DOI: 10.1111/bjh.18134

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

ABSTRACT

Posters

ALL, AML MDS & Bone Marrow Failure

BSH22-PO01 | Oral Azacitidine (Oral-AZA) in Patients with Acute Myeloid Leukaemia (AML) in First Remission after Intensive Chemotherapy (IC): Long-Term Overall Survival (OS) Results from the Phase 3 QUAZAR AML-001 Trial

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Abstract Content: Results from the randomized, placebo (PBO)-controlled, phase 3 QUAZAR AML-001 trial of Oral-AZA (CC-486) in patients (pts) with AML in remission after intensive chemotherapy (IC) and ineligible for stem cell transplant showed significantly prolonged overall survival (OS) vs. PBO: 24.7 months vs. 14.8 months (mo), respectively ($p < 0.001$) (Wei, 2020). Kaplan-Meier (KM) OS curves for Oral-AZA and PBO showed convergence at later time point after about 48 mo. At primary data cutoff (July 2019), 125/472 (26.5%) pts were either still receiving treatment (Tx) with Oral-AZA ($n = 45$) or PBO ($n = 26$) or were alive in survival follow-up ($n = 26$ and $n = 28$). We assessed longer term OS for pts in QUAZAR AML-001 after >1 year of additional follow-up.

Eligible patients (age ≥ 55 years with newly diagnosed AML, intermediate/poor-risk cytogenetics at AML diagnosis [Dx], ECOG PS ≤3, first complete remission [CR] or CR with incomplete blood count recovery [CRi] after IC [induction ± consolidation] before screening) were randomised 1:1 to Oral-AZA 300 mg or PBO QD for 14 days/28-day Tx cycle within 4 months after CR/CRi. Oral-AZA patients could continue to receive Tx in an extension phase after trial unblinding (July 2019) if they continued to benefit; PBO patients had Tx discontinued and were followed for OS. KM estimated OS was calculated from time of randomisation until death, withdrawal of consent or loss to follow-up (log-rank test). Baseline (BL) demographical and disease characteristics were compared between patients who were alive (on-Tx and/or in survival follow-up) for ≥3 years from randomisation (Long-term [LT] Survivors) and those who died or were censored before 3 years.

Of 472 patients randomised to Oral-AZA ($n = 238$) or PBO ($n = 234$), 39 patients (16%) in the Oral-AZA arm continued into the extension phase at trial unblinding. Overall, 31.4% Oral-AZA and 15.5% PBO patients received >24 months of Tx. By follow-up in September 2020, 54 (23%) Oral-AZA patients were alive in survival follow-up, 31 (13%) of whom were still receiving Oral-AZA in the extension phase; 165 patients (69%) died, and 19 patients (8%) had withdrawn consent or were lost to follow-up. In the PBO arm, 35 patients (15%) remained alive, 176 (75%) died and 23 (10%) had withdrawn consent or were lost to follow-up. The median OS in each arm remained unchanged from the primary cut-off date at median follow-up of 51.7 months (24.7 months vs. 14.8 months with Oral-AZA vs. PBO, respectively, $p = 0.0008$). KM OS curves, however, showed greater separation at long-term follow-up, with 3-year estimated survival rates of 37.4% vs. 27.9% in Oral-AZA and PBO arms respectively (Δ +9.5% [95% CI 0.9%, 18.1%]).

There were 140 patients (29.7%) in the LT Survivors cohort, 83 in Oral-AZA and 57 in PBO arms. Compared with patients who died or were censored before 3 years, LT Survivors were more likely to have intermediate-risk cytogenetics (95% vs. 82%) and *NPM1* mutation (45% vs. 22.5%) at AML Dx, and were less likely to be MRD+ at BL (33% vs. 52%). Seventy-one percent (34/48) of LT Survivors with post-IC MRD+ at BL vs. 15% (26/172) in the <3-year cohort achieved MRD negativity on-study ($p < 0.0001$).

Analysis at long-term follow-up showed greater separation of Oral-AZA and PBO KM OS curves at later timepoints than in the primary analysis, indicating a sustained, long-term OS benefit with Oral-AZA. Intermediate-risk cytogenetics and *NPM1* mutations at AML Dx, and absence of detectable MRD post-IC, were associated with long-term survival in QUAZAR AML-001.

Disclosure of Interest: A. Wei Conflict with: Novartis, Astellas, Pfizer, MacroGenics, AbbVie, Genentech, Servier, Celgene, Amgen, AstraZeneca, Janssen, Conflict with: Novartis, Celgene, AbbVie, Servier, AstraZeneca and Amgen, Conflict with: Walter and Eliza Hall Institute, H. Döhner Conflict with: Oxford Biomedicals, Novartis, Janssen, Jazz, Helsinn, GEMoaB, Celgene, BMS, AstraZeneca, Berlin-Chemie, Astex, Astellas, Roche, Amgen, Abbvie, Agios, Conflict with: Pfizer, Novartis, Jazz, Helsinn, Celgene, BMS, Astellas, Amgen, Abbvie, Agios, H. Sayar Conflict with: BMS, F. Ravandi Conflict with: Taiho, Xencor, Celgene, Amgen, Bristol Myers Squibb, Syros Pharmaceuticals, Astex, Agios, Jazz, Abbvie AstraZeneca, Novartis, Conflict with: Taiho, Xencor, Celgene, Amgen, Bristol Myers Squibb, Prelude, Syros Pharmaceuticals, Astex, Agios, Jazz, Abbvie, Conflict with: Celgene, Bristol Myers Squibb, P. Montesinos Conflict with: Stemline/Menarini, Forma Therapeutics, Glycomimetics, Daiichi Sankyo, Celgene, Tolero Pharmaceutical, Astellas Pharma, Conflict with: Novartis, Janssen, Pfizer, Daiichi Sankyo, Karyopharm, Celgene, Teva, Abbvie, Conflict with: Novartis Janssen, Incyte, Pfizer, Sanofi, Daiichi Sankyo, Karyopharm, Celgene, Teva, Abbvie, H. Dombret Conflict with: Amgen, Incyte, Jazz, Pfizer, Abbvie, BMS-Celgene, Daiichi Sankyo, Conflict with: Amgen, Incyte, Jazz, Novartis, Pfizer, Servier, D. Selleslag Conflict with: Novartis, Celgene, Amgen, Amgen Cilag, AbbVie, Alexion, GlaxoSmithKline, Merck, Pfizer, Sanofi, Takeda, Incyte, Teva, K. Porkka Conflict with: AbbVie, Astellas, BMS/Celgene, Incyte, Novartis, Pfizer, Conflict with: AbbVie, Astellas, BMS/Celgene, Incyte, Novartis, Pfizer, J. H. Jang: None Declared, B. Skikne Conflict with: Bristol Myers Squibb, C. L. Beach Conflict with: Bristol Myers Squibb, Y. O. Tian Conflict with: Bristol Myers Squibb, T. Chevassut Conflict with: BMS, Abbvie, Jazz, AstraZeneca, Pfizer, G. Roboz Conflict with: Celgene, MEI Pharma, Astellas, Jazz, Amgen, Mesoblast, Agios, Novartis, Otsuka, Janssen, AbbVie, Daiichi Sankyo, Helsinn, AstraZeneca, Bayer, Actinium, Astex, Glaxo SmithKline, Bristol Myers Squibb, Blueprint, Medicines, Jasper Therapeutics, Janssen, Pfizer, Roche/Genentech, Conflict with: Janssen, Conflict with: Bristol Myers Squibb.

BSH22-PO03 | Functionally Active Cytotoxic T Lymphocytes & Notch-1 in Peripheral Blood and Bone Marrow of Acquired Aplastic Anaemia Patients and Their Correlation with Disease Severity

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Abstract Content: Introduction & Aim: Acquired aplastic anaemia (aAA) is an autoimmune disorder, characterised by hypocellular bone marrow (BM) and peripheral blood (PB) pancytopenia. It is believed that cytotoxic T lymphocytes (CTLs; CD8+) destroy haematopoietic stem cells, leading to BM failure. The hallmark of active CTLs is perforin-mediated granule exocytosis. CD107a lines granule membrane. Surface expression of CD107a is induced on CTLs upon degranulation and is important for efficient perforin delivery. Additionally, expansion and effector functions of CTLs require notch signalling. Notch receptor and its ligands—Delta-like-1 (DLL-1), Jagged-1 (JAG-1) are involved in notch signalling. In this study, we have evaluated the frequency and function of CTLs; mRNA level of NOTCH-1 and its ligands in PB and BM of newly diagnosed, untreated aAA patients compared with healthy controls. Furthermore, patients were stratified as per disease severity into non-severe (NSAA), severe (SAA), very severe (VSAA) aplastic anaemia.
Method: Heparinised PB and BM paired samples were collected from 20 untreated aAA patients; 10 PB and 10 BM samples were from healthy controls. IRB approval and signed consent taken. Mononuclear cells isolated by ficoll hypaque density gradient centrifugation. Perforin-specific CD8 + T cells, stained *ex vivo*. For CD107a expression, cells were activated with anti-CD3/CD28 for 6 h. Cells identified as CD8 + perforin+; CD8 + CD107a+. Stained cells acquired in BD FACS Calibur. Data were analysed with FlowJo software. Real-time PCR was used for relative mRNA expressions of NOTCH-1, DLL-1, JAG-1. Mann–Whitney T test and Pearson correlation coefficient for statistical analysis. Data are shown as median.
Results: Increased % of CD8 + perforin+, CD8 + CD107a + cells in patient PB (16.2, 13.6) and BM (13.5, 13.8) as compared with healthy control PB (7.3, 6.9) and BM (9.5, 6.3) respectively. Elevated mRNA level of NOTCH-1, DLL-1, JAG-1 in PB (0.008173, 0.001381, 0.001384 vs. 0.001274, 0.0003046, 0.0004119) and BM (0.01360, 0.002093, 0.004487 vs. 0.00293, 0.0004607, 0.0009612) of patients than controls respectively. $p < 0.05$. No difference within patient PB and BM values. Among severity groups, VSAA+SAA had higher % of CD8 + perforin+, CD8 + CD107a + in PB (22.7,18.3), BM (23.50, 18.8) than NSAA PB and BM (15.5, 12.1; 13.90, 13.40) respectively. Likewise, raised mRNA level of NOTCH-1, DLL-1, JAG-1in SAA + VSAA than NSAA.

Positive correlations between CTLs and disease severity of patients.

Conclusion: Phenotypically defined CTLs are increased in aAA and represent an abnormally activated immune system. Aberrant expression of notch-1 and its ligands might be responsible for the generation of highly activated CTLs. These can be assessed in PB and BM. Excessive perforin production might lead to immune-mediated damage in aAA. The altered expression of CD107a might be an important functional marker responsible for inducing apoptosis in haematopoietic progenitors. The imbalance in CTLs and molecules also varies with disease severity. Positive correlations between CTLs and disease severity, denote the stimulated state of immune cells. Thus, disruption of immunopathology appears to take part in aAA. Furthermore, our study can be utilised to administer targeted drug therapy against Notch-1. Inhibiting Notch signalling at its different stages might help in restoring CTL balance in aAA.

Abstract Table:

Total number of patients	20
NSAA	10
SAA + VSAA	5 + 5
Males	12
Females	8
Median age & range (in years)	21(12–35)

Disclosure of Interest: None Declared.

BSH22-PO04 | Performances of Targeted RNA Sequencing for the Analysis of Fusion, Mutation, Exon Skipping and Expression in Haematological Tumours

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Abstract Content: RNA sequencing technique brings infinite potential for the diagnosis of haematological malignancies, because of its ability to analyse fusion genes, gene mutations, gene jumps and gene expression. However, its analytical performance is rarely described in diagnostic samples. Using the targeted panel of 507 genes related to haematological malignancies in 50 clinical samples and 20 healthy control samples, we detected 30 common known fusion genes, which were 100% consistent with the results of quantitative real-time polymerase chain reaction (qPCR). Meanwhile, two rare fusion genes were detected but not be detected by conventional detection methods such as qPCR and fluorescence in situ hybridisation (FISH). Additionally, we found that 91.3% (19/21) missense mutations identified at the DNA level were detected at the RNA level. All the nonframeshift ins/del mutations (3/3) and frameshift variants (4/4) were detected, but none splicing mutation (0/2) were detected, which were subjected to mRNA decay. All 10 cases with IKZF gene skipping identified by qPCR or multiplex ligation-dependent probe amplification (MLPA) were detected. Regarding the analysis of gene expression, 100% (20/20) cases with CRLF2 gene overexpression identified by qPCR were consistent with the results of targeted RNA sequencing. We conclude that targeted RNA sequencing may improve the fusion gene diagnosis rate of haematological tumours. Gene mutations at RNA level are not suitable for analysing clonal evolution but they are a powerful supplement to the molecular characteristics of the disease. The standardisation of RNA sequencing experimental operation, panel design and the improvement of biological information pipeline are very important factors for its use in standard diagnostic procedures. Targeted RNA sequencing is a very convenient tool for haematological tumour diagnosis to detect gene fusion, gene mutation, exon skipping and gene expression.

Disclosure of Interest: None Declared.

BSH22-PO05 | Beyond the In-Practice CBC: The Research CBC Parameters-Driven Machine Learning Predictive Modelling for Early Differentiation among Leukaemias

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Abstract Content: A targeted and timely treatment can be a beneficial tool for patients with haematological emergencies (particularly acute leukaemias). The key challenges in the early diagnosis of leukaemias and related haematological disorders are their symptom-sharing nature and prolonged turnaround time as well as the expertise needed in reporting confirmatory tests. The present study made use of the potential morphological and immature fraction-related parameters (research items or cell population data) generated during complete blood cell count (CBC), through artificial intelligence (AI)/machine learning (ML) predictive modelling for early (at the premicroscopic level) differentiation of various types of leukaemias: acute from chronic as well as myeloid from lymphoid. The routine CBC parameters along with research CBC items from a haematology analyser in the diagnosis of 1577 study subjects with haematological neoplasms were collected. The statistical and data visualisation tools, including heat-map and principal component analysis (PCA), helped in the evaluation of the predictive capacity of research CBC items. Next, research CBC parameter-driven artificial neural network (ANN) predictive modelling was developed to use the hidden trend (disease's signature) by increasing the auguring accuracy of these potential morphometric parameters in differentiation of leukaemias. The classical statistics for routine and research CBC parameters

showed that as a whole, all study items are significantly deviated among various types of leukaemias (study groups). The CPD parameter-driven heat-map gave clustering (separation) of myeloid from lymphoid leukaemias, followed by the segregation (nodding) of the acute from the chronic class of that particular lineage. Furthermore, acute promyelocytic leukaemia (APML) was also well individuated from other types of acute myeloid leukaemia (AML). The PCA plot guided by research CBC items at notable variance vindicated the aforementioned findings of the CPD-driven heat-map. Through training of *ANN* predictive modelling, the CPD parameters successfully differentiate the chronic myeloid leukaemia (CML), AML, APML, acute lymphoid leukaemia (ALL), chronic lymphoid leukaemia (CLL) and other related haematological neoplasms with AUC values of 0.937, 0.905, 0.805, 0.829, 0.870 and 0.789, respectively, at an agreeably significant (10.6%) false prediction rate. Overall practical results of using our *ANN* model were found quite satisfactory with values of 83.1% and 89.4.7% for training and testing datasets respectively. We proposed that research CBC parameters could potentially be used for early differentiation of leukaemias in the haematology–oncology unit. The CPD-driven ANN modelling is a novel practice that substantially strengthens the predictive potential of CPD items, allowing the clinicians to be confident about the typical trend of the 'disease fingerprint' shown by these automated potential morphometric items.

Disclosure of Interest: R. Z. Haider: None Declared, T. Shamsi Conflict with: No, Conflict with: No, Conflict with: No, Conflict with: No.

BSH22-PO06 | One size fits all: A fixed (not weight-adjusted) dose of prophylactic liposomal amphotericin B is not associated with a higher rate of breakthrough invasive fungal infections in patients with higher weight

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Abstract Content: At University Hospitals Birmingham NHS Foundation Trust, liposomal amphotericin B is recommended as first-line prophylaxis against invasive fungal infection (IFI) in high-risk haematology inpatients (including but not limited to patients undergoing stem cell transplant, high-intensity induction chemotherapy for AML or ALL and immunosuppression for graft versus host disease [GvHD]). We use a standard dose of 50 mg every other day (EOD) regardless of weight. Alternative approaches are to use higher doses proportional to patient weight such as 1 mg/kg or higher. 50 mg is the standard vial size of proprietary liposomal amphotericin B, as such our approach makes calculating and administering doses easier, with the additional benefit of lower cost. A potential concern has been that a 50 mg dose may under-dose larger patients and may lead to an increased risk of breakthrough IFI. We, therefore, evaluated clinical outcomes in this high-risk cohort of patients.

We reviewed the clinical records of all haematology inpatients over a 2-year period who received 50 mg liposomal amphotericin B EOD as prophylaxis against IFI from January 2019 to December 2020 (114 patients). The most common indication for prophylaxis was induction chemotherapy for acute leukaemia (56%), followed by previous IFI undergoing chemotherapy or transplant (16%), immunosuppression for GvHD (10%), stem cell transplant with high-risk features (8%), cord blood transplant (4%) and other (7%). Failure of prophylaxis was defined pragmatically as the clinical decision of the treating team to initiate antifungal treatment.

The mean duration of prophylaxis was 18.5 days. Of 114 patients, 31 (27%) had treatment initiated for an IFI. Of these, one met the criteria for probable IFI, 17 for possible IFI and 13 did not meet criteria but treatment was started based on judgement of the clinical team. There was no significant difference in the body mass index (BMI) of patients treated for an IFI *versus* those not treated for an IFI (24.8 kg/m^2 vs. 25.4 kg/m^2, $p = 0.60$), nor was there any significant difference in weight (72.2 kg vs. 76.5 kg, $p = 0.39$). Analysed categorically, there was no significant difference in the rate of treatment for IFI in patients defined as obese (BMI ≥30 kg/m^2) compared with non-obese (30% vs. 27%, $p = 0.76$), nor was there any difference in rates of IFI in those with a very high weight (≥90 kg) compared with patients <90 kg (22% vs. 29% $p = 0.51$). Tolerability was generally good with 4 patients (3.5%) stopping prophylaxis due to adverse events.

In summary, larger patients (based on BMI, weight and obesity) on a standardised dose of antifungal prophylaxis were not more likely to be treated for a suspected IFI. We believe our experience offers evidence in support of using a flat 50 mg EOD dose of liposomal amphotericin B for prophylaxis of IFI in high-risk haematology patients regardless of weight.

Disclosure of Interest: None Declared.

BSH22-PO07 | Venetoclax and Azacitidine Combination in Chemotherapy Ineligible Untreated Patients with Therapy-related Myeloid Neoplasms, Antecedent Myelodysplastic Syndromes or Myelodysplastic/Myeloproliferative Neoplasms

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Abstract Content: Patients (pts) with therapy-related myeloid neoplasms (tMN), antecedent myelodysplastic syndrome, or antecedent myelodysplastic/myeloproliferative neoplasms (A-MDS/MPN) may have poor outcomes due to age and adverse genetic/karyotypic features. In the VIALE-A study, pts with tMN and A-MDS/MPN unfit for intensive chemotherapy treated with venetoclax (Ven) and azacitidine (Aza) demonstrated superior response rates and overall survival (OS) than Aza alone. Herein, the efficacy and safety of Ven + Aza among pts with tMN and A-MDS/MPN are described.

Data were pooled from pts enrolled in VIALE-A (NCT02993523) comparing pts who received Ven + Aza or placebo (Pbo) + Aza and a prior phase 1b study (NCT02203773) where pts received Ven + Aza. Enrolled pts were ≥ 18 years, treatment-naïve with no prior exposure to hypomethylating agents, and ineligible for intensive chemotherapy. Pts on Ven + Aza received Ven 400 mg orally (days 1–28) and Aza (75 mg/m^2; days 1–7/28-day cycle). Composite complete remission rate (CRc; complete remission [CR] + CR with incomplete haematological recovery [CRi]), duration of response (DoR) and OS were assessed. Disease assessments were per modified International Working Group response criteria for AML.

In this pooled analysis, tMN was observed in (Ven + Aza/Pbo + Aza) 31/9 and A-MDS/MPN in 59/26 pts. Poor-risk cytogenetics were observed in 18 (58%)/6 (67%) with tMN (5 or 5q deletion [del]: 4/1; 7 or 7q del: 6/1; complex [≥3 clonal abnormalities]: 10/4), and 19 (32%)/13 (50%) with A-MDS/MPN (5 or 5q del: 10/5; 7 or 7q del: 6/1; complex: 14/9). *TP53* mutation was observed in 5 /3 pts with tMN and 8/0 pts with A-MDS/MPN.

Pts with tMN received a median (Ven + Aza/Pbo + Aza) of 5/4 cycles of treatment. CRc was achieved by 19 (61%)/1 (11%). The mDoR was not reached (NR) (95% CI: 17.8, NR)/8.5 (NR, NR) months. The mOS was 16.4 (95% CI: 4.1, NR)/11.3 (0.6, 17.5) months.

Pts with A-MDS/MPN received a median (Ven + Aza/Pbo + Aza) of 9/5 cycles of treatment. CRc was achieved by 39 (66%)/7 (27%) pts with mDoR of 17.3 (95% CI: 9.6, NR)/5.8 (1.1, NR) mos. The mOS was 15.9 (95% CI: 11.5, NR)/10.1 (4.7, 14.5) mos.

Common grade ≥3 adverse events (Ven + Aza/Pbo + Aza) were febrile neutropenia (tMN: 39%/11% and A-MDS/MPN: 36%/12%) neutropenia (tMN: 29%/33%; A-MDS/MPN: 39%31%) and thrombocytopenia (tMN: 32%/33%; A-MDS/MPN: 39%/62%).

Ven + Aza compared to Aza monotherapy resulted in higher CRc rates with longer DoR and median OS among treatment-naïve pts with tMN and A-MDS/MPN ineligible for intensive chemotherapy. The safety profile was similar to overall pts with the Ven + Aza combination. Outcomes by cytogenetic and molecular risk groups will be presented.

Acknowledgements: The authors thank the patients and their families, the study coordinators and support staff. The authors also acknowledge all investigators of M14-358 and M15-656 studies.

Statistical support was provided by Yinghui Duan, Ph.D. of AbbVie.

Medical writing support was provided by Dalia Majumdar, Ph.D., an employee of AbbVie.

Venetoclax is being developed in collaboration between AbbVie and Genentech. AbbVie and Genentech provided

financial support for the study and participated in the design, study conduct, analysis and interpretation of data, as well as the writing, review and approval of the abstract. No honoraria or payments were made for authorship.

Disclosure of Interest: V. Pullarkat M.D. Conflict with: Advisory board fees and fees for serving on a speakers bureau from AbbVie, Genentech, Pfizer, Jazz, Novartis, Servier and Amgen, K. W. Pratz M.D. Conflict with: Grant support and advisory board fees from AbbVie, Conflict with: Grant support from Agios, Daiichi Sankyo and Millennium, Conflict with: Advisory board fees from Astellas, Boston BioMedical and Celgene., H. Döhner M.D. Conflict with: Advisory role for Abbvie, Agios, Amgen, Astellas, Astex Pharmaceuticals, Celgene, Janssen, Jazz, Helsinn, Novartis, Oxford Biomedicals, Roche, Conflict with: Research funding from Amgen, Bristol Myers Squibb, Celgene, Jazz Pharmaceuticals, Novartis, Pfizer, C. Recher M.D. Conflict with: Research grants from Abbvie, Amgen, Novartis, Celgene, Jazz Pharmaceuticals, Agios, Chugai, Maat Pharma, Astellas, Roche and Daiichi-Sankyo, Conflict with: An advisory role for Abbvie, Sunesis, Janssen, Jazz Pharmaceuticals, Novartis, Celgene, Otsuka, Astellas, Daiichi-Sankyo, Macrogenics, Roche and Pfizer, M. J. Thirman M.D. Conflict with: Grant support, consulting fees and advisory board fees from AbbVie, Janssen and Pharmacyclics, grant support from Gilead Sciences, Merck, Syndax, TG Therapeutics and Tolero, Conflict with: Consulting fees and advisory board fees from AstraZeneca, Celgene and Roche/Genentech, C. D. DiNardo M.D. Conflict with: Consultant/advisory board member for AbbVie, Agios, Bayer, Celgene, Daiichi-Sankyo, Jazz, Immune Onc., Medimmune and Notable Labs, Conflict with: Research funding from AbbVie/Genentech, Agios, Calithera, Celgene, Daiichi Sankyo, Novartis, P. Fenaux M.D. Conflict with: Research funding from Abbvie, Celgene/BMS, Janssen, Agios, A. C. Schuh M.D. Conflict with: Consultant/Advisory Board/Research Support from, AbbVie, Agios, Amgen, Astellas, Celgene/BMS, GlycoMimetics, Jazz, Novartis, Phebra, Pfizer and Teva., A. H. Wei M.D. Conflict with: Grant support and consulting fees from AbbVie, Servier, Novartis, AstraZeneca., Conflict with: Consulting fees from Genentech, Pfizer, Celgene, Helsinn, BMS, Janssen, Amgen, Astellas, Conflict with: Royalties from the Walter and Eliza Hall Institute of Medical Research., A. Pigneux M.D. Conflict with: Investigator in an AbbVie funded trial, J.-H. Jang M.D. Conflict with: Investigator in an AbbVie funded trial, G. Juliusson M.D. Conflict with: Advisory board for AbbVie, Astellas, Celgene, Novartis, Conflict with: Research collaboration with Amgen and Novartis., Y. Miyazaki M.D. Conflict with: Honoraria from Novartis, Celgene, Sumitomo Dainippon, Nippon Shinyaku, Chugai, Otsuka, Astellas and Kyowa-Kirin, Conflict with: Research funding from Chugai, and Sumitomo Dainippon, D. Selleslag M.D. Conflict with: Advisory role for Abbvie, Sunesis, Janssen, Novartis, Celgene, Otsuka, MSD, Daiichi-Sankyo, Pfizer, Takeda, Astellas, Teva, M. L. Arellano M.D. Conflict with: Advisory board for Gilead, Kite Pharma, Inc, Syndax Pharmaceuticals, Inc., Conflict with: Research funding from Cephalon Oncology, K. Naqvi M.D. Conflict with: Employee of Genentech and may hold Roche stock or stock options, J. Yu Ph.D Conflict with: Employee of AbbVie and may hold stock or stock options, J. A. Ridgeway DNP, NP-C Conflict with: Employee of AbbVie and may hold stock or stock options, J. Potluri M.D. Conflict with: Employee of AbbVie and may hold stock or stock options, M. Konopleva M.D. Conflict with: Grant support and consulting fees from AbbVie, Genentech, F. Hoffmann La-Roche, Stemline Therapeutics, Forty-Seven, Conflict with: Consulting fees from Amgen and Kisoji, grant support from Eli Lilly, Cellectis, Calithera, Ablynx, Agios, Ascentage, AstraZeneca, Rafael Pharmaceutical, Sanofi, Conflict with: Royalties and stock options from Reata Pharmaceutical Inc., and patent US 7795305 B2 on CDDO-compounds and combination therapies, licensed to Reata Pharmaceutical.

BSH22-PO08 | CPX-351 Treatment for Acute Myeloid Leukaemia in England: Real-world Outcomes in Adults Aged <60 Years

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Abstract Content: CPX-351 (Vyxeos® liposomal) is a dual-drug liposomal encapsulation of daunorubicin and cytarabine in a synergistic 1:5 molar ratio. Since November 2018, NICE has recommended the use of CPX-351 for adults with newly diagnosed, therapy-related acute myeloid leukaemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) due to either prior myelodysplastic syndrome (MDS)/chronic myelomonocytic leukaemia (CMML) or *de novo* AML with myelodysplasia-related cytogenetic changes. The pivotal phase 3 study of CPX-351 enrolled patients aged 60 to 75 years with t-AML or AML-MRC, and thus there are limited data on outcomes for younger adults treated with CPX-351. The aim of this retrospective study was therefore to describe the characteristics and overall survival (OS) of younger adults (aged 18 to 59 years) with AML in England who were treated with CPX-351.

This study utilised the Cancer Analysis System (CAS) database available through the National Cancer Registration and Analysis Service (NCRAS), which systematically collects and curates population-level data about cancer diagnoses, treatments and outcomes across England. A diagnosis of t-AML or AML-MRC between 01/01/2013 and 31/03/2021 was determined either directly using International Classification of Diseases for Oncology, Third Edition (ICD-O-3) codes or indirectly using non-specific ICD-O-2, ICD-O-3 or ICD-10 AML codes in combination with prior systemic anticancer therapy or radiotherapy (t-AML) or a prior diagnosis of MDS/CMML (AML-MRC; other

AML-MRC subtypes could not be specifically identified and are included in the unspecified AML subgroup). OS was estimated from the diagnosis date or landmarked from the haematopoietic cell transplantation (HCT) date.

Of the 211 patients with AML who were treated with CPX-351, 60 (28%) were aged 18 to 59 years and are described here. The median (interquartile range [IQR]) age was 53 years (46, 58), with 12 patients aged 18 to 44 years and 48 patients aged 45 to 59 years; 21 (35%) patients had secondary AML (t-AML or prior MDS/CMML), nine (15%) had other AML-MRC and 30 (50%) had unspecified *de novo* AML. No patient had received prior azacitidine therapy.

The cut-off date for OS was 31/08/2021, giving a median (IQR) follow-up of 13.8 months (6.1, 20.9). Overall, 31 patients had died, with an estimated median (95% confidence interval [CI]) OS of 18.5 months (11.0, not estimable) and survival probabilities (95% CI) of 0.59 (0.48, 0.73) at 1 year and 0.44 (0.32, 0.60) at 3 years. Early mortality rates were 3% at 30 days and 10% at 60 days. To date, 29/60 (48%) patients have undergone HCT, including 29/50 (58%) with ≥3 months of follow-up; 21 patients underwent HCT following CPX-351 and eight following subsequent salvage therapy. When landmarked from the HCT date, median (95% CI) OS was not reached (16.5 months, not estimable), with survival probabilities (95% CI) of 0.83 (0.70, 0.98) at 1 year and 0.61 (0.43, 0.86) at 2 years. In a treatment patterns analysis, 14 patients had died without salvage therapy and 19 were alive without receiving subsequent therapy by the end of the study period. The most common salvage treatment after CPX-351 was fludarabine, cytarabine and granulocyte-colony stimulating factor (FLAG)–based therapy (n = 12).

In conclusion, this study provides real-world survival outcomes in patients aged 18 to 59 years with AML who were treated with CPX-351 in England. The median OS was 18.5 months and the median OS post-HSCT had not been reached.

Disclosure of Interest: A. Legg Conflict with: employee: Jazz Pharmaceuticals, Conflict with: stock or stock options: Jazz Pharmaceuticals, A. Reich Conflict with: employee of IQVIA Inc., which was contracted by Jazz Pharmaceuticals for the conduct of this analysis, E. Wilkes Conflict with: employee of IQVIA Inc., which was contracted by Jazz Pharmaceuticals for the conduct of this analysis, G. Medalla Conflict with: employee: Jazz Pharmaceuticals, Conflict with: stock or stock options: Jazz Pharmaceuticals.

BSH22-PO09 | High GLI-1 expression predicts poor prognosis in AML patients

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Abstract Content: Background: Acute myeloid leukaemia (AML) is a clinically and biologically complex heterogenous disease that is characterised by broad-spectrum molecular alterations as a result of deregulation of many signalling pathways that can be considered as potential therapeutic targets. The glioma-associated oncogene homolog 1 (Gli1) transcription factor is defined as the terminal effector of the Hedgehog (Hh) signalling pathway, a fundamental pathway in embryonic development and stem cell biology. Gli1 is tightly regulated during development and tissue patterning in embryonic life and has a potential role in controlling cell cycle so its aberrant activation has been associated with the development of many cancer landmarks, as proliferation, angiogenesis, metastasis, survival, metabolic renewal and resistance to chemotherapy. This work aimed to assess Gli1 expression as a prognostic marker in AML patients.

Subjects and Methods: The clinical specimens were obtained from 43 newly diagnosed non-APML AML patients and 10 normal control samples. Real-time qPCR was carried out to detect Gli1 mRNA expression level in bone marrow mononuclear cells (BMMNC). The relation of Gli1 mRNA levels with clinical parameters and prognostic factors were evaluated.

Results: Gli1 was over expressed in our patients' bone marrow samples compared to control samples. There was no statistically significant difference in the Gli1 mRNA expression among different age groups, between males and females, or between different FAB subtypes, (p = 0.65), (p = 0.18), (p = 0.37). No correlation was observed between Gli1 mRNA level and haemoglobin level, total leucocytic count, platelets count, peripheral or bone marrow blasts at diagnosis. There was statistically significant difference in Gli1 expression among different risk categories being highest in 15 patients with poor risk (87.73 + 115.18) compared to intermediate risk (5.22 + 3.9) (p = 0.001) and favourable risk groups (4.15 + 3.03) (p = 0.001). Those who harboured mutant allele of FLT3 had significantly higher levels of Gli1 gene than patients carrying the wild one. The levels of Gli1 mRNA were significantly higher in 26 de novo non-APL AML patients who did not achieve complete remission (CR) after induction chemotherapy, compared with 17 patients who achieve CR (p = 0.004). Significantly higher levels of expression were seen in those who failed to achieve CR in each subgroup of patients with favourable risk, wild FLT3 allele, alive patients or in those who did not complete the journey.

Conclusion: GLI overexpression can be considered as a negative prognostic factor in AML. In addition, it may offer a novel target for therapy in AML patients in near future.

Key words: AML, Gli1, poor prognosis.

Disclosure of Interest: None Declared

BSH22-PO10 | Single-centre experience of Liposomal Daunorubicin and Cytarabine (CPX-351) for the Treatment of Poor risk AML

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Abstract Content: CPX-351 is a liposomal preparation of daunorubicin and cytarabine in a synergistic 1:5 molar ratio, resulting in enhanced uptake into leukaemia cells, and has been found to result in a superior median survival as compared to standard daunorubicin + cytarabine (DA 7 + 3). In Dec 2018 CPX-351 was NICE approved for the treatment of adults with secondary AML (sAML) and AML with myelodysplastic related changes (AML-MRC) in the UK.

Since 2017, we treated 34 patients who received 60 cycles of CPX via standard commissioning, clinical trials and compassionate use. All patients had baseline cytogenetics and 33/34 had a NGS myeloid molecular panel performed. Of these 30 patients received CPX as first line and four received it after prior AML- therapy (3 primary refractory disease and 1 early relapse of MLL-rearranged AML). Of the 30 patients receiving upfront CPX, 11 were female and 19 male with a median age of 63.5 years (range 23–76 years). Of these only 11 patients met the current NICE criteria for CPX approval (10 were AML-MRC and 1 was sAML). Of the remaining 19 upfront-treated patients 12 had a diagnosis of AML-NOS and seven had a diagnosis of MDS-EB2 of whom had a complex karyotype and five had poor risk molecular features (3 with p53 deletions and two with an ASXL-1 mutation +/− RUNX-1 mutation). Overall, by standard ELN cytogenetic or molecular criteria 15/30 patients would be classified as poor risk, 13 as standard risk and 2 as good risk.

All 34 patients received a 3-day induction cycle of CPX 44/100 mg/m^2; 18 patients had a second cycle at the 44/100 mg/m^2 dose (17 receiving 2 day and 2 receiving 3 day cycles) and one patient received the lower 29/65 mg//m^2 consolidation dose. Six patients received a third cycle at the lower 29/65 mg/m^2 dose, with just one patient receiving a fourth cycle. Haematological toxicity was severe with a median duration of grade 4 thrombocytopenia of 35 days postcycle 1 (5 patients had no platelet recovery), 27 days after cycle 2 (2 patients failed to recover platelets) and 20 days after cycle 3. Grade 4 neutropenia was also prolonged. Complete remission (CR) was achieved in 22/34 patients (65%), while 9/34 patients failed to achieve CR and three patients died prior to count recovery. Of the nine patients who were refractory to CPX, five were poor risk and four were standard risk by ELN criteria. Of the 11/34 patients who achieved CR who had an MRD marker, six (55%) remained positive post CPX indicating residual disease. Five out of 22 (22.7%) patients who initially achieved a CR post CPX relapsed. Seventeen out of 34 (50%) patients are alive at a median of 24 months post-CPX completion of whom 21 were allografted (1 in prolonged aplasia). Of the 11 patients meeting NICE criteria for CPX, seven (63.6%) achieved CR and of which four were allografted; one died in CR of a cardiac event and two were unfit for transplant. All four remain alive at a median of 17 months post-transplant (range 4–30 months).

Our data confirm the efficacy of CPX in a difficult cohort of AML patients. The haematological toxicity was profound and reduction to the lower dose of 29/65 mg/m^2 dose for cycle 2 for patients in remission is now routinely done. The value of CPX-351 in the management of patients not meeting current NICE criteria (e.g. high-grade MDS with adverse genetic features and in refractory disease) suggests that an expansion of its use beyond its license might be beneficial for these patients who otherwise have a dismal prognosis.

Disclosure of Interest: T. Taylor: None Declared, J. Byrne Conflict with: Advisory board, G. Errico: None Declared, Y. Lwin: None Declared, A. Drewry: None Declared, J. Kenny: None Declared.

BSH22-PO11 | Purified phospholipase A2 from Pseudechis australis snake venom—A novel anticancer agent for the treatment of precursor-B acute lymphoblastic leukaemia

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Abstract Content: Acute lymphoblastic leukaemia (ALL) is a haematological malignancy, with an incidence rate of 790 cases per year in the United Kingdom. Of these, approximately 75% represent precursor-B ALL (pre-B ALL), a subtype of ALL characterised by immature development of B-lymphocytes. Standard treatment for pre-B ALL often involves multidrug regimens of chemotherapy agents alone or in combination with transplantation. These treatments, despite their clinical effectiveness are often poorly tolerated by patients. As such, there is an unmet clinical need to develop effective and better-tolerated therapies for the treatment of pre-B ALL.

Previously, our group has purified and pooled together three phospholipase A_2 enzymes from *Pseudechis australis* snake venom. The compound, termed PA-PLA_2 has been shown to induce necrotic cell death in two pre-B ALL cell line models. This study aims to build on these findings, employing RNA sequencing to fully elucidate PA-PLA_2's mechanism of action and exploring the systemic effects of PA-PLA_2 treatment.

Reh, SD-1, C2C12 and SH-SY5Y cell lines were used, with cell viability assessed using CellTiter-Glo. RNA sequencing

was conducted on harvested RNA from Reh and SD-1 cells under control and PA-PLA$_2$-treated conditions (Reh; 1 μg/ml and SD-1; 25 μg/ml) with data analysed using DeSeq2, Gene Set Enrichment Analysis and Database for Annotation, Visualisation and Integrated Discovery (DAVID).

Coagulation assays studying fibrinogen levels, prothrombin (PT) and activated partial thromboplastin times (APTT) were performed on citrated blood from four donors, treated with 1, 5 or 50 μg/ml PA-PLA$_2$.

In each experimental series, at least three independent experiments were performed. Data were analysed using Excel and GraphPad Prism where $p < 0.05$ was considered as significant.

Pathway and gene ontology analysis of PA-PLA$_2$-treated Reh cells revealed enrichment of tumour necrosis factor and toll like-receptor signalling pathways ($p < 0.0001$). Of the 319 enriched genes, the majority were involved in the inflammatory and immune response ($p < 0.0001$). For PA-PLA$_2$-treated SD-1 cells, DAVID analysis revealed enrichment of the PI3K/Akt signalling pathway as well as genes involved in signal transduction ($p < 0.001$). The REACTOME gene set 'RIPK1_MEDIATED_REGULATED_NECROSIS' was also found to be enriched in PA-PLA$_2$-treated Reh cells ($p < 0.01$). Pretreatment with the RIPK1 inhibitor, necrostatin-1 (30 μM) for 24 h was shown to rescue cell viability after PA-PLA$_2$ treatment (0–100 μg/ml) ($p < 0.05$) in both cell lines.

Neuronal (SH-SY5Y) and muscle (C2C12) cell viability was shown to be intact after 1 μg/ml PA-PLA$_2$ treatment ($p > 0.05$) with coagulation analysis of PA-PLA$_2$-treated blood samples revealing no changes, compared to the normal range in fibrinogen levels and PT. Extension of the APTT following treatment with 1 μg/ml PA-PLA$_2$ was observed, however, in two of the four sets of donor samples.

This study builds on previous findings, demonstrating PA-PLA$_2$'s anticancer action as involving inflammatory, immune and cell survival pathways, with RIPK1 implicated as a possible effector. Coagulation analysis did reveal PA-PLA$_2$ to induce an anti-coagulant phenotype, however, neurotoxicity and myotoxicity were not observed at low doses PA-PLA$_2$ treatment suggesting that PA-PLA$_2$ is tolerated well. Overall, this study elucidates mechanisms of action of PA-PLA$_2$ on pre-B ALL cell lines and supports the investigation of its potential therapeutic use for the treatment of pre-B ALL.

Disclosure of Interest: None Declared.

BSH22-PO12 | Management of non-severe aplastic anaemia: laboratory workup and treatment patterns

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Abstract Content: Background: Non-severe aplastic anaemia (NSAA) is a rare and heterogeneous disease characterised by a wide range cytopenias type and severity and variable evolution into myeloid neoplasms. Given the limited representation of NSAA patients in clinical trials, data on clinical workup and therapeutic strategies adopted are largely lacking.

Material and methods: We evaluated all patients diagnosed with NSAA at a single tertiary haematological center in the last 20 years. We collected baseline haematological features, bone marrow biopsies, flow-cytometry (FCM) results of marrow aspirates and mutational status by next-generation sequencing (NGS) for 69 genes involved in myeloid neoplasms. Different management strategies were registered retrospectively and categorised in 1) immunosuppressive therapy (IST, steroid ± ciclosporin, CyA), 2) eltrombopag + IST, and a watch & wait. Responses were evaluated according to 2009 Marsh criteria.

Results: We included 25 patients, mainly females (64%) and with a median age of 48 years (17–91) (Table 1). The most frequent cytopenia was thrombocytopenia ($N = 22$) and 1/3 of cases were transfusion dependent. Bone marrow samples showed a median cellularity of 15% (range 5–30), with dyserythropoiesis in 44%, dysmyelopoiesis in 16% and reticulin fibrosis (MF-1) in 16% of patients. Bone marrow microenvironment by FCM appeared enriched for lymphocytes (22% of the total cellularity, range 7–58), particularly T lymphocytes (median 72%, range 58–97). A minor infiltrate of monocytes (median 3.3%, range 0.6–5) and mast-cells (median 0.5%, range 0.02–2) was also detected. This reflects the prominent T-cell mediated autoimmunity, with minor features of chronic inflammation.

Nine patients were studied by NGS for mutations in myeloid genes and seven had negative results, while one patient harboured NF1 and U2AF1 mutations (VAF 4.7% and 4.9% respectively), and one with a concurrent familiar history of myeloid neoplasm harboured a germline SBDS mutation (VAF 48%) confirmed on cutaneous biopsy.

During a median follow-up of 21 months (range 1–187), 16 patients received treatment. These patients showed more profound cytopenias and a higher frequency of small PNH clones ($p = 0.02$) as compared to untreated cases (Table 1). Eight patients were treated with IST and the other 8 with eltrombopag plus IST. The overall response rate (CR + PR) in the former group at 3, 6 and 12 months were 66%, 100% and 100% respectively. In the second one, the corresponding

response rates were 57%, 49% and 100%, with no significant differences between treatment groups.

Seven patients (43%) experienced one or more adverse events (AEs), mostly grade 1 or 2 according to CTCAE. Grade 3/4 toxicities were all registered in the eltrombopag plus IST group and consisted in retinal thrombosis, gastroenteritis, diarrhoea and acute hepatitis. The sudden rise of transaminases and bilirubin levels was registered in 3 patients and led to treatment discontinuation. Single-agent eltrombopag was subsequently readministered due to loss of platelet response in all patients, with no further toxicity to date.

In conclusion, we observed a high heterogeneity of NSAA patients. FCM showed a prominent T-cell infiltrate, consistent with disease pathogenesis. Treatment with IST +/− eltrombopag led to a significant clinical improvement, however, the occurrence of G3 liver toxicity in patients treated with CyA plus eltrombopag demands for further studies and advice close monitoring of liver function tests.

Disclosure of Interest: None Declared.

Abstract Table 1: Baseline features and outcome in NSAA patients

	Steroids ± Ciclosporin ***N*** **= 8**	**Eltrombopag ± Ciclosporin and Steroids** ***N*** **= 8**	**Untreated** ***N*** **= 9**
Median age, years (range)	26.5 (20–72)	51 (35–91)	45 (17–63)
Male, *N* (%)	4 (50%)	2 (25%)	3 (33%)
Female, *N* (%)	4 (50%)	6 (75%)	6 (66%)
Transfusion dependence, *N* (%)	2 (25%)	6 (75%)	0
Median follow-up, days (range)	546 (24–1507)	566 (152–1999)	1037 (185–5688)
Laboratory values, median (range)			
Hb, g/dl	9.6 (7.7–13.9)	9.0 (6.1–11.5)	12.9 (10.1–15)*
ANC ×10^9/l	1.02 (0.46–1.38)	1.25 (0.59–4.99)	1.42 (0.57–5.25)
ALC ×10^9/l	1.40 (0.68–2.1)	1.21 (0.37–2.12)	1.17 (1.02–2.84)
PLT ×10^9/l	37 (18–61)	23 (6–64)	111 (59–216)*
Reticulocytes ×10^9/l	0.05 (0.039–0.104)	0.06 (0.009–0.108)	0.04 (0.029–0.098)
Endogenous EPO U/l	414 (3.9–1052)	119 (85.5–898)	17 (14–40)
LDH, UI/l	179 (151–243)	197 (140–347)	180 (136–322)
Treatment response[1]			
3 months—sample size, *N*	6	7	
CR, *N* (%)	1 (16%)	4 (57%)	—
PR, *N* (%)	3 (50%)	—	—
6 months—sample size (*N*)	5	6	
CR, *N* (%)	1 (20%)	1 (16%)	—
PR, *N* (%)	4 (80%)	2 (33%)	—
12 months—sample size (*N*)	3	6	
CR, *N* (%)	—	—	—
PR, *N* (%)	3 (100%)	6 (100%)	—
Adverse events			
Grade 1 and 2	Gengival Hypertrophy Striae rubrae	CMV reactivation EBV reactivation Diabetes Diarrhoea Gengival Hypertrophy Hirsutism	0
Grade 3 and 4		Retinal thrombosis Acute hepatitis Diarrhoea Gastroenteritis	

*p value <0.05 in untreated versus treated patients.

[1]Response criteria according to "Guidelines for the diagnosis and management of aplastic anemia", Marsh 2009.

