1-, 3- and 5-years were 78.8%, 55.0% and 42.0% respectively, which were comparable to the national statistics. Multivariate analysis showed that International Staging System (ISS) stage 3 predicts poor overall survival, HR 3.33 (95% CI 1.25 – 8.87, P = 0.016), after adjusting for age and ASCT. Median progression free survival (PFS) was 24 months. Multivariate analysis showed that patients with an ISS stage 3 with HR 4.89 (95% CI 1.91 – 12.57, P = 0.001) and patients who did not have ASCT with HR 0.32 (95% CI 0.12 – 0.86, P = 0.023) predict poor PFS. However, comparing overall survival of MM diagnosed in 2009 – 2014 and 2015 – 2020 showed no significant difference. The median time to first relapse, second relapse and third relapse were 21 months, 15 months and 8 months respectively.

In conclusion, our single centre data demonstrated comparable outcomes to the national data but did not show any difference in overall survival in MM over the last decade. ISS stage 3 is a strong predictor of overall survival and PFS in MM.

Disclosure of Interest: None Declared

BSH2021-PO-195

The significance of lymphocytosis in routine clinical practice: data from the South East Scotland Cancer Network

Gabrielle E. Clark*, Christopher Mullen, Laura E. McGlinchey, Victoria Campbell

Abstract Content:

Lymphocytosis is a frequent finding; in younger patients it is usually transient and reactive; in older patients a persistent lymphocytosis may reflect an underlying lymphoproliferative disorder. Immunophenotyping (IPH) is a technique that allows the protein expression of cell populations to be measured, highlighting clonal populations. In South East Scotland IPH is carried out on cases with a lymphocyte count >5x10⁹/L for >3 months.

Disclosure of Interest: None Declared
Most participants were survivors of haematological malignancies with a median age of 71 years (range 31–86 years) and slight male predominance (59%). 97% had a lymphocyte count >5 × 10^9/L with a mean lymphocyte count of 10.95 x 10^9/L (range 1.03–62.56 x 10^9/L). The mean duration of lymphocytosis prior to immunophenotyping being performed was 405 days. 36% were associated with additional abnormal haematological parameters - unexplained anaemia (15%), thrombocytopenia (16%) and thrombocytosis (5%). An abnormal population was detected in 82% of all cases; 94% showed B cell clonality. The remaining 6% were T cell, confirmed by T cell receptor studies. 64% had a CLL score of 4–5, with a mean absolute clonal population count of 8.57 x 10^9/L (range 1.85–52.55 x 10^9/L). These patients were diagnosed with CLL (23), SLL (1), monoclonal B-cell lymphocytosis and no diagnosis was recorded for 2. Of the remaining 36% diagnoses included a range of indolent and aggressive non-Hodgkin’s lymphoma. In concordance with BCSH guidelines for CLL reporting approximately 80% of cases to be asymptomatic at diagnosis 69% were asymptomatic at the time of testing. This compares to those tests which originated from within haematology with a median age of 71 years (range 31–94 years) and slight male predominance (61%). The mean lymphocyte count was higher at 12.93 x 10^9/L (range 0.65–195.26 x 10^9/L). The mean duration of lymphocytosis prior to immunophenotyping being performed was 281 days. A higher proportion, 55%, were associated with additional abnormal haematological parameters - unexplained anaemia (31%), thrombocytopenia (18%) and thrombocytosis (6%). Interestingly an abnormal population was detected in fewer of the cases originating from haematology at 67%; 76% showed B cell clonality. The remaining 24% were T cell, confirmed by T cell receptor studies. 72% had a CLL score of 4–5, with a mean absolute clonal population count of 16.21 x 10^9/L (range 0.01–185.50 x 10^9/L). These patients received a diagnosis of CLL (11), SLL (1), monoclonal B-cell lymphocytosis (4) and 2 were not diagnosed with a lymphoproliferative disorder. A higher proportion, 47%, reported symptoms at the time of testing; symptoms reported by more than 5% included fatigue weight loss, sweating, lymphadenopathy and infection.

We recognise our threshold for IPH is below that of many centres. In specifying persistence for >3 months we show a good predictive value, though we accept the clinical significance of a small clonal lymphocyte population is less clear. It is clear national guidelines are required to standardise practice.

Disclosure of Interest: None Declared

### Abstract Table: Table 1. Participant Demographics Table

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Disclosure of Interest: None Declared
BSH2021-PO-197
How does survival differ by treatment route in elderly DLBCL?
Catherine Turner*, Dominic Gordon-Walker†1, David Sparksman2, Nimish Shah3, Nick Morley1
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Abstract Content: Diffuse Large B Cell Lymphoma (DLBCL) accounts for approximately 40% of all Non-Hodgkin Lymphoma (NHL). Despite the availability of numerous DLBCL treatments such as curative anthracycline-based regimens and palliative chemotherapy/steroids/radiotherapy, there is a sparsity of research focusing on survival outcomes in the elderly. We discuss data from a multi-centre UK study with a focus on survival outcomes for DLBCL in the >80 age group and compare intravenous, oral and palliative therapies.

Survival data were retrospectively collected (N = 173) alongside patient demographics from both Norwich (over an eight-year period) and Sheffield (over a five-year period) University Hospitals. Three treatment groups were identified for analysis: intravenous chemotherapy (RCHOP/RGCPV/R-PMitCEBO/R-miniCHOP/RCVP/VEDEX, N = 89); oral chemotherapy (Chlorambucil/Etoposide, N = 17) and palliative (steroids/palliative radiotherapy, N = 67). Each patient was grouped based on the first treatment modality they received. Overall survival (OS) was analysed by age (Spearman’s correlation) and sex (Mann-Whitney U). A multivariate analysis (Cox regression) assessed both age and treatment in relation to OS. Post-hoc Kruskal-Wallis testing described specific differences between treatment groups. Median survival by treatment is reported.

Age was significantly negatively correlated with OS (P = 0.011) whereas there was no significant difference in OS between sexes (P = 0.653). The median OS values by treatment were 1.95 years (intravenous chemotherapy), 0.57 years (oral chemotherapy) and 0.21 years (palliative). The subsequent multivariate survival analysis showed OS varied significantly between treatment groups (P < 0.001) - in this model, age did not retain its significance (P = 0.965). Post-hoc testing revealed that intravenous chemotherapy conferred significantly greater OS than both oral chemotherapy and palliative treatment (P = 0.041 and P < 0.001 respectively). Oral chemotherapy OS and palliative treatment OS were not significantly different (P = 0.22).

To conclude, we have shown that age and treatment each significantly predict OS; however, when these variables are included together in a multivariate analysis, treatment remains the only significant predictor. This interaction likely relates to patients being pre-selected into treatment groups by age for example, more intensive intravenous therapies are more likely to be offered to the younger patient demographic. This study also shows that it may be reasonable not to burden patients with tablet chemotherapy when choosing between oral and palliative options but better-powered analyses are required. Additionally, we show that whilst intravenous therapies lead to a longer OS, it is not clear to what extent this is due to its superiority as a treatment or because of a bias wherein it is selectively offered to patients with a better outlook – this is an area for further research.

Reference:

Disclosure of Interest: None Declared

BSH2021-PO-198
Multicentre analysis on the outcome and incidence of invasive cerebral aspergillosis in haematology patients following ibrutinib treatment
William Ashley-Fenn1, Harriet Potter2, Kieran Toms2, Diana Lobo3, Vita Cedei4, Nicola Gill5, Aida Raja6, Federica Masieri5, Mamatha Karanth6, Steve Bougatsias6, Luke Bibby, Andrew Hodson6, Mahesh Prahladan7,8
1St Catharine’s College, 2School of Clinical Medicine, University of Cambridge, 3Haematology, East Anglia University Hospitals NHS Foundation Trust, 4Biotechnology Unit, Directorate of Life Science, School of Engineering, Arts, Science and Technology, 5Biotechnology Unit, Directorate of Life Science, School of Engineering, Arts, Science and Technology, University of Suffolk, Ipswich, 6Haematology, West Suffolk Hospital, Bury St Edmunds, 7Haematology Oncology, East Suffolk and North Essex Foundation NHS Trust, Ipswich, 8Masters in Genomics programme, University of Cambridge, Cambridge, United Kingdom

Abstract Content: Ibrutinib is a small molecule inhibitor of Bruton’s tyrosine kinase (BTK). This enzyme is a key component of the B cell receptor (BCR) pathway, responsible for B cell proliferation and differentiation, through the activation of multiple transcription factors. Thus, it has emerged as a novel therapy for B cell malignancies, including chronic lymphocytic leukaemia (CLL), mantle cell lymphoma, and Waldenström’s macroglobulinemia. An association between BTK inhibitor use and invasive fungal infections has also been postulated, as the blockage of BTK pathway inhibits downstream calcineurin Nuclear factor of activated T-cells (NFAT) pathway, resulting in defective neutrophil recruitment.

We performed a retrospective study of electronic patient records from 2 level-three and 1 level-two centres in East Anglia cancer network, to investigate the incidence of patients treated with Ibrutinib who developed invasive cerebral aspergillosis since 2015. Here we present a qualitative narrative of the clinical presentations, management and outcomes of such patients. 229 patients were identified as having received treatment with Ibrutinib for either CLL or B cell lymphomas since 2015. Of these, 3 patients contracted cerebral aspergillosis: 2 cases were confirmed upon biopsy and culture, whereas 1 case was treated as a presumptive diagnosis on the basis of radiological evidence. All of these patients presented to a level-three centre between May 2020 and October 2020. Patient ages were within the range of 65-85 years. Two of the patients presented with intracerebral infections within 5 months and the third patient after 4 years of first starting Ibrutinib.

The symptoms at presentation included headache, visual disturbances, confusion and ataxia. MRI of the head, staging CT scan, peripheral blood Aspergillus PCR, beta-D glucan fungal antigen tests, lumbar puncture and microscopy were done in all three patients. MRI of the head showed ring-enhancing lesions present within the frontal, occipital and/or parietal lobes. 2 patients underwent further investigation with stealth guided biopsy and culture, confirming the diagnosis of cerebral aspergillosis. Of note, one patient was confirmed to also have pulmonary aspergillosis on CT chest.

In 2 patients, a combined procedure with neurosurgical intervention followed by a minimum of 6 months of antifungal treatment with either Voriconazole or Isavuconazole. One patient had radical resection of the cerebral fungal mass. Both patients who underwent combined modality had complete recovery with no objective neurological deficits.

For 1 of these patients, complete resolution of the cerebral lesions was noted after 8 months of therapy, whilst the other patient showed
a partial response on follow-up MRI scan after 2 months of treatment, with complete neurological recovery.

The final patient was deemed medically unfit for neurosurgery and passed away 31 days later.

We present a case-series of 3 patients who developed cerebral aspergillosis following use of ibrutinib therapy. Previous data has indicated that patients on BTK inhibitors may be at particular risk of developing invasive intracerebral aspergillosis. Further clinical and molecular data and genomic analysis could be considered to better understand these recent cases of intracerebral aspergillosis within a localised area, and to risk-stratify patients who may require prophylactic antifungal treatment.

Abstract Table: Reference


Disclosure of Interest: None Declared

**BSH2021-PO-199**

Audit and case series of Primary CNS lymphoma at a single centre between 2010 and 2020 excluding those treated with MATRIX chemotherapy or Autologous Stem Cell Transplant.

**Patrick Sarkies**, **Nimish Shah**, **Kris Bowles**, **Victoria Willimott**, **Cesar Gomez**

1 Haematology, Norfolk and Norwich University Hospital, Norwich, United Kingdom

Abstract Content: Background: Primary CNS lymphoma is a rare Non-Hodgkin Lymphoma which usually requires treatment with intensive combination chemotherapy. The combination of high dose methotrexate, cytarabine, rituximab and thiopeta (MATRIX) improves survival but can be associated with significant toxicity. For patients where MATRIX is unsuitable less intensive chemotherapy combinations such as rituximab, methotrexate and temozolomide or procarbazine have shown some efficacy. We audited all primary CNS lymphoma patients who were not fit for intensive frontline therapy at a single centre Teaching hospital.

**Aim:** To review the diagnosis, treatment and survival of primary CNS lymphoma patients who were not fit for high intensity chemotherapy and consolidation with autologous stem cell transplant over a 10-year period.

**Methods:** We identified patients with a diagnosis of primary CNS lymphoma between 2010 and 2020. Patients were excluded if they received MATRIX chemotherapy, had systemic disease, or underwent stem cell transplant. Baseline patient characteristics included age, sex, performance status, LDH and co-morbidities. Cases were reviewed for details of diagnostic tests and staging through to therapy and overall survival.

**Results:** 16 eligible patients were identified, (M=9 F=7). Median age at diagnosis was 66 and most patients had a performance status of 1 or 2 (n = 12). The majority (69%) had one or more comorbidities. Diagnostic brain biopsy was performed in 88% and 94% underwent staging MRI brain and CT scan. Eleven patients (69%) proceeded to chemotherapy within a median time of 14 days. Chemotherapy included high dose methotrexate (n = 3), rituximab/methotrexate/te-mozolomide (n = 5), rituximab/methotrexate/cytarabine (n = 2), methotrexate/cytarabine (n = 1). Initial methotrexate dose was 3 gm or 3.5 gm2 in 94% (n = 10). A minority (36%) completed four cycles of high dose methotrexate and dose reductions or omissions occurred in 27% of patients. 82% had response assessed via brain imaging (90% via MRI) and 11% (n = 1) had complete response (CR), 33% (n = 3) partial response (PR) and 56% (n = 5) progressive disease. 73% proceeded to whole brain radiotherapy after chemotherapy. Maintenance temozolomide was given in 2/3 of eligible patients, one completing 5 cycles and the other 9 cycles. Median overall survival was 10 months (range 0.5–66 months). The cause of death was disease progression in the majority (63%) of all patients.

**Conclusion:** This audit demonstrated compliance with national guidelines as the majority had brain biopsy proven diagnosis, appropriate staging and response assessment and at least 3 gm2 methotrexate. Only 44% achieved a PR (33%) or CR (11%) and the overall survival was poor. The majority of patients did not complete the planned four cycles of methotrexate. This correlates with larger studies where poorer outcomes were found in patients who did not complete four cycles of methotrexate (Martinez-Calle et al., Br J Haem 2020). Treatment of this patient group remains challenging and further work is needed to find suitable and effective treatments. It is

Abstract Table: Chemotherapy regimens, methotrexate cycles and survival

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essential to consider early support from palliative care services in the management of these patients.

MTX (methotrexate), R-MTX-T (rituximab, methotrexate, temozolomide) R-MTX-ARAC (rituximab, methotrexate, cytarabine), MTX-ARAC (methotrexate, cytarabine), PD (progressive disease) TR (treatment related) SR (systemic relapse) *alive at time of writing ***4th cycle withheld instead of dose reduction

Disclosure of Interest: None Declared

BSH2021-PO-200
Immunoglobulin replacement therapy - The unexpected advantages of a Pandemic in one Haematology Unit
Ramya -*, Hajer Oun, Kinda Al-Hourani, Rha Green, Alistair Hart

Abstract Content: Secondary antibody deficiency (SAD) is common in patients with many haematological malignancies and is a major cause of morbidity and mortality. National guidance assures Immunoglobulin Replacement Therapy (IGRT) is used in those patients with SAD who are most likely benefitted. The COVID pandemic, gave us an opportunity, to review our practice, with the brief pause of long-term immunoglobulins (IGs), to forego any non-essential hospital attendances.

The objectives of this study were to review the use of IGRT against national guidance and to identify if this COVID “drug holiday” increased the infection or hospital admission rates. All patients receiving IGRT had case note review and were interviewed at clinic attendance. Base IG levels were measured after the drug holiday of 4 months, and challenged with Penumvax (Merck Sharp & Dohme, UK). A month after this had their functional antibodies remeasured.

Twenty-six patients on IGs, with the median duration of 5 years, were retrospectively reviewed. There were 15 (58%) males and 11 (42%) females. The median age of this cohort was 72 years (range 57-83 years). Based on their baseline IG level, 2 Groups, Group 1 (IG < 5 g/L, n = 12) and Group 2 (IG >5 g/L, n = 14), were formed. Group 1 returned onto IGRT. Group 2 patients were further assessed based on baseline functional antibody level, presence and severity of underlying respiratory, or other co-morbidities, incidence of infections and their need for antibiotics.

Three died during this period, due to progression of their disease or other medical causes. Functional antibodies were checked in the remaining 11 patients of the Group 2. Four had levels > 15 mg/L and did not receive a vaccine challenge. Two of these received long term antibiotics. Seven patients underwent a vaccine challenge and were monitored for response and any adverse outcomes. Response was seen in 4 of the 7 patients. However, despite good response, two returned onto IVIGs and only two received antibiotics. Hence, a total of 7 returned to IGRT, 4 (28%) received prophylactic antibiotics. All these 4 were followed up for a median duration 6 months with no evidence of increased infection or mortality.

Recurrent chest infection was the most common cause for commencing IGRT in ninety two percent (24) with proven Haemophilus influenza or pneumococcal infection in 7 (27%). Life threatening infection was seldom seen. Solitary four from Group 2 had recurrent outpatient infections needing treatment antibiotics, of which two were switched to long-term antibiotics. It was evident that 8 (57%) had received prophylactic antibiotics prior to or while on IGs.

The challenges encountered during re-introduction of IGs were, existence of COPD or end organ damage in 9 (64%) patients from Group 2 and ischaemic heart disease in 4 (29%). Whilst cost savings was not an end point of this study it is apparent that savings could be achieved by this strict use of guidance as well as ensuring the most appropriate use of an expensive drug.

IGRT is an effective but expensive therapy in long term SAD patients. Careful application of guidance can reduce the number of patients receiving regular therapy and save drug budget but also chair time in busy Units. It would appear that drug holidays appear to be reasonably tolerated and could be recommended in these patients while covering with prophylactic antibiotics. Rationalising the use of IGRT in SAD will enable better, wider and effective delivery of health care.

Disclosure of Interest: None Declared

BSH2021-PO-201
Immunotactoid Glomerulonephritis in a donor kidney
Chinonye Onyeocha1*, Shulakshana Soondron1, Amin Islam2, Simon Hallam3
1Haematology, Mid and south Essex University Hospitals NHS Foundation Trust, Essex, 2Haematology, Queen Mary University, London , 3Haematology, Bart’s Health NHS Trust, London , London, United Kingdom

Abstract Content: Immunotactoid Glomerulonephritis is a very rare glomerular disease, found in less than 1 in 100 kidney biopsies. This is usually associated with disorders including CLL, B cell disorders, Hepatitis C virus and Autoimmune Disease. The prognosis is variable with 50% of patients progressing to End Stage Renal Failure within 5 years. Small Lymphocytic Lymphoma (SLL) along with
Chronic Lymphocytic Leukaemia (CLL) is the most common Haematological malignancy in Caucasian population. Majority of the patients are asymptomatic. About one third patient never require treatment. The diagnosis of CLL is made on peripheral blood immunophenotyping. When less than $5 \times 10^9/L$ B lymphocytes in the peripheral blood are present, the diagnosis is usually made from either bone marrow biopsy or tissue from the nodal mass. CLL/SLL patients presenting with isolated extramedullary involvement such as bladder wall, kidney involvement with nephrotic range proteinuria have been described but failing renal graft post-transplant due to Immunotactoid Glomerulopathy is extremely rare.

We report the case of a 69-year-old lady with declining renal function six weeks after receiving a live kidney from her husband for presumed Diabetic Nephropathy. Apart from moderate anaemia her full blood counts were all normal pre transplant with a normal white cell differential. She engrafted well with normalisation of her renal functions and continued immunosuppression. She was reviewed by the renal team with lethargy. Blood tests revealed worsening anaemia, deranged renal function and proteinuria on urine dipstick test. Investigations failed to reveal the cause of her early graft failure. A renal biopsy performed demonstrated Proliferative Glomerulopathy thought to be infectious in origin initially. She received antibiotics with nil improvement. A screen ruled out viral aetiology. Additional investigations revealed mildly elevated Kappa/Lambda ratio of 4.2 with small amount of IgM 3 gm/L monoclonal band on protein electrophoresis. Electron microscopy from repeat renal biopsy showed light chain deposit consistent with the rare entity, Immunotactoid Glomerulonephritis. The case was discussed in joint Renal, Haematology and Haematopathology Multidisciplinary meeting. A presumptive diagnosis of SLL/CLL was suggested. Bone marrow biopsy showed 75% infiltration with small mature lymphoid cells. Immunohistochemistry confirmed the diagnosis of SLL/CLL. PET CT showed widespread low volume lymphadenopathy. Her husband was investigated with no evidence of SLL/CLL found. A joint MDT decision was made to treat with Chlorambucil and Obinutuzumab. Creatinine level returned to normal after only 1 cycle of treatment. A Repeat Bone marrow and Flow cytometry post chemotherapy did not show any evidence of SLL infiltration therefore considered to be in Complete Haematological Remission.

This is an extremely rare case of Immunotactoid Glomerulopathy where undiagnosed SLL infiltrated her donor renal graft. This case highlights the possibility of SLL as the aetiologic cause for declining renal function in native kidney. As peripheral blood lymphocyte count was normal with no palpable adenopathy, CLL was not considered. We suggest when dealing with Immunotactoid Glomerulopathy, consider early evaluation for Lymphoproliferative disorder. Correct diagnosis in a timely manner led to the salvage of the transplant kidney.

Disclosure of Interest: C. Onyeocha: None Declared, S. Soondron: None Declared, A. Islam Conflict with: Consultant Haematologist, S. Hallam: None Declared

BSH2021-PO-202
Bendamustine therapy in low grade B-cell lymphoproliferative disorders: a District General Hospital experience
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Abstract Content: Bendamustine Therapy in Low Grade B-cell Lymphoproliferative Disorders: A District General Hospital experience
Bendamustine has been licensed to treat indolent advanced Non-Hodgkin’s Lymphoma (NHL) in England since 2018. It has fewer side effects than traditional alternatives including R-CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) and R-CVP (cyclophosphamide, vincristine, prednisolone). Dose modifications are not needed for age and renal function, making it suitable for older patients who may have multiple comorbidities. Here we report our experience of Bendamustine-based regimes in terms of its efficacy and tolerability, focusing particularly on its use in older patients.

Our cohort comprised 91 low grade B-cell lymphoma patients commenced on Bendamustine-based chemotherapy between January 2015 and August 2020. Median age was 73 years (range 37-88), with 59 patients aged ≥70 and 19 patients aged ≥80. Patients received either Bendamustine monotherapy or Bendamustine-Rituximab (R-Benda). A total of 442 cycles of chemotherapy were given. 57/91 patients completed all six cycles. Reasons for early discontinuation of therapy included minimal response or intolerance to the chemotherapy, disease progression and planned cessation of therapy after optimal response. Two patients passed away during treatment. Of the whole cohort (n = 91): neutropenic sepsis or fever requiring hospitalisation occurred in 23 patients; grade 3-4 toxicity requiring transfusions with blood products (packed red cells and/or platelets) occurred in 27 patients; granulocyte colony stimulating factor was used in 29 patients. In a separate analysis of patients aged ≥80 (n = 19): neutropenic sepsis or fever requiring hospitalisation occurred in 4 patients; grade 3-4 toxicity requiring transfusions with blood products occurred in 6 patients; granulocyte colony stimulating factor was used in 4 patients. There was no statistically significant difference in the proportion of each side effect occurring in elderly patients compared with the whole cohort (Chi square test, $P > 0.05$).

The most common non-haematological complications were constipation (n = 19) and skin rash (n = 18). Two patients were hospitalised with constipation. There was no need for hospital admissions or intravenous interventions for those with skin rash. In those aged ≥80: 4 patients had constipation and 3 patients had a skin rash. Despite observed toxicities leading to delayed chemotherapy cycles, we found that 57 of 91 patients completed 6 cycles of chemotherapy. Complication rates were not increased in the elderly over-80-years patients. Our experience shows that Bendamustine as a single agent, or combined with Rituximab is well tolerated and a safe viable treatment option for all low grade B-cell lymphoproliferative disorders.

Disclosure of Interest: None Declared

BSH2021-PO-203
Management of patients with Diffuse Large B cell Lymphoma not fit for anthracycline based chemotherapy at North Wales Cancer Center
Durgadevi Moratuwagama1, Sumita Raj1 and Department of Haematology, Glan Clwyd Hospital
1Haematology, Betsi Cadwaladr University Health Board, Rhuddlan, United Kingdom

Abstract Content: Management of patients with Diffuse Large B cell Lymphoma not fit for anthracycline based chemotherapy at North Wales Cancer Center
RCHOP chemotherapy is the standard of care for Diffuse Large B cell Lymphoma (DLBCL). However, not all patients can tolerate RCHOP chemotherapy, due to associated comorbidities, especially due to cardiac comorbidities which make them unsuitable for anthracycline-based chemotherapy. For these patients, it is our practice to offer RGCVP chemotherapy, which is less cardio-toxic and better tolerated.
The aim of the study is to see how well RGCVP chemotherapy is tolerated and to assess the outcome of the patient receiving above chemotherapy.

All patients with a histologically proven DLBCL, treated with RGCVP chemotherapy from October 2013 –October 2018 were included in the study. The following data was collected from clinical notes and electronic records: histological sub type, history of cardiac disease, number of chemotherapy cycles completed, outcome of the treatment (Complete response/partial response/progressive disease/ death due to disease).

24 patients were identified to be on RGCVP over the study period; 18 patients were identified as having DLBCL and the rest T cell/ Follicular lymphoma. Only the patients with DLBCL were included in this study. 13 were males. Age ranged from 69–90 years and the mean age was 82 years. According to histological sub types, there were 12 patients with activated B cell histology, one with germinal center B cell type, three with double hit , one with double expresser, and one unknown/undocumented.

Out of the 18 patients, 13(72%) were alive at the time of the study. 10 patients tolerated all 6 cycles (10/18=55%). At the end of treatment 9 patients achieved complete metabolic response (50%) and 3 had excellent partial responses (16%), giving an overall response rate of 66%. 5(28%) were deceased. 3 progressed on chemo, 2 patients died of pneumonia and end stage pulmonary fibrosis. Five out of 18 patients had their cardiac history documented previously.

Subgroup analysis of the outcome of elderly patients with DLBCL treated with R-CHOP from UK NCRI RCHOP14 vs 21 trial, shows CR rates of 62% vs 67%, and overall response rate was 91% for both. In our cohort, in patients who were not fit for anthracycline based treatment, RGCVP gave a CR rate of 50% and an overall response of 66%. Hence it appears that RGCVP can be offered with curative intent in this subgroup of patients, who carry an inferior prognosis compared to young and fit elderly patients who can tolerate anthracycline based RCHOP chemotherapy.

It appears that documentation of cardiac history needs improvement.

References:

Disclosure of Interest: None Declared

BSH2021-PO-204
A single centre study to assess delivery of vaccination advice to patients with chronic lymphocytic leukaemia
Grace Cox1,4, David Allsup 1
1Hull York Medical School, University of Hull, Hull, United Kingdom

Abstract Content: Chronic lymphocytic leukaemia (CLL) causes an accumulation of malignant B lymphocytes in the blood, lymph nodes and spleen. These white blood cells are less competent at dealing with infections which compromises the immune response. Treatment for CLL involves chemoimmunotherapy which causes further immunosuppression. The combined result is a burden of infection, accounting for 50–60% of deaths in CLL patients. To reduce infections the British Society for Haematology released guidance in 2018 recommending pneumococcal vaccination and seasonal influenza vaccination in people with early stage CLL.1 Despite this guidance being available, it is unknown whether it is being offered in practice.

The primary objective of this project was to gain a better understanding of the current vaccination advice given to patients with CLL in secondary care. Additional objectives included investigation into possible barriers to the delivery of appropriate vaccination advice to patients with haematological malignancies, and how these barriers could be overcome.

A 10-question anonymous online survey looking into vaccination advice given to patients with CLL was produced and sent to healthcare professionals involved in the management of patients with CLL. These involved members of the regional haematology multidisciplinary team, the nurses in the chemotherapy day unit, four wards managing haemato-oncology and oncology patients, and the junior medical staff at the Queens Medical Centre. The survey was open from 23/10/2020- 14/02/2021 and generated 29 responses which were then analysed.

The results found that 72% of people surveyed were aware of the 2018 guidelines from the British Society of Haematology. Despite this, when asked ‘to what proportion of CLL patients that you see, do you offer vaccination advice?’ the mean average was 54%. The most interesting responses related to people’s perception of efficacy of the vaccinations with only 35% of respondents saying they believed that they were effective in protecting people with CLL from infections. The respondents who expressed reservations regarding the efficacy of vaccinations reported the main reason/s were they didn’t know enough about it and also there was insufficient evidence available. When respondents were asked what could be done to improve the vaccination uptake, the most common suggestion was to have a standard letter to be given at diagnosis. Other recommendations included patient leaflets/posters, and further education and data on the optimum delivery of the vaccines.

In conclusion there is inconsistency in the delivery of vaccination advice to people with CLL by healthcare professionals. There is also significant variability of respondents’ views concerning perceived efficacy of vaccinations in preventing infections in these patients. A standard letter given to the patient at diagnosis should be considered to ensure that all people with CLL get appropriate and timely vaccination advice.


Disclosure of Interest: None Declared
Red Cell Disorder

BSH2021-PO-205
C3 Inhibition with pegcetacoplan in patients with paroxysmal nocturnal hemoglobinuria: results from the Paddock and Palomo trials
Raymond Wong1,4, Kalina Ignatova2, Humphrey Pullon3, Jameela Sathar4, Pimjai Niparuck5, Tontanai Numnbenjapon6, Eric Tse2, Surapol Issaragrisil6, Eloy Roman8, Ismail Amine9, Lisa Tan11, Carl di Casoli12, Pascal Deschatelets12, Cedric Francois12, Federico Grossi12, Andrija Bogdanovic13
1Sir YK Pao Centre for Cancer & Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, NT, Hong Kong, 2National Specialized Hospital for Active Treatment of Hematologic Diseases, Sofia, Bulgaria, 3Waikato Hospital, Hamilton, New Zealand, 4Department of Hematology, Ampang Hospital, Petaling Jaya, Malaysia, 5Ramathibodi Hospital, Division of Hematology, Department of Medicine, Phramongkutklao College of Medicine, Bangkok, Thailand, 6Department of Medicine, The University of Hong Kong, Pok Fu Lam, Hong Kong, 7Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand, 8Lakes Research, Miami, FL, United States, 9Hematology Department, Tokuda Hospital, Sofia, Bulgaria, 10Lisa Tan Pharma Consulting Ltd, Cambridge, United Kingdom, 11Apelli Pharmaceuticals, Waltham, MA, United States, 12Clinic of Hematology, Clinical Center of Serbia, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Abstract Content: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, life-threatening hematologic disease characterized by chronic complement-mediated red blood cell (RBC) hemolysis. The current standard treatment for patients with PNH is eculizumab (ECU) or ravulizumab, both C5 inhibitors (C5i). C5i reduce intravascular hemolysis (IVH), but extravascular hemolysis (EVH) can be significant in a subset of C5i-treated patients. Pegcetacoplan is a C3 inhibitor targeted to control both IVH and EVH. The PADDOCK and PALOMINO studies assessed the safety and preliminary efficacy of pegcetacoplan in complement inhibitor-naive patients.

PADDOCK was a phase 1b, open-label, pilot study (NCT02588833) with 2 cohorts. Subjects in cohort 1 (n = 3) received pegcetacoplan at a suboptimal subcutaneous dose of 180 mg/day for 28 days; subjects in cohort 2 (n = 20) received pegcetacoplan 270-360 mg/day subcutaneously for up to 1 year. Subjects could participate in both cohorts (n = 1). PALOMINO was a phase 2a, open-label, single-cohort study (NCT03593200) in which subjects received pegcetacoplan 270 mg/day for up to 1 year (n = 4). Both studies enrolled subjects ≥18 years old diagnosed with PNH and no prior treatment with ECU. Primary efficacy endpoints in both studies were change from baseline (CBF) in lactate dehydrogenase (LDH), haptoglobin, and hemoglobin (Hb). Secondary efficacy endpoints included CBF in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score and number of packed RBC transfusions. Primary safety endpoints were the incidence and severity of treatment emergent adverse events (TEAEs).