Education & Professional

BSH22-PO13 | Reporting Language in Haematological Malignancies

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Abstract Content: While there is existing research for reporting language, there has been none within haematology. Pathological reporting is crucial for diagnoses by means of peripheral blood films and trephines. Discrepancies in the interpretation of this language can ultimately affect patient treatment. Existing literature has suggested that there are different perspectives between reporters and service users. Reporters may purposefully attach ambiguity to diagnoses to reflect the limitations of a sample. These may include lack of a complete clinical picture and the quality of a sample. There may also be a medicolegal factor; reporters may not want to be attached to absolute diagnoses when this is not completely certain. Service users may prefer more unequivocal language to definitively guide management. There are also other wider factors surrounding reporting that may affect a diagnosis, for example more regular interdepartmental discussions. Reported cases on HMDS (HODS) were accessed to generate the following eight commonly used adjunct terms: 'suspicious of', 'compatible with', 'diagnostic of', 'suggestive of', 'in keeping with', 'consistent with', 'features are those of' and 'cannot be excluded'. A questionnaire was then created which allowed responders to express the level of certainty they attach to each term, expressed as a percentage. Participants were also asked to rank the terms according to their certainty and to express if the term had more weighting if it was for a positive diagnosis or that of a remission. There was a total of 47 responders, of which 33 were self-described as reporters and 14 as service users. Two responses, one reporter and one service user, were excluded. Reporters consisted of consultant histopathologists, biomedical scientists, consultant haematologists and haematology trainees. Consultant haematologists also made up the majority of the service user group, as the role could be applied to both. Consultant clinical oncologists and haematology trainees also featured here. Quantitative data analysis allowed comparison between these two groups. An unpaired t-test was calculated for each term, comparing the mean certainty of the reporter and service user groups. In 2/8 terms, there was a statistically significant difference in this value. These terms were 'suspicious of' and 'compatible with'. The mean certainty that reporters perceived for 'suspicious of' was 59.45% and for service users this was 45.38%. For 'compatible with' the mean certainty for reporters was 82.47% and for service users this was 71.92%. The term with the overall highest mean certainty was 'diagnostic of' and the term with the least was 'cannot be excluded'. The terms with the overall greatest range of certainty were 'suspicious of' and 'cannot be excluded'; both 70% and the term with the least range was 'diagnostic of'; 10%. These data have shown that there is discrepancy between reporters and service users for these adjunct terms, namely 'suspicious of' and 'compatible with'. It also shows that there is a wide range of interpretations generally for most terms. Therefore, more consideration should be applied to the usage of these adjunct terms and departments might consider how they standardise such reporting. The next step in this project is to gather a focus group and gain more in-depth qualitative data. This would be to discuss not only the terms used in the questionnaire, but the wider themes of communication previously described.

Disclosure of Interest: None Declared.

Abstract Table:

	Suspicious of	Compatible with	Diagnostic of	Suggestive of	In keeping with	Consistent with	Features are those of	Cannot be excluded
Overall mean	55.39	79.42	97.80	68.61	83.31	85.84	88.59	29.88
R mean	59.45	82.47	97.72	68.83	85.44	87.65	89.58	30.17
SU mean	45.38	71.92	98.00	68.08	78.08	81.54	86.15	29.17
Overall range	70 (20–90)	60 (40–100)	10 (90–100)	60 (30–90)	60 (40–100)	50 (50–100)	50 (50–100)	70 (0–70)
R range	70 (20–90)	60 (40–100)	10 (90–100)	60 (30–90)	60 (40–100)	50 (50–100)	50 (50–100)	70 (0–70)
SU range	55 (25–80)	50 (50–100)	10 (90–100)	50 (40–90)	50 (50–100)	50 (50–100)	40 (60–100)	50 (10–60)

BSH22-PO14 | Audit outcomes of the Referral Pathway for Haematology Patients to the Intensive Care Facility at the University Hospital of Wales During the COVID Pandemic

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Abstract Content: Patients with haematological conditions can become critically ill due to their underlying disease or secondary to treatment complications. The BSH published guidelines on the management and admission to intensive care unit (ICU) of critically ill adult patients with haematological malignancies in 2015 (Wise et al, BJHaem) Here we present the first published data on compliance with this guideline at the University Hospital of Wales, Cardiff.

We performed a retrospective study of 30 haematology patients referred to ICU between September 2020 and July 2021. Patients were identified from an intensive care database and individual patient data were collected using patients' medical records. The BSH audit template was used to evaluate the patient pathway. Additional data such as performance status, advanced care planning were assessed and are shown in the table below.

All were monitored by NEWS score throughout admission. Referral to ICU was made by haematology registrars in 42%, medical registrars in 26% and haematology consultants in 32%. Sixteen (53%) patients had ICU reviews as part of planned discussions which occurred at a median of 23 (2–243) h of becoming unwell, whereas 14 (47%) patients were reviewed by ICU at the time of a crash call. Importantly, the majority (66%) of crash calls occurred outside normal working hours highlighting the importance of adequate out of hours (OOH) medical cover. With regards to communication, 68% of patients admitted to ICU had documentation with either patient or relative at the time of ICU admission.

Of the patients referred, 19 (63%) were accepted for admission to the ICU. The average length of hospital stay prior to ICU admission was 17 days and the average length of stay in ICU was 5 (1–58) days. The majority of patients (68%) had sepsis and 14 (74%) required invasive ventilation. Eight cases were neutropenic and had a higher death rate of 75% compared with 55.6% of non-neutropenic patients. Overall, mortality rate during ICU stay was 68%. By contrast, in eight patients who were initially deferred but later accepted, the mortality rate was 75%. These patients were accepted for transfer to ICU typically 2–3 days after the initial deferral. Haematology inputs were documented in 89% of patients during the ICU stay.

In summary, clear documentation of escalation plans and resuscitation status is essential to enabling prompt treatment decisions in a deteriorating patient. Our audit highlights the need for improvement in this area and we take lessons from medical admissions during the COVID pandemic where all patients have a clear escalation plan. The data also highlighted the majority of crash calls occurred OOH. A recent introduction of a remodified critical care outreach service, PART (patient at risk team) will be crucial for service development and coordination of care between ICU and haematology. In a COVID era regular ICU and haematology communication may be challenging thus virtual mortality and morbidity meetings can be helpful. Communication with patients and families is encouraged at all phases of care with more emphasis around the ICU admission. A re-audit is planned in 1 year to evaluate practice which will evaluate the additional benefit of the PART team in co-ordination of care.

Disclosure of Interest: None Declared.

Abstract Table:

Parameter (documented at time of admission)	Stem cell transplant (BUT) *n* = 12	General haematology *n* = 18
Performance status	91.6%	55.6%
Prognosis	100%	66.7%
Escalation plans	33.3%	5.6%
Resuscitation status	16.7%	16.7%

BSH22-PO15 | Choose your own story: Combining interactive voting technology with high-fidelity patient simulation for undergraduate transfusion teaching

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Abstract Content: Transfusion is a common, high risk but potentially life-saving clinical intervention where effective education is critical. In haematology teaching, a key task is to enable learners to relate basic science to the clinical setting. As previously demonstrated in preclinical teaching at Newcastle University, lecture theatre-based simulations can illuminate clinical relevance to large groups of students. With interactive voting technology, the entire group of students is able to apply their knowledge to the simulated case (Guilding 2016). Using this interactive format, we devised a transfusion revision session based on two simulated emergencies. Our cases pivoted on the commonest causes of transfusion-related death in the 2020 SHOT report: transfusion-associated circulatory overload and transfusion delays.

Preclinical medical students at University of Bristol receive lectures introducing transfusion concepts and science. Following these lectures, our practical session was delivered for all second-year medical students in three

separate sessions (166 students in total; approximately 55 in each group) each lasting 90 min. Interactive simulated emergencies were interwoven with a lecture revising relevant transfusion concepts, such as blood group compatibility. SimMan was visible at the front of the lecture room. During the simulation sections, clinical teaching fellows and haematology registrars played the roles of the doctor and patient. The lecture screen showed SimMan's vital signs as on a patient monitor. The entire lecture room engaged with clinical decision-making using the smartphone-based quiz app Mentimeter. At key points, the students were asked to vote on the app on the best course of action. For example during the second unit of red blood cell transfusion, SimMan desaturated with bibasal crackles and became tachycardic. Students had to choose between administering adrenaline, antibiotics, chlorphenamine, diuretics or a fluid bolus. The option with the most votes was followed and the students saw the clinical outcome in real time.

Feedback was very positive. 105 of 146 responders (72%) agreed or strongly agreed that the use of SimMan enhanced their learning experience on a 5-point Likert scale (88% response rate). Overall, students reported enjoying the use of voting technology and described the session as very interactive. Analysis of free-text qualitative feedback highlighted two main themes:

- The simulations embedded the learning in the clinical context: students described the session as 'very clinically focussed' and appreciated the 'clinical relevance'
- The session was engaging: students described it as an 'exciting emergency', 'engaging' and 'feels realistic'

Our session demonstrates a highly engaging and interactive format for large group teaching. Undergraduate haematology teaching poses particular challenges in the need to relate extensive conceptual content to clinical practice. Our sessions showed that engagement with realistic simulated scenarios can bring basic haematological principles to life. In institutions without access to SimMan, the session could be delivered effectively with an affordable patient monitor app such as SimMon. Combining simulation with interactive voting technology could be applied to a range of topics, such as neutropenic sepsis or acute painful crisis in sickle cell disease, to facilitate engaging and clinically focussed large group haematology teaching.

Disclosure of Interest: None Declared.

BSH22-PO16 | Under or delayed transfusion: Risk factors leading to patient deaths

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Abstract Content: The urgent provision of blood components is vital for life-threatening bleeding and severe anaemia. A rapid, focussed approach is required as delays or undertransfusion can result in preventable death or end-organ damage. This review looks at cases of under or delayed transfusion of blood components reported to Serious Hazards of Transfusion (SHOT), the UK haemovigilance scheme from 2010 to 2019. The diagnosis and reasons for transfusion were reviewed together with the outcomes.

Sixty-eight cases are included in the analysis. In 42/68 (61.8%) the transfusion priority was emergency or urgent. Of these, nine were paediatric cases and in 8/9 (88.9%), there were errors in prescription or transfusion volumes and one was failure to have platelets available.

Twenty-two out of 68 (32.4%) patients died, 16 (16/22, 72.7%) deaths were related to the transfusion event. Red cell transfusions were indicated in all these cases except one who required only FFP. Out of the 16 transfusion-related deaths, 10 were in patients with gastrointestinal (GI) bleeding. GI bleeding was not recognised in a timely manner in four patients who were not transfused at all. There was a failure to activate the major haemorrhage procedure in 4 cases. One patient was undertransfused due to fear of transfusion-associated circulatory overload. The other transfusion-related deaths included a patient with major obstetric haemorrhage, two cases of abdominal aortic aneurysm, one patient with autoimmune haemolytic anaemia (death was from a cerebrovascular event related to severe anaemia), one bleeding during surgery for fractured neck of femur and a patient with severe coagulopathy who did not receive FFP.

Twenty-seven out of 68 (39.7%) patients required various blood cell components without red cells. FFP alone was needed in 23 cases and of these, 21 were transfused an insufficient amount usually one bag instead of a standard dose of 4. One case was a major haemorrhage delay and the other was failure to give 4 units to a sick patient with coagulopathy. Eight of these cases were in patients with liver disease.

Two cases of undertransfusion of cryoprecipitate were reported where the dose given for each adult was one pool instead of the recommended two. One of these was a person with liver disease, the other had low fibrinogen. Two cases involved only platelet transfusions—platelets were not available for a baby undergoing cardiac surgery; this resulted in chest being kept open and transfusion of additional components for bleeding while waiting for platelets to arrive. The other case was a person with chemotherapy-induced

cytopenias for whom platelets were ordered (count 10×10^9/l) but not given.

Transfusion delays and undertransfusions are preventable. GI bleeding can be difficult to recognise and assess and can be particularly severe in elderly patients on anticoagulants. Improved decision-making, patient monitoring and education, addressing factors contributing to errors, building safer systems and continued vigilance are vital in improving transfusion safety. All staff responsible for authorisation of blood component transfusion must be aware of the different component indications and the appropriate dose calculations for fresh frozen plasma and cryoprecipitate for all age groups.

Disclosure of Interest: None Declared.

BSH22-PO17 | Reducing Unnecessary Blood Tests on a Haematology Ward at Salisbury NHS Foundation Trust

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Abstract Content: Laboratory blood testing is an effective tool in managing patients on a haematology ward. However, we felt that excessive blood testing was performed at Salisbury NHS Foundation Trust - a sentiment we expect to be widespread across the NHS. Salisbury is a district general hospital and its haematology ward covers a mix of patients including those undergoing intensive chemotherapy and autologous stem cell transplantation. Consultant ward rounds are twice weekly and as such blood test organisation is primarily led by the ward-based junior doctors. At Salisbury, we proposed a Blood Test Schedule (BTS) for all haematology inpatients with the aim of using the minimum effective number of blood tests without compromising patient care and retaining junior doctor autonomy.

Notwithstanding the Becton Dickinson manufacturing global shortage of blood tube bottles, many other good reasons to strive to use the minimum effective number of blood tests exist. These include reducing patient discomfort, bruising, infection, thrombophlebitis, iatrogenic anaemia and its consequences and reducing costs of materials and staff time in the ward and laboratory. Additionally, the environmental impact of creating unnecessary waste and its processing are significant.

The BTS has four defined levels of blood testing intensity, namely levels A-D. Level A patients require the most intensive blood testing and include acute leukaemia, high-grade lymphoma and symptomatic myeloma patients alongside those undergoing intensive chemotherapy or autologous stem cell transplant. Level A patients require daily testing of FBC, U&E, LFT, CRP, Bone Profile and Magnesium. The BTS defines levels B, C and D with decreasing blood panels and reducing frequencies and is designed to allow patients to move between levels as their clinical progress allows.

Using the BTS as a benchmark of appropriate blood testing, a retrospective audit was conducted on the haematology ward at Salisbury in January 2021. This audit was performed across a 2-week period and is equivalent of 85 inpatient days with a balanced spread of patients across BTS levels A-D. Overall this showed 10.4% of tests taken were inappropriate. The audit cycle was then completed with a prospective audit following the introduction of the BTS in July 2021. Again, a 2-week period was evaluated equivalent of 117 inpatient days with a balanced spread across levels A-D as per the BTS. The second audit cycle showed improvement in number of unnecessary blood tests done with a reduction to 6.9% from 10.4% yielding a 3.5% improvement across the first implementation of this new schedule.

This 3.5% reduction in blood testing accounts for 15 blood tests per fortnight. The average cost to Salisbury per blood test is £3.15. As such this is a cost saving of £47.25 per fortnight equivalent to £1228.50 per year. With ongoing use and perfect implementation of the BTS the potential annual saving could reach £3276 per year alongside the non-quantifiable reduction in patient harm and improved environmental impact.

We propose the application of our Blood Test Schedule to be made available for use across Haematology Wards in the NHS. We have not tested this in the allogeneic stem cell transplant setting and these should be excluded pending further analysis. With speciality-specific modifications similar Blood Test Schedules could be created for other specialities to optimise blood test usage across the NHS.

Disclosure of Interest: None Declared.

BSH22-PO18 | A multidisciplinary approach to improvement of a bone marrow biopsy service: advice from both service users and service providers

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Abstract Content: Local patient complications of bone marrow biopsy (BMB) prompted a review of our service in a UK tertiary haematology centre that performs approximately 1000 BMBs per year. BMB is a necessary diagnostic tool within haematology; it is invasive, with low rates of serious adverse events. However, there is uncertainty around less severe but patient-relevant complications.

An online survey of staff who request or perform BMB was undertaken in advance of discussion of the complication events at a morbidity and mortality meeting. The survey was fed back at a subsequent departmental education meeting. Survey comments and feedback during the meetings were recorded. This provided a forum for extensive discussion; staff expressed a desire for change in the service and offered many ideas to improve service efficiency, patient experience

and to mitigate risk. A multidisciplinary team (MDT) was motivated to form a service improvement group.

A patient survey was distributed to 100 patients that had recently used the service; 44 surveys were returned. Feedback was mostly positive and results were shared with staff. Information about the procedure, feeling reassured or relaxed and minimising pain was mentioned by several patients, reminding us that addressing patient uncertainty, anxiety and analgesia is imperative.

Additional activities were undertaken to understand how the service currently runs. Day unit nursing and medical, administration and laboratory staff met to map the process from BMB request to results. A time in motion study of several BMBs was performed to record the time taken for each procedure and how this time was divided. From preparation to documentation, the range was 68–90 min. The standard time allocated to a doctor who is often unassisted in the procedure room is 45 min. A snapshot audit identified that some of the time taken was to make the laboratory requests or review anticoagulation, which are intended to be done in advance; occasionally, cancellations resulted. We have reviewed this data to identify targets to increase efficiency and staffing support.

To date, a new patient information leaflet has been created to address the clarity and depth of information provided to patients, including more detailed postprocedural advice and departmental contact details. A preprocedure checklist will be trialled as suggested by a survey respondent. The Standard Operating Procedure is under review to clarify roles, responsibilities and processes, particularly in the context of increasing molecular monitoring out of region. Incident reporting of complications has been encouraged. A 'Patient Safety Registrar' will work with our Patient Safety Manager to oversee quarterly discussions of incidents within our departmental teaching because we have found that this improved staff engagement during this project. We have found that this MDT approach integrated into departmental teaching has resulted in excellent engagement, idea generation and momentum despite the staffing pressures during the Covid-19 pandemic. Progress will be reviewed after a year.

Disclosure of Interest: None Declared.

BSH22-PO19 | Home transfusions—balancing safety with individualised care

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Abstract Content: Blood transfusions are an essential part of supportive care for certain patient cohorts, particularly those on palliative care. Most transfusions occur in the hospital setting, including community hospitals. Transfusion in the patient's home supports individualised care, reduces demand on acute services and inconvenience for patient travel to hospital. Decision to undertake home transfusions requires assessment of risks and benefits, with regular review. Risk of acute transfusion reaction in any setting is rare but can result in major morbidity or death. This review looks at adverse events and reactions reported to Serious Hazards of Transfusion (SHOT), the UK haemovigilance scheme, where the transfusion was performed in the patient's home.

SHOT cases submitted 2010–2020 were identified using the terms 'home', 'home transfusion' and 'patient's home'. Data were manipulated in MS Excel identifying reactions (febrile, allergic and hypotensive [FAHR], transfusion-associated circulatory overload [TACO]) and events (right blood right patient (RBRP), avoidable, delayed and over/under-transfusion [ADU], incorrect blood component transfused—specific requirements not met [IBCT-SRNM]).

20 cases of home transfusion were identified. FAHR accounted for 10/20 cases, IBCT-SRNM (3/20), HSE (3/20), RBRP (2/20), TACO (1/20) and ADU (1/20). Where patient sex was recorded, 12/19 were male. Age range 3–90 years (median 66, SD 24.9). Red cell components were implicated in 12/20 cases, platelet concentrates in 7/20 cases and one fresh frozen plasma. Patient underlying condition was haematological in 12/20 cases, others included pancytopaenia, angiodysplasia, metastatic cancer and anaemia. Chronic anaemia was the indication in 8/12 red cell transfusion cases and prophylaxis for 4/7 of platelet transfusions. Reactions (n–11) were febrile (5/11), allergic reactions (3/11), TACO (1/11), 1 anaphylaxis and 1 unclassified. 7/11 patients (6 FAHR and 1 TACO) required hospital admission as a result of the reaction. Four patients were identified as not suitable for home transfusion after the event, SHOT expert review noted one patient should have been ineligible in the first place due to risk of TACO. Adverse events (n = 9) included cold chain failures (2/9), one failure to inform the laboratory of home transfusion, failure to provide irradiated red cells (2/9), errors in labelling (2/9), incorrect administration rate, failure to provide antigen-negative blood and delay due to an incorrect Hb result.

There are no data regarding the number of home transfusions in the UK, therefore it remains unclear whether reactions and errors are over-represented in these cases. Careful consideration should be given to the eligibility of patients to receive home transfusion, particularly the risk of TACO and previous transfusion reactions, before this regime is implemented. No data were available regarding staff performing the transfusions, nurses administering home transfusions must be transfusion trained and competent in identification and management of reactions. There must be robust processes for urgent transfer to hospital. There are no national guidelines for safe practice for home transfusions, including informed consent. Home transfusion is an increasingly important component of patient care, particularly during the COVID-19 pandemic to minimise risk for vulnerable patients, the infrastructure supporting this must have patient safety at its core.

Disclosure of Interest: None Declared.

BSH22-PO20 | Endocrine Complications in Patients with Thalassaemia: A Single Centre Experience

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Abstract Content: Aims: Endocrine complications secondary to iron overload is not uncommon in Thalassaemia patients and affects almost all major endocrine glands. The UK Thalassemia Society (UKTS 2016) has described practice standards for endocrine review in all such patients receiving blood transfusion. This audit aims to examine the practice at our centre in comparison to national standards.
Methods: We did a retrospective audit of all Thalassaemia patients followed up in our centre in 2019–2020. Variables included were demographical data and annual review and treatment of diabetes, thyroid/gonadal function and bone profile.
Results: Out of a total of 34 patients (mean age ± 30 years; 56% female & 44% male) 79% had Beta thalassaemia major, 9% Beta thalassaemia intermedia; 6% Allograft beta thalassaemia major; 3% HbE/Beta and 3% HbS/Beta.
Eight out of17 females (24%) were diagnosed with hypogonadism and were currently on HRT. Three out of 12 males (25%) had low morning testosterone levels and were on LA Testosterone injections (Nebido). Annual TFT was checked in 23 out of 34 (68%) patients—six (18%) patients were diagnosed with hypothyroidism and were on Thyroxine treatment. Nineteen patients had normal TFT. Six patients did not have annual TFT checked. 12/34 (35%) patients were diagnosed with diabetes – all have regular annual reviews and CV risk assessments. Four (12%) patients had IFG/IGT. Fructosamine level was checked in 16/34 (47%) patients. Six of these 12 patients were on Insulin, four on oral hypoglycaemic agents and two are diet controlled.
Calcium level was checked in 27 out of 34 (79%) patients—five of them (15%) had hypocalcaaemia. Vitamin D was checked in 22 out of 34 (65%) patients—nine (26%) had Vitamin D insufficiency, six (18%) had Vitamin D deficiency. Thus, 44% of those tested had some form of Vitamin D deficiency. DEXA scan performed in 21 out of 34 (62%) patients—10 (29%) had osteoporosis and six (18%) had osteopenia. Thus, 47% of the Thalassaemia patients had some decrease in their BMD.
Conclusion: Review of endocrine complications in patients with Thalassaemia is crucial for early recognition and intervention where necessary. In comparison to UKTS standards, our centre monitored endocrine complications annually at significantly higher rate than national standards (100% vs. 54%; $p < 0.0001$). Especially good was vitamin D level monitoring (65% vs. 54%) and DEXA scanning (62% vs. 50%).
Review of hypogonadism (59% vs. 62%), thyroid function (68% vs. 94%), calcium levels (79% vs. 92%), diabetes screening (35% vs. 57%) and PTH level estimation (12% vs. 90%) were performed at much lower rates compared with national standards.
Thus, it appears that while the annual review is performed well for all patients in our centre, there are gaps in adherence to national standards in certain specific endocrine reviews. We are planning to plug this gap after appropriate interventions which will help improve our current practice.
Disclosure of Interest: None Declared.

BSH22-PO21 | The Haematology Taster Day—Inspiring the next generation of haematologists

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Abstract Content: We designed and organised the first national Haematology Taster Day to inform junior doctors about a career in haematology and attract them to the specialty. The day was supported by the British Society of Haematology (BSH).
Haematology is often seen as a highly complex, academic specialty with doctors who are sometimes jokingly referred to as 'vampires who prefer microscopes, blood films and coagulation cascades to patients' (Eccles & Sanders, 2009). We wanted to showcase our specialty, highlighting the importance of teamwork, effective communication with patients and their families and the exciting and ever-changing nature of haematology which makes keeping up to date with current research a must. We wanted to illustrate what working in haematology looks like while demystifying aspects of the specialty that are less known to junior doctors, such as "the lab".
We advertised via email to UK training programme leads and through the BSH website. Due to restrictions in travel and face-to-face teaching we organised a virtual event with interactive talks by doctors and specialist nurses as well as break-out group tutorials. Topics included 'a day in the life of a haematology consultant /registrar', 'the emotional side of working in haematology', 'the lab", "interesting cases", as well as talks on out of programme opportunities and the application process. Forty junior doctors (74% IMT, 24% Foundation doctors, 2% Clinical Fellows) attended with a further 60 on the waiting list for the next event.
Participants completed a pre and postcourse feedback form, which highlighted potential barriers to applying for haematology training. These included concerns about the requirement to perform procedures, the competitive nature of the specialty, and the prospect of sitting further exams. Trainees were also concerned about the emotional aspects of haematology and heavy workload within the specialty.
The postcourse feedback was extremely positive. Participants rated all speakers highly and were on average 15% more likely to apply for haematology. The success of our first Haematology Taster Day demonstrates that there is an

appetite from junior doctors to find out more about our specialty. We plan to run this day on an annual basis and hope to be able to offer a face-to-face format next year. Greater use of social media and publicity from previous attendants should enable us to attract more applicants with each successive year.

Disclosure of Interest: None Declared.

BSH22-PO22 | Strangers in a foreign land: Foundation year 1 doctors' introduction and experiences in Haematology-Oncology

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Abstract Content: The foundation programme is a unique time in medical careers, with short-term rotations in different clinical environments. Haemato-oncology is a highly specialised service, with its own set of specific conditions, investigations and treatments and Foundation doctors may have had minimal exposure to these as students. There are also unusual emotional challenges to the work in this department. Patients are often young, deteriorations can be sudden, and there are often strong bonds formed with patients. St Bartholomew's is a tertiary Haemato-oncology centre which performs autologous and allogeneic stem cell transplantation, requiring doctors to have an understanding of complex procedures and treatments. Providing sufficient induction to Foundation year 1 (F1) doctors rotating into the Haemato-oncology department is crucial to doctor wellbeing, patient safety and the smooth running of the service.

We conducted a quality improvement project focussed on evaluating current induction materials, collecting feedback from previous F1 doctors about their experience on the rotation, and creating an improved induction pack for future F1 doctors. Trainees who had completed 4-month rotations in Haemato-oncology at St Bartholomew's Hospital over the past 1–2 years responded to our survey outlining their opinion on the induction materials. We used both qualitative and quantitative approaches through binary and free text questions, to identify what information doctors saw as crucial for adequate orientation to the speciality and job role.

The initial survey was sent to seven previous F1 doctors. Results highlighted more than half of previous trainees did not read the entire induction document provided by the department. While the majority reported that it helped prepare them, 42% felt it did not translate to the real experience. Half of the trainees reported they felt the document was not specific or tailored to F1 doctors, asking for 'shorter, more visual and less dense information', with 'more practical tips specific to the F1 role'. Trainees also felt induction was an important time to discuss the emotional demands of the job, with some trainees quoting it as the most emotionally challenging job they had during foundation training.

Using information from the surveys, advice of our senior colleagues and our own daily experience as F1 doctors in the department, we produced a new comprehensive induction booklet. We considered how to make it user friendly, digestible and easy to refer back to. We have now collected data from the first F1 doctors to use our booklet, and will continue to do so in each rotation for ongoing development. Our initial feedback shows all of respondents read the whole booklet and found the material balanced and easy to read. One respondent reported it as a 'good concise resource of what to expect'. We have also commenced a regular debrief session co-led by a haematologist and psychologist to allow space for junior doctors to consider the emotional impact of their role.

It is important to consider junior doctors and the role they play in the team. By improving induction, the knowledge, efficiency and cohesion of the team are enhanced, which can benefit patient care. Our work demonstrates the potential for empowering junior doctors to review and improve their induction, and to draw attention to aspects of the job which may be less obvious to more senior colleagues.

Disclosure of Interest: None Declared.

BSH22-PO23 | Developing the role of the Haematology ward in undergraduate medical education with the creation of a novel clinical placement

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Abstract Content: Within healthcare in the United Kingdom, there is an ever-increasing demand for more doctors. To try and improve supply, the government has increased the number of medical school places available. In order to train this increased number of medical students effectively, novel ways are required to enhance the number of clinical placements available. Within our trust and medical school, haematology wards have generally been neglected when creating clinical placements. Furthermore, medical students at our medical school get very little exposure to clinical haematology. Our undergraduate education department and haematology department have liaised to create a new trial clinical placement for year 6 (Y6) medical students as part of a senior medicine placement.

Two Y6 medical students were attached to the haematology ward for each allocated 4-week placement. A total of ten Y6 medical students rotated through five clinical placements. A comprehensive day one trust and ward induction was provided to students. Learning objectives were extrapolated from the medical school curriculum, with the focus of the placement on developing generic F1 level clinical skills. Ward-based experience was complimented with two formal sessions each of simulation teaching and bedside teaching delivered by clinical teaching fellows. At the end of each

placement students were invited to complete an anonymous electronic feedback survey with a short series of Likert scale and free text questions. Following the completion of the initial five placements, medical ward staff were invited to complete a corresponding anonymous electronic feedback survey.

In total, eight out of 10 students completed the feedback survey. All students had either never been on a Haematology ward or had spent less than a week on a Haematology ward. Following the placement 87.5% (7/8) of students reported that their confidence in clinical Haematology had improved. 87.5% (7/8) of students agreed or strongly agreed that they had been able to achieve the senior medicine learning outcomes. 87.5% (7/8) students agreed or strongly agreed that Haematology was a useful placement for senior medicine.

In total, six doctors completed the feedback survey; two F1/SHOs, two registrars and two consultants. Most doctors (5/6) spent several hours a day interacting with the students, with junior doctors spending more time teaching medical students than consultants. 33.3% (2/6) of respondents agreed or strongly agreed that they were aware of the learning objectives of Y6 medical students. 66.7% (4/6) of respondents agreed or strongly agreed that Y6 medical students displayed expected levels of professionalism. One respondent did raise concerns regarding attendance. All respondents agreed or strongly agreed that Y6 medical students were a valuable addition to the team, with 83.3% (5/6) agreeing or strongly agreeing that they enjoyed having Y6 medical students on the ward.

Overall, we have been able to create a feasible and effective clinical placement in Haematology that has simultaneously enabled students to achieve their learning objectives and improve their confidence in Haematology. Furthermore, the addition of medical students has enhanced the experience and enjoyment of staff. Our experience demonstrates the valuable role the Haematology ward can have in undergraduate medical education. We plan to build on this role with the development of further clinical placements in Haematology across different undergraduate year groups.

Disclosure of Interest: None Declared.

General Haematology Including ITP & Myeloproliferative Disorders

BSH22-PO24 | Does Early Intervention in Myelofibrosis Impact Outcomes? A Pooled Analysis of the COMFORT I and II Studies

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Abstract Content: Myelofibrosis (MF) is characterised by cytopenias, splenomegaly, burdensome symptoms and poor overall survival (OS). Few studies have investigated if earlier intervention with targeted MF therapies affects response and OS. In a pooled analysis of the COMFORT I and II trials of ruxolitinib (RUX), patients (pts) who received RUX at randomisation or after crossover from placebo (PBO) or best available therapy (BAT) had improved OS. The objective of this analysis was to assess the association of MF disease duration before treatment with disease outcomes using pooled COMFORT data.

COMFORT I (NCT00952289) and COMFORT II (NCT00934544) were phase 3 trials of RUX *versus* PBO or BAT, respectively, in pts with intermediate-2 or high-risk MF. In this post hoc analysis, data from RUX-treated pts in both studies were combined (RUX group), and data from the PBO/BAT arms were pooled (control group). Pt subgroups were defined based on disease duration before treatment initiation (≤12 months or >12 months from diagnosis). Assessments included frequency of thrombocytopenia (platelets [PLT] <100 Gi/l or PLT transfusion) and anaemia (haemoglobin <100 g/l or red blood cell transfusion) events, spleen volume response (SVR; spleen volume reduction ≥35% from baseline [SVR35]), symptom response (MF-Symptom Assessment Form total symptom score [TSS] reduction ≥50% from baseline [TSS50]; available in COMFORT I only), and OS. OS was assessed using the Kaplan–Meier method; pts randomised to PBO/BAT were included in the PBO/BAT group regardless of crossover. A multivariable analysis (MVA) using a logistic regression model was used to examine factors associated with SVR.

There were 525 pts in the analysis (RUX: ≤12 months, $n = 84$; >12 months, $n = 216$; PBO/BAT: ≤12 months, $n = 66$; >12 months, $n = 159$). The median age across groups ranged from 65 to 70 years. Baseline clinical characteristics were generally similar across subgroups, but pts with shorter *versus* longer disease duration were slightly younger with higher

Abstract Table: Clinical Outcomes of Patients With MF Stratified by Disease Duration Before Treatment Initiation

Outcome	RUX		PBO/BAT	
	MF ≤ 12 months (*n* = 84)	MF > 12 months (*n* = 216)	MF ≤ 12 months (*n* = 66)	MF > 12 months (*n* = 159)
SVR				
Change from baseline in spleen volume, mean				
Wk 24	−34.7	−28.8	8.2	6.2
Wk 48	−35.6	−27.5	14.7	5.7
Patients with SVR35,[†] %				
Wk 24	47.6	32.9	0	0.6
Wk 48	44.0*	26.9	0	0
Duration of SVR, median (95% CI), wks	NR (135.0–NR)	229.6 (108.0–NR)	NA	NA
TSS (COMFORT I)				
Change from baseline in TSS, mean	*n* = 38	*n* = 91	*n* = 31	*n* = 72
Wk 24	−52.4	−43.5	30.3	46.7
Patients with TSS50,[‡] %	*n* = 41	*n* = 114	*n* = 47	*n* = 106
Wk 24	56.1	39.5	8.5	3.8
OS				
Deaths, %	34.5	45.8	47.0	54.1
240-wk survival, % (95% CI)	63.3* (51.4–73.0)	56.8 (49.4–63.5)	49.4 (35.7–61.7)	40.7 (32.3–48.8)

Abbreviations: BAT, best available therapy; MF, myelofibrosis; NA, not assessed; NR, not reached; OS, overall survival; PBO, placebo; RUX, ruxolitinib; SVR, spleen volume response, SVR35, spleen volume reduction ≥35% from baseline; TSS, total symptom score; TSS50, TSS reduction ≥50% from baseline.

*Significant difference ($p < 0.05$) *versus* MF >12 months.

[†]SVR35 data were missing from 111 patients at Week 24 (RUX ≤12 months, *n* = 9; RUX >12 months, *n* = 28; PBO/BAT ≤12 months, *n* = 20; PBO/BAT >12 months, *n* = 54) and 222 patients at Week 48 (RUX ≤12 months, *n* = 17; RUX >12 months, *n* = 50; PBO/BAT ≤12 months, *n* = 47; PBO/BAT >12 months, *n* = 108).

[‡]TSS50 data were missing from 76 patients (RUX ≤12 months, *n* = 3; RUX >12 months, *n* = 23; PBO/BAT ≤12 months, *n* = 16; PBO/BAT >12 months, *n* = 34).

blood counts. Among pts who received RUX, fewer thrombocytopenia events were observed among those treated earlier (≤12 months vs. >12 months), with differences seen as early as Wk 4–8 on treatment (18% vs. 33%) and sustained over time; a similar trend was observed for anaemia events (Wk 4–8, 59% vs. 72%). The proportion of pts with SVR35 was greater among those who initiated RUX earlier (≤12 months vs. >12 months) at Wk 24 (48% vs. 33%; $p = 0.0610$) and 48 (44% vs. 27%; $p = 0.0149$; Table). A numerically greater proportion of pts who initiated RUX at ≤12 months vs. >12 months achieved TSS50 at Wk 24 (56% vs. 40%; $p = 0.0829$; Table). OS at Wk 240 was improved among pts who initiated RUX at ≤12 months vs. >12 months (63% [95% CI, 51%–73%] vs. 57% [95% CI, 49%–64%]; $p = 0.0430$; Table). Comparatively, OS was longer with RUX *versus* PBO/BAT regardless of disease duration. A sensitivity analysis using a 24-mo cutoff was also conducted but yielded weaker associations between disease duration and SVR, TSS and OS. In the MVA, a significantly greater binary SVR was seen among pts with shorter (≤12 months) vs. longer (>12 months) MF disease duration (odds ratio, 2.1; $p = 0.022$).

These findings suggest that earlier RUX initiation in MF may improve clinical outcomes, including cytopenias, SVR, symptom burden and OS. While 'watch and wait' remains a common treatment approach for newly diagnosed patients, these data suggest that pts with MF may benefit from earlier intervention. Additional studies to further evaluate the impact of early intervention are warranted.

Disclosure of Interest: C. Harrison Conflict with: Celgene, Novartis, Conflict with: AOP Orphan Pharmaceuticals, Celgene, CTI BioPharma Corp., Gilead Sciences, Incyte Corporation, Janssen, Novartis, Promedior, Roche, Shire, Sierra Oncology, J.-J. Kiladjian Conflict with: AbbVie, AOP Orphan, BMS, Incyte Corporation, Novartis, A. M. Vannucchi Conflict with: BMS, Novartis, Incyte Corporation, R. A. Mesa Conflict with: AOP, Incyte Corporation, La Jolla Pharma, Novartis, Sierra, Conflict with: AbbVie, Celgene, CTI, Genentech, Gilead, Incyte Corporation, Sierra, J. E. Hamer-Maansson Conflict with: Incyte Corporation, S. Verstovsek Conflict with: Celgene, Incyte Corporation, Novartis, Sierra Oncology, Conflict with: AstraZeneca, Blueprints Medicines Corp., Celgene, CTI BioPharma Corp., Genentech, Gilead, Incyte Corporation, ItalPharma, Novartis, NS Pharma, PharmaEssentia, Promedior, Protagonist Therapeutics, Roche, Sierra Oncology.

BSH22-PO25 | Treatment free responses and long-term outcomes in ITP patients with an optimal response to thrombopoietin receptor agonists

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Abstract Content: Immune thrombocytopenia (ITP) is an autoimmune bleeding disorder, characterised by antibody-mediated platelet destruction and reduced platelet production (Audia et al., 2017). While the mortality associated with ITP is low, patients with resistant disease suffer from considerable morbidity (Portielje et al., 2001). Thrombopoietin receptor agonists (TPO-RA) offer chronic ITP patients an effective long-term therapy to maintain a stable platelet count (Ghanima et al., 2019).

The TRAIT study reported real-life data in 267 adult patients across 15 centres, who received either Eltrombopag or Romiplostim for ITP (Cooper et al., 2018). Within this post hoc analysis, we propose novel patterns of response beyond the binary classification of responder and non-responder (Table 1).

Results: Two hundred and sixty-two patients were included in the 1-year analysis, with a mean age of 55 when commencing their first TPO-RA. 52% (135/262) were female and 48% (127/262) were male. The median time to commence TPO-RA in patients diagnosed with ITP after 2009, was 1.7 years. Eighty-one percent (213) of participants were diagnosed with primary ITP (pITP), and 19% (49/262) TPO-RA with secondary ITP (sITP).

1-year analysis: 55% (144/262) were classed responders, with at least 80% of recorded platelet counts above 30 x 10^9/l for 1 year. Responders achieved a median platelet response above 100 × 10^9/within 3 weeks of TPO-RA initiation. Of the total responders, 32% (84/262) satisfied the criteria of having an 'optimal' response, with 100% of recorded platelet counts above 30 x 10^9/l for 1 year (Table 1).

Median weekly platelet counts for optimal, intermediate and poor responders at 52 weeks were 129 × 10^9/l, 75 × 10^9/l and 40 × 10^9/l respectively (Table 1). Optimal responders maintained a median platelet count above 100 × 10^9/l for 45/52 weeks, compared to poor responders who recorded 0/52 median weekly platelet counts above 100 × 10^9/l (Table 1).

Abstract Table 1: A comparison of demographics and outcomes based on subclassifications

	Optimal responders	Intermediate responders	Poor responders	TFR
Proportion of total patients (%)	32% (84/262)	23% (59/262)	45% (119/262)	17%
Mean age at commencing TPO-RA (years)	57	56	54	59
Gender (male/female)	M: 50% F: 50%	M: 46% F: 54%	M: 49% F:51%	M: 43% F: 57%
Mean time to TPO-RA from diagnosis of ITP (diagnosed post 2009)	18 months	20 months	22 months	13 months
ITP diagnosis (primary/secondary)	Primary: 81% Secondary: 19%	Primary: 80% Secondary: 20%	Primary: 81% Secondary: 19%	Primary: 59% Secondary: 41%
Platelet count (×10^9/l): 26 weeks 52 weeks	105 129	78 75	51 40	106 144
Number of total weekly median platelet counts > 100 × 10^9/l (52 weeks)	45/52	21/52	0/52	45/52
Proportion achieving TFR	21% (18/84)	18% (11/60)	13% (15/119)	—
Time to achieving TFR (months)	12	25	15	—

Definitions:*Responders*: Optimal responders + intermediate responders;
Optimal responders: 100% of recorded platelet counts above 30 × 10^9/l between 21 days and 1 year since commencing TPO-RA, and have not required rescue therapy within that time frame;
Intermediate responders: More than 80% of recorded platelet counts above 30 × 10^9/l between 21 days and 1 year since commencing TPO-RA and have not required rescue therapy within that timeframe;
Poor responders: Less than 80% of recorded platelet counts above 30 × 10^9/l between 28 days and 1 year since commencing TPO-RA, AND/OR have required rescue therapy between 21 days and 1 year since commencing TPO-RA;
Treatment free response: 100% of platelet counts above 30 × 10^9/l for 3 months after cessation of TPO-RA.

Twenty-six percent (67/262) of participants required at least one rescue therapy between 21 days and 1 year of commencing TPO-RA. IVIG (48%) and corticosteroids (39%) were the most common rescue therapies prescribed.

2-year analysis: Of the responders, 90 out of 144 had data available to be analysed at 24 months. Seventy-three percent (66/90) had 100% of platelet counts above 30 between 12 and 24 months. Only 6% (5/90) required rescue therapy between 12 and 24 months.

Treatment free response: Treatment free response (TFR) was achieved in 17% (44/262) of patients. The average time to TFR was 16 months. Logistic regression indicated a statistically significant association between TFR with both earlier commencement of TPO-RA from diagnosis (p = <0.05) and sITP (p = <0.05). Of the patients who achieved a TFR, 41% were optimal responders, on average achieving a TFR within 12 months of commencing their TPO-RA.

Conclusion: Eltrombopag and Romiplostim can provide a durable platelet response for up to 2 years, with a sustained response observed in 17% of patients when treatment has stopped. TFR was associated with earlier initiation of TPO-RA (p = <0.05) and secondary ITP (p = <0.05). The subclassification of 'optimal responders', achieved a higher proportion of TFR (Table 1). TFR rate in this cohort is likely under-reported as two-thirds remained on TPO-RA at the end of the study period.

Clinicians can use these subclassifications to predict long-term outcomes for patients on TPO-RA. Our data suggest optimal responders can trial a cessation of therapy after 12 months of TPO-RA use.

*Funded in part by a research collaboration with Novartis and Imperial College London NIHR BRC. Statistical analysis and writing were conducted independently by Imperial College London.

Disclosure of Interest: A. Charania: None Declared, A. Ervin Conflict with: Novartis, G. Adams: None Declared, N. Cooper Conflict with: Rigel, Novartis, Amgen, UCB, Grifols, Sanofi, Conflict with: Rigel, Novartis.

BSH22-PO26 | Outcomes before and after dose reduction in patients with newly diagnosed chronic myeloid leukaemia receiving bosutinib or imatinib

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Abstract Content: Background: Bosutinib is approved for patients with Philadelphia chromosome-positive chronic myeloid leukaemia (CML), at a starting dose of 400 mg once daily (QD) in newly diagnosed patients in chronic phase (CP). This analysis evaluated the impact dose reduction has on the outcomes of bosutinib and imatinib in patients with CP CML.

Methods: In the open-label BFORE trial, 536 patients with newly diagnosed CP CML were randomised to receive 400 mg QD bosutinib (N = 268) or imatinib (N = 268; 3 untreated). Dose could be reduced to 300 mg QD for toxicity. Following sponsor approval, dose reduction to bosutinib 200 mg QD was permitted for 4 weeks maximum; after this time, dose escalation or treatment discontinuation was required. Maintenance of response after dose reduction was defined as having a response >6 months after the first reduction. Database lock: 12th June 2020, 5 years after the last patient enrolled.

Results: In the bosutinib arm, dose reduction to 300 (without further reduction) or 200 mg QD was seen in 82 (31%) and 33 (12%) patients, and median time to dose reduction was 85 and 205 days. In the imatinib arm, 50 (19%) patients had a dose reduction to 300 mg QD, and median time to dose reduction was 92 days. Most common (≥2% of patients) treatment-emergent adverse events (TEAEs) leading to dose reduction were increased alanine aminotransferase (8%), thrombocytopenia (7%), diarrhoea (7%), increased lipase (6%), increased aspartate aminotransferase (4%), nausea (4%), neutropenia (3%), rash (3%) and abdominal pain (2%) with bosutinib and neutropenia (4%) with imatinib.

Of the patients who remained on 400 mg QD bosutinib (n = 153) or imatinib (n = 214), respectively, 120 (78%) and 139 (65%) achieved major molecular response (MMR). Among patients who had a bosutinib dose reduction to 300 mg QD, 51 out of 82 (62%) had MMR >6 months after dose reduction: 14 (17%) maintained MMR before and after dose reduction and 37 (45%) achieved MMR for the first time after dose reduction. Seven (9%) patients had MMR before dose reduction but discontinued treatment before the next >6 months assessment. In the imatinib arm, 32 out of 50 (64%) patients had MMR >6 months after dose reduction: nine (18%) maintained MMR before and after dose reduction and 23 (46%) achieved MMR for the first time after dose reduction. One (2%) patient had MMR before dose reduction but discontinued treatment before the next >6 months assessment and one (2%) patient lost a previously attained MMR after dose reduction. Among patients who had a bosutinib dose reduction to 200 mg QD, 12/33 (36%) had MMR >6 months after dose reduction: seven (21%) maintained MMR before and after dose reduction and five (15%) achieved MMR for the first time after dose reduction. Six (18%) patients had MMR before dose reduction but discontinued treatment before the next >6 months assessment. Similar trends were seen for the complete cytogenetic response.

Conclusions: Management of TEAEs through bosutinib or imatinib dose reduction enabled patients to continue treatment, with a substantial number of patients achieving MMR for the first time after dose reduction.

Disclosure of Interest: D. Milojkovic Conflict with: Incyte, Pfizer, Novartis, Bristol-Myers Squibb, Conflict with: Pfizer, M. W. Deininger Conflict with: Ariad, Blueprint Medicine, Bristol-Myers Squibb, Galena Biopharma, Incyte, Novartis, Pfizer, Conflict with: Bristol-Myers Squibb, Celgene, Gilead Sciences, Incyte, Novartis, Pfizer, Conflict with: Ariad, Blueprint Medicine, Bristol-Myers Squibb, Galena Biopharma, Incyte, Novartis, Pfizer, T. H. Brümmendorf Conflict with: Janssen, Merck, Novartis, Pfizer, Conflict with: Novartis, Pfizer, Conflict with: Novartis, Pfizer, F. Cervantes Conflict with: Novartis, Pfizer, Incyte, Celgene, F. Huguet Conflict with: Novartis, Incyte, Pfizer, A. Viqueira Conflict with: Pfizer, E. Leip Conflict with: Pfizer, S. Purcell Conflict with: Pfizer, J. E. Cortes Conflict with: Amphivena Therapeutics, Astellas Pharma, Bio-Path Holdings Inc, BiolineRx, Bristol Myers Squibb, Daiichi Sankyo, Jazz Pharmaceuticals, Novartis, Pfizer, Takeda, Conflict with: Astellas Pharma, Bristol Myers Squibb, Daiichi Sankyo, Immunogen, Jazz Pharmaceuticals, Merus, Novartis, Pfizer, Sun Pharma, Takeda, Tolero Pharmaceuticals, Tovagene.

BSH22-PO27 | Pelabresib (CPI-0610) monotherapy in patients with myelofibrosis—update of clinical and translational data from the ongoing MANIFEST trial

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Abstract Content: Pelabresib (CPI-0610) is an investigational, selective, oral small-molecule inhibitor of bromodomain and extraterminal domain (BET) proteins that can modify the expression of genes involved in nuclear factor kappa B (NF-κB) signalling in patients (pts) with myelofibrosis (MF). Here we present updated results, based on a data cut off as of 10 September 2021, from Arm 1 of MANIFEST (NCT02158858), an ongoing, global, open-label Phase 2 study, investigating pelabresib monotherapy in pts with advanced MF who are refractory/resistant, ineligible or intolerant to Janus kinase inhibitor (JAKi) treatment and typically have a very poor prognosis.

Eligibility criteria are MF pts with Dynamic International Prognostic Scoring System (DIPSS) risk category of ≥ intermediate-2, platelets ≥75 × 109/l and ≥2 symptoms measurable (score ≥1) per Myelofibrosis Symptom Assessment Form (MFSAF) v4.0. Additional criteria include red blood cell (RBC) transfusion dependence (TD) per Gale criteria in the TD cohort or spleen volume of ≥450 cc by computed tomography/magnetic resonance imaging in the non-TD cohort. Pts were enrolled as TD (defined as ≥2 U RBCs/month over 12 weeks [wks]) and non-TD if TD criteria were not met. The primary end-point in TD cohort is RBC transfusion independence (TI; defined as no transfusion for ≥12 wks) and ≥ 35% spleen volume reduction (SVR35) at Wk 24 in the non-TD cohort. Secondary end-points include number of pts with ≥50% total symptom score reduction (TSS50) per MFSAF v4.0 at Wk 24 and safety. Additional exploratory end-points include changes in plasma levels of proinflammatory cytokines and bone marrow morphology/fibrosis. Pts with assessment at Wk ≥24 and those discontinued without Wk 24 assessment are included in the analysis of the corresponding end-point.

As of 10 September 2021, 86 pts were treated for a median treatment follow-up of 22 months (reverse Kaplan–Meier estimate, 95% confidence interval [CI] 10–25). In the TD cohort, 16% (4/25) pts achieved TI. In the non-TD cohort, 18% (7/38) pts achieved SVR35 at Wk 24. At Wk 24, 11% (7/38) of all evaluable pts achieved SVR35 (median change: −24%) and 28% (18/64) pts achieved TSS50 (median change: −40%). 86 pts were evaluable for safety. The most common (≥20%) treatment-emergent adverse events (TEAEs) of any grade irrespective of causal association were thrombocytopenia (38%), diarrhoea (34%), nausea and asthenic conditions (33% each), anaemia (24%), dysgeusia and respiratory tract infections (23% each), pruritus (22%) and constipation (21%).

For the exploratory end-point, a panel of 68 cytokines, including those known to be NF-κB targets linked to inflammation and elevated in MF pts, were evaluated in plasma samples obtained at baseline (BL) and during therapy. Cytokines were clustered in six groups based on their overexpression pattern at BL compared with healthy donors and downregulation by pelabresib. 21 cytokines, which are involved in the tumour necrosis factor receptor-2 (TNFR2) noncanonical NF-kB pathway, interleukin 10 (IL-10), IL-4, IL-13, IL-18 signalling and associated with myelofibrosis pathogenesis, were the most strongly downregulated. Downregulation was observed by Day 14 and sustained through 24 wks.

Data suggest pelabresib monotherapy was generally well tolerated and suggested signals of clinical activity in MF pts refractory/resistant, ineligible or intolerant to JAKi treatment.
Disclosure of Interest: N. Curto-Garcia: None Declared, M. Kremyanskaya Conflict with: Protagonist Therapeutics, Conflict with: Protagonist Therapeutics, Incyte, Constellation, Bristol Myers Squibb, Astex, Chimerix, Astellas, J. Mascarenhas Conflict with: Incyte, Roche, CTI Biopharm, Merck, AbbVie, Novartis, Geron, Kartos, PharmaEssentia, Constellation, Celgene/BMS, Sierra Oncology, Genentech/Roche, Gilead, Promedior, Prelude, Galecto, Geron, Conflict with: Incyte, Roche, Forbius, CTI Biopharm, Merck, AbbVie, Novartis, Geron, Kartos, PharmaEssentia, Merus, Conflict with: Incyte, Roche, CTI Biopharm, Merck, Novartis, Kartos, PharmaEssentia, Constellation, Celgene/BMS, Sierra Oncology, Genentech/Roche, Gilead, Promedior, F. Palandri Conflict with: CTI, Conflict with: Novartis, Celgene, AOP, Sierra Oncology, A. M. Vannucchi Conflict with: Novartis, Incyte, BMS, AbbVie, S. Verstovsek Conflict with: Novartis, Celgene, Incyte, Sierra Oncology, Constellation, Conflict with: Novartis, AstraZeneca, Blueprint Medicines Corp, Celgene, CTI BioPharma, Genentech, Gilead, Incyte, Ital Pharma, NS Pharma, PharmaEssentia, Promedior, Protagonist Therapeutics, Roche, Sierra Oncology, C. Harrison Conflict with: Novartis, Celgene, Constellation, Conflict with: Novartis, Celgene, CTI BioPharma, Gilead Sciences, Shire, Roche, Janssen, Promedior, AOP Orphan Pharmaceuticals, Sierra Oncology, Incyte, AbbVie, BMS, Geron, Galacteo, Keros, P. Bose Conflict with: Incyte, BMS, Celgene, CTI BioPharma, Blueprint Medicines, Kartos, Constellation, Pfizer, Astellas, NS Pharma, Promedior, Conflict with: Incyte, BMS, Celgene, CTI BioPharma, Blueprint Medicines, Kartos, Sierra Oncology, Novartis, G. J. Schiller Conflict with: BMS/Celgene, Incyte, Agios, Amgen, Jazz, Ono, Novartis, Pharma, AstraZeneca, Kaiser Permanente, Evidera, NCI, Conflict with: Abbvie, Actinium Pharmaceuticals, Actuate, Arog, Astellas, Celator, Constellation, Daiichi-Sankyo, Deciphera, Delta-Fly, Forma, FujiFilm, Gamida Cell, Genentech-Roche, Geron, Incyte, Karyopharm, Kite/Gilead, Mateon, Onconova, Pfizer, PrECOG, Regimmune, Samus, Sangamo, Stemline, Takeda, Tolero, Trovagene, Agios, Amgen, Jazz, Elevate, Bio, Ono, Novartis, Sanofi, Biomed Valley Discoveries, Eli Lilly, Sellas, Ariad, Cyclacel, MedImmune, Ambit, Leukemia&Lymphoma Society, Bluebird Bio, Boehringer-Ingleheim, Cellerant, CTI BioPharma, Janssen, Kura Oncology, Millennium, National Marrow Donor Program, NIH, Onyx, Pharmamar, UC Davis, UCSD, Conflict with: Astellas, BMS/Celgene, Incyte, Kite/Gilead, Pfizer, Stemline, Agios, Amgen, Jazz, Sanofi, Johnson&Johnson, ASH Foundation, Pharmacyclics, R. Rampal Conflict with: Abbvie, CTI, Sierra Oncology, Novartis, BMS/Celgene, Stemline, Disc Medicine, Blueprint, Pharmaessentia, Incyte, Jazz, Kartos, Conflict with: Stemline, Incyte, Constellation, M. W. Drummond Conflict with: Novartis, BMS, CTI, V. Gupta Conflict with: Novartis, BMS/Celgene, Abbvie, Pfizer, Roche, Constellation, Sierra Oncology, Conflict with: Incyte, Conflict with: Novartis, BMS/Celgene, Abbvie, Constellation, Sierra Oncology, Incyte, A. Patriarca Conflict with: Novartis, Amgen, Takeda, Incyte, Pfizer, Argenix, N. Granacher Conflict with: Abbvie, Conflict with: Abbvie, Constellation, MPN-RF, CR&T, Conflict with: Abbvie, European LeukemiaNet, J. Scandura Conflict with: Abbvie, Conflict with: Abbvie, Constellation, MPN-RF, CR&T, Conflict with: Abbvie, European LeukemiaNet, W. Prejzner: None Declared, L. L. Teichmann Conflict with: Pfizer, R. Hoffman Conflict with: Abbvie, Novartis, Kartos, G. Colak Conflict with: Constellation, Z. Ren Conflict with: Constellation, S. Bobba Conflict with: Constellation, J. Cui Conflict with: Constellation, S. Efuni Conflict with: Constellation, M. Talpaz Conflict with: Novartis, Imago, Celgene, Conflict with: Takeda, Novartis, Conflict with: Novartis, BMS, Constellation, A. J. Mead Conflict with: Abbvie, BMS/Celgene, Novartis, Conflict with: BMS/Celgene, Conflict with: Abbvie, BMS/Celgene, Novartis.

BSH22-PO28 | EMT transcription factor Zeb1 plays a critical role in adult T-cell maturation and survival during ontogenesis

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Abstract Content: We have identified Zeb1, a member of the zinc finger homeobox E-box binding transcription factors, as a key player in normal haematopoietic stem cell function and multilineage differentiation fates. Previous data have shown that Zeb1 is essential for T cell development, yet little is known about the function of Zeb1 in T-cells throughout ontogeny.
To explore this issue, we employed a conditional genetic approach using the Vav-iCre system, which deletes gene expression at d11 of embryonic development. Young adult mice engineered to be deficient in Zeb1 using this system displayed reduced thymus weight characterised by hypocellularity which leads to thymus atrophy, and reduced frequency of double-positive (DP) cells and a reduction of T cells in peripheral blood (PB), Spleen (SP) and Bone Marrow (BM). Total cell numbers were altered in double-negative (DN), DP, CD4+ and CD8+ cells from Zeb1 ablated mice. In particular, T-cell subset development was impaired in the thymus. There was a significant increase in immature DN cells contrasting with a significant reduction in the proportion of DP cells, which can be ascribed to impaired positive selection and cell survival of thymocytes. Immunophenotypic analysis showed an incremental differentiation block in DN1 and the opposite pattern in the transition of DN2/DN3 and DN4. In mature T-cell subsets, loss of Zeb1 causes a pronounced expansion in effector and memory T-cell frequency and

a dramatic reduction in naive T cells in the thymus while the absolute cell counts reveal that there is a depletion of naive, central and effectors CD4+ and CD8+ cells leading to an increase in PD-1 (programmed cell death protein 1) frequency. This reduction in naive CD4+ and CD8+ cells is also observed in BM, SP and PB and leads to an altered ratio of CD4:CD8. RNA-Seq analysis of transcriptome differences reveal that there is an increase in cell adhesion molecules in Zeb1-deleted mice, associated up-regulation of Cdh1, EpCAM and Itgb4 and a dysregulation of epithelial markers. In the thymus, Zeb1 deletion leads to a reduction of the receptor CXCR4, associated with cellular migration. These changes leading to T cell dysfunction imply that Zeb1 malfunction may contribute to premature immunological ageing, characterised by immunosenescence (including decrease in naive T cells and CD62L) and exhaustion of T-cells (increased chemokine expression and high levels of PD-1 and FAS).

Altogether, we identify Zeb1 as an indispensable regulator of transcriptional programming for T-cell development and survival throughout ontogenesis. This data may have implications for understanding Zeb1-mediated regulation of lymphoid malignancies, immunosurveillance of solid cancers and cancer immunotherapy.

Disclosure of Interest: None Declared.

BSH22-PO29 | Association of red blood cell distribution width and lactate dehydrogenase with disease transformation in essential thrombocythaemia and polycythaemia vera patients: a UK cohort study using electronic health records

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Abstract Content: Patients living with essential thrombocythaemia (ET) or polycythaemia vera (PV) are at risk of disease transformation to secondary myelofibrosis (SMF) and/or acute myeloid leukaemia (AML), which results in poorer outcomes for these patients. Prognostic markers for disease transformation are pivotal in ensuring earlier and potentially more successful therapeutic management. While the role of haemoglobin, platelets and white blood cells (WBC) for prognosis has repeatedly been described in the literature, the importance of other biomarkers, such as red blood cell distribution width (RDW) and lactate dehydrogenase (LDH) for prognosis is less certain.

Electronic health records for patients diagnosed with either ET or PV were collected from two UK NHS trusts (Chelsea & Westminster Hospital NHS Foundation Trust and Oxford University Hospitals NHS Foundation Trust) between 2008 and 2020. Patients entered the cohort on the day of their earliest recorded ET or PV diagnosis (index date) and were observed until transformation to SMF or AML, death, loss to follow-up, or 5 years after index event. Analysis was adjusted for age, sex, Charlson Comorbidity Index (CCI) and laboratory measurements at index date, including blood counts (RDW, haemoglobin, platelets, WBC, % neutrophils, % lymphocytes, % monocytes) and LDH). Any laboratory tests recorded within ±30 days of index date were included to account for potential time differences between investigations and diagnosis. When a laboratory test was not recorded within this time frame, multiple imputation with M = 100 and predictive mean matching was used to impute likely values. Competing-risks survival regression was used to determine the association of one standard deviation (SD) increase in RDW and LDH with the risk of transformation to SMF or AML, where death was considered a competing risk. To validate our findings, we repeated all analyses in an independent patient cohort from the NHS Greater Glasgow and Clyde health board in Scotland for medical records collected between 2000 and 2020.

A total of 1049 patients were identified at our English trusts, including 620 ET and 429 PV patients. After 5 years of follow-up (median 2.1 years), an estimated 6.8% (95% CI 4.2–11.1) and 4.0% (95% CI 2.2–7.1) of patients had undergone transformation to either SMF or AML. After adjusting for other covariates, an increase in RDW by one SD (19.1% vs. 15.5%) was associated with a 2.6-fold increase in the risk of transformation for patients (HR = 2.56; 95% CI 1.20–5.47, $p = 0.019$; Figure 1). A one SD increase in LDH (411.5 U/l vs. 268.8 U/l) was similarly associated with a 2.2-fold increase in risk of transformation (HR = 2.21; 95% CI 1.37–3.55, $p = 0.002$). Analysis of an independent cohort of 761 ET and 1009 PV patients from Scotland resulted in very similar estimates for RDW (HR = 2.47, 95% CI 1.30–4.72, $p = 0.014$) and LDH (HR = 2.23, 95% CI 1.38–3.61, $p = 0.003$).

Increased levels of RDW and LDH were found to be associated with increased risk of disease transformation while controlling for established prognostic factors in two independent patient cohorts in England and Scotland. Integration of these novel markers in the development of prognostic scores of disease transformation in both ET and PV should be considered.

Disclosure of Interest: P. Rockenschaub Conflict with: Sensyne health employee, L. Carpenter Conflict with: Sensyne health employee, G. Hatton Conflict with: Sensyne health employee, S. D'Abrantes Conflict with: Sensyne health employee, E. Sims Conflict with: Sensyne health employee, N. Scott-Ram Conflict with: Sensyne health employee, A. Ducès Conflict with: BMS employee, G. Emanuel Conflict with: BMS employee, A. Mead Conflict with: Work on the manuscript, grants, consulting fees, payment for lectures, attending meetings and participation on advisory board in the past 36 months, M. Drummond Conflict with: Work on the manuscript, payment for lectures, expert testimony and attending meetings in the past 36 months, N. Lipunova Conflict with: Sensyne health employee.

BSH22-PO30 | Real-World Outcome of Patients with Myelofibrosis Treated with Ruxolitinib in the West of Scotland: A Retrospective Multicentre Analysis

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Abstract Content: Myelofibrosis (MF) is a chronic myeloproliferative neoplasm that can present either de novo (PMF) or secondary to essential thrombocythaemia or polycythaemia vera (SMF). It is associated with a significant disease burden. The JAK2 driver mutation is identified in approx. 60% of patients with PMF. Following on from the phase III COMFORT-I and COMFORT-II trials, the JAK-inhibitor Ruxolitinib was accepted by the Scottish Medicines Consortium in March 2015 for the treatment of disease-related splenomegaly or symptoms in adult patients with MF (irrespective of DIPSS score). The aim of our study was to evaluate real-world practise and outcome in patients with MF treated with Ruxolitinib in the West of Scotland.

All patients with MF treated with Ruxolitinib in the West of Scotland between Dec 2013 and Dec 2019 were identified retrospectively using electronic prescribing records. Overall survival (OS) and event-free survival (time to death, transformation or discontinuation; EFS) were calculated using the Kaplan–Meier method. Descriptive statistics were used to report other outcomes.

One hundred and fifty-seven patients were eligible for analysis. Demographics: 56% male, median age at diagnosis 67.5 years, 56% primary MF. One patient was lost to follow-up. The median DIPSS score at presentation and at time of starting therapy was 2 (Int-1). Cytogenetic results were available in 59% of patients: 69% favourable, 20% unfavourable, 11% very high risk by MIPSS criteria. For patients with SMF, median MYSEC-PM score was 14.1 (Int-2). The median time from diagnosis to starting Ruxolitinib was 6.5 months.

Spleen size was assessed radiologically at diagnosis in 72% (median 17.3 cm) and at commencement of Ruxolitinib in 68% (median 18.9 cm). Improvement in splenomegaly was documented in 51% (improvement range 1–15.3 cm). 38% of patients were transfusion-dependent pre-Ruxolitinib; 20% of these achieved transfusion independence.

The median duration of therapy was 26.5 months (indication: splenomegaly 29%, constitutional symptoms 41%, both 17%, not recorded 13%). The median starting dose and maximum tolerated dose was 10 mg BD (range 5–20 mg BD) and 15 mg BD (range 10–20 mg BD) respectively. Eleven percent of patients reached the target dose of 25 mg BD. 32% of patients discontinued Ruxolitinib (43% due to disease progression /transformation; 35% due to intolerance).

Median OS from time of starting Ruxolitinib was 5.6 years in all patients, 4.0 years in PMF and 6.8 years in SMF. The median EFS was 4.9 years in all patients, 3.1 years in PMF and 5.3 years in SMF. Leukaemic transformation was seen in 10% of patients.

Allogenic stem cell transplant was planned in 11% of patients. By the end of follow-up, 78% of these patients had undergone transplant. Forty-three percent (n = 6) of these patients died either from disease or transplant complications.

8% (n = 13) of patients experienced a second malignancy (non-melanoma skin cancer 62% (n = 8), seminoma 8% (n = 1), carcinoma of unknown primary 8% (n = 1), other solid organ tumour 23% (n = 3).

Forty-two percent of patients had died by the end of the study period (progressive MF 30%, leukaemic transformation 12%, haemorrhage 10%, infection 24%, cardiovascular disease 5%, other /not recorded 19%).

This study confirmed the real-world benefit of Ruxolitinib in controlling disease-related symptoms or splenomegaly in this cohort of patients with MF treated in the West of Scotland. This cohort notably included patients with Int-1 MF. OS and outcome data are similar to that in the published literature.

Disclosure of Interest: None Declared.

BSH22-PO31 | Transfusion Independence is Associated with Improved Overall Survival in Myelofibrosis Patients Receiving Momelotinib

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Abstract Content: Momelotinib (MMB) is a potent JAK1, JAK2 and ACVR1 inhibitor with clinical activity against the hallmark features of myelofibrosis (MF), namely anaemia,

constitutional symptoms and splenomegaly, across the continuum of JAKi naïve or previously JAKi-treated intermediate/high-risk MF patients as demonstrated in the previously conducted Phase 3 SIMPLIFY-1 & -2 clinical trials (S1, S2). S1 enrolled JAKi-naïve patients with MF (n = 432) double-blind randomised 1:1 to MMB or ruxolitinib (RUX). S2 enrolled patients with MF with haematological toxicity during prior RUX therapy (n = 156) randomised 2:1 to open-label MMB or best available therapy (BAT; consisting of RUX in 88% of patients). In both trials, following the 24-week randomised treatment (RT) period, patients could continue MMB (MMB → MMB) and those randomised to RUX/BAT could cross-over to MMB (RUX/BAT→MMB) for extended treatment (ET).

Previously published data from the SIMPLIFY studies demonstrate robust overall survival (OS) for MMB-treated patients in S1 and S2 (median not reached and 34.3 months respectively) with a maximum follow-up of approximately 5 years and median of 2.9 years in S1 and 2.3 years in S2.

OS data for patients receiving MMB in S1 and S2 are reported here for subgroups defined by Week 24 (W24) transfusion independence (TI) responders *versus* non-responders, and also other efficacy end-points. Survival was estimated using KM analysis with descriptive log-rank tests for comparison applied (all pvalues are descriptive).

As previously reported, W24 TI rates were higher in the MMB arms of S1 (67% vs. 49%) and S2 (43% vs. 21%). In S1, W24 TI responders in the MMB group show an OS advantage, with median OS not reached and 3-year survival of 80% (HR = 0.30; $p < 0.0001$) compared to MMB TI non-responders. Similarly in S2, W24 TI responders in the MMB group show a trend towards better OS compared to TI non-responders (HR = 0.57; $p = 0.0652$). The HRs in S1 for MMB responders *versus* non-responders for W24 SRR and TSS were 0.59 ($p = 0.0904$) and 0.65 ($p = 0.1657$) respectively. Alternative analyses using OS defined from W24 demonstrated consistent results.

These new analyses suggest JAKi naïve patients receiving MMB who maintain or achieve TI at W24 have favourable OS compared to MMB TI non-responders, with a similar trend observed in S2. These findings are consistent with anaemia and transfusion dependency being key predictors of shortened OS in MF and suggest that TI response at W24 may become a surrogate for clinical benefit, supporting the clinical relevance of MMB's differentiated pro-erythropoietic ACVR1 inhibition.

Disclosure of Interest: None Declared.

BSH22-PO32 | Longitudinal and Individual Symptom Analyses of Momelotinib and Ruxolitinib-Treated Myelofibrosis Patients from SIMPLIFY-1

Ruben Mesa[1,*], Stacy Hudgens[2], Libby Floden[2], Jeanne Palmer[3], Vikas Gupta[4], Donal McLornan[5], Mary Frances McMullin[6], Jean-Jacques Kiladjian[7], Lynda Foltz[8], Uwe Platzbecker[9], Laura M. Fox[10], Adam Mead[11], David Ross[12], Stephen Oh[13], Andrew Perkins[14], Michael F. Leahy[15], Samineh Deheshi[16], Rafe Donahue[17], Barbara Klencke[17], Srdan Verstovsek[18]

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Abstract Content: Clinical trials investigating JAK1/JAK2 inhibitors for myelofibrosis (MF) subjects have measured symptom improvement as a minimum 50% reduction in total symptom score (TSS) at the end of a 24-week treatment period. This landmark analysis is based on postbaseline score changes from Weeks 21 (W21) to 24 and requires vastly different absolute TSS improvements for patients with very high or low baseline (BL) TSS to reach responder status. A phase 3 clinical study, SIMPLIFY-1, randomised 432 intermediate and high-risk JAK inhibitor (JAKi) naive MF patients 1:1 to momelotinib (MMB) or ruxolitinib (RUX). Non-inferiority on the MPN-SAF TSS response rate end-point at W24 was not met (MMB: 28% vs. RUX: 42%); however, improvement in each of the seven TSS items was similar for MMB *versus* RUX. To understand the discrepancy, we applied item analysis and mixed effect models for repeated measures (MMRM) to SIMPLIFY-1.

Analyses were conducted in the intention-to-treat (ITT) population and in a symptomatic subset (selected as subjects with BL TSS ≥10). The distributions of TSS items were examined at BL and shift in scores at W24 (health state shifts) were assessed. GEE models were used to estimate item-level odds ratios using multiple predictive imputations for missing data. MMRM compared mean change in TSS from BL to W24 using data from all visits. The meaningful change threshold (MCT) was determined using Patient Global Impression of Change.

BL scores across items were heterogenous in the MMB and RUX groups; the proportion of subjects with no or mild symptoms (0- to 3- on a 0- to 10-point scale) ranged from 36% (tiredness) to 77% (itching). Distributions of BL scores were different across arms with all items in the MMB arm reporting more severe or very severe symptoms (scores of 7–10) at BL compared to RUX. Despite the imbalance in BL scores, item-level health state shifts showed similar improvements for MMB and RUX. Categorical responder analysis showed no significant differences on any items. Odds ratios for each between-group comparison ranged from 0.75 to 1.20.

MMRM mean TSS change at W24 was 6.35 (MMB) vs. 7.87 (RUX) in the ITT and 8.80 (MMB) vs. 10.46 (RUX) in the symptomatic subset. Mean TSS were near the within-subject MCT of 8 points in the ITT and exceeded the MCT in the symptomatic subset. The between-group difference was 1.52 (95% CI: [0.196, 2.847]) in the ITT and 1.67 (95% CI: −0.134, 3.468) in the symptomatic subset.

Comparable item health state shifts at W24 and similar improvements in mean TSS as shown by MMRM, with a minimal between-group difference of 1.52 on the 70-point scale in context of an 8-point MCT suggest MMB provides clinically relevant and comparable symptom improvements to RUX; these analyses require further validation in independent datasets. Imbalance in BL symptom scores in MMB subjects may have contributed to the inability to demonstrate non-inferiority in TSS response rate at W24.

Disclosure of Interest: None Declared.

BSH22-PO33 | Effects of cessation of venesection on ferritin level and liver function among older patients with haemochromatosis as a result of the Covid-19 pandemic

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Abstract Content: COVID- 19 has had a profound impact on the delivery of healthcare services within the NHS. To relieve burden, elective procedures were ceased. This included venesection, the treatment for haemochromatosis, a disease characterised by excessive dietary iron absorption. Evidence suggests that a physiological result of ageing is reduced iron absorption. Therefore, an arbitrary cut-off age for venesection cessation was established at over 70, in attempt to limit adverse outcomes. However, management guidelines state that treatment is required lifelong, though there is no evidential basis for this. Therefore, the purpose of this study is to explore the effect of cessation of venesection on serum ferritin (SF) level and liver function in patients aged over 70 at the Royal Derby Hospital (RDH). Primarily, it was to assess whether venesection cessation was safe.

Haemochromatosis patients, aged over 70 at RDH were the group of interest. Only those who were receiving maintenance venesection at the time of treatment cessation (SF < 150 μg/l) were included. Using the software CITO, their genotypes were identified and only those with HFE mutation were selected. The sample group was composed of 44 patients with conventional HFE hereditary haemochromatosis (biallelic HFE mutation) and seven with monoallelic HFE mutation, who were used as a comparator. SF, ALT, ALP and GGT levels before and after venesection cessation were collected. Statistical analyses were conducted using STATA, to test for a significant difference between blood test parameters before *versus* after treatment cessation. The rate of change in SF per day was calculated for both groups.

Patients did not receive treatment for a median of 403 days (1 year and 38 days). No significant difference was noted between GGT, ALT and ALP levels before *versus* after treatment cessation. There was a statistically significant increase in SF before *versus* after treatment cessation ($z = -4.532$), $p < 0.001$) at the 99% confidence level. The median SF before treatment cessation was 74 μg/l compared to 124.5 μg/l just before treatment re-initiation. However, this did not prove to be clinically significant, as only 1/44 patients had a SF that rose above the normal reference range of 30–400 μg/l. There was a statistically significant difference in the rate of change in SF per day between patients with biallelic HFE mutation (median = was 0.14 μg/l/day) compared to patients with monoallelic HFE mutation (median = 0.10 μg/l/day) at the 95% confidence level.

Venesection cessation was safe for patients aged over 70 with HFE haemochromatosis at RDH. The results suggest that venesection does not need to be lifelong, but can safely be paused- not ceased, after the age of 70 for 5-year intervals. Results can facilitate the establishment of new clinical guidelines for the treatment of haemochromatosis.

Abstract Table:

	Overall	Male	Female
Median age	75.5	74	76
Median year of birth	1946	1946	1945
Median year of diagnosis	2013	2012	2016
Median age at diagnosis	67	66	71
Median days off treatment (days)	403		

Disclosure of Interest: None Declared.

BSH22-PO34 | Improved Transfusion Independence Rates for Momelotinib *versus* Ruxolitinib in Anaemic Jaki Naïve Myelofibrosis Patients Independent of Baseline Platelet or Transfusion Status

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Abstract Content: Momelotinib (MMB) is a potent JAK1, JAK2 and ACVR1 inhibitor with clinical activity against the hallmark features of myelofibrosis (MF), namely anaemia, constitutional symptoms and splenomegaly, across the continuum of JAKi naïve or previously JAKi-treated intermediate/high-risk MF patients as demonstrated in the previously conducted Phase 3 SIMPLIFY-1 & -2 clinical trials (S1, S2). S1 was conducted in JAKi-naïve patients with MF (n = 432) double-blind randomised 1:1 to MMB or ruxolitinib (RUX). MMB demonstrated a statistically non-inferior splenic response rate (SRR) to RUX at the W24 landmark analysis in S1 but did not meet significance for total symptom score (TSS) response. Low SRR and TSS response was observed for RUX in patients with low platelets, while MMB elicited consistent SRR and TSS response across the platelet subsets, comparable to the response in the ITT. Transfusion independence (TI) at W24 was higher for MMB *versus* RUX patients across all PLT strata. Progressive anaemia is a common occurrence in MF with nearly all MF patients requiring transfusions as their disease advances. Given the prognostic importance of Hgb and transfusion status in MF patients including evidence that achieving or maintaining transfusion independence by Week 24 with momelotinib is associated with improved OS in S1 and S2, we expanded the previously reported retrospective platelet subset analysis to explore the W24 TI response rates for MMB and RUX randomised patients in S1 by baseline Hgb and PLT levels and transfusion status.

The data presented here suggest that the prognostically important W24 TI rate was substantively higher in anaemic patients receiving MMB *versus* RUX, irrespective of the degree of anaemia. MMB is also more effective relative to RUX in achieving or maintaining TI in JAKi naïve patients irrespective of baseline PLT count or baseline transfusion status. Together with data suggesting that TI response at W24 with momelotinib is associated with a survival advantage, these data further support the potential TI benefits of inhibiting ACVR1 in addition to JAK1 and JAK2 with MMB in MF patients.

Abstract Table:

	TI response at Week 24	
	MMB	**RUX**
ITT population	67% (143/215)	49% (107/217)
Baseline Hgb level		
Hgb <8	29% (8/28)	18% (4/22)
Hgb <10	47% (40/86)	27% (26/95)
Hgb <12	62% (99/159)	37% (61/164)
Hgb <14	67% (136/204)	45% (87/195)
Hgb ≥14	64% (7/11)	91% (20/22)
Baseline PLT count		
PLTs <150	62% (29/47)	43% (24/56)
PLTs <300	68% (93/136)	48% (62/128)
PLTs ≥300	63% (50/79)	51% (45/89)
Baseline transfusion status		
TI	81% (119/147)	62% (94/152)
TR	53% (8/15)	31% (4/13)
TD	30% (16/53)	17% (9/52)

Abbreviations: Hgb, haemoglobin; ITT, intent-to-treat; MMB, momelotinib; PLT, platelet; RUX, ruxolitinib; TD, transfusion dependent; TI, transfusion independent; TR, transfusion requiring.

Disclosure of Interest: None Declared.

BSH22-PO35 | Characterisation of Cardiovascular Risk in a Contemporary Cohort of Patients with Myeloproliferative Neoplasms

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Abstract Table:

MPN subtype	Event rate		Mean QRISK3 score
	Arterial	Venous	
Essential Thrombocythaemia (n = 262)	14.5% (38/262)	9.9% (26/262)	12.9%
Polycythaemia Vera (n = 108)	18.5% (20/108)	20.4% (22/108)	13.6%
Primary Myelofibrosis (n = 31)	12.9% (4/31)	16.1% (5/31)	16.6%
Secondary Myelofibrosis (n = 36)	19.4% (7/36)	36.1% (13/36)	19.8%
Total (n = 437)	15.8% (69/437)	15.1% (66/437)	13.9%

Abstract Content: Myeloproliferative neoplasms (MPNs) are heterogenous diseases caused by excess clonal haemopoiesis, which include polycythaemia vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (MF). While they are associated with an increased risk of thrombotic complications, the full extent of thrombotic complications and the impact of cardiovascular risk (CVR) factors remains incompletely defined. We performed a retrospective analysis of a large contemporary cohort to characterise the incidence of arterial and venous events, and CVR.

All patients with PV, ET and MF who attended for review at a major tertiary referral centre between 2020 and 2021 were included. Previous arterial events (defined as myocardial infarction, ischaemic stroke/transient ischaemic attack and peripheral arterial thromboembolism) and previous venous events (defined as pulmonary embolism, deep venous thrombosis, abdominal and cerebral venous thrombosis), *JAK2* mutation status and CVR factors (type 2 diabetes (T2DM), hypertension (HTN), smoking status, atrial fibrillation (AF), chronic kidney disease (CKD), autoimmune disease, steroid use and family history) were recorded in order to calculate a QRISK3 score, which is a widely accepted tool used to calculate an individual's 10-year risk of developing ischaemic cardio/cerebrovascular disease.

Four hundred and thirty-seven patients with PV (24.7%) (108/437), ET (60.0%) (262/437) and MF (15.3%) (67/437) were included. The median age was 66 years (IQR 24 years). 56.1% were female.

The incidence of previous arterial events was 15.8% (69/437): the majority were cerebral (62.3%); the remainder coronary (33.3%) or peripheral (4.4%). Among MPN subtypes, the incidence of arterial events was 14.5% in ET, 18.5% in PV, 12.9% in primary MF and 19.4% in secondary MF. 15.1% of patients had a previous venous event, with the highest incidence in patients with secondary MF (36.1%), followed by PV (20.4%), primary MF (16.1%) and ET (9.9%).

The most common CVR factors were HTN in 39.6% (173/437) and positive smoking history in 38.3% (167/437). Where applicable, a QRISK3 score was calculated in 93.8% (410/437), with the mean score being 13.9% (a calculated score of >10% represents a high CVR category).

71.9% (314/437) of our cohort were *JAK2* V617F positive. There was a trend towards a higher incidence of arterial (17.8% vs. 10.6%; p = 0.32) and venous (15.9% vs. 13%; p = 0.82) events in those with a *JAK2* V617F mutation but this was not statistically significant.

MPN patients continue to demonstrate a high prevalence of vascular morbidity. 15.8% (69/437) patients had arterial events with 62.3% in cerebral circulation. 15.1% (66/437) had venous events. The high prevalence of venous events is unexplained, although it is possible that referral bias may play a part. While the presence of *JAK2* V617F has been known to confer a higher risk of thrombosis in MPN patients, this was not statistically significant in our cohort as the incidence of previous arterial and venous events in the *JAK2* V617F wild type group was greater than expected, possibly due to overrepresentation of MF in this group.

MPN patients have a high CVR as shown by the elevated mean QRISK3 score. Aggressive management of CVR factors should continue to be part of standard treatment introduced early in the diagnosis of MPN.

Disclosure of Interest: None Declared.

BSH22-PO36 | Pegylated Interferon is an effective and well-tolerated cytoreductive agent in patients with myeloproliferative neoplasms aged over 60 years

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Abstract Content: Pegylated Interferon (PegIFN) is the recommended first-line cytoreductive therapy in patients aged <40 years with essential thrombocythaemia (ET) or polycythaemia vera (PV). However, its use in patients >60 years is often limited due to concerns about tolerability. In this

study, we evaluate the efficacy and tolerability of PegIFN in patients >60 years at University College London Hospitals (UCLH).

Using electronic medical records, we identified patients with ET, PV or myelofibrosis at UCLH who commenced treatment with PegIFN between 2010 and 2020 and were aged >60 years on starting therapy. Data were collected until April 2021 to allow a minimum of 1-year follow-up. Complete Haematological responses were defined as per standard European Leukaemia Net criteria. Adverse events (AE) were graded 1–5 according to Common Terminology Criteria for Adverse Events (CTCAE). Thrombosis risk was graded according to IPSET criteria for ET patients. Patients with PV were classed as high risk if they were aged >65 or had a previous history of thrombosis.

Eighteen patients were included in the study. The median age was 75.1 years (range 63–91), 61% were female. Ten out of 18 (56%) had a diagnosis of ET, seven out of 18 (39%) of PV and 1/18 (6%) of post-ET myelofibrosis. Fifteen out of 18 (83%) were positive for *JAK2*V617F, and two out of 18 (17%) were positive for *CALR* mutation. Ten out of 18 (56%) had significant cardiovascular co-morbidities at diagnosis. Five out of 18 (28%) had arterial or venous thromboembolic disease at diagnosis. Sixteen out of 18 (89%) were high-risk for thromboembolic events at diagnosis.

Seventeen (94%) patients had PegIFN as a second- or third-line agent. Of these, 15 out of 17 had received hydroxycarbamide (HU) as first-line therapy; two out of 17 had interferon alpha. PegIFN was started at a median age of 70 years (range 50–86) and continued for 5.7 years (range 2–13). Twelve out of 18 (67%) patients achieved complete remission (CR) on PegIFN monotherapy; 1 out of 18 (6%) achieved CR on PegIFN and HU combination therapy, and the remaining 5 out of 18 (28%) achieved a partial remission (PR). The median time to CR was 5 months (range 1–40 months).

Ten out of 18 (56%) had grade 1–2 AEs including skin rashes, cytopenia and fatigue. Three out of 18 (17%) developed a major thromboembolic event while on treatment (brachial artery embolism, transient ischaemic attack and a non-ST elevation myocardial infarction). Of these, two out of three failed to achieve a CR on PegIFN and required ongoing venesection. The third had suboptimal response due to dose escalation limited by grade 3 neutropenia.

Thirteen patients (72%) remained on pegIFN at the end of the study period. Of those who discontinued, three out of five stopped due to cytopenias, one out of five died during the study period of Covid-19 infection and one out of five transformed to myelodysplastic syndrome.

In this study, we present a group of patients who were at high risk for thrombosis due to their age and cardiovascular risk factors. The majority of AEs documented were grade 1–2, with only three out of 18 (17%) patients discontinuing due to AEs. The rate of CR 72% similar to that quoted in imminent studies including MPN-RC (Knudsen et al, 2018) and DALIAH trials (Mascarenhas et al, 2018), which recruited larger numbers of youngers ET and PV patients on PegIFN.

Over 20% of MPN patients develop resistance or intolerance to HU (Sever et al, 2014); therefore, there is a need for alternative cytoreductive agents. Our study demonstrates PegIFN to be effective and well-tolerated for use in patients >60 years and is an excellent cytoreductive option in this cohort.

Disclosure of Interest: None Declared.

BSH22-PO37 | Iron Status of Pregnant Women with Sickle Cell Disease (SCD)

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Abstract Content: Anaemia is a common complication of SCD and pregnancy. SCD patients with severe, symptomatic anaemia are commonly treated with red cell transfusions, which may predispose them to iron overload, iron toxicity, organ dysfunction and damage. Iron deficiency anaemia (IDA) in pregnancy is associated with increased risk of preterm delivery, low birth weight babies, placenta abruption, small for gestational age babies and maternal death. Though iron supplementation in pregnancy is recommended by WHO in regions where iron deficiency (ID) is common, there is no clear consensus on the role of routine iron supplementation in pregnant women with SCD.

In a cross-sectional study to test the hypothesis that there is no significant difference between iron status of pregnant women with SCD, pregnant HbAA and non-pregnant SCD controls; we recruited 50 pregnant women with SCD (HbSS and HbSC), 50 pregnant HbAA and 50 non-pregnant women with SCD as controls. We confirmed their Hb phenotypes, determined haematological indices, serum iron, total iron binding capacity (TIBC) and serum ferritin concentrations. Differences between categorical variables were determined using chi-squared test, unpaired Student's *t*-test to compare differences in two means and ANOVA to compare differences in the mean of greater than two groups. A p-value <0.05 was considered statistically significant at 95% CI.

Nine (18%) pregnant women with SCD (7 HbSS and 2 HbSC) were iron deficient (serum iron <10 µmol/l, TIBC >75 µmol/l and serum ferritin <30 ng/ml); compared to 13 (26%) pregnant HbAA women, and one (2%) non-pregnant SCD control. The odds of iron deficiency (ID) in pregnant SCD women was 0.11 (95% CI 0.01–0.91, p = 0.041) compared to non-pregnant SCD controls. None of our study subjects had iron overload (serum iron >30 ng/ml, TIBC <40 µmol/l and serum ferritin >800 ng/ml). There was no association between ID and: gravidity (p = 0.525), parity (p = 0.322), Hb phenotype (p = 0.389) and frequency of blood transfusion (p = 0.182) among the groups studied.

Abstract Table: Iron studies and haematological indices

Variable	Pregnant SCD	Pregnant HbAA	Non-Pregnant SCD	*p* Value
Haematological indices				
Hb (g/dl)	8.84 ± 1.44	10.46 ± 1.38*	8.03 ± 1.93*+	<0.001
MCV (fl)	90.24 ± 10.39	85.32 ± 7.06*	77.28 ± 8.31*+	<0.001
MCH (pg)	29.37 ± 3.95	28.50 ± 2.62*	24.49 ± 3.27*+	<0.001
MCHC (g/dl)	32.53 ± 2.02	33.46 ± 2.63*	31.63 ± 1.56*+	<0.001
Reticulocyte count (%)	3.92 ± 2.59	0.85 ± 0.71*	2.92 ± 1.63*+	<0.001
Iron studies				
Serum Fe (μmol/l)	24.17 ± 7.58	17.09 ± 6.98*	21.75 ± 5.60+	<0.001
TIBC (μmol/l)	68.90 ± 11.27	71.80 ± 15.06	64.06 ± 9.92+	0.007
Serum Ferritin (ng/ml)	80.77 ± 10.03	26.61 ± 3.55*	101.39 ± 9.77+	<0.001

Mean values with * are statistically significantly different from the SCD/Pregnant group at $p < 0.05$. Mean values with + are statistically significantly different from the HbAA/pregnant group at $p < 0.05$.

There were statistically significant differences in the serum iron ($p < 0.001$), serum ferritin ($p < 0.001$) and TIBC ($p = 0.007$) between the study and control groups (Table). HbAA controls had the lowest mean serum iron, highest mean TIBC and lowest mean serum ferritin compared with the SCD subjects; pregnant and non-pregnant. Haematological indices showed statistically significant differences between study and control groups ($p < 0.001$). Pregnant HbAA controls had the highest mean Hb concentration and lowest mean reticulocyte count. Pregnant women with HbSS disease had significantly higher mean serum ferritin concentration (106.08 ± 17.39 vs. 59.21 ± 9.70, $p = 0.018$), reticulocyte count (4.97 ± 3.15 vs. 3.03 ± 1.57, $p = 0.007$) but a lower mean Hb concentration (7.81 ± 1.09 vs. 9.72 ± 1.08, $p < 0.001$) compared to pregnant HbSC women.

Our study demonstrated the occurrence of ID in pregnant women with SCD. None of the subjects had iron overload. The fact that the prevalence of ID was lower in pregnant HbSS women compared to HbAA controls may suggest increased intestinal iron absorption in pregnant HbSS women, however, this is insufficient, because ID was commoner in these women than in their non-pregnant counterparts. With the known deleterious effect of ID on both mother and baby, we recommend that iron supplementation should be considered in selected pregnant women with SCD, especially when adequate nutritional intake cannot be guaranteed.

Disclosure of Interest: None Declared.

BSH22-PO38 | Enhancing chronic myeloid leukaemia (CML) patient safety and treatment management—Development of a management and audit tool for patients on tyrosine kinase inhibitor (TKI) therapy

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Abstract Content: The advent of TKI therapy over 20 years ago has fundamentally changed the outcomes for patients diagnosed with CML, so that a disease that was once severely life limiting, is now managed as a chronic condition. Life expectancy is now almost equivalent to those of matched controls with management more focussed towards control of long-term side effect profiles of TKI therapy and quality of life issues. Indeed, approaches to sustained remission free of treatment are the aim for appropriate cohorts of patients. While imatinib remains for many in the United Kingdom the drug of choice for first-line therapy, several further TKIs have since been licensed, which can provide deeper responses and overcome resistance to initial therapy. However, the increasing treatment options along with differential side effect profiles with the newer agents add to a level of complexity that can often result in suboptimal management in the outpatient settings. Partly in recognition of this, both the British Society for Haematology (BSH) and European Hematology Association have issued guidance on the diagnosis and management of CML.

The challenge for Haematology Departments, such as in Musgrove Park Hospital, Taunton, which serves a population of around 500 000, is effective implementation of these guidelines to ensure patient safety and optimisation of outcomes. Therefore, the aim was to generate a system to integrate patient information and guideline recommendations to enhance treatment plans and understanding, multidisciplinary team communication and patient outcomes.

An initial audit was performed on current practice and adherence to current national guidance. In this audit, while good adherence to BCR/ABL monitoring at 3/6/12 month milestones was noted, there was poorer adherence to guidance regarding monitoring of side effects and detailed correspondence to GPs. Using the dataset obtained and software already in use by the Haematology Department to manage CML patients, we were able to modify our datasheets to derive a working proforma tool. This occurred in three phases. First, we modified the existing CML patient data entry sheet, inputting baseline risk assessment criteria, response criteria at milestones and up to six lines of therapy, recording causes of any cessation in lines of therapy and mutation analysis. Second, we created a live audit tool. The aim of this was to

best support the clinician with summarising patient information and providing basic analysis to highlight patient safety concerns and aid treatment management. Third, a clinical letter template was developed in the Trust systems to enable clearer communication of treatment management plans.

In summary, we have developed a system which provides clear, visual, fail-safe prompts allowing appropriate management of TKI therapy and better adherence to BSH guidelines. Its implementation in the outpatient setting should allow optimisation of patient management of TKI therapy. A follow-up audit once the management/audit tool is implemented in clinics will be completed.

Disclosure of Interest: None Declared.