At baseline in both studies, mean LDH was >8x upper limit of normal (ULN) and mean Hb and FACIT-Fatigue scores were below normal (see Table). At Day 365, mean LDH levels were decreased to <2x ULN in PADDOCK and within normal range in PALOMINO. In both studies at Day 365, mean Hb was increased to within normal range and FACIT-Fatigue scores were increased by >6 points (>3; clinically meaningful). A decrease in the number of subjects requiring transfusions was also observed; after the initiation of pegcetacoplan dosing, 13/20 PADDOCK subjects and 4/4 PALOMINO subjects were transfusion-free. Overall, 143 TEAEs were reported in 19/22 subjects (86.4%) in PADDOCK cohorts 1 and 2, of which 35 were either possibly or probably related to pegcetacoplan (most of which were associated with injection site reactions). Thirteen serious adverse events (SAEs) were reported in PADDOCK. Three SAEs (aplastic anemia, abdominal neoplasm, and hypersensitivity) led to pegcetacoplan discontinuation. The aplastic anemia SAE was fatal and considered not related to pegcetacoplan. In PALOMINO, 60 TEAEs were reported in 3 (75.0%) subjects, of which 52 were possibly treatment-related with the most common treatment-related TEAE being injection site reactions and skin erythema. One SAE (rib fracture) was reported and was considered not related to pegcetacoplan. In PALOMINO, no TEAEs led to death, pegcetacoplan discontinuation, or study discontinuation.

In the PADDOCK and PALOMINO studies, pegcetacoplan was demonstrated to be safe long-term and improved hematological and clinical parameters in patients with PNH. PADDOCK and PALOMINO exhibit the therapeutic potential of pegcetacoplan in the treatment of PNH and support further evaluation in the ongoing phase 3 PRINCE trial (NCT04085601) in complement inhibitor-naive patients.

Abstract Table: Table. Primary, secondary, and pharmacodynamic endpoints

<table>
<thead>
<tr>
<th>Parameter, units</th>
<th>Normal range</th>
<th>PADDOCK Cohort 2 Mean (SD)</th>
<th>PALOMINO Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (n = 20)</td>
<td>Day 365 (n = 17)</td>
<td>Baseline (n = 4)</td>
</tr>
<tr>
<td>LDH, U/L</td>
<td>120–250</td>
<td>2388.8 (1014.13)</td>
<td>306.5 (324.67)</td>
</tr>
<tr>
<td>Haptoglobin, g/L</td>
<td>0.14–2.58</td>
<td>0.043 (0.013)</td>
<td>0.110 (0.123)</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>11.9–18</td>
<td>8.38 (1.828)</td>
<td>12.14 (2.002)</td>
</tr>
<tr>
<td>FACIT-Fatigue, points</td>
<td>43.6*</td>
<td>34.6 (10.56)</td>
<td>42.5 (8.47)</td>
</tr>
<tr>
<td>Reticulocyte count, x10⁶ cells/L</td>
<td>10–110</td>
<td>194.9 (62.16)</td>
<td>96.4 (33.36)</td>
</tr>
<tr>
<td>Total bilirubin, μmol/L</td>
<td>3–20</td>
<td>42.60 (25.59)</td>
<td>13.90 (5.62)</td>
</tr>
<tr>
<td>Clonal distribution of type II and type III PNH RBCs, %</td>
<td>–</td>
<td>39.8 (21.39)</td>
<td>84.0 (21.04)</td>
</tr>
<tr>
<td>C3 deposition on type II and type III PNH RBCs, %</td>
<td>–</td>
<td>1.5 (1.80)</td>
<td>0.4 (0.57)</td>
</tr>
</tbody>
</table>

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LDH, lactate dehydrogenase; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; PNH, Paroxysmal Nocturnal Hemoglobinuria; RBCs, red blood cells

*Population norm

**Disclosure of Interest:** R. Wong Conflict with: Alexion (Consultancy, Honoraria, Research Fund and Speakers Bureau), Apellis (Research Funding and Speakers Bureau), Roche (Consultancy, Honoraria, Research Fund and Speakers Bureau), K. Ignatova: None Declared, H. Pullon: None Declared, J. Sathar Conflict with: Roche (Honoraria), Novo Nordisk (Honoraria), Bayer (Honoraria), P. Niparuck: None Declared, T. Numbenjapon: None Declared, E. Tse Conflict with: MSD (Research funding), Janssen (Research funding), S. Issaragrisil Conflict with: Alexion (Speakers Bureau), Novartis (Speakers Bureau), E. Roman Conflict with: Alexion (Speakers Bureau), Novartis (Speakers Bureau), I. Amine Conflict with: Acibadem City Clinic Tokuda Hospital (Current employment), L. Tan Conflict with: Apellis (Consultancy and Patents & Royalties), C. di Casoli Conflict with: Novartis (Honoraria, Steering committee), Alexion (Honoraria, Research Funding), Biocrypt (Honoraria, Data monitoring committee), Apellis (Consultancy, Honoraria, Research Funding), Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), P. Deschatelets Conflict with: Apellis (Current Employment and Current equity holder), C. Francois Conflict with: Apellis (Current Employment and Current equity holder), F. Gossi Conflict with: Apellis (Current Employment and Current equity holder), A. Bogdanovic Conflict with: Novartis (Consultancy, membership on an entity’s board of directors or advisory committees, and speakers bureau), Takeda (Membership on an entity’s board of directors or advisory committees, and speakers bureau), Pfizer (Membership on an entity’s board of directors or advisory committees), Apellis (Investigator fee in clinical trial)

**Abstract Content:** The phase 3 MEDALIST study evaluates the safety and efficacy of luspatercept in patients (pts) with lower-risk myelodysplastic syndromes (LR-MDS; defined as IPSS-R Very low-, Low-, and Intermediate-risk) with ring sideroblasts requiring red blood cell (RBC) transfusions who are ineligible for, intolerant, or refractory to erythropoiesis-stimulating agents (NCT02631070). We assessed the effect of luspatercept on biomarkers of erythropoiesis and their relationship to clinical benefit (CB; i.e., RBC transfusion independence ≥8 weeks and/or modified haematological improvement-erythroid by IWG 2006 criteria) in the primary treatment phase (Wks 1–24).

Pts (N = 229) were randomised 2:1 to luspatercept 1.0 mg/kg (up to 1.75 mg/kg; n = 153) or placebo (PBO; n = 76) subcutaneously every 3 wks. Reticulocyte count was evaluated in blood samples collected at baseline (BL) and during Wks 1–24. Serum biomarkers (soluble transferrin receptor 1 [sTfR1], erythroferrone [ERFE], erythropoietin [EPO]) were measured by ELISA. Bone marrow (BM) erythroid precursors (EP) were assessed by cytomorphology from BM aspirates.

In pts receiving luspatercept, starting at 8 days after first dose (55.1 vs 34.5 × 10^11/L at BL, P < 0.0001), mean reticulocyte count increased from BL and remained elevated throughout the evaluation period. Mean EPO levels significantly increased within 6 weeks after first dose (440.1 vs 220.4 IU/L at BL, P < 0.0001) and remained elevated throughout Week 25. Levels of sTfR1 (P < 0.0001), EPO (P < 0.0001), and EP (P = 0.0010) were also elevated at Wk 25 vs BL (Table). The 16-wk mean transfusion burden (TB) was significantly reduced at Wk 25 vs BL (7.2 vs 11.0 units, P < 0.0001). In the PBO arm, EPO levels, reticulocyte count, and 16-wk TB in contrast remained largely unchanged, while levels of sTfR1 (P < 0.0001), EP (P = 0.0010), and ERFE (P = 0.0431), were significantly decreased at Wk 25 vs BL. Mean BL EP were higher in 87 pts receiving luspatercept with CB (31.3%) vs 63 pts without CB (26.5%; P = 0.0298); however no statistically significant differences in BL, ERFE, EPO, sTfR1, reticulocyte count, and 16-wk TB were observed in either group. Pts with luspatercept and CB at Wk 25 experienced a significantly greater increase in reticulocyte count (2.7 vs 1.8 mean fold increase from BL, P = 0.0017), but not EPO levels (2.9 vs 4.3 mean fold increase from BL, P = 0.1370) vs pts without CB. Changes in erythropoiesis-related biomarkers (EPO, ERFE, and sTfR1) did not vary significantly between pts with and without CB. The ratio of reticulocyte/sTfR1 was calculated to examine whether luspatercept affects erythroid maturation. This ratio was reasoned to approximate the proportion of late-stage erythropoiesis (reticulocytes) within total erythropoiesis (sTfR1). Mean ratio of reticulocyte/sTfR1 was increased in luspatercept pts with CB (2.2 in Wk 25 vs 1.5 at BL, P < 0.0001) and no CB (1.9 in Wk 25 vs 1.3 at BL, P = 0.0071).

In the MEDALIST trial, luspatercept-treated pts experienced an increase of erythropoiesis-associated biomarkers. Increased blood reticulocyte counts was associated with CB and was higher in pts with expanded BM erythropoiesis (as measured by EP) at BL. With the observation that the ratio of reticulocytes/sTfR1 increased during luspatercept treatment, this suggests that the efficacy of luspatercept

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**Table:** Table. Erythropoiesis biomarkers in Weeks 1–24 of the MEDALIST trial

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Luspatercept N = 153</th>
<th>P value (Wk 25 vs BL)</th>
<th>PBO N = 76</th>
<th>P value (Wk 25 vs BL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood reticulocyte count (n), ×10^7/L</td>
<td>34.5 (135)</td>
<td>71.9 (108)</td>
<td>&lt;0.0001</td>
<td>38.4 (68)</td>
</tr>
<tr>
<td>Serum sTfR1 level, mean (n), nM</td>
<td>32.7 (143)</td>
<td>42.8 (125)</td>
<td>&lt;0.0001</td>
<td>31.6 (74)</td>
</tr>
<tr>
<td>Serum ERFE level, mean (n), ng/mL</td>
<td>20.9 (137)</td>
<td>27.0 (122)</td>
<td>&lt;0.0001</td>
<td>22.9 (68)</td>
</tr>
<tr>
<td>Serum EPO level, mean (n), IU/L</td>
<td>220.4 (152)</td>
<td>662.9 (120)</td>
<td>&lt;0.0001</td>
<td>215.5 (74)</td>
</tr>
<tr>
<td>BM EP level, mean (n), %</td>
<td>29.3 (150)</td>
<td>34.3 (130)</td>
<td>0.0010</td>
<td>29.9 (75)</td>
</tr>
<tr>
<td>16-week transfusion burden, mean (n), RBC units</td>
<td>11.0 (153)</td>
<td>7.2 (128)</td>
<td>&lt;0.0001</td>
<td>11.5 (76)</td>
</tr>
</tbody>
</table>
**BSH2021-PO-207**

"Superiority of Pegcetacoplan Compared to Eculizumab in Patients with Paroxysmal Nocturnal Hemoglobinuria, Regardless of Prior Transfusion Requirement: Analysis at 16-weeks of PEGASUS Phase 3 Randomized Trial"

Regis Peffault De Latour1, Carlos M De Castro2, Jeffrey Szer3, Kensuke Usuki4, Peter Hillmen5, Morag Griffin5, Mohamed Hamdani6, Temitayo Ajayi6, Hisakazu Nishimori7, Ilene C Weitz8

1French Reference Center for Aplastic Anemia and Paroxysmal Nocturnal Hemoglobinuria, Public Assistance-Hospital of Paris, University of Paris, Paris, France, 2Duke University School of Medicine, Durham, North Carolina, United States, 3Clinical Haematology, Peter MacCallum Cancer Centre & Royal Melbourne Hospital, Melbourne, Australia, 4Hematology, NTT Medical Center Tokyo, Tokyo, Japan, 5Haematology, St James University Hospital, Leeds, United Kingdom, 6Apellis Pharmaceuticals, Inc., Waltham, Massachusetts, United States, 7Hematology and Oncology, Okayama University Hospital, Okayama, Japan, 8Hematology, University of Southern California Keck School of Medicine, Los Angeles, California, United States

**Abstract Content:** Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, hemolytic disease characterized by chronic complement-mediated hemolysis. PEGASUS, a phase 3, randomized, open-label, controlled trial (NCT03500549), assessed the efficacy and safety of pegcetacoplan compared to ECU in patients with PNH. Pegcetacoplan, a C3 inhibitor targeting the proximal complement pathway, was superior to eculizumab (ECU) for the primary endpoint of hemoglobin (Hb) change from baseline at week 16, and improved clinical and hematologic parameters. Additional pre-specified analyses assessed if any groups of patients might experience further benefit from pegcetacoplan.

PNH patients (≥18 years) and Hb levels <10.5 g/dL despite receiving treatment with ECU for ≥3 months were eligible for inclusion. Patients entered a 4-week run-in period with ECU plus twice-weekly pegcetacoplan (1080 mg, self-administered subcutaneously). On study day 1, patients were stratified based on baseline platelet count and prior transfusion requirements, and randomized 1:1 to monotherapy with pegcetacoplan or ECU for 16 weeks. The primary endpoint was change in Hb level from baseline to Week 16. Key secondary endpoints were transfusion avoidance and adverse events (AEs). Primary and key secondary endpoints were also analyzed by subgroups based on baseline age, sex, race, number of packed red blood cell transfusions (<4 vs ≥4) within the 12 months prior to baseline and platelet count at screening (<100,000/mm³ vs ≥100,000/mm³) to investigate outcomes independent of disease activity.

Pegcetacoplan treatment was associated with significantly greater increases in Hb levels than ECU at week 16, regardless of prior transfusions or baseline platelet count (Table). At week 16, mean Hb significantly increased from baseline in the pegcetacoplan group and decreased in the ECU group. The proportion of transfusion-free patients was similar in the pegcetacoplan group, regardless of age (≤65 years, 87.1%; >65 years, 80%), sex (female, 81.5%; male, 92.9%), race (Asian, 100%; black, 100%; white, 75.0%), transfusion strata (<4 vs ≥4) within the 12 months prior to baseline and platelet count at screening (<100,000/mm³ vs ≥100,000/mm³), and diagnosis (4 (9.8%) patients with pegcetacoplan and 9 (23.1%) with ECU, leading to study drug discontinuation in 3 (7.3%) patients on pegcetacoplan.

In this prespecified stratified analysis of the PEGASUS study of patients with PNH and persistent anemia, pegcetacoplan demonstrated superiority to ECU in Hb level with transfusion avoidance in most PNH patients regardless of prior transfusion numbers and platelet count. The safety profile of pegcetacoplan was comparable to ECU.

**Abstract Table:** Table. Hb Change from Baseline (g/dL) and Transfusion Avoidance at Week 16

<table>
<thead>
<tr>
<th>Hemoglobin (g/dL)</th>
<th>Pegcetacoplan</th>
<th>Eculizumab</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LS Mean (SE)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Population</td>
<td>2.37 (0.36)</td>
<td>-1.47 (0.67)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>n = 41</td>
<td>n = 39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4 transfusions</td>
<td>2.97 (0.36)</td>
<td>-0.01 (0.49)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>n = 20</td>
<td>n = 16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥4 transfusions</td>
<td>2.11 (0.60)</td>
<td>-4.02 (2.40)</td>
<td>0.0278</td>
</tr>
<tr>
<td>n = 21</td>
<td>n = 23</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Red Cell Disorder

<100,000/mm³ platelets

<table>
<thead>
<tr>
<th>Platelet Count</th>
<th>Pegcetacoplan</th>
<th>Eculizumab</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100,000/mm³</td>
<td>3.23 (0.67)</td>
<td>-1.84 (1.09)</td>
<td>0.0007</td>
</tr>
<tr>
<td>≥100,000/mm³</td>
<td>2.18 (0.40)</td>
<td>-0.92 (0.74)</td>
<td>0.0009</td>
</tr>
</tbody>
</table>

Transfusion Avoidance, %

<table>
<thead>
<tr>
<th>Total Population</th>
<th>Pegcetacoplan</th>
<th>Eculizumab</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35/41 (85.4%)</td>
<td>6/39 (15.4%)</td>
<td>0.81</td>
<td>(0.64, 0.99)</td>
</tr>
</tbody>
</table>

<4 transfusions

<table>
<thead>
<tr>
<th>Pegcetacoplan</th>
<th>Eculizumab</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18/21 (85.7%)</td>
<td>1/23 (4.3%)</td>
<td>0.54 (0.26, 0.81)</td>
</tr>
</tbody>
</table>

≥4 transfusions

<table>
<thead>
<tr>
<th>Pegcetacoplan</th>
<th>Eculizumab</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17/20 (85.0%)</td>
<td>5/16 (31.3%)</td>
<td>0.66 (0.47, 0.85)</td>
</tr>
</tbody>
</table>

<100,000/mm³ platelets

<table>
<thead>
<tr>
<th>Pegcetacoplan</th>
<th>Eculizumab</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25/29 (86.2%)</td>
<td>6/30 (20.0%)</td>
<td>0.83 (0.62, 1.00)</td>
</tr>
</tbody>
</table>

≥100,000/mm³ platelets

<table>
<thead>
<tr>
<th>Pegcetacoplan</th>
<th>Eculizumab</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/12 (83.3%)</td>
<td>0/9 (0.0%)</td>
<td>0.81 (0.64, 0.99)</td>
</tr>
</tbody>
</table>

*Values are change from baseline at Week 12; no transfusion-free patients with uncensored data remained in this stratum in the ECU group at Week 16.

Disclosure of Interest: R. Peffault De Latour Conflict with: Novartis, Pfizer and Alexion (Consultancy), Conflict with: Novartis, Pfizer, Amgen and Alexion (Grant/Research Support), Conflict with: Novartis, Pfizer, and Alexion (Honoraria), C. M. De Castro Conflict with: Apellis (Consultancy), Conflict with: Alexion and Apellis (Grant/Research Support), Conflict with: Novartis (Honoraria, Steering Committee); Alexion and Apellis (Honoraria); Biocryst (Honoraria, Data monitoring committee), J. Szer Conflict with: Novartis, Alexion and Apellis (Consultancy), Conflict with: Takeda, Pfizer, Novartis, Prevail Therapeutics and Alexion (Speakers Bureau); Prevail Therapeutics and Alexion (Membership on an entity’s Board of Directors or advisory committees), K. Usuki Conflict with: Alexion, Apellis, Chugai, and Novartis (Grants/Research Support), Conflict with: Alexion and Novartis (Speakers Bureau), P. Hillmen Conflict with: Alexion, Apellis, Abbvie, AstraZeneca, Janssen and Roche (Consultancy), Conflict with: Alexion, Apellis, Abbvie, Gilead, Janssen, Pharmacycics and Roche (Grants/Research Support), Conflict with: Alexion, Apellis, Abbvie, AstraZeneca, Janssen and Roche (Speakers Bureau), M. Griffin Conflict with: Biocryst (Membership on an entity’s Board of Directors or advisory committees); Alexion (Honoraria, conference support), M. Hamdani Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), T. Ajayi Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), H. Nishimori: None Declared, I. C. Weitz Conflict with: Alexion and Apellis (Consultancy); Conflict with: Alexion and Apellis (Speakers Bureau); Alexion and Apellis (Honoraria).

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Comparative effectiveness of pegcetacoplan versus ravulizumab in patients with paroxysmal nocturnal hemoglobinuria previously treated with eculizumab: a matching-adjusted indirect comparison

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1Apellis Pharmaceuticals, Inc., Waltham, Massachusetts, 2Analysis Group, Boston, Massachusetts, United States

Abstract Content: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired hematologic disease characterized by complement-mediated red blood cell hemolysis. Currently available treatment options for PNH include the C5 inhibitors (C5i) eculizumab (ECU) and ravulizumab. C5i reduce intravascular hemolysis (IVH), but extravascular hemolysis (EVH) can be significant in a subset of C5i-treated patients. Pegcetacoplan is a targeted C3 inhibitor being developed to control both IVH and EVH to improve hematological and clinical outcomes. The PEGASUS study (NCT03500549) is a phase 3, open-label, randomized controlled trial evaluating the efficacy and safety of pegcetacoplan compared with ECU.

PEGASUS enrolled patients ≥18 years of age with PNH and hemoglobin (Hb) levels <10.5 g/dL despite ECU treatment for ≥3 months. Individual patient data from PEGASUS were used to adjust for baseline differences compared to aggregate published results from the randomized 302 study comparing ravulizumab and ECU among patients with PNH with previous ECU treatment (Kulasekarakaraj et al., Blood 2019). PEGASUS and 302 had similar eligibility criteria; however, PEGASUS required Hb <10.5 g/dL and absolute reticulocyte count >1x upper limit of normal while 302 did not. Propensity score weighting was used to balance demographic and clinical characteristics. Outcomes were assessed at Week 16 in PEGASUS and Week 26 in 302. Outcomes evaluated included transfusion avoidance, total transfused units of packed red blood cells (PRBCs), Hb stabilization, and change in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score. Unadjusted mean and least-squares mean change in FACIT-Fatigue score were compared for PEGASUS and the 302 study, respectively. Weighted Wald tests and 95% confidence intervals (CIs) were computed for comparisons of categorical and continuous outcomes.

Sixty-eight patients from PEGASUS (36 pegcetacoplan; 32 ECU) and 195 from the 302 study (97 ravulizumab; 98 ECU) were included. Among pegcetacoplan and ravulizumab patients, mean age after matching was 46.4 years, 48.5% were female, and 51.5% were white. Overall, 51.5% received ≥4 transfusions in the 12 months before screening in PEGASUS. The adjusted difference in proportion of transfusion avoidance was 71.4% (95% CI, 53.5–89.3%; P < 0.0001) for pegcetacoplan vs ravulizumab, indicating that pegcetacoplan is associated with 71.4% more patients who avoided transfusions than ravulizumab. The difference in mean PRBC units transfused during follow-up was −5.7 units (95% CI, −7.2 to −4.2; P < 0.0001) for pegcetacoplan vs ravulizumab, indicating that pegcetacoplan is associated with 5.7 fewer PRBC units transfused during treatment than ravulizumab. The adjusted difference in proportion of Hb stabilization was 75.5% (95% CI, 56.4–94.6%; P < 0.0001), suggesting that pegcetacoplan is associated with 75.5% more patients who achieved Hb stabilization than ravulizumab. The adjusted difference in mean change from baseline in FACIT-Fatigue score was 8.2 points (95% CI, 3.8–12.6; P = 0.0003), indicating that pegcetacoplan is associated with an improvement that is 3x a clinically meaningful improvement (>3-points).

MAIC results suggest an improvement in transfusion avoidance, Hb stabilization, and fatigue and a reduction in the total number of PRBC units transfused for patients who received pegcetacoplan, a C3 inhibitor, in PEGASUS, vs patients who received ravulizumab, a C5 inhibitor, in the 302 study.
Abstract Table:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PEGASUS study Pegcetacoplan (n = 36)</th>
<th>Eculizumab (n = 32)</th>
<th>302 Study Ravalizumab (n = 97)</th>
<th>Eculizumab (n = 98)</th>
<th>Difference (95% CI)</th>
<th>P Value^c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusion avoidance, %b^d</td>
<td>89.47%</td>
<td>13.18%</td>
<td>87.60%</td>
<td>82.70%</td>
<td>71.39% (53.50, 89.28)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Transfusion requirements, mean^b,c</td>
<td>0.13</td>
<td>4.92</td>
<td>4.30</td>
<td>3.40</td>
<td>-5.69 (-7.20, -4.18)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hemoglobin stabilization, %c^d</td>
<td>89.47%</td>
<td>13.18%</td>
<td>76.30%</td>
<td>75.50%</td>
<td>75.49% (56.38, 94.60)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Change from baseline FACIT-Fatigue, mean^c,d</td>
<td>10.03</td>
<td>0.38</td>
<td>2.01</td>
<td>0.54</td>
<td>8.19 (3.79, 12.58)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

^aThe P value for the anchored comparison after matching is calculated using the weighted Wald test (i.e. chi-square test for categorical endpoints; z test for continuous endpoints). ^bFor the endpoints related to hemoglobin, the following baseline characteristics were used for matching: age at first infusion of study drug, female, white, Asian, history of aplastic anemia, and lactate dehydrogenase. ^cTransfusion requirement is defined as the total number of units of packed red blood cells transfused during follow-up. ^dHemoglobin stabilization is defined as the avoidance of ≥2 g/dL decrease in hemoglobin level in the absence of transfusions from baseline through the end of the follow-up period. ^eFor endpoints related to fatigue, the following baseline characteristics were used for matching: age at first infusion of study drug, weight, history of aplastic anemia, and lactate dehydrogenase. ^fThe least-squares mean change from baseline in FACIT-Fatigue was extracted for the 302 study. The corresponding standard error was converted to standard deviation. ^gFACIT-Fatigue data were available for 67 of the 68 patients in the PEGASUS study.

Disclosure of Interest: R. Bhak Conflict with: Apellis (Grant/Research Support), N. Mody-Patel Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), S. B. Baver Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), C. Kunzweiler Conflict with: Apellis (Grant/Research Support), C. Yee Conflict with: RTI-HS Health Solutions (Reports Consultant/Advisory Board), Conflict with: Apellis (Research Funding), S. Sundaresan Conflict with: RTI-HS Health Solutions (Reports Consultant/Advisory Board), C. Yee Conflict with: Apellis (Research Funding), S. Krishnan Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), S. P. Sarda Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company)

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Effects of Luspatercept on Health-Related Quality Of Life Outcomes For Patients With Transfusion-Dependent Beta-Thalassaemia In The BELIEVE Trial


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Abstract Content: Luspatercept, a first-in-class erythroid maturation agent, provided clinically meaningful reductions in red blood cell transfusion (RBCT) burden in patients (pts) with transfusion-dependent (TD) β-thalassaemia in the phase 3 BELIEVE trial
Abstract Table: Table. Proportion of pts achieving clinically meaningful improvement in SF-36<sup>a</sup> and TranQol<sup>b</sup> primary domains, luspatercept responders vs PBO

<table>
<thead>
<tr>
<th>Domain</th>
<th>Treatment</th>
<th>Definition of clinical response</th>
<th>Up to Wk 48, n/N (%)</th>
<th>Up to Wk 24, n/N (%)</th>
<th>Up to Wk 24, n/N (%)</th>
<th>Up to Wk 48, n/N (%)</th>
<th>Up to Wk 48, n/N (%)</th>
<th>Up to Wk 24, n/N (%)</th>
<th>Up to Wk 48, n/N (%)</th>
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<tbody>
<tr>
<td>SF-36: GH</td>
<td>Luspatercept responder</td>
<td>TB reduction ≥ 33% at any 12-week interval</td>
<td>31/157 (19.6)</td>
<td>18/97 (18.6)</td>
<td>7/23 (30.4)</td>
<td>13/91 (14.3)</td>
<td>14/91 (15.4)</td>
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<tr>
<td></td>
<td>PBO</td>
<td></td>
<td>13/91 (14.3)</td>
<td>13/91 (14.3)</td>
<td>13/91 (14.3)</td>
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<td>SF-36: PF</td>
<td>Luspatercept responder</td>
<td>TB reduction ≥ 50% at any 12-week interval</td>
<td>27/157 (17.2)</td>
<td>21/97 (21.7)</td>
<td>8/23 (34.8)</td>
<td>15/91 (16.5)</td>
<td>12/91 (13.2)</td>
<td>12/91 (13.2)</td>
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<tr>
<td></td>
<td>PBO</td>
<td></td>
<td>15/91 (16.5)</td>
<td>15/91 (16.5)</td>
<td>15/91 (16.5)</td>
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<td>12/91 (13.2)</td>
<td>12/91 (13.2)</td>
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<tr>
<td>SF-36: PCS</td>
<td>Luspatercept responder</td>
<td>TI at any 8-week interval</td>
<td>44/157 (28.0)</td>
<td>26/97 (26.8)</td>
<td>11/23 (47.8)</td>
<td>18/91 (19.8)</td>
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<td>18/91 (19.8)</td>
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<td>15/91 (16.5)</td>
<td>15/91 (16.5)</td>
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<tr>
<td>TranQol total score</td>
<td>Luspatercept responder</td>
<td>TI at any 12-week interval</td>
<td>34/160 (21.3)</td>
<td>22/98 (22.5)</td>
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</tr>
<tr>
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<td></td>
<td>PBO</td>
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</tbody>
</table>

Significant values are shown in bold font.
<sup>a</sup>Within-pt clinically meaningful change from baseline was defined as 3.8–7.0-point improvement, based on the prespecified domain-specific cutoff values for the domains of the SF-36 questionnaire;
<sup>b</sup>Within-pt clinically meaningful change from baseline was defined as a ≥4-point change for the TranQol total score and ≥0.5 standard deviations of the pooled domain score for other domains of the TranQol questionnaire.

GH, Global Health; PBO, placebo; PCS, Physical Component Score; PF, Physical Functioning; PH, Physical Health; pt, patient; SF-36, 36-item Short Form Health Survey; TB, transfusion burden; TI, transfusion independence; TranQol, Transfusion-dependent Quality of Life questionnaire; wk, week.

The impact of luspatercept on health-related quality of life (HRQoL), however, is not well understood. Here we evaluate the effects of luspatercept + best supportive care (BSC, including RBCT and iron chelation therapy) vs placebo (PBO) + BSC on HRQoL.

336 pts were randomised to receive luspatercept (1.0 mg/kg, titration up to 1.25 mg/kg every 3 weeks; n = 224) or PBO (n = 112) subcutaneously for ≥48 weeks + BSC. The generic 36-item Short Form Health Survey (SF-36) and thalassemia-specific Transfusion-dependent Quality of Life questionnaire (TranQol) were used to assess HRQoL at screening (≥4 weeks prior to first study dose) and every 12 weeks up to 48 weeks of treatment. The HRQoL-evaluable population included all pts who completed the HRQoL assessment at screening with ≥1 post-screening assessment visit and the primary analysis assessed changes from baseline between groups through Wk 48. TranQol and SF-36 questionnaires were considered complete if ≥75% and 50% of items, respectively, were answered at a given time point. The primary domains of interest were: TranQol total score and Physical Health (PH); and the SF-36 Physical Component Summary (PCS), Physical Functioning (PF), and General Health (GH). ANCOVA models adjusting for baseline domain scores and geographic region were used to compare changes from baseline. All other exploratory domains assessed the proportion of pts achieving a clinically meaningful improvement in domain scores between pts on luspatercept achieving a clinical response (i.e. ≥33% or 50% reduction in RBCT burden over 12 weeks; transfusion independence (TI) for any 8 or 12 weeks) and PBO.

The HRQoL-evaluable population was 212 (94.6%) in the luspatercept arm and 104 (92.9%) in the PBO arm. At Week 48, HRQoL questionnaire compliance rates among pts on treatment were >87.5% for both questionnaires. Although GH, Role-Emotional, and Role-Physical domain scores were impaired in the BELIEVE population, baseline scores were similar to the US general population for most SF-36 domains. There was no difference in mean scores for all primary and exploratory domains between treatment groups at Weeks 24 and 48, and scores were stable over time. Pts receiving luspatercept who achieved ≥50% reduction in RBCT burden over 12 weeks were significantly more likely than pts receiving PBO to achieve a clinically meaningful improvement in PCS (31.1% vs 16.5%; P = 0.024) and PF (30.0% vs 13.2%; P = 0.007) at Wk 48 (Table). Statistically significant differences were observed between luspatercept and PBO pts achieving TI for any 8 or 12 weeks for some SF-36 domains. Although the proportion of pts with improved scores was higher with luspatercept, especially at Wk 48, no statistical differences were seen in pts achieving ≥33% reduction in RBCT burden for either SF-36 or TranQol domains.

Luspatercept + BSC reduced transfusion burden while sustaining HRQoL over time through Wk 48 in adult pts with TD β-thalassemia. Luspatercept responders were more likely to achieve clinically meaningful improvements in HRQoL.

This abstract was previously published (Cappellini et al., Blood 2020;136[Sl1]-S9).