Laboratory Haematology and Transfusion

BSH22-PO39 | Assessing the utility of peripheral blood monocyte analysis and the fraction of classical monocytes (CD14 + ve CD16-ve) in the diagnosis of Chronic Myelomonocytic Leukaemia

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Abstract Content: Chronic Myelomonocytic Leukaemia (CMML) often poses a diagnostic challenge when utilising WHO diagnostic criteria, given inter-reporter variability of myelodysplastic changes. Selimoglu-Buet *et al.*(2015; Blood) reported increased classical monocytes (cMo, CD14 +ve, CD16 −ve) in CMML, although the high diagnostic specificity and sensitivity reported utilising their >94% threshold has not been reproduced by all groups. This study aimed to introduce a local flow cytometric assay, as described by Selimoglu-Buet *et al.,* as an additional diagnostic tool in CMML, determining sensitivity and specificity. A 6-colour flow cytometric panel was developed based on established protocols. Monocytes were selected on CD45 and side scatter, and contaminant cells were removed via exclusion gating, using CD16 (Granulocytes), CD56 (Natural Killer Cells), CD2 (T-cells) and CD24 (B-cells). Monocyte subsets were subpopulated based on CD16 *versus* CD14 expression into classical (CD14 + ve/CD16-ve), intermediate (CD14 +ve/CD16 +ve) and non-classical subsets (CD14 −ve/CD16 +ve). Peripheral blood samples were analysed in normal controls (n = 20) and patients with either a reactive new-onset monocytosis (n = 20) or CMML (n = 20). Samples with less than 10 000 monocyte events were excluded from the analysis. Table 1 details peripheral monocytes populations within the analysed groups. Patients with CMML had a significantly higher proportion of cMos than normal controls and those with a reactive monocytosis ($p < 0.001$; Kruskal–Wallis). There was no significant difference in cMos percentages between normal controls and those with reactive monocytosis (p 0.97; Mann–Whitney). The proportion of intermediate monocytes ($p < 0.01$; Mann–Whitney) and non-classical monocytes in CMML patients were significantly lower compared to normal controls and those with a reactive monocytosis and non-classical monocytes in CMML were significantly lower than normal controls ($p < 0.01$; Mann–Whitney). The local CMML population included patients with high-risk disease and a mixture of patients falling under the CMML0,1 and 2 and MPD/MDS classifications. A >94% cut-off for cMos gave a sensitivity and specificity of 25% and 100%, respectively, whereas >71.96% cut-off gave a sensitivity and specificity of 90% and 72.5%. This work confirms that CMML patients have increased cMos, a useful additional diagnostic tool in this uncommon cross-over syndrome, especially for individuals with >94% cMos (100% specificity). Reduced specificity at lower cut-offs, may be speculatively improved, in revised diagnostic criteria, utilising a myeloid next-generation sequencing assay, in addition to integrating current WHO criteria.

Abstract Table 1: Gives indices for local groups tested using the monocyte subset assay

Subset	Group		
	Normal (%)	Reactive Monocytosis (%)	CMML (%)
Classical			
Median	60.67	63.74	86.78
Interquartile Range (IQR)	21.14	24.88	19.31
Intermediate			
Median	27.05	28.53	6.12
IQR	21.80	17.51	16.63
Non-classical			
Median	7.29	2.10	1.47
IQR	5.03	5.44	2.82

Disclosure of Interest: None Declared.

BSH22-PO40 | Sickle screening of Blood Donors in Scotland using High-Performance Liquid Chromatography. Are we opening Pandora's box?

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Abstract Content: The Scottish National Blood Transfusion Service introduced sickle (Hb S) screening of blood donors in 2021 to allow the provision of Hb S negative blood for sickle

cell disease patients; neonates and intrauterine transfusions in Scotland, in line with the British Society for Haematology and Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) Guidelines respectively. No baseline donor ethnicity data were available to predict likelihood of Hb S in donors.

High-performance liquid chromatography (HPLC) was chosen as the screening method because it is a high throughput, fully automated process. The latter is helpful for Good Manufacturing Practice, which is an integral part of a Blood Establishment's remit, reducing the potential for transcription errors in the Laboratory Information Management System which could result in patients with special requirements receiving inappropriate component transfusion. Hb S confirmation is done at an external laboratory.

HPLC identifies all haemoglobin (Hb) variants present so donor management is more complex. As Hb variants have potential implications for donor health or reproduction, SNBTS felt an ethical duty to inform donors of abnormal variants including Hb S and elevated HbA1c >8%, which is potentially suggestive of diabetes mellitus (DM), accepting the risk that this strategy may lead to an increase in donor deferrals and an adverse effect on the blood supply. Donors who are Hb S carriers can continue to donate if there is no history of filter blockage leading to donation discards; donors with elevated HbA1c >8% with a history of DM who meet the JPAC donor selection criteria are allowed to continue donating but advised to inform their GP of the result and their history of blood donation and donors with elevated HbA1c >8% and no history of DM and those with other Hb variants are deferred from donating, subject to external investigation and clearance for future donation.

Three months post implementation, 2333 donors were screened. 2303 donors (98.7%) had normal HPLC; no Hb S positive donors were identified; 28 donors (1.2%) with elevated HbA1c >8% (14 with known history of DM) were found and 2 donors (0.1%) had other Hb variants. 17 donors (0.7%) (2 with unidentified Hb variants, 14 with elevated HbA1c >8% and no known history of DM and 1 with DM who did not declare diagnosis of DM or insulin use) were deferred from donating.

16 of the donors deferred were surveyed to find out results of external investigations. Of the five respondents, one was found to be a Hb C carrier and four were found to have Type 2 DM. All five donors intend to return to donate in future.

Hb S screening of blood donors in Scotland using HPLC has proven an efficient way to meet the blood specification requirements of certain patient cohorts without a high level of donor attrition or negative impact on the Scottish blood supply.

Disclosure of Interest: None Declared.

BSH22-PO41 | Maternal Allo-antibodies: A 10-year review at the Royal Bolton Hospital

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Abstract Content: Background: Testing women during pregnancy for the presence of clinically significant antibodies is an important factor in predicting the potential risk of Haemolytic disease of the foetus and the newborn (HDFN). Anti-D, anti-c and anti-K are the antibodies which most often result in HDFN that requires antenatal intervention. Despite the introduction of antenatal anti-D Ig, anti-D remains one of the most commonly detected maternal antibodies. UK guidelines recommend that women should have an ABO, RhD and antibody screen taken at booking and 28 weeks' gestation. Pregnancies at significant risk of HDFN should be referred to a foetal medicine unit. All neonates born to women with clinically significant maternal alloantibodies should have cord bloods taken at delivery to monitor the effects of the maternal antibody. The aims of this retrospective review were to estimate the incidence of clinically significant maternal alloantibodies in the population of patients who received their maternity care at the Royal Bolton Hospital and review the outcome of the foetus and neonate.

Methods: Data on the antibody specificities were retrieved from the laboratory information management system (Labcentre). Clinical information on the management of the pregnancy and clinical outcomes for the neonate was collected from the maternity clinical records (E3.NET 1.7, Euroking). All data were collected and maintained in an excel spreadsheet prospectively.

Results: Between January 2011 and December 2020, 475 pregnancies were identified with maternal clinically significant alloantibodies. A total of 362 women had maternal antibodies, of which 88 women had multiple pregnancies. We excluded 27 pregnancies due to transfer of care, miscarriages, intrauterine death and termination of pregnancy, leaving 448 cases. There were no foetal or neonatal deaths that were attributed to the maternal alloantibodies. The most common antibodies detected were Anti-M, anti-E, anti-D and anti-c detected in 126 (28.1%), 101 (22.5%), 75 (16.7%) and 44 (9.82%) of pregnancies respectively. A total of 104 (23.2%) cases resulted in a positive DAT at delivery. Of these 104 cases, there were 27 cases where the women or neonates required treatment, three in the antenatal period with an intrauterine transfusion, 21 in the postnatal period with either transfusion or phototherapy and three pregnancies required treatment in both the antenatal and postnatal periods (Table 1).

Discussion: All pregnancies at high risk of HDFN were managed jointly between the Joint Obstetric Haematology Clinic and Fetal Medicine Unit. The majority of cases that required treatment were due to anti-D and anti-c. None of the cases that resulted in treatment were due to anti-K. The

Abstract Table: The treatment requirements and antibodies for cases where the neonate had a positive DAT at delivery

Treatment	Cases (n = 30)* (27 pregnancies, 3 had two different treatments)	Antibody responsible
Intrauterine Transfusion (IUT)	6* (22.2%)	1 anti-c & 5 anti-D
Phototherapy	13 (48.1%)	3 anti-c, 1 anti-E, 1 anti-Fy[a] & 8 anti-D
Exchange transfusion	9* (33.3%)	9 anti-D
Top-up transfusion	2 (7.4%)	1 anti-D & 1 anti-E

three cases that required an IUT and an exchange transfusion were due to anti-D, all with levels above 15iu (59.5iu, 82.29iu and 19.18iu). Further work will look to evaluate the management and testing protocols of these 448 cases and effects of the newly implemented cell free foetal DNA testing for RhD negative women.

Disclosure of Interest: None Declared.

BSH22-PO42 | An audit of compliance with BCSH haemoglobinopathy patients transfusion requirements and antibody prevale prevalence in UK tertiary centre hospital blood bank

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Abstract Content: Background: Patients, with Sickle cell disease (SCD) and Thalassaemia (T), should receive Rh/K matched blood and be extended antigen typed to reduce the risk of alloimmunisation.

A retrospective audit checked request orders and patient history in the laboratory information system of Cambridge University Hospital.

There were 174 (SCD = 160, T = 14) haemoglobinopathy patients registered at our hospital.

Extended phenotyping was not recorded in 3 (21.4%) of T patients and 32 (20%) of SCD patients. Eighty-five (53.1%) of the SCD patients had an extended phenotype recorded and 9 (64.3%) of T patients. Only two (14.3%) T patients had a recorded genotype and 43 (26.9%) of sickle patients.

Twenty-two (13.8%) of SCD patients had allo antibodies compared to 3 T (21.4%) of thalassaemia patients. The specificities are listed in Figure 1.

All the patients with antibodies were typed for Rh/K as well as extended antigen typing. There were a total of 45 antibodies (with 16 different antibody specificities).

In SCD patients, the most common alloantibody was anti-M. This was followed by Rh antibodies anti-e and anti-C.

In T patients, the most common alloantibody was anti-E followed by anti-K and anti-Fya.

There were only three autoantibodies in sickle cell patients and one autoantibody in thalassaemia patients. Five sickle patients (3.1%) had Rh variants (3 x e, 2 x D and 3 x C) recorded. All of these patients had extended phenotyping.

The auto-antibodies were directed against in one case each against e, Jka and Fyb and in three cases against Jkb.

Conclusion: Although genotyping results are held on an NHSBT server and can be accessed through SpICE, it would be a safer, leaner way of working to have them easily accessible to BMS staff, issuing blood to patients, on the local LIMS. Ideally checking of the SpICE system should be automated into the BMS workflow when issuing blood.

Most significant among the antibodies is the detection of 3.1% anti-e, Anti-C, AND Anti-E antibodies, which could be indicative of a possible transfusion errors in the past and require further investigation.

Robust processes are required to ensure the communication of the haemoglobinoathy diagnosis to blood bank in all cases.

Abstract Table 1: Specificity of antibodies found in patient cohort

	SCD	T
anti-Fy1	1	1
anti-Jks	1	
anti-e	5	
anti-C	5	
anti-Leb	1	
anti-Lea	4	
anti-Jkb	3	
anti-Jka	2	
anti-Kpa	2	
anti-Cw	4	
anti-S	3	
anti-M	6	
anti-E	3	2
anti-Kpa	4	1

Disclosure of Interest: S. Makki: None Declared, V. Garcia Conflict with: Novartis, R. Auturally: None Declared, R. Jolley Conflict with: GBT, Novartis, C. Newsam: None Declared, K. Philpott: None Declared, T. Foukaneli: None Declared, E. Dickens: None Declared, M. Besser Conflict with: Novartis, GBT, Amgen, Agios, Conflict with: Sanofi, Hemeo,

BSH22-PO43 | Time to first plasma exchange in TTP—a regional Scottish experience

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Abstract Content: Acquired thrombotic thrombocytopenic purpura (TTP) is a rare disorder, caused by the development of antibodies against the von Willebrand factor (VWF) cleaving protein ADAMTS13, leading to the accumulation of ultra-large multimers of VWF and platelet aggregation. A low index of suspicion is needed as untreated mortality is high. Plasma exchange (PEX) has reduced this, although early deaths do occur. It is recommended that treatment with PEX is initiated as soon as possible and preferably within 4–8 h regardless of time of day of presentation.

We report the experience of PEX in cases of suspected TTP across two Scottish National Blood Transfusion Service (SNBTS) centres. This was performed as part of a review into apheresis service provision by SNBTS in Scotland. Due to the geography of Scotland, patients may have to be transferred considerable distances to their nearest tertiary centre. The SNBTS Therapeutic Apheresis Registry (STAR) was used to identify all cases of patients who were urgently referred for PEX for suspected TTP from May 2019 to May 2021.

Clinical details, including patient demographics, time taken from initial referral to first PEX and patient outcomes were obtained from hospital electronic records.

Twenty-seven patients were identified (M: F 11:16), mean age was 54 years (range 8–86 years). Thirteen of the 27 cases had TTP (12 acquired, 1 congenital). Other diagnoses included small vessel vasculitis (n = 1), haemolytic uraemic syndrome (HUS) (n = 4), aplastic anaemia (n = 1), atypical HUS (n = 3), disseminated intravascular coagulation (DIC) (n = 2), malignancy-associated thrombotic microangiopathy (TMA) (n = 1), microangiopathic haemolytic anaemia (MAHA) secondary to pancreatitis (n = 1) and in one case no cause was identified.

There was a significant difference in time to first PEX between those who received PEX for TTP in a health board that had an apheresis unit (Greater Glasgow and Clyde, and Lothian) when compared with those that required patient transfer (Tayside, Forth Valley, Lanarkshire, Ayrshire and Arran) (mean time = 4 h 16 min vs. 8 h 46 min, p = 0.017). Despite this, there was no significant difference in mean duration of stay between those who received PEX within a health board that hosts an apheresis unit and those who were transferred (22.7 days vs. 26 days, p = 0.83).

Causes of delay to PEX included difficulties with patient transfer (n = 4), difficulties establishing central venous access (n = 2) and delay due to a combination of both difficulties with central venous access and patient transfer (n = 1).

Of the TTP cases, all patients survived. Morbidity was seen in four patients with ischaemic stroke (n = 2), type 2 myocardial infarction (n = 1), venous thromboembolism (VTE) (n = 2) and one patient had both ischaemic stroke and a VTE).

Four patients who did not have TTP subsequently died. In these patients, the underlying diagnoses were DIC from malignancy, DIC from sepsis, TMA from metastatic breast carcinoma and HUS.

In summary, our data show that time from referral to initial PEX is longer for patients transferred to another health board and does exceed the recommended 8 h. However, the outcomes of these patients in terms of mortality and mean duration of hospital stay were comparable with those patients who received PEX locally, although we acknowledge that this series contains a small number of patients.

Disclosure of Interest: None Declared.

BSH22-PO44 | Comparative Study of Diagnostic Accuracy Between Rotational Thromboelstometry and Conventional Coagulation Tests

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Abstract Content: ROTEM (Rotational thromboelastometry) is a point of care viscoelastic haemostasis analyser that is being increasingly used in the diagnosis and management of coagulopathy. This novel diagnostic test aids in understanding coagulation pathways and bedside identification haemostasis disorders. When compared to Conventional coagulation techniques like Prothrombin time (PT), partial thromboplastin time (aPTT), platelet count & fibrinogen, viscoelastic methods like ROTEM resemble in vivo haemostasis, require one device to evaluate multiple coagulation factors, do not require centrifuge, measures cloth strength and dynamics. ROTEM has a faster turnaround time but requires more expensive reagents. The primary objective was to assess the diagnostic accuracy of ROTEM compared with conventional coagulation tests.

It was a cross-sectional, diagnostic evaluation test conducted in a tertiary care hospital in South India, among 109 patients above 18 years requiring coagulation assessment. In all the cases, both conventional tests and ROTEM were performed simultaneously. Comparison between standard conventional coagulation tests and ROTEM test (EXTEM, INTEM, FIBTEM) was done using SPSS AUC-ROC curve, standard error assessment and difference of $p < 0.05$ was taken as statistically significant.

The mean age of the study population was 42.7 years with 52.3% males and 47.7% females. The mean turnaround time (TAT) for ROTEM 11.2 min was around three times lesser than that of CCT 33.5 min. Fibrinogen had an excellent correlation (r >0.8) with A5 (Amplitude at 5th minute), A10

(Amplitude at 10 min) and MCF (Maximum clot firmness) of FIBTEM, compared to strong correlation with EXTEM (r >0.6) and INTEM (r >0.5). Also, AUC ROC for all these parameters was above 0.9 with >80% sensitivity and specificity. EXTEM parameters A5, A10, MCF & ALPHA had >70% sensitivity and specificity in diagnosing coagulopathy. A5 parameters have a strong correlation with MCF parameters and hence help in the early detection of clot firmness and coagulopathy. Platelet count had a significant correlation with A5, A10 & MCF of EXTEM. But clotting time (CT) and clot formation time (CFT) of EXTEM and INTEM do not correlate strongly with PT and APTT parameters of CCT and hence these values are not interchangeable. ROTEM was used more commonly for the management of trauma followed by PPH, surgery, snake bite and GI bleed.

We could conclude that FIBTEM, EXTEM and INTEM parameters can be used as surrogates to fibrinogen levels with great sensitivity and specificity. Significant reduction in TAT by ROTEM leads to early bedside identification and resuscitation of coagulopathy. ROTEM provides a global portrait of the clot formation within whole blood and allows for interaction between whole blood elements including platelet, fibrinogen and coagulation factors.

Disclosure of Interest: None Declared.

BSH22-PO45 | Assessment of intoxication indexes in local cold injury

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Local cold injury (LCI) is a medical and social problem. The unsatisfactory results of treatment of local cold injury are mainly due to errors in the diagnostics of the extent of damage and prediction of the outcomes of frostbite for the early periods of injury (Nizamoglu, 2016, Gonzaga, 2016). LCI is accompanied by processes of tissue damage, cells death and inflammation, which leads to developing intoxication. The different ratios and indexes of haematological parameters have been used as inflammatory and intoxication markers (Ostrovskii, 2006, Jiang, 2017).

In our study, we aimed to evaluate Leucocytic Intoxication Index (LII), Total Intoxication Index (TII) and Integral Intoxication Index (III) in rats with LCI. LII, TII—indicate the inflammation of various origins and III—can detect endogenous intoxication.

The research was performed on hairless rats in accordance with the requirements of the Bioethics Committee of the IPC&C of NAS of Ukraine and in conformity with the EU Directive 2010/63/EU for animal experiments. The LCI was performed using a cryoprobe (–192.0–194.8°C) with a diameter of 8.0 mm. The animals were divided into the control group (intact rats) and two experimental groups. The duration of cryo-exposure will be 30, 60 seconds (LCI_{30} and LCI_{60}).

After 4 h, LII after LCI_{30} increased 7.0 times; after LCI_{60} increased 4.2 times, TII remained unchanged, III increased by 2.2 with LCI_{30} and 1.8 with LCI_{60} to the control. It was noted that LII with LCI_{60} was 1.7 times lower than with LCI_{30}; in our opinion, this is due to an increased volume of the zone of local tissue hypothermia and a slower restoration of blood circulation in the LCI zone. The results obtained indicate that the indexes used to establish the presence of an acute inflammatory process but are not informative in assessing the severity of LCT.

One day later, the LII values with LCI_{30} and LCI_{60} exceeded the indicators in the control group by 6.5 and 12.2 times, TII increased only after LCI_{60} by 2.1 times, the III increased by 4.2 and 10.2 times respectively. It should be noted that the values of LII, TII and III with LCI_{60} were higher than with LCI_{30} by 1.9, 1.7 and 2.4 times, respectively, which indicates the possibility of establishing the severity of LCI. At this time of observation, indexes allow us to simultaneously confirm the presence and severity of acute inflammation and endogenous intoxication, making it possible to judge the severity of LCI.

The use of indexes based on assessing the relationship between different types of blood cells is a promising direction in determining the systemic manifestations of LCI. These indexes reveal the presence and severity of inflammation and intoxication caused by tissue destruction during LCI and can be easily calculated. The results obtained can help improve the quality of diagnosis and treatment of LCI.

Disclosure of Interest: None Declared.

BSH22-PO46 | Improving compliance with blood and platelet transfusion thresholds on a tertiary haematology ward

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Abstract Content:

Restrictive transfusion thresholds are accepted as optimal blood management for patients receiving transfusions.[1] Unnecessary blood transfusions result in increased blood product shortages (exacerbated by the COVID-19 pandemic),[2] adverse patient outcomes and significant costs to health systems.[3]

To improve transfusion practice, we aimed to minimise inappropriate transfusions through exploring and targeting areas of noncompliance with locally agreed red blood cell (RBC) and platelet transfusion thresholds of 80 g/l and $10*10^9$/l respectively.

Abstract Table:

	Aug 2020	Feb 2021	May 2021	Jun 2021
Percentage compliance and fraction of RBCs and Platelets transfused				
Appropriate RBC transfusions	89% (73/82)	81% (52/57)	93% (83/89)	95% (88/93)
Appropriate platelet transfusions	97.7% (129/132)	97% (70/72)	97% (76/79)	97%(112/115)

We conducted a retrospective multicycle audit over 4 months (Aug 2020, Feb 2021, May 2021 and Jun 2021) for all patients on the Haematology–Oncology ward. Standards were set at 100% compliance with local hospital guidelines. We analysed the number of RBC and platelet transfusions, pre- and post-transfusion haemoglobin and platelet counts, and clinical indications for transfusion.

Actions implemented following each cycle composed of departmental meetings, teaching for foundation doctors and trainees, trust guideline updates and creation of a RBC transfusion checklist on our electronic 'EPIC' prescribing system.[4]

Percentage compliance for RBC transfusions improved from 89% to 95% following actions implemented per audit cycle. Inappropriate RBC transfusions associated with discharge decreased from 10% to 1% and transfusion of two RBC units without appropriate increment decreased from 10% to 3%.

Although percentage compliance of platelet transfusions did not improve from Aug 2020 to Jun 2021, they were consistently higher (97%) compared to RBC transfusions. This may be secondary to differing causes for inappropriate platelet transfusions detected each cycle. Despite inappropriate HLA-platelet use detected in the latest cycle, there are improvements in documentation to justify platelet transfusions outside normal threshold (100% in latest cycle), total number of platelets transfused and transfusion associated with discharge.

Our audit has been successful in improving overall transfusion practice on the Haematology–Oncology ward. Ongoing education and re-audit will ensure this is maintained.

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Disclosure of Interest: None Declared.

BSH22-PO47 | HIV, Hepatitis B and C viruses and syphilis coinfection among blood donors in hospital settings

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Abstract Content: HIV, Hepatitis B and C viruses and syphilis coinfection among blood donors in hospital settings.

There is a heavy burden of HIV-HBV and HIV-HCV coinfection in the developing world, including India. There is a probability that co-infection with HIV and HBV can progress to chronic hepatitis B and hence increased liver-related mortality. Hepatitis C coinfection has been found to be more common in HIV-positive individuals and is associated with an increased mortality and morbidity. Co-infection with HCV and HIV has been associated with rapid decline in the CD4 count and rapid progression of HIV infection. Therefore, this study was planned to assess seroprevalence of these co-infections with HIV, HBV, HCV and Treponema palladium (TP) and to assess associated factors in donor history for them. A retrospective observational study was conducted in the department of transfusion medicine (TM) at a tertiary-level healthcare centre between January 2019 and December 2021. A total of 18 819 donor samples were subjected to screening for TTIs by two different methods simultaneously ECLIA and mini-pool NAT testing. All donors with co-infections were identified and necessary records for identifying associated factors were obtained from the donor screening form as well as the reactive donor counselling form. When tested by ECLIA, the seroprevalence for co-infection with HCV and TP was 0.0053% (1/18 819). The seroprevalence for co-infection with HBV and HIV was 0.010% (2/18 819). The seroprevalence for co-infection with HBV and VDRL was 0.015% (3/18 819). The seroprevalence for co-infection with HIV and TP was 0.021% (4/18 819). When tested by NAT, the prevalence of co-infection with HCV and VDRL was 0.0053% (1/18 819). The prevalence of co-infection with HBV and HIV was 0.010% (2/18 819). The prevalence of co-infection with HBV and TP was 0.010% (2/18 819). The prevalence of co-infection with HIV and TP was 0.021% (4/18 819). Out of the 10 reactive cases, three factors were found to be significantly (p-value<0.05) associated with co-infection replacement donations, first-time donors and male donors. Blood safety is a challenge in India because of the high prevalence of HIV, HCV, HBV and TP. There is a relatively low percentage of volunteer donors, repeat donors and female donors. Many factors favour coinfections. However, with our study, we found that voluntary donations,

repeat donors and female donations are safer as compared to replacement donors, first-time donors and male donors. Therefore, it is of utmost importance to screen and counsel donors, promote voluntary and repeat donations and to know the rates of these coinfections among otherwise healthy blood donors at risk of transmitting these TTIs.
Disclosure of Interest: None Declared.

CCBSH22-PO48 | Haematological changes & in-hospital mortality in severe COVID-19

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Abstract Content: COVID-19 is an acute respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first detected in China (December 2019) but now widespread. The aim of this study was to investigate the main haematological changes in severe cases of COVID-19 and if full blood count results at admission can be used to determine in-hospital mortality risk.
This retrospective observational study included laboratory results of confirmed cases of hospitalised patients with SARS-CoV2 infection in Jersey between March and December 2020 (subject to inclusion criteria), split into two subgroups based on outcome (non-survivors *versus* survivors). Statistically significant changes between groups were defined by probability (p) <0.05, using t-test, Mann–Whitney test, or X^2/Fisher exact test, as appropriate. Multivariate and univariate logistic models were used to determine risk factors for in-hospital mortality.
A total of 81 cases (out of 113 available cases) were included in this study: median age: 75 years; 48 patients were men (59.3%); 27 non-survivors (33.3%) and 18 (22%) required intensive care.
Non-survivors showed the following statistically significant changes compared to survivors: non-survivors were older (median age: 82 vs. 74 years, $p = 0.003$); 70.4% presented with marked lymphopenia (median: 0.63 vs. 0.99×10^9/l, $p = 0.025$), 55.6% with raised creatinine (median: 103.0 µmol/l, $p = 0.024$), 40.7% with elevated white blood cells (WBC) (median: 9.5 vs. 7.3×10^9/l, $p = 0.042$) and 14.8% with lower mean cell haemoglobin concentration (MCHC) (32.99 vs. 33.79 g/dl, $p = 0.030$).
Univariate analysis showed age ≥ 82 years was significantly associated with death (odds ratio [OR] = 4.210, $p = 0.005$). Multivariate logistic analysis identified the following risk factors for in-hospital mortality: lymphocytes $<0.85 \times 10^9$/l (OR = 6.694, $p = 0.004$), WBC $>9.5 \times 10^9$/l (OR = 4.855, $p = 0.015$) and creatinine >100 µmol/l (OR = 3.280, $p = 0.049$). Full blood count results on hospital admission can be used to identify COVID-19 patients with higher mortality risk. In-hospital mortality risk was shown to be 6.7 times higher in patients presenting with a lymphocyte count $<0.85 \times 10^9$/l, 4.9 times higher in patients presenting with a WBC $>9.5 \times 10^9$/l and 3.3 times higher for those presenting with creatinine levels over 100 µmol/l. Age ≥ 82 years was significantly associated with death. Additionally, this study suggests male gender is a risk factor for hospital admission in COVID-19.
Disclosure of Interest: None Declared.

BSH22-PO49 | ABO-related D-dimer elevation and severity In SARS-cov2-infected Tunisian patients

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Abstract Content: Introduction: The blood group is an important biological parameter in the development of several infectious, bacterial or viral diseases. Many studies have shown that virus SARS-cov2 preferentially attaches to the epithelial cells of people with blood group A (affinity between protein S and antigen A).
The main objective of the study was to find the relationship between blood group, D-dimer level and the severity of infection SARS-cov2.
Patients and Methode: This is an exposure-non exposure descriptive study (SARS-cov2 infection+) of 133 Tunisian patients included consecutively between January and April 2021 at Rabta hospital. The patients were subdivided into groups according to the presence or absence of antigen A. The phenotype distribution of SARS-cov2 patients was compared with that of a control group of 2801 patients not affected by SARS-cov2 and with the blood group distribution of a blood donor population ($N = 3072$).
Results: During the study, 133 Tunisian patients were included. Group A (group A and AB) was present in 39.8% of patients ($N = 53$) *versus* non-A group (group O and B) in 60.2%. The average D-dimer level was 7291.59 ng/ml in group A *versus* 3047.34 ng/ml in non-A group with a statistically significant difference ($p = 0$). The rate of resuscitation was higher in group A (34.6%) *versus* non-A group (11.1%) with a statistically significant difference ($p = 0.02$). The period of hospitalisation was longer in group A (average 15.06 days) *versus* non-A group (average 10.08 days) with a statistically significant difference ($p = 0.02$). The blood type was not independently associated with the mortality rate. It was 19.2% in group A *versus* 13.9% for the NON-A group with a difference not statistically significant ($p = 0.5$).
Conclusion: This study suggests the ABO blood group could be one of the factors that play a role in determining SARS-cov2 susceptibility severity with more need for resuscitation and an increase in the period of hospitalisation. A large study would be interesting to confirm these results.
Disclosure of Interest: None Declared.

BSH22-PO50 | RDW: useful prognostic marker in acute COVID-19 infection

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Abstract Content: COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has been associated with over 5 million deaths worldwide since December 2019.

Red cell distribution width (RDW) is a routine full blood count parameter that reflects the level of change in size between red cells (anisocytosis) and has been widely researched as an independent predictor of mortality in different hospital settings, including critically ill patients with sepsis. This study aims to investigate if RDW results on admission may be used as a prognostic marker in patients with acute COVID-19 infection.

This retrospective study included 81 hospitalised patients with COVID-19 at the General Hospital in Jersey (Channel Islands, UK), subject to inclusion criteria. Differences between groups were calculated using the *t* test if data were normally distributed, otherwise the Mann–Whitney test was used. $p < 0.05$ was considered significant for all tests. Area under curve (AUC) and the 95% confidence interval (CI) were determined to establish optimal cut-off point that maximised sensitivity and specificity to predict death by the Youden's index. Logistic regression was then used to determine the odds of in-hospital mortality.

Non-survivors were found to be significantly older (median age: 82 years; overall range: 50–94 vs. 74 years; overall range: 28–92 in survivors; $p = 0.003$) and presented with higher RDW when compared with survivors (14.1 vs. 13.4; $p = 0.028$). A total of 63 patients (78%) received ward-based care, while 18 patients (22%) required intensive care. Men accounted for most deaths (males: 16 deaths, 59.3% vs. females: 11 deaths, 40.7%), although the mortality rate in males and females was undistinguishable (males: 33.3% vs. females: 33.3%).

Multivariate logistic analysis demonstrated that RDW >14% on admission was associated with a 5-fold increased mortality risk in hospitalised patients with COVID-19 (OR = 5.335 [95% CI 1.524–18.674]; $p = 0.009$). This association was shown to be independent of age and other potential confounders such as lymphocyte count, white cells, or creatinine levels.

This study confirms the prognostic potential of RDW in hospitalised patients with COVID-19. Identifying patients with higher risk of in-hospital mortality may enable prioritisation of resources and targeted treatments, which could ultimately improve outcomes.

Disclosure of Interest: None Declared.

Lymphoma, CLL

BSH22-PO52 | First Interim Analysis of ALPINE Study: Results of a Phase 3 Randomised Study of Zanubrutinib *versus* Ibrutinib in Patients with Relapsed/Refractory Chronic Lymphocytic Leukaemia/Small Lymphocytic Lymphoma

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Abstract Content: Treatment of chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) has been transformed with inhibitors of B-cell receptor signalling, such as Bruton tyrosine kinase (BTK) inhibitors. The first-generation BTK inhibitor ibrutinib is a standard of care in CLL/SLL. Zanubrutinib is an irreversible next-generation BTK inhibitor designed to maximise BTK occupancy and minimise off-target inhibition. It was hypothesised that the increased specificity of zanubrutinib may minimise toxicities related to ibrutinib off-target inhibition and that more

complete and sustained BTK occupancy may improve efficacy outcomes. Activity and tolerability of zanubrutinib in patients with CLL/SLL has been demonstrated in early phase trials. ALPINE (BGB-3111-305; NCT03734016) is a global, randomised, phase 3 study comparing zanubrutinib *versus* ibrutinib in patients with relapsed/refractory (R/R) CLL/SLL. Here we present the results of a preplanned interim analysis scheduled approximately 12 months after the first 415 out of 652 patients were enrolled.

Patients with R/R CLL/SLL were randomly assigned 1:1 to receive zanubrutinib 160 mg twice daily or ibrutinib 420 mg once daily until disease progression. Randomisation was stratified by age (<65 years vs. ≥65 years), geographical region, refractory status and del17p/TP53 mutation status. The primary end-point was overall response rate (ORR) as determined by investigators using the 2008 International Workshop on CLL guidelines and the Lugano criteria for SLL. Sample size was calculated to provide 90% power to demonstrate non-inferiority of zanubrutinib to ibrutinib response ratio at the non-inferiority margin of 0.8558. A hierarchical testing approach was implemented to test the superiority of zanubrutinib over ibrutinib in ORR if non-inferiority was demonstrated.

Between 5 Nov 2018 and 20 Dec 2019, 415 patients were randomised. Treatment groups were well balanced for demographical and disease characteristics: age ≥ 65 years 62.3% vs. 61.5%, male 68.6% vs. 75%, >3 prior lines of therapy 7.3% vs. 10.1%, del17p 11.6% vs. 12.5%, TP53 mutated without del17p 8.2% vs. 5.8%, in zanubrutinib and ibrutinib arms respectively. At a median follow-up of 15 months, ORR was significantly higher with zanubrutinib *versus* ibrutinib (78.3% vs. 62.5%, 2-sided $p = 0.0006$ compared with a prespecified alpha of 0.0099 for interim analysis). ORR was higher in patients with del11q (83.6% vs. 69.1%) and del17p (83.3% vs. 53.8%) with zanubrutinib, as were overall 12-month progression-free survival (PFS; 94.9% vs. 84.0%) and overall survival rates (97.0% vs. 92.7%). The rate of atrial fibrillation/flutter, a prespecified safety end-point, was significantly lower with zanubrutinib *versus* ibrutinib (2.5% vs. 10.1%, 2-sided $p = 0.0014$, compared with a prespecified alpha of 0.0099 for interim analysis). Rates of major bleeding (2.9% vs. 3.9%), and adverse events leading to discontinuation (7.8% vs. 13.0%) or death (3.9% vs. 5.8%) were also lower with zanubrutinib. Rate of neutropenia was higher with zanubrutinib (28.4% vs. 21.7%), while grade ≥3 infections were lower with zanubrutinib (12.7% vs. 17.9%).

In this interim analysis of a randomised, phase 3 ALPINE study in patients with R/R CLL/SLL, zanubrutinib was shown to have a superior response rate, an improved PFS, and a lower rate of atrial fibrillation/flutter compared with ibrutinib. These data support that more selective BTK inhibition, with more complete and sustained BTK occupancy, results in improved efficacy and safety outcomes.

Disclosure of Interest: P. Hillmen Conflict with: Janssen, Abbvie, Pharmacyclics, Roche, Gilead, Conflict with: Janssen, Abbvie, Pharmacyclics, Astra Zeneca, SOBI, Beigene, B. Eichhorst Conflict with: Janssen, Roche, Novartis, AbbVie, Gilead, Celgene, ArQule, AstraZeneca, Oxford Biomedica (UK), MSD, Conflict with: Janssen, Gilead, Roche, AbbVie, BeiGene, Astra Zeneca, Conflict with: Janssen, Gilead, Roche, AbbVie, Novartis, Celgene, AstraZeneca, Adaptive Biotechnologies, Hexal, J. R. Brown Conflict with: Abbvie, Acerta/Astra-Zeneca, Beigene, Bristol-Myers Squibb/Juno/Celgene, Catapult, Eli Lilly, Genentech/Roche, Janssen, MEI Pharma, Morphosys AG, Nextcea, Novartis, Pfizer, Rigel, Conflict with: Gilead, Loxo/Lilly, SecuraBio, Sun, TG Therapeutics, Conflict with: Invectys, N. Lamanna Conflict with: Abbvie, AstraZeneca, BeiGene, Genentech, Janssen, Pharmacyclics, Conflict with: Abbvie, AstraZeneca, BeiGene, Genentech, Loxo, MingSight, Octapharma, Oncternal, TG Therapeutics, S. O'Brien Conflict with: Amgen, Astellas, Celgene, GlaxoSmithKline, Janssen Oncology, Aptose Biosciences Inc., Vaniam Group LLC, AbbVie, Alexion, Verastem, Juno Therapeutics,Vida Ventures, Autolus, Johnson and Johnson, Merck, Bristol Myers Squibb, NOVA Research Company, Gilead, Pharmacyclics, TG Therapeutics, Pfizer, Sunesis, Conflict with: Kite, Regeneron, Acerta, Caribou, Gilead, Pharmacyclics, TG Therapeutics, Pfizer, Sunesis, Conflict with: Gilead, Pharmacyclics, TG Therapeutics, Pfizer, Sunesis, C. S. Tam Conflict with: Beigene, Conflict with: Abbvie, Janssen, Beigene, Conflict with: AbbVie, Janssen, Beigene, L. Qiu: None Declared, M. Kazmierczak: None Declared, K. Zhou: None Declared, M. Šimkovič Conflict with: Astra Zeneca, AbbVie, Conflict with: Beigene, Janssen-Cillag, Astra Zeneca, Conflict with: University Hospital Hradec Králové, AbbVie, Gilead, Janssen-Cilag,, J. Mayer Conflict with: BeiGene, A. Gillespie -Twardy: None Declared, M. Shadman Conflict with: Abbvie, Genentech, AstraZeneca, Sound Biologics, Pharmacyclics, Beigene, Bristol Myers Squibb, Morphosys, TG Therapeutics, Innate Pharma, Kite Pharma, Adaptive Biotechnologies, Epizyme, and Atara Biotherapeutics, Conflict with: Mustang Bio, Celgene,Bristol Myers Squibb, Pharmacyclics, Gilead, Genentech, Abbvie, TG Therapeutics, Beigene, AstraZeneca, Sunesis, Atara Biotherapeutics, A. Ferrajoli Conflict with: Beigene, Astra-Zeneca, Conflict with: Janssen, Beigene, Astra-Zeneca, P. S. Ganly Conflict with: BeiGene, R. Weinkove Conflict with: AbbVie Ltd, Janssen-Cilag, Conflict with: Wellington Zhaotai Therapies Ltd, Conflict with: Beigene Ltd, AbbVie Ltd, Janssen-Cilag, T. Salmi Conflict with: BeiGene Switzerland GmbH, BeiGene, M. Ji Conflict with: BeiGene (Beijing) Co., Ltd., J. Yecies Conflict with: BeiGene, Ltd., K. Wu Conflict with: BeiGene, W. Novotny Conflict with: BeiGene, J. Huang Conflict with: BeiGene, W. Jurczak Conflict with: BeiGene, Conflict with: BeiGene, Janssen, Astra Zeneca, Loxo, TGH therapeutics, Tellios.

BSH22-PO53 | Subcutaneous Epcoritamab in Combination With Rituximab and Lenalidomide in Relapsed or Refractory Follicular Lymphoma: Preliminary Phase 1/2 Results

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Abstract Content: Patients (pts) with relapsed or refractory (R/R) follicular lymphoma (FL) develop increasingly aggressive disease with each line of treatment. Despite high overall response rates (ORRs) with rituximab and lenalidomide (R^2) in R/R FL, the disease remains incurable. Epcoritamab (DuoBody-CD3xCD20) is a subcutaneously administered bispecific antibody that binds to CD20 on B cells and CD3 on T cells, activating T cells to kill $CD20^+$ malignant B cells. Single-agent epcoritamab had manageable safety and substantial antitumour activity in pts with heavily pretreated B-cell non-Hodgkin lymphoma (NHL) in the first-in-human phase 1/2 EPCORE NHL-1 trial (NCT03625037). In pts with R/R FL (median prior lines of therapy: 5), epcoritamab (0.76–48 mg) had an ORR of 90% (9/10) and a complete response rate of 50% (5/10). These data supported initiation of EPCORE NHL-2 (NCT04663347), a phase 1/2 trial evaluating epcoritamab in combination with standard B-cell NHL therapies. We present preliminary results from arm 2, which is evaluating epcoritamab + R^2 in R/R FL.

Adults with R/R $CD20^+$ FL received epcoritamab in a dose-escalation phase followed by an expansion phase at the recommended phase 2 dose (RP2D) + R^2 for 12 cycles (28 days/cycle). Step-up dosing and corticosteroids were required during cycle 1 to mitigate cytokine release syndrome (CRS). Responses were evaluated by position emission tomography/computed tomography.

As of September 16, 2021, 29 pts had received epcoritamab + R^2 (3 received epcoritamab 24 mg, 26 received 48 mg). The median age was 67 years; 66% had one prior line of therapy (range, 1–5). Eleven (38%) pts had progressed within 24 months of initial (prior) therapy, and eight (28%) progressed within 24 months of first immunochemotherapy. The median follow-up was 2.8 (range, 0.2–8.5) months. The median number of cycles initiated was 3 (range, 1–8). Treatment-emergent adverse events (TEAEs) in >25% of pts were CRS (48%; 28% grade [G] 1, 14% G2, 7% G3), injection-site reaction (41%; all G1/2), all infections (38%; 31% G1/2, 7% G3), constipation (28%; all G1/2) and cough (28%; all G1/2). The majority of CRS events occurred in cycle 1; CRS events resolved with standard management. No dose-limiting toxicities were reported for epcoritamab. No immune effector cell-associated neurotoxicity syndrome events, clinical tumour lysis syndrome events, or fatal TEAEs were observed. All 21 efficacy-evaluable pts responded (ORR: 100%; 21/21), with 81% (17/21) achieving a complete metabolic response (CMR); 95% of responders (20/21) remained in response and continued to receive study treatment.

These data suggest that epcoritamab can be combined with R^2 with a manageable safety profile and no new safety findings. The combination showed encouraging preliminary activity, with nearly all pts achieving early CMR and no relapses observed.

Encore statement: This abstract was previously presented in part at the American Society of Hematology Annual Meeting and Exposition, December 11–14, 2021, Atlanta, GA, USA and virtual.

Funding statement: This study was funded by Genmab A/S and AbbVie.

Disclosure of Interest: K. M. Linton Conflict with: Genmab, Roche, Conflict with: Genmab, Roche, Celgene, Beigene, Blood Cancer UK, Roy Castle Lung Cancer Foundation, Conflict with: Aptitude Health, Hartley Taylor, Kite, Karyopharm, B. Wahlin Conflict with: Roche, Conflict with: Gilead Sciences, Roche, S. Leppä Conflict with: Orion, CHO Pharma USA, Conflict with: Genmab, Novartis, Roche, Takeda, Bayer, Celgene, Nordic Nanovector, Conflict with: Incyte, MSD, University of Helsinki and Helsinki University Hospital, Finnish Cancer Organizations, F. Morschhauser Conflict with: F. Hoffmann-La Roche Ltd, Gilead, Epizyme, AbbVie, Genentech, Inc., Servier, BMS, Novartis. Roche, Conflict with: Janssen, Celgene, Incyte, Genmab, Chugai, AstraZenenca, B. Elliott Conflict with: Genmab, T. Liu Conflict with: Genmab, M. Cota Stirner Conflict with: AbbVie, A. Abbas Conflict with: Genmab, L. Falchi Conflict with: Genmab, AbbVie, Conflict with: Genmab, AbbVie, Roche, Genetech.

BSH22-PO54 | SEQUOIA: Results of a Phase 3 Randomised Study of Zanubrutinib *versus* Bendamustine + Rituximab in Patients with Treatment-Naïve Chronic Lymphocytic Leukaemia/Small Lymphocytic Lymphoma

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Abstract Content: Zanubrutinib (zanu) is a selective next-generation Bruton tyrosine kinase (BTK) inhibitor designed to have high specificity for BTK and minimal off-target effects. SEQUOIA (NCT03336333) is an open-label, global phase 3 study that randomised treatment naïve (TN) patients with chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) without del(17p) to receive zanu 160 mg twice daily until progressive disease or unacceptable toxicity, or bendamustine 90 mg/m^2 on day 1 and 2 and rituximab 375 mg/m^2 in cycle 1, 500 mg/m^2 in cycles 2–6 for 6 × 28-day cycles (BR). Adult patients who met International Workshop on CLL (iwCLL) criteria for treatment were eligible if they were ≥ 65 years or unsuitable for treatment with fludarabine, cyclophosphamide and rituximab. Central verification of del(17p) status by fluorescence in situ hybridisation was required. Patients were stratified by age (<65 years vs. ≥65 years), Binet Stage (C vs. A/B), immunoglobulin heavy chain gene (IGHV) mutational status and geographical region. The primary end-point was independent review committee (IRC)-assessed progression-free survival (PFS). Secondary end-points included PFS by investigator assessment (INV), overall response rate (ORR; by IRC and INV), overall survival (OS) and safety. Responses for CLL and SLL were assessed per modified iwCLL criteria and Lugano criteria respectively. Adverse events (AEs) were recorded until disease progression.

From 31 Oct 2017–22 Jul 2019, 479 patients without del(17p) were randomised to zanu (n = 241) and BR (n = 238). Treatment groups were well balanced for demographical and disease characteristics (zanu vs. BR): median age, 70.0 years vs. 70.0 years; unmutated IGHV, 53.4% (125/234) vs. 52.4% (121/231); and del(11q), 17.8% vs. 19.3%. At median follow-up (26.2 months), PFS was significantly prolonged with zanu *versus* BR as assessed by IRC (hazard ratio [HR] 0.42, 95% CI 0.28–0.63, 2-sided $p < 0.0001$), and INV (HR 0.42, 95% CI 0.27–0.66, 2-sided $p = 0.0001$). Treatment benefit for zanu was observed across subgroups for age, Binet stage, bulky disease and del(11q) status and for patients with unmutated IGHV (HR 0.24, 2-sided $p < 0.0001$), but not for mutated IGHV (HR 0.67, 2-sided $p = 0.1858$). Estimated 24-mo PFS (IRC) (zanu vs. BR) was 85.5% (95% CI 80.1%–89.6%) vs. 69.5% (95% CI 62.4%–75.5%); ORR by IRC was 94.6% (95% CI 91.0%–97.1%) vs. 85.3% (95% CI 80.1%–89.5%); complete response rate was 6.6% vs. 15.1%; ORR by INV was 97.5% (95% CI 94.7%–99.1%) vs. 88.7% (95% CI 83.9%–92.4%); estimated 24-mo OS was 94.3% (95% CI 90.4%–96.7%) vs. 94.6% (95% CI 90.6%–96.9%).

AEs of interest occurring during the full reporting period (pooled terms, zanu vs. BR) included atrial fibrillation (any grade [gr]: 3.3% vs. 2.6%), bleeding (any gr/gr≥3: 45.0%/3.8% vs. 11.0%/1.8%), hypertension (any gr: 14.2% vs. 10.6%), infection (any gr/gr≥3: 62.1%/16.3% vs. 55.9%/18.9%) and neutropenia (any gr/gr≥3: 15.8%/11.7% vs. 56.8%/51.1%). Treatment discontinuation due to AEs occurred in 20 patients (8.3%) vs. 31 patients (13.7%) (zanu vs. BR) and AEs leading to death occurred in 11 patients (4.6%) vs. 12 patients (5.3%). No sudden deaths were reported.

In this global registrational trial, zanu demonstrated statistically significant improvement in PFS compared with BR as assessed by IRC. Superiority was also observed in PFS by INV and ORR by IRC and INV. Zanu was well tolerated,

with low rates of atrial fibrillation. These data support the potential utility of zanu in the frontline management of patients with TN CLL/SLL.

Disclosure of Interest: T. Munir Conflict with: Abbvie, AstraZeneca, Roche, Alexion, Janssen, Morphosys, Sobi, K. Giannopoulos Conflict with: Abbvie, Amgen, Astra-Zeneca, Bei-Gene, Janssen, Sanofi-Genzyme, Novartis, Takeda, Roche, Karyopharm, GSK, Sandoz, Conflict with: Abbvie, Amgen, Astra-Zeneca, Bei-Gene, Janssen, Sanofi-Genzyme, Novartis, Takeda, Roche, Gilead, TG Therapeutics, Conflict with: Polish Myeloma Consortium, Next Generation Hematology Association, Abbvie, Amgen, Astra-Zeneca, Bei-Gene, Janssen, Sanofi-Genzyme, Novartis, Takeda, Roche, Karyopharm, GSK, Gilead, Sandoz, Pfizer, Teva, W. Jurczak Conflict with: Abbvie, Astra Zeneca, Beigene, Celgene, Debbiopharm, Epizyme, Incyte, Janssen, Merck, Roche, Takeda, TG Therapeutics, M. Šimkovič Conflict with: AbbVie, AstraZeneca, Janssen-Cilag, Conflict with: University Hospital Hradec Kralove, AbbVie, Merck, Eli Lilly, J&J, AstraZeneca, Gilead, Janssen-Cilag, M. Shadman Conflict with: Abbvie, Genentech, AstraZeneca, Sound Biologics, Pharmacyclics, Beigene, Bristol Myers Squibb, Morphosys, TG Therapeutics, Innate Pharma, Kite Pharma, Adaptive Biotechnologies, Epizyme, Eli Lilly and Atara Biotherapeutics, Adaptimmune, Conflict with: Mustang Bio, Celgene, Bristol Myers Squibb, Pharmacyclics, Gilead, Genentech, Abbvie, TG Therapeutics, Beigene, AstraZeneca, Sunesis, Atara Biotherapeutics, GenMab, Conflict with: Abbvie, Genentech, AstraZeneca, Sound Biologics, Pharmacyclics, Beigene, Bristol Myers Squibb, Morphosys, TG Therapeutics, Innate Pharma, Kite Pharma, Adaptive Biotechnologies, Epizyme, Eli Lilly and Atara Biotherapeutics, Adaptimmune, A. Österborg Conflict with: BeiGene, Gilead, L. Laurenti Conflict with: Roche, AbbVie, Conflict with: AbbVie, Roche, BeiGene, Janssen, AstraZeneca, P. Walker Conflict with: BeiGene, Acerta, S. 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Trněný Conflict with: Janssen, Gilead Sciencies, Takeda, Bristol-Myers Squibb, Amgen, Abbvie, Roche, MorphoSys, Incyte, Novartis, Conflict with: First Faculty of Medicine, Charles University General Hospital in Prague, Janssen, Gilead Sciences, Bristol-Myers Squibb, Amgen, Abbvie, Roche, Astra Zeneca, MorphoSys, Incyte, Portolla, Takeda, Novartis, Gilead, D. M. Brander Conflict with: AbbVie, Genentech, Pharmacyclics, Pfizer, TG Therapeutics, Verastem, Conflict with: AbbVie, ArQule, Ascentage, AstraZeneca, BeiGene, DTRM, Genetech, Juno/Celgene/BMS, LOXO, MEI Pharma, Novaris, Pharmacyclics, TG Therapeutics, Conflict with: NCCN, I. W. Flinn Conflict with: AbbVie, AstraZeneca, BeiGene, Century Therapeutics, Genentech, Gilead Sciences, Great Point Partners, Hutchison MediPharma, Iksuda Therapeutics, Janssen, Juno Therapeutics, Kite Pharma, MorphoSys, Novartis, Nurix Therapeutics, Pharmacyclics, Roche, Seattle Genetics, Servier Pharmaceuticals, Takeda, TG Therapeutics, Unum Therapeutics, Verastem, Vincerx Pharma, Yingli Pharmaceuticals, Conflict with: AbbVie, Acerta Pharma, Agios, ArQule, AstraZeneca, BeiGene, Calithera Biosciences, Celgene, Constellation Pharmaceuticals, Curis, Forma Therapeutics, Forty Seven, Genentech, Gilead Sciences, IGM Biosciences, Incyte, Infinity Pharmaceuticals, Janssen, Juno Therapeutics, Karyopharm Therapeutics, Kite Pharma, Loxo, Merck, MorphoSys, Novartis, Pfizer, Pharmacyclics, Portola Pharmaceuticals, Rhizen Pharmaceuticals, Roche, Seattle Genetics, Takeda, Teva, TG Therapeutics, Trillium Therapeutics, Triphase Research & Development Corp., Unum Therapeutics, Verastem, S. Grosicki: None Declared, E. Verner Conflict with: Janssen Cilag Pty Ltd, B. S. Kahl Conflict with: Genentech, ADCT, Abbvie, AstraZeneca, BeiGene, Pharmacyclics, BMS, TG Therapeutics, Teva, Janssen, MEI, Conflict with: Genentech, ADCT, Abbvie, Acerta, AstraZeneca, BeiGene, P. Ghia Conflict with: AbbVie, AstraZeneca, ArQule/MDS, BeiGene, Celgene/Juno/BMS, Janssen, Roche, Conflict with: AbbVie, AstraZeneca, Janssen, Gilead, Sunesis, Conflict with: AbbVie, AstraZeneca, ArQule/MDS, BeiGene, Celgene/Juno/BMS, Janssen, Roche, J. Li: None Declared, T. Tian Conflict with: BeiGene, AbbVie, L. Zhou Conflict with: BeiGene USA, Inc., BeiGene, Ltd., C. Marimpietri Conflict with: BeiGene USA, J. C. Paik Conflict with: BeiGene USA, Inc., BeiGene, Ltd., A. Cohen Conflict with: BeiGene, J. Huang Conflict with: BeiGene, Protara, Protara Therapeutics, J. R. 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BSH22-PO55 | Pirtobrutinib, A Highly Selective, Non-covalent (Reversible) BTK Inhibitor In Previously Treated CLL/SLL: Updated Results From The Phase 1/2 BRUIN Study

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Abstract Content: Covalent BTK inhibitors (BTKi) have transformed the management of chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL), but many patients (pts) will require additional treatment. Pirtobrutinib is a highly selective, non-covalent (reversible) BTKi that inhibits both wild type (WT) and C481-mutated BTK with equal low nM potency.

BRUIN is a phase 1/2 multicentre study (NCT03740529) of oral pirtobrutinib monotherapy in pts with advanced B-cell malignancies who have received ≥2 prior therapies. Pirtobrutinib was dose escalated in a standard 3 + 3 design in 28-day cycles. The primary objective for phase 1 was to determine the recommended phase 2 dose (RP2D) and the primary objective of phase 2 was overall response rate (ORR); secondary objectives included duration of response, progression-free survival, overall survival, safety and tolerability and pharmacokinetics. Response was assessed every 8 weeks from cycle 3, and every 12 weeks from cycle 13 and was measured according to the iwCLL 2018 criteria, including PR with lymphocytosis (PR-L). Safety was assessed in all pts.

As of 27 September 2020, 323 pts with B-cell malignancies (170 CLL/SLL, 61 MCL, 26 WM, 26 DLBCL, 13 MZL, 12 FL, 9 RT and 6 other) were treated on seven dose levels (25–300 mg QD). Among the 170 pts with CLL/SLL, the median age was 69 (36–88) years. The median number of prior lines of therapies was 3 (1–11). The majority of the CLL/SLL pts had received a prior BTKi (86%), an anti-CD20 antibody (90%) or a chemotherapy (82%). High-risk molecular features such as 17p deletion, TP53 mutation, and unmutated IGHV were present in 25% (20/81), 30% (27/91) and 88% (71/81) of pts respectively. No dose-limiting toxicities (DLTs) were reported and maximum-tolerated dose (MTD) was not reached (n = 323). 200 mg QD was selected as the RP2D. Fatigue (20%), diarrhoea (17%) and contusion (13%) were the most frequent treatment-emergent adverse events (TEAEs) regardless of attribution or grade seen in ≥10% of pts (n = 323). The most common adverse event of grade ≥3 was neutropenia (10%). Treatment-related haemorrhage and hypertension occurred in five (2%) and four (1%) pts respectively. One percent of pts discontinued due to TEAEs. One hundred and thirty-nine CLL/SLL pts were efficacy-evaluable with a median follow-up time of 6 months (0.16–17.8+). The ORR was 63% (95% CI 55–71) among the 139 efficacy evaluable pts with 69 PRs (50%), 19 PR-Ls (14%), 45 SDs (32%) and 1 PD (1%), and 5 (4%) discontinued prior to first response assessment. Among the 121 BTKi pretreated pts, the ORR was 62% (95% CI 53–71). Responses deepened over time with an ORR of 86% among the pts with at least 10 months' follow-up. ORR was similar in pts who discontinued prior BTKi due to progression (67%), or adverse events or other reasons (52%). Of the 88 responding pts, all except five remained on therapy (4 progressed and 1 achieved a

PR and electively discontinued treatment to undergo transplant). The longest-followed responding patient had been on treatment for 17.8+ months.

Pirtobrutinib demonstrated promising efficacy in heavily pretreated CLL/SLL pts following multiple prior lines of therapy and in pts with BTK C481 mutations. Pirtobrutinib was well tolerated and exhibited a wide therapeutic index. Updated data, including approximately 100 new pts with CLL and an additional 10 months since the prior data cut will be presented.

Disclosure of Interest: A. Mato Conflict with: Genentech, Adaptive Biotechnologies, DTRM BioPharma, LOXO: Consultancy, Nurix, Pharmacyclics LLC, an AbbVie Company, BeiGene, Sunesis, Janssen, TG Therapeutics, Genmab, AbbVie, Acerta/AstraZeneca, Johnson and Johnson, Conflict with: Genentech, Adaptive Biotechnologies, DTRM BioPharma, LOXO: Consultancy, Nurix, Pharmacyclics LLC, an AbbVie Company, BeiGene, Sunesis, Janssen, DSMB, TG Therapeutics, Genmab, AbbVie, Acerta/AstraZeneca, Johnson and Johnson, Conflict with: MSKCC: Current Employment, J. Pagel Conflict with: AstraZeneca; Gilead; Pharmacyclics/AbbVie; BeiGene; Epizyme; MEI Pharma; Kite, a Gilead Company; Actinium Pharmaceuticals; Incyte/MorphoSys: Consultancy, Conflict with: Former Employee: Swedish Cancer Institute, Seattle; Loxo Oncology at Lilly, Stamford, CT, USA, C. 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Munir Conflict with: Janssen, Abbvie, AstraZeneca, Alexion, Apellis, Gilead, Novartis: Honoraria; Janssen, Abbvie, AstraZeneca, Morphosys, Alexion, Gilead, Novartis: Membership on an entity's Board of Directors or advisory committees, E. Lech-Maranda Conflict with: Gilead, Conflict with: Takeda: Membership on an entity's Board of Directors or advisory committees; Janssen-Cilag: Membership on an entity's Board of Directors or advisory committees; Amgen: Membership on an entity's Board of Directors or advisory committees; Sanofi: Membership on an entity's Board of Directors or advisory committees; AbbVie: Membership on an entity's Board of Directors or advisory committees; Roche: Membership on an entity's Board of Directors or advisory committees; Gilead: Membership on an entity's Board of Directors or advisory committees; Novartis: Membership on an entity's Board of Directors or advisory committees, T. Eyre Conflict with: Roche, Abbvie, Incyte, Secura Bio, Loxo Oncology, Conflict with: AstraZeneca, Gilead/KITE, Beigene, Conflict with: Janssen, Roche, AstraZeneca, Abbvie, Gilead/KITE, Secura Bio, Beigene, Loxo Oncology: Honoraria; Abbvie, Gilead/KITE: Travel to conferences; Gilead/KITE: Travel support for conferences, Speakers Bureau; Loxo Oncology: Membership on an entity's Board of Directors or advisory committees, J. Woyach Conflict with: AbbVie Inc, ArQule Inc, AstraZeneca Pharmaceuticals LP, Janssen Biotech Inc, Pharmacyclics LLC, an AbbVie Company, Conflict with: AbbVie Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Conflict with: Gilead Sciences Inc: Other: Data & Safety; AbbVie Inc, ArQule Inc, Janssen Biotech Inc, AstraZeneca, Beigene: Other: Advisory Committee, W. Wierda Conflict with: Genzyme Corporation, Conflict with: Xencor; Gilead Sciences; Karyopharm; Acerta Pharma Inc.; KITE Pharma; Pharmacyclics LLC, an AbbVie Company; Sunesis; Miragen; Oncternal Therapeutics, Inc.; AbbVie: Research Funding; Loxo Oncology, Inc.; Juno Therapeutics, GSK/Novartis, Cyclacel, Janssen, Genentech, AstraZeneca, C. Cheah Conflict with: TG Therapeutics, AstraZeneca, MSD, Janssen, Roche, Gilead, Loxo/Lilly, Beigene, Ascentage pharma, Conflict with: AbbVie; Celgene, MSD, Roche, Conflict with: Honoraria, Other: advisory: Ascentage pharma, Beigene, Loxo/Lilly, TG Therapeutics; AstraZeneca, MSD, Janssen, Gilead; Other: advisory and travel expenses Roche, J. 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Biomedicine: Research Funding; Ribon Therapeutics: Research Funding; Evelo Biosciences: Research Funding; Aileron Therapeutics: Research Funding; Portola Pharmaceuticals: Research Funding; Phoenix Molecular Designs: Research Funding; Jacobio: Research Funding; Placon Therapeutics: Research Funding; Forma Therapeutics: Research Funding; Ciclomed: Research Funding; Clovis: Research Funding; Curis: Research Funding; Cyteir Therapeutics: Research Funding; Daiichi Sankyo: Research Funding; Effector Therapeutics: Research Funding; Eli Lilly: Research Funding; Janssen: Research Funding; Jounce Therapeutics: Research Funding; Klus Pharma: Research Funding; Kymab: Research Funding; Loxo Oncology: Research Funding; LSK Biopartners: Research Funding; Lycera: Research Funding; Mabspace: Research Funding; AstraZeneca: Research Funding; Bicycle Therapeutics: Research Funding; BioNTech: Research Funding; Boehringer Ingelheim: Research Funding; Takeda: Research Funding; Tesaro: Research Funding; TopAlliance: Research Funding; Vedanta: Research Funding; Verastem: Research Funding; Vigeo: Research Funding; Xencor: Research Funding, Conflict with: Funding; Hengrui, Genentech/Roche: Research Funding; Genentech/Roche: Membership on an entity's Board of Directors or advisory committees; Pfizer: Membership on an entity's Board of Directors or advisory committees; Celgene: Membership on an entity's Board of Directors or advisory committees; EMD Serono: Membership on an entity's Board of Directors or advisory committees, Janssen: Membership on an entity's Board of Directors or advisory committees, Exelixis: Membership on an entity's Board of Directors or advisory committees; Bayer: Membership on an entity's Board of Directors or advisory committees; Pharmacyclics: Membership on an entity's Board of Directors or advisory committees; Abbvie: Membership on an entity's Board of Directors or advisory committees; Alexion, AstraZeneca Rare Disease: Other: Study investigator, B. Fakhri Conflict with: Loxo/Lilly, M. Barve: None Declared, C. Tam Conflict with: Roche, Loxo, Janssen, BeiGene, AbbVie, Conflict with: Janssen, AbbVie, Conflict with: Honoraria: Pharmacyclics, Novartis, Roche, Janssen, BeiGene, AbbVie,, D. Lewis Conflict with: Loxo Oncology at Lilly: Membership on an entity's Board of Directors or advisory committees, J. Gerson Conflict with: Loxo Oncology at Lilly, Conflict with: Abbvie, Genentech: Membership on an entity's Board of Directors or advisory committees, A. Alencar Conflict with: Amgen; BeiGene; Celgene; Epizyme; Incyte; Janssen; Karyopharm; Kite Pharma; Seattle Genetics, C. Ujjani Conflict with: Lilly and Beigene, Conflict with: Loxo; Adaptive Biotechnologies; AstraZeneca, AbbVie, Pharmacyclics, Conflict with: Epizyme, AstraZeneca: Membership on an entity's Board of Directors or advisory committees; Kite, a Gilead Company: Honoraria; ACDT: Honoraria; Gilead: Honoraria; TG Therapeutics: Honoraria, I. 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Biosciences: Other: All research funding payments made to Sarah Cannon Research Institute, Research Funding; Forty Seven: Other: All research funding payments made to Sarah Cannon Research Institute, Research Funding; Pharmacyclics LLC, an AbbVie Company: Consultancy, Other: All consultancy and research funding payments made to Sarah Cannon Research Institute, Research Funding; Novartis: Consultancy, Other: All consultancy and research funding payments made to Sarah Cannon Research Institute, Research Funding; Calithera Biosciences: Other: All research funding payments made to Sarah Cannon Research Institute, Research Funding; Nurix Therapeutics: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute; ArQule: Other: All research funding payments made to Sarah Cannon Research Institute, Research Funding; TG Therapeutics: Consultancy, Other: All consultancy and research funding payments made to Sarah Cannon Research Institute, Research Funding; Agios: Other: All research funding payments made to Sarah Cannon Research Institute, Research Funding; Verastem: Consultancy, Other: All consultancy and research funding payments made to Sarah Cannon Research Institute, Research Funding; Unum Therapeutics: Consultancy, Other: All consultancy and research funding payments made to Sarah Cannon Research Institute, Research Funding; Yingli Pharmaceuticals: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute; Acerta Pharma: Other: All research funding payments made to Sarah Cannon Research Institute, Research Funding; Seagen: Consultancy, Other: All consultancy and research funding payments made to Sarah Cannon Research Institute, Research Funding; Triphase Research & Development Corp.: Other: All research funding payments made to Sarah Cannon Research Institute, Research Funding; Century Therapeutics: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute; Hutchison MediPharma: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute; Vincerx Pharma: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute; Sarah Cannon Research Institute: Current Employment; Servier Pharmaceuticals: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute; Yingli Pharmaceuticals: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute; Seagen: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute; Servier Pharmaceuticals: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute; Unum Therapeutics: Consultancy, Other: All consultancy payments made to Sarah Cannon Research Institute, Research Funding; Johnson & Johnson: Current holder of individual stocks in a privately held company; Seattle Genetics: Research Funding, S. Sundaram: None Declared, S. Ma Conflict with: Loxo: Research Funding; AstraZeneca: Honoraria, Research Funding, Speakers Bureau; Juno: Research Funding; Beigene: Research Funding, Speakers Bureau; Abbvie: Honoraria, Research Funding; Janssen: Research Funding, Speakers Bureau; TG Therapeutics: Research Funding; Pharmacyclics: Research Funding, Speakers Bureau, D. Jagadeesh: None Declared, J. Rhodes Conflict with: AstraZeneca, Beigene, SeaGen, J. Taylor: None Declared, O. Abdel-Wahab Conflict with: H3B Biomedicine: Consultancy, Research Funding; Foundation Medicine Inc: Consultancy; Merck: Consultancy; Prelude Therapeutics: Consultancy; LOXO Oncology: Consultancy, Research Funding; Lilly: Consultancy; AIChemy: Current holder of stock options in a privately held company, Membership on an entity's Board of Directors or advisory committees; Envisagenics Inc.: Current holder of stock options in a privately held company, Membership on an entity's Board of Directors or advisory committees, P. 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Schuster Conflict with: Abbvie: Consultancy, Research Funding; Incyte: Research Funding; TG Theraputics: Research Funding; Tessa Theraputics: Consultancy; Acerta Pharma/AstraZeneca: Consultancy; Nordic Nanovector: Consultancy; Novartis: Consultancy, Honoraria, Patents & Royalties, Research Funding; Alimera Sciences: Consultancy; BeiGene: Consultancy; Juno Theraputics: Consultancy, Research Funding; Loxo Oncology: Consultancy; Genentech/Roche: Consultancy, Research Funding; Merck: Research Funding; Pharmacyclics: Research Funding; Adaptive Biotechnologies: Research Funding; Celgene: Consultancy, Honoraria, Research Funding, D. Wang Conflict with: Loxo Oncology at Lilly: Current Employment, B. Nair Conflict with: Loxo Oncology at Lilly: Current Employment, Current equity holder in publicly traded company, E. Zhu Conflict with: Loxo Oncology at Lilly: Current Employment, Current equity holder in publicly traded company, D. 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Research Funding; MEI Pharma: Consultancy, Research Funding; Janssen: Consultancy; Celgene: Consultancy; TG Therapeutics: Consultancy, Research Funding; BMS: Consultancy, Research Funding; Merck: Consultancy; Research to Practice: Consultancy; Takeda: Consultancy; Ascentage Pharma: Consultancy, Research Funding, J. Brown Conflict with: Genentech/Roche: Consultancy; Invectys: Other: Data Safety Monitoring Committee Service; SecuraBio: Research Funding; Sun: Research Funding; TG Therapeutics: Research Funding; Loxo/Lilly: Research Funding; Eli Lilly and Company: Consultancy; MEI Pharma: Consultancy; Morphosys AG: Consultancy; Nextcea: Consultancy; Janssen: Consultancy; Novartis: Consultancy; Pfizer: Consultancy; Rigel: Consultancy; Acerta/AstraZeneca: Consultancy; Beigene: Consultancy; Gilead: Research Funding; Abbvie: Consultancy; Bristol-Myers Squib/Juno/Celegene: Consultancy; Catapult: Consultancy, W. Jurczak Conflict with: European Medicines Agency, Sandoz-Novartis, Janssen China R&D, BeiGene, Epizyme, Acerta, AstraZeneca: Consultancy; AstraZeneca, BeiGene, Janssen, Loxo Oncology, Sandoz, Roche: Membership on an entity's Board of Directors or advisory committees; AbbVie, AstraZeneca, Bayer, BeiGene, Celtrion, Celgene, Debbiopharm, Epizyme, Incyte, Janssen, Loxo Oncology, Merck, Mei Pharma, Morphosys, Novo Nordisk, Roche, Sandoz, Takeda, TG Therapeutics, Pharmacyclics, Affirmed, Gilead Sciences, Nordic Nanovecto: Research Funding; Maria Sklodowska-Curie National Research Institute of Oncology: Current Employment; Jagiellonian University: Ended employment in the past 24 months.

BSH22-PO56 | Pirtobrutinib, A Highly Selective, Non-covalent (Reversible) BTK Inhibitor In Previously Treated Mantle Cell Lymphoma: Updated Results From The Phase 1/2 BRUIN Study

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Abstract Content: Covalent BTK inhibitors (BTKi) have transformed the management of mantle cell lymphoma (MCL), but these treatments are not curative and the majority of patients (pts) will require additional treatment. Covalent BTKi share pharmacological liabilities (e.g. low oral bioavailability, short half-life) that collectively may lead to suboptimal BTK target coverage, for example in rapidly proliferating tumours with high BTK protein turnover such as MCL. To address these limitations, pirtobrutinib, a highly selective, non-covalent (reversible) BTKi that inhibits both wild type (WT) and C481-mutated BTK with equal low nM potency were developed.

BRUIN is a multicentre phase 1/2 study (NCT03740529) of oral pirtobrutinib monotherapy in pts with advanced B-cell malignancies who have received ≥2 prior therapies. Pirtobrutinib was dose-escalated in a standard 3 + 3 design in 28-day cycles. The primary objective for phase 1 was to determine the recommended phase 2 dose (RP2D) and the primary objective of phase 2 was overall response rate (ORR); secondary objectives included duration of response (DoR),

progression-free survival (PFS), overall survival (OS), safety and tolerability and pharmacokinetics. Efficacy evaluable pts included all dosed pts who underwent their first response evaluation or discontinued therapy. Response was assessed every 8 weeks from cycle 3, and every 12 weeks from cycle 13 and was measured according to Lugano Classification. Safety was assessed in all pts (CLL/SLL and NHL).

As of 27 September 2020, 323 pts (170 CLL/SLL, 61 MCL, 26 WM, 26 DLBCL, 13 MZL, 12 FL, nine RT and six other NHL [other transformation, B-PLL and hairy cell leukaemia]) were treated on seven dose levels (25–300 mg QD). The median age was 69 (range 50–87) years for MCL pts. Among the 61 MCL pts, the median number of prior lines of therapy was 3 (range, 1–8) and a majority of them had received a prior BTKi (93%), an anti-CD20 antibody (98%) or chemotherapy (92%). No DLTs were reported and MTD was not reached (n = 323). Two hundred milligram of QD was selected as the RP2D. Fatigue (20%), diarrhoea (17%) and contusion (13%) were the most frequent treatment-emergent adverse events regardless of attribution or grade seen in ≥10% of pts (n = 323). The most common adverse event of grade ≥3 was neutropenia (10%). Treatment-related haemorrhage and hypertension occurred in five (2%) and four (1%) pts respectively. Five (1%) pts discontinued due to treatment-related adverse events. At the efficacy cutoff date, 52 prior BTKi-treated MCL pts were efficacy evaluable with an ORR of 52% (95% confidence interval 38–66; 13 complete response (CR) [25%], 14 partial response (PR) [27%], nine stable disease (SD) [17%]), 11 progressive disease (PD) [21%] and 5 [10%] discontinued prior to first response assessment). The median follow-up was 6 months (range 0.7–18.3+). Responses were observed in nine out of 14 pts (64%) with prior autologous or allogeneic stem cell transplant, and two out of two with prior CAR-T-cell therapy.

Pirtobrutinib demonstrated promising efficacy in heavily pretreated, poor-prognosis MCL following multiple prior lines of therapy, including a covalent BTKi. Pirtobrutinib was well tolerated and exhibited a wide therapeutic index. Updated data, including approximately 60 new pts with MCL and an additional 10 months since the prior data cut will be presented.

Disclosure of Interest: M. Wang Conflict with: Acerta Pharma, Loxo Oncology, Bayer Healthcare, Kite Pharma, BeiGene, Janssen, Genentech, DTRM Biopharma (Cayman) Limited, AstraZeneca, Pharmacyclics, InnoCare, Epizyme, Oncternal, CStone, VelosBio, Juno, Miltenyi Biomedicine GmbH, Conflict with: Acerta Pharma, Loxo Oncology, Kite Pharma, BeiGene, Janssen, AstraZeneca, Pharmacyclics, InnoCare, Molecular Templates, Oncternal, Celgene, Juno, Lilly, VelosBio, BioInvent, Conflict with: Honoraria: Acerta Pharma, Kite Pharma, CAHON, BeiGene, Anticancer Association, Janssen, Dava Oncology, The First Afflicted Hospital of Zhejiang University, Physicians Education Resources (PER), Imedex, Scripps, Chinese Medical Association, AstraZeneca, Clinical Care Options, Epizyme, Hebei Cancer Prevention Federation, Mumbai Hematology Group, BGICS, OMI, Newbridge Pharmaceuticals, Moffit Cancer Center, Miltenyi Biomedicine GmbH, *N.* Shah Conflict with: Epizyme, Miltenyi Biotec, Lilly, Conflict with: Miltenyi Biotec, Lilly, Conflict with: Honoraria: Miltenyi Biotec, Lilly, A. Alencar Conflict with: Amgen, BeiGene, Celgene, Epizyme, Incyte, Janssen, Karyopharm, Kite Pharma, Seattle Genetics, J. Gerson Conflict with: Loxo Oncology at Lilly, Conflict with: Membership on an entity's Board of Directors or advisory committees: Abbvie, Genentech, M. Patel Conflict with: EMD Serono, Evelo Biosciences, Prelude Therapeutics; Qilu Puget Sound Biotherapeutics; Revolution Medicines; Ribon Therapeutics, Hutchinson MediPharma; Florida Cancer Specialists; Mirati Therapeutics; Lycera; Millennium Pharmaceuticals; Mabspace; Macrogenics; Merck; Daiichi Sankyo; Effector Therapeutics; Cyteir Therapeutics; ADC Therapeutics; Vedanta; Loxo Oncology; Forma Therapeutics, Genentech/Roche, Gilead, GlaxoSmithKline; LSK Biopartners; ModernaTX; ORIC Pharmaceuticals; Pfizer; Phoenix Molecular Designs; Placon Therapeutics, Portola Pharmaceuticals, Boehringer Ingelheim; Eli Lilly; Curis:; Jacobio; Acerta Pharma; AstraZeneca; Ciclomed; BioNTech; Clovis; Checkpoint Therapeutics; Celgene; Calithera; Bicycle Therapeutics; Artios Pharma; TopAlliance; Janssen; Stemline Therapeutics; Seven and Eight Biopharmaceuticals; Taiho; H3 Biomedicine; Vigeo; Tesaro; Aileron Therapeutics; Agenus; Ignyta; Xencor; Syndax; Synthorx; Incyte; Kymab; Hengrui; Verastem; Takeda; Klus Pharma; Jounce Therapeutics, Conflict with: Other: Study investigator: Alexion, AstraZeneca Rare Disease; Membership on an entity's Board of Directors or advisory committees: Genentech/Roche, Pfizer, Exelixis, Bayer; Pharmacyclics; Abbvie, EMD Serono, Celgene, Janssen, B. Fakhri Conflict with: Loxo/Lilly, W. Jurczak Conflict with: European Medicines Agency, Sandoz-Novartis, Janssen China R&D, BeiGene, Epizyme, Acerta, AstraZeneca, Conflict with: AbbVie, AstraZeneca, Bayer, BeiGene, Celtrion, Celgene, Debbiopharm, Epizyme, Incyte, Janssen, Loxo Oncology, Merck, Mei Pharma, Morphosys, Novo Nordisk, Roche, Sandoz, Takeda, TG Therapeutics, Pharmacyclics, Affirmed, Gilead Sciences, Nordic Nanovecto, Conflict with: Jagiellonian University: Ended employment in the past 24 months, Conflict with:: Membership on an entity's Board of Directors or advisory committees: BeiGene, Janssen, Loxo Oncology, Sandoz, Roche; Current Employment: Current Employment: Maria Sklodowska-Curie National Research Institute of Oncology, X. Tan: None Declared, K. Lewis Conflict with: AstraZeneca, Roche, Conflict with: Honoraria: Roche, AstraZeneca, Janssen; Patents & Royalties: Janssen, Novartis, T. Fenske Conflict with: Pharmacyclics; Servier Pharmaceuticals; MorphoSys; TG Therapeutics, KaryoPharm; CSL Therapeutics; Biogen; Beigene; ADC Therapeutics; Adaptive Biotechnologies; AbbVie, Conflict with: Speakers Bureau: Sanofi; Kite (Gilead); Seattle Genetics; KaryoPharm; Bristol-Myers Squibb; AstraZeneca, C. Coombs Conflict with: AbbVie, Conflict with: H3 Biomedicine, Incyte, Loxo Oncology, Conflict with: Served on teering committees for AbbVie and Loxo Oncology, has served on independent

review committees for AbbVie and Octapharma, has received honoraria from AbbVie, AstraZeneca, Beigene, Genentech, LOXO oncology, MEI Pharma, Novartis, TG Therapeutics, I. Flinn Conflict with: Takeda,; Kite, a Gilead Company, Pharmacyclics LLC, an AbbVie Company, TG Therapeutics: Consultancy, Nurix Therapeutics, Juno Therapeutics, Roche, Unum Therapeutics, Seagen, AstraZeneca, Verastem, Yingli Pharmaceuticals, Novartis, AbbVie, BeiGene, Genentech, Gilead Sciences, Great Point Partners, Iksuda Therapeutics, Janssen, Century Therapeutics, Hutchison MediPharma, Vincerx Pharma, Servier Pharmaceuticals, Yingli Pharmaceuticals, Seagen, Servier Pharmaceuticals, Unum Therapeutics, Conflict with: Celgene, Acerta Pharma, Takeda, Kite, a Gilead Company, Pharmacyclics LLC, an AbbVie Company, ArQule, Agios, TG Therapeutics, Triphase Research & Development Corp, Forma Therapeutics, Merck, Juno Therapeutics, Roche, Calithera Biosciences, Unum Therapeutics, Seagen, AstraZeneca, Verastem, MorphoSys: Consultancy, Incyte, Karyopharm Therapeutics, Infinity Pharmaceuticals, Curis, Novartis, Pfizer, Trillium Therapeutics, Portola Pharmaceuticals, Rhizen Pharmaceuticals, Teva, AbbVie, BeiGene, Genentech, Gilead Sciences, Janssen, Unum Therapeutics, Conflict with: Other: All research funding payments made to Sarah Cannon Research Institute: Celgene, Acerta Pharma, Takeda, Forty Seven, ArQule, Agios, Triphase Research & Development Corp, Forma Therapeutics, Merck, Calithera Biosciences, Constellation Pharmaceuticals, Loxo; Incyte, Karyopharm Therapeutics, Infinity Pharmaceuticals, Curis, Pfizer, Trillium Therapeutics, Portola Pharmaceuticals, Rhizen Pharmaceuticals, Teva; Other: All consultancy and research funding payments made to Sarah Cannon Research Institute: Kite, a Gilead Company; Pharmacyclics LLC, an AbbVie Company, TG Therapeutics, Nurix Therapeutics, Juno Therapeutics, Roche, Unum Therapeutics, Seagen, AstraZeneca, Verastem, Yingli Pharmaceuticals, MorphoSys, Novartis, AbbVie, BeiGene, Genentech, Gilead Sciences, Great Point Partners, Iksuda Therapeutics, Janssen, Century Therapeutics, Hutchison MediPharma, Vincerx Pharma, Servier Pharmaceuticals, Yingli Pharmaceuticals, Seagen, Servier Pharmaceuticals, Unum Therapeutics; Sarah Cannon Research Institute: Current Employment; Johnson & Johnson: Current holder of individual stocks in a privately held company; Seattle Genetics: Research Funding, D. 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BSH22-PO57 | Completed Induction Phase Analysis of MAGNIFY: Phase 3b Study of Lenalidomide + Rituximab (R2) Followed By Maintenance in Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

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Abstract Content: Patients (Pts) with relapsed indolent NHL (iNHL) have limited treatment options. Lenalidomide +rituximab (R^2) has shown complimentary activity and is tolerable in untreated and relapsed/refractory (R/R) pts with iNHL (RELEVANCE*: N Engl J Med* 2018 and AUGMENT: *J Clin Oncol*. 2019).

MAGNIFY is a phase 3b trial in pts with R/R follicular lymphoma (FL) gr1–3b, transformed FL (tFL), marginal zone lymphoma (MZL), or mantle cell lymphoma (MCL; NCT01996865). In the induction phase, lenalidomide 20 mg PO on days (d) 1–21 of a 28-d cycle (c) + rituximab (R) IV at 375 mg/m^2/wk c1 and then every 8 weeks starting with c3 (R^2) are administered for 12c. Pts with stable disease, partial response, or complete response/complete response unconfirmed (CR/CRu) were randomised 1:1 to R^2 *versus* R-maintenance for 18 months. Data presented here are the complete analysis of the induction phase in efficacy-evaluable pts with FL grades 1–3a or MZL (FL gr3b, tFL and MCL not included). The focus of this interim analysis was overall response rate (ORR) by 1999 IWG criteria in the induction intention-to-treat population.

As of March 5, 2021, 394 pts (318 [81%] FL gr1–3a; 76 [19%] MZL) enrolled. The median follow-up was 40.6 months (range, 0.6–79.6). The median age was 66y (range, 35–91), 328 (83%) had stage III/IV disease, with a median of 2 prior therapies (94% prior R-containing). ORR was 71% with 42% CR/CRu (Table). All pts have completed R^2 induction (n = 232, 59%) or discontinued study treatment (n = 162, 41%). 141 pts (36%) prematurely discontinued both lenalidomide and R, primarily due to adverse events (AEs) (n = 54, 14%) or progressive disease (n = 42, 11%). The majority of pts who completed induction have been randomised and entered maintenance (n = 217). The median duration of response was NR (95% CI, 43.9 months–NR), and median progression-free survival in the induction safety population (n = 393) was 50.5 months (95% CI, 39.5–NR). Efficacy results are reported in the table by histology subgroups, and R-refractory, double-refractory and early relapse statuses. Most common all-grade AEs were 47% fatigue, 43% neutropenia, 37% diarrhoea, 30% nausea and 30% constipation. Grade 3/4 AEs occurring in ≥5% of pts included 37% neutropenia (10 pts [3%] had febrile neutropenia), 8% leukopenia, 6% thrombocytopenia, 5% anaemia and 5% fatigue.

These data represent complete analysis of all pts in the induction phase of MAGNIFY which continues to support that R^2 is active with a tolerable safety profile in pts with R/R FL grade 1–3a and MZL, including R-refractory, double-refractory and early relapse pts.

Disclosure of Interest: F. Lansigan Conflict with: Celgene/BMS, Conflict with: Celgene/BMS, D. J. Andorsky Conflict with: Abbvie, Celgene/BMS, Conflict with: Abbvie, Celgene/BMS, Epizyme, M. Coleman Conflict with: Abbvie,Bristol Myers, Celgene, Genentech, Gilead, BeiGene, Innocare, Merck, Pfizer, Roche, Conflict with: immunomedics, A. Yacoub Conflict with: Incyte, Novartis, CTI Biopharma, ACCELERON PHARMA, Agios, J. M. Melear Conflict

Abstract Table: Efficacy for induction R[2] in R/R iNHL

	ORR, *n* (%)	CR/CRu, *n* (%)	DOR, median (95% CI), months	PFS, median (95% CI), months*
All FL gr 1–3a + MZL, *N* = 394	279 (71)	164 (42)	NR (43.9–NR)	50.5 (39.4–NR)
Histology				
FL gr 1–3a, *n* = 318	230 (72)	134 (42)	NR (45.8–NR)	51.1 (38.7–NR)
MZL, *n* = 76	49 (64)	30 (39)	39.0 (29.4–NR)	41.2 (29.9–NR)
R-refractory				
Yes, *n* = 140	84 (60)	47 (34)	NR (34.7–NR)	27.4 (18.1–38.4)
No, *n* = 254	195 (77)	117 (46)	NR (43.9–NR)	NR (49.7–NR)
Double refractory				
Yes†, *n* = 85	43 (51)	21 (25)	27.4 (17.7–NR)	18.1 (15.5–25.9)
No, *n* = 309	236 (76)	143 (46)	NR (45.8–NR)	NR (41.6–NR)
Early relapse				
Yes‡, *n* = 133	86 (65)	43 (32)	37.0 (24.9–NR)	27.4 (20.3–41.6)
No, *n* = 261	193 (74)	121 (46)	NR (NR–NR)	NR (41.4–NR)

*If pts in maintenance at cutoff, response assessments also contributed to PFS.

†Refractory to both R (monotherapy or combo) and alkylating agent.

‡Progressed or relapsed ≤2 years of initial diagnosis after 1 l systemic treatment.

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BSH22-PO58 | Mosunetuzumab in Combination with Lenalidomide Has a Manageable Safety Profile and Encouraging Activity in Patients with Relapsed/Refractory Follicular Lymphoma: Initial Results from a Phase Ib Study

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Abstract Content: Mosunetuzumab (M), a CD20xCD3 bispecific antibody, has demonstrated high and consistent response rates in high-risk relapsed/refractory (R/R) follicular lymphoma (FL) patients (pts), with early evidence of a favourable benefit/risk profile. Lenalidomide (Len) is clinically active in FL pts. M + Len offers potentially additive/synergistic efficacy via potent immunomodulatory activity. We present data from an ongoing Phase Ib study

(NCT04246086) evaluating safety and activity of M + Len in R/R FL pts.

Pts with R/R FL (Grade [Gr] 1–3a) and ≥1 prior systemic anti-cancer therapy were enrolled to receive 12 cycles of M + Len (Cycle [C]1 duration: 21 days; C2–12: 28 days). In C1, step-up doses of M (intravenous [IV] infusion) were given on Day (D)1 (1 mg), and D8 (2mg), with the target dose (30 mg) given on C1D15 and on D1 of C2–12. Len (20 mg) was administered orally on D1–21 of C2–12. No hospitalisation was mandated. Primary objective: to evaluate M + Len safety. Secondary objective: to assess response and long-term efficacy outcomes. Cytokine release syndrome (CRS) was reported using American Society for Transplantation and Cellular Therapy (ASTCT) criteria, responses were assessed with PET-CT using standard criteria.

At data cut-off (31 May 2021) 27 pts were enrolled. The median age was 59 years (range: 31–79 years), 12 pts (44%) were male and Eastern Cooperative Oncology Group (ECOG) performance status was 0 (18 pts, 67%) or 1 (9 pts, 33%). The median number of prior therapy lines was 1 (1–4); three pts (11%) had disease progression (PD) <24 months (m) from the start of first-line therapy. Sixteen pts (59%) had been on study for 0–3 m, 8 (30%) for 3–6 m, 2 (7%) for 6–9 m and 1 for >9 m.

Twenty pts (74%) experienced ≥1 adverse event (AE) of any Gr. The most common AE was CRS (8 pts, 30%). Gr3–4 AEs and serious AEs occurred in eight pts (30%) each. There were no Gr5 AEs. AEs relating to M and Len occurred in 20 (74%) and 10 pts (37%) respectively. No AEs led to the withdrawal of M or Len; two pts had M-related AEs leading to M dose delays, six pts (22%) had Len-related AEs leading to Len dose interruption and/or reduction. CRS events were Gr1 (7/8 pts) or Gr2 (1/8 pts). Six out of eight pts experienced CRS events in C1D1–7; two out of eight had Gr1 CRS events in C2. The median time to CRS onset was 1 day after the first dose (1–28 days); median duration was 3 days (2–5 days). All CRS events were resolved without sequelae. No pts required tocilizumab, ICU admission, high flow oxygen, or vasopressor support. Five pts (19%) reported 14 events of Gr3–4 neutropenia between D41 and 218, lasting 6–16 days, all resolved, with one pt receiving primary granulocyte colony-stimulating factor (G-CSF) prophylaxis and two pts receiving G-CSF treatment. No febrile neutropenia events occurred.

The efficacy-evaluable population (13 pts) included all pts who had been assessed for response at any time on the study, withdrawn from treatment/study prior to reaching their first response assessment, or were on the study long enough to reach their first scheduled response assessment (planned per protocol for D15–21). The objective response rate at data cut-off was 92%. Complete (10 pts, 77%) and partial (2 pts, 15%) metabolic response (PMR) and stable disease (1 pt, 8%) were observed. One pt with initial PMR experienced PD after C8. M + Len appears to have an acceptable safety profile in R/R FL pts with ≥1 prior therapy line and encouraging preliminary anti-lymphoma activity. These data support initiation of a randomised Phase III study of M + Len *versus* rituximab+Len.

Disclosure of Interest: F. Morschhauser Conflict with: F. Hoffmann-La Roche Ltd, Servier, Novartis, Epizyme, AbbVie, Bristol-Myers Squibb, Genentech, Inc., Gilead, Conflict with: Honoraria: F. Hoffmann-La Roche Ltd, Chugai, Janssen; Membership on an entity's Board of Directors or advisory committees: F. Hoffmann-La Roche Ltd, Novartis, Genmab, Epizyme, AbbVie, Bristol-Myers Squibb, Celgene, Incyte, Gilead, AstraZeneca; Speakers Bureau: F. Hoffmann-La Roche Ltd, M. Bishton Conflict with: Cellitron, Tevapharma, BMS, Gilead, F. Hoffmann-La Roche, Conflict with: Honoraria: Celltrion, Tevapharma, Bristol-Myers Squibb, Gilead; Membership on an entity's Board of Directors or advisory committees: F. Hoffmann-La Roche Ltd, Conflict with: Nottingham University Hospitals NHS Trust, T. A. Eyre Conflict with: LOXO Oncology, Incyte, BeiGene, Janssen, KITE/Gilead, Secura Bio, AstraZeneca, Conflict with: BeiGene, AstraZeneca, Conflict with: Honoraria: LOXO Oncology, Incyte, BeiGene, Janssen, KITE/Gilead, Secura Bio, AstraZeneca; Speakers Bureau: Janssen, KITE/Gilead, AstraZeneca, Conflict with: Oxford University Hospitals NHS Foundation Trust, E. Bachy Conflict with: Roche, Takeda, Incyte, Conflict with: Daiishi, Conflict with: Honoraria: Novartis, KITE/Gilead, G. Cartron Conflict with: Roche, Celgene-BMS, Conflict with: Honoraria: Gilead, Novartis, Janssen, Roche, Celgene-BMS, AbbVie, Sanofi, Takeda, L. Ysebaert Conflict with: AbbVie, AstraZeneca, Gilead, Janssen, F. Hoffmann-La Roche Ltd, Conflict with: Honoraria: AbbVie, AstraZeneca, Gilead, Janssen, F. Hoffmann-La Roche Ltd; Speakers Bureau: AbbVie, AstraZeneca, Gilead, Janssen, F. Hoffmann-La Roche Ltd, S. Bobillo Conflict with: F. Hoffmann-La Roche, Conflict with: Speakers Bureau: F. Hoffmann-La Roche Ltd, Gilead, N. C. Gutierrez: None Declared, E. Budde Conflict with: Kite Pharma, Genentech, Conflict with: Genentech, AstraZeneca, C. P. Fox Conflict with: F. Hoffmann-La Roche, Conflict with: Membership on an entity's Board of Directors or advisory committees: F Hoffmann-La Roche, A. Knapp Conflict with: Employee: F. Hoffmann-La Roche, Conflict with: F. Hoffmann-La Roche, M. Yaqub Conflict with: Employeee: Genentech, Inc./F. Hoffmann-La Roche Ltd, Conflict with: Genentech/F. Hoffmann-La Roche, M. C. Wei Conflict with: Employee: Genentech, Inc.; Stockholder: F. Hoffmann-La Roche, Conflict with: Genentech, F. Hoffmann-La Roche, C. O'Hear Conflict with: Employee: Genentech, Inc.; Stockholder: F. Hoffmann-La Roche, Conflict with: Genentech, F. Hoffmann-La Roche, H. Li Conflict with: Employee: F. Hoffmann-La Roche, Conflict with: F. Hoffmann-La Roche, E. Purev Conflict with: Employee: Genentech, Conflict with: Genentech, W. Townsend Conflict with: F. Hoffmann-La Roche Ltd, Celgene (Bristol-Myers Squibb), Conflict with: Honoraria: F. Hoffmann-La Roche Ltd, Celgene (Bristol-Myers Squibb).