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NOVARTIS Company, PRODIGANT Company (research funding), V. Viprakasit Conflict with: BMS, Novartis (consultancy, honoraria, research funding, speakers bureau); Agios Pharmaceuticals, Ionis Pharmaceuticals, La Jolla Pharmaceuticals, Protagonist Therapeutics, Vifor Pharma (consultancy, research funding), J. B. Porter Conflict with: Agios Pharmaceuticals, bluebird bio, Inc., BMS (consultancy, honoraria); La Jolla Pharmaceuticals, Protagonist Therapeutics, Silence Therapeutics, Vifor Pharmaceuticals (honoraria), O. Hermine Conflict with: AB Science (consultancy, current equity holder in publicly-traded company, honoraria, patents & royalties, research funding); Alexion, BMS, Intherex, Novartis (research funding), E. J. Neufeld Conflict with: Acceleron Pharma (consultancy, other: DSMB); BMS, Genentech, Novo Nordisk, Octapharma, Takeda (consultancy); Pfizer (membership on an entity’s board of directors or advisory committees); ApoPharma/Chiesi, Imara Pharma (other: DSMB service); Bayer (other: DSMB, A. A. Thompson Conflict with: bluebird bio, Inc., BMS (consultancy, research funding); Baxalta, Biomarin, CRISPR/Vertex (research funding); Novartis (consultancy, honoraria, research funding), D. Tang Conflict with: BMS (current employment, current equity holder in publicly-traded company), P. Yu Conflict with: Evidera (current employment), S. Guo Conflict with: BMS (consultancy), J. K. Shetty Conflict with: BMS (current employment), D. Mitvec Conflict with: BMS (current employment), T. Zinger Conflict with: Gelgene, a Bristol-Meyers Squibb company (current employment), E. L. Beattstrom Conflict with: Acceleron Pharma (current employment, current equity holder in publicly-traded company); BMS (current equity holder in publicly-traded company), E. N. Oliva Conflict with: BMS (consultancy, honoraria, patents & royalties, speakers bureau); Abbvie, Alexion, Agenus, Apellas, Novartis (consultancy)

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Risk Factors for Thrombotic Events in Patients with PNH: A Nested Case-Control Study in the International PNH Registry

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Abstract Content: Although thrombotic events (TEs) are the leading cause of paroxysmal nocturnal hemoglobinuria (PNH)-related mortality, the risk factors predictive of TEs are not well established. Previous studies have reported that the proportion of PNH cells, elevated lactate dehydrogenase (LDH), age, thrombosis at diagnosis, and treatment may impact TE risk. The International PNH Registry (NCT01374360) is an observational cohort study containing the largest database of safety, quality-of-life, and outcome data from patients with PNH. Here, we analyzed patient data from the Registry to identify risk factors for TEs.

Data from Registry patients who were untreated at enrollment, had an incident TE after enrollment, non-zero follow-up time, and with documented birthdate, sex, enrollment date, treatment status, and country were included in this analysis. Up to five controls were
selected from the risk set for each TE case matched on age (±5 years at Index Date), gender, country, and history of bone marrow disease (BMD). Cases that could not be matched with at least one control were excluded from the study. Univariate conditional logistic regression was used to estimate odds ratios (ORs) with 95% Wald confidence intervals (CIs) of TE associated with candidate risk factors: glycoprophosphatidylinositol (GPI)-deficient granulocytes, GPI-deficient erythrocytes, LDH ratio, recent high-disease activity (HDA; defined as within six months prior to the index date, LDH ratio ≥1.5xULN, and hemoglobin <10 g/dL or at least one of the following symptoms: abdominal pain, dyspnea, dysphagia, fatigue, hemoglobinuria, and/or male erectile dysfunction), LDH ratio and number of HDA symptoms, history of TE, history of major adverse vascular event (MAVE), and recent prophylactic anticoagulant (PA) use.

Due to the strict eligibility criteria, 57 TE cases and 189 non-TE controls met the conditions and were matched for the case-control study. The mean age at Index Date was 46.8 years for TE cases and 47.1 years for non-TE control. Cases were more likely to have a clone size of ≥50% GPI-deficient granulocytes, an LDH ratio ≥1.5xULN, recent HDA, and a history of TE or MAVE, compared with controls. From univariate analyses, the following factors were found to be associated with statistically significantly increased risk of TE: recent HDA (OR, 2.65; 95% CI, 1.10–6.61), LDH ≥1.5xULN and 2–3 HDA symptoms (OR, 8.61; 95% CI, 1.46–96.96), LDH ≥1.5xULN and ≥4 HDA symptoms (OR, 14.50; 95% CI, 1.70–209.25), and a history of TE (OR, 3.60; 95% CI, 1.41–9.24) or MAVE (OR, 2.17; 95% CI, 0.96–4.80), and recent PA use (OR, 4.35; 95% CI, 1.57–13.13). Despite not all patients having available data for each parameter assessed, and the relatively small number of TE cases identified, several factors that were statistically significantly associated with increased TE risk were identified.

These factors included ≥50% GPI-deficient granulocyte clone size, LDH ratios ≥1.5xULN, recent HDA, LDH ≥1.5xULN plus HDA symptoms, a history of TE or MAVE, and recent PA use compared with non-TE controls; for recent PA use, these patients were most likely at increased risk of TE, which may explain why they received treatment. Our data add to the findings of previously published studies 10, 11 by expanding the results to a broader patient population. These results highlight the importance and urgency of identifying and monitoring risk factors for TE in patients with PNH to inform treatment decisions.

BSH2021-PO-212

"Improvements in Fatigue and Physical Function Evaluated Through Changes in Clinical Outcomes in Paroxysmal Nocturnal Hemoglobinuria: Post-Hoc Analyses from the PEGASUS Study"

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Abstract Content: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, hemotologic disease characterized by complement-mediated hemolysis, thrombosis, impaired bone marrow function, and anemia. In a randomized phase 3 trial (PEGASUS; NCT03500549), pegcetacoplan demonstrated a statistically significant improvement in hemoglobin (Hb) levels compared to eculizumab (ECU) at Week 16 in PNH patients with partial response to prior ECU treatment. The objective of these post-hoc analyses was to explore relationships between patient-reported measures of fatigue and physical functioning with clinical and hematological parameters, namely Hb levels, absolute reticulocyte count (ARC), and indirect bilirubin levels from baseline to Week 16 in PNH patients.

Adult patients with PNH and Hb levels <10.5 g/dl despite treatment with ECU for ≥3 months were eligible for the study. Patients started a 4-week run-in period with both ECU and twice-weekly pegcetacoplan (1080 mg, self-administered subcutaneously) before 1:1 randomization to either monotherapy for 16 weeks. Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy (FACIT)–Fatigue scale and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC-QLQ-C30) questionnaire, which also evaluates physical functioning. Convergent validity was assessed using Spearman correlations. To evaluate responsiveness to change, patients were grouped by increases in Hb levels (>1 g/dl, ≥2 to <2 g/dl, and ≥2 g/dl), decreases in ARC (≥70x10⁵ cells/L and <70x10⁵ cells/L) and decreases in indirect bilirubin levels (≥7.6 µmol/L and <7.6 µmol/L). Cut points were determined based on the median splits for each variable.

At Week 16 (n = 80; intent-to-treat), FACIT-Fatigue scores were significantly correlated with Hb (r = 0.47, P < 0.0001), ARC (r = -0.37, P < 0.01) and indirect bilirubin (r = -0.25, P < 0.05). EORTC-QLQ-C30 fatigue scores were correlated with ARC (r = 0.28, P < 0.05), but not with Hb or indirect bilirubin. EORTC-QLQ-C30 physical function scores were correlated with Hb (r = 0.45, P < 0.0001), ARC (r = -0.28, P < 0.05), and indirect bilirubin (r = -0.26, P < 0.05). Patients with larger decreases in ARC (F = 0.15, P = 0.0002) and indirect bilirubin (F = 15.8, P = 0.0002) showed improvements in FACIT-Fatigue scores (9.3 for ARC; 9.2 for indirect bilirubin). Groups with greater improvements in Hb over 16 weeks also showed the largest improvement in FACIT-Fatigue scores (F = 9.0, P < 0.0001), with the largest fatigue reduction observed in the Hb group with an increase of ≥2 g/dl (11.3-point improvement in FACIT-Fatigue score). Fatigue and physical functioning, as defined by the EORTC-QLQ-C30, also demonstrated improvements across the three outcomes measured. Patients with larger decreases in ARC (F = 6.1, P = 0.02) and indirect bilirubin levels (F = 7.6, P = 0.007), and greater improvements in Hb levels (F = 4.1, P = 0.0093), showed the greatest improvement in fatigue. Similarly, patients in both groups showed the greatest improvement in physical function (F = 7.7, P = 0.007 for ARC; F = 8.4, P = 0.005 for indirect bilirubin levels, F = 4.1, P = 0.0103 for Hb levels).

The results of the current study in PNH patients demonstrate that fatigue and physical functioning outcomes are correlated with improvements in clinical and hematological parameters. The FACIT-Fatigue and EORTC-QLQ-C30 scales appear to be useful and valid patient-reported measures for assessing meaningful change in PNH.

Disclosure of Interest: A. Röth Conflict with: Alexion, Apellis, Biocryst, Novartis, Roche and Sanofi (Consultancy), Conflict with: Alexion and Roche (Grant/Research Support), W. R. Lenderking Conflict with: Evidera (Current employment), S. P. Sarda Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), S. B. Baver Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), M. Hamdani Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), R. Hsieh Conflict with: Evidera (Current employment), S. Shaffer Conflict with: Evidera (Employment), M. Yeh Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), D. Cell Conflict with: Evidera and Apellis (Consultancy), Conflict with: FACIT.org (President/Owner), Conflict with: President/Owner of FACIT.org

BSH2021-PO-213

Discharge opioid prescribing in patients with sickle cell anaemia after an admission for a sickle cell crisis

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Abstract Content: Many patients with sickle cell anaemia present with pain and are treated with opioid analgesics during their admission. At Sheffield Teaching Hospitals (STH), the palliative medicine team work closely with the haematology department to provide support and guidance for managing opioids during a painful crisis. There are departmental haematology guidelines on the management of a sickle cell crisis which includes advice for opioid prescribing on admission and on discharge. The guidance advised the minimum necessary doses of oral opioids should be used. A maximum of 5 days should be dispensed of only one type of opioid and should not be continued by a community prescriber unless previously agreed by the palliative medicine or haematology team. A clear plan for patient follow-up is essential to review their pain and opioid use. The aim of this audit was to review whether discharge medications and prescriptions were compliant with hospital guidelines and to establish if safe opioid prescribing practices occurred within the haematology department. This project was approved by the Clinical Effectiveness Unit at STH.

A retrospective review was conducted of patient discharge letters dating from September 2019–September 2020 (inclusive). During this time, 74 patients were admitted with a sickle cell crisis. All were admitted under the care of the haematology team, except one patient who was admitted under the care of the obstetrics team. 59 of these patients were discharged home with opioid analgesics and were included in the audit. Length of admission ranged from 1-21 days, with 5.1 days being the average length of stay. The results are summarised in Table 1. Standard compliance had been set at 100% for all areas looked at.

The audit results (Table 1) highlighted that in a third of patients (34%) a maximum dose for when required opioid medications was missed. 31% of patients who were not taking immediate release (IR) opioids prior to admission were discharged home with greater than 5 days of IR medication. 71% of discharge letters appropriately stated where future opioid medications would be dispensed. Care must be taken to avoid opioids being prescribed from the community without haematology or palliative care input and involvement.

Since this audit, changes have been implemented. New guidance with clear instructions for opioid prescribing have been developed.
and circulated amongst the haematology team. This guidance will also be included at the rotational induction for junior doctors who work in the department. At present we are working towards a discharge box on the electronic software which is specifically for patients with sickle cell which can act as a prompt for safe prescribing. When a patient is admitted we plan to document whether any opioid prescriptions have been issued by their general practitioners (GPs) in the 12 months prior to the attendance.

The audit had limitations which included a small sample size, however, despite this, valuable information has been gained. Due to restrictions from information governance, we were unable to access patient Summary Care Records to review historical opioid prescribing by GPs. We hope community prescribing can be captured during the next audit cycle.

The use of opioid analgesics in the management of pain for a sickle cell crisis remains an essential aspect of care. For any physician managing patients who take opioids, careful prescribing can prevent harm and long-term complications.

**Abstract Table:**

**Table 1: Audit results.**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Standard compliance % and Numbers</th>
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<tbody>
<tr>
<td>1) There will be a clear plan for opioid analgesics on the discharge letter.</td>
<td>31/59 (53%) patients had clear instructions documented on the discharge letter.</td>
</tr>
<tr>
<td>2) That opioids will be prescribed in accordance with STH guidelines.</td>
<td>17/36 (47%) patients who do not usually take as required immediate release (IR) opioids were prescribed a maximum of 5 days worth of IR opioids.</td>
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<td></td>
<td>11/36 (31%) were prescribed &gt;5 days of opioid analgesics.</td>
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<td></td>
<td>8/36 (22%) were not prescribed any IR opioid analgesia for discharge.</td>
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<tr>
<td></td>
<td>19 patients were discharged on a sustained release opioid.</td>
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<td>4 (21%) patients were not discharged with immediate release analgesics.</td>
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<tr>
<td></td>
<td>11 (58%) were prescribed an appropriate immediate release dose.</td>
</tr>
<tr>
<td></td>
<td>4 (21%) were not prescribed an appropriate immediate release dose.</td>
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<tr>
<td></td>
<td>Of the 14 patients who were not discharged on ‘strong’ analgesics (oxycodeone/morphine – as required/regular).</td>
</tr>
<tr>
<td></td>
<td>14/14 (100%) of these were prescribed one prn analgesic on discharge of tramadol/codeine or dihydrocodeine.</td>
</tr>
<tr>
<td>3) To ensure that opioid prescriptions are not continued by the GP unless specifically requested to do so with clear follow up if this is the case.</td>
<td>42/59 (71%) of opioids on discharge appropriately stated where future prescriptions will be obtained from.</td>
</tr>
<tr>
<td>4) A clear follow up plan is documented on discharge.</td>
<td>42/59 (71%) of patients had evidence of appropriate and timely follow up documented on the discharge letter.</td>
</tr>
<tr>
<td></td>
<td>13/13 (100%) patients with palliative care follow up had a sole prescriber.</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

**Abstract Content:**

Seroxim ferritin is under requested in the 1 to 5 age group: relationship between mean corpuscular volume and serum ferritin

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**Abstract Content:** Serum ferritin is under requested in the 1 to 5 age group: relationship between mean corpuscular volume and serum ferritin

Iron deficiency (ID) in early childhood has consistently been found to be associated with poorer motor, behavioural and cognitive outcomes. Diagnosis of ID is aided by several biomarkers, most commonly serum ferritin (SF). The World Health Organisation (WHO) defines ID as SF <12 µg/l in children under 5 years, and <15 µg/l for individuals over 5 years of age. A depleted mean corpuscular volume (MCV), termed microcytosis, may be a helpful correlate of ID. While less conclusive, evidence suggests that microcytosis, indicated by MCV <<74fl, is also associated with poorer cognitive outcomes in 2-year-old children and can be an earlier marker of functional ID compared to commonly used reference limits of SF. This study aimed to (a) explore the relationship between SF and MCV in a cohort of children aged 1-5 years, and (b) examine SF requests for this group.

The study was a five-year retrospective analysis of electronic laboratory data (2016 - 2020) of children aged 1-5 years, held at the Haematology Department of Cork University Hospital, a department that services the Cork and Kerry region and receives up to 250000 SF requests per annum for all age groups. SF was available for a total of 2326 children, and those with both an MCV and SF available were included for whole group analysis (n = 2112). A c-reactive protein (CRP) was available for 239 children in this sample, and sub-group analysis was conducted on those with CRP <5 mg/l (n = 204). ID was interpreted as per WHO criteria.

The proportion of children found to have ID and microcytosis is described in Table 1. SF requests were estimated to comprise 0.2% of total requests over the five-year period. A weak positive correlation was found between SF and MCV for both groups, but stronger for SF ≤10 µg/l (Table 2). Area under the curve (AUC) analysis demonstrated that a SF cut-off of 15.5 µg/l best predicted microcytosis for both the whole group (AUC = 0.698, P = 0.00; sensitivity 54% and specificity 76%), and the sub-group (AUC = 0.636, P = 0.034; sensitivity 54% and specificity 72%).

In conclusion, findings demonstrate that a child may have depleted SF while still maintaining a normal MCV. Only the most severe deficiency manifests as microcytosis consistently, confirming bone marrow compensates until iron stores deplete over time. Therefore, we conclude that SF remains an essential test despite a normal MCV for diagnosing ID in children aged 1-5 years. Surprisingly, findings suggest that SF is an underutilised test in this vulnerable cohort, given the small number of SF requests for children aged 1-5 compared to total requests for all children and adults.

**Abstract Table:**

**Table 1. Proportion of children with iron deficiency (ID) and microcytosis (MCV<74fl) in whole group and identified subgroup.**

<table>
<thead>
<tr>
<th>Group</th>
<th>Iron deficiency n (%)</th>
<th>Microcytosis n (%)</th>
<th>ID and microcytosis n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole group</td>
<td>365 (17)</td>
<td>317 (15%)</td>
<td>131 (6%)</td>
</tr>
<tr>
<td>(n = 2112)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sub-group</td>
<td>38 (18)</td>
<td>28 (14%)</td>
<td>11 (5%)</td>
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</table>

*Disclosure of Interest: None Declared*
Table 2. Spearman moment correlations showing relationship between iron deficiency (ID) and microcytosis (MCV <74fl) for whole group and identified subgroup.

<table>
<thead>
<tr>
<th>Group</th>
<th>Spearman r,</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole group</td>
<td>0.27***</td>
</tr>
<tr>
<td>Sub-group</td>
<td>0.23**</td>
</tr>
<tr>
<td>Whole group with SF ≤10 µg/l</td>
<td>0.48***</td>
</tr>
<tr>
<td>Sub-group with SF ≤10 µg/l</td>
<td>0.49*</td>
</tr>
</tbody>
</table>

*p <0.05  **p <0.01***  ***p < 0.001

Disclosure of Interest: None Declared

BSH2021-PO-215

Efficacy and safety of ravulizumab in older patients aged >65 years with paroxysmal nocturnal hemoglobinuria in the 301 and 302 phase 3 extension studies


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Abstract Content: In the two largest phase 3 studies in patients with paroxysmal nocturnal hemoglobinuria (PNH), ravulizumab given every 8 weeks was noninferior to eculizumab given every 2 weeks across all efficacy endpoints. However, data on efficacy and safety of ravulizumab in patients aged ≥65 years with PNH are limited.

This study demonstrated the efficacy and safety of ravulizumab in patients with PNH aged >65 years.

The population included patients from two phase 3 studies that assessed ravulizumab vs eculizumab in complement-inhibitor-naïve (301; NCT02946463) and -experienced patients (302; NCT03056940) adults with PNH. In study 301, patients were aged ≥18 years with a confirmed PNH diagnosis by flow cytometry and had a lactate dehydrogenase (LDH) level ≥1.5x upper limit of normal (ULN; 246 UL/L). In study 302, patients were aged ≥18 years with a confirmed PNH diagnosis by flow cytometry, were clinically stable on ≥6 months eculizumab and had a LDH level ≤1.5x ULN. Patients were randomized to either ravulizumab or eculizumab for 26 weeks after which all received ravulizumab up to 52 weeks. This analysis stratified patients by age: ≥65 or >65 years. Outcomes of interest included proportion of patients achieving LDH ≤1.5x upper limit of normal (ULN), percentage of patients achieving treatment transfusion avoidance (TA), hemoglobin (Hgb) stabilization, breakthrough hemolysis (BTH) and FACIT-fatigue score. Treatment emergent adverse events (TEAEs) were assessed as an indicator of safety.

A total of 58 patients aged ≥65 years and 383 patients aged <65 years were included, with similar medical history at baseline. Results for primary and secondary endpoints for the two subgroups were comparable across studies and efficacy was maintained through 52 weeks. In complement inhibitor-naïve and -experienced patients, mean LDH levels in both age groups were maintained below 1.5x ULN. In both studies, 93.0%-94.5% patients aged ≤65 years and 42.9%-83.3% >65 years who avoided transfusions in the primary evaluation period (BL–26 weeks) continued to avoid transfusion from 27 to 52 weeks, respectively. The number of BTH events was low. No patients treated with ravulizumab had BTH events associated with suboptimal free C5 inhibition. No BTH events were reported in older patients in this analysis. In both studies, 87.3%–91.9% patients aged ≤65 years and 50%–90% >65 years achieved Hgb stabilization through 52 weeks, respectively. A clinically significant 3-point change was seen in FACIT-fatigue scores (indicating improvements in fatigue), with higher scores observed for ravulizumab in both subgroups.

One patient discontinued the extension of study 301 due to lung cancer onset during the 52-week period and died following discontinuation. There were no meningococcal infections in any patients through 52 weeks. Headache, fatigue, pyrexia, nasopharyngitis and upper respiratory tract infection were the most frequent TEAEs. The incidence of TEAEs reported during ravulizumab treatment up to 52 weeks did not increase vs the 26-week period, with few events and no difference between subgroups.

The effectiveness of ravulizumab for reducing intravascular hemolysis, avoiding transfusion and stabilizing hemoglobin levels was similar in patients aged ≥65 years and patients aged 18–64 years. Ravulizumab was well tolerated in patients aged >65 years with no additional safety concerns compared to patients ≤75 years. The small sample size of PNH patients >65 years limits interpretation of the data.


BSH2021-PO-216

The therapeutic mechanisms that are unique in a sickle cell pain management programme. A grounded theory

Ji Yeon Park*, Sue Holttum, Alexa Duff

Abstract Content: Sickle cell disease (SCD) is the most common life-limiting and lifelong genetic disorder in the UK with pain as the main disease characteristic. Pain management programmes (PMPs) are multidisciplinary-led interventions for people with chronic pain to improve functioning and promote self-management. Recently, sickle cell pain management programmes (SCPMPs) have emerged as management options. This study aimed to explore the therapeutic mechanisms that are perceived to be present in SCPMPs.

Ten participants were recruited from two haematology services, in which eight participants had attended SCPMPs and two participants had attended non-specific PMPs. Additionally, two group facilitators were recruited from a haematology service where the SCPMP is
Paroxysmal Nocturnal Hemoglobinuria from the Pegasus Phase 3 Trial
Effect of Pegcetacoplan on Quality of Life in Patients with Paroxysmal Nocturnal Hemoglobinuria with Eculizumab

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1Hematology, University Hospital Essen, University of Duisburg-Essen, Essen, 2University of Ulm and Institute of Transfusion Medicine and Immunogenetics, German Red Cross Blood Transfusion Service, and University Hospital Ulm, Institute of Transfusion Medicine, Ulm, Germany, 3Hematology, St James University Hospital, Leeds, United Kingdom, 4Duke University School of Medicine, Durham, North Carolina, United States, 5Clinical Haematology, Peter MacCallum Cancer Centre & Royal Melbourne Hospital, Melbourne, Australia, 6Hematology, NTT Medical Center Tokyo, Tokyo, Japan, 7Center of Clinical Investigations, Hospital Saint-Louis; Public Assistance-Hospital of Paris; University of Paris, Paris, France, 8Apellis Pharmaceuticals, Inc., Waltham, Massachusetts, United States, 9Hematology, Oncology, Hemostasiology and Stem Cell Transplantation, University Hospital RWTH Aachen, Aachen, Germany

Abstract Content: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, life-threatening hematologic disease characterized by chronic complement-mediated red blood cell (RBC) hemolysis. The current standard treatment for patients with PNH is eculizumab (ECU) or ravulizumab, both C5 inhibitors. Despite the proven efficacy of anti-C5 therapy in the control of intravascular hemolysis, 72% of patients have persistent hemolytic anemia despite ECU treatment and 36% require transfusions, resulting in significant impact on quality of life (QoL) including persistent fatigue. Pegcetacoplan is a C3 inhibitor that has the potential to control both intravascular and extravascular hemolysis in patients with PNH. QoL was evaluated in the PEGASUS study (NCT03500549), a phase 3, open-label, randomized, controlled trial evaluating the efficacy and safety of pegcetacoplan compared with ECU.

PEGASUS enrolled patients ≥18 years of age with PNH and hemoglobin (Hb) levels <10.5 g/dL despite receiving treatment with ECU for ≥3 months. Patients entered a 4-week run-in period in which they received ECU plus twice-weekly pegcetacoplan (1080 mg, administered subcutaneously) and were then randomized 1:1 to monotherapy with pegcetacoplan or ECU for 16 weeks. The primary endpoint was change from baseline in Hb levels. QoL assessments included the Linear Analog Scale Assessment (LASA) and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Scale (EORTC QLQ-C30) scores. The LASA consists of 3 sections asking respondents to rate their perceived level of functioning on a scale from 0 to 100 and contains specific domains for activity level, ability to carry out daily activities, and overall QoL. EORTC QLQ-C30 contains 30 questions comprising 5 functional scale scores, 9 individual symptom items and one overall health and QoL item. Change from baseline in the QoL instruments to Week 16 was analyzed using a mixed model for repeated measures.

Eighty patients were included in the analysis (pegcetacoplan, n = 41; ECU, n = 39; intention-to-treat set). Mean (SD) of the total of the 3 LASA scores for each treatment group were comparable at baseline (pegcetacoplan, 161.0 [67.99]; ECU, 156.7 [61.27]). The difference in the least-squares mean change from baseline in LASA scores using data censored for transfusion in the intention-to-treat set was 59.10 (95% CI, 16.88, 101.32; Table) at Week 16 for the comparison of pegcetacoplan with ECU. At Week 16, the

Disclosure of Interest: None Declared

Table 1 Main Themes categorised on the experience of the SCPMP.

<table>
<thead>
<tr>
<th>Categories</th>
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<tbody>
<tr>
<td>1. Not talking about pain</td>
<td></td>
</tr>
<tr>
<td>2. Learning about pain and techniques</td>
<td></td>
</tr>
<tr>
<td>3. New ways of talking to friends and family</td>
<td></td>
</tr>
<tr>
<td>4. Sharing and relating</td>
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<tr>
<td>5. Learning together</td>
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<tr>
<td>6. Exploring your pain</td>
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<tr>
<td>7. Increased positive experiences of self</td>
<td></td>
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<tr>
<td>8. Accept and make changes</td>
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Red Cell Disorder

provided. Semi-structured interviews were conducted with each participant and were analysed using a grounded theory methodology.

All participants from the SCPMPs described a shift in their experiences of pain and being more able to discuss their pain. This shift was important as it appeared to facilitate identifying and accepting the pain and the condition. Some participants described the acceptance as allowing them to modify their internal stigma, which may have contributed to the development of a more positive sickle cell identity through acceptance and change (Table 1). Acceptance allowed the participants to do more despite pain, rather than relying on trying to alleviate pain through using opioids. SCPMP attendees also identified the shared understanding of SCD as helping in the acceptance process in contrast to non-specific PMP attendees, who felt less understood as they felt that they had to explain SCD to other group members. The categories identified from the data can be seen in Table 1.

The unique medical experiences of SCD was an important variation in the SCPMP when compared to general PMPs, which was important in normalising and relating to each other about SCD moving towards an acceptance of pain. The process of talking about pain for people with SCD helped them to understand and respond differently to the sickle pain. Therefore, the study indicates that SCPMPs and other psychological treatment such as by acceptance and commitment therapy are important.

The findings showed an interaction of racial stigma towards people of Afro-Caribbean descent, and the stigmatisation against people using opioids, contributes to the sickle cell patients’ experience of pain management. The interaction between stigma and pain management raises implications for clinicians working with SCD, and highlights the need to develop compassionate understanding for those accessing services.

Despite pain being a main characteristic of SCD, many participants in this study highlighted that they had never received information about pain, (e.g. differences between acute crises and chronic pain), during their hospital appointments with haematology doctors or nurses. Therefore, one of the clinical implications from the study is that it may be useful for haematology services to consider other ways of making such information accessible to patients and families.

The study suggests that not talking about pain is a barrier to accessing treatment and support for pain management and SCD. It adds to the current literature on those with SCD having a unique experience and this needing an adapted response. Therefore, the therapeutic processes that can occur within a SCPMP provide tentative support for the acceptability of a SCPMP.

Abstract Table:

<table>
<thead>
<tr>
<th>Categories</th>
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<tbody>
<tr>
<td>1. Not talking about pain</td>
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<tr>
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<tr>
<td>8. Accept and make changes</td>
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</table>
Disclosure of Interest: A. Roth Conflict with: Alexion, Apellis, Biocryst, Novartis, Roche and Sanofi (Consultancy), Conflict with: Alexion and Roche (Grant/Research Support), Conflict with: Alexion, Apellis, Biocryst, Novartis, Roche and Sanofi (Honoraria), B. Höchsmann Conflict with: Novartis, Roche, Alexion and Apellis (Consultancy), Conflict with: Alexion Grant/Research Support), Conflict with: Novartis, Roche, Alexion and Apellis (Honoraria), M. Griffin Conflict with: Biocryst (Membership on an entity’s Board of Directors or advisory committees); Alexion (Honoraria, Steering Committee); Biocryst (Membership on an entity’s Board of Directors or advisory committees); Alexion and Apellis (Honoraria); Biocryst (Honoraria, Data monitoring committee); J. Sier Conflict with: Novartis, Alexion and Apellis (Consultancy), Conflict with: Takeda, Pfizer, Novartis, Prevail Therapeutics and Alexion (Honoraria); Takeda, Pfizer, Novartis and Alexion (Speakers Bureau); Prevail Therapeutics and Alexion (Membership on an entity’s Board of Directors or advisory committees); K. Usuki Conflict with: Alexion, Apellis, Chugai, and Novartis (Grants/Research Support), Conflict with: Alexion and Novartis (Speakers Bureau), J. Soret: None Declared, M. Hamdani Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), T. Ajayi Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), S. P. Sarda Conflict with: Apellis (Current Employment and Current equity holder in publicly-traded company), J. Panse Conflict with: Blueprint Medicines, Amgen, F. Hoffman-La Roche Ltd., MSD, Grunenthal, Bristol Myers Squibb and Apellis (Consultancy), Conflict with: Blueprint Medicines, F. Hoffman-La Roche Ltd., MSD, Grunenthal, Bristol Myers Squibb and Apellis (Honoraria), Blueprint Medicines, Amgen, Novartis, Boehringer Ingelheim, Alexion, F. Hoffman-La Roche Ltd., MSD, Grunenthal, Bristol Myers Squibb and Apellis (Membership on an entity’s Board of Directors or advisory committees); Chugai, Pfizer, Novartis, Boehringer Ingelheim and Alexion (Speakers Bureau)

Abstract Table: Table. Week 16 LASA and EORTC QLQ-C30 secondary endpoints and mixed model for repeated measures (MMRM) analyses.

<table>
<thead>
<tr>
<th>Metric</th>
<th>Pegcetacoplan N = 41 least square mean (SE)</th>
<th>Eculizumab N = 39 least square mean (SE)</th>
<th>Difference (95% CI) in least square mean</th>
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<tbody>
<tr>
<td>LASA score</td>
<td>49.4 (10.3)</td>
<td>−9.7 (19.0)</td>
<td>59.1 (16.9, 101.3)</td>
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<tr>
<td>EORTC QLQ-C30 Global Health Status/QoL</td>
<td>15.9 (3.6)</td>
<td>−2.7 (8.5)</td>
<td>18.6 (0.1, 37.1)</td>
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<tr>
<td>Functional Scales</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical functioning</td>
<td>16.9 (2.1)</td>
<td>4.1 (3.6)</td>
<td>12.9 (4.9, 20.9)</td>
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<tr>
<td>Role functioning</td>
<td>15.4 (3.9)</td>
<td>−9.0 (7.0)</td>
<td>24.4 (8.8, 40.0)</td>
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<td>Emotional functioning</td>
<td>8.0 (3.4)</td>
<td>3.9 (7.2)</td>
<td>4.1 (−11.6, 19.8)</td>
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<tr>
<td>Cognitive functioning</td>
<td>5.8 (3.3)</td>
<td>−3.8 (6.4)</td>
<td>9.6 (−4.5, 23.6)</td>
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<tr>
<td>Social functioning</td>
<td>15.1 (3.0)</td>
<td>3.8 (6.4)</td>
<td>11.3 (−2.4, 24.9)</td>
</tr>
<tr>
<td>Symptom Scales</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>−22.9 (3.3)</td>
<td>−22.6 (6.6)</td>
<td>−0.2 (−35.3, −6.2)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>−0.3 (1.6)</td>
<td>−0.3 (3.9)</td>
<td>0.0 (−6.4, 8.4)</td>
</tr>
<tr>
<td>Pain</td>
<td>−0.7 (4.3)</td>
<td>2.0 (7.8)</td>
<td>−2.5 (−20.4, 14.9)</td>
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<td>Dyspnea</td>
<td>−20.1 (3.5)</td>
<td>−5.6 (7.0)</td>
<td>−14.6 (−29.9, 0.8)</td>
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<td>Insomnia</td>
<td>−9.2 (4.0)</td>
<td>16.9 (7.1)</td>
<td>0.3 (−15.7, 16.3)</td>
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<td>Appetite loss</td>
<td>−3.8 (3.4)</td>
<td>4.2 (7.0)</td>
<td>−8.0 (−23.2, 7.3)</td>
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<td>Constipation</td>
<td>3.0 (3.3)</td>
<td>1.2 (8.1)</td>
<td>1.8 (−15.7, 19.3)</td>
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<td>Diarrhea</td>
<td>0.3 (3.7)</td>
<td>1.7 (8.2)</td>
<td>−1.4 (−19.3, 16.5)</td>
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<td>Financial difficulties</td>
<td>−6.8 (3.9)</td>
<td>0.6 (6.3)</td>
<td>−7.4 (−21.8, 7.0)</td>
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</tbody>
</table>

SE, standard error; CI, confidence interval.

pegcetacoplan group showed an improved mean score in the global health status/QoL and all functional scales of the EORTC QLQ-C30, while the ECU group showed a mean decrease from baseline in the global health status/QoL and role functioning scale score (positive values indicating better functioning). Significant improvements in the fatigue and dyspnea scales were observed for pegcetacoplan compared with ECU (fatigue, −20.7 [−35.3, −6.2]; dyspnea, −14.6 [−29.9, 0.8]). Compared with the ECU group, most symptom parameters were improved (negative values indicating improvement) in the pegcetacoplan group at Week 16.