BSH22-PO59 | Real-World Experience of Rapid Obinutuzumab Administration: Time to Change Obinutuzumab Infusion Rates

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Abstract Content: Administration of obinutuzumab to patients with B-cell lymphoproliferative malignancies places significant demands on chemotherapy unit resources as slow infusion rates are currently advised in the drug monograph to mitigate against the high rates of infusion-related reactions (IRR) reported in initial therapeutic clinical trials. However, three clinical trials have now demonstrated tolerance of rapid obinutuzumab infusions in selected patient groups. We report our updated real-world experience following protocol change at our centre in October 2018 to permit 90-min obinutuzumab infusions from cycle 2 onwards in lower-risk patients who experienced no greater than grade 2 IRR events during cycle 1 treatment and who have a lymphocyte count $<5 \times 10^9$/l prior to rapid infusion (in patients with CLL).

Demographical data, medical and nursing notes and chemotherapy prescription records were reviewed to evaluate protocol compliance and infusion outcome for all 42 patients who received obinutuzumab within the department during a 30-month period between October 2018 and April 2021.

Thirty-five patients with a median age of 71 years received a total of 161 90-min obinutuzumab infusions during the 30-month period for treatment of follicular lymphoma ($n = 18$, in combination with bendamustine, CVP or CHOP chemotherapy) or chronic lymphocytic leukaemia ($n = 17$, in combination with chlorambucil or venetoclax). A median of 4- to 90-min infusions per patient was administered. No IRR events occurred during any 90-min infusions, despite 17 patients (48%) in this cohort experiencing grade 1 or 2 IRR events during their first cycle of treatment administered using standard obinutuzumab incremental infusion rates. An estimated 281.75 h of chemotherapy unit chair time was saved over the 30-month period due to reduction in infusion time from 195 min per dose to 90 min per dose.

Our real-world experience supports previously published clinical trial data and brings the reported number of patients to have received rapid obinutuzumab infusions globally to 253 with only a single ≥grade 3 IRR event reported within the GAZELLE trial. Rapid obinutuzumab infusions are well tolerated in selected patients from cycle 2 onwards and this change in practice has the potential to lead to meaningful improvements to chemotherapy unit capacity during this period of persistent strain on healthcare systems. We advocate for review of obinutuzumab administration guidance for lower-risk patients in light of growing evidence to demonstrate the safety and utility of rapid infusions.

Disclosure of Interest: J. Cunningham: None Declared, D. Sparksman: None Declared, D. Gordon-Walker: None Declared, P. Sarkies: None Declared, R. De Silva: None Declared, M. Small: None Declared, A. Collins: None Declared, N. Shah Conflict with: AbbVie, Janssen, Roche.

BSH22-PO60 | Outcomes and prognostic factors for adult patients with Post-Transplant Lymphoproliferative Disorders: the Thames Valley experience

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Abstract Content: Post-transplant lymphoproliferative disorders (PTLD) are a serious complication of solid organ and haematopoietic stem cell transplants. Historically, PTLD have been divided reflecting the temporal vicinity of the onset to the transplant procedure and the presence of EBV copies in histological samples. The International Prognostic Index (IPI) remains the more widely used prognostic model at diagnosis. However, the risk-stratified sequential approach currently in use is mainly based on the histology at diagnosis and the response to Rituximab monotherapy.

In our study, we audited our practice, we validated in our cohort the currently used prognostic indices, and we hypothesised that additional clinical or laboratory features could improve prognostication at baseline.

To explore this, we collected data on 91 consecutive patients diagnosed with PTLD and treated at Oxford University Hospitals (OUH) or one of the regional hospitals, between 2012 and 2020. Descriptive statistics were used for patient characteristics and management. Univariate and multivariate analyses were performed using Cox-regression models. The level of significance was set at $p < 0.05$. Statistical tests were performed using IBM SPSS v27. Inpatient location at time of first-line treatment was used as a surrogate marker for ECOG ^{3}3. IPI and PTLD score were calculated only when all the variables of the prognostic score were available or when the missing value would not change the class assignation.

The median age at diagnosis was 52 years. Renal transplants represented 69.2% of patients, whereas 89% of PTLD showed a monomorphic histology, with DLBCL-like PTLD being the most common type (60/91 patients). EBV positivity was demonstrated in 47.3% of biopsies. 60.4% of patients presented with advanced disease stage and 78% had extranodal involvement. All patients had reduction of immunosuppression (RIS) at diagnosis and 33% of patients received Rituximab monotherapy as first-line systemic therapy. Of these, 19% and 31% achieved CR and PR, respectively, with comparable OS. The median OS was similar also between patients treated with Rituximab or immunochemotherapy

(35.2%) in first line. In our cohort, the ORR and CR rate were 56.7% and 47.8%% respectively. The median OS was 2.7 years and TRM was 10%. Surgical resection of localised PTLD of the gastrointestinal tract coupled with RIS resulted in a 100% cure rate (5/5 patients). We confirmed the strong association between the risk stratification of IPI (low vs. high) and PTLD score and patient outcome (OS, EFS, PFS). In multivariate analysis, we found that the albumin level adds significant prognostic power to the IPI and PTLD score. Indeed, a deranged albumin allows the identification of a subset of high-risk patient with a particularly poor outcome, whereas a normal value seems to mitigate the negatively prognostic impact of high-risk scores at baseline.

Our study, in line with the published literature, confirms that a sequential risk-stratified approach can result in good outcomes, sparing chemo-related toxicities in a group of patients who remains in long-term complete remission after Rituximab monotherapy. We corroborated the utility of the IPI and PTLD score in risk-stratifying patients and we found that these may be even improved if albumin was added as a variable. Furthermore, all five of our patients with early stage disease treated with surgical resection achieved long-term remission without further treatment.

Abstract Table:

	Total *N*	Median OS
Median OS according to IPI and Albumin value		
IPI low, Alb normal	20	68 185
IPI low, Alb abnormal	16	not reached
IPI high, Alb normal	11	77 327
IPI high, Alb abnormal	21	1848
Overall	68	68 185

Chi-square 16 415; $p = 0.001$

Disclosure of Interest: None Declared.

BSH22-PO61 | The MCL Biobank Observational Study comes of age

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Abstract Content: Mantle cell lymphoma (MCL) accounts for 6–8% of non-Hodgkin lymphoma and exhibits a highly heterogeneous clinical course. A subset of patients follow an indolent course allowing initial therapy to be deferred with no detrimental effect on survival.[1] This group of patients classically present with extra nodal disease and are *SOX11* negative.[2]

The MCL Biobank Observational Study is a prospective study designed to investigate differences between indolent and aggressive forms of MCL. Newly diagnosed patients with MCL aged 16 and over were recruited from 73 NHS sites across the UK from October 2014 to October 2019. Patients were enrolled within 90 days of diagnosis and prior to receiving therapy. Here we present an update of patient characteristics and outcome from the MCL Biobank.

Baseline patient characteristics, blood and saliva samples were collected at registration along with tissue blocks where available. The primary outcome measure was time to treatment. Secondary outcome measures included overall survival (OS). Patients were followed up at a minimum of 6-monthly intervals. OS was defined as time from MCL diagnosis to death as a result of any cause or date to last follow-up and was estimated using the Kaplan–Meier method. We defined the watch and wait (W&W) subset as those patients that did not require treatment within 180 days of diagnosis. Clinical data are held at the Peninsula Clinical Trials Unit and biological samples are stored at the University of Liverpool GCP Facility.

A total of 593 patients were recruited. Patient characteristics are shown in Table 1. Nineteen patients have been lost to follow-up. Tissue blocks have been received at the Biobank for 419 participants (of which 83% have proceeded to treatment and 17% remain under observation). Blood samples including anticoagulated and clotted blood are available for 539 patients (of which 82% have proceeded to treatment and 18% remain under observation). Saliva samples are available for 572 patients (of which 83% have proceeded to treatment and 17% remain under observation).

Of the 593 patients, 375 (63%) received treatment within 180 days of diagnosis. Initial treatment was deferred for over 180 days in 218 patients (37%) with a median time to treatment in this subgroup of 546 days (range 196–1847 days). The estimated median follow-up at the time of analysis was 1348 days. The estimated 3-year OS of the whole population was 73.1%. Of the 593 patients, 98 (17%) remain on W&W at the time of last follow-up. Initial analysis shows Rituxumab-Bendamustine ($n = 89$) and R-CHOP ($n = 76$) were the most commonly used regimens, with 107 patients treated within the ENRICH study.

The MCL Biobank Observational Study's creates a unique national database and tissue repository for further characterising indolent and aggressive forms of MCL. With further analysis and collaboration, we seek to elucidate further biological differences between indolent and aggressive disease and, in doing so, discover and validate novel predictive markers and drug targets that will pave the way to a more tailored approach to therapy and disease monitoring.

References

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2. G Clot, P Jares, E Giné, *et al.* A gene signature that distinguishes conventional and leukaemic nonnodal mantle cell

Abstract Table: Patient characteristics.

Characteristic	All patients (*n* = 593) No.	Early treatment (*n* = 375) No.	W&W (*n* = 218) No.
Age, years			
Median	70	70	70
Range	30–93	32–92	30–93
Sex			
Male	426 (72%)	282 (75%)	144 (66%)
Female	167 (28%)	93 (25%)	74 (34%)
Ann-Arbor Stage			
I–II	87/569 (15%)	30/365 (8%)	57/204 (28%)
III–IV	482/569 (85%)	335/365 (92%)	147/204 (72%)
ECOG performance score			
0	327/588 (56%)	180/371 (49%)	147/217 (68%)
1	197/588 (34%)	146/371 (39%)	51/217 (23%)
2	49/588 (8%)	38/371 (10%)	11/217 (5%)
3	15/588 (3%)	7/371 (2%)	8/217 (4%)
Bone marrow involvement	271/347 (78%)	202/252 (80%)	69/95 (73%)
Elevated LDH	201/561 (36%)	166/360 (46%)	35/201 (17%)
Lymphocytosis (>4.0 × 10^9/l)	190/590 (32%)	128/375 (34%)	62/215 (29%)

Abbreviations: ECOG, European Cooperative Oncology Group; LDH, lactate dehydrogenase.

lymphoma helps predict outcome. Blood, 132 (4) (2018), pp. 413–422.

Disclosure of Interest: S. Mant: None Declared, G. Naylor: None Declared, N. Crosbie: None Declared, P. Clinical Trials Unit: None Declared, M. Oates: None Declared, A. Pettitt: None Declared, S. Rule Conflict with: Employment Astra Zeneca, D. Lewis: None Declared

BSH22-PO62 | BRUIN CLL-322: A Phase 3 Open-Label, Randomised Study of Fixed Duration Pirtobrutinib plus Venetoclax and Rituximab *versus* Venetoclax and Rituximab in Previously Treated Chronic Lymphocytic Leukaemia/Small Lymphocytic Lymphoma (Trial in Progress)

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Abstract Content: Covalent Bruton's Tyrosine Kinase (BTK) inhibitors (BTKi) have transformed the management of chronic lymphocytic leukaemia/small lymphocytic

lymphoma (CLL/SLL), but these treatments are not curative and the majority of patients will require additional treatment. The MURANO study established the time-limited combination of 2 years venetoclax plus rituximab as a clinically important regimen for patients with R/R CLL/SLL. However, that trial almost exclusively enrolled patients who were never treated with a covalent BTKi, a population less relevant in the context of today's standard of care. Pirtobrutinib is a highly selective, non-covalent BTKi that inhibits both wild type (WT) and C481-mutated BTK with equal low nM potency. In a phase 1/2 BRUIN trial, pirtobrutinib achieved pharmacokinetic exposures that exceeded its BTK IC96 at trough, was well tolerated, and demonstrated promising efficacy in CLL/SLL patients regardless of prior therapy, number of prior lines of therapy, or BTK C481 mutation status (Mato et al. *Lancet* 2021;39 710 277:892–901). Therefore, adding fixed duration pirtobrutinib to the time-limited MURANO regimen may allow for even deeper and more prolonged disease control, and generate a clinically relevant dataset in a BTK-pretreated CLL/SLL population.

BRUIN CLL-322 is a randomised, open-label, global phase 3 study comparing fixed duration pirtobrutinib plus venetoclax and rituximab (PVR) *versus* venetoclax and rituximab (VR) in patients with CLL/SLL who have received prior therapy. To ensure relevance in the modern therapy context, a minimum of 80% of patients must have had a prior covalent BTKi. Approximately 600 patients will be randomised 1:1. Randomisation will be stratified by 17p deletion (yes/no) and prior BTKi experience (discontinuation due to progressive disease *versus* due to other reasons *versus* no prior BTKi exposure).

Eligible patients are adults with a diagnosis of CLL/SLL and requirement for therapy per iwCLL 2018 criteria who have received prior therapy that may or may not include a covalent BTKi. The unlimited number of lines of prior therapy are allowed. Key exclusion criteria include CNS involvement by CLL/SLL, Richter transformation at any time pre-enrolment, history of allogeneic stem cell transplant (SCT) or autologous SCT or chimeric antigen receptor (CAR) T-cell therapy within 60 days and prior therapy with a BCL2 inhibitor or non-covalent BTKi.

The primary end-point is progression-free survival (PFS) per iwCLL assessed by an independent review committee. Secondary end-points include overall response rate (ORR), overall survival (OS), time to next treatment (TTNT), event-free survival (EFS), safety and tolerability and patient-reported outcomes. This global study is currently enrolling patients (NCT04965493).

Disclosure of Interest: A. Mato Conflict with: AstraZeneca, AbbVie,Sunesis,PharmacyclicsLLC,Janssen,LOXO,Adaptive Biotechnologies, BeiGene, Acerta, DTRM BioPharma, Johnson and Johnson, TG Therapeutics, Genetech, Conflict with: Nurix, AbbVie, Sunesis, Pharmacyclics LLC, Janssen,, LOXO, Adaptive Biotechnologies, BeiGene, Acerta, Genmab, DTRM BioPharma, Johnson and Johnson, Genetech, W. Wierda Conflict with: Genzyme Corporation, Conflict with: GSK/Novartis, Xencor, Genetech, Janssen, Cyclacel, Loxo Oncology Inc, Pharmacyclis LLC, Karyopharm, Oncternal Therapeutics, Miragen, Sunesis, KITE Pharma, Juno Therapeutics, Acerta, Gilead Sciences, AbbVie, AstraZeneca, J. Pagel Conflict with: Pharmacyclics, AbbVie, Gilead, Epizyme, AstraZeneca, BeiGene, MEI Pharma, Kite, Incyte/MorphoSys, Actinium Pharmaceuticals, Conflict with: Former employee: Center for Blood Disorders and Stem Cell Transplantation, Swedish Cancer Institute; Current employee: Loxo Oncology at Lilly, Stamford, CT, USA, M. Davids Conflict with: Eli Lilly and Company, Janssen, Celgene, BeiGene, Adaptive Technologies, AbbVie, MEI Pharma, Merck,Takeda, Research To Practice, Pharmacyclics, TG Therapeutics, MEI Pharma, Novartis, BMS, Verastem, AstraZeneca, Genentech, Ascentage Pharma, Conflict with: Pharmacyclics, TG Therapeutics, MEI Pharma, Novartis, BMS, Verastem, AstraZeneca, Genentech, Surface Oncology, Ascentage Pharma, P. L. Zinzani Conflict with: Verastem, Novartis, MSD, EUSAPHARMA, Conflict with: Roche, KYOWA KIRIN, BMS, SERVIER, Verastem, Novartis, Incyte, JANSSEN CILLAG, TAKEDA, EUSAPHARMA, GILEAD, Beigene, TG Therapeutics, CELLTRION, BMS, SERVIER, Verastem, SANDOZ, ADC Therap, Y. Lu Conflict with: Eli Lilly and Company: current employee and current equity holder in publicly traded company, H. Liu Conflict with: Loxo Oncgy at Lilly: Current employee; AstraZeneca: Previous employess, S. Shahda Conflict with: Loxo Oncgy at Lilly: Current employee and Current equity holder in publicly traded company, C. C. Leow Conflict with: Loxo Oncgy at Lilly: Current employee and Current equity holder in publicly traded company, C. Tam Conflict with: Janssen, AbbVie, Beigene, Conflict with: Honaria: LOXO, Beigene, Janssen, AbbVie, J. Woyach Conflict with: Abbvie, ArQule Inc, Janssen, AstraZeneca, Pharmacyclis LLC, Conflict with: Loxo Oncology, AbbVie, Conflict with: Advisory: Abbvie, ArQule Inc, Janssen, AstraZeneca, Biegene; Data and Safety: Gilead Sciences Inc, T. Eyre Conflict with: Roche, Loxo Oncology, Incyte, Secura Bio, Abbvie, Conflict with: Beigene, Gilead/KITE, AstraZeneca, Conflict with: Honoraria: Roche, Beigene, Gilead/KITE, Loxo Oncology, Janssen, Secura Bio, AstraZeneca, Abbvie; Travel Support for Conferences: Gilead/KITE, Abbvie; Speakers Bureau: Gilead/KITE; Membership on an entity's Board of Directors or advisory committees: Loxo Oncology.

BSH22-PO63 | Bisphosphonate prophylaxis in Lymphoma patients treated with steroid containing regimens

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Abstract Content: Chemotherapy regimens for lymphoma frequently incorporate high doses of glucocorticoids and observational studies have highlighted increased risks of subsequent osteoporotic bone fractures. Greater numbers of often elderly patients, at higher risk of osteoporosis, are now treated with curative intent. The recent randomised controlled trial SIESTA, shows that primary prophylaxis of weekly alendronate for lymphoma patients on steroid containing chemotherapy was safe, effective, demonstrated improved T scores on densitometry and reduced bone resorption supported by biochemical analyses. Our department introduced a guideline on the use of primary alendronate prophylaxis in patients with lymphoma treated with regimens incorporating glucocorticoids. Consideration of alendronate prophylaxis was recommended for regimens containing >30 mg/m^2 prednisolone for >3 days and one risk factor for osteoporosis; males >65 years, females >50 years, history of osteopenia/osteoporosis, bone involvement with lymphoma, prolonged immobility.

The objective of the study was to investigate fracture frequency (within 2 years of treatment start), in two consecutive cohorts of patients, treated pre and postguideline.

Data were collected retrospectively on all patients with lymphoma who received >1 cycle of any of CHOP/CVP, DA EPOCH, ESHAP, GDP, (+/− antibody) BEACOPP/BEACOPDAC and ChlVPP-PABLOE between years 2018 and 2020.

A total of 162 patients were identified. The baseline demographics are outlined in Table 1.

In the pre and post guidelines cohorts; 56 (65%) vs. 60 (78%) patients were considered high fracture risk, 25 (29%) vs. 23 (30%) had pre-existing osteoporosis and only two and six high-risk patients were on bisphosphonates at presentation. Prophylactic bisphosphonates were prescribed in nine (16%) and 31 (51%) high-risk patients, respectively, prior to and following implementation of the guideline.

In the pre and post guideline cohorts; seven out of 86 patients (8%) (4 male, 3 female) vs. 5/76 patients (6.8%) (1 male, 4 female) sustained fractures following chemotherapy, with a median age of 73.8 years (59–84 years) vs. 59 years (range 30–77 years). The median time from initiation of chemotherapy to fracture was 4 months (2–19) vs. 6 months (1–19 months). Of those patients who sustained fractures, five out of seven (pre) *versus* three out of seven (post)had pre-existing osteoporosis but were not prescribed bisphosphonates, while one out of seven (pre-) *versus* one out of five (post-)sustained a fracture while on prophylaxis.

Most fractures occurred in patients treated with RCHOP (n = 5 vs. n = 4) and in patients with Diffuse large B cell Lymphoma (n = 5 vs. n = 3).

In conclusion, while alendronate prescription was more frequent following the guideline, many high-risk patients did not receive prophylaxis. Improved guideline adherence, and a larger cohort would be required to establish the efficacy of alendronate prophylaxis in this clinical context.

Abstract Table:

Criteria	Pre	Post
Median age	65.5	68
Sex	86	76
Male/Female	53/33	37/36
Diagnosis		
1. DLBCL	46	54
2. Follicular Lymphoma	15	1
3. Hodgkin Lymphoma	13	1
4. Others	12	11
Chemotherapy		
1. R-CHOP	70	57
2. Others	15	19

Disclosure of Interest: None Declared.

BSH22-PO64 | Efficacy of Mogamulizumab in Mycosis Fungoides by Patient Blood Involvement and Time to Response Analysis in Mycosis Fungoides and Sézary Syndrome: A post hoc analysis of the MAVORIC Study

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Abstract Content: Cutaneous T-cell lymphomas (CTCL) are rare forms of non-Hodgkin lymphoma, presenting primarily in the skin. Mycosis fungoides (MF) and Sézary syndrome (SS) account for around two-thirds of all CTCL cases.

MAVORIC (NCT01728805) was an open-label, phase 3 study comparing mogamulizumab (Moga) to vorinostat (Vori) in MF and SS patients. Previously published post hoc MAVORIC data has shown trends to higher multicompartmental efficacy with Moga in MF and SS patients with increasing baseline blood tumour burden (Scarisbrick J, et al. Efficacy and Safety of Mogamulizumab by Patient Blood Classification. Presented at the 16th EADO Congress, 12–14 October 2020, Virtual). This subset of patients may experience an increased risk of disease progression and worse survival (Agar 2010, Am Soc J Clin Oncol). This post hoc analysis of MAVORIC

Abstract Table: Efficacy analyses for ORR, PFS and TTNT by IA in MF patients by baseline blood classification

	B0		B1		B2	
	Vori (*N* = 61)	Moga (*N* = 63)	Vori (*N* = 27)	Moga (*N* = 29)	Vori (*N* = 11)	Moga (*N* = 13)
PFS[a], Months, median (*n*)	4.37 (37)	4.7 (39)	2.83 (23)	8.43 (17)	4.7 (9)	11.4 (10)
HR (95% Cl)	0.99 (0.63, 1.56)		0.36 (0.17, 0.76)		0.68 (0.26, 1.73)	
p-value	0.8638		0.0033		0.5549	
ORR[b], % (*n*)	6.6 (4)	15.9 (10)	7.4 (2)	20.7 (6)	9.1 (1)	46.2 (6)
RD (95% CI)	9.3 (−2.3, 21.6)		13.3 (−6.7, 34.2)		37.1 (−3.1, 68.5)	
p-value	0.0819		0.223		0.0325	
TTNT[a], Months, median (*n*)	4.13 (48)	6.77 (46)	3.13 (21)	11.9 (18)	6.6 (8)	19.63 (6)
HR (95% Cl)	0.70 (0.47, 1.06)		0.40 (0.19, 0.86)		0.54 (0.18, 1.68)	
p-value	0.0992		0.0018		0.2054	

Abbreviations: CI, confidence interval; CR, complete response; HR, hazard ratio; IA, Investigator's Assessment; MF, mycosis fungoides; Moga, mogamulizumab; ORR, overall response rate; PFS, progression-free survival; PR, partial response; RD, risk difference; TTNT, time-to-next treatment; Vori, vorinostat.

[a]*N* numbers are No. pts evaluable for end-point /No. pts with B-class at baseline.

[b]*N* numbers are No. pts with global response (CR + PR) /No. MF pts with B-class at baseline.

data examined the efficacy of Moga and Vori in MF patients stratified by baseline blood classification, and analysed time to global response (TTR) for Moga by disease subtype.

In MAVORIC, patients were randomized 1:1 to receive either Moga (intravenous, 1.0 mg/kg weekly for the first 28-day cycle, then on days 1 and 15 of subsequent cycles) or Vori (oral, 400 mg daily). Vori patients who experienced disease progression or intolerable toxicity could cross over to the Moga treatment arm.

In this analysis, efficacy outcomes (progression-free survival [PFS], global overall response rate [ORR] and time-to-next-treatment [TTNT]) by investigator assessment (IA) for MF patients (Moga, *n* = 105; Vori, *n* = 99) were stratified by baseline blood involvement, where B0 indicates absence of significant blood involvement and B1 and B2 indicate low- and high- blood tumour burden respectively. Analysis of TTR by IA by disease subtype was performed for Moga-responders (*N* = 52).

Moga-treated MF patients showed numerically superior results compared to Vori patients for PFS, ORR and TTNT and there was a trend with Moga to improved results for all analysed end-points with escalating baseline B-class (Table). Superiority was seen from statistically significant results for Moga *versus* Vori for MF B1 patients for PFS (8.43 vs. 2.83 months, $p = 0.003$) and TTNT (11.9 vs. 3.13 months, $p = 0.002$), and for MF B2 patients for ORR (46.2% vs. 9.1%, $p = 0.033$). TTR analysis by IA in Moga patients showed a more variable range of values for MF compared to SS; median (range) TTR was 3.07 (0.93–27.83) months vs. 4.72 (0.93–16.17) months for MF and SS respectively.

Moga-treated MF patients show a trend to improvement in PFS, ORR and TTNT with increasing blood tumour burden. Statistically significant improvement is seen for MF patients with blood involvement (B1 and B2) treated by Moga *versus* Vori. While median TTR with Moga is shorter in MF patients, the greater range suggests that in some cases, clinical responses may occur later than those in SS patients.

Disclosure of Interest: M. Beylot-Barry Conflict with: Kyowa Kirin, Recordati, Conflict with: Celgene, Roche, Conflict with: Kyowa Kirin, N. Booken Conflict with: Kyowa Kirin, Recordati, Takeda, Conflict with: Recordati, C. Weishaupt Conflict with: Bristol Meyer-Squibb, Kyowa Kirin, Novartis, Pierre Fabre, Roche Pharma, Sanofi, SUN Pharma, M. Medley Conflict with: Employee of Kyowa Kirin International, W. Sun Conflict with: Employee of Kyowa Kirin Pharmaceutical Development, J.-P. Rosen Conflict with: Employee of Kyowa Kirin International.

BSH22-PO65 | Undiagnosed Lymphadenopathy Pathway—Is a Haematology-led service warranted?

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Abstract Content: Lymphadenopathy of unknown cause is a frequent reason for patient referral for further investigation, and has a differential diagnosis, including lymphoma. Optimising the patient pathway and ensuring efficient and timely diagnosis, especially in the setting of a suspected cancer is important for patient experience, health economics and clinical outcome. Current referral pathways for undiagnosed lymphadenopathy in ABUHB are via site-specific specialist clinics for preliminary investigation and tissue diagnosis, according to location of pathological lymphadenopathy. Where no appropriate route of referral is obvious, and the clinical picture is highly suggestive of lymphoma, cases may be referred directly to haematology. Local guidelines on choice of appropriate pathway are available to primary and secondary care clinicians. A suggested restructuring

of the current referral and diagnostic pathway provoked the Haematology Lymphoma team to perform an audit of all lymph node biopsies processed by the Health Board's Histopathology department during a 1-year period, to assess whether an alteration to the current pathway was warranted; in particular, whether creating a central, haematology-led diagnostic clinic, similar to the Royal Marsden lymph node diagnostic clinic, is appropriate. Three hundred and seventy-three histology samples were identified. The clinical record, pathology results and radiological investigations for each lymph node biopsy sample were reviewed. Data were collected on site and method of biopsy, speciality team organising biopsy, inpatient/outpatient status, and whether or not the Lymphoma team was involved in the patient's care prior to diagnosis. Surgical biopsy or radiological-guided needle core biopsy is required for lymphoma diagnosis. Among 373 samples, 18 cases were excluded due to lack of available results, 44 samples obtained by fine-needle aspirate or bronchoalveolar lavage were excluded as unsuitable for lymphoma diagnosis and 111 cases where biopsy was taken for staging of a known non-haematological malignancy were excluded. Among 200 radiological core/surgical excisional biopsies, a new diagnosis of haematological malignancy was made in 51 cases (25.5%). Radiological-guided core biopsy was adequate for diagnosis in 80.4%. Fifteen out of 51 new lymphoma diagnoses were made in patients who were hospitalised under a medical or surgical team; 36 cases of new haematological malignancy were diagnosed via an outpatient pathway. In 57 out of 200 cases (28.5%) histology showed reactive lymphadenopathy, and 68 out of 200 biopsies (34%) showed a non-haematological cancer. These data show that among 200 cases of undiagnosed lymphadenopathy, just one in four cases were due to haematological malignancy, insufficient to warrant a change of the current diagnostic pathway such that all cases of undiagnosed lymphadenopathy would be referred to haematology. The Royal Marsden model may not be applicable in a general hospital setting.

Disclosure of Interest: None Declared.

BSH22-PO66 | Clinical Outcomes in Relapsed DLBCL Patients Approved for CAR-T Therapy— A Single-Centre Study

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Abstract Content: Chimeric antigen receptor (CAR)-T cell therapy can be an effective treatment strategy for patients with relapsed or refractory Diffuse Large B-cell Lymphoma (DLBCL). However, a significant proportion of progress despite CAR-T and its use can be complicated by treatment-related toxicities. CAR-T cell therapy was first approved for use in Scotland in September 2019. Two CAR-T products have been approved by the Scottish Medicines Consortium for DLBCL: Axicel (Yescarta, Kite) and Tisagen (Kymriah, Novartis). Eligibility for CAR-T-cell therapy is considered at the Scottish

Abstract Table:

	Total ***N*** **= 22** ***N*** **= 18 day 100**	**Axi-cel** ***N*** **= 13** ***N*** **= 10 day 100** **0**	**Tisagen** ***N*** **= 9**
CRS, *N* (%)			
Any grade	21 (95)	13 (100)	8 (89)
Grade 3+	3 (13.6)	2 (15.4)	1 (22.2)
ICANS, *N* (%)			
Any grade	10 (45.5)	9 (69)	1 (11)
Grade 3+	4 (18.2)	4 (30.8)	0 (0)
Tocilizumab use, *N* (%)	18 (81)	12 (92)	6 (66.7)
Steroid use, *N* (%)	12 (54.5)	9 (69.2)	3 (33.3)
ICU/HDU admission, *N* (%)	8 (36.4)	5 (38.4)	3 (33.3)
HDU admission	5 (22.7)	2 (15.38)	3 (33.3)
ICU admission	5 (22.7)	4 (30.7)	1 (11.1)
Grade 3+ cytopenia, *N* (%)			
D28 neutro−/thrombopenia (*N* = 22)	7 (31.8)/10 (45.5)	6 (46.2)/9 (69.2)	1 (4.5)/1 (13.6)
D100 neutro−/thrombopenia (*N* = 17)	2 (11.1)/5 (27.7)	2 (20)/5 (50)	0 (0)/0 (0)

CAR-T multidisciplinary team meeting (MDT). We present the clinical outcomes data for all patients treated in Scotland with SMC approved CAR-T-cell therapy for DLBCL.

Data were retrospectively collected for those patients approved by the CAR-T MDT using medical records and the CAR-T database. This included baseline characteristics at the time of approval, treatment toxicity and postinfusion treatment outcomes.

A total of 55 patients were submitted for discussion at the Scottish CAR-T MDT between 01/11/2021 and 30/09/2021. Of these 43 patients were approved for CAR-T therapy, and a total of 29 were subsequently treated. Reasons for not reaching infusion of CAR-T following MDT approval included: clinical deterioration secondary to progressive disease (7), inadequate fitness for CAR-T cell therapy following review at CAR-T treating centre (5), and failed collection or failed manufacturing of the CAR (2).

In terms of baseline characteristics, the median age of patients treated was 61 (40–75), 29 of 55 patient had advanced stage III/IV at presentation to the MDT, 23 had *De Novo DLBCL* (the remainder had transformed follicular) and extranodal disease involvement was found in 24 of 55 patients at presentation to the Scottish CAR-T MDT. Of the 29 patients treated following MDT approval, a total of 23 were treated in Scotland with SMC-approved CAR for DLBCL. The remainder were either treated through clinical trial entry, infused in NHS England or are awaiting infusion. For the 23 patients treated with an SMC-approved CAR in this time frame, the overall response rates were 61.9% and 57.9% at 3 and 6 months respectively. Complete metabolic remission was achieved in 47.6% of patients at 3 months and in 47.4% at 6 months. The majority of patients experienced treatment-related toxicity. This is summarised in the table attached.

Outcomes for CAR-T use in Scotland are inline with previously reported ORR and CMR rates in real-world data studies, which show that this is an effective form of treatment for previously relapsed or refractory diffuse large B-cell lymphoma patients. However, there remain issues with rapidly progressing disease prohibiting infusion of manufactured CAR-T as well as treatment-related toxicity which can result in significant morbidity and treatment burden. In light of this, further real-world data will be useful in identifying objective factors which might preclude patients from CAR-T therapy.

Disclosure of Interest: None Declared.

BSH22-PO67 | Real-World Outcomes for Dexamethasone, Rituximab and Cyclophosphamide (DRC) in the Treatment of Waldenström Macroglobulinaemia: An Eight-Year Retrospective Review

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Abstract Content: Waldenström macroglobulinaemia (WM) is a subtype of lymphoplasmacytic lymphoma (LPL) characterised by monoclonal immunoglobulin (Ig) M gammopathy, bone marrow infiltration and the presence of the MYD88 mutation in approximately 90% of patients. Although there is no clear first-line treatment for symptomatic WM, British Society of Haematology (BSH) guidelines recommend personalised, rituximab-containing regimes that include agents such as cyclophosphamide, fludarabine or bendamustine. The combination of dexamethasone, rituximab and cyclophosphamide (DRC) is widely used, especially in older and frailer patients, as it is often better tolerated with less associated myelotoxicity.

We conducted a single-centre, retrospective study at Norfolk and Norwich University Hospital—level 3, tertiary haematology unit. All patients who underwent treatment for WM with DRC from January 2014 to September 2021 were identified electronically and included. Data were collected and analysed for patient demographics, disease characteristics, response to treatment and associated toxicities. Standardised categorical response definitions were used to evaluate treatment effect.

Overall, 66 patients were identified of whom 36 (64%) were male and 20 (36%) female. The median age at the start of treatment with DRC was 75 years (range 42–90), with a median serum paraprotein level before treatment of 20.9 g/l (range 0.8–64.7). The median number of treatment cycles was 6.5 (range 1–8).

In our cohort, overall response rate (ORR) was 71%, with 21% displaying stable disease (SD) and 7% meeting criteria for progression (PD). Fifty-five percent of patients displayed a partial response (PR) or better and 16% had a minor response (MR). The median time to 50% reduction in serum paraprotein was 3.9 months (range 0.8–11.2). Overall 2-year progression-free survival (PFS) was 54% and 2-year PFS for patients that demonstrated a PR or better was 87%. Five patients (8%) experienced side-effects (all myelosuppression) that were classified as being of Grade 3 severity or higher.

The findings of our study show less favourable results when compared with seminal data (Dimopoulos MA, et al. *J Clin Oncol*. 2007 Aug; 25 [22]:3344–9) which provided the first empirical evidence to support the use of DRC in WM (Table 1). These results may be explained by heterogeneity in baseline patient co-morbidities and worse performance status, as well as individual changes to DRC dosing schedules deemed necessary by clinicians at our centre due to the real-world patients being older, frailer and having more co-morbidities.

DRC remains an effective treatment for symptomatic WM with a favourable toxicity profile, especially when used in frail patients as first-line therapy. However, there remains an unmet need to continue to improve the outcomes of this subset of patients with WM.

Abstract Table: Comparison of Patient Characteristics and Outcome Data with Study by Dimopoulous et al, 2007.

	Current study	Dimopoulous et al, 2007
Number of participants	66	72
Median age; range (years)	75; 42–90	69; 33–89
% Male	64	62.5
Overall Response Rate (%)	71	83
Complete Response (%)	0	7
Partial Response or Very Good Partial Response (%)	55	67
Minor Response (%)	16	9
Overall 2-year PFS (%)	54	67
2-year PFS for patients who responded to DRC (%)	60	80
Grade 3 or 4 Neutropenia (%)	8	9

Disclosure of Interest: None Declared.

BSH22-PO68 | Identification of a Novel Proliferating Cell Fraction in Chronic Lymphocytic Leukaemia with High Expression of IgM and Chemokine Receptors

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Abstract Content: Chronic lymphocytic leukaemia (CLL) is characterised by the accumulation of malignant $CD5^+$ B cells in the peripheral blood (PB), secondary lymphoid tissues and bone marrow. Previous studies using incorporation of ^{2}H-labelling of DNA in vivo demonstrated subclonal heterogeneity in PB CLL cell fractions based on surface expression of CXCR4 and CD5. The $CXCR4^{lo}CD5^{hi}$ fraction was shown to be enriched in recently born proliferating cells while the $CXCR4^{hi}CD5^{lo}$ fraction consists of quiescent cells thought to reflect their migratory and B cell receptor (BCR) signalling histories in tissue. While these fractions have since been more closely examined, the remaining bulk PB CLL population has been left relatively unexplored leaving other therapeutically relevant cell fractions undetected.

Here, we analysed the phenotype of subpopulations of PB cells from 22 CLL patients using flow cytometry to identify fractions of activated and proliferating cells. $CD19^+CD5^+$cells were divided into nine fractions based on CXCR4/CD5 densities, each containing 1%–2% of the total clonal $CD19^+CD5^+$ population. Surprisingly, we detected enrichment for $Ki67^+$ proliferating cells and high expression of AID in the fraction with high expression levels of both CXCR4 and CD5 ($CXCR4^{hi}CD5^{hi}$), demonstrating that $CXCR4^{lo}CD5^{hi}$ cells are not the only proliferating fraction in the blood. Moreover, we could detect mitotic cells in the $CXCR4^{hi}CD5^{hi}$ fraction using imaging flow cytometry of a nuclear stain. This $CXCR4^{hi}CD5^{hi}$ fraction showed the highest surface expression levels of IgM, CD86, CCR7 and CXCR5 of all the fractions assessed ($p < 0.05$), indicating they are highly activated and primed for migration to lymph nodes (LN) for further activation and proliferation. In support, mimicking LN environment stimulation with CD40L, IL4 and IL21 in vitro induced extensive proliferation of $CXCR4^{hi}CD5^{hi}$ as well as $CXCR4^{lo}CD5^{hi}$ cells, while $CXCR4^{hi}CD5^{lo}$ cells remained quiescent.

Proliferation of CLL cells occurs predominantly in secondary lymphoid tissues. To examine the phenotype of proliferating CLL cells in LNs, we analysed a fine-needle aspirate obtained from an enlarged cervical node of a *de novo* U-CLL patient with mutated *TP53* and rapidly progressing disease. Expression levels of both Ki67 and surface IgM were highest in the $CXCR4^{hi}CD5^{hi}$ fraction which was expanded to 20% of the $CD19^+CD5^+$ population in the LN, while $CXCR4^{lo}CD5^{hi}$ cells (accounting for 2% of the bulk LN population) expressed very low surface IgM and Ki67 levels, suggesting $CXCR4^{hi}CD5^{hi}$ cells may be the most proliferative cells in this patient.

Ibrutinib effectively targets proliferating $CXCR4^{lo}CD5^{hi}$ cells, however, the impact of ibrutinib on the $CXCR4^{hi}CD5^{hi}$ fraction remains unknown. Exposure of ibrutinib to PB CLL cells for 48 h in vitro resulted in selective depletion of the $CXCR4^{lo}CD5^{hi}$ fraction as expected; however, persistent cells after 48 h ibrutinib administration in vitro were exclusively of the $CXCR4^{hi}$ phenotype.

In conclusion, we have identified a potentially dangerous fraction of proliferating cells in the PB of CLL patients with high expression of IgM and chemokine receptors open for both migration to tissue and receipt of BCR signals. Furthermore, these $CXCR4^{hi}CD5^{hi}$ cells in the periphery may closely mirror activated cell phenotypes found in tissues and may represent critical targets for therapeutic intervention, particularly in high-risk CLL patients refractory to BCR inhibitor therapies.

Disclosure of Interest: None Declared.

BSH22-PO69 | Anthracycline-Induced Cardiotoxicity

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Abstract Content: Anthracyclines are a highly effective class of chemotherapy used to treat approximately 50%–80% of patients with lymphoma. The use of anthracyclines is complicated by the development of cardiotoxicity. Cardiotoxicity encompasses an early asymptomatic phase where abnormalities in cardiac biomarkers such as troponin may be present, leading to the development of left ventricular systolic dysfunction and heart failure. It is estimated that 9%–25% of patients develop left ventricular systolic dysfunction and 2%–5% heart failure following treatment.

Abstract Table:

Cardiac abnormality	Number of patients affected *(Out of the 25 patients who have completed chemotherapy)*	Comments
Abnormal troponin during chemotherapy	19 (76%)	- High sensitivity troponin T is measured at our Trust. A value of >14 ng/l is abnormal - The number of patients who developed an abnormal troponin value is higher than anticipated and requires longer term follow-up to determine its significance
Confirmed cardiotoxicity	4 (16%)	- A diagnosis of cardiotoxicity is made if there is a drop in the left ventricular ejection fraction of >10% from baseline, to a value of <50% on echo
Presumed cardiotoxicity	2 (8%)	- Both patients developed an abnormal troponin during treatment which triggered an echo. Both echos demonstrated left ventricular systolic dysfunction, however, there were no baseline echos to compare to. The patients were therefore treated as having presumed cardiotoxicity - This highlights the importance of obtaining a baseline echo in all patients who receive anthracycline chemotherapy and is recommended in Cardiology and Oncology guidelines

In 2020, we introduced a clinical pathway for outpatients receiving anthracycline chemotherapy for haematological malignancies at our Trust. The pathway is based on recent European Cardiology and Oncology guidelines and is comprised of three steps; a baseline cardiovascular risk assessment (including clinical assessment, ECG, echo and troponin measurement), surveillance during chemotherapy and recommendations for long-term cardiac follow-up. High-risk patients undergo an echo halfway through chemotherapy and at the end of treatment. The majority are also seen in the cardio-oncology service. Non-high-risk patients have troponin and symptom monitoring before each cycle and if abnormalities develop, this triggers an echo and referral to cardio-oncology.

We performed a prospective audit to assess adherence to the pathway and report the incidence of cardiotoxicity in our study population.

Thirty-four patients with lymphoma were treated with anthracycline chemotherapy between August 2020 and November 2021. The most common diagnoses were diffuse large B cell lymphoma (63%) and Hodgkin lymphoma (20%). The median age was 56 years (IQR 37–73), with 32% females. The median cumulative dose of anthracyclines was 300 mg/m^2. At the time of audit, 25 patients had completed chemotherapy and nine patients had chemotherapy ongoing. Eleven (32%) patients were deemed high-risk and 23 (68%) not-high risk for developing cardiotoxicity. Of the 11 high-risk patients, four (36%) were referred to cardio-oncology for optimisation prior to starting chemotherapy. At baseline, 55% of all patients had an ECG, 85% an echo and 76% a troponin performed.

In high-risk patients, echo and troponin surveillance was appropriately performed in 90% and 89% of cases respectively. In non-high-risk patients, 64% of patients developed an abnormal troponin, with a subsequent referral for an echo and to cardio-oncology in 85% and 64% of patients respectively.

In those who completed chemotherapy, 4/25 (16%) developed cardiotoxicity and 2/25 (8%) presumed cardiotoxicity (Table). One of the four confirmed cases of cardiotoxicity developed heart failure. All patients have been commenced on appropriate cardiac medications and are under surveillance by cardio-oncology. One patient had chemotherapy delayed by 1 week, while waiting an echo.

In summary, the adherence to a novel anthracycline pathway has been good with minimal impact upon chemotherapy care. Patients who developed cardiotoxicity were identified at an early timepoint and commenced on cardiac medications, which may be associated with a higher likelihood for cardiac recovery. A high proportion of patients developed asymptomatic troponin abnormalities during treatment indicating early myocardial injury. Patients are now entering longer term follow-up and the pathway will be re-audited in 6 months to establish longer term outcomes, the significance of abnormalities during treatment and ongoing adherence to the pathway.

Disclosure of Interest: None Declared.

BSH22-PO70 | BRUIN MCL-321: A Phase 3 Open-Label, Randomised Study of Pirtobrutinib *versus* Investigator Choice of BTK Inhibitor in Patients with Previously Treated, BTK Inhibitor Naïve Mantle Cell Lymphoma (Trial in Progress)

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Abstract Content: Covalent Bruton's Tyrosine Kinase (BTK) inhibitors (BTKi) have transformed the management of relapsed mantle cell lymphoma (MCL), but these treatments are not curative and the majority of patients will require additional treatment. Covalent BTKi share pharmacological liabilities (e.g. low oral bioavailability, short half-life) that collectively may lead to suboptimal BTK target coverage especially in rapidly proliferating tumours with high BTK protein turnover such as MCL. To address these limitations, pirtobrutinib, a highly selective, non-covalent BTKi that inhibits both wild type (WT) and C481-mutated BTK with equal low nM potency was developed. In the phase 1/2 BRUIN study, pirtobrutinib achieved pharmacokinetic exposures that exceeded its BTK IC96 at trough, was well tolerated and demonstrated promising efficacy in heavily pretreated, poor-prognosis MCL patients, most of whom had prior treatment with a covalent BTKi[1]. The purpose of this randomised study is to determine whether pirtobrutinib is superior to investigator's choice of covalent BTKi in patients with previously treated MCL.

BRUIN MCL-321 is a randomised, open-label, global phase 3 study comparing pirtobrutinib monotherapy *versus* investigator's choice of covalent BTKi monotherapy (ibrutinib, acalabrutinib or zanubrutinib) in patients with previously treated, BTKi naïve MCL. Approximately 500 patients will be randomised 1:1. Randomisation will be stratified by sMIPI risk (low/intermediate *versus* high), comparator BTKi (ibrutinib *versus* acalabrutinib/zanubrutinib) and number of prior lines of therapy (1 vs. ≥2).

Eligible patients are adults aged ≥18 years with a confirmed diagnosis of MCL (cyclin D1 overexpression, and ≥1 B-cell marker) who have received ≥1 prior line of systemic therapy for MCL that did not include a prior BTKi. Patients must have measurable disease per Lugano criteria and must have progressed on or relapsed following the most recent line of therapy prior to study enrolment. Key exclusion criteria include a history of current or prior central nervous system (CNS) involvement, significant cardiovascular disease, stroke or intracranial haemorrhage within 6 months of randomisation, and allogeneic stem cell transplant (SCT), autologous SCT or chimeric antigen receptor (CAR) T-cell therapy within 60 days of randomisation.