Although no statistical tests for noninferiority were performed on these QoL endpoints based on the trial protocol, substantial and clinically relevant improvements in QoL were consistently observed with pegcetacoplan compared with ECU at Week 16 across both LASA and EORTC QLQ-C30 scores. Disease-specific QoL tools may provide additional information on these differences.

BSH2021-PO-218
Injection-Site Reactions in the Randomized Phase 3 PEGASUS Trial of Pegcetacoplan Compared with Eculizumab for Individuals with Paroxysmal Nocturnal Hemoglobinuria

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1Medical Oncology/Hematology, University of Louisville, Louisville, KY, 2Jane Anne Nohl Division of Hematology Keck School of Medicine, University of Southern California, Los Angeles, CA, 3John Thuerer Cancer Center, Hackensack University Medical Center, Hackensack, NJ, 4Clinical Oncology Pharmacy, University of Louisville, Louisville, KY, 5Apellis Pharmaceuticals, Waltham, MA, United States

Abstract Content: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired hematological disease characterized by complement-mediated red blood cell hemolysis. Pegcetacoplan is an investigational C3 inhibitor for the treatment of PNH. The PEGASUS trial (NCT03500549; n = 80) was a phase 3, randomized, open-label, head-to-head, 16-week study of pegcetacoplan vs eculizumab (ECU) in patients receiving ECU ≥3 months and having hemoglobin (Hb)
Red Cell Disorder

Abstract Table: Table. Situational Analysis of ISRs.

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Drug type</th>
<th>Volume per site (mL)</th>
<th>Delivery</th>
<th>Frequency</th>
<th>Most frequent ISRs</th>
<th>ISR incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pegcetacoplan</td>
<td>PEGylated peptide</td>
<td>~10</td>
<td>20–40 min over 2 sites</td>
<td>Twice weekly</td>
<td>Erythema, swelling</td>
<td>37%~41%</td>
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<tr>
<td>Immunoglobulin with hyaluronidase</td>
<td>Immuno-globin</td>
<td>≤600</td>
<td>~1–2 mL/min over 2 sites</td>
<td>Monthly</td>
<td>Discomfort, pain</td>
<td>38–65%</td>
</tr>
<tr>
<td>Deferoxamine</td>
<td>Small molecule</td>
<td>10–20</td>
<td>Continuous pump over 8–24 hours</td>
<td>Daily</td>
<td>Pain, swelling, reddening, itching, blistering, burning</td>
<td>50%</td>
</tr>
<tr>
<td>Daratumumab and hyaluronidase</td>
<td>Monoclonal antibody</td>
<td>15</td>
<td>Injected over 3–5 min</td>
<td>Weekly to monthly</td>
<td>Erythema, itching, swelling, bruising</td>
<td>10%</td>
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<tr>
<td>Certolizumab pegol</td>
<td>PEGylated antibody fragment</td>
<td>~1</td>
<td>Short injections at up to 2 sites</td>
<td>Monthly</td>
<td>Erythema, bruising, discolaration, pain, swelling</td>
<td>5%</td>
</tr>
<tr>
<td>Pegfilgrastim</td>
<td>PEGylated growth factor</td>
<td>0.6</td>
<td>Single injection at 1 site</td>
<td>Once per Chemotherapy cycle</td>
<td>Pain, redness</td>
<td>8%</td>
</tr>
</tbody>
</table>

ISR, injection-site reaction.

*Per prescribing information. **From review of the literature. ^From PEGASUS randomized controlled period.

levels <10.5 g/dl despite ECU treatment. Pegcetacoplan is self-administered via a 20-ml subcutaneous infusion, which may lead to injection-site reactions (ISRs). ISR safety outcomes from the PEGASUS trial are reported and compared to ISR rates from similarly administered treatments from published literature.

PEGASUS trial participants received twice-weekly subcutaneous infusions of 1080 mg pegcetacoplan plus their current ECU dose in an initial 4-week run-in period, followed by a 16-week 1:1 randomized controlled period, where participants received pegcetacoplan or ECU intravenous monotherapy. The primary endpoint was the mean change from baseline in Hb levels at Week 16. Safety was a secondary endpoint and included monitoring incidence of ISR, adverse events (AE), and treatment-emergent AEs (TEAEs). To evaluate pegcetacoplan-associated ISRs in the context of similar treatments, a situation analysis was performed to identify therapies comparable to pegcetacoplan. Inclusion criteria were subcutaneously administered drugs with similar injection volumes (>10 mL) or PEGylation (with ≥0.5-mL injections). ISR rates and management strategies reported with identified drugs were evaluated from the prescribing information and published literature.

Patients were randomized to receive either pegcetacolan (n = 41) or ECU (n = 39). TEAEs were reported in 69 participants (86.3%) during the run-in period and in 36 and 34 participants (87.8% and 87.2%) in the pegcetacolan and ECU arms, respectively, during the randomized controlled period. Most ISRs occurred during treatment initiation, as 58% of pegcetacolan patients experienced ISRs during the initial run-in period compared to 37% in the randomized controlled period. 2.6% of pegcetacolan patients experienced ISR. No ISR TEAEs were serious, severe, or led to study drug discontinuation.

Five drugs with comparable delivery to pegcetacolan were identified and evaluated for ISR data: immunoglobulin with hyaluronidase, deferoxamine, daratumumab and hyaluronidase, certolizumab pegol, and pegfilgrastim (see Table). Reported ISR rates varied between evaluated drugs from 5–65% of patients but were generally mild, resolved quickly, and decreased following the initial treatment. Prevention or management strategies for ISRs included ice packs, injection-site rotation, and empowering patients to gain comfort in self-administration through training and other initiatives.

PEGASUS trial ISRs observed with pegcetacolan treatment were greater in the initial treatment period and reduced after 4 weeks, suggesting ISRs decreased over time, as the patients became more comfortable with self-injection. ISRs were often mild or manageable and pegcetacolan patients on average reported higher quality of life than ECU treated patients, indicating these events are likely not a barrier to treatment. Comparable trends for reported ISRs have been observed with drugs delivered similarly to pegcetacolan; management strategies for ISRs with these drugs may potentially be useful for reactions observed with pegcetacolan.


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British Journal of Haematology, 2021, 193, (Suppl. 1), 77–232
Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hematopoietic stem cell disease characterized by uncontrolled complement activation on the surface of PNH blood cells, which can lead to hemolytic anemia. Aplastic anemia is a closely related rare bone marrow disorder and commonly treated with immunosuppressive therapy (IST). Previous research has shown that IST is effective when used concomitantly with eculizumab, regardless of the sequence of treatment initiation; however, there is less evidence in patients with PNH who may require concomitant ravulizumab and IST.

The efficacy and safety of concomitant ravulizumab and IST was assessed in patients with PNH who received ravulizumab up to 52 weeks and those who switched to ravulizumab following the 26 weeks of treatment with eculizumab during the primary evaluation period; transfusion requirements were also assessed.

Patient data from Study 301 (NCT02946463) were stratified by concomitant IST use during the primary evaluation period and extension period of this phase 3, multicenter, randomized, active-controlled, open-label, multicenter study. There was a 26-week primary evaluation period in which patients ≥18 years old with a diagnosis of PNH received either ravulizumab or eculizumab, followed by an extension, in which all patients received ravulizumab. Efficacy data were collected at the end of the primary evaluation period (through week 26) and through week 52 of the extension period. Data from week 52 were compared with week 26 data to assess treatment response. Safety variables were also assessed.

In the 26-week primary evaluation period, 246 patients received either ravulizumab or eculizumab, and 243 of these patients then received ravulizumab during the extension period, of which, 28 received concomitant IST. For lactate dehydrogenase (LDH) normalization (LDH levels ≤ 1x upper limit of normal; ULN), 50.0% of patients on IST maintained the treatment response from week 26 to week 52 vs 75.5% of patients without IST. Patients on IST had a numerically lower mean change in LDH levels compared with patients without IST at week 26, compared with baseline. A total of 75.0% of patients taking IST maintained transfusion avoidance through 52 weeks vs 89.9% of patients without IST; this may be related to a coexisting condition such as bone marrow disease in those who required IST. A similar proportion of patients on IST (88.9%) and without IST (87.6%) maintained stabilized hemoglobin levels through week 52 (avoidance of >2 g/dL decrease in hemoglobin levels from baseline in the absence of transfusion). Furthermore, numerically higher proportion of patients without concomitant IST achieved Hgb stabilization vs patients with concomitant IST.

Patients treated with IST received, on average, more transfusions than patients without IST. In the non-IST and concomitant IST groups, the number of pRBC/WBT and units of pRBC transfused decreased after initiation of a C5 inhibitor. This was more prominent in patients without concomitant IST vs patients with concomitant IST. Safety results were similar between both subgroups.

Despite a limited number of patients with available data for evaluating the effects of IST, ravulizumab was effective and well tolerated in patients with PNH irrespective if IST use over 52 weeks of treatment. Patients receiving concomitant IST and C5 inhibitor therapy continue to need more transfusions, which may be due to underlying bone marrow disease.


Red Cell Disorder

BSH2021-PO-220

Inconsistent Complement Inhibition In Patients With Paroxysmal Nocturnal Haemoglobinuria (PNH) On Eculizumab - 5 Year Experience From The National PNH Service Leeds

Rachael Jones1,2, Petra Muus1, Talha Munir1, Alexandra Pike1, Louise Arnold1, Jeannifer Gachev1, Brioni Forrest1, Peter Hillmen1, Morag Griffin1

1PNH Service, Department of Haematology, St James University Hospital, Leeds, United Kingdom

Abstract Content: Paroxysmal Nocturnal Haemoglobinuria (PNH) is a rare acquired disorder characterised by intravascular haemolysis and thrombosis. Patients with symptomatic PNH are commenced on the complement inhibitor eculizumab (600 mg weekly for 5 weeks then 900 mg 2 weekly). This monoclonal antibody targets C5 in the complement cascade, halting terminal complement activation thus inhibiting intravascular haemolysis. In some patients intravascular haemolysis is not adequately controlled. Patient symptoms, transfusion requirements and raised Lactate dehydrogenase (LDH) levels are indicators for suboptimal control of PNH and review of eculizumab dosing. The 50% haemolytic complement (CH50) test assesses capability of serum complement components of the classical pathway to lyse sheep red blood cells pre-coated with rabbit anti-sheep red blood cell antibody. Patients with complement inhibited PNH should demonstrate absent lysis. We tested if incomplete complete blockade as determined by CH50 activity would be better to confirm underdosing than LDH value.

The National PNH Service reviewed patients on eculizumab who underwent CH50 assay between January 2015 and March 2020. Serum samples were obtained 24 hours prior to patients’ eculizumab infusions for CH50 assay; LDH values were routinely collected. Complete complement blockade was defined as <10% CH50 activity; intravascular haemolysis was indicated by LDH value >1.5x upper limit of normal (ULN). Confidence intervals were set at 95% and significance set at P < 0.05.

In the study period, 327 tests (median 2, range 1–8) were carried out in 146 patients (median age 54 years, range 16–89; 74 female). 81% (265) were successful; 19% (62) were unsuccessful due to processing errors. Of the successful tests, 74% (197 in 127 patients) indicated complete complement blockade and 26% (68 in 38 patients) indicated incomplete blockade. Of the patients with incomplete blockade, 68% (26) demonstrated complete blockade on repeat testing and 32% (12) had their eculizumab dose increased. Repeat testing was carried out in 10/12 patients post dose increase; 8 indicated complete blockade; 2 patients were incompletely blocked and received a further dose increase. Further testing indicated complete blockade in 1 patient; 1 required a third dose increase due to incomplete blockade and transfusion requirement.

Corresponding LDH values were analysed; median LDH for the complete blockade group was 1.16xULN (range 0.54–2.16) and 1.28xULN (range 0.76–2.38) for the incomplete blockade group. LDH values were not significantly higher in the incomplete blockade group compared to the complete blockade group, P = 0.08. There was no significant difference in LDH values pre- and post-dose increase, P = 0.38. Correlation coefficient shows that CH50 activity was positively correlated with LDH value, r(123)=0.18, P = 0.04.
We report the effective utilisation of CH50 analysis where there is clinical concern of suboptimal control of PNH. All patients demonstrating haemolytic activity on CH50 assays indicated subsequent complement blockade following increase of eculizumab dose. A positive correlation between CH50 activity and LDH values was shown however this is not sufficient to guide clinical decisions. LDH values of the incomplete blockade group were not significantly higher than those with complete blockade, suggesting the use of LDH values as an assessment of complement inhibition in patients is not sufficient to guide eculizumab dose increases.


BSH2021-PO-221
The use of hydroxycarbamide in sickle cell patients across the South Thames Sickle and Thalassaemia Network
Kathryn McVinnie1,*, Sara Stuart-Smith1
1Haematology, Kings College Hospital, London, United Kingdom

Abstract Content: Hydroxycarbamide (HU) is the only currently licensed medication for the treatment of sickle cell disease patients in the UK. Other medication options such as L-glutamine, Voxelotor and Crizanlizumab are licensed in USA. The South Thames Sickle and Thalassaemia Network (STSTN) represents almost a third of patients with homozygous SS sickle cell disease (HbSS) and sickle cell beta-zero thalassaemia heterozygotes (HbSβthal) in England. We annually audit our use of HU in patients with sickle cell disease across our network. Here we present the data regarding HU use between 2017 and 2020.

The aim of our audit was to quantify HU use across different sites and determine how this has changed over time, particularly following the 2018 British Society of Haematology (BSH) guidelines1. We also consider possible strategies to increase HU uptake in eligible patients.

Between 2017 and 2020, annual email questionnaires were sent out to lead haemoglobinopathy clinicians in the network. Data describing each unit’s cohort was recorded, and the proportion of eligible patients was calculated. Patients were considered eligible for HU treatment if they had HbSS or HbSβthal but were not on current transfusion programmes. Some centres also had patients with genotypes other than HbSS or HbSβthal who were on HU. There was also a small number who were on both transfusion and HU. The full findings are outlined in the table.

In conclusion, there is wide variation in HU use across our network, suggesting some inequity of provision. Overall, the median percentage of eligible patients on HU has increased over the audited years. This may reflect the 2018 BSH Guidelines1, which promoted consideration of HU in HbSS or HbSβthal patients in all those above 9 months of age. There is no specified target for HU uptake in the 2018 guideline, which may explain why individual unit’s targets are varied, and why many units do not have a target.

There are limitations to the data collected. It does not assess compliance to HU, nor prescribing practice in terms of maximal tolerated dose or minimum effective dose. There are patients who attend more than one hospital so might have been counted twice, and it does not provide a clear assessment of the use of HU in other genotypes.

We propose that the availability of improved educational resources for patients would encourage shared decision-making between patients and clinicians and help increase HU uptake. We share the Kings College Hospital HU decision-making tool as an option to help patients access the information needed to make an informed choice. This has been in use at King’s College Hospital since 2018, and was extensively revised following input by patients at King’s College Hospital Sickle Cell Disease Patient Support Group. The tool was also recently updated in the light of the current audit results. It will be made available to teams working across the STSTN as an open-access resource on STSTN website for staff, service users and their families/carers. We hope that this will enable clear informed discussions and facilitate wider uptake of HU.

Acknowledgements: We thank staff across all trusts in the STSTN for collating and sharing their data; and the King’s Adult Sickle Cell Beta-Zero Thalassaemia Thal Network – John Wiley & Sons Ltd

Abstract Table:

<table>
<thead>
<tr>
<th>Hospital code</th>
<th>No of patients with HbSS and HbSβthal, 2019</th>
<th>Adults or children?</th>
<th>No on HU, 2019</th>
<th>% on HU 2017</th>
<th>% on HU 2018</th>
<th>% on HU 2019</th>
<th>No. of HbSS/ HbSβthal on transfusion</th>
<th>Target % of HbSS/ HbSβthal on HU</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>Adults</td>
<td>189</td>
<td>40</td>
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<td>50</td>
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<td>n/a</td>
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Median % 30 39 43

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British Journal of Haematology, 2021, 193, (Suppl. 1), 77–232
Support Group for their contributions and insights into the joint decision-making tool.

References


Disclosure of Interest: None Declared

BSSH2021-PO-223
Methaemoglobinemia and G6PD in a patient for major surgery: Diagnostic dilemma & therapeutic enigma
Arum V. J*, Aboobacker Rafi, Deepak Charles, Susheela Innah

Abstract Content: The aim was management of a patient with two rare mutations.

27-year old female presented with history of swelling on the right side of the neck for 2 years with recurrent pain which made her approach our hospital for surgery. She was referred to haematology for fitness as the anaesthetist detected a saturation gap. A detailed evaluation revealed a history of dark brown coloured blood on cuts, giddiness and easy fatigability. On examination, she had cyanosis in the oral cavity and tongue. Considering all the positive finding including saturation gap, a decision was taken to evaluate for methaemoglobinemia.

Radiological evaluation confirmed the diagnosis of a branchial cyst. Workup revealed Methaemoglobin levels of 68.47% (<2%) and NADH cytochrome B5 reductase 10.82(30-40 IUg/Hb). Genetic analysis revealed a novel mutation (R192C) in CYB5R3 gene (Arg192Cys) which is associated with an autosomal recessive congenital methaemoglobinemia type 1.

Vitamin C and Niacin were started & samples were sent to analyse for G6PD deficiency as the plan was to start methylene-blue during surgery. The G6PD genetic study was suggestive of the G6PD Kerala-Kalyan pathogenic heterozygous variant (949 G→A; 24.5%) which deferred the use of methylene-blue.

A multidisciplinary team decided to avoid methylene blue & dehydration, along with monitoring for acidosis, hypoxia, sensorium & renal function intra-operatively & plan for hyperbaric oxygen therapy and exchange transfusion, if needed.

She was reassessed after 1 month on being Vitamin-C and Niacin with a pulse-oximetry evaluation which showed a drastic improvement. She was prehydrated. Anaesthetic agents which could induce haemolysis were avoided. Propofol & atracurium were used for induction & muscle relaxation respectively. Maintenance of anaesthesia was achieved using oxygen, air, sevoflurane with a target saturation of 93%. The surgery and post-operative period were uneventful. She was discharged on postoperative day 4 with the lab parameters within an acceptable range.

Even though the combined deficiency is rare, care should be taken to evaluate for G6PD deficiency in methaemoglobinemia, before initiating methylene blue as it may lead to life-threatening haemolysis. A multidisciplinary evaluation and management are necessary to avoid adverse outcome and thereby improve patient satisfaction

Abstract Table:

<table>
<thead>
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<td>RS</td>
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<td>Soft, Non-tender</td>
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<td>NoFND, WNL</td>
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<td>84% in RA</td>
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<td>ABG PO2</td>
<td>98</td>
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Disclosure of Interest: None Declared

BSSH2021-PO-223
Transfusion requirements in adult patients with paroxysmal nocturnal hemoglobinuria with or without a history of bone marrow disorder receiving ravulizumab and eculizumab: results from a phase 3 non-inferiority study extension A Risitano¹, T Munir²-5, J Ho Jang⁶, G-W Lee⁷, W Wanachiwanawin⁸, H Schrezenmeier⁶,7,8, Y Yonemura⁹, R Pavan¹⁰, J Wang¹⁰, A Kulagin¹¹, A Kulasekararaj¹²,¹³, F Sicre de Fontbrune¹⁴, A Roth¹⁵

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Abstract Content: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare and life-threatening hematologic disorder leading to hemolytic anemia, which can occur concomitantly with bone marrow disorders (BMD), such as aplastic anemia (AA) and myelodysplastic syndrome (MDS). Accordingly, patients with PNH often require red blood cell (RBC) transfusions to treat anemia due to hemolysis or bone marrow failure. The efficacy of ravulizumab in patients with PNH with an underlying pathologic of AA or MDS, and the impact of ravulizumab on transfusion burden as measured by number of transfusions and total packed RBC (pRBC) units transfused over a 52-week period were assessed.

This phase 3 multicenter, randomized, active-controlled, open-label study (NCT02946463) enrolled complement-inhibitor-naïve patients with PNH. Patients were aged ≥ 18 years with a confirmed diagnosis of PNH by flow cytometry and lactate dehydrogenase (LDH) level ≥ 1.5x the upper limit of normal (ULN; 246 U/L). Patients received either ravulizumab or eculizumab for 26 weeks, after which all patients received ravulizumab from weeks 27 to 52. Efficacy outcomes included the proportion of patients achieving transfusion avoidance (TA), number of pRBC units transfused and the number of pRBC or whole blood transfusions (WBT) received from baseline to 26 and 52 weeks of treatment.

Of the 246 patients included in the study, 79 had history of AA (32.1%) and 15 (5.3%) had history of MDS. Baseline characteristics were comparable between treatment groups. TA was maintained through 52 weeks in 87.1–91.3% of patients with AA. All patients (n = 3; 100%) with a history of MDS who achieved TA in weeks 0 to 26 maintained TA in weeks 27 to 52. Specifically, 75.6% (n = 31) of ravulizumab-ravulizumab patients with history of AA avoided transfusions from baseline to 26 weeks and 78.0% (n = 32) avoided transfusions from week 27 to 52. In the eculizumab-ravulizumab...
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arm, 60.5% (n = 23) of patients with history of AA avoided transfusion in both treatment periods. Additionally, 42.9% (n = 3) of patients with PNH and history of MDS avoided transfusion from baseline to 26 weeks and 57.1% (n = 4) avoided transfusion from week 27 to 52. In the eculizumab-ravulizumab arm, no patients with PNH and history of MDS avoided transfusion from baseline to 26 weeks and 16.7% (n = 1) avoided transfusion from week 27 to 52. Ravulizumab-treated patients with PNH and history of AA or MDS in both treatment periods had numerically fewer transfusions (AA, 30; MDS, 5) and units of pRBC/WBT transfused (mean units: AA, 1.2; MDS, 0.7), per patient, compared with patients who switched from eculizumab to ravulizumab from week 26 to 52 (transfusions: AA, 66; MDS, 17; mean units: AA, 2.7; MDS, 4.2). However, the exploratory nature of the analysis and the smaller number of patients with MDS limits interpretation of the data.

This analysis demonstrates that majority of ravulizumab-treated patients with PNH and a history of AA avoided the need for transfusion. Patients who avoided transfusion during the 26 weeks of the study, maintained their response in the extension period. Patients treated with ravulizumab for the 52-week period had numerically fewer transfusions and units of pRBC/WBT transfused compared with patients who received eculizumab followed by ravulizumab. This confirms that the complete and sustained inhibition of free C5 over time with ravulizumab may result in reduced transfusion needs in patients with PNH regardless of a history of BMD.


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A delayed diagnosis of Blue rubber bleb nevus syndrome: characterized by refractory iron deficient anemia

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Abstract Content: Blue rubber bleb nevus syndrome (BRBNS) is a rare congenital disease characterized by multifocal venous malformations with involvement of skin and gastrointestinal (GI) tract. Approximately 200 cases have been reported, the most frequent clinical manifestations are GI bleeding, and rare complications such as intussusception, volvulus, and intestinal infarction can also occur during the disease. Many cases are undiagnosed or misdiagnosed. Here we represent a case with delayed diagnosis of BRBNS after treatment of refractory iron deficient anemia for 12 years.

A 25-year-old female with a complaint of discontinuous pallor and fatigue for 12 years was admitted to the hospital. She received intermittent blood transfusion due to refractory anemia. Melena, hematemesis, menorrhagia or any other blood-loss events were denied. She showed a height of 145 cm and a weight of 43 kg, mild pallor was noted and two small cutaneous bluish nodules were found in limbs. A series of laboratory findings demonstrated severe microcytic hypochromic anemia (hemoglobin 49 g/L, mean corpuscular volume 70.5 fl, mean corpuscular hemoglobin 18.5 pg, mean corpuscular hemoglobin concentration 263 g/L). Serum iron was 1.76 µmol/L and total iron binding capacity was 94.25 µmol/L. Both bone marrow smear and biopsy revealed reduction of iron staining. Although fecal occult blood test (FOBT) was negative for three times, colonoscopy indicated a sessile polyp measuring approximately 1.8*1.8 cm located in ascending colon about 60 cm from the anus, which was rough and bluish. At a distance of 30 cm from the edge of the anus, the sigmoid colon was hyperemic and congested with mucosal erosions and ulcers, the rectum showed blue mucosa with multiple site erosions located at the 10 cm from the anus. Capsule endoscopy showed the small intestine mucosa was blue and the blood vessels were large and tortuous. Hence, she was diagnosed as BRBNS.

To improve the level of anemia, we administered 4 units of packed red blood cells transfusion and intravenous infusion of 200 mg iron sucrose three times a week regularly. What is expected, we observed a significant increase of hemoglobin. The levels of hemoglobin rise from 56 g/L to 89 g/L in two weeks. To obtain long-term curation, she received a sigmoid-colecotomy to remove the gastrointestinal lesions. Multiple purple lesions of sigmoid colon and rectum were showed by the using of laparoscope, and hemangioma was identified by histologic features. All the data were consistent with the diagnosis of BRBNS. The hemoglobin was maintained at the normal level after surgery. The underlying disease was confirmed by GI endoscopy and capsule endoscopy. To obtain long-term curation, this patient received sigmoid-colecotomy to remove the gastrointestinal lesions, and the level of hemoglobin maintained normal after surgery.

BRBNS is caused by double (cis) mutations in the TEK gene (also known as TIE2). Unregulated angiogenesis is constitutively active in BRBNS due to somatic mutations. Sirolimus is an angiogenesis inhibitor and was recently reported as a successful treatment option for BRBNS, however, the dose and duration remained uncertain. In conclusion, refractory IDA and chronic occult bleeding from GI tract could happen due to BRBNS. Clinicians should keep in mind to detect the underlying diseases from GI tract by endoscopy. Precision diagnosis and appropriate intervention could booster to upgrade the quality of life for patients.

Disclosure of Interest: None Declared

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Epidemiological characters of adult egyptian sickle cell anemia patients: a single center experience

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Abstract Content: Sickle cell anemia (SCA) is a chronic problem with growing with ages consequences. It starts with birth & continues to add complication throughout the patient’s life. During his childhood the patient develop a psychological bond with his treating team which makes it traumatic to him when he is transferred to adult hematolgy service which might lead to loss of interest in receiving treatment and skipping follow up visits which eventually
leads to increased complications and either stopping treatment or developing treatment related adverse events.

The Aim of this study is to outline the Demographic characters of Egyptian SCA patients on regular follow up at an adult academic hematology center in Egypt and the characters of their disease.

This is a descriptive study regarding Adult (above the age of 18) SCA patients on follow up with the clinical hematology unit Oncology center Mansoura University, Dakahlia, Egypt who had recorded follow up visits on our System in the period between 2005 and 2021 regarding their age at diagnosis, sex, baseline criteria, presence of crisis or not method of diagnosis and their follow up regimen.

By reviewing the data on our system over the period of 1-1-2005 and 1-1-2021 we found that we have 39 SCD anemia patients with 19 males (48.7%) and 20 females (51.3%). The average age at referral to our center was 24 years with the range of 14.6-37.4 years. The median follow up of our patients was 114.8 months (357 – 6). Out of our 35 patients twenty five (71.4 %) were referred to us from the pediatric service while the remaining ten (28.6%) were newly diagnosed at our unit. Using Hemoglobin electrophoresis twenty eight patients (71.8 %) had done this investigation which showed that 11 (39%) had sickle-thalassemia while the rest were pure SCA. Spleen was surgically removed in 7 (17.9 %), Non-visualized in 8 (20.6%) while the remaining 22 had spleen measurable by ultrasonography. 12 (30.7%) patients had HCV infection, Twenty four (61.5 %) were non transfusion dependent while the remaining 11 (28.2 %) required monthly transfusion. As regard all our 39 patients were accounted for at the time of data analysis.

Children with SCA need a more smooth transfer from their pediatric service to adult service to help them to be more adherent to the treatments available for them to ensure longer and more stable remissions and wait strategy with regular tonics or the major used line corticosteroids and if the patient fails this immunosuppressive drugs might be added or replace corticosteroids with the increased use of monoclonal antibodies especially rituximab and splenectomy still remains an option for resistant cases with certain types of chemotherapeutic agents. The burden of such medications and their associated toxicities affect the patient adherence to therapy itself and follow up dates which requires meticulous and tailored treatment choices for each patient to decrease disease complications and treatment related adverse events and ensure the patient compliance.

Aims: The Aim of this study is to outline the Demographic characters of Egyptian AIHA patients on regular follow up at an adult academic hematology center in Egypt and the characters of their disease.

Methods: This is a descriptive study regarding Adult (above the age of 18) AIHA patients on follow up with the clinical hematology unit Oncology center Mansoura University, Dakahlia, Egypt who had recorded follow up visits on our System in the period between 2005 and 2021 regarding their age at diagnosis, sex, baseline criteria, presence of crisis or not method of diagnosis and their follow up regimen.

Results: By reviewing the data on our system over the period of 1-1-2005 and 1-1-2021 we found that we have 228 AIHA anemia patients with 25 males (10.8%) and 203 females (89.2%). The average age at diagnosis at our center was 45 years with the range of 16 – 72 years, The median follow up of our patients was 61 months (180 – 6). All patients with follow up under 6 months were excluded from final analysis. 77.9% of our patients were primary AIHA while the remaining 22.1% were secondary from which 41.6% were secondary to Viral hepatitis, 16.6% to both of Myelodysplastic syndrome and Systemic lupus erythematosi and 8.3% to pregnancy, rheumatoid arthritis and Antiphospholipid syndrome. The average hemoglobin at diagnosis was 7 gm/dl with the range (3 – 12), average White blood cell count was 8 x10^3/ ml (3 – 67) and platelets average was 205 x10^3/ ml (5 - 387). 15.2% of our patients had immune thrombocytopenia and were considered to be having Evan’s syndrome while the other 84.8 had normal platelets count. As regard direct coomb’s test 91.5 % were positive while the remaining 8.5 % were negative while the indirect coomb’s test was test was positive in 71.2 % and negative in 28.2 %. 75% of our patients required packed red blood cells transfusion during their course of the disease while the rest were not transfused.

Conclusion: Patients with AIHA need more care and psychological support with increasing the awareness regarding their disease characters and complications with an increased need for further progress in the treatments available for them to ensure longer and more stable remissions.