The primary end-point is progression-free survival (PFS) per Lugano criteria assessed by an independent review committee (IRC), with the goal of demonstrating superiority of pirtobrutinib over investigator's choice of covalent BTKi. Secondary end-points include overall response rate (ORR), duration of response (DoR), investigator-assessed PFS per Lugano criteria, overall survival, event-free survival, time to treatment failure, time to next treatment, PFS2 (time from randomisation to disease progression on next line of treatment or death from any cause), safety and tolerability and patient-reported outcomes. This global study is currently enrolling patients (NCT04662255).

[1]Mato et al. *Lancet* 2021;397 (10277):892–901.

Disclosure of Interest: T. Eyre Conflict with: Secura Bio, Roche, Loxo Oncology, Incyte, Abbvie, Conflict with: Gilead/KITE, AstraZeneca, Beigene, Conflict with: Honoraria: Secura Bio, Beigene, AstraZeneca, Roche, Abbvie, Loxo Oncology, Gilead/KITE, Janssen; Travel Support for Conferences: Abbvie, Gilead/KITE; Speakers Bureau: Gilead/KITE; Membership on an entity's Board of Directors or advisory committees: Loxo Oncology, N. Shah Conflict with: Incyte, Lilly, Miltenyi Biotec, Kite, Epizyme, Legend Umoja, Conflict with: Miltenyi Biotec, Lilly, Conflict with: Miltenyi Biotec, Lilly, S. Le Gouill: None Declared, M. Dreyling Conflict with: Incyte, Gilead/Kite, Bayer HealthCare Pharmaceuticals, Genmab, BeiGene, Celgene, Novartis, Janssen, Roche, Astra Zeneca, Conflict with: Abbvie, Gilead/Kite, Bayer HealthCare Pharmaceuticals, Janssen, Roche, Celgene, Conflict with: Speakers Bureau: Incyte, Gilead/Kite, Bayer HealthCare Pharmaceuticals, Amgen, Celgene, Astra Zeneca, Roche, Novartis, Janssen, E. Vandenberghe Conflict with: Honoraria: Jansnens, Abbvie, W. Jurczak Conflict with: Abbvie, AstraZeneca, BeiGene, Celtrion, Celgene, Debbiopharm, Epizyme, Incyte, Janssen, Loxo Oncology, Merck, Mei Pharma, Morphosys, Novo Nordisk, Roche, Sandoz, Takeda, TG Therapeutics, Conflict with: Membership on an entity's Board of Directors or advisory committees: Astra Zeneca, BeiGene, Janssen, Loxo Oncology, Sandoz, Roche, Y. Wang Conflict with: Incyte, Novartis, InnoCare, Genentech, MorphoSys, LOXO

Oncology, Conflict with: Membership on an entity's Board of Directors or advisory committees: LOXO Oncology, Eli Lilly, Incyte, TG Therapeutics, C. Cheah Conflict with: Gilead, Ascentage pharma, Beigene, AstraZeneca, Loxo/Lilly, Janssen, Roche, TG Therapeutics, Conflict with: Roche, Celgene, AbbVie, MSD: Consultancy, Conflict with: Honoraria: MSD: Consultancy, Gilead, Ascentage pharma, Beigene, AstraZeneca, TG Therapeutics, Roche, Loxo/Lilly, Janssen; Advisory: MSD: Consultancy, Gilead, AstraZeneca, TG Therapeutics, Loxo/Lilly, Janssen, Roche, Beigene, Ascentage pharma; Travel expenses: Roche, M. Gandhi Conflict with: Honoraria: Karyopharm Therapeutics, TG Therapeutics, GlaxoSmithKline, C. Chay: None Declared, J. Sharman Conflict with: BeiGene, TG Therapeutics, AbbVie, BMS, AstraZeneca, Lilly, Pharmacyclics LLC, an AbbVie Company, Conflict with: Current holder of stock options in a privately held company, Membership on an entity's Board of Directors or advisory committees: Centessa, D. Andorsky Conflict with: Abbvie, Celgene/BMS, Conflict with: Abbvie, Celgene/BMS, Epizyme, M. Yin Conflict with: Loxo Oncology at Lilly: Current Employment; AstraZeneca: Ended employment in the past 24 months, M. Balbas Conflict with: Nektar Therapeutics: Current equity holder in publicly traded company, Ended employment in the past 24 months; Loxo Oncology at Lilly: Current Employment, Current equity holder in publicly traded company, J. Kherani Conflict with: Loxo Oncology at Lilly: Current Employment, Current equity holder in publicly traded company, M. Wang Conflict with: AstraZeneca, Bayer Healthcare, BeiGene, CSTone, DTRM Biopharma (Cayman) Limited, Epizyme, Genentech, InnoCare, Janssen, Juno, Kite Pharma, Loxo Oncology, Miltenyi Biomedicine GmbH, Oncternal, Pharmacyclics, VelosBio, Conflict with: Acerta Pharma, AstraZeneca, BeiGene, BioInvent, Celgene, Innocare, Janssen, Juno, Kite, Pharma, Lilly, Loxo Oncology, Molecular Templates, Oncternal, Pharmacyclics, VelosBio, Conflict with: Honoraria: Acerta Pharma, Anticancer Association, AstraZeneca, BeiGene, CAHON, Chinese Medical Association, Clinical Care Options, Dava Oncology, Epizyme, Hebei Cancer Prevention Federation, Imbruvica, Imedex, Janssen, Kite Pharma, Miltenyi Biomedicine GmbH, Moffit.

Myeloma

BSH22-PO71 | CARTITUDE-2 Cohort B: Efficacy and Safety of Ciltacabtagene Autoleucel, a Chimeric Antigen Receptor T-Cell Therapy Directed Against B-Cell Maturation Antigen, in Patients With Multiple Myeloma and Early Relapse After Initial Treatment

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Abstract Content: Ciltacabtagene autoleucel (cilta-cel) is a chimeric antigen receptor T-cell (CAR-T) therapy with two B-cell maturation antigen (BCMA)-targeting single-domain antibodies. CARTITUDE-2 (NCT04133636) is a phase 2, multicohort study evaluating the safety and efficacy of cilta-cel in patients with multiple myeloma (MM) in various disease settings. Here, we present the first results from CARTITUDE-2 Cohort B, which enrolled patients following early relapse after initial therapy that included a proteasome inhibitor (PI) and immunomodulatory drug (IMiD).

Eligible patients had MM, received 1 prior line of therapy (PI and IMiD required), had disease progression ≤12 months after autologous stem cell transplantation (ASCT) or frontline therapy, and were naive to CAR-T or anti-BCMA therapies. A single cilta-cel infusion at a target dose of 0.75×10^6 CAR+ viable T cells/kg was given 5–7 days after start of lymphodepletion (300 mg/m^2 cyclophosphamide and 30 mg/m^2 fludarabine daily for 3 days). The primary objective was minimal residual disease (MRD) negativity at 10^{-5}. Adverse events were graded by Common Terminology Criteria for Adverse Events version 5.0 (cytokine release syndrome [CRS]) and immune effector cell associated neurotoxicity syndrome (ICANS) by American Society for Transplantation and Cellular Therapy (ASTCT) criteria.

As of data cutoff on April 15, 2021, 18 patients (median age 57.0 years [range: 44–67]; 78% men) received cilta-cel. The median follow-up was 4.7 months (range: 0.6–13.5) and the median time from diagnosis to enrolment was 1.1 years (range: 0.5–1.9). Two (11.1%) patients had high cytogenetic risk and 5 (27.8%) had bone marrow plasma cells >30%; 14 (77.8%) patients had prior ASCT, and 15 (83.3%) were refractory to their prior therapy. The overall response rate was 88.9% (95% CI: 65.3–98.6), with 27.8% of patients (95% CI: 9.7–53.5) achieving ≥complete response (CR) and 66.7% (95% CI: 41.0–86.7) achieving ≥very good partial response. The median time to first response was 0.9 months (range:

0.9–2.6), median time to best response was 1.4 months (range: 0.9–11.8) and median time to ≥CR was 1.8 months (range: 0.9–11.6). Of 13 patients with ≥3 months follow-up, five (38%) achieved ≥CR. All MRD-evaluable patients ($n = 9$) were MRD negative at 10^{-5}. Haematological treatment-emergent adverse events (TEAEs) in ≥20% of patients were neutropenia (88.9%), thrombocytopenia (61.1%), anaemia (50.0%), leukopenia (27.8%) and lymphopenia (22.2%). Fifteen (83.3%) patients had CRS (1 grade 4); the median time to onset was 8 days (range: 5–11) and median duration was 4 days (range: 1–7). One patient had ICANS (grade 1). One patient experienced movement and neurocognitive TEAEs (grade 3) on Day 38 post cilta-cel infusion. No study deaths were reported post cilta-cel infusion.

In patients who experienced early clinical relapse or treatment failure to initial therapy, a single cilta-cel infusion resulted in early and deep responses, with a manageable safety profile. Responses continue to deepen, and follow-up is ongoing. These data support the continued investigation of cilta-cel in earlier lines of therapy and incorporation into potentially curative frontline regimens.

Disclosure of Interest: N. W. C. J. Van de Donk Conflict with: Amgen, Bayer, BMS/Celgene, Janssen, Novartis, Roche, Servier, Takeda, Conflict with: Amgen, Cellectis, Janssen, Conflict with: BMS/Celgene, M. Delforge Conflict with: Amgen, Celgene, Janssen, Sanofi, Conflict with: Amgen, Celgene, Janssen, Sanofi, M. Agha: None Declared, A. D. Cohen Conflict with: AstraZeneca, BMS/Celgene, Genentech/Roche, GlaxoSmithKline, Janssen, Oncopeptides, Takeda, Conflict with: GlaxoSmithKline, Novartis, Y. C. Cohen Conflict with: GlaxoSmithKline, Janssen, Neopharm/Promedico, Takeda, Conflict with: Karyopharm, Takeda, Conflict with: GlaxoSmithKline, Janssen, Neopharm/Promedico, Takeda, J. Hillengass Conflict with: Adaptive, Axxess Network, Beijing Life Oasis Public Service Center, Beijing Medical Award Foundation, Bristol Myers Squibb, Curio Science, GlaxoSmithKline, Oncopeptides, Oncotracker, Sanofi, Skyline, S. Anguille: None Declared, T. Kerre Conflict with: BMS, Celgene, Elyad, Janssen, Novartis, Pfizer, W. Roeloffzen: None Declared, J. M. Schecter Conflict with: Janssen, K. C. De Braganca Conflict with: Janssen, H. Varsos Conflict with: Janssen, L. Wang: None Declared, M. Vogel Conflict with: Janssen, E. Zudaire Conflict with: Janssen, C. Corsale Conflict with: Janssen, M. Akram Conflict with: Legend Biotech USA, D. Geng Conflict with: Legend Biotech USA, T. Nesheiwat Conflict with: Legend Biotech USA, L. Pacaud Conflict with: Legend Biotech USA, P. Sonneveld Conflict with: Amgen, Celgene/BMS, Janssen, Karyopharm, Takeda, Conflict with: Amgen, Celgene/BMS, Janssen, Karyopharm, Skyline Dx, Takeda, Conflict with: Amgen, Celgene/BMS, Janssen, Karyopharm, Skyline Dx, Takeda, S. Zweegman Conflict with: Janssen, Takeda, Conflict with: BMS, Janssen, Oncopeptides, Sanofi, Takeda.

BSH22-PO72 | First Results From CC-92480-MM-002: A Phase 1/2 Study Of The Potent, Novel CELMoD Agent CC-92480, In Combination With Dexamethasone And Bortezomib In Patients With Relapsed/Refractory Multiple Myeloma

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Abstract Content: CC-92480, a potent cereblon E3 ligase modulator (CELMoD®) agent, has shown marked synergy with proteasome inhibitors, dexamethasone (DEX) and CD38 monoclonal antibodies (mAbs) in myeloma cells. CC-92480 + DEX demonstrated a manageable safety profile with promising preliminary efficacy in patients (pts) with relapsed/refractory multiple myeloma (RRMM). Here we report preliminary results from the CC-92480 + bortezomib (BORT) + DEX cohort of the phase 1/2 study, CC-92480-MM-002 (NCT03989414).

Key eligibility criteria were: RRMM; 2–4 prior regimens, including lenalidomide (LEN); and documented progressive disease during or after the last myeloma therapy. Over a 21-day cycle (C), oral CC-92480 was administered at specified cohort doses (0.3, 0.6 and 1.0 mg) on days (D) 1–14 with subcutaneous BORT (1.3 mg/m^2) on D1, 4, 8 and 11 of C1–8 and on D1 and 8 after C8. DEX (20 mg/day or 10 mg/day if >75 years of age) was given on D1, 2, 4, 5, 8, 9, 11 and 12 of C1–8 and on D1, 2, 8 and 9 after C8. Primary objectives were to evaluate safety and preliminary efficacy, and to determine the maximum tolerated dose (MTD)/recommended phase 2 dose (RP2D). Immunophenotyping, pharmacodynamics (PD) and Ikaros/Aiolos protein levels were also assessed.

Nineteen pts received CC-92480 + BORT+DEX as of May 26, 2021, with a median age of 66 (50–83) years and median time since initial diagnosis of 4.8 (1.9–17.1) years. The median number of prior regimens was three (2–4) and prior therapies included stem cell transplantation (57.9%), BORT (78.9%), carfilzomib (21.1%), LEN (100%), pomalidomide (47.4%) and CD38 mAbs (36.8%); four pts had extramedullary disease and four were triple-class refractory. The median follow-up was 8 (1.0–19.2) months; the median number of cycles received was 10 (1–28), with nine pts continuing treatment and 5 pts discontinuing due to progressive disease. At least one treatment-emergent adverse event (TEAE) was reported in all pts, with 18 pts having grade (Gr) 3/4 TEAEs. Most frequent Gr 3/4 TEAEs were neutropenia (36.8%; no febrile neutropenia), thrombocytopenia (21.1%), anaemia (10.5%), insomnia (10.5%) and hyperglycaemia (10.5%). One pt had Gr 3/4 infection, eight pts had Gr 1/2 peripheral neuropathy and five pts experienced serious TEAEs (none related to study treatment). Dose reductions of CC-92480, BORT and DEX, occurred in five, seven and eight pts, respectively; four pts had dose reductions due to TEAEs. Two pts discontinued because of TEAEs (dysgeusia and pre-existing colon neoplasm). The MTD was not reached and no pt had dose-limiting toxicity; two deaths occurred (due to myeloma progression and colon neoplasm). The overall response rate across all doses was 73.7% (14/19 pts), with responses observed at all dose levels. The median time to first response was 0.95 (0.7–3.3) months and median duration of response was 10.4 (5.5–not reached) months. Plasma exposures of CC-92480 + BORT+DEX were consistent with previous analysis of CC-92480 + DEX. PD studies of CC-92480 + BORT+DEX treatment, showed potent degradation of substrates 3–6 h after treatment and reduced levels of mature B cells. A CC-92480 dose of 1.0 mg was selected as the RP2D.

In pts with RRMM, CC-92480 + BORT+DEX appears to be safe and well tolerated with encouraging preliminary efficacy. These results support further development of CC-92480 in combination regimens in RRMM. A CC-92480 + BORT+DEX expansion cohort is ongoing at the RP2D in the CC-92480-MM-002 study.

Disclosure of Interest: P. G. Richardson Conflict with: Oncopeptides, Celgene/BMS, Takeda, Karyopharm (research funding, honoraria), Conflict with: Janssen, Sanofi, Secura Bio, GSK, Regeneron, AstraZeneca, Protocol Intelligence (honoraria), E. M. Ocio Conflict with: Amgen, Bristol Myers Squibb, GSK, Janssen, Oncopeptides, Pfizer, Sanofi, Takeda (honoraria or consultancy), N. Raje Conflict with: BMS, Amgen, Pfizer, Takeda, GSK, Janssen (consultancy); Bluebird bio (consultancy, research funding), Conflict with: Bluebird bio, Conflict with: Caribou, Immuneel (Scientific advisory board), T. Gregory: None Declared, D. White Conflict with: Amgen, Celgene/BMS, GSK, Janssen, Karyopharm, Sanofi (grants, honoraria); Pfizer (grants), Conflict with: Antengene, Forus (honoraria); Takeda (Data safety monitoring board), A. Oriol Conflict with: Sanofi, GSK, BMS, Amgen (honoraria), I. Sandhu Conflict with: Celgene/BMS, Amgen, Janssen, Forus (honoraria), M.-S. Raab Conflict with: Amgen, BMS, Janssen (consultancy, honoraria, Participation on a Data Safety Monitoring Board or Advisory Board), Conflict with: Roche, Art Tempi, Blue Star, Sanofi, Takeda (honoraria); Novartis, GSK (honoraria, payment for expert testimony); Abbvie (payment for expert testimony), R. LeBlanc Conflict with: BMS Canada (participation on advisory board), C. Rodriguez Valdes Conflict with: BMS, Janssen, Takeda, Amgen, Oncopeptides, Karyopharm (consultancy), S. Trudel Conflict with: GSK, BMS (consultancy, grants, honoraria); Roche (consultancy), Conflict with: Janssen (grants, honoraria); Pfizer, Amgen (grants), Conflict with: Sanofi, Forus (honoraria), R. Wäsch Conflict with: Janssen (consultancy, honoraria, support for attending meetings and/or travel, participation on a Data Safety Monitoring Board or Advisory Board); Novartis, Celgene/BMS (consultancy, participation on a Data Safety Monitoring Board or Advisory Board); Amgen (consultancy), Conflict with: Takeda (honoraria, support for attending meetings and/or travel); Sanofi (honoraria); Gilead (Support for attending meetings and/or travel), A. Perrot Conflict with: Takeda, Sanofi (grants), Conflict with: Abbvie, Amgen, BMS/Celgene (honoraria); Janssen (honoraria, participation on a Data Safety Monitoring Board or Advisory Board), N. J. Bahlis Conflict with: Pfizer, Celgene/BMS (grants, honoraria, participation on a Data Safety Monitoring Board or Advisory Board), Conflict with: Janssen, Abbvie, Amgen, Genentech, Karyopharm, Sanofi (honoraria, participation on a Data Safety Monitoring Board or Advisory Board), Z. Zhou Conflict with: BMS (stock or stock option), M. Lamba Conflict with: BMS, Pfizer (stock or stock option), M. Amatangelo Conflict with: BMS (employment, stock or stock options), T. Civardi: None Declared, J. Katz: None Declared, P. Maciag Conflict with: BMS (stock or stock option), T. Peluso Conflict with: BMS (employment), M. A. Dimopoulos Conflict with: Amgen, Takeda, Beigene, BMS, Janssen (honoraria, participation in advisory boards).

BSH22-PO73 | A Comparison of the Clinical Characteristics, Treatment Response and Survival of Patients With and Without Light Chain Glycosylation on their Monoclonal Protein in Patients Treated with Carfilzomib, Cyclophosphamide, Lenalidomide and Dexamethasone (KCRD) in the Myeloma XI Trial

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Abstract Content: N-linked glycosylation of the light chain (LC) component of monoclonal proteins is emerging as a post-translational modification of interest in patients with plasma cell dyscrasias. It can be detected using intact light chain mass spectrometry (MS) assays and has been reported to be associated with an increased risk of progression from MGUS. However, no studies have compared the presenting characteristics and outcomes of patients with myeloma with and without LC glycosylation.

Two hundred and ninety-three patients treated with KCRD in the Myeloma XI trial who had residual serum available for MS testing from baseline or the end of the first cycle of induction chemotherapy were included in this study. Baseline samples underwent immune precipitation using antisera specific for IgG, IgA, IgM, total kappa, total lambda, free kappa and free lambda, then were eluted and reduced, spotted onto target plates and analysed by matrix-assisted laser desorption/ionisation time-of-flight MS. MS spectra were assigned as being consistent with LC glycosylation if there were higher mass peaks with a polytypic distribution present in the MS spectra at the $[M + 1H]^{1+}$ and $[M + 2H]^{2+}$ charge states. Minimal residual disease (MRD) was assessed centrally by flow cytometry as part of the trial protocol (sensitivity of 4×10^{-5}).

Two hundred and sisty-six out of 293 (90.8%) patients had no evidence of LC glycosylation and 26/293 (8.9%) had MS spectra consistent with LC glycosylation. In 1/293 (0.3%) patients the main monoclonal protein had no evidence of LC glycosylation, but there was a small second monoclonal protein only detectable by MS with spectral appearances suggestive of glycosylation. Due to the mixed glycosylation picture of the monoclonal proteins detected by MS, this patient was excluded from the comparisons between patients with and without LC glycosylation.

There was no significant difference in the level of the involved free LC levels (iFLC) at presentation between patients with and without LC glycosylation (median iFLC 480 mg/l vs. 435 mg/l, 0.93), however, patients with LC glycosylation had a better renal function at presentation (median creatinine 78.5 mmol/l vs. 94.0 mmol/l $p < 0.01$, median GFR 80.8 ml/min vs. 67.5 ml/min, $p = 0.02$). There was no difference in the age at presentation between patients with and without LC glycosylation (58.0 vs. 60.4 years, $p = 0.44$). Beta-2-microglobulin and albumin levels did not significantly differ between patients with and without LC glycosylation (median beta-2-microglobulin 3.2 mg/l vs. 3.4 mg/l, $p = 0.50$, median albumin 40.2 g/l vs. 40.0 g/l, $p = 0.96$).

MRD results were available for 131/292 (44.8%) of patients from post induction and there was no difference in the rate of MRD negativity achieved between patients with and without LC glycosylation (7/10 (70%) vs. 76/121 (62.8%), $p = 0.91$). At day +100 post ASCT, MRD results were available for 166 out of 292 (56.8%) patients and there was no significant difference in the rate of MRD negativity between patients with and without LC glycosylation (12/14 (85.7%) v. 112/152 (73.7%), $p = 0.50$). After a median follow-up of 43.7 months, there is no difference in progression-free survival (PFS) between patients with and without LC glycosylation (median PFS 50.0 months vs. not reached (NR), $p = = 0.62$). To date, there is also no difference in overall survival (OS) (median OS NR v.NR, $p = 0.92$).

In this study, LC glycosylation was not associated with poorer responses to treatment or reduced survival in patients with newly diagnosed symptomatic myeloma.

Disclosure of Interest: H. V. Giles Conflict with: The Binding Site Ltd, B. Kishore: None Declared, M. Drayson Conflict with: Abingdon Health, N. Wright Conflict with: The Binding Site Ltd, G. Cook: None Declared, R. de Tute: None Declared, M. Kaiser Conflict with: AbbVie, BMS/Celgene, Janssen, GSK, Karyopharm, Pfizer, Seattle Genetics and Takeda, Conflict with: BMS/Celgene, G. Morgan Conflict with: BMS, Janssen, Karyopharm and Oncopeptides, G. Jackson Conflict with: Celgene, Amgen, takeda, GSK, J and J, and Oncopeptides, G. Pratt Conflict with: Amgen, The Binding Site Ltd, Celgene/BMS, Gilead, Janssen, and Takeda.

BSH22-PO74 | Free Light Chain-Specific Antisera Improves the Sensitivity of Matrix-assisted Laser Desorption/Ionisation-Time of Flight Mass Spectrometry (MALDI-TOF MS) for the Detection of Residual Disease in Patients with Free Light Chain Only Multiple Myeloma

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Abstract Content: Mass spectrometry (MS) is emerging as a highly sensitive technique for the identification and follow-up of monoclonal proteins (MP). However, there are

conflicting reports about its sensitivity for the detection of low-level free light chain (FLC) MP.

In this study, the sensitivity of MALDI-TOF MS for detecting FLC MP was analysed in 48 patients with FLC only myeloma who were treated with carfilzomib, lenalidomide, cyclophosphamide and dexamethasone in the Myeloma XI trial. Responses were classified using the IMWG criteria with an additional category of nCR for patients who were immunofixation negative but did not have bone marrow confirmation. sFLC ratios were considered abnormal in follow-up samples if they were skewed towards the involved FLC. Samples were tested twice by MS: first using antisera specific for IgG, IgA, IgM, total kappa and total lambda (EXENT); and then with antisera specific for free kappa (FK) and free lambda (FL) light chains (FLC-MS).

Monoclonal light chains (LC) were detectable in 46/48 (95.8%) patients using the EXENT assay and 1/48 (2.1%) patients had an equivocal result. 47/47 (100%) of baseline samples had detectable monoclonal LC using the FLC-MS assay. The patient with insufficient serum for FLC-MS testing had monoclonal FK detectable by EXENT and Freelite and had 200 mg FK/g creatinine in the urine. The EXENT-negative patient had abnormal sFLC results (FK 83.49 mg/l, FL 7.2 mg/l, sFLC ratio 11.596) but had 0 g FK/g creatinine in their urine. 5/48 (10.4%) samples had an intact MP with the same LC isotype and mass-to-charge ratio as the FLC MP, suggesting these patients may have progressed from an intact immunoglobulin-secreting MGUS.

34/48 (70.8%) patients had serum available for MS testing from post induction (PI). Nine out of 34 (26.5%) samples had an abnormal sFLC ratio. Residual monoclonal FLC were detectable in five out of nine (55.6%) and eight out of nine (88.9%) samples by EXENT and FLC-MS respectively. In FLC-MS negative sample, the sFLC ratio was skewed due to suppressed levels of the uninvolved FLC and the patient was MRD negative by flow cytometry. Twenty-one out of 27 (77.8%) patients in ≥nCR had a normal sFLC ratio; residual FLC MP was detectable in two out of 21 (9.5%) of these samples by EXENT and six out of 21 (28.6%) by FLC-MS.

Thirty out of 48 (62.5%) patients had serum available for MS testing from day+100 post ASCT. Five out of 30 (16.7%) had an abnormal FLC ratio of which only one out of five (20%) had residual disease detectable by FLC-MS. MRD results were available for three out of four (75%) of the FLC-MS negative patients and three out of three (100%) were MRD negative. FLC-MS positivity was associated with reduced progression-free survival (PFS) (31.0 months vs. not reached (NR), $p = 0.04$) but there was no significant difference between the PFS of patients with and without an abnormal sFLC ratio (75% PFS 24.7 vs. 35.4 months, $p = 0.482$). FLC-MS positivity was also associated with reduced overall survival (OS) survival (75% OS 39.0 months vs. NR, $p = 0.021$). Twenty-four out of 28 (85.7%) patients in ≥nCR had a normal sFLC ratio and residual MP was detectable in two out of 24 (8.3%) and six out of 24 (25.0%) by EXENT and FLC-MS respectively. There was a trend towards reduced PFS and OS in FLC-MS-positive patients in ≥nCR (median PFS 31.0 months vs. NR, $p = 0.11$ and 75% OS 42.6 months vs. NR, $p = 0.08$).

In conclusion, FLC-MS provided greater sensitivity for the detection of monoclonal FLC compared to standard techniques and EXENT and persistent positivity at day+100 post ASCT was associated with reduced PFS and OS.

Disclosure of Interest: H. V. Giles Conflict with: The Binding Site Ltd, B. Kishore: None Declared, M. Drayson Conflict with: Abingdon Health, N. Wright Conflict with: The Binding Site Ltd, G. Cook: None Declared, R. de Tute: None Declared, C. Pawlyn Conflict with: Celgene/BMS, Janssen and Sanofi, M. Kaiser Conflict with: AbbVie, BMS/Celgene, Janssen, GSK, Karyopharm, Pfizer, Seattle Genetics and Takeda, Conflict with: BMS/Celgene, S. North Conflict with: The Binding Site Ltd, G. Morgan Conflict with: BMS, Janssen, Karyopharm and Oncopeptides, G. Jackson Conflict with: Celgene, Amgen, takeda, GSK, J and J, and Oncopeptides, G. Pratt Conflict with: Amgen, The Binding Site Ltd, Celgene/BMS, Gilead, Janssen, and Takeda.

BSH22-PO75 | Randomised, Phase 3 Study of Bortezomib, Lenalidomide and Dexamethasone Followed by Ciltacabtagene Autoleucel *Versus* Bortezomib, Lenalidomide and Dexamethasone Followed by Lenalidomide and Dexamethasone Maintenance in Patients With Newly Diagnosed Multiple Myeloma Not Intended for Transplant: CARTITUDE-5

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Abstract Content: Autologous stem cell transplant (ASCT) is the standard of care treatment for transplant-eligible patients with newly diagnosed multiple myeloma (NDMM). For patients with NDMM who are ineligible or decline ASCT, the bortezomib, lenalidomide and dexamethasone (VRd) regimen is an effective treatment option. Ciltacabtagene autoleucel (cilta-cel) is a chimeric antigen receptor T-cell (CAR-T) therapy with two B-cell maturation antigen (BCMA)–targeting single-domain antibodies. A single infusion of cilta-cel in the phase 1b/2 CARTITUDE-1 study

(NCT03548207) resulted in deep and durable responses in heavily pretreated patients with relapsed/refractory multiple myeloma (MM).

The randomised, phase 3 CARTITUDE-5 study (NCT04923893) will compare the efficacy of cilta-cel *versus* lenalidomide and dexamethasone (Rd) maintenance when given after VRd induction in patients with NDMM who are ineligible or decline ASCT.

Eligible patients (target recruitment: N = 650) are aged ≥18 years with a diagnosis of MM based on International Myeloma Working Group criteria, measurable disease at screening and Eastern Cooperative Oncology Group performance status ≤1. Patients are eligible if they are not candidates for or decline high-dose chemotherapy with ASCT as initial treatment. Key exclusion criteria include a frailty index ≥2 based on the Myeloma Geriatric Assessment Score, prior CAR-T or BCMA-targeting therapy, or prior therapy for MM or smoldering myeloma (exception of a short course of steroids or one cycle of VRd). Enrolled patients will receive five to six cycles (21-day [d]) of VRd (one cycle permitted prior to screening): 1.3 mg/m^2 s.c. bortezomib: d 1, 4, 8 and 11; 25 mg oral lenalidomide: d 1–14 and 20 mg oral dexamethasone: d 1, 2, 4, 5, 8, 9, 11 and 12. Patients without disease progression will be randomised 1:1 to the cilta-cel arm or Rd maintenance (control) arm. Patients in the cilta-cel arm will undergo apheresis and receive bridging therapy (2 additional VRd cycles) before cilta-cel infusion at a target dose of 0.75 × 10^6 CAR+ viable T cells/kg 5–7 d after lymphodepletion (i.v. cyclophosphamide 300 mg/m^2 and fludarabine 30 mg/m^2 daily for 3 d) followed by a treatment-free observation period. Patients in the control arm will receive two additional VRd cycles followed by Rd maintenance in 28-d cycles (25 mg oral lenalidomide: d 1–21 and 40 mg oral dexamethasone: d 1, 8, 15 and 22) until disease progression or unacceptable toxicity. The primary end-point is progression-free survival (PFS). Secondary endpoints include sustained minimal residual disease (MRD)-negative complete response (CR); MRD-negative CR rate at 9 months; overall MRD-negative CR rate; overall survival; patients achieving ≥CR; time to subsequent anti-myeloma therapy; PFS on next-line therapy; incidence and severity of adverse events; pharmacokinetic and pharmacodynamic markers and changes in health-related quality of life.

Findings from this randomised, phase 3 study can provide insights into the efficacy and safety of cilta-cel after VRd in patients with NDMM. A single infusion of cilta-cel after VRd *versus* continuous treatment with Rd until disease progression may offer patients the benefit of a treatment-free period.

Disclosure of Interest: D. Dytfeld Conflict with: Janssen Cilag, Conflict with: Celgene, Conflict with: Celgene, Janssen Cilag, B. Dhakal: None Declared, M. Agha: None Declared, S. Manier Conflict with: Abbvie, Amgen, Celgene – Bristol Myers Squibb, Janssen, Novartis, M. Delforge Conflict with: Amgen, Celgene, Janssen, Sanofi, Conflict with: Amgen, Celgene, Janssen, Sanofi, S. Kuppens Conflict with: Janssen, S. Afifi Conflict with: Janssen, W. Deraedt Conflict with: Janssen, A. Taraseviciute-Morris Conflict with: Janssen, J. M. Schecter Conflict with: Janssen, J. Gilbert Conflict with: Janssen, F. Yalniz Conflict with: Janssen, E. Florendo Conflict with: Legend Biotech, L. Pacaud Conflict with: Legend Biotech, V. Hungria Conflict with: Abbvie, Amgen, Celgene – Bristol Myers Squibb, Janssen, Sanofi, Takeda, Conflict with: Amgen, Celgene – Bristol Myers Squibb, Janssen, Sanofi, S. Z. Usmani Conflict with: Abbvie, Amgen, Array BioPharma, Celgene – Bristol Myers Squibb, EdoPharma, GSK, Janssen, Janssen Oncology, Merck, Pharmacyclics, Sanofi, Seattle Genetics, SkylineDX, Takeda, Conflict with: Amgen, Array BioPharma, Celgene – Bristol Myers Squibb, GSK, Janssen, Janssen Oncology, Merck, Pharmacyclics, Sanofi, Seattle Genetics, SkylineDX, Takeda, Conflict with: Amgen, Celgene – Bristol Myers Squibb, Janssen, Sanofi, Takeda, M.-V. Mateos Conflict with: Adaptive Biotechnologies, Amgen, Celgene – Bristol Myers Squibb, Janssen, Oncopeptides, Pfizer, Regeneron, Roche, Sanofi, Sea-Gen, Takeda.

BSH22-PO76 | The impact of a delayed diagnosis on myeloma patients' quality of life

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Abstract Content: Myeloma has one of the longest times to diagnosis of any cancer. A quarter of myeloma patients wait over 10 months before getting the right diagnosis and the median time from first symptom to diagnosis is 163 days. Despite these statistics, there is no evidence on what it is like to live with the consequences of a delayed diagnosis.

Using an online survey, we looked at the impact of delayed diagnosis on the quality of life of myeloma patients to understand how different diagnosis experiences affect patients, their families and friends.

Of the 1324 survey participants, we found that 50% of myeloma patients reported a delayed diagnosis of myeloma (GP visit >3 months prior to diagnosis or diagnosis via A&E), compared to 30% who reported a timely diagnosis (Diagnosis within 3 months of GP visit, no visits to A&E). Patients who received a delayed diagnosis experienced a significantly greater impact on their quality of life compared to those who receive a timelier diagnosis: 49% of those with a delayed diagnosis reported a high impact on their quality of life, compared to 30% who received a timely diagnosis (Two-tailed test, $p < 0.05$). Significantly more patients with a timely diagnosis of myeloma reported that myeloma had a low impact on quality of life: 28% of those with a timely diagnosis report a low impact on quality of life, compared to 17% with a delayed diagnosis (Two-tailed test, $p < 0.05$).

Our results showed that patients with a delayed diagnosis experienced more negative physical effects due to their myeloma than patients with a timely diagnosis. More patients with a delayed diagnosis reported a lack of energy/weakness/fatigue (80% with a

delayed diagnosis vs. 74% with a timely diagnosis), pain (78% vs. 63%), spine fractures (34% vs. 26%), other bone fractures (29% vs. 16%), spinal cord compression (21% vs. 15%) and kyphosis (21% vs. 15%) compared to patients with a timely diagnosis.

The psychosocial and financial impacts of myeloma were also significantly greater for those with a delayed diagnosis. Patients receiving a delayed diagnosis identified a greater impact on their mobility/physical activity/ability to exercise, ability to work, ability to take part in social events, ability to enjoy life, be independent, carry out family responsibilities and spend quality time with friends and family. 16% of patients with a delayed diagnosis reported that myeloma had a major effect on financial difficulties compared to 9% for those with a timely diagnosis. Myeloma also had a significantly greater impact on mental health for those with a delayed diagnosis (36%) compared to those with a timely diagnosis (23%) (Two-tailed test, $p < 0.05$).

Our findings show for the first time that a delayed diagnosis of myeloma has a significantly greater impact on the quality of life of patients. Patients who received a delayed diagnosis experienced significantly more negative physical impacts, particularly relating to the spine, as well as psychosocial impacts that affect their overall quality of life. There is a need to ensure that all patients receive the right care and treatment that allow them to have a good quality of life after a diagnosis of myeloma, and our results show that this is particularly important for those who have a delayed diagnosis and as a result experience more physical and psychosocial effects.

Disclosure of Interest: A. Capper Conflict with: This project was supported by Amgen. They had no editorial control over the content/outputs., S. McKinlay: None Declared.

BSH22-PO77 | Treatment delivery and outcomes in elderly myeloma patients at The Royal Bournemouth hospital; Real-life data

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Abstract Content: Patients diagnosed with myeloma over the age of 75 have been identified as a high-risk group. Co-morbidities, frailty and treatment-related toxicity are all contributing factors. The added complexity of treating older patients with myeloma can restrict treatment options and impact upon overall survival.

We retrospectively evaluated treatment lines and outcomes in patients with myeloma over the age of 75 years at The Royal Bournemouth Hospital (RBH). RBH is a busy district general servicing a population with a high average age and almost double the national incidence of myeloma. Using real-world data, our aim was to assess how age can impact on the delivery of treatment and outcomes in this elderly myeloma population.

Retrospective data were collected using electronic records to identify all patients diagnosed with myeloma at RBH over a 5-year period, from 2015 to 2019. We collected data on patients over the age of 75 including: number of lines of therapy, regimens given, indication for discontinuation, number of infections requiring hospitalisation and overall survival.

One hundred and twenty-one patients were diagnosed with myeloma at RBH in this study period. The average age at diagnosis was 73 years. Fifty-three patients (43.8%) were over 75 years old. The average number of lines of therapy in the over 75 years group was 1.4. Ten patients (19%) had no systemic treatment and were managed with the best supportive care; 23 patients (43%) received one line of therapy; ten patients (19%) had two lines and 10 patients (19%) had three or more lines.

In the over 75 years group, the commonest reason for discontinuation of therapy was the completion of fixed duration treatment, followed by disease progression. Other reasons included recurrent infection, frailty, cardiac events, patient choice and palliation. The average time from diagnosis to death was 18 months. The mean number of infections requiring hospitalisation per patient was 2. Patients receiving three or more lines of therapy had an average of 4.3 hospital admissions compared to 1.2 admissions in patients who received less than three lines of therapy. Eleven patients had documented use of Levofloxacin.

These results demonstrate that most patients over the age of 75 with myeloma will not proceed beyond their first line of therapy. Preserving treatment lines for first or second relapse should therefore be deemed unnecessary and not in the best interest of this patient group.

The reason patients received fewer treatment lines is likely due to increased co-morbidities, reduced performance status and increased treatment-related toxicity. We also found that hospital admissions from infection were more likely in patients over 75 years old who received three or more lines of therapy. Twenty percent of patients received Levofloxacin prophylaxis (this would now be standard therapy for 1st line induction treatment).

These findings support the need for a personalised approach to treatment in the elderly. Rather than measuring success in terms of depth and duration of remission as with younger patients, factors such as tolerability and quality of life should have greater influence. With 63% of patients not going on to receive second-line therapy, the choice of treatment at diagnosis should be the best possible for that individual acknowledging many will not receive treatment beyond this line. Infection prophylaxis, close initial monitoring and regular clinical review to manage early toxicities are keys in this group of vulnerable patients.

Disclosure of Interest: None Declared.

BSH22-PO78 | Real-world outcomes of myeloma patients who fulfil the SLiM part only of the SLiM-CRAB criteria and who underwent monitoring during the COVID-19 pandemic: a single centre analysis

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Abstract Table:

	ALL PATIENTS *n* = 22 (%)	PATIENTS WHO PROGRESSED TO TREATMENT *n* = 9 (%)	PATIENTS WHO REMAIN UNDER OBSERVATION *n* = 13 (%)
Median age (range)	70.5 (41–92)	67 (41–88)	74 (55–92)
Sex			
Male	15 (68)	7 (78)	8 (62)
Female	7 (32)	2 (22)	5 (38)
Isotype			
IgG	13 (59)	3 (33)	10 (77)
IgA	5 (23)	3 (33)	2 (15)
Light chain	4 (18)	3 (33)	1 (8)
ISS			
I	16 (73)	6 (67)	10 (77)
II	5 (23)	2 (22)	3 (23)
III	1 (4)	1 (11)	0 (0)
Revised-ISS			
I	5 (23)	2 (22)	3 (23)
II	13 (59)	6 (67)	7 (54)
III	0 (0)	0 (0)	0 (0)
Not known	4 (18)	1 (11)	3 (23)
Cytogenetics			
Normal	9 (41)	3 (33)	6 (46)
1q gain	4 (18)	2 (22)	2 (15)
Unknown	9 (41)	4 (55)	5 (39)
Median bone marrow infiltrate % (range)	20% (10–60%)	40% (20–60%)	14% (10–60%)
Positive SLiM criteria			
WBMRI	13 (59)	2 (22)	11 (84)
Marrow infiltrate	1 (5)	1 (11)	0 (0)
SFLC ratio	4 (18)	3 (34)	1 (8)
SFLC and WBMRI	2 (9)	2 (22)	0 (0)
Marrow and WBMRI	1 (5)	0 (0)	1 (8)
Marrow, SFLC & WBMRI	1 (5)	1 (11)	0 (0)
Reason for treatment			
Anaemia	n/a	2 (22)	n/a
Pathological fracture		1 (11)	
Lytic lesion		1 (11)	
Progression on WBMRI		1 (11)	
Renal		2 (22)	
Renal & anaemia		1 (11)	
Patient choice		1 (11)	
Median follow-up	12 months		
Number progressed to symptomatic myeloma	9 (41)	n/a	n/a
Median TTP	Not Reached	3.8 months	n/a

Abstract Content: International Myeloma Working group (IMWG) diagnostic criteria for myeloma (MM) requires the presence of ≥10% clonal plasma cells alongside a MM defining event—traditionally a CRAB feature (hypercalcaemia, renal impairment, anaemia, bone disease). In 2014, three biomarkers were added (≥60% plasma cells in the marrow, light chain ratio ≥100 and ≥2 focal lesions on MRI), each associated with around an 80% probability of developing CRAB features within 2 years. These biomarkers are the SLiM criteria and the recommendation is that such patients are treated.

In March 2020 UK Myeloma Forum issued guidance for MM therapy during the Covid-19 pandemic, recommending patients who fulfil the SLiM part only of the SLiM/CRAB (SLiM positive) or who only have anaemia should be monitored.

There is a lack of real-world data available to validate the recommendation to treat based on SLiM criteria. The impact of not treating these patients during the Covid-19 pandemic remains unknown. We conducted a retrospective analysis of the outcomes of SLiM positive patients at Nottingham University Hospitals (NUH) NHS Trust who underwent observation rather than treatment during the Covid-19 pandemic.

SLiM positive patients were detected via the MM MDT min from 1st April 2020–30 Nov 2021. Time to progression (TTP) was defined as the time from diagnosis of SLiM positive MM until the time systemic therapy was initiated (day 1 cycle 1). Decision to treat was based on development of CRAB features, worsening of SLiM criteria and patient choice.

22 SLiM positive patients were identified. Patient characteristics and outcomes for the entire cohort and for those who did and did not progress are shown in Table 1. No patients were R-ISS stage III and 1q gain was the only high-risk cytogenetic abnormality detected. This may suggest higher risk patients are more likely to present with CRAB features and less likely to be SLiM positive.

The median follow-up was 12 months. Forty-one percent of patients progressed to require therapy in keeping with the IMWG data suggesting 80% of SLiM positive patients will progress over a 2-year period. The median TTP was not reached. For those patients who did progress, the median TTP was 3.8 months. Reasons for progression are shown in Table 1. Overall survival (OS) was 100% hence no suggestion thus far that observation of SLiM positive patients during the Covid-19 pandemic increased MM-related mortality.

The majority who remained under observation were SLiM positive on WBMRI alone. In contrast, the majority who did progress had been SLiM positive on SFLC ratio, marrow infiltrate or a combination of features.

We acknowledge the small numbers and relatively short follow-up of this study. Results thus far are in keeping with the IMWG finding that SLiM positive patients have around an 80% chance of progression at 2 years. There is a suggestion that patients who present with SLiM criteria only may have genomically lower risk disease. OS has not been affected thus far by monitoring SLiM patients. Our results also suggest that patients SLiM positive due to SFLC ratio or BM infiltration are more likely to require early intervention than those positive on WBMRI. We recommend a future multicentre UK wide analysis of the outcome of SLiM positive patients during Covid-19. Results would help counsel UK MM patients regarding when to offer treatment and potentially help develop a UK-based biomarker model to predict risk of progression.

Disclosure of Interest: None Declared.

BSH22-PO79 | Haematology clinic presentation of benign plasma cell granuloma and lymphomatoid granulomatosis with intracranial involvement—A case series

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Abstract Content: Plasma cell granuloma (PCG) and lymphomatoid granuloma (LG) are rare inflammatory non-neoplastic lesions. Central nervous system lesions are rare—a recent review identified around 50 cases with isolated intracranial involvement worldwide. Traditional management includes surgery, steroids and radiotherapy. LG lesions have been reported as responsive to Rituximab. We report three cases of benign intracranial lesions as the only site of involvement, not amenable to surgery, presenting to the haematology clinic. There is limited evidence on the use of systemic chemoimmunotherapy, and our cases highlight the difficulties in treating these rare pathologies.

Case 1. A 25-year-old with known hypothyroidism presented with seizures and visual disturbance. Diagnostics confirmed intracranial PCG with limited CD20 expression. Although initially steroid-responsive, she suffered disease progression radiologically with seizure recurrence on attempted tapering. Intrathecal hydrocortisone was unsuccessful, and radiotherapy not attempted due to toxicity concerns. She received regular Rituximab over 26 months (initially weekly for 4 doses, later monthly, and then 2 monthly over 2 years). She achieved a complete response and remained in remission at clinic discharge (30 months after final Rituximab).

Case 2. A 72-year-old with known myasthenia gravis presented with auditory hallucinations and lower limb weakness. A frontal lobe lesion biopsy confirmed LG with CD20 and EBER positivity. EBV PCR on peripheral blood was detectable but below the lower limit of quantification. Mycophenolate (myasthenia gravis treatment) was weaned, and steroids commenced with no clinical improvement. She was switched to Rituximab, resulting in significant lesion reduction based on interim neuroimaging 6 weeks later. Unfortunately, she deteriorated with recurrent infection and died eight weeks after the first Rituximab administration.

Case 3. A 50-year-old female presented with headaches, visual disturbance, weakness and memory impairment. Neuro-imaging revealed a peri-trigonal lesion, confirmed to be PCG on biopsy. There was limited CD20 expression.

Although initially steroid-responsive, she failed to respond to Rituximab. The latter was complicated by possible cardiotoxicity (palpitations and slightly reduced ejection fraction). Her disease was refractory to intravenous cyclophosphamide and prednisolone (10 cycles). She suffered postradiation symptom flare following stereotactic radiotherapy (20 gy in 10 fractions), requiring tapering steroids. Radiological appearances remain stable with an unchanged symptom complex (memory impairment and left-sided neglect).

Key morphological features of PCG are polyclonality with an inflammatory infiltrate and fibrosis. There were no clear antigenic triggers in our cases, although Case 1 and 2 had an autoimmune history (hypothyroidism and myasthenia gravis respectively). The role of immunosuppression in driving aetiology remains unclear but speculatively contributive. Although slow-growing and benign lesions, significant clinical morbidity is associated with these lesions. We highlight difficulties in diagnosing and treating these rare inflammatory disorders, which are best managed in an expert centre with multidisciplinary input. With non-resectable lesions, radiotherapy and steroids are most employed. Our cases show that Rituximab monotherapy and cyclophosphamide responses are variable, and outcomes do not appear to correlate with CD20 expression.