Disclosure of Interest: None Declared

BSH2021-PO-226

EPIDEMIOLOGICAL CHARACTERS OF ADULT EGYPTIAN Auto Immune Haemolytic ANEMIA PATIENTS: A SINGLE CENTER EXPERIENCE

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Abstract: Background: Auto immune Haemolytic anemia (AIHA) is a widely used title for a variety of anemia types which are mostly diagnosed by exclusion and comprises a lot of symptoms and signs with a myriad of complications. No age is immune with majority being middle-aged with a significant female predominance over male patients. It could be primary or secondary to many factors but mostly other immune disorders. The treatment may include a watch and wait strategy with regular tonics or the major used line corticosteroids and if the patient fails this immunosuppressive drugs might be added or replace corticosteroids with the increased use of monoclonal antibodies especially rituximab and splenectomy still remains an option for resistant cases with certain types of chemotherapeutic agents. The burden of such medications and their associated toxicities affect the patient adherence to therapy itself and follow up dates which requires meticulous and tailored treatment choices for each patient to decrease disease complications and treatment related adverse events and ensure the patient compliance.

Aims: The Aim of this study is to outline the Demographic characters of Egyptian AIHA patients on regular follow up at an adult academic hematology center in Egypt and the characters of their disease.

Methods: This is a descriptive study regarding Adult (above the age of 18) AIHA patients on follow up with the clinical hematology unit Oncology center Mansoura University, Dakahlia, Egypt who had recorded follow up visits on our System in the period between 2005 and 2021 regarding their age at diagnosis, sex, baseline criteria, presence of crisis or not method of diagnosis and their follow up regimen.

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Conclusion: Patients with AIHA need more care and psychological support with increasing the awareness regarding their disease characters and complications with an increased need for further progress in the treatments available for them to ensure longer and more stable remissions.

Disclosure of Interest: None Declared

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Thalassemia awareness among Iraqi people in 2018

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Abstract: Thalassemia is an autosomal recessive disease which is common in Iraq with prevalence of 35.7 per 100000. It is the most common type of hereditary anemia registered in Iraq in 16 thalassemia centers in 2015. It’s a life threatening condition with many complications which if not managed could cause death in early age.

This study aimed to assess the awareness of Iraqi people about thalassemia regarding disease transmission and prevention and to find their source of information about the disease, as developing good awareness is the first and the most advantageous road to establish a successful prevention program.

This study involved 418 participants who were from medical and non-medical field, those in medical field were considered as control group for comparison. It was conducted for one month duration as an online survey using a self-structured questionnaire which was tested for validity, unidimensionality and reliability in a pilot study of 40 participants. Each participant who had heard about the disease was given a score (0-5) based on their knowledge.

All participants were informed about the goal of the survey and they gave their consent.

The data was analyzed using Social Sciences program (SPSS) version 24.
69.1% had heard about the disease previously, those had a mean score of 3.47 out of 5.

87.6% knew that consanguineous marriage increase the risk of the disease and 89.4% claimed that it is a noncommunicable disease. The lowest rate of knowledge was about the preventability of the disease with only 46.2% confirmed that the disease can be prevented.

The family history of thalassemia was more common among non-medical field but this predominance was non-significant.

No significant correlation was found between the score with the age, the family history and gender.

The difference in knowledge among medical and non-medical was statistically significant.

People awareness about thalassemia was relatively good, the highest awareness was for the contiguity of the disease and the lowest awareness was for the preventability. A Control strategy should be directed to elevate the awareness level about Thalassemia in the community.

Disclosure of Interest: None Declared
Thrombosis and Haemostasis

BSH2021-PO-228
Implications of the Covid-19 Pandemic for Patients on Long-term Anticoagulants: A DOAC Switching Program in a Teaching Hospital Based Anticoagulant Service

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Abstract Content: The COVID-19 pandemic poses a challenge of ensuring safe monitoring of patients on Vitamin K Antagonists (VKAs). In March 2020, national guidance was issued on safe switching of VKAs to Direct Oral Anticoagulants (DOACs), in order to minimise healthcare interaction and protect vulnerable patients from COVID-19 by reducing monitoring requirements. Leeds Teaching Hospitals (LTH) achieved this by adapting an established clinic within the anticoagulation service with over 6000 patients on VKAs.

We describe the response of our service, the patient group switched, and the experiences of patients and staff involved.

Existing face-to-face “DOAC clinics” were changed to almost exclusively telephone clinics. A screening pro forma set up on DAWN AC Software was used to determine patient eligibility. Selected patients were provided with written information. Baseline blood tests were performed at INR clinics prior to the switching appointment. Appointments with a specialist provided clinical assessment for suitability and enabled patients to safely discuss their options regarding anticoagulant therapy and access their chosen medication via their GP. If required, follow-up calls were scheduled at 2 weeks post-switch.

Primary care pharmacists, GPs and ward-based teams provided similar services, offering some additional capacity. A small proportion of face-to-face appointments were also offered when necessary.

In March 2020, our service had 6153 patients on VKAs of which 4601 had licensed indications for DOAC therapy. Mean time in therapeutic range (TTR) for eligible patients was 80%, averaging 14 monitoring appointments each in the preceding year. 12 weeks later, 791 patients had received a switching consultation of whom 779 had switched from a VKA to a DOAC. Mean TTR on VKA therapy for this group was 75%, with an average of 16 appointments each in the previous year.

Analysis of 200 patients switched by our clinic identified that 77 changed to apixaban, 86 to edoxaban, and 37 to rivaroxaban. The mean age was 79 and 35% previously required home visits for INR monitoring. 25% of patients received a follow-up phone call 2 weeks after switching. 27% reported adverse effects from the new treatment, mostly minor. After 6 months, 93% remained on a DOAC. 9 patients changed to a different DOAC, 8 reverted to a VKA and 4 had anticoagulation stopped indefinitely.

In this small cohort, 5.5% of patients died within 6 months of switching compared with 1% in a randomly selected group of patients who continued on a VKA. Further work is on-going to assess the significance of these findings.

20 patients were surveyed on their experience of the clinic. All found the process straightforward and felt switching instructions were clear. Most obtained their new medication easily, although 2 reported having to prompt their GP. 3 patients felt they would have benefitted from a follow-up call but did not receive one.

The staff survey showed full agreement that the Covid pandemic justified rapid expansion of the DOAC switching program and overall the staff experience was positive.

This service model was largely successful, resulting in safe and effective uptake of guidelines. Learning points will be embedded going forward. The apparent difference in death rate in the switching cohort requires further investigation. The service design would be easy to emulate by other hospital-based anticoagulant services and could benefit patients throughout the COVID-19 pandemic and beyond.

Disclosure of Interest: None Declared

BSH2021-PO-229
Chronic oral coagulation and COVID-19; Does it make any difference?

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Abstract Content: Hypothesis: We hypothesize that COVID-19 patients on chronic oral anticoagulants (OAC) for other co-morbidities have reduction in in-hospital complications by decreasing the overall clot burden compared to patients, not on chronic oral anticoagulants (N-OAC).

Methods: A single center retrospective study was performed to determine the impact of OAC therapy on in-hospital COVID-19 related complications. The outcomes measured included; all-cause mortality, upgrade to intensive care unit (ICU), need for invasive mechanical ventilation (IMV), and acute kidney injury (AKI) necessitating dialysis by decreasing the overall clot burden. Independent t-test and binary logistic regression analysis were performed to calculate mean differences and adjusted odds ratios (aOR) with its 95% confidence interval (CI), respectively. Odds ratios were also adjusted for co-morbidities (hypertension, Chronic kidney disease, Obstructive pulmonary disease, diabetes mellitus) and whether patient received steroids or tocilizumab while hospitalized.

Results: A total of 193 COVID-19 patients were included, 43 in the chronic OAC group* and 150 in the N-OAC group. The mean age, baseline comorbidities and other medications used during hospitalization were similar in both groups. The mean age, baseline comorbidities and other medications used during hospitalization were similar in both groups. The mean age, baseline comorbidities and other medications used during hospitalization were similar in both groups. Unadjusted odds were controlled for varying proportions of baseline characteristics. The adjusted odds for in-hospital mortality (aOR 2.39, 95% CI 0.82-6.91, P = 0.10), upgrade to ICU (aOR 1.02, 95% CI 0.36-2.84, P = 0.96), need for IMV (aOR 0.93, 95% CI 0.32-2.72, P = 0.89) and AKI (aOR 0.46 95% CI 0.07-2.70, P = 0.38) were not significant between patients on OAC and N-OAC (table 1).

There was also no difference in most of the inflammatory biomarkers between the two groups except D-dimers level (table 2). The mean for lactate dehydrogenase (LDH) (483 vs 430 U/L, P = 0.41), serum ferritin (1397 vs 1219 NG/ML, P = 0.61) and C-reactive protein (CRP) (115 vs 133 MG/L, P = 0.24) remained identical, while the D-dimers levels (745 vs 2812 NG/ML, p value: 0.01) were significantly higher in the N-OAC group.

Conclusions: While there were few patients in chronic OAC group and our results are not significant, chronic OAC in patients with COVID-19 does not appear to reduce complications. Similarly, there was no statistically significant difference in markers of chronic inflammation (LDH, CRP, Ferritin) except d-dimer levels between two groups. Future research is needed to ascertain the role of chronic OAC in COVID-19 hospitalizations.

*: Vitamin K antagonists 15/43, Direct oral anticoagulants 28/43)
Abstract Table:

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Disclosure of Interest: None Declared

**BSH2021-PO-230**

**Reversal of anticoagulation with PCC – every minute counts**

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Abstract Content: The Serious Hazards of Transfusion (SHOT) haemovigilance scheme collects and analyses anonymised information relating to errors of blood transfusion reported in the United Kingdom (UK). Prothrombin Complex Concentrate (PCC) is a human blood product used to reverse the effect of warfarin and direct oral anticoagulants in patients with life, limb or sight-threatening haemorrhage. PCC should be given within an hour of the decision being made, particularly in intracranial haemorrhage (ICH). Delays or omissions in administration can lead to serious morbidity or death. PCC is contraindicated in some conditions such as myocardial infarction and unstable angina. SHOT has collected data on errors relating to PCC since 2014 to identify areas for improving patient safety.

Incidents reported to SHOT 2014 to 2019 were reviewed. Search terms were ‘PCC’, ‘warfarin’, ‘Octaplex’ and ‘Beriplex’. The identified reports were examined for trends including reason for administration, type of error, reasons for delays in administration and mortality.

Fifty reports were identified, the majority related to PCC indicated to reverse warfarin (31/50, 62.0%) in patients aged 49 to 94 (mean 79) years. Reversal was mainly indicated for urgent surgery (17/50, 34.0%), haemorrhage (16/50, 32.0%) and ICH (11/50, 22.0%). Within the ICH cohort, where administration of PCC within 60 minutes is critical, 7/11 (63.6%) reports related to delays in administration. PCC requests most often originated from emergency departments (15/50, 30.0%), anaesthesia (5/50, 10.0%) and general surgery (5/50, 10.0%). Most errors originated in the clinical area (41/50, 82.0%). Errors resulted in delays to administration of PCC in 20/50 cases, 40.0%; inappropriate order and/or prescription of PCC in 12/50 (24.0%), and order/prescription of the wrong component in 7/50 (14.0%). Reasons for delays in administration included: insufficient laboratory stock, errors in prescription, errors in administration, communication errors, inappropriate referral for approval, electronic ordering systems, patient transfers, delays in obtaining coagulation test results, delays in laboratory testing and in collection of products. Only 8 reports contained details on the length of delays in administration, these ranged from 1.8 to over 24 hours. In 2 cases patient deaths were reported; one directly, and one possibly, related to delays.

It is unlikely that all cases are reported; this review provides valuable learning that can be utilised to improve processes and reduce delays. Inclusion of all relevant details in reports would optimise learning. Rapid administration of PCC is critical in these elderly, vulnerable patients, particularly in ICH where delays can lead to devastating consequences. Lack of knowledge about PCC by staff treating these emergency cases and delays caused by patient transfers are avoidable. Every effort must be made to improve local systems and reduce the ‘door to needle’ time for administering PCC in these patients.

Disclosure of Interest: None Declared

**BSH2021-PO-231**

**Use of the HemosIL AcuStar ADAMTS13 functional assay as the basis for Bethesda style inhibitor detection in acquired Thrombotic Thrombocytopenic Purpura**

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Abstract Content: Acquired Thrombotic Thrombocytopenic Purpura (TTP) is a rare disorder characterised by the production of autoantibodies against the metalloprotease ADAMTS13. The severe deficiency of this metalloprotease causes von Willebrand factor to circulate in the plasma as ultra-large multimers which are able to aggregate to platelets and cause the formation of micro-thrombi. Functional assays to measure ADAMTS13 activity and inhibitors are fundamental for the diagnosis, management and prognosis of acquired TTP. The aim of this study was to investigate the possibility of replacing the current method for the detection of ADAMTS13 inhibitors (Technozym® ADAMTS13 inhibitor ELISA) with a Bethesda-style Assay (BA) based upon the measurement of ADAMTS13 residual activity by the HemosIL® AcuStar ADAMTS13 activity assay, providing a quicker technique for the detection of ADAMTS13 inhibitors and, therefore, a faster turnaround time for the diagnosis of acquired TTP. Twenty six samples from patients presenting with an ADAMTS13 activity of <10% (16 female and 10 male) were used for the measurement of ADAMTS13 inhibitor activity. Test samples were serially diluted in buffer and an equal amount of normal pooled plasma was added and incubated at 37°C for 1 hour. Samples were then measured for ADAMTS13 residual activity by the AcuStar and the Bethesda Units (BU) were calculated and compared to the ELISA. The AcuStar ADAMTS13 activity based assay showed a positive correlation ranging from 0.4-17.0 BU compared to 1-152 IU/ml for the ELISA. The relation between inhibitor titre and activity was not completely linear with factors such as the type of inhibitor (either neutralising or non-neutralising) and the immunoglobulin subgroup suggested as contributing to this. The residual activity measured by the AcuStar ADAMTS13 activity assay provided results quicker than its comparator (able to be performed by basic technical staff in approx. 2 h whilst the ELISA took approx. 3-5 h). The results suggest the HemosIL® AcuStar ADAMTS13 activity Bethesda assay to be more sensitive than the ELISA in samples with a reduced level of inhibitor and the use of pre-analytical heat-treatment (36°C for 30 min) increased the sensitivity of the assay. In conclusion, the use of a Bethesda-style assay and the measurement of ADAMTS13 residual activity by the HemosIL® AcuStar ADAMTS13 activity assay can detect neutralising autoantibodies against ADAMTS13 and can support the diagnosis and management of acquired TTP.

Disclosure of Interest: None Declared
Management of Spontaneous Intra-Cranial Haemorrhage whilst on a Direct Oral Anticoagulant is less well known than Warfarin

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Abstract Content: Side effects of anticoagulation include increased risk of bleeding and spontaneous Intra-Cranial Haemorrhage (ICH), a serious, potentially life-threatening condition. Between 2012 and 2015 NICE approved Direct Oral Anticoagulants (DOCAs) for treatment of Venous Thromboembolism (VTE) and as primary stroke prevention for patients with Atrial Fibrillation (AF)1,2. ICH management varies depending on the oral anticoagulant used, with different approaches advised for Vitamin K Antagonists, Direct Thrombin Inhibitors, and Factor Xa Inhibitors.

We reviewed adherence to local ICH management guidelines following the introduction of DOACs. All spontaneous ICH cases at Wirral University Teaching Hospital between 1st July 2018 and 30th June 2019 were audited. Aims were to establish: indications for anticoagulation; anticoagulants used; adherence to trust policy for ICH management; and clinical outcomes.

Cases of spontaneous ICH in anticoagulated patients were retrospectively identified through the local stroke database. Case notes were reviewed to assess patient demographics, anticoagulation used, management initiated, and clinical outcomes.

20 cases of spontaneous ICH in anticoagulated patients were identified within 12 months. Ages ranged from 52 to 94 years and 60% were female. 80% were anticoagulated for AF, versus 20% for VTE. Anticoagulants used were: DOACs (65%), Warfarin (30%), and Enoxaparin (5%). Review of other risk factors for ICH demonstrated: no patients were taking anti-platelet drugs; all had a normal platelet count; one patient on Warfarin had an INR >3; and 60% had an established diagnosis of hypertension. 45% obtained a CT head scan within an hour of admission, with 70% scanned within two hours.

All Warfarinised patients, except one palliated at admission, received Vitamin K and Prothrombin Complex Concentrate (PCC). In contrast, PCC was administered to 58% of patients on DOACs who were actively treated. The one patient on Dabigatran did not receive Idarucizumab. Across both groups, PCC and Vitamin K were administered within two hours of the CT scan in 60% of cases treated.

Two patients experienced VTE complications whilst anticoagulation was suspended. Mortality during admission was 83% in patients on Warfarin, and 31% of those on DOACs.

Adherence to ICH management guidelines was related to the anticoagulant used. Clinicians appeared familiar with management of ICH in patients on Warfarin: all actively treated patients on Warfarin received Vitamin K and PCC. Variability was identified in the management of patients on DOACs as only 58% received PCC, and use of a reversal agent on Dabigatran was not considered. Despite this, mortality was higher in those on Warfarin. Further work is required to educate clinicians on the management of ICH in patients on DOACs and to encourage earlier, appropriate administration of PCC, Vitamin K and Idarucizumab.

Disclosure of Interest: None Declared

Major non elective orthopaedic surgery on a severe haemophilia A patient on emicizumab (without inhibitors): a case study

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Abstract Content: A gentleman in his 60s weighing 92 kg, with severe haemophilia A without inhibitors had recently switched to two weekly emicizumab prophylaxis due to poor venous access. He had a background of reduced joint mobility affecting his ankles, knees and elbows. Unfortunately, he had a mechanical fall at home, landing on his left hip. Paramedic review at home felt a fracture was unlikely. As he was tender over his hip, the on-call haemophilia consultant advised a bleed dose of Refacto AF, aiming for a peak FVIII level of ~50 IU/dL. Despite a few days of factor replacement, the patient’s pain did not improve and so review by the Emergency department (ED) was organised. Hip X-rays revealed a Garden type IV neck of femur fracture and an orthopaedic review took place.

Specialist coagulation blood tests were requested through ED. These included bowine chromogenic FVIII (101.2 IU/dL) and an emicizumab level (45.9 µg/ml). Close liaison between the Haemophilia, Laboratory and Orthopaedic teams resulted in a total hip replacement being scheduled for the next morning. Pre-operative peak FVIII level of ~400 IU/dL was achieved (2000 IU Refacto AF®). There were no intra-operative bleeding complications. Post-operatively twice daily factor doses achieved peak FVIII levels of ~400 IU/dL. After achieving a peak of 1000 IU Refacto AF® BD. From D+3 to D+5 factor replacement was reduced (1000 IU Refacto AF® BD), aiming for peak FVIII levels of ~50 IU/dL. Mechanical but not chemical thromboprophylaxis was prescribed. On day of discharge (D+5), he was mobilising with elbow crutches without pain. No further outpatient factor was given and the patient continued with fortnightly emicizumab. There was no breakdown of bleeding.

There are currently no guidelines advising on the haemostatic management around major surgery for patients with severe haemophilia A (with and without inhibitors) on emicizumab. In particular there is no consensus on how long to sustain peak FVIII levels >100 IU/dL and when to stop factor replacement. For this patient, emicizumab alone was sufficient to support ongoing rehabilitation. This case highlights the importance of tailoring haemostatic plans according to the patient. Furthermore we may be able to safely use shorter courses of factor replacement alongside emicizumab following major orthopaedic surgery.

Disclosure of Interest: None Declared

For women with a previous venous thromboembolism, is standard dose thromboprophylaxis adequate in pregnancy?

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Abstract Content: Background: PA-VTE is associated with a high rate of morbidity, and pulmonary embolism (PE) is still one of the leading causes of maternal deaths in the developed world. Royal College of Obstetricians and Gynaecologists (RCOG) guidelines on prevention of venous thromboembolism were updated in the guideline

Disclosure of Interest: None Declared

We performed a retrospective study to evaluate the utility of these guidelines in 290 pregnancies between 2015-2019.

Methods: We retrospectively identified 290 pregnancies from our local data-base, in whom a past VTE was recorded. Of these, 190 cases had a past history of VTE. For each record, we determined the recommended strategy of thromboprophylaxis according to RCOG guidelines.

Results: Appropriate weight-related thromboprophylaxis with Dalteparin had been used in all cases. Four cases were found to have breakthrough VTEs (2.11%). Of these, one case had very poor compliance, a second case had a severe thrombotic tendency with a background of both antiphospholipid syndrome and Factor V Leiden heterozygosity. The third had a recurrence very early in her 10th pregnancy at the time of positive pregnancy test and therefore before TP was commenced. She later had postpartum thrombophlebitis despite recommended TP, although her compliance was thought to be poor. The final case had no extra risks to explain failure of the TP. Excluding the 1st and 3rd cases as these did not primarily constitute a failure of TP, the frequency of recurrence reduced to 1%.

Discussion & Conclusion: The frequency of recurrence of VTE was low, in keeping with the New Zealand study of Cox et al, who reported 1.2% recurrence rate on TP with Enoxaparin. The earliest Netherland study of van Lennep et al with Nadroparin TP had a 5.5% recurrence rate, but all cases were in ‘high risk’ women, as in our 2nd case. Although we use low molecular weight heparins interchangeably there are differences in their half-lives and other characteristics which could also impact on recurrence risk.

We conclude that for the vast majority of cases standard weight-adjusted TP is adequate prevention for PA-VTE.

Disclosure of Interest: None Declared

BSH2021-PO-235


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Abstract Content: The COVID-19 pandemic onset in March 2020 resulted in the rapid implementation of virtual clinics throughout the NHS to minimise infection transmission in hospitals. This transformation may become permanent after the pandemic, in line with the NHS Long Term Plan (2019). This envisaged the increasing use of virtual/remote (telephone and video) “Attend Anywhere” consultations to improve convenience for patients, enhance clinic capacity, and more productive use of consultant time. Despite these potential benefits, there is limited research into the safety, acceptability and suitability of virtual/remote clinics for patients in different clinical services.

We evaluated patient preferences and feasibility for the future use of virtual/remote consultations by conducting a telephone survey of patients remotely ‘attending’ thrombosis and anticoagulation clinics at a single London NHS Trust during the COVID-19 pandemic. At the end of each telephone consultation, patients were asked two questions: (1) ‘In the current climate of the COVID-19 pandemic, what would your preference be in terms of being seen in future clinics – face to face, video or telephone?’. (2) ‘Do you have access to a smartphone or computer that you could use with video consultations in the future or can you get support from a family member/friend to do this?’. Patient preferences were analysed by median age group, gender, and new/follow-up status.

A total of 51 patients [23 females (45.1%) and 28 males (54.9%)] were surveyed. Median age was 65.5 years (range 23 – 100 years). There were 16 new and 35 follow-up patients with 42 patients attending consultant-led thrombosis clinics and 9 attending nurse/pharmacist-led anticoagulant clinics. 42 patients were seen because of venous thromboembolism (VTE), 6 because of atrial fibrillation (AF), and 3 for other conditions. 45 patients (88.2%) preferred a specific type of consultation and 6 patients (11.8%) showed no preference. 33 of 45 patients (64.7%) preferred virtual/remote consultation, whereas 12 patients (23.5%) preferred face-to-face contact. Out of the 33 patients who preferred a virtual/remote consultation, 17 (33.3%) preferred only telephone, 8 (15.7%) preferred only video, and 8 (15.7%) preferred either video or telephone. These proportions were similar in females and males, aged under and over 65, and new compared to follow-up patients. 37 patients (72.5%) had access to a smartphone or computer. Median age of patients who had access was 65.5 years (range 23-91 years), and in patients who did not have access was 76.0 years (range 29-100 years).

The majority of patients preferred virtual/remote consultations for the future. Telephone consultations appeared more popular than video consultations, despite most patients having access to a smartphone or computer. The findings may be influenced by the methodology of the survey being conducted at the end of a phone consultation and during the COVID-19 pandemic. Remote/virtual thrombosis clinics seem likely to continue for many patients after the COVID pandemic. Further research is needed to identify the factors that determine individual patient preferences and the clinical implications and safety of different types of consultation.

Disclosure of Interest: None Declared

BSH2021-PO-236


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Abstract Content: Thrombotic events are a major contributor to morbidity and mortality in Covid-19 infection. This study looked at the outcomes of thrombosis, mortality and bleeding in critically unwell patients with Covid-19 when applying a local escalated thromboprophylaxis protocol based on a D-dimer cut-off value.

This study was approved by the NHS Health Research Authority (REC, 20/HR/2977) and included adult patients with positive polymerase chain reaction nasopharyngeal swab for Covid-19 who were admitted to critical care from March to April 2020 at Barking, Havering and Redbridge University Hospitals NHS Trust. Data was collected retrospectively and patients were classified in two subgroups (standard and escalated thromboprophylaxis) based on whether they received any higher than standard anticoagulation prophylaxis for at least seven days during their inpatient stay. Patient survival and negative composite outcome (deaths and combined arterial and venous thromboses) were compared (log-rank test) on days 30 and 90 from patient admission to Intensive Care Unit (ICU).

83 patients were included with an average length of stay of 41.6 days and an overall mortality of 44.5% at 90 days from admission to ICU. D-dimer values >3 mg/L were observed in 93% of the patients. The combined arterial and venous thrombosis rates were similar.
between the two sub-groups while similar numbers of significant bleeding events were also observed (Table 1). Despite a reduction by a third in the number of deaths at 30 and 90 days from ICU admission in patients receiving escalated doses of thromboprophylaxis the reported reduction was not statistically significant (p = -.14 and 0.09 respectively).

This study confirms the high incidence of thrombosis in severe Covid-19 infection reported to be 31% in retrospective studies. The crosstalk between inflammation and coagulation has been implicated in the development of a prothrombotic state in critically unwell patients and could partly explain the role of low molecular weight heparins at improving morbidity and mortality in view of their anti-inflammatory properties. The significant variability of D-dimer levels during hospitalisation and organisational challenges during the pandemic limited the application of a local thromboprophylaxis protocol based on the D-dimer. Current NICE guidance recommends considering escalation to intermediate dose of anticoagulation for patients requiring advanced respiratory support pending results from randomised clinical trials on the best anticoagulation strategy in Covid-19 infection.

Notwithstanding the limitations of this small, retrospective study these findings suggest that while D-dimer is not a useful tool of thromboprophylaxis stratification, escalated doses of prophylactic anticoagulation may lead to lower mortality in severe Covid-19 infection.

Abstract Table: Table 1. Comparison of clinical outcomes between the standard and escalated thromboprophylaxis dose.

<table>
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<th>Escalated dose (40 patients)</th>
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<tr>
<td></td>
<td>D30 [N*, (%)]</td>
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<tr>
<td>Thrombosis</td>
<td>8 (18.6)</td>
<td>7 (17.9)</td>
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<tr>
<td>Bleeding (WHO grade 3)</td>
<td>3 (7.0)</td>
<td>2 (5.1)</td>
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<tr>
<td>Death</td>
<td>20 (46.5)</td>
<td>12 (30.8)</td>
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<tr>
<td></td>
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</table>

*N*: number of patients

Disclosure of Interest: None Declared

BSH2021-PO-237

ADAMTS13 activity trends in TTP patients with COVID-19 infection

Rebecca J. Shaw1*, Jessica Kenworthy2, Ashley Lawson2, Cheng-Hock Toh1, Tina Dutt2

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Abstract Content: Thrombotic thrombocytopenic purpura is a rare but potentially fatal diagnosis caused by deficiency in von-Willebrand cleaving protease, ADAMTS13. One third of patients will relapse and 1 in 3 will die. TTP patients are at high risk of thrombosis. This study of ADAMTS13 levels in TTP patients with COVID-19 infection was performed to understand the role of ADAMTS13 in the development of thrombotic complications, the impact on COVID-19 infection and the potential role of ADAMTS13 in the development of COVID-19. This study confirms the high incidence of thrombosis in severe Covid-19 infection reported to be 31% in retrospective studies. The crosstalk between inflammation and coagulation has been implicated in the development of a prothrombotic state in critically unwell patients and could partly explain the role of low molecular weight heparins at improving morbidity and mortality in view of their anti-inflammatory properties. The significant variability of D-dimer levels during hospitalisation and organisational challenges during the pandemic limited the application of a local thromboprophylaxis protocol based on the D-dimer. Current NICE guidance recommends considering escalation to intermediate dose of anticoagulation for patients requiring advanced respiratory support pending results from randomised clinical trials on the best anticoagulation strategy in Covid-19 infection.

Notwithstanding the limitations of this small, retrospective study these findings suggest that while D-dimer is not a useful tool of thromboprophylaxis stratification, escalated doses of prophylactic anticoagulation may lead to lower mortality in severe Covid-19 infection.

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*N*: number of patients

Disclosure of Interest: None Declared

BSH2021-PO-238

Optimising COVID-19 thromboprophylaxis within the critical care unit of a large UK-based teaching hospital

Louis Gardner1*, Donna Kelly2, Katherine Smith1, Paul Nwajiugo1, Shobana Anpalakhan1, Kate Talks2, Brigit Greystoke3, Kathryn Musgrave1,4

1Northern Centre for Cancer Care, 2Department of Anaesthetics and Critical Care, 3Haematology Department, The Newcastle upon Tyne Hospitals NHS Foundation Trust, 4Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom

Abstract Content: COVID-19 is associated with increased rates of venous thromboembolism (VTE), particularly in the critically ill population. The optimum dose of thromboprophylaxis for critically ill patients is unclear. In this work, we aimed to audit the
effectiveness of dosing low molecular weight heparin thromboprophylaxis by weight and anti-Xa level in critically ill patients with COVID-19.

The Newcastle upon Tyne NHS Hospital Foundation Trust implemented a new thromboprophylaxis protocol for all patients on critical care units who were PCR positive for SARS-CoV-2. Enoxaparin thromboprophylaxis was initially dosed by patient weight, followed by an anti-Xa level measured at 3 days, with dosage adjustment if necessary, to achieve a peak level of 0.2-0.4 IU/mL. Patients without COVID-19 were given standard dose thromboprophylaxis (enoxaparin 40 mg daily). Electronic medical records of critically ill patients admitted between 1st April and 15th May 2020, were reviewed retrospectively. Statistical analysis was performed using Fisher’s exact test for categorical variables and the unpaired t test for continuous.

We identified 274 critical care patients, 34 were COVID-positive, 240 were COVID-negative. Both groups had a similar proportion of male participants and the groups did not vary in either age or weight (see Table 1). All patients eligible for thromboprophylaxis received it, and 15 (45%) of COVID-positive patients had anti-Xa levels performed and thromboprophylaxis adjusted as appropriate.

Overall, 4 (12%) COVID-positive individuals developed a VTE compared to 9 (4%) in the COVID-negative group, this difference was not significant ($P = 0.66$). All VTE events within the COVID-positive group occurred within the pulmonary vasculature ($n = 4, 12\%$), this was significantly different to the number of pulmonary thromboses in the COVID-negative group ($n = 3, 1\%$, $P < 0.05$).

Every thrombus in the COVID-positive group occurred within subsegmental pulmonary arteries. The COVID-negative group included three thrombi in the segmental pulmonary vasculature, three deep vein thromboses, two portal vein thromboses and one left ventricular thrombus. There was no significant difference in the rates of major bleeding, between the groups, one (3%) in the COVID-positive group compared to 4 (2%) in the COVID-negative group ($P = 0.48$, see Table 1).

The rates of VTE in this study were generally low, and in comparison to previous work, not higher in individuals with COVID-19. All VTE events in the COVID-positive group were within the pulmonary subsegmental arteries. Thromboprophylaxis adjusted by weight and anti-Xa level was not associated with an increased risk of bleeding. Future studies should consider prospectively comparing thromboprophylaxis adjusted by weight and anti-Xa level to standard thromboprophylaxis in the critically ill population.

References:

Abstract Table: Table 1: Demographics and results from clinical audit. %—percentage, kg =kilogram.

<table>
<thead>
<tr>
<th></th>
<th>COVID-positive</th>
<th>COVID-negative</th>
<th>$P$ value</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
<td>34</td>
<td>240</td>
<td></td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>64 (27-82)</td>
<td>60 (18-88)</td>
<td>$0.06$</td>
</tr>
<tr>
<td>Male (%)</td>
<td>21 (62)</td>
<td>132 (55)</td>
<td>$0.58$</td>
</tr>
<tr>
<td>Already on anticoagulation</td>
<td>2</td>
<td>12</td>
<td>$0.68$</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

BSH2021-PO-239
Perioperative management of anticoagulation: an audit of complications
Paul Armitage,* Paul Armitage,* Richard Gooding1, Patrick Mensah2
1University of Leicester, 2University Hospitals of Leicester, Leicester, United Kingdom

Abstract Content: The optimal haematological management of a patient on anticoagulation during the perioperative period is a commonly faced challenge. During this period, low-molecular-weight heparin (LMWH) is often given to bridge the gap between the cessation of standard anticoagulation and surgery and then back to full anticoagulation postoperatively. However, an individual’s overall risk is difficult to assess, and the rate of bleeding and thromboembolic complications surrounding periods of bridging anticoagulation is a challenge to study in a clinical environment. This audit aimed to assess the prevalence of bleeding and thromboembolic complications in the perioperative period of patients with increased thromboembolic risk, and therefore investigated the efficacy and safety of the anticoagulant bridging guidelines in University Hospitals of Leicester (UHL).

An audit population was selected to include patients who had an operation or invasive procedure planned at UHL between 01-01-17 and 31-12-18 ($n = 424$). Exclusion criteria were applied in this population, removing patients with incomplete surgical discharge summaries or whose operations had been cancelled or postponed. For those included in the audit ($n = 277$), clinical and demographic data were collected, and the bridging guideline followed was identified. The occurrence of haematological complications in the 90 days following surgery was established using the surgical discharge summaries and imaging reports.

22 (7.9%) patients experienced a perioperative haematological complication, with 21 (91.3%) bleeding and 2 (8.7%) thromboembolic complications reported, of which two were for a single patient. Complications ranged in severity from minor surgical site bleeding to pulmonary embolism, and occurred across a range of surgical specialties, with the highest proportion of complications per operation reported in gynaecology, ENT, general surgery and breast surgery (43.5%, 17.4%, 17.4% and 8.7%, respectively). Complications were more prevalent when following the high-risk bridging guidelines, where higher doses of LMWH were given (10.6% for high-risk guidelines, 5.9% for low-risk guidelines).
During the audit timeframe, a higher rate of bleeding complications was reported compared with perioperative thromboembolic events. These complications occurred throughout the audit population but were observed at higher rates in certain surgical specialties and at larger prescribed LMWH doses. The high-risk UHL guidelines were associated with greater complication rates, although the overall complication prevalence at UHL was lower than that reported in the literature at other centres.

Disclosure of Interest: None Declared

BSH2021-PO-240
Management of surgery, menorrhagia and childbirth for patients with unclassified bleeding disorders: a systematic review of cohort studies
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1Haemostasis and Thrombosis Centre, Guy’s and St Thomas’ NHS Foundation Trust, London, UK. 2Cardiff Haemophilia Centre, University Hospital of Wales, Cardiff, UK. 3West Midlands Adult Comprehensive Care Haemophilia & Thrombosis Centre, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK. 4Systematic Review Initiative, NHS Blood and Transplant, Oxford, UK. 5Haemophilia & Thrombophilia Centre, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

Abstract Content: Introduction: Unclassified bleeding disorders account for 2-6% of all new bleeding disorder registrations in the UK. The management of the bleeding phenotype associated with these disorders is poorly described.

Aim: Systematic review and meta-analysis to determine the bleeding rates associated with tranexamic acid, desmopressin, platelet transfusion, fresh frozen plasma and recombinant activated factor VII, for patients with unclassified bleeding disorders undergoing surgery, childbirth or with menorrhagia.

Methods: We searched for randomized controlled trials in MEDLINE, Embase, The Cochrane Central Register of Controlled Trials, PubMed, ISI Web of Science and the Transfusion Evidence Library from inception to 24th February 2020. Where appropriate, data were pooled using the metaprop function of STATA. The quality of evidence was assessed using Grading of Recommendations, Assessment, Development and Evaluations (GRADE) guidelines.

Results: Two studies with 157 participants with unclassified bleeding disorders were identified. The pooled risk of minor bleeding for patients undergoing surgery treated with peri-operative tranexamic acid was 11% (95% confidence interval 3 to 20%; n = 52; I² = 0%). The risk of desmopressin and tranexamic acid in combination was 3% (95% confidence interval 0 to 7%; n = 71; I² = 0%). There were no instances of major bleeding. In one procedure, 1/71 (1.4%), treated with a combination of desmopressin and tranexamic acid the patient had a line-related deep vein thrombosis. There were too few patients treated to prevent post-partum haemorrhage or for menorrhagia to draw conclusions.

Conclusion: The GRADE quality of evidence was very low suggesting considerable uncertainty over the results. However both tranexamic acid, and the combination of tranexamic acid and desmopressin have high rates of haemostatic efficacy and are associated with few adverse events.

Disclosure of Interest: M. Desborough Conflict with: Advisory boards for Takeda and Portola, unrelated to this work, S. Obaji: None Declared, G. Lowe: None Declared, C. Doree: None Declared, W. Thomas Conflict with: Advisory boards for Daiichi Sankyo, AbbVyn and Sanofi, speaking fees from Takeda, Bayer, Pfizer and support to attend the ISTH Congress by Novo Nordisk, unrelated to this work

BSH2021-PO-241
Retrospective study: assessment of utility of the pregnancy-adapted YEARS algorithm in predicting presence of PE in pregnant women with suspected PE.
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1Haematology, University of Leicester Medical School, 2Haematology, University Hospitals of Leicester, Leicester, United Kingdom

Abstract Content: Introduction: Pregnancy-associated Venous thromboembolism (PA-VTE) is one of the leading causes of maternal morbidity and mortality in the UK, with untreated pulmonary emboli (PE) having a 15-30% risk of mortality. The current assessment of PEs in pregnancy is difficult and unreliable, leading to the clinical need for better diagnostic strategies in this area of medicine. There is debate as to whether an algorithm such as the pregnancy-adapted YEARS score (which uses clinical signs, D dimer level and clinical likelihood of PE) can be helpful in this respect in order to simplify this diagnostic process; the algorithm has been subject to conflicting reports on its efficacy, especially considering the conclusions of the DiPEP biomarker study in 2018 which showed no correlation between D dimer and VTE in pregnancy. The following small study analyses the utility of using the YEARS algorithm in relation to pulmonary emboli in pregnant women.

Methods: From a local data base, women who had suffered a pregnancy associated PE were identified and notes obtained on those who had also had a d-dimer performed in pregnancy. There were a full set of data available for 36 women. The pregnancy-adapted YEARS algorithm was applied retrospectively to assess the utility. The criteria are summarised in figure and include presence of: 1. Clinical signs of a deep vein thrombosis, 2. Haemoptysis 3. Pulmonary embolus as most likely diagnosis and d dimer level

Results: A total of 36 cases of pregnancy associated PE were identified, of which 23 were antenatal and 13 were postnatal events. YEARS score was 1-3 in all cases. D-dimer was raised above the threshold in all but 2 cases (520-9,530 ng/ml). CTPA or V/Q scans were performed and PE confirmed in 30 cases and no PE in 4 cases. Two women had d dimer below the threshold and on CTPA did not have a PE.

Conclusion: No PEs were missed but the score predicted presence of PE in 11% which had negative scans. These were antenatal suspected VTEs in all four cases. It is reassuring that no VTEs were missed but the specificity of the algorithm is low as dependent on the experience of the assessor as to whether PE is ‘the most likely diagnosis’

Abstract Table:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>d-dimer &lt; 500</th>
<th>d-dimer &gt; 500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs DVT</td>
<td>0 criteria</td>
<td>OR ≥1 criteria</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>+ddimer &lt; 1000</td>
<td>+ddimer ≥ 1000</td>
</tr>
<tr>
<td>PE most likely diagnosis</td>
<td>+ddimer &lt; 500</td>
<td>+ddimer &gt; 500</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared
The COVID pandemic has had countless effects globally, and in particular on the health services in the UK and elsewhere. We sought in a questionnaire to investigate and document any changes in practice within haemostasis laboratories in response to the pandemic.

A questionnaire was sent to participants in the UK NEQAS BC laboratory programme. The following data summarises responses from 179 participants (both UK and non UK).

151 centres (84%) indicated that the repertoire of tests performed in their laboratory changed as a consequence of the pandemic. A number of centres had added D-Dimer testing, anti-Xa for heparin control, Clauss fibrinogen assays, additional APTT reagents, and argatroban assays. One centre noted temporary suspension of lupus, thrombophilia and platelet function tests.

128 centres (73%) indicated the quantity of tests performed in their laboratory changed significantly as a consequence of the pandemic. 83 centres reported increase DDimer testing, 24 saw an increase in fibrinogen assays, and 30 an increase in anti-Xa assays for heparin control. 10 centres saw an increase in coagulation screening requests, and others reported increased antithrombin assays, ADAMTS13 assays, and lupus investigations. 38 centres reported a decrease in test requests, in some cases for specialist tests, and in others due to reduced levels of outpatient or GP work.

Just 22 (12%) of centres reported that the turnaround time of tests performed in their laboratory changed significantly as a consequence of the pandemic. The majority of these reported extended turnaround times, reasons included staffing, changes to practice such as emptying of centrifuges, and batching of tests. Some centres reported reduced turnaround times particularly for anti-Xa assays.

Throughout 2020, UK NEQAS BC maintained their scheduled EQA programmes, and return rates remained close to average levels, demonstrating the ability of laboratories to participate in and prioritise quality assurance of their haemostasis tests. However it is clear that changes in testing practices, both in terms of tests performed and volume of tests, was experienced in a large majority of haemostasis laboratories in the last year.

Disclosure of Interest: None Declared

Reduction in Hospital Associated Thrombosis at Hampshire Hospitals (HHFT) due to innovative cross specialty collaboration during COVID-19 pandemic.

Tracy May1 on behalf of Tracy May, Tamara Everington, Helen Lewis, Sarah Mangles, Udaya Reddy, Ben Harris, Tamara Everington1,2 on behalf of Tracy May, Tamara Everington, Helen Lewis, Sarah Mangles, Udaya Reddy, Ben Harris and Tracy May, Tamara Everington, Helen Lewis, Sarah Mangles, Udaya Reddy, Ben Harris

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Abstract Content: Hospital associated thrombosis (HAT) is a well-recognised complication of hospital care. This risk can be reduced by careful VTE risk assessment on admission with use of thromboprophylaxis appropriate to bleeding risk. HHFT has consistently achieved >95% VTE risk assessment & thromboprophylaxis in line with NICE guidance for inpatients. Every HAT is subject to root cause analysis (RCA) to identify whether or not this event might have been preventable, & any learning is fed back into the organisation.

Early in the pandemic it became clear that patients hospitalised with COVID-19 illness were at very high risk of VTE & other thrombotic events. This was both because more severe COVID-19 disease is seen in older patients and patients with other health conditions which are already associated with VTE risk, and, because of inherent COVID-19 disease characteristics. This risk did not appear to be well mitigated with standard thromboprophylaxis & it was unclear whether this was due to overwhelming thrombophilia or suboptimal responses to heparins. A new enhanced thromboprophylaxis protocol was developed & introduced across the Trust to support patients admitted with COVID-19 infection.

As several patients had been found to have low Protein C or S levels, a single dose of IV Vitamin K 10 mg was introduced as standard at admission. Enhanced thromboprophylaxis was then given with enoxaparin on a twice daily regime (the standard starting dose for normal BMI & creatinine clearance was 40 mg bd compared to the 40 mg od they would otherwise have received). All patients had anti-Xa activity checked 3–4 hours post dose after 48 hours with subsequent anti-Xa monitoring frequency dependent on clinical stability & measured responses. The target for primary prophylaxis was anti-Xa level 0.4–0.7 iu/dl with a target of 0.7–1.2 iu/dl for thrombosis treatment.

A daily multi-disciplinary MDT was established to discuss patients & thrombosis consultants advised on appropriate dose titration where assays were out of range or there were clinical concerns around poor renal function, bleeding risks or other specific patient factors. Anti-Xa assays were run 7 days a week during peaks of infection. Patients with severe kidney injury were typically managed with once daily enoxaparin.

Continued close monitoring of HAT cases through RCA has shown that our incidence of HAT is lower than pre-COVID-19, with an approximate 50% reduction in the absolute number of events. Following implementation of the new protocol, analysis of data from April 2020 to December 2020 has shown only 2 HATs were identified in patients with COVID-19 and these were low severity VTE events in patients who had had appropriate thromboprophylaxis. Importantly, in addition, no serious bleeding or other adverse consequences resulted from the introduction of this enhanced thromboprophylaxis protocol.

The pandemic has brought significant changes in hospital care with intermittent suspension of elective activity, altered patterns of working and a much higher proportion of patients already at high risk of VTE requiring extended time on critical care for treatment of COVID-19. Despite this, our rate of HAT has fallen. We believe this results from an innovative & directly measured multidisciplinary approach which could open the door to new opportunities in reduction of HAT.

Disclosure of Interest: None Declared

Changes to coagulation factors in critically ill patients with SARS-CoV-2 infection

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1Haematology, 2Pathology, University Hospitals Of Leicester, Leicester, United Kingdom, 3Obstetrics and Gynaecology, Ioannina Hospital G. Hatzikosta, Ioannina, Greece

Abstract Content: Background: Severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2) is a coronavirus with human
infection initially reported in China which rapidly evolved in a pandemic designated as COVID-19 by the World Health Organisation. The development of coagulation test abnormalities and associated coagulopathy seen in SARS-CoV-2–infected patients is a major component of the disease leading to high morbidity and mortality.

**Aim:** To establish the changes to the circulating coagulation factors for critically ill patients with SARS-CoV-2 infection.

**Methods:** Blood samples from 22 patients with confirmed SARS-CoV-2 infection managed on an intensive care unit were analysed. The following coagulation tests were performed: prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, coagulation factors FII, FV, FVII, FVIII, FIX, FX, FXI and FXII. Demographics and clinical outcome data for thrombosis and death were collected. Statistical analysis to determine differences between SARS-CoV-2–infected patients and a control population of 39 subjects was performed using one-way ANOVA. Results are expressed as mean and were considered statistically significant for \( P < 0.05 \).

**Results:** Results of coagulation factors are seen in table 1. 15 patients were male and 7 female with a mean age of 55 years (ranging from 37 to 69). 10/22 eventually died and 12 survived and were discharged. Seven thrombotic events occurred, 6 of which were venous and 1 arterial. Coagulation screening tests were abnormal in 21/22 patients; FV and FIX were significantly higher in SARS-CoV-2–infected patients. FXI was lower in the cohort studied. No changes were seen in coagulation factors FII, FX, FVII an FXII.

**Conclusion:** Abnormalities of coagulation screening tests are common in ICU patients with COVID-19 infection. The abnormalities of screening tests are rarely associated with clinically relevant coagulation factor deficiencies. The prothrombotic state is likely driven, at least in part, by elevation of coagulation factors. Significant elevations of fibrinogen and FVIII were seen, in keeping with infection-induced inflammatory changes. Elevation of FV and FIX in an acute inflammatory state appears to be a new finding.

**Abstract Table:**

<table>
<thead>
<tr>
<th>Patients, ( n = 22 )</th>
<th>Control population, ( n = 39 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>FII (IU/dl) ±SD</td>
<td>94.81 ± 19.82</td>
</tr>
<tr>
<td>FV (IU/dl) ±SD</td>
<td>148.81 ± 30.92</td>
</tr>
<tr>
<td>FVII (IU/ dl) ±SD</td>
<td>109 ± 33.11</td>
</tr>
<tr>
<td>FX (IU/dl) ±SD</td>
<td>102.63 ± 21.05</td>
</tr>
<tr>
<td>FIX (IU/dl) ±SD</td>
<td>146.81 ± 31.96</td>
</tr>
<tr>
<td>FXI (IU/dl) ±SD</td>
<td>91.2 ± 37</td>
</tr>
<tr>
<td>FXII (IU/dl) ±SD</td>
<td>78.8 ± 28.26</td>
</tr>
</tbody>
</table>

**Disclosure of Interest:** None Declared

**BSH2021-PO-245**

**Thrombotic complications among hospitalized Covid-19 patients in a tertiary care hospital in Karachi, Pakistan**

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**Abstract Content:** Introduction: Severe Acute respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection results in a hypercoagulable state and an increased incidence of arterial and venous thrombotic events has been reported in patients. To date, there has been no study from Pakistan on thrombotic events in coronavirus disease 2019 (Covid-19) patients.

**Material and methods:** A retrospective observational study of hospitalized patients with at least one positive SARS-CoV-2 PCR result was carried out in Aga Khan University Hospital, Karachi, Pakistan from March 2020 to June 2020. Clinical, laboratory and radiological data were reviewed for evidence of arterial or venous thrombotic events.

**Results:** A total of 709 Covid-19 patients were admitted from March 2020 to June 2020. Thrombotic events were identified in 8.4% (64) cases; 48 (75%) were male and 16 (25%) were females. Mean age was 64.25 ± 14.41 years, 6 (9.4%), 7 (10.9%), 26 (40.6%), 25 (39.1%) had mild, moderate, severe and critical Covid-19 respectively. 56 (87.5%) had arterial and (12.5%) had venous thrombotic events. Myocardial injury was reported in 50 cases (78.1%); Non ST segment elevation myocardial infarction in 49 (76.6%) and ST segment elevation MI in 1 case (1.6%), radiologically confirmed pulmonary embolism in 5 cases (7.8%). 6 (9.4%) had ischemic stroke, there was one case of cerebral venous sinus thrombosis, one case of acute limb ischemia and one case of vascular access thrombosis was reported. Median D Dimer level on admission were 2.20 mg/L (IQR 1.0–7.9) and maximum Dimer levels were 7.7 mg/L (IQR 2.5–15.6). 29 (45.3%) patients died, there was a statistically significant difference (\( p \text{-value} < 0.0009 \)) between D-Dimer levels among survivors and non-survivors (8.75 ± 9.9 vs 13.384 ± 9.43 mg/ml).

**Conclusion:** There was a high prevalence of thrombotic events in Covid-19 patients which highlights the use of appropriate anti-coagulation and monitoring via D-Dimer levels. Certain limitations of the study include lack of cardiac catheterization for confirmation of MI and possible underestimation of thrombotic events due to logistical issues in radiological screening of patients.

**Disclosure of Interest:** None Declared
Proton pump inhibitor (PPI) if co-prescribed antiplatelets or SSRI

Safety Standards: ISTH major bleeding

Ischaemic stroke, systemic embolism and venous thromboembolism

DOAC discontinuation or switching to an alternate anticoagulant

Results: 286 patients were audited. 58% were male and 42% were female. The proportion of patients aged < 65, 65-74 and > 74 were 11.2%, 29.0% and 59.8%. Mean duration of follow up was 23 months.

99.3% of patients were dosed according to the SPC. DOACs were prescribed within licensed indications for 98.6% of patients. Two patients were prescribed DOACs for a left ventricular thrombus (LVT).

39.5% of patients were monitored less often than recommended. Dose modifications were required for 5.3%. Of the 31 patients on SSRI or antiplatelets, 18 (58.1%) were prescribed a PPI. 92% of patients remained on their initial DOAC with only three (1.0%) patients discontinuing anticoagulation completely.

Seven (2.4%) patients suffered a major bleeding event. Three (1.0%) patients suffered a thrombotic event. No bleeding or thrombotic events occurred with 30 days of switching. No fatal bleeds or thrombotic events occurred. 15.4% of patients died of other causes.

Discussion: The discontinuation rate of DOACs was low, perhaps due there being no first choice DOAC in our centre. Off licence DOAC prescribing was seen only for LVT. The management of LVT is poorly evidence based and where warfarin control is poor, DOACs are an attractive option.

The 23 month mean follow up period is strength of our audit. A significant number of patients were not monitored as frequently as recommended. The adverse event rate was too low for us to draw any conclusions about the impact this may have had. The high mortality rate is likely related to the age of our audit population.

The empirical switching strategy without INR monitoring was shown to be safe and practical. No patients in the audit were switched within three months of a thrombotic event or major bleeding event. INR monitoring during switching should continue in this higher risk group. Our strategy represents a pragmatic way to transition from warfarin to a DOAC in the COVID-19 era and beyond.

Disclosure of Interest: None Declared

BSH2021-PO-247

Predictors for prognosis in patients with nonfatal Pulmonary Embolism in COVID-19 pandemic

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Abstract Content: Pulmonary embolism (PE) is a devastating clinical problem with the high mortality rate, including mortality due to recurrent PE.

Aim: The objective of this study was to determine predictors for short- and middle-term prognosis of patients with pulmonary embolism (PE) and the clinico-instrumental predictors of poor outcome.

Method: This was a single-center prospective study of inpatients admitted in Institut of Cardiology of RM, with first-time PE (during 2020), within the national research project 2020-2023, focused on patients with venous thromboembolism. Clinical data were collected from patients with objectively confirmed PE, and a 1-year follow up was conducted.

Results: Eighty-four patients with PE, on age 59.3 ± 12.5 years (62.9% men), were selected in the study. Pulmonary embolism was confirmed by CT angiography in all the patients, while DVT was confirmed by ultrasound in 34 patients. Study population was followed up for 9.7 months. Multivariate regression analysis was done where right ventricular (RV) diameter (mean 3.74 cm), mean PASP (66 ± 23 mm Hg), RV hypokinesis, presence of RV thrombi, decreased ratio TAPSE/PASP < 0.4 (0.038, 95% CI, 0.025–0.055, P < 0.0001) measured by echoCG, d-dimer level at baseline 3615.5 ± 420.3 ng/mL and number of comorbidities (3.4 ± 0.7) entered the model. D-dimer level was revealed as a predictor for the length of hospitalization (β = 10.97, P = 0.05) and RV diameter as a factor for duration of anticoagulation (β = 29, P = 0.05), active cancer (OR = 6.142, 95% CI 1.233–30.587) and COVID history (OR=4.1, 95% CI, 4.3–80) were associated with a poor prognosis for acute PE in the short term (in hospital). Cox regression analysis showed that elevated pulmonary artery systolic pressure (PASP, >55 mmHg) (HR = 6.240, 95% CI, 2.307–37.013) and active cancer with PE (HR = 3.700, 95% CI, 1.010–13.562) were associated with an increased risk of mid-term mortality after a follow-up period of 1 years.

Conclusion: Our results show that the baseline measurement of these parameters independently influence both the short-term and middle-term prognosis of patients with nonfatal PE.

Disclosure of Interest: None Declared

BSH2021-PO-248

A multi-professional approach to improving awareness of cancer-associated thrombosis amongst people with cancer at the Northern Centre for Cancer Care in the United Kingdom

Iona Cutforth1*, Katherine Smith1, Karen Christie2, Lisa Pashby2, Sumantha Gabrieli3, Kathryn Musgrave1,4

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Abstract Content: Venous thromboembolism (VTE) is a leading cause of death in people with cancer1. However, nearly 3 out of 4 people with cancer are unaware of their risk of developing cancer-associated thrombosis (CAT)2.

The aim of this project was to assess the level of awareness of their increased risk of VTE, and associated symptoms, amongst outpatients with a diagnosis of cancer and to develop interventions to increase awareness.

Between January and March 2020, consecutive individuals receiving outpatient chemotherapy in the Northern Centre for Cancer Care, Newcastle upon Tyne, UK, were interviewed by medical clinicians. The survey assessed understanding of the term venous thrombosis, ability to recall a discussion with a healthcare professional about their increased thrombotic risk due to cancer, and recall of common symptoms of thrombosis. Interventions involved a multi-professional approach including the use of a patient-focused education video, patient information cards and regular training of nurses, doctors and pharmacists. The survey was repeated eight months following the interventions. Statistical analysis was completed using Fishers exact test.

The initial survey included 33 individuals. Fewer than half (42%) either understood what a VTE was or could recall having a discussion about thrombotic risk with a healthcare professional (39%). The majority of individuals could identify at least one symptom of VTE (64%).

Following the implementation of the interventions, the survey was repeated with 51 individuals. Most individuals could recall discussing the increased thrombotic risk with a healthcare professional (75%, P < 0.01). Despite an increase in number, there was no significant
difference in the proportion of individuals who understood the term VTE (61%, $P = 0.12$) or an increase in the number of symptoms they could remember (78%, $P = 0.21$).

A multi-professional approach with a range of interventions improved out-patient awareness of cancer-associated thrombosis risk.

**References**


**Disclosure of Interest:** None Declared

**BSH2021-PO-249**


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Abstract Content: Haemophilia is a rare inherited disorder with a frequency of approximately 1 in 10,000 births globally. Haemophilia A (deficiency of coagulation factor VIII) is commoner (80-85%) than haemophilia B (coagulation factor IX deficiency).

The quality of life and life expectancy of patients with haemophilia have improved over the decades with improved treatment. As a result, age related comorbidities became more prominent in this population. Although a lower incidence of cardiovascular diseases (CVD) was speculated among haemophiliacs due to hypoagglutinability, results from recent research in different ethnicities have challenged this hypothesis.

Haemophilia treatment centre at National Hospital of Sri Lanka (NHSL), the largest in the country was chosen for this study. All patients who consented and age ≥ 18 years (109) were recruited. Data on socio-demography, CVD events and risk factors were collected using an interviewer administered questionnaire. Seated blood pressure and anthropometric measurements were taken following standard techniques. Blood samples were collected for fasting plasma glucose and for lipid profile from those who had not been diagnosed to have diabetes mellitus (DM) and hyperlipidaemia respectively. Samples were analyzed on fully automated biochemistry analyzers using validated assay methods and appropriate quality control. The data were analyzed using SPSS 20 software. Prevalence of CVD was calculated and the prevalence of risk factors were compared with that of age matched males from the general population. $P$ values < 0.05 were considered significant.

Mean age of the participants was 37.7 years (SD 12.8). Majority were Sinhalese (84.4%, $n = 92$) Buddhists (77.1%, $n = 84$) and employed (76.1%, $n = 83$) with a monthly income ≥50000 Sri Lanka Rupees among 73.5% participants ($n = 80$). There were 92 (84.4%) patients with haemophilia A and 56 (51.4%) with factor levels below 1%. Most of the patients were on prophylaxis (57.8%, $n = 63$) while 81.7% ($n = 89$) had never detected inhibitors. Prevalence of at least one CVD (angina, myocardial infarction, coronary artery bypass grafting or non-hemorrhagic stroke) among study subjects was 2.8% ($n = 3$). There were 10 (9.2%), 30 (27.5%), 13 (11.9%) and 4 (3.7%) study subjects with DM, hypertension, current smoking and obesity (BMI ≥30 kg/m2) respectively. There were 32 (29.4%) and 37 (29.4%) study subjects with waist circumference ≥90 cm and waist hip ratio ≥0.9 respectively. Lipid profile revealed 38 (34.9%) study subjects with total cholesterol ≥200 mg/dl, 43 (39.5%) with LDL cholesterol ≥150 mg/dl, 25 (22.9%) with triglycerides ≥150 mg/dl and 58 with (53.2%) with HDL cholesterol <40 mg/dl. DM showed significant association with factor levels below 5% ($P = 0.038$). Statistically significant higher prevalence of BMI ($P < 0.00001$), waist circumference ($P < 0.00001$) and dyslipidemia ($P < 0.00001$) were found among study subjects compared to the age matched healthy males from Sri Lanka diabetes and cardiovascular study (Katulanda et al., 2018).

The study signify an increased prevalence of risk factors for CVD among patients with haemophilia and the need for preventive measures. Prevalence of hypertension, which was found to be significantly increased in patients with haemophilia in some of the published data, did not show any statistically significant difference from the general population in the current study. Further studies using larger sample size is recommended to further validate these findings.

**Disclosure of Interest:** T. Vithanage Conflict with: This research was supported with a financial grant from AJ Medicchem International, Sri Lanka., V. Ratnamalala: None Declared, C. Wickramaratne: None Declared, G. Katulanda: None Declared, C. Rodrigo: None Declared

**BSH2021-PO-250**

Evaluation of plasma fibrinogen level in patients who have undergone extracorporeal circulation

Sonia Mahjoub*, Asma Chamakh, Fakher Ghedira, Neila Ben Romdhane, Raouf Denguir

Abstract Content: Introduction: Extracorporeal circulation (ECC) produces serious insults to the coagulation process leading to impaired haemostasis and increased postoperative hemorrhage. Many studies have been focused on analyzing the changes of parameters of coagulation testing during and after ECC in order to identify patients at risk for increased postoperative blood loss, including fibrinogen as it represents a key protein in the coagulation cascade.

In this study, we sought to evaluate the modifications of fibrinogen level during and after ECC and to determine the relationship between fibrinogen level and postoperative bleeding.

**Materials and methods:** A total of 30 patients undergoing cardiac surgery under ECC were included in a prospective observational study. Postoperative bleeding volume was registered at 1 hour, 2 hours, 6 hours and 24 hours after surgery. Laboratory variables (hemoglobin, hematocrit, platelet count, prothrombin rate, activated partial thromboplastin time, fibrinogen level) were assessed in pre (T1), per (T2), post ECC (T3) and 24 hours after surgery (T4). Plasma fibrinogen concentration was determined according to the method by Claus.

**Results:** There were 30 patients with an average age of 54.4 years old (18-79 years old). Based on the surgery indication, Patients were split up into three groups: coronary insufficiency (P) ($N = 12$), valvulopathy (V) ($N = 14$) and other reasons (C) ($N = 4$). Two patients had fibrinogen levels below the lower normal limit of 2 g/l before initiating ECC. The mean fibrinogen concentration was respectively 3.41 g/l, 2.42 g/l, 2.46 g/l and 4.16 g/l at T1, T2, T3 and T4. A statistically significant difference between the preoperative (T1) and post ECC (T3) and postoperative (T4) fibrinogen level was noticed. Among groups, there was no statistical difference of fibrinogen level at T4. On the other side, based on the falls rate of
hemoglobin between T1 and T4 which was estimated at 2.5 g/dl, we defined two groups (N = 15). The rate of falls of preoperative fibrinogen concentration between the two groups was not statistically significant contrary to preoperative hemoglobin level and postoperative bleeding volume at 24 hours. However, there was an inverse correlation between preoperative fibrinogen level and chest tube drain volume after 6 hours (P = 0.83, R = -0.41). Besides, fibrinogen levels were significantly decreased after termination of ECC (T3-T1) (P = 0.03) in the latter groups. A positive correlation between preoperative fibrinogen and prothrombin rate was also noted (R=0.71, P < 0.001). No patient had received concentrated of fibrinogen in per or postoperative period.

Conclusion: In summary, our results demonstrate, in a small number, a correlation between preoperative fibrinogen level and postoperative bleeding volume outlining the importance of fibrinogen analysis in providing information about risk of severe postoperative bleeding and blood use. A large multicenter study is needed to prove causality and initiate countermeasures in order to control postoperative hemorrhage and thus reduce blood transfusion.

Disclosure of Interest: None Declared

BSH2021-PO-251
A Rare Presentation of ST-segment Elevation Myocardial Infarction Associated with Ovarian Stimulation in the Absence of Ovarian Hyperstimulation Syndrome
Keun Young Kim1,*, Yasmine Gerai2, Apurwa Prasad1, Na Hyun Kim1, Chenyu Sun, Sami Hussein1, Pratikshya Thapa1, Raghu Ramadurai2
1Internal Medicine, Amita Health Saint Joseph Hospital, 2Cardiology, Amita Health Saint Mary of Nazareth Hospital, Chicago, United States

Abstract Content: Follitropin Beta is a recombinant human follicle stimulating hormone (rFSH) used to stimulate ovarian follicular growth in women. Both venous and arterial thrombosis have been reported in association with ovarian stimulation with and without ovarian hyperstimulation syndrome (OHSS). We present a rare case of ST-segment elevation myocardial infarction (STEMI) associated with Follitropin Beta use. There were no signs or symptoms of OHSS. To our knowledge, this is the first case of STEMI in the absence of OHSS associated with ovarian stimulation. A 47-year-old female athlete presented with sudden onset chest pain. She had no previous episodes of chest pain. There was no family history of heart diseases, strokes or sudden deaths. She denies smoking, alcohol intake or any illicit drug use. Electrocardiogram revealed ST segment elevation in the anterior leads. Her high sensitivity troponin was elevated to 296 pg/ml. Percutaneous coronary angiogram showed 100% occlusion of the mid left anterior descending coronary artery. Two stents were placed. The patient reported multiple past IVF attempts that failed. She was currently on ovulation induction therapy with Follitropin Beta. Last Follitropin Beta injection was 28 days ago. She had no previous miscarriage or venous thromboembolism. Evaluation for hypercoagulable disorders including inherited thrombophilia and antiphospholipid syndrome was negative with normal results for heparin studies, Protein C and S deficiency, prothrombin mutation, anticardiolipin antibody, antithrombin III deficiency and Factor V Leiden mutation. She was discharged on dual antiplatelet therapy, atorvastatin and lisinopril after being monitored in the ICU. She was counselled to discontinue follitropin beta injections.