Disclosure of Interest: None Declared.

BSH22-PO80 | Epidemiology of multiple myeloma in UK and Republic of Ireland

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Abstract Content: Introduction: Multiple myeloma (MM) is the third most common blood cancer diagnosed each year. Despite considerable treatment advances, survival rates remain poor. To date, limited research has focussed on the impact of geography on MM patient outcomes.

Objective: To investigate the epidemiology of MM across the United Kingdom and Republic of Ireland (ROI) using publicly available data.

Methods: The most recent cancer registry statistics/reports for England, Scotland, Wales, Northern Ireland (NI) and ROI were explored for MM (ICD-10: C90) incidence and survival data. For each country, crude and age-standardised incidence rates and 1- and 5-year net survival estimates were extracted by sex, age group, geographical settings and other variables of interest (e.g. stage at diagnosis, admission process) if available. Findings were narratively compared.

Results: The most recent publicly available cancer registry statistics for the UK nations and ROI includes MM cases diagnosed in 2019, with the exception of Wales which currently reports on MM diagnoses up to 2018. Across the United Kingdom and ROI, n = 6772 people were diagnosed with MM in the most recent reported year (n = 6420 UK [n = 5521 England, n = 436 Scotland, n = 277 Wales, n = 186 NI] and n = 352 ROI). MM incidence rates varied across the investigated nations, with NI recording the highest incidence rate (age-standardised rate [ASR] 11.1 per 100 000) compared to Scotland which had the lowest (ASR 8.2 per 100 000). Incidence was higher among males and increased with advancing age with the highest rates observed for the 85–89 age group. Across the nations, 1-year net survival varied between 81.6% and 84.1% with NI reporting the highest survival and Scotland and Wales the lowest. Reported 5-year net survival ranged between 51.8% and 64% with ROI (2014–2018) recording the highest survival and NI (2010–2014) the lowest (however, diagnosis timeframes did vary between registries). In NI, MM patients with an emergency admission (up to 30 days prior to diagnosis) recorded the lowest 5-year survival (38.6% vs. no emergency/elective admission (52.2%) *versus* elective admission (60.5%); this information was only reported by the NI cancer registry.

Conclusion: While the findings highlight variation in MM epidemiology across the United Kingdom and ROI, further investigation of cancer registration practices for MM and harmonisation of the data is needed to enable more comparable analysis.

Disclosure of Interest: None Declared.

BSH22-PO81 | Outcomes of Patients (pts) with Previously Treated Multiple Myeloma (MM) from European Countries and the United Kingdom, Treated with Selinexor, Bortezomib and Dexamethasone (XVd) *Versus* Bortezomib and Dexamethasone (Vd): A Post Hoc Analysis from the BOSTON Trial

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Abstract Content: In Phase 3, randomised, multicentre BOSTON study, XVd was associated with significant improvements in progression-free survival (PFS), overall response rate (ORR) and rates of peripheral neuropathy (PN), with favourable trends in overall survival (OS) *versus* standard twice-weekly Vd.

This is a retrospective subgroup analysis of the BOSTON trial (N = 402) of XVd *versus* Vd in pts with MM and 1–3 prior therapies. We performed post hoc analyses on the

outcomes of pts from European countries (EC), including Austria, Belgium, Bulgaria, Czech Republic, France, Germany, Greece, Hungary, Italy, Poland, Romania, Russia, Serbia, Spain, Ukraine and the United Kingdom (UK) where 74% (297; XVd = 139, Vd = 158) of pts were from EC and 9% (36; XVd = 19, Vd = 17) were from the UK.

Demographics and baseline characteristics were similar in both arms including pts with 1 prior *versus* 2–3 prior lines of therapy (EC 50%; UK 53%) *versus* (EC 50%; UK 47%). Notably, the number of frail pts as defined by a simplified frailty score (using the Charlson Comorbidity Index, Eastern Cooperative Oncology Group performance status score and age) was greater in the EC subgroup (35%) compared to the UK (11%) and the number of pts with previous autologous stem cell transplantation (ASCT) was lower (EC 34%; UK 72%). No pts in the UK group had renal impairment (creatine clearance <30 min/ml) compared to 4% of EC pts. The PFS was significantly longer in pts in the XVd arm of both subgroups: EC pts 13.93 months (mo) (95% confidence interval [CI] 11.76- not reached [NR]) vs. Vd 9.43 months (95% CI 7.23–10.87; p = 0.002; HR 0.62, 95% CI 0.45–0.86); UK pts XVd NR (95% CI 16.56-NR) vs. Vd 9.43 months (95% CI 5.78-NR; p = 0.036; HR = 0.39, 95% CI 0.14–1.13). The OS in EC pts was NR for XVd (95% CI NR-NR) and 24.84 for Vd (95% CI 21.22-NR; p = 0.06; HR 0.71, 95% CI 0.46–1.09), and in UK pts, NR for XVd (95% CI 18.27-NR) and Vd (95% CI 21.22-NR; p = 0.294; HR = 0.67, 95% CI 0.16–2.84). The ORR for EC was 76.3% for XVd vs. 62.0% for Vd (p = 0.004), and UK: 84.2% for XVd and 52.9% for Vd (p = 0.023).

The most common adverse events (AEs) of any grade in EC and UK pts for XVd *versus* Vd were thrombocytopenia (EC 58% vs. 27%; UK 63% vs. 47%), PN (EC 35% vs. 47%; UK 47% vs. 53%) and fatigue (EC 35% vs. 17%; UK 84% vs. 59%). Serious AEs occurred in 50% (XVd) vs. 39% (Vd) of EC pts and 71% (XVd) vs. 46% (Vd) UK pts. Dose reduction due to AE occurred in 66% (XVd) vs. 45% (Vd) in the EC pts and 95% (XVd) vs. 71% (Vd) in the UK pts.

Of the UK pts, 6 on XVd and 14 on Vd received subsequent therapy. Lenalidomide and daratumumab were the most common treatments for the pts in the XVd arm (XVd 83.3% and 66.7%; Vd 64.3% and 35.7% respectively). No pts in the XVd arm received carfilzomib or isatuximab, which accounted for 7.1% of subsequent treatments in the Vd arm. Similarly, 52 pts from the XVd arm and 91 from the Vd arm received subsequent therapy in the EC pts. Lenalidomide, pomalidomide and daratumumab were the most common in the XVd arm (XVd 46% and 25% and 25%; Vd 43% and 17% and 23% respectively).

In summary, XVd significantly improved PFS and ORR in both EC and UK populations with significant improvement in OS in the EC population and a trend towards improvement in the UK population. Both patient populations had manageable AEs. The data presented here align with the results of the overall population and support the use of the XVd combination for pts with previously treated MM.

Disclosure of Interest: R. Benjamin: None Declared, M. Garg: None Declared, S. Basu Conflict with: advisory board to Sanofi, Pfizer, and Bristol Myers Squib, Y. Chai Conflict with: Employee of Karyopharm, A. DeCastro Conflict with: Employee of Karyopharm, F. Boulhabel Conflict with: Employee of Karyopharm, J. Shah Conflict with: Employee and stockholder of Karyopharm, H. Auner Conflict with: Takeda and Karyopharm, Conflict with: Amgen, Conflict with: speaker's bureau role for Janssen.

BSH22-PO82 | A META-ANALYSIS OF THE RATE OF MALIGNANT PROGRESSION OF MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE: PRELIMINARY FINDINGS FROM A SYSTEMATIC REVIEW

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Abstract Content: Monoclonal gammopathy of undetermined significance (MGUS) is an asymptomatic premalignant condition preceding multiple myeloma (MM) and other haematological malignancies (HM). Clinically the rate of progression from MGUS to HM is important; current guidelines from the International Myeloma Working Group (IMWG) report this rate as "around 1% per year", however, variation has been reported by ethnic groups, MGUS type and clinical features. A systematic review of the published literature was conducted to investigate the rate of MGUS progression to support clinical practice.

Four electronic databases (Embase, Medline, Pubmed and Web of Science) were searched from database inception to 11/12/2019 using key words and MeSH subject headings for "MGUS", "haematological malignancy" and "progression". Studies were reviewed against predefined eligibility criteria by two independent reviewers. For studies reporting progression events and person-years of follow-up, a random-effects meta-analysis model was used to produce a pooled rate of MGUS progression to HM and MM. Studies reporting on cumulative rates of progression at specified time-points (1, 5 and 10-year) were included in a narrative synthesis.

Overall, 36 papers met the inclusion criteria; 12 studies (sample size: 114–17 963; follow-up 3.3–42.1 years) were included in the meta-analysis. In preliminary analyses, the annual pooled rate of MGUS progression was 1.1% (95% CI 0.9–1.3) to HM and 0.9% (95% CI 0.7–1.1) to MM.

In total, 18 studies contributed to the narrative synthesis on MGUS progression to HM (sample size: 52–17 963; follow-up 2.1–34.1 years) and 10 studies reported on MGUS progression to MM (sample size: 75–2046, follow-up: 2.1–17 years). These narrative syntheses highlighted the heterogeneity of research, which encompassed key traits like methods, sample sizes and follow-up duration. Studies were also mainly conducted in Europe, being particularly scarce in Asia.

Between meta-analysis and narrative synthesis, only seven studies reported on IgM-MGUS progression to Waldenström's macroglobinaemia or HM, which could not be clearly synthesised in either analysis due to differing reporting; these papers indicated higher progression rates in IgM-MGUS than non-IgM.
Preliminary findings from this systematic review support current IMWG guidelines on the rate of MGUS progression to HM. However, as the majority of studies included were limited to geographical areas within Europe and USA, further research reflecting population and clinical diversity is needed.
Disclosure of Interest: None Declared.

BSH22-PO83 | Are we looking for Monoclonal Gammopathy of Renal Significance (MGRS)? An audit of investigations in current clinical practice

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Abstract Content: Monoclonal gammopathy of unknown significance (MGUS) is a premalignant condition defined as the presence of a monoclonal protein with no evidence of plasma cell/B-cell-related malignancy. The risk of progression from MGUS to a related malignancy is approximately 1% per year. MGUS patients are closely monitored for signs of progression allowing for rapid initiation of treatment.
In 2012, the International Kidney and Monoclonal Gammopathy Research Group (IKMG) introduced the term Monoclonal Gammopathy of Renal Significance (MGRS). MGRS is the clonal proliferation of a nephrotoxic monoclonal protein without meeting the criteria for any other plasma cell/B-cell malignancy. The diagnosis of MGRS allows for the initiation of urgent treatment required to prevent further deterioration in renal function. Updated diagnostic criteria from the IKMG made renal biopsy essential for diagnosis of MGRS. Consequently, the IKMG set out an algorithm to guide clinicians on when to consider a renal biopsy. The parameters measured to evaluate the need for a renal biopsy include urine albumin creatinine ratio (ACR).
This audit was conducted in the Clatterbridge Cancer Centre Liverpool (CCC-L) a leading cancer centre in the Northwest of England. Urine ACR was chosen as the parameter to audit as it is a cheap, non-invasive, quantitative investigation. The primary outcome of this audit is to assess the number of MGUS patients who had an ACR measured at diagnosis in the Myeloma clinic from January 2014 to December 2020.
Data were collected retrospectively from electronic clinic letters and notes. The date of diagnosis was defined as the date of clinic letter in which diagnosis was first confirmed. Patients were considered to have had an ACR performed at diagnosis if ACR was measured between 28 days prior to and post the date of diagnosis. ACR performed during disease was defined as any ACR measured from 28 days prior to date of diagnosis and date of death/data collection.
Data from 503 patients (249 females, 254 males) were analysed. The median age at diagnosis was 73. Table 1 shows data for patients who had an ACR measurement performed at diagnosis and during disease. There is a trend towards greater compliance to measuring ACR at diagnosis in successive years from 2014 to 2019 (Table 1). This trend reverses in 2020 when only 40.0% of patients had an ACR measured at diagnosis. For all patients where ACR was performed during disease; 56.8% (n = 179) had the highest ACR measurement of <3.0 mg/mmol with only 14.0% (n = 44) having the highest ACR measurement of >30.0 mg/mmol. If ACR was performed at diagnosis it was more commonly repeated if the value was higher; the frequencies with which ACR was repeated were 85.7% (n = 12), 65.1% (n = 28) and 28.4% (n = 31) when ACR value at diagnosis was >30.0 mg/mmol, 3.0–30.0 mg/mmol and <3.0 mg/mmol respectively.
This audit has shown an increased recognition for the importance of ACR measurement with increased compliance year on year. A likely hypothesis for the reduced measurements in 2020 is the need for remote clinic appointments during the Coronavirus 2019 (Covid-19) pandemic. Following IKMG

Abstract Table: Frequency of ACR performed by year of diagnosis

Year of diagnosis	Total *n*	ACR at diagnosis *n* (%)	ACR at diagnosis and repeated *n* (%)	Any ACR performed during disease *n* (%)
2014	4	0 (0.0)	0 (0.0)	3 (75.0)
2015	99	11 (11.1)	11 (11.1)	51 (51.5)
2016	79	5 (6.3)	5 (6.3)	36 (45.6)
2017	81	15 (18.5)	11 (13.6)	45 (55.6)
2018	90	41 (45.6)	20 (22.2)	65 (72.2)
2019	95	72 (75.8)	21 (22.1)	84 (88.4)
2020	55	22 (40.0)	3 (5.5)	31 (56.4)
All years	503	166 (33.0)	71 (14.1)	315 (62.6)

Patients are considered to have had an ACR performed at diagnosis if performed 28 days prior to or post the date of diagnosis (considered as date of clinic letter in which diagnosis was confirmed). Patients are considered to have had an ACR performed during disease if any ACR has been performed between 28 days prior to date of diagnosis and death or time of data collection if alive at time of analysis. Data are presented as total number and percentage of cases diagnosed in that year.
Abbreviation ACR: Urinary albumin:creatinine ratio.

guidelines 14.0% ($n = 44$) of patients would be advised to have a renal biopsy due to their ACR measurement of >30.0 mg/mmol. Further evaluation of this patient cohort is required to audit compliance with other parameters suggested by the IKMG. A diagnostic pathway to be used at the earliest opportunity for MGUS patients may then be developed.
Disclosure of Interest: None Declared.

Red Cell Disorder

BSH22-PO84 | Quality of Life and Symptom Burden of Paroxysmal Nocturnal Haemoglobinuria Among Patients Receiving C5 Inhibitors in the United States and Europe

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Abstract Content: Paroxysmal nocturnal haemoglobinuria (PNH) is a rare disease with the most prominent symptoms being haemolytic anaemia, haemoglobinuria, thrombosis and fatigue. Complement C5 inhibition with eculizumab or ravulizumab is the current standard of care. Despite improvements in morbidity and mortality, some patients continue experiencing haemolysis and suboptimal quality of life (QoL). This study aimed at investigating the symptom burden of PNH in patients currently treated with a C5 inhibitor, globally.
Adult patients with a self-reported diagnosis of PNH were recruited through patient advocacy groups in the United States (US) and Europe (EU: UK, France and Germany): Aplastic Anaemia and myelodysplastic syndrome (MDS) International Foundation, Patient Support, Hémoglobinurie Paroxystique Nocturne (HPN) France and Stiftung lichterzellen respectively. Patients treated with Eculizumab or Ravulizumab completed an online cross-sectional questionnaire. FACIT (Functional Assessment of Chronic Illness Therapy) was used to measure fatigue scores. Descriptive statistics are reported here.
A total of 193 adult patients were enrolled (122 patients in the US, and 71 in EU) including 20 UK patients. Current medications included Eculizumab (EU:69%, US:29%) or Ravulizumab (EU:31% US:71%); most patients were on treatment for ≥3 months: EU:98.6% US:96.7%. The most recent haemoglobin level was <12 g/dl (mean ± SD; EU:10.19 ± 1.97, US:10.17 ± 2.04) for the majority of patients (EU:85.7%, US:84.2%), indicating that most remained anaemic. Among patients whoever received a red blood cell transfusion and were on treatment for ≥1 year, (EU:35.0%, US:35.2%) received ≥1 transfusion in the previous year, and 18% (EU) and 22% (US) received ≥4. Fatigue was the most commonly reported symptom (EU:63.4%, US:78.7%) (Figure 1). FACIT scores (EU:35.0 ± 13.7, US:32.1 ± 13.4) were lower than in the general population (43.5) indicating higher levels of fatigue. Breakthrough haemolysis was experienced by US:40% and EU:39% patients.
Despite improved standard of care, PNH patients still experience a substantial burden of illness. There is a need for newer treatments allowing better clinical and haematological outcomes for PNH patients.
This study was sponsored by Apellis Pharmaceuticals, Inc., and Swedish Orphan Biovitrum AB and both companies reviewed the abstract.

Abstract Table: Figure 1: Patient-reported current symptoms and those experienced at diagnosis.

Disclosure of Interest: S. Sonecha Conflict with: Employee of Sobi, J. Matos Conflict with: Employee of Cerner Enviza (Previously Kantar Health), T. Mnif Conflict with: Employee of Cerner Enviza (Previously Kantar Health), H. Costantino Conflict with: Employee of Cerner Enviza (Previously Kantar Health), K. Lehrhaupt Conflict with: Employee of Cerner Enviza (Previously Kantar Health), P. Le Calve Conflict with: Employee of Cerner Enviza (Previously Kantar Health), S. sarda Conflict with: Employee of ApeIIis Pharmaceuticals, Inc., S. baver Conflict with: Employee of ApeIIis Pharmaceuticals, Inc., J. fishman Conflict with: Employee of ApeIIis Pharmaceuticals, Inc., Z. hakimi Conflict with: Employee of Swedish Orphan Biovitrum AB, E. persson Conflict with: Employee and shareholder of Swedish Orphan Biovitrum AB, R. Desgraz Conflict with: Employee of ApeIIis Pharmaceuticals, Inc., B. Lui Conflict with: Employee of ApeIIis Pharmaceuticals, Inc., J. Panse Conflict with: Blueprint Medicines, Amgen, Chugai, Pfizer, Novartis, Boehringer Ingelheim, Alexion, F. Hoffman-La Roche Ltd, MSD, Grunethal, Bristol Myers Squibb, Apellis Pharmaceuticals, J. Nazir Conflict with: Employee of Sobi.

BSH22-PO85 | Retrospective analysis of the burden of vaso-occlusive events experienced by sickle cell disease (SCD) patients in the integrated health and social care system in North West London

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Abstract Content: Vaso-occlusive crises (VOC) are a key clinical feature of sickle cell disease (SCD). These

Abstract Table:

Known comorbidies identified via primary and secondary coding systems	Overall population (*n* = 1007) *N* (%)	No VOCs (*n* = 715) *N* (%)	Low-frequency VOCs (*n* = 67) *N* (%)	High-frequency VOCs (*n* = 225) *N* (%)
Pain	456 (45)	160 (22)	35 (52)	180 (80)
Kidney	83 (8)	35 (5)	8 (12)	30 (13)
Bone	129 (13)	31 (4)	14 (21)	71 (32)
Lung	243 (24)	80 (11)	21 (31)	103 (46)
CNS	62 (6)	25 (3)	8 (12)	26 (12)
Leg Ulcer	44 (4)	14 (2)	4 (6)	12 (5)
infections	149 (15)	45 (6)	13 (19)	82 (36)
Spleen	46 (5)	<5 (<5)	5 (7)	37 (16)
Eye	60 (6)	23 (3)	10 (15)	25 (11)
Cardiac	227 (23)	90 (13)	24 (36)	100 (44)
Priapism	11 (1)	<5 (<5)	<5 (<5)	7 (3)
Gall bladder and liver	110 (11)	32 (4)	6 (9)	58 (26)
Allergy to medicines	161 (16)	48 (7)	11 (16)	97 (43)
Consequences of opioid use	19 (2)	0 (0)	<5 (<5)	16 (7)
Consequences of transfusion	65 (6)	12 (2)	<5 (<5)	48 (21)

unpredictable, painful events are a frequent cause of hospitalisation. Using patient data from the longitudinally linked Discover dataset, covering a registered population of 3.4 million in North West London, this study aimed to quantify the frequency of VOCs. and resource utilisation consumed across all type of healthcare services.

The data extraction from the Discover dataset covered the period of 1st April 2015 until 31st March 2020 and the demographic over 16 years old. A description of VOC from published literature was used to identify a list of relevant diagnostic codes in the Discover dataset. The overall SCD population was divided into three groups: no VOC (patients who had no VOC recorded during the 5-year data collection period), low frequency (patients who had no more than 1 VOC recorded in any single year) and high frequency of VOC (patients who had 2 or more VOC recorded in any single year). The three groups were characterised by demographics and level of concomitant comorbidities. Resource utilisation by each group was quantified by extracting the total number of interactions recorded by healthcare service, primary care, inpatient, outpatient, A&E, community and mental healthcare services. The costs to commissioners were extracted from the costs defined locally in the Discover dataset.

In the total population of 1 945 730, over the age of 16 contained in the Discover dataset, 1007 patients were identified with a recorded diagnosis of SCD. The number of SCD patients with no records of a VOC, low-frequency VOC and high-frequency VOC were 715 (71%), 67 (7%) and 225 (22%) respectively. The high proportion of patients with no records of a VOC may be due to under-recording. The average number of healthcare interactions per patient per year was higher in the high-frequency VOC group (27) compared with the low-frequency VOC group (14) and the no VOC group (8). The most frequently used healthcare service was the outpatient setting, regardless of VOC frequency. This was followed by the inpatient setting in the high-frequency group, community setting in the low-frequency group and GP setting in the no VOC group. The number of inpatient stays for the 715 patients in the no VOC group was 1491, for the 67 patients in the low frequency group was 556 and for the 225 patients in the high frequency group was 6283.

The most frequent long-term conditions affecting individuals with SCD were anxiety (15%), hypertension (12%) and depression (12%), followed by diabetes (7%) and asthma (7%). The frequency of comorbidities increased with increasing VOC frequency.

The average cost per year per patient for the local commissioner was £4170, £12 780 and £38 024 for the no VOC, low-and high-frequency VOC groups respectively. However, these costs are an underestimation of the overall NHS costs as they do not include specialised services such as blood transfusions.

This study showed the disease burden of patients who do not experience high rates of VOCs is still considerable. The data in the Discover dataset confirm that patients with a higher rate of VOCs have a greater disease burden associated with increased healthcare cost.

Disclosure of Interest: S. J. Collington Conflict with: Novartis Pharmaceuticals UK Limited, A. Nawaz Conflict with: Novartis Pharmaceuticals UK Limited, S. Walder Conflict with: Novartis Pharmaceuticals UK Limited, S. Prashar: None Declared, S. Houston: None Declared, C. Cohen: None Declared, D. M. Layton Conflict with: Agios, Cerus, and Novartis.

BSH22-PO86 | The Pharmacokinetics, Pharmacodynamics And Safety Of Intravenous Pegcetacoplan Administration In Healthy Subjects

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Abstract Content: Subcutaneous (SC) Pegcetacoplan (PEG) is an FDA-approved C3-targeted therapy for PNH and a broad inhibitor of the complement cascade. Intravenous (IV) PEG administration may allow for more rapid and robust reduction of uncontrolled complement activation. Pharmacokinetics (PK) and pharmacodynamics (PD) of IV PEG in acetate-buffered saline treatment in a Phase 1 single ascending dose study (ACTRN12616000700437) in healthy subjects were assessed for safety.

On Day 1, 4 cohorts with PEG doses (200 mg, 600 mg, 1500 mg, 2300 mg) received a bolus of PEG IV (or matching placebo) administered over 30 min. Blood samples for PK analyses of PEG concentration and PD analyses of alternative complement pathway haemolytic activity (AH50), total complement haemolytic activity (CH50), C3 and C3a levels were collected at 15, 30 and 60 min, 4, 8, 12 and 24 hrs and Days 3, 4, 5, 6, 7, 8, 15, 22, 29 and 43. Safety monitoring was from Day 2–8 by physical examination, ECG, haematology, serum chemistry, monitoring for injection site reaction (ISR) and treatment-emergent adverse events (TEAEs). Follow-up safety assessments were on Days 15, 22, 29 and 43.

Twenty subjects were allocated 4:1 to PEG or placebo per cohort (PEG-200 mg, $n = 4$; PEG-600 mg, $n = 4$; PEG-1500 mg, $n = 4$; PEG-2300 mg, $n = 4$; pooled placebo, $n = 4$). After a single IV dose, peak concentration (C_{max}) of PEG was observed at 1 hr postdose (infusion start) for most cohorts (mean serum concentration: PEG-200 mg, 61 µg/ml; PEG-600 mg, 193 µg/ml; PEG-2300 mg, 708 µg/ml) except PEG-1500 mg (occurred at 4 hrs, 542 µg/ml). PEG concentration at the end of infusion was similar to the observed C_{max}. Drug exposure increased in a dose-proportional manner. PEG concentration declined mono-exponentially, with a terminal elimination half-life from 201 to 285 hrs. Total body clearance of PEG after IV administration was 0.013 L/h. Volume of distribution was between 3.7 and 4.9 L. Variability across all PK parameters was generally low (CV% ≤ 30). AH50 response to PEG was dose-related and immediate decreases in mean AH50 values were detected at 1 hr in all PEG cohorts, with 1500 and 2300 mg doses decreasing AH50 to undetectable levels (Table). Decreases in mean AH50 values were maintained for at least 12, 72, 144 and 168 hrs after single doses of 200, 600, 1500 and 2300 mg PEG respectively. All PEG groups had an initial rapid decrease at 1 hr in mean C3a levels, with all doses having trough mean C3a levels within 24 hrs of dosing. Dose-related decreases in mean C3a were not observed, all doses recorded a max mean decrease in 48%–58%. No changes were seen with placebo for C3a. C3 and CH50 results will be forthcoming. Of the 20 subjects, 11 (55.0%) experienced TEAEs, with the most common being headache ($n = 6$, 37.5%), upper respiratory infections attributed to seasonal viral infection ($n = 2$, 12.5%) and diarrhoea ($n = 2$, 12.5%). No serious adverse events, deaths or severe TEAEs occurred. One subject (5.0%) in the PEG-2300 mg cohort experienced a moderate TEAE (infusion-related reaction, dizziness, clamminess, nausea) that led to study discontinuation.

Administration of IV PEG in a sodium acetate solution has a favourable safety profile, increases PEG serum concentrations and decreases complement activity within 1 hr postdose. Although the safety and efficacy of SC PEG treatment have been demonstrated in patients with PNH, IV PEG administration could serve as a useful therapeutic option for patients with a need for rapid control of complement activity.

Disclosure of Interest: M. Yeh Conflict with: Apellis Pharmaceuticals, Inc. (current employment and equity holder), F. Grossi Conflict with: Apellis Pharmaceuticals, Inc. (current employment and equity holder), H. Ping Conflict with: Apellis Pharmaceuticals, Inc. (current employment), P. Deschatelets Conflict with: Apellis Pharmaceuticals, Inc. (current employment and equity holder).

Abstract Table: Pharmacokinetics and Pharmacodynamics of Intravenous Pegcetacoplan in Healthy Subjects

Day 4	**Mean (SD)**	42.4 (11)	126.8 (25.7)	337.3 (40.1)	382.3 (22.1)	100.3 (14.1)	80.5 (39.92)	72.5 (59.12)	42.8 (25.79)	0 (0.0)
Day 5	**Mean (SD)**	39.2 (11.1)	113.7 (21.6)	278.8 (29.4)	338 (44.2)	101 (10.33)	95 (30.61)	77.5 (44.16)	70.8 (10.75)	5.5 (11)
Day 6	**Mean (SD)**	33.4 (7.4)	108.2 (23.9)	258.5 (33.9)	319 (40.7)	97.5 (5.8)	81 (36.04)	84.5 (40.96)	84.8 (12.34)	21 (30.18)
Day 7	**Mean (SD)**	34 (8.3)	96.2 (12.9)	233.5 (30.4)	300.7 (29.5)	94.8 (7.68)	80 (38.97)	84 (46.5)	95.3 (7.27)	32.5 (45.73)
Day 8	**Mean (SD)**	30.1 (9.3)	95.2 (18.7)	222.5 (26.4)	286.7 (47.6)	98.8 (2.22)	99.5 (30.88)	101.8 (28.24)	102.8 (9.95)	56 (36.47)
Day 15	**Mean (SD)**	18.3 (5.9)	51.7 (12)	128.3 (9.5)	183.3 (20.6)	99 (19.97)	126.8 (15.97)	92 (11.17)	109 (12.33)	115.5 (9.95)
Day 22	**Mean (SD)**	10.5 (3.5)	33.7 (1.2)	65.7 (12.2)	112.7 (23.1)					
Day 29	**Mean (SD)**	6 (2)	20.1 (2.2)	38.1 (9.2)	76.9 (19.7)	96.7 (26.39)	108.8 (12.69)	83.3 (19.99)	103.5 (9.26)	109.3 (2.06)
Day 43	**Mean (SD)**	1.9 (0.9)	7.8 (2.3)	13.5 (3.3)	30.2 (15.4)	107.3 (19.5)	98.8 (16.26)	81.3 (15.13)	104.8 (8.66)	118.3 (16.98)

Pharmacokinetics (pegcetacoplan serum concentration, µg/ml) and pharmacodynamics (AH50, U/ml) of pegcetacoplan following intravenous administration in healthy subjects.
Twenty healthy subjects were randomised into four cohorts four with ascending PEG doses (200, 600, 1500, 2300 mg) and matching placebo.

BSH22-PO87 | Association of CR1 and C3 polymorphisms with C3-mediated extravascular haemolysis in Paroxysmal Nocturnal Haemoglobinuria

April Joy Baral[1]*, Claire Mckinley[2], Rosie Fellows[1], Thomas Hallam[1], Thomas Cox[1], Daniel Payne[3], Stephen Richards[2], Alexandra Pike[2,4], Richard Kelly[4], Morag Griffin[4], Peter Hillmen[2], Kevin Marchbank[1], David Kavanagh[1], Darren Newton[2], Claire Harris[5]

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Abstract Content: Paroxysmal nocturnal haemoglobinuria (PNH) is a rare clonal haematological stem cell disorder characterised by impaired regulation of the alternative (AP) and terminal complement pathways. Loss of CD59 expression leads to the destruction of PNH erythrocytes (E) via intravascular haemolysis that is prevented by treatment with anti-C5 antibody, eculizumab. However, approximately 30% of patients still require blood transfusion. This is associated with C3 fragment accumulation on PNH-E due to the loss of CD55 expression leading to erythrophagocytosis and extravascular haemolysis (EVH). C3b fragment accumulation on PNH-E is regulated by binding of complement regulators such as complement receptor type 1 (CR1) to C3b with the enzyme factor I (FI) forming an AP trimolecular complex (TMC) which inactivates C3b.

We hypothesise that single nucleotide polymorphisms (SNP) in complement receptor 1 (CR1) and C3 influence susceptibility to EVH by influencing C3b and iC3b inactivation on PNH-E surface.

Forty-two PNH patients treated with eculizumab were genotyped for their SNP in C3 (rs2230199, S/F) and CR1 (rs11118133, H/L). C3 loading on PNH-E of patients was measured by flow cytometry as part of the routine analysis at the Leeds Haematological Malignancy Diagnostic Service (HMDS). Of the 42 patients, 23 required atleast one event of transfusion within the last 12 months of data acquisition. Lactate dehydrogenase (LDH) and haemoglobin levels and reticulocyte count were also recorded. Recombinant soluble CR1 (sCR1) constructs were generated and C3 variants were purified from human plasma using classic chromatography techniques to study CR1:C3b variant interaction, including AP regulatory TMC (C3b:CR1:FI) formation using surface plasmon resonance (SPR). Healthy donors were genotyped for their CR1 density polymorphism to study its effect in C3b inactivation on E. C3b-coated streptavidin beads were incubated with solubilised E from CR1 H/H or H/L donors and iC3b/C3dg conversion was measured using flow cytometry.

Patients with high CR1 expression showed a trend for a lower mean percentage of C3 loading on PNH-E compared to patients with intermediate CR1 expression. Patients homozygous for C3-S showed a trend for a higher mean percentage of C3 loading on PNH-E and significantly lower haemoglobin levels compared to patients who were heterozygous (C3 S/F.) Of the 14 patients with the combined polymorphism, CR1 H/L C3 S/S, 11 received at least one transfusion. No transfusions were recorded from 3 patients with combined polymorphisms, CR1 H/L C3 S/F and CR1 H/L C3 F/F. Using SPR, we observed stronger binding and more TMC formation for C3b-F with CR1 and FI than with C3b-S. CR1 decayed C3-F convertase (C3b-F:Bb) more effectively than the convertase formed by C3b-S. Solubilised E from a CR1 H/H donor converted iC3b more effectively to C3dg compared to E from CR1 H/L donors.

Our data indicate that both CR1 density and C3 S/F polymorphism may influence C3b loading on PNH-E, with higher C3 fragments influencing EVH risk. Slower decay of C3-S convertase (C3b-S:Bb), weaker binding of C3b-S to CR1, and decreased regulatory TMC formation with FI suggest a potential mechanism for the association of the C3-S variant with EVH risk. Our data also indicate that E from individuals with lower CR1 expression convert the phagocytic opsonin iC3b to C3dg more slowly. The evidence suggests multiple mechanisms that increase C3 loading on PNH-E can enhance erythrophagocytosis.

Disclosure of Interest: A. J. Baral: None Declared, C. Mckinley: None Declared, R. Fellows: None Declared, T. Hallam Conflict with: Gyroscope Therapeutics, T. Cox: None Declared, D. Payne: None Declared, S. Richards: None Declared, A. Pike: None Declared, R. Kelly: None Declared, M. Griffin: None Declared, P. Hillmen: None Declared, K. Marchbank Conflict with: Catalyst Biosciences ltd, Gemini Therapeutics, Freeline, Idorsia Pharmaceuticals ltd, Purespring Therapeutics, D. Kavanagh Conflict with: Gyroscope Therapeutics, D. Newton: None Declared, C. Harris Conflict with: Gyroscope Therapeutics, Q32 Bio, Chinook Therapeutics, Biocryst Pharmaceuticals, Freeline, Conflict with: Ra Pharmaceuticals.

BSH22-PO89 | Real-World Experience of Patients With Sickle Cell Disease Treated With Voxelotor: A Multicenter, Retrospective Study

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Abstract Content: Sickle cell disease (SCD) is an inherited systemic disorder in which sickle haemoglobin (HbS) polymerisation triggers red blood cell sickling, chronic haemolytic anaemia and recurrent episodes of vaso-occlusion. SCD-related complications lead to acute and chronic life-threatening events, cumulative organ damage, and early mortality. Oxbryta® (voxelotor) tablets are approved in the United States for treatment of SCD in adults and adolescents aged ≥12 years, based on the efficacy and safety data from the randomised, placebo-controlled, multicentre HOPE trial. Voxelotor is an oral, once-daily HbS polymerisation inhibitor that has been shown to increase haemoglobin (Hb) levels and reduce markers of haemolysis.

The Retrospective Study to Evaluate Outcomes in Patients with Sickle Cell Disease Treated with Oxbryta (RETRO) is a multicentre, postmarketing, retrospective study that collects and characterises real-world laboratory and clinical data on adults and adolescents (aged ≥12 years) with SCD treated with voxelotor. RETRO included approximately 200 patients with SCD from 10 US study sites. A steering committee provided independent SCD expertise to inform the design and conduct of the voxelotor registry. Clinical and laboratory data were collected from 1 year before and up to 1 year after the initiation of voxelotor. Patients with documented SCD who received voxelotor treatment for ≥2 consecutive weeks were included in this analysis.

A total of 140 patients whose data were entered at 10 sites at the time of data cutoff (October 7, 2021) were included (mean age (SD): 32.7 (13.36) years; 55.7% female and 87.1% HbSS genotype). The mean (SD) duration of voxelotor treatment was 53.2 (23.1) weeks. The initial prescribed voxelotor dose strength (*n*, %) was mostly 1500 mg (122, 87.1%). Reason for prescription (*n*, %) included reduction of anaemia (90. 64.3%), reduction in pain (44, 31.4%), reduction in frequency of vaso-occlusive crises (34, 24.3%), reduction in the need for blood transfusion (12, 8.6%) and other (27, 19.3%); more than 1 reason may have been selected. In 99 patients with recorded baseline and post-treatment Hb values, the peak observed post-treatment Hb (mean [SD]) was 9.4 (2.17) g/dl, an increase in 1.5 (1.6) g/dl from baseline (7.9 [1.75] g/dl). Sixty percent (59/99) of patients had a clinical response (Hb increase in ≥1.0 g/dl from baseline) within 12 months of voxelotor treatment. Change in haemolytic markers was also evaluated. In patients with recorded baseline and post-treatment reticulocyte percentage (N = 83) and indirect bilirubin (N = 84), the mean (SD) minimum observed post-treatment value was 7.6% (5.1%) for reticulocyte percentage, a decrease in 3.4% (5.7%) compared with baseline (11.1% [6.4%]), and 2.5 (2.0) mg/dl for indirect bilirubin, a decrease in 1.3 (2.4) mg/dl compared with baseline (3.8 [2.7] mg/dl). The most common non-SCD-related treatment-emergent adverse events (AEs) were diarrhoea, headache and rash (Table); 43 (30.7%) patients reported ≥1 AE, and most non-SCD-related AEs were mild in severity.

RETRO is the first multicentre, retrospective study to examine the real-world effectiveness of voxelotor and describe the observed changes in laboratory and clinical outcomes after ≥2 weeks of therapy. This study shows that voxelotor treatment was associated with increased Hb levels and decreased haemolytic markers. The safety data are consistent with those from the HOPE trial.

This study was supported by Global Blood Therapeutics.

Abstract Table: Treatment-Emergent Adverse Events Not Related to Sickle Cell Disease

	Voxelotor, *n* (%) (*N* = 140)
Patients with any adverse event	43 (30.7)
Adverse events with (≥5%) incidence	
Diarrhoea	19 (13.6)
Headache	11 (7.9)
Rash	8 (5.7)
Uncoded	17 (12.1)

Disclosure of Interest: B. Andemariam Conflict with: CRISPR/Vertex, Pfizer, Cyclerion, Sanofi Genzyme, GBT, CHNCT, Novartis, Conflict with: Novartis, Conflict with: CRISPR/Vertex, Pfizer, Cyclerion, Sanofi Genzyme, I. Osunkwo Conflict with: Terumo, Acceleron, Pfizer, Chiesi, Cyclerion, Emmaus, GBT, Novartis, Forma Therapeutics, Conflict with: GBT, Novartis, Forma Therapeutics, Micella Biopharma, M. Idowu Conflict with: Pfizer, Ironwood, Forma Therapeutics, Conflict with: GBT, Novartis, N. Shah Conflict with: bluebird bio, CSL Behring, GBT, Conflict with: GBT, Novartis, Conflict with: GBT, Novartis, Alexion, R. Drachtman: None Declared, A. Sharma: None Declared, A. Glaros Conflict with: GBT, M. Achebe

Conflict with: Fulcrum Therapeutics, Pharmacosmos, A. Nero Conflict with: GBT, Editas Medicine, Bluebird Bio, Novartis, S. Curtis Conflict with: GBT, C. Minniti Conflict with: GBT, Novartis, NovoNordisk, Roche, Forma, Agios, Chiesi.

BSH22-PO90 | Pegcetacoplan Treatment In Patients With Paroxysmal Nocturnal Haemoglobinuria And Baseline Haemoglobin Levels At Or Above 10 g/dl

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Abstract Content: Paroxysmal nocturnal haemoglobinuria (PNH) is a rare and life-threatening disease characterised by chronic complement-mediated haemolysis, thrombosis and some degree of bone marrow dysfunction. Pegcetacoplan, a C3 complement-inhibitor approved by the FDA for adults with PNH, demonstrated improved haemoglobin (Hb) levels for patients with PNH with screening levels <10.5 g/dl and prior suboptimal response to C5-inhibitor eculizumab (Hillmen P, et al., *N Engl J Med*, 2021 384 (11):1028–1037) or complement-inhibitor naïve patients with PNH (Wong RS, et al., *Blood,* 2020 136 [Supplement 1]). While these studies have demonstrated positive results for patients with lower baseline Hb levels, the efficacy and safety of pegcetacoplan in patients with baseline Hb ≥10.0 g/dl has not been evaluated. This post hoc analysis evaluated the efficacy and safety of pegcetacoplan in a subgroup of patients with PNH with baseline Hb levels ≥10.0 g/dl at 16 and 48 weeks from the PADDOCK (NCT02588833) Phase 1b and PEGASUS (NCT03500549) Phase 3 studies.

PADDOCK evaluated pegcetacoplan treatment (270–360 mg/day subcutaneously) in complement-inhibitor naïve patients. PEGASUS enrolled patients that remained anaemic despite stable eculizumab treatment (≥3 months) with Hb levels <10.5 g/dl at the screening visit. PEGASUS patients were randomised 1:1 to eculizumab or pegcetacoplan (1080 mg subcutaneously 2× weekly) during the randomised controlled period (RCP) through Week 16. Patients who received pegcetacoplan during the RCP continued with pegcetacoplan monotherapy through Week 48 of the open-label period.

The post hoc analysis included adult patients with PNH with baseline Hb levels ≥10.0 g/dl and no transfusions within 14 days of the baseline measurement. For PEGASUS, only patients treated with pegcetacoplan in the RCP were included. Mean Hb levels, absolute reticulocyte count (ARC), lactate dehydrogenase (LDH) levels, Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scores, and percentage of patients with Hb response (≥1 g/dl Hb increase without transfusion) were evaluated at Week 16 and Week 48.

Overall, 12 patients were included in the post hoc analysis: six PADDOCK and six PEGASUS patients (baseline Hb range: PADDOCK, 10.0–11.0 g/dl; PEGASUS, 10.0–10.8 g/dl). In this subgroup of patients treated with pegcetacoplan, improvements from baseline to Week 16 were seen in mean Hb levels, ARC, LDH levels and FACIT-Fatigue scores (Table). Similar results were also seen at Week 48 in both trials (Table), demonstrating the sustained effect of pegcetacoplan. Most patients in this subgroup also achieved a Hb response at Week 16 and 48 (Table). Clinically significant increases (≥3 points) in mean FACIT-Fatigue scores were observed at both Week 16 and 48 (Table). No thrombotic incidents occurred and no additional safety signals were observed in this subgroup of patients.

While this patient population had near normal Hb at baseline, they also had elevated ARC prior to pegcetacoplan therapy, suggesting ongoing haemolysis which was improved after pegcetacoplan treatment initiation. Overall, these results suggest pegcetacoplan can be efficacious long-term in patients with PNH with less severe anaemia regardless of prior complement-inhibitor treatment, which results in further clinical improvements in markers of haemolysis and quality of life. The safety profile of pegcetacoplan was similar to results from previous studies.

Disclosure of Interest: J. Panse Conflict with: Blueprint Medicines, MSD, Grunenthal, Bristol Myers Squibb, Apellis Pharmaceuticals and F. Hoffmann-La Roche Ltd (consultancy, honoraria and membership on an entity's Board of Directors or advisory committees); Amgen (consultancy and membership on an entity's Board of Directors or advisory committees); Chugai and Pfizer (speakers bureau) and Novartis, Alexion and Boehringer Ingelheim (membership on an entity's Board of Directors or advisory committees and speakers bureau), N. Daguindau: None Declared, S. Okuyama: None Declared, R. Peffault de Latour Conflict with: Novartis, Pfizer and Alexion Pharmaceuticals Inc. (consultancy, honoraria and research funding); Apellis Pharmaceuticals Inc. and Swedish Oprhan Biovitrum AB (consultancy and honoraria); Amgen (research funding),

Abstract Table:

	PADDOCK			PEGASUS		
	Baseline *N* = 6	**Week 16*** *N* = 5	**Week 48*** *N* = 5	**Baseline** *N* = 6	**Week 16** *N* = 6	**Week 48** *N* = 6
Mean Haemoglobin Levels, g/dl (Normal Reference Range, 12.0–18.0 g/dl)	10.5	12.7	12.0	10.3	12.4	12.6
Haemoglobin Response, *n* (%)	--	5 (100%)	3 (60.0%)	--	5 (83.3%)	4 (66.7%)
Mean Absolute Reticulocyte Count, ×10^9 cells/l (Normal Reference Range, 30–120 × 10^9 cells/l)	198.8	115.6	121.4	252.5	70.0	99.8
Mean Lactate Dehydrogenase Levels, U/l (Normal Reference Range, 113–226 U/l)	1935.8	242.8	241.6	211.6	149.0	220.5
Mean FACIT-Fatigue Scores (General Population Norm, 43.6; Cella D, et al., *Cancer*, 2002;94 (2):528–538)	36.7	45.2	44.0	24.3	38.8	34.0

*One PADDOCK patient stopped dosing at Day 29 and left the study due to physician decision; therefore Week 16 and Week 48 data are out of a total *N* = 5.

P. Schafhausen Conflict with: Blueprint Medicines and Swedish Orphan Biovitrum AB (membership on an entity's Board of Directors or advisory committees); Alexion and Bristol Myers Squibb (honoraria, membership on an entity's Board of Directors or advisory committees, and speakers bureau); MSD and Novartis (honoraria and membership on an entity's Board of Directors or advisory committees), N. Straetmans Conflict with: Alexion (membership on an entity's Board of Directors or advisory committees), M. Al-Adhami Conflict with: Apellis Pharmaceuticals, Inc. (current employment), T. Ajayi Conflict with: Apellis Pharmaceuticals, Inc. (current employment), M. Yeh Conflict with: Apellis Pharmaceuticals, Inc. (current employment and equity holder).

BSH22-PO91 | Predictors for improvement in patient-reported outcomes: post hoc analysis of a phase 3 randomised, open-label study of eculizumab and ravulizumab in complement inhibitor-naïve patients with paroxysmal nocturnal haemoglobinuria (PNH)

Hubert Schrezenmeier[1,2], Austin Kulasekararaj[3,*], Lindsay Mitchell[4], Regis Peffault de Latour[5], Timothy Devos[6], Shinichiro Okamoto[7], Richard Wells[8], Evan Popoff[9], Antoinette Cheung[9], Karissa Johnston[9], Jimmy Wang[10], Philippe Gustovic[11], Alice Wang[10], Ioannis Tomazos[10], Yogesh Patel[10], Jong Wook Lee[12]

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Abstract Content: Patients with PNH have uncontrolled terminal complement activation that can lead to thrombosis, organ damage, intravascular haemolysis (IVH) and clinical

sequelae. PNH is also associated with debilitating patient-reported outcomes (PROs), such as fatigue, dyspnoea and pain that contribute to a poor quality of life (QoL). Although improvements in clinical outcomes are associated with C5 inhibitor (C5i) therapy in patients with PNH, the relationship between clinical outcomes and fatigue