Our case of a 47-year-old athletic female with no underlying cardiovascular risk factors warrants awareness that ACS could be a rare yet serious condition associated with ovarian stimulation. Hemocoagulation has been considered to be a contributing factor to thromboembolism in patients with OHSS. Our patient developing ACS in the absence of OHSS suggests additional pathophysiology in inducing hypercoagulable state with ovarian stimulation. As rhFSH administration increases serum estradiol levels, a hypercoagulable state induced from increased plasma estrogen levels is plausible. Further analysis of serum estrogen levels in patients developing thromboembolic events with ovarian stimulation may provide guidance into risk stratification of thromboembolic events and the need for prophylactic anticoagulation accordingly.

No current guidelines on prophylactic anticoagulation during ovarian stimulation exist. Data is lacking in safety and efficacy of anticoagulation in patients who develop thromboembolism after ovarian stimulation. Further research is warranted to establish anticoagulation guidelines in ovarian stimulation.

As our patient did not present with OHSS, and was free of any cardiovascular risk and hypercoagulable conditions, the risk of major thromboembolic events associated with exogenous gonadotropin administration for ovarian stimulation is emphasized. Clinicians should be prompted to evaluate for cardiovascular risk and discuss the risk of thromboembolic events when considering ovarian stimulation. Further studies are needed to provide guidance in anticoagulation therapies and risk stratification for thromboembolic events in ovarian stimulation.

Disclosure of Interest: None Declared

BSH2021-PO-252
Management appropriateness and outcomes of patients with acute pulmonary embolism in COVID-19 pandemic
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Abstract Content: Background: Some studies show a poor adherence to published guidelines and on the bed outcomes of patients with acute pulmonary embolism (PE).

Aim: Assessment of adherence to the recommendations of recent Pulmonary Embolism management guidelines and their influence on the final results, in conditions of the COVID-19 pandemic.

Method: In this prospective study of a single academic center, within the national research project 2020-2023, focused on patients with venous thromboembolism, admitted to the emergency department (n = 86) of the Institute of Cardiology, RM (during 2020), we evaluated the rate of patients who were assisted according to international guidelines, the causes of non-adherence and their influence on the final result. Outcomes consisted of all-cause mortality, PE-related mortality, recurrent venous thromboembolism (VTE) and major bleeding events during the first month of follow-up after diagnosis.

Results: In this prospective study we included 88 of patients (mean age 59.3 ± 12.5 years (62.9% men) with acute symptomatic PE diagnosis, of whom 80% underwent early TTE (during the first 24 hours). Of these 25% met the primary endpoint within 7 day, including 5.8% deaths, 14% systemic thrombolysis, 12% requiring vasopressor due to systemic hypotension, a patient develop MI of RV. Overall, 88 patients (69% (95% CI 18–81%) did not receive guideline-adherent PE management. Patients receiving non-adherent management were significantly more likely to experience prolonged hospitalization (adjusted odds ratio (OR) 2.34 (95% CI 1.57–4.61)) all-cause mortality (OR 0.99 (95% CI 1.57–2.61)) or PE-related mortality (OR 3.02 (95% CI 1.42–8.42); P < 0.05) during follow-up. Non-adherent management was also a significant independent predictor of recurrent VTE: PE (OR 2.09 (95% CI 1.11–4.02); P = 0.05), DVT (OR 3.29 (95% CI 1.11–5.02); P = 0.04), and major
bleeding (OR 1.95 (95% CI 1.66–2.34); P < 0.01). The most common cause of non-adherence was the lack of availability of investigations and healthcare for epidemiological reasons (32%).

**Conclusion:** PE management that does not adhere to guidelines for indications related to diagnostic investigation, adequate anticoagulation, thrombolytics and inferior vena cava filters is associated with worse patient outcomes.

**Disclosure of Interest:** None Declared

**BSH2021-PO-253**

**Venous thromboembolism awareness among medical students in south-eastern Nigeria. A multicenter survey**

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**Abstract Content:** The burden of venous thromboembolism (VTE) can be reduced through awareness programs as VTE is largely preventable. We sought to determine the level of knowledge among medical students in the South-East Nigeria.

We carried out a descriptive cross-sectional study on clinical students at four medical schools in south-eastern Nigeria: Abia State University Teaching Hospital (ABSUTH), Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (COOUTH), Enugu State University of Technology Teaching Hospital (ESUT-TF) and University of Nigeria Teaching Hospital (UNTH). The pre-tested, pre-validated Ipsos-Reid questionnaire (a VTE awareness questionnaire) version draft -11 was used.

A total of 784 students were surveyed with a mean age of 23.5 ± 3.0. Our respondents showed high level of awareness (99.1%) of VTE. Majority, 638 (87.6%) of the respondents correctly described vein thrombosis as “a blood clot in a vein”. A little above half of them knew how clot felt in the leg (51.0%) and lungs (57.5%). Their level of awareness of the possible risk factors for VTE were all above 57%. However, majority (56.7%) showed poor knowledge of VTE. The relationship between medical school and level of perception was statistically significant, having P-value = <0.0001. While the adjusted odd ratio of 0.6 (95% CI: 0.35–0.96) implies that sex of respondents did not influence level of knowledge, being in 400 level, with an AOR = 1.5 (95%CI: 0.80–2.69) may have influenced the level of knowledge.

Awareness of VTE was high among our medical students but overall knowledge was low. Institution and level of study were found to be determinants of VTE knowledge and perception. This may be a call to curriculum adjustment in our medical schools.

**Disclosure of Interest:** None Declared

**BSH2021-PO-254**

**Review of Utility of Royal College of Obstetricians and Gynaecologists (RCOG) guidelines in predicting pregnancy-related VTE (PA-VTE)**

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**Abstract Content:** Background: Guidelines for pregnancy and post-partum thromboprophylaxis are largely expert-based, and differ widely from country to country. We performed a retrospective analysis of the RCOG guidelines to assess the utility in predicting pregnancy-related VTE (PA-VTE)

**Methods:** A local database was used to identify women who had suffered a PA-VTE, and the notes reviewed to assess their RCOG score. 290 previously pregnant women were identified, and of these 225 had no previous history of VTE. The notes were obtained and review of risk factors as listed in RCOG were available for 216 cases.

**Abstract Table:**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Level of Perception</th>
<th>Bivariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Agree</td>
<td>Disagree/Not Sure</td>
<td>X²</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>48 (60.8)</td>
<td>365 (53.8)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>31 (39.2)</td>
<td>313 (46.2)</td>
</tr>
<tr>
<td>Age (in years)</td>
<td>18–22</td>
<td>26 (32.9)</td>
<td>260 (38.3)</td>
</tr>
<tr>
<td></td>
<td>23–27</td>
<td>47 (59.5)</td>
<td>361 (53.2)</td>
</tr>
<tr>
<td></td>
<td>≥27</td>
<td>6 (7.6)</td>
<td>57 (8.4)</td>
</tr>
<tr>
<td>School</td>
<td>ABSUTH</td>
<td>33 (41.8)</td>
<td>142 (20.9)</td>
</tr>
<tr>
<td></td>
<td>COOUTH</td>
<td>9 (11.4)</td>
<td>131 (19.3)</td>
</tr>
<tr>
<td></td>
<td>ESUT-TF</td>
<td>16 (20.3)</td>
<td>130 (19.2)</td>
</tr>
<tr>
<td></td>
<td>UNTH</td>
<td>21 (26.6)</td>
<td>275 (40.6)</td>
</tr>
<tr>
<td>Level</td>
<td>400 Level</td>
<td>48 (60.8)</td>
<td>240 (35.4)</td>
</tr>
<tr>
<td></td>
<td>500 Level</td>
<td>31 (39.2)</td>
<td>140 (20.6)</td>
</tr>
<tr>
<td></td>
<td>600 Level</td>
<td>26 (32.9)</td>
<td>298 (44.0)</td>
</tr>
</tbody>
</table>
Results: Those with 4 or more risk factors were analysed in a separate submission; table 1 shows the results of number of risk factors and number of women who did or did not have a PA-VTE. For 3 risk factors, those women who suffered a clot did so prior to 28 weeks.

Conclusion: There is no clear predictive value of the RCOG guidance from this small study

Abstract Table:

<table>
<thead>
<tr>
<th>no. of risk factors</th>
<th>no. of women with no VTE</th>
<th>no. of women with VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>17 (61%)</td>
<td>11 (39%)</td>
</tr>
<tr>
<td>1</td>
<td>45 (66%)</td>
<td>23 (34%)</td>
</tr>
<tr>
<td>2</td>
<td>46 (79%)</td>
<td>12 (21%)</td>
</tr>
<tr>
<td>3</td>
<td>39 (32%)</td>
<td>83 (68%)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

BSH2021-PO-255

Hyperfibrinogenemia in patients with aggressive non-Hodgkin's lymphoma

Buruiana Sanda*, Robu Maria

Abstract Content: Patients with aggressive non-Hodgkin Lymphoma (NHL) have an increased risk of venous thromboembolism. Many factors contribute to the pathogenesis of thrombotic events. Hyperfibrinogenemia has one of the prothrombotic risk factors.

The purpose of the article is assessment of the frequency of hyperfibrinogenemia in new patients with aggressive NHL. The study included 59 new patients (38 – women and 21 – men) with aggressive B-cell NHL in accordance with the International Historical and Cytological Classification of Tumors of Hematopoietic and Lymphatic Tissue proposed by the WHO (2016). The frequency of increased fibrinogen levels was analyzed according to gender, age, stage of the disease, the presence of B-symptoms (defined as the presence of fever >38 °C, drenching night sweats or ≥10% loss in body weight in the 6 months preceding diagnosis) and the location of the primary tumor focus.

Hyperfibrinogenemia was confirmed in 17.9% of cases, at new patients who received treatment at the Hematological Center of the Oncological Institute of the Republic of Moldova, aged from 32 to 77 years, whose average age was 49.4 years. A comprehensive study revealed the higher incidence of increased fibrinogen in women (12.8%) versus men (5.1%) and in advanced stages of the disease (III and IV) with B systemic signs of intoxication – 85.7%. The nodal primary tumor focus (mainly in the peripheral lymph nodes and mediastinum) was in 57% of cases in the form of conglomerates of lymph nodes from 2.5 to 7 cm and in 43% of cases lymphoma developed extranodally: stomach, spleen and uterus.

The detection of hyperfibrinogenemia, large size of lymph nodes and advanced stage of the disease with B signs of intoxication are risk factors for the development of thromboembolic events in new patients with aggressive B-cell NHL.

Disclosure of Interest: None Declared

BSH2021-PO-256

Acquired Thrombotic Thrombocytopenic Purpura - Single Centre Experience

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1Internal Medicine, 2Nephrology, 3Haematology, SEHA- Tawam Hospital, AlAin, United Arab Emirates

Abstract Content: Introduction: Thrombotic thrombocytopenic purpura (TTP) is a rare microangiopathic disorder that results from deficiency of ADAMTS13 leading to increase of ultra-large von Willebrand factor (ULVWF) multimers. The cardinal clinical features of TTP including fever, thrombocytopenia, microangiopathic hemolytic anemia, neurological and renal involvement. Acquired TTP is characterized by production of autoantibodies against ADAMTS13 and low ADAMTS13 activity. TTP can be secondary to various clinical conditions including infection, drugs, malignancy and transplantation. The mortality is high if not recognised and treated early. Therapeutic plasma exchange (TPX), immunosuppressive drugs and rituximab are standard treatment protocol. The clinical data about TTP is limited in Middle East region. We studied the outcomes of acquired TTP in a tertiary hospital in United Arab Emirate.

Method: a retrospective chart review study was conducted at Tawam hospital over three years January 2018 to January 2021. Inclusion criteria were adult patient (age ≥ 16 years), with diagnosis of TTP based on clinical features and initial laboratory testing and confirmed by low ADAMTS13 activity and positive inhibitors. Demographic, clinical presentation, and laboratory data were collected and descriptive analysis was used. Therapeutic modalities, management outcomes and 30 days mortality rate were studied.

Results: Five patients had TTP during the study period, all patients were expatriates, with mean age of 29.8 years and 60% were males (n = 3). Majority of the patients were previously healthy with mean body mass index 37.27 kg/m2. The clinical presenting symptoms were fever (80% (n = 4)), bleeding episode (60% (n = 3)), jaundice (40% (n = 2)), and neurological symptoms (60% (n = 3)). All patients had renal impairment with mean serum creatinine (139.6 micromol/L) and one patient needed renal replacement therapy. There was an evidence of microangiopathic haemolytic anaemia with mean haemoglobin level of 72.4 g/L, elevated LDH (mean 856.8 IU/L), retic count (mean 157.58 × 10^9/L), schistocytes in blood film, and thrombocytopenia (mean 19.6 × 10^9/L). Three patients (60%) had bacterial infections (Salmonella species, Group B, Streptococcus mitis/Streptococcus oralis, Haemophilus influenzae). Our cohorts of patients fulfilled the clinical criteria of acquired TTP supported by low ADAMTS13 activity and elevated ADAMTS13 inhibitors. Daily therapeutic plasma exchange sessions were used with FFP replacement fluid without major complications. Majority of patients (80%) needed critical care admission, three required mechanical ventilation and all received broad spectrum antibiotics. Steroid therapy (100%, n = 5) was given either in oral prednisolone form or pulse therapy using methylprednisolone. Rituximab therapy was given for three patients. Two patients were diagnosed with new conditions along with TTP (systemic lupus erythematosus, Hairy cell leukemia). The median duration of hospitalization ranged from 8 to 32 days, and mortality was high (40%, n = 2). Outpatient follow up clinic visits at 3, and 6 months showed no evidence of recurrence in two patients.

Conclusion: The mortality rate of acquired TTP was high (40%) in our cohort. TPX is the standard therapy followed by the use of rituximab if indicated. Bacterial infections might contribute to acquired TTP and managing both conditions is fundamental.

Disclosure of Interest: None Declared
Abstract Table: Table 1: Clinical characteristics and outcomes of acquired TTP patients (n = 5).

<table>
<thead>
<tr>
<th>Cases</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, sex</td>
<td>31 years old</td>
<td>26 years old</td>
<td>35 years old</td>
<td>28 years old</td>
<td>29 years old</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Comorbid conditions</td>
<td>Previously healthy</td>
<td>Previously healthy</td>
<td>Previously healthy</td>
<td>Depression, CKD, asthma,</td>
<td>Previously healthy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>chronic thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>Hb with evidence of MAHA</td>
<td>50 g/L</td>
<td>69 g/L</td>
<td>92 g/L</td>
<td>97 g/L</td>
<td>54 g/L</td>
</tr>
<tr>
<td>Platelet count</td>
<td>36 x10^9/L</td>
<td>6 x10^9/L</td>
<td>24 x10^9/L</td>
<td>24 x10^9/L</td>
<td>8 x10^9/L</td>
</tr>
<tr>
<td>Bleeding episode</td>
<td>Lower GI bleeding</td>
<td>Gum bleeding</td>
<td>No</td>
<td>No</td>
<td>Per vaginal bleeding</td>
</tr>
<tr>
<td>Renal involvement</td>
<td>Yes, Cr 167 micromol/L</td>
<td>Yes, Cr: 113 micromol/L</td>
<td>Yes, Cr: 103 micromol/L</td>
<td>Yes, Cr: 208 micromol/L</td>
<td>Yes, Cr: 107 micromol/L</td>
</tr>
<tr>
<td>Neurological</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>headache</td>
<td>seizure, SAH</td>
</tr>
<tr>
<td>Blood or sputum culture</td>
<td>Salmonella species, Group B</td>
<td>Negative</td>
<td>Streptococcus mitis/</td>
<td>Strept oralis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADAMTS13 activity</td>
<td>0.3 IU/mL</td>
<td>&lt;0.08 IU/mL</td>
<td>&lt;0.08 IU/mL</td>
<td>&lt;7 %</td>
<td>&lt;7 %</td>
</tr>
<tr>
<td>ADAMTS13 inhibitor</td>
<td>24 units/ml</td>
<td>&gt;93 units/ml</td>
<td>27 units/ml</td>
<td>48.1 U/ml</td>
<td>38.0 U/ml</td>
</tr>
<tr>
<td>Diagnosis TTP</td>
<td>Acquired TTP</td>
<td>Acquired TTP</td>
<td>Acquired TTP</td>
<td>Acquired TTP</td>
<td>Idiopathic, possible drug</td>
</tr>
<tr>
<td>Associated conditions</td>
<td>Hairy cell leukemia</td>
<td>idiopathic</td>
<td>Infection</td>
<td>Idiopathic</td>
<td>SLE</td>
</tr>
<tr>
<td>Critical care admission</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>RBC transfusion</td>
<td>36 RBC units</td>
<td>9 RBC units</td>
<td>2 RBC units</td>
<td>2 RBC units</td>
<td>17 RBC units</td>
</tr>
<tr>
<td>Platelet transfusion</td>
<td>28 PLT</td>
<td>4 PLT</td>
<td>2 PLT</td>
<td>2 PLT</td>
<td>30 PLT</td>
</tr>
<tr>
<td>TPX sessions</td>
<td>4 sessions (5.25 L FFP)</td>
<td>7 sessions (4 L FFP)</td>
<td>7 sessions (4 L FFP)</td>
<td>1 session (4.75 L FFP)</td>
<td>6 sessions (3 L FFP)</td>
</tr>
<tr>
<td>Rituximab therapy</td>
<td>No</td>
<td>Yes (1 dose)</td>
<td>Yes (2 doses)</td>
<td>Yes (4 doses of Rituximab)+</td>
<td>No, MMF 1000 mg</td>
</tr>
<tr>
<td>Duration of hospitalization</td>
<td>8 days</td>
<td>8 days</td>
<td>14 days</td>
<td>32 days</td>
<td>25 days</td>
</tr>
<tr>
<td>Outcomes / mortality</td>
<td>Death</td>
<td>Recovered</td>
<td>Recovered</td>
<td>Death</td>
<td>Recovered</td>
</tr>
</tbody>
</table>
Diagnostic uncertainty in a case of thrombotic microangiopathy

Clare Brown¹**, Jennifer Easterbrook¹, Julia Anderson¹
¹Haematology, NHS Lothian, Edinburgh, United Kingdom

Abstract Content: Thrombotic microangiopathies (TMAs) are a group of disorders characterised by microangiopathic haemolytic anaemia (MAHA), thrombocytopenia and microvascular thrombosis. Establishing their cause is essential as urgent plasma exchange is required in cases of thrombotic thrombocytopenic purpura (TTP). We present a case of thrombotic microangiopathy where the distinction between primary or systemic aetiology proved challenging.

A 71-year-old female with a background of breast cancer (treated successfully with surgery and chemotherapy 4 years ago) presented with a 4-week history of weight loss and back pain in the context of a recent transient ischaemic attack (TIA). On examination observations were within normal limits and there was no focal neurology and no signs of malignancy.

Blood results were in keeping with a MAHA: haemoglobin 74 g/L, mean cell volume 103 fl, platelet count 55x10⁹/L, haptoglobin undetectable, bilirubin 159 µmol/L, reticulocytes 416x10⁹/L and direct antiglobulin test negative. The blood film revealed marked red cell fragmentation and occasional spherocytes. Vitamin B12 and folate levels were normal and there was evidence of a mild acute kidney injury with a raised troponin of 151 ng/L. Coagulation screen was normal and D-dimer was 3037 ng/ml. Tumour markers, virology and autoimmune screen were unremarkable. CT scan showed no evidence of malignancy.

The PLASMIC score was 5, correlating with an intermediate risk of severe ADAMTS13 deficiency. Urgent plasma exchange, methylprednisolone and folic acid were commenced for presumed TTP. ADAMTS13 blood samples were sent away to England for urgent analysis.

Towards the end of her first plasma exchange, the patient’s conscious level dropped which was felt to be secondary to a TIA. Oozing was noted from her central line site. Despite four plasma exchanges she continued to deteriorate neurologically. The ADAMST13 result returned as normal on day 3 and therefore plasma exchange was stopped. Bone marrow aspiration revealed erythroid hyperplasia (in keeping with haemolysis) only. The patient developed unilateral weakness with reduced conscious level requiring intubation and ventilation and CT imaging of her head revealed no cause. After a further haemodynamic deterioration and given the lack of identifiable precipitant for the MAHA, a decision was made to palliate and she died on the same day.

Posthumously, the bone marrow trephine was reported as metastatic carcinoma, likely primary breast invasive lobular carcinoma.

This case illustrates the difficulties in distinguishing cases of primary and systemic TMA. From the outset, there were reasonable grounds to suspect that this patient had a malignancy-associated TMA (given her background of breast cancer and the chronicity of her presenting symptoms). However in the absence of positive findings of malignancy, proceeding to plasma exchange was justified. As her condition progressed there were other features which went against a diagnosis of TTP including oozing of blood from her line sites and the lack of early response to plasma exchange.

This case has helped to strengthen our centre’s case for provision of local ADAMTS13 activity testing. Where there is diagnostic uncertainty, rapid confirmatory tests would have spared our patient unnecessary interventions.

Disclosure of Interest: None Declared
Lower Limb Oedema in Beckwith-Wiedemann Syndrome
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Abstract Content: We present a case of inferior vena cava agenesis (IVCA) associated with bilateral deep venous thrombosis (DVT) in a patient with Beckwith-Wiedemann syndrome (BWS). In adult patients with BWS presenting with bilateral lower limb oedema, specific aetiological factors should be considered. These include cardiomyopathy and intra-abdominal tumours. Congenital malformations of the IVC, through causing relative venous stasis, can lead to lower limb oedema either directly or indirectly by favouring lower limb venous thromboembolism, however, they are yet to be reported as an associated feature of BWS.

Given its life threatening potential, the prompt initiation of treatment for bilateral DVT is paramount. In BWS patients however, this can prove more complicated. Due to overgrowth, the above average birth weight can continue throughout childhood. In this case the patient’s weight reached 170 kg, impacting on anticoagulation choice, as direct oral anticoagulants have a limited evidence base in patients with a body mass above 120 kg. Furthermore, the presence of IVCA leads to a long term increased venous thrombosis risk. Therefore, patients with IVCA and bilateral DVT warrant specialist consideration and may benefit from a multidisciplinary team management, with haematology and vascular surgery input.

Conclusion: Here we showcased a rare cause for bilateral lower limb oedema, respectively bilateral deep venous thrombosis complicating IVCA in a patient with Beckwith-Wiedemann syndrome. The importance of this case lies in its novelty, as the association between IVC agenesis and BWS has not yet been described. Furthermore, the treatment of DVT in such situations requires special consideration, taking into account the patient’s weight and the presence of a significant, predisposing vascular abnormality.

Disclosure of Interest: None Declared

Assessment of Vitamin K Level in Newborns Presenting with Bleeding in Population of Rural Sindh, Pakistan
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Abstract Content: Background: Vitamin K deficiency bleeding (VKDB) has been classified by age of onset into early (<24 hours), classical (days 1–7) and late (1 week to 6 months), and by etiology into idiopathic and secondary in 1999 by the Pediatric and Perinatal Subcommittee of ISTH. Limited data are available on the relative frequencies of early, classical, and late vitamin K deficiency bleeding and exact level of vitamin K has not been assessed before in the population of Sindh. The method used in present study is a direct measurement of vitamin K concentration by photospectrometrical assay (ELISA) that has not been used previously in any local study of Pakistan. Other studies have used PIVKA (Protein Induced in Vitamin K Absence) to assess the deficiency, which is not a specific indicator.

Objectives: 1- To assess Vitamin K level in newborns presenting with bleeding. 2- To determine demographic profile of Vitamin K Deficiency Bleeding (VKDB) patients.

Methods: This descriptive cross-sectional study was conducted at the department of Pathology and department of Pediatrics LUMHS from 1996 to 2015. The total sample size was 114 newborns, 72 from term and 42 from preterm infants.

Abstract Table

<table>
<thead>
<tr>
<th>Type</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early (&lt;24 hrs)</td>
<td>4</td>
<td>3.5</td>
</tr>
<tr>
<td>Classical (day 1 to day 7)</td>
<td>19</td>
<td>16.7</td>
</tr>
<tr>
<td>Late (day 8 up to 180 days)</td>
<td>19</td>
<td>16.7</td>
</tr>
<tr>
<td>other causes of bleeding</td>
<td>72</td>
<td>63.2</td>
</tr>
<tr>
<td>Total</td>
<td>114</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

A rare case of Acquired Factor 8 inhibitor in a patient with Autoimmune Hemolytic Anemia successfully treated with steroids and rituximab
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Abstract Content: Introduction: Acquired Hemophilia A (AHA) is a rare disorder caused by autoantibodies directed against clotting factor VIII. The estimated incidence is 1.3 to 1.5 cases per million population per year. AHA is often underdiagnosed in real-world clinical setting as it often occurs in the elderly population with multiple comorbidities and medications that interfere with coagulation. Mortality is estimated to be above 20%. Although steroids and cyclophosphamide are the first-line treatment, there is increasing evidence on the effectiveness of immune tolerance regimens and rituximab. This report adds to the growing evidence that rituximab has efficacy in AHA.

Case Presentation: This is a 93-year-old female with no history of hematological disorders who presented with left facial swelling. Examination showed a tender, firm mass over the left face consistent with a hematoma. Initial lab work revealed Coombs positive autoimmune hemolytic anemia. After 48 hours, she developed multiple ecchymoses throughout the body and developed hemorrhagic shock requiring transfusion of four units of packed red blood cells. She was found to have a massive, 15 cm left gastrocnemius hematoma.

Coagulation studies revealed prolonged aPTT and low levels of Factor VIII. The mixing study was consistent with the presence of Factor VIII inhibitors. She was treated with intravenous danamethasone for five days, followed by oral prednisone for three weeks, and rituximab weekly for four doses. Factor VIII levels normalized and the bleeding subsided; hemoglobin level remained stable and hemolytic markers continued to trend down indicating a good response to the treatment.

Discussion: This case prompts clinicians to consider acquired factor inhibitors in the setting of major bleeding in a patient with no prior history of a bleeding disorder or anticoagulation use. Such presentation warrants further workup, including mixing study, when coagulation results are abnormal. Secondary causes of AHA, including malignancy, must be worked up, although >50% of reported cases are idiopathic. AHA is eminently treatable and therefore a prompt diagnosis is vital. The first-line treatment is the combination of steroids and cyclophosphamide. However, there is increasing evidence on the effectiveness of rituximab, similarly to our patient who had a good response and did not develop life-threatening bleeding manifestations. Clinical studies are required to assess the efficacy of rituximab as a treatment for eradication of factor VIII inhibitors.

Disclosure of Interest: None Declared

BSH2021-PO-262
A Rare Case of Bi-atrial Thrombi in a Stage IV Pancreatic Cancer Patient with Atrial Fibrillation on Warfarin
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Abstract Content: Atrial fibrillation (AF) is the most common arrhythmia and can result in adverse consequences of reduced cardiac output or formation of atrial thrombus. AF-related systemic thromboembolic events are the leading cause of mortality and morbidity in AF patients. Thus patients are placed on anticoagulants after risk stratification.

We present an unusual case of a 78-year old male with Stage IV pancreatic cancer and underlying AF who was found to have bi-atrial thrombi while on warfarin therapy. CT abdomen and pelvis for routine surveillance revealed small thrombi within the right atrium and left atrial appendage, which was new compared to his most recent CT imaging performed 3 months prior. At the time of imaging, the patient was noted to have supra-therapeutic prothrombin time-international normalized ratio (PT-INR) of 3.3. The patient was admitted for national normalized ratio (PT-INR) of 3.3. The patient was admitted to low molecular weight heparin therapy as this regimen is safe, and effective anticoagulation therapy.

Disclosure of Interest: None Declared

BSH2021-PO-263
A rare cause of diffuse peripheral and central thromboses
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Abstract Content: Catastrophic Antiphospholipid Syndrome (cAPS) is the most severe form of Antiphospholipid Syndrome with a high mortality. We present the case of a fifty year old lady with recurrent thromboses, initially treated with endovascular stents, progressing to require immunosuppression and anticoagulation. A fifty year old lady presented with bilateral leg and abdominal pain. Co-morbidities included Diabetes Mellitus and three miscarriages. Examination revealed pulse deficits in the lower limbs with gangrene on her toe digits. CT angiogram demonstrated complete thrombus of the Infernal Aorta and an Aortic stent was inserted. Two weeks later readmission occurred with leg pain; Doppler revealed a tight stenosis at the distal aortic region which mandated kissing stent insertion. One month later the patient presented with bilateral leg pain and necrotic right toes; this led to a right foot amputation. A triphasic finger colour change was noted with livedo reticulans on her lower limbs; a decision to institute Iloprost and Methylprednisolone ensued. Antiphospholipid antibodies returned showing triple positivity. Management subsequently included the addition of Rituximab, Plasma Exchange, IVIG and Sildenafil. Two months later readmission occurred with lower limb paralysis due to a complete thrombus of the Aortic B-Iliac stent- thrombolysed with good result. No further endovascular stenting was advised due to risk of embolic seeding. We have described a case of cAPS on a previously asymptomatic patient who presented with diffuse thrombosis. Our patient suffered from organ infarction, recurrent vascular occlusion over a period of 12 months and previous pulmonary emboli. Livedo reticulans and gangrene were demonstrated. cAPS accounts for less than 1% of APS with a mortality of 50%; this means early specialist input is important. The cAPS registry demonstrates that the majority of patients are female (72%) with a mean age of 37 years, 46% have primary APS, 40% suffer from SLE and 9% from other Autoimmune diseases. This patient does not have a secondary autoimmune condition. The most common clinical features to present before cAPS develops include foetal loss, previous DVT or thrombocytopenia- two of which our patient demonstrated. The prognosis and clinical features of cAPS have been shown to depend on the extent of thrombosis, organs affected and the presence of a systemic immune response. Our patient required aggressive treatment due to accelerating thrombosis as demonstrated by new gangrene, ongoing livedo reticulans and thrombocytopenia. Our case demonstrates the importance of keeping a high index of suspicion for cAPS as up to 46% will have this as their first presenting feature of APS. The diagnosis was secure with high titre of IgG anticardiolipin antibody, anti-Beta-2 glycoprotein 1 antibodies and Lupus Anticoagulant. Patients may present to surgical specialties in view of peripheral vascular signs and symptoms. It would be appropriate to identify patients with APS early to prevent multiple surgeries or endovascular stents, as they are frequently not successful. This case highlights the need for discussion and education within the multi-disciplinary setting for patients with APS. Finally, the risk of immunosuppression for patients who have received Rituximab can persist for up to 12 months following treatment. This patient’s risk stratification was high in view of COVID-19 and she was advised to shield until government guidelines ended.

Disclosure of Interest: None Declared
Research of influence of virus inactivating agent on the activity of Thrombin

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Abstract Content: Bleeding and thrombotic complications are usually cause of mortality in hematology patients, that is why it is important to control of factor coagulations.

Thrombin concentrate’s is often used in surgical practice to prepare fibrin sealant to promote hemostasis or with platelet concentrates to prepare gels to wound healing and also in coagulation studies. The obtained thrombin concentrate must have a high specific activity, and to ensure viral safety for both patients and medical professionals.

In our laboratory, a method for producing thrombin concentrate by dye-ligand affinity chromatography was done. We got the thrombin concentrate with an activity of 1500–2000 NIH/ml by this method. The technological scheme included 2 stages of viral inactivation: solvent-detergent and thioycanate methods.

Previous studies of these virus-inactivating substances on the activity of thrombin have been conducted to determine the possibility of their use in this technology.

Thrombin activity was determined according to the standard procedure according to the requirements of the National Institute Health (National Institute of Health; NIH) at a clotting time of 1 ml of 0.1% a solution of fibrinogen in 0.15 M NaCl with 0.01 M Tris-HCl buffer, at pH 7.3 and adding 0.01–0.05 ml of thrombin solution at a temperature of 37°C.

To investigate the effects of chemicals inactivators of viruses on the activity of Thrombin in the studied reaction the mixture was added their buffered solutions of various concentrations. The sample without the addition of chemical reagents was used as control.

At increase in the investigated solution concentration of Triton X-100 from 0.001 to 0.025 g/l appreciable growth was observed of Thrombin activity (from 1.1 to 1.7 units NIH/ml), and then at concentrations from 0.025 to 0.04 g/l – drop of activity. The increase of thrombin activity has been directly proportional depended on the concentration of Tween 80 (0.0016–0.04 g/l). Solvent three-(n-butyl)-phosphate in concentration from 0.0016 to 0.04 g/l insignificantly reduced thrombin activity.

Ammonium thiocyanate (NH4SCN) by changing the concentration in the reaction’s mixture from 0.0032 to 0.04 M/l significantly reduced the activity of Thrombin (fall was up to 80%).

To determine the reversibility or irreversibility of inhibition of thrombin activity, chemical reagents were removed from of the investigated solutions in stages by the method of ultradiafiltration (filters Amicon Ultra-0.5 10 kD, Millipore).

Thus, research has shown that high concentrations of inactivators reduced the activity of thrombin. The Thrombin activity recovered when removing them from the reaction mixture. These properties allow to effectively use these virus-activating reagents in one technological scheme of purification of plasma proteins using pre-fractionation and dye-ligand affinity chromatography on silica sorbents, which will significantly improve the safety of concentrate.

Disclosure of Interest: None Declared

Prothrombin time, activated partial thromboplastin time and platelets indices of mortuary workers exposed to formaldehyde, a base line study in Calabar, Nigeria

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Abstract Content: Introduction: The toxicity of embalming chemicals especially formaldehyde to human system including carcinogenicity and other adverse health effects have been reported. This study was done to provide information on the effect of formaldehyde on the Prothrombin Time, Activated Partial Thromboplastin Time and Platelet indices of mortuary workers.

Method: A total of 64 subjects were recruited for the study based on convenience sampling method in Calabar, Cross River State. The test group comprised of 32 mortuary workers with age ranging from 18–60 years from three different mortuaries within Calabar Cross River State Nigeria. Thirty two non-mortuary workers of the same age bracket from Calabar Municipality served as control. Sample collection was by venopuncture and method of analysis was by the use of automated haematology analyzer for platelet indices while Prothrombin time test and activated partial thromboplastin time test were analysed using One Quick’s stage method. Data generated was presented as mean ± standard deviation using tables. Student’s t-test and one way ANOVA were used to test the hypothesis. An error probability <0.05 was considered significant.

Abstract Table:

Table 1. PT, APTT, Platelet count, MPV, and PDWC of mortuary workers

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mortuary Workers</th>
<th>Non Mortuary Workers</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT (%)</td>
<td>0.19 ± 0.08</td>
<td>0.17 ± 0.06</td>
<td>0.14</td>
</tr>
<tr>
<td>MPV (fl)</td>
<td>10.05 ± 1.19</td>
<td>8.74 ± 0.74</td>
<td>0.00</td>
</tr>
<tr>
<td>PDWC (%)</td>
<td>32.94 ± 10.96</td>
<td>16.12 ± 1.14</td>
<td>0.00</td>
</tr>
<tr>
<td>Platelets (×109/l)</td>
<td>189.63 ± 77.35</td>
<td>191.47 ± 65.43</td>
<td>0.918</td>
</tr>
<tr>
<td>PT</td>
<td>12.09 ± 1.77</td>
<td>12.34 ± 1.15</td>
<td>0.505</td>
</tr>
<tr>
<td>APTT</td>
<td>32.63 ± 4.79</td>
<td>35.28 ± 3.13</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Table 2. PT, APTT, Platelet count, MPV and PDWC of mortuary workers based on duration of exposure

<table>
<thead>
<tr>
<th>Parameters</th>
<th>less than 5 years</th>
<th>greater than 5 years</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets (×109/l)</td>
<td>216.14 ± 86.69</td>
<td>169.00 ± 64.30</td>
<td>0.087</td>
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<tr>
<td>PCT (%)</td>
<td>0.23 ± 0.09</td>
<td>0.16 ± 0.06</td>
<td>0.009</td>
</tr>
<tr>
<td>MPV (fl)</td>
<td>10.79 ± 0.94</td>
<td>9.47 ± 1.05</td>
<td>0.001</td>
</tr>
<tr>
<td>PDWC (%)</td>
<td>39.86 ± 2.18</td>
<td>27.44 ± 11.96</td>
<td>0.001</td>
</tr>
<tr>
<td>PT</td>
<td>11.79 ± 1.96</td>
<td>12.54 ± 1.39</td>
<td>0.245</td>
</tr>
<tr>
<td>APTT</td>
<td>32.32 ± 4.74</td>
<td>33.08 ± 5.02</td>
<td>0.666</td>
</tr>
</tbody>
</table>

PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time Test; PCT, plateletcrit; MPV, mean platelet volume; PDWC, platelet distribution width

Result: The Prothrombin time of control subjects (12.34 ± 1.15) were slightly higher than that of Mortuary workers (12.09 ± 1.77), but this difference was not statistically significant as P-value = 0.505, whereas the activated partial thromboplastin time of the control was statistically significant higher than that of Mortuary workers P-value <0.05. This study also shows that Mean platelet volume and Platelet...
distribution width were significantly increased ($P = 0.000$) in mortuary workers when compared to non-mortuary workers. The Platelet count of mortuary workers were also decreased when compared to non-mortuary workers. Three (9.4%) of thirty two mortuary workers had giant forms of platelet. The result also shows that Long term exposure to formaldehyde can cause a significant ($P < 0.05$) reduction in the Platelet count, mean platelets volume, plateletcrits and platelets distribution width but had no effect on prothrombin time and activated partial thromboplastin time test of mortuary workers. There was a significant negative correlation ($r = -0.528; -0.549$ respectively) between age and platelet count and plateletcrit.

**Conclusion:** This study has shown that exposure to formaldehyde has a negative alteration on the Prothrombin Time, Activated Partial Thromboplastin Time Test, Platelet count and Platelet indices of mortuary workers.

**Disclosure of Interest:** None Declared
BSH2021-PO-266
Long term outcome of beta thalassemia major patients post allogeneic hematopoietic stem cell transplant-a single center study from pakistan

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Abstract Content: β-Thalassemia major (BTM) is characterized by deficient or absent synthesis of the β-globin chains. Sibling matched allogeneic hematopoietic stem cell transplant (HSCT) is only established curative treatment for BTM major patients.

Objective: 1. To analyze post-transplant outcome in terms of Overall Survival (OS) and Disease free survival (DFS). 2. Methodology: It is a Descriptive case series including data of 309 patients undergoing HSCT at Armed Forces Bone Marrow Transplant center, Rawalpindi from October 2001 till April 2020. Sampling technique was non probability consecutive sampling. All the thalassemia patients undergoing HSCT were included and those undergoing second bone marrow transplant were excluded. Mean age at BMT is 68.25 +/- 55 months (11.2 mo 16 yrs 8 mo).OS and DFS were calculated on the basis of Pesaro risk classification. Assessment of acute GVHD of skin, gut and liver will be made clinically as per Glucksberg-Seattle criteria (GSC). For hemorrhagic cystitis patients will be followed after conditioning for dysuria, microscopic and macroscopic haematuria. Probabilities of OS and DFS following transplant were estimated by Kaplan-Meier method and significance was assessed by log-rank test.

Results: The OS was 77.7% and DFS was 65.7%. Class risk analysis showed a significantly higher OS and DFS in class I and class II compared to class III high risk group. Acute GVHD was seen in 122 (39.5%) patients and HC was seen in 33 (13.3%) patients The incidence of grade I acute GVHD was 75 (24.3%) cases .grade II in 34 (11.0%) cases ,grade III in 3 (1.0%) cases and grade IV in 8 (2.6%) cases. Among HC 2 (0.8%) patients developed grade I, 20 (8.09%) developed grade II, 10 (4.04%) grade III and I (0.40%) patients developed grade IV hemorrhagic cystitis

Conclusion: Our study showed significantly higher OS and DFS in class I and II as compared to class III risk group. These results are comparable to international data (Lucarelli G et al).So HSCT is a reasonable option for the treatment considering improved OS and DFS in beta thalassemia patients

Conflict of Interest: “none to declare”

Ethical approval and Funding Disclosure: Permission of the hospital ethical committee was sought before conducting this study. Participants were explained about the purpose of the study and informed written consent was obtained. There is no funding disclosure.

Abstract Table:

<table>
<thead>
<tr>
<th>Risk Class</th>
<th>percentage n (%)</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>32 (10%)</td>
</tr>
<tr>
<td>II</td>
<td>85 (28%)</td>
</tr>
<tr>
<td>III</td>
<td>192 (62%)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None Declared

BSH2021-PO-267
Outcomes of allogeneic transplantation with non-myeloablative conditioning in patients with myelodysplastic and overlap syndromes

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Abstract Content: Allogeneic hematopoietic stem cell transplant (Allo-HSCT) remains an important option in treating a wide range of haematological malignancies. Reduced intensity conditioning (RIC) is less toxic than traditional myeloablative conditioning, and more suitable for elderly and significantly comorbid patients. We have previously reported the successful use of truly non-myeloablative T-replete conditioning with fludarabine and cyclophosphamide (FluCy). However, there is concern that without prior intensive chemotherapy, the FluCy conditioning may not facilitate effective engraftment in myeloid disorders such as atypical chronic myeloid leukemia (aCML), chronic myelomonocytic leukemia (CMLM), myelodysplastic syndrome (MDS) and other MDS/MPN overlap. This study retrospectively evaluated the outcomes of patients who underwent FluCy-conditioned Allo-HSCT with or without prior cytoreductive treatments.

Data was collected for patients with the above conditions who had FluCy Allo-HSCT at St Bartholomew’s Hospital between January 2015 and December 2020. Information including chimerism results and disease outcomes was compiled by reviewing inpatient notes, outpatient letters and pathology results on both the local electronic patient record system and transplant protocol documents.

27 patients were included in this study, 19 of which (70%) were male. The median patient age at transplant was 64 years old. 29.6% of the patients had a sibling donor and the rest had fully matched-unrelated donors. The majority (81.4%) of patients had a form of MDS (MDS-E1, MDS EB-2 or therapy-related MDS) as the diagnosis. The remaining patients had either CMLM-1, CMLM-2 or CML.

The 27 patients in this analysis are split into two groups. Group A comprises 21 patients who had FluCy conditioning with no prior high-intensity chemotherapy or hypomethylating agents alone. The remaining 6 (group B) had high-intensity chemotherapy treatment prior to their FluCy transplant.

Achievement of full whole blood and T-cell chimerism occurred in 12/21 (57.1%) patients in group A and 4/6 (66.7%) in group B. The mean number of days to achieve full whole blood and T-cell chimerism was 180 and 155 respectively in group A, and 138 and 136 days respectively for group B.

No patients had primary graft failure. Secondary graft failure occurred in 6/21 (28.6%) of patients in group A and 2/6 (33.3%) in group B. Overall survival at one year was 14/19 (73.7%) in group A and 4/6 (66.6%) in group B; two patients in group A were not yet one year from transplantation. One year remission-rates in surviving patients were 7/14 (50%) in group A and 3/4 (75%) in group B. Chronic graft-versus-host disease rates in survivors were 3/14 (21.4%) in group A and 2/4 (50%) in group B.

Despite the benefit of reduced toxicity in FluCy conditioning regimes, in this pathologically defined patient cohort 40% of patients did not achieve full donor chimerism (FDC) and the secondary graft failure rate is significantly higher than in a previously reported FluCy series in patients mainly with Acute Myeloid Leukaemia. More
patients also achieved FDC in that study. Although limited by a small sample size, there was minimal difference between failure rate in those receiving intensive chemotherapy prior to transplant and those who did not. Patients with the diagnoses described above may require alternative strategies to facilitate sustained engraftment in the context of RIC allo-HSCT such as more myelosuppressive conditioning.

**Disclosure of Interest:** None Declared

**BSH2021-PO-268**

**Bortezomib for refractory haemolytic anaemia post allogeneic haematopoietic stem cell transplantation**

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**Abstract Content:** The incidence of haemolytic anaemia (HA) is 2-4% post allogeneic haematopoietic stem cell transplantation (allo-HSCT) with a median onset 3-10 months post-transplant. Autoimmune haemolytic anaemia (AIHA) post allo-HSCT arises due to expansion of autoreactive donor B cells targeting donor red cells and may be due to lack of peripheral tolerance and low levels of T regulatory cells. Risk factors include use of T cell depletion, unrelated donors, chronic GVHD and use of PBSC or umbilical cord donors. It is distinct from ABO mismatch driven haemolysis resulting from ABO mismatch between donor and host. This leads to delayed host versus graft driven haemolysis post engraftment or pure red cell aplasia. Only 30-50% of patients achieve a complete response to steroids and often run a relapsing course. Second line agents include MMF, ciclosporin, IVIG and Rituximab. Higher response rates can be seen with Rituximab which targets autoreactive B cells. Proteasome inhibition with Bortezomib (BZ) is a potential third line treatment option targeting autoreactive plasma cells.

Three cases of refractory haemolytic anaemia post allo-HSCT treated with BZ were identified. All received BZ 1.3 mg/m² weekly for management of refractory HA. Data was obtained from patient electronic records. Patient 1 developed DAT negative HA on Day 30 post T deplete reduced intensity conditioned (RIC) matched unrelated donor (MUD) allo-HSCT (major ABO mismatched). He was refractory to first line therapy with corticosteroids and to second line therapy including Rituximab. He commenced BZ at 4 months post onset of haemolysis and received 11 doses over 4 months. He remains transfusion independent at 11 months post last dose and has weaned off corticosteroids completely. Patient 2 developed DAT Positive AIHA (IgG3+, IgM1+ and C3d2+ with pan-reactive auto-antibody (Ab)) 8 months post T deplete RIC MUD allo-HSCT for treatment of Myelodysplastic Syndrome. He was refractory to corticosteroids and a further 4 agents including Rituximab. He commenced BZ 29 months following onset of AIHA and received 13 doses over 31 months. An improvement in haemoglobin (Hb) and haemolytic markers and a reduction in transfusion requirements was seen but response has been incomplete. He remains on prednisolone 5 mg and MMF 250 mg daily 71 months post allo-HSCT. Patient 3 developed DAT positive AIHA (IgG3+, C3d3+, pan-reactive auto-Ab) 4 months post RIC double umbilical cord allo-HSCT for treatment of T-PLL. He was refractory to 5 modes of therapy including Rituximab and commenced BZ at 5 months post onset of AIHA. He received 8 doses of BZ over 2 months and is now transfusion independent, has been weaned off immunosuppression and has normalization of Hb and haemolytic markers at 30 months post allo-HSCT. BZ was well tolerated in all 3 patients with no adverse events.

**Disclosure of Interest:** None Declared

**BSH2021-PO-269**


Peadar O'Donohoe1, James Angus1,*, Mark Evans2, Tracey Ellison2

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**Abstract Content:** Hepatic veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) is a potentially fatal complication that
can occur after haematopoietic cell transplantation (HCT) conditioning or chemotherapy with or without HCT. The most severe form of VOD/SOS is associated with multi-organ dysfunction/failure and a mortality rate of >80% if untreated. Defibrotide is approved by the European Medicines Agency for the treatment of severe VOD/SOS post-HCT in patients aged ≥1 month. Based on the number of patients undergoing HCT reported to the British Society of Bone and Marrow Transplantation and available commissioned defibrotide use data from National Health Service (NHS) England, the estimated incidence of severe VOD/SOS among patients with first HCT (allo- genetic or autologous) in England from 2019-2020 was approximately 2.5%. Here, we used the Hospital Episode Statistics (HES) database to evaluate the overall incidence and burden of VOD/SOS in England.

In this retrospective analysis, data for patients with first HCT from April 2010 to March 2020 were obtained from HES (copyright 2021; reused with the permission of NHS Digital; all rights reserved), a data warehouse containing details of admissions, outpatient appointments, and accident/emergency department attendances at NHS hospitals. Two groups were created based on ICD-10 diagnostic codes: those coded for VOD/SOS 100 days post-HCT, regardless of disease severity, (VOD/SOS patients) and those not-coded for VOD/ SOS 100 days post-HCT (non-VOD/SOS patients). In both groups, information was collected on patient demographics, length of hospital stay, outpatient visits, and incidence of ICD-10 codes for bleeding complications based on McDonald, et al. (Clin Epидemiol 2018). Among VOD/SOS patients, data was collected on use of X831 (Blood Products Band 1), the OPCS code associated with advanced blood-derived therapeutics, including defibrotide.

Of the 32,147 records identified, 342 (1.06%) were coded for VOD/SOS (of any severity) within 100 days post-HCT. The mean length of hospital stay was 45.7 days for VOD/SOS patients and 23.9 days for non-VOD/SOS patients, and the mean number of outpatient appointments was 11.5 and 7.5, respectively. Overall, bleeding complications were coded in 4,749/32,147 (14.8%) patients within 100 days post-HCT, whereas 170/342 (49.7%) VOD/SOS patients had a bleeding complication. Among patients with codes for VOD/SOS and bleeding, 57/170 (33.5%) had also a code for X831. Similarly, in patients with codes for VOD/SOS and no bleeding, 151/172 (29.7%) were coded for X831.

The incidence of VOD/SOS in this analysis was lower (at 1.06%) than the approximately 2.5% incidence rate for severe VOD/SOS obtained from NHS England commissioning data, suggesting that VOD/SOS may be under-coded in the HES database, possibly due to under-diagnosis. On average, VOD/SOS patients experienced numerically longer hospital stays and more outpatient appointments per patient compared to non-VOD/SOS patients. Patients with VOD/SOS appeared to have higher rates of bleeding complications (49.7%) than the overall HCT population (14.8%); however, bleeding rates were similar in VOD/SOS patients with and without code X831. Given the burden of disease associated with VOD/SOS, appropriate diagnosis and coding is important for improving patient outcomes. Potential under-coding and under-diagnosis of VOD/SOS in the HES database emphasizes the need for appropriate use of VOD/SOS diagnostic codes.

Disclosure of Interest: P. O’Donohoe Conflict with: employee of Jazz Pharmaceuticals, Conflict with: holds stock ownership and/or stock options in Jazz Pharmaceuticals, J. Angus Conflict with: employee of Jazz Pharmaceuticals, Conflict with: holds stock ownership and/or stock options in Jazz Pharmaceuticals, M. Evans Conflict with: employee of Harvey Walsh which was contracted by Jazz Pharmaceuticals for the conduct of this analysis, T. Ellison Conflict with: employee of Harvey Walsh which was contracted by Jazz Pharmaceuticals for the conduct of this analysis.


BSH2021-PO-270

Outcomes of patients with acute Graft versus Host Disease managed with extra-corpooreal photopheresis: a single centre service evaluation following initial commissioning by NHS England

Julia Wolf*, James Griffin

Abstract Content: Graft versus host disease (GVHD), a frequent complication of allogeneic haematopoietic stem cell transplant (HSCT), is associated with significant morbidity and mortality. Response to first line corticosteroid therapy is frequently inadequate with 40-50% of patients being refractory or dependent (Abu-Dalle, et al. 2014). Extra-corpooreal photopheresis (ECP) is an apheresis based immune-modulatory therapy that is licenced for GVHD treatment and, having previously been funded for chronic GVHD, was commissioned for second line use in acute GVHD by NHS England in April 2017.

We retrospectively analysed data from electronic and paper records of all adult and paediatric patients (n = 30) who underwent ECP at our centre between April 2017 and April 2020. Patients with eight or less procedures (n = 4) were excluded. GVHD was graded according to modified Glucksberg criteria. Response was assessed according to EBMT–NHS–CIBMTR taskforce criteria.

Data on 26 patients (mean age 35.8 years; mean follow up 13.6 months) was analysed. GVHD was diagnosed after a mean of 37 days following HSCT and 82.6 days following donor lymphocyte infusion. Most patients had severe GVHD (73% Grade 3/4) affecting two or three organs. 50% of patients were steroid refractory and dependent respectively, ECP was initiated at a mean overall time of 50.6 days following diagnosis. This was reduced to 25.3 days in the steroid refractory subgroup. Notably, ECP initiation was significantly slower in 2017 (mean 111 days) than in more recent years (average mean 36.6 days in 2018-2020). All patients received an intensive ECP schedule and no serious adverse events were recorded.

Responses were as follows: active in 30.7% (n = 8), controlled in 46.2% (n = 12), inactive in 7.7% (n = 2), resolved in 15.4% (n = 4). Despite this, our maximum response rates are encouraging. 76.9% (n = 20) of patients achieved a complete response (CR) with a further 15.4% (n = 4) demonstrating partial responses. Most patients were able to stop or reduce immunosuppression. 69.2% (n = 18) developed chronic GVHD and 61.5% (n = 13) died – GVHD was felt to be causative in nine of these.

Prospective data on ECP in the setting of acute GVHD remains limited and no randomised controlled trials have yet reported. Greinix, et al (2006) reported encouraging CR rates of 82% for cutaneous, 61% for liver and 61% for gut GVHD. However, CR in triple organ GVHD was only seen in 25% with poor overall survival of 11% in non-responders. Similar responses were reported by Messina, et al (2003) and Perotti, et al. (2010). A more recent meta-analysis (Abu-Dalle, et al. 2014) showed pooled CR rates of 53% in five heterogeneous prospective studies. Our study cohort demonstrated CR in 76.9% of patients across all organs. While encouraging, this is the best recorded response and four patients required further GVHD therapy. ECP was started relatively late overall - earlier initiation was seen in more recent years but also in patients who subsequently died. This likely reflects the higher number of patients with steroid refractory, triple organ and severe GVHD in that group. Acute GVHD necessitating ECP remains associated with high mortality rates in our cohort. However, most patients were able to significantly reduce or stop immunosuppression and ECP was well tolerated with no recorded adverse events, making it a useful treatment modality.

While this study is limited by its retrospective nature it adds real world data to an expanding field of research.
Abstract Content: Recipients of bone marrow transplantation experience higher psychological distress than the general cancer population, which may impact on long-term psychological outcomes, biological outcomes, quality of life and survival. However, little is known about psychological care services (PCS) in transplant centres (TCs) internationally. We report on the first UK national survey to explore the provision of psychological care in bone marrow transplantation and clinicians’ perceptions of it.

The survey was developed in liaison with experienced bone marrow transplant clinicians and clinical psychologists. It explored psychological care workforce, psychological care scope, psychological screening and clinician perceptions, using both closed and open questions that were directed to participants according to their professional role. The survey was sent online to all 24 UK adult TCs that perform both allografts and autografts. It was sent to 3 healthcare professionals at each TC who have recognised roles in bone marrow transplantation: a clinical nurse specialist, physician and specialist psychological practitioner (SPP), apart from 2 TCs that had no designated SPP where it was sent to 2 clinicians each. A descriptive and content analysis of responses was performed.

100% TCs participated with an overall participant response rate of 89% (62/70). The SPP workforce is variable. 67% of all TCs have an SPP based outside the haematology service with 1 TC having no designated SPP within the hospital. In contrast to this, 33% of all TCs have an SPP based within the haematology service and 17% of all TCs have the SPP embedded in the transplant team although this is limited to the allograft service only in 2 TCs. However, 87% of all participants feel that the SPP needs to be embedded within the transplant team in order to improve patients’ quality of life and psychological outcomes. The scope of the service is variable and limited with regards to non-patient facing support. The PCS provides training of the transplant team on psychological skills in only 11/21 TCs whilst participants indicate a greater need for staff psychological support overall. Psychological screening is performed in 11/23 TCs pre-transplant and 12/23 TCs post-transplant. However, 90% of doctors and nurses feel that psychological screening should be performed on all patients pre and post-transplant. Overall, psychological care provision is not considered adequate by physicians. In TCs where the SPP is based in the haematology service, 86% (n = 6) of physicians rate their PCS to be adequate for both allograft and autograft, compared to 15% (n = 2) and 38% (n = 5) of physicians respectively in TCs where the SPP is based outside the haematology service. Similarly, 53% (n = 10) of SPP’s find psychological care to be inadequate in the pre-transplant period.

Analysis of participant comments reveals the following themes as barriers to psychological care delivery: limited resources (time, funding, staff and space), lack of SPP involvement in the transplant multidisciplinary team, limited availability of SPPs with experience in bone marrow transplantation, poor responsiveness of the PCS and poor coordination to identify patients in need.
BSH2021-PO-273
Ruxolitinib for management of Graft versus host disease: Real world experience from a developing country
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Abstract Content: Introduction: Treatment options for steroid resistant graft versus host disease (GVHD) are limited.

Objectives: To assess efficacy and safety of Ruxolitinib in steroid resistant or refractory GVHD in real world setting.

Methods: From November 2018 to January 2020, 10 consecutive patients with steroid dependent/refractory GVHD post HSCT were included in the study.

Results: The study included 4 male and 6 female patients. Median age at transplant was 19 years (1-34 years). Indications of transplant included: acute myeloid leukemia (n = 3), thalassemia major (n = 2) and one patient each of myelodysplastic syndrome, acute lymphoblastic leukemia, aplastic anemia, Fanconi anemia, SCID. Eight patients (80%) received matched related donor transplant and 2 (20%) received haploidentical HSCT. Median donor age was 27.5 years (4-37 years), gender mismatch was present in 8 (80%), while 5 donors (50%) were multiparous females.

Eight patients received Myeloablative, 1 non-myeloablative and 1 reduced intensity conditioning, 1 patient had received craniospinal radiotherapy prior to transplant. Stem cell source was BMH (40%), PBSC (40%) and both (20%). Median CD34 dose was 4.81x10⁶/kg. GVHD prophylaxis was Cyclosporine plus methotrexate in 8 (80%), cyclosporine plus mycophenolate in 1 and cyclosporine alone in 1. One patient had steroid refractory acute GVHD at day 63, five had overlap syndrome and 4 had extensive chronic GVHD. Five (50%) patients had at least 3 prior lines of treatment. Most commonly used dose of Ruxolitinib was 0.3 mg/kg or a flat dose of 20 mg daily. Median duration of treatment was 140 days (16-660). Ruxolitinib was well tolerated apart from 2 patients developing tuberculosis and CMV reactivation each and 1 developing pulmonary aspergillosis. Overall response rate as per NIH criteria were 90% (complete 70%, partial 20%), time to best response was 44 days (10-95 days). OS, DFS and GRFS of study population was 100%, 90% and 70% respectively

Conclusion: Our data show that Ruxolitinib is a safe and effective treatment for steroid dependent/refractory acute and chronic GVHD.

Disclosure of Interest: None Declared

BSH2021-PO-274
Implications of ABO incompatibility in Allogeneic Hematopoietic Stem Cell Transplantation
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Abstract Content: Background: The allogeneic hematopoietic stem cell transplantation (HSCT) is the preferred treatment option in many patients diagnosed with known malignant and non-malignant hematological conditions. The implications of ABO incompatibility (ABO-IC) in the allogeneic hematopoietic stem cell transplantation (HSCT) was studied based on two endpoints. The primary end-point was defined as the graft outcome (GO) in the form of a successful engraftment and the secondary end-point was to observe the median overall survival [MOS] of the recipient. Therefore, we wished to see the impact of ABO-IC on the post-transplant GO and or any associated complications.

Patients and Methods: We retrospectively identified among 28 patients [five autologous HSCT; 23 allogeneic HSCT] who underwent 29 HSCT procedures at our center between 2016 and 2020. Out of the 23 patients who received allogeneic HSCT, four underwent allogeneic HSCT from bone marrow [HSCT-M] in the OT settings, and 19 underwent allogeneic HSCT through apheresis [HSCT-A] at our blood centre. P value less than 0.05 was considered to be statistically significant.

Results: Amongst the twenty three allogeneic HSCT, around 4.0% [n = 0/23] patient-donor pairs were ABO-IC (major), 22% [n = 0/23] were ABO-IC (minor) and the rest 74% [n = 17/23] were completely ABO compatible [ABO-C]. All the patient-donor pairs were matched related donors. In minor ABO-IC transplantations, mild delayed hemolytic reaction occurred more frequently compared to major ABO-IC transplantations (P < 0.001). Neutrophil engraftment was slightly delayed in ABO-IC patient-donor pairs when compared ABO matched donor pairs according to median engraftment time. None of the patients showed any adverse reactions due to HSCT transfusions. There was however, an increased need of irradiated packed red blood cell [PRBC] and single donor apheresis platelet [SDAP] requirement in ABO-IC as against ABO-C [five PRBC vs three PRBC; three SDAP VS one SDAP (P = 0.04)]. Total nine patients expired [50 % (n = 3/6) ABO-IC versus 35% (n = 6/17) ABO-C; P = 0.041]

Conclusion: ABO-IC transplants were associated with decreased MOS and slightly reduced GO in the form of delayed neutrophil engraftment. More blood components were required in ABO-IC as against ABO-C HSCT post transplantation.

Key words: ABO Incompatibility; Hematopoietic Stem Cell Transplantation (HSCT); Graft Outcome; Median Overall Survival; Successful Engraftment; Graft versus Host Disease (GVHD)

Disclosure of Interest: None Declared

BSH2021-PO-275
Influence of ABO and D antigen discrepancies in allogeneic stem cell transplant: A single center study from Bangladesh
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Abstract Content: Allogeneic stem cell transplant (SCT) is a curative option for a variety of malignant and non-malignant hematological diseases. Transplant outcomes are strongly influenced by the degree of human leukocyte antigen (HLA) matching. ABO and Rh antigens are inherited independently of HLA complex and their incompatibilities are not a barrier in SCT. Three ABO mismatches are: major (recipient plasma antibody reacts to donor red blood cell antigen), minor (recipient RBC antigen reacts with donor plasma antibody) and bidirectional comprises both of them. When D antigen status differs between recipient and donor, the SCT is D antigen mismatch. Immediate or delayed hemolysis, pure red cell aplasia, delayed engraftment and graft versus host disease (GVHD) are immunohematological problems in various mismatches. Different strategies to prevent these are graft manipulation, reducing recipient’s isoagglutinin titer by plasma exchange and using donor type secretor plasma before transplant. The aim is to study the effect of ABO and D antigen mismatch on outcome of allogeneic SCT.
This is a retrospective case study over a period of 16 months. Total 10 patients of acute myeloid leukemia, diffuse large B cell lymphoma and acute undifferentiated leukemia were included. The study group include children and adults (age range 8-51 years for patient and 8-53 years for donors). 7 donors were full HLA matched and 3 were haploidentical. All patients received transplant from their related donors (9 siblings and 1 parent) after myeloablative conditioning. 2 of all transplants were ABO mismatched (one major, one minor) and 2 were major RhD mismatched (recipient RhD negative and donor RhD positive). Peripheral blood stem cells were collected by leukocytapheresis procedure. While infusion was given after premedication, each patients were monitored closely for any signs of hemolysis. Clinical and laboratory monitoring for post SCT complications were done carefully. Post-transplant events were managed by various antimicrobial agents, GVHD prophylaxis and other supporting therapies. Both recipient and donor grouping were considered for transfusion. All packed red blood cells (PRBCs) and platelets were irradiated at a dose of 25 Gy to prevent any risk of acute transfusion induced GVHD.

Total blood volume was processed 1.5-2 times and collection was avr. 181 ml. Cell dose was 0.8-26 x 10^6/kg body weight (Avr. 9.5). The major ABO mismatch needed no manipulation as isoagglutinin titer was 1:8 for IgM and 1:16 for IgG, but in minor mismatch donor’s IgM was 1:512 and IgG was 1:256 and plasma reduction was done. There were no graft failure. Successful engraftment was 100% with average engraftment of neutrophil in ABO identical was day 13 and day 18 in ABO mismatch and day 12 in RhD mismatch. Platelet engraftment in ABO identical was day 12 and in ABO mismatch and RhD mismatch it was day 17 and 13. GVHD (grade I -II) developed in minor ABO mismatch and in 2 patients of ABO identical SCT. Transfusion support was higher in major ABO mismatch group (2 PRBCs, 7 platelet concentrates and 1 apheretic platelet) compared to minor (1 PRBC, 2 platelet concentrates and 1 apheretic platelet). All patients were alive at the last follow up and one died before engraftment. This study revealed that ABO and RhD mismatch does not hamper engraftment but ABO mismatch require higher blood transfusion support and overall survival rate till date was same in all groups.

Disclosure of Interest: None Declared
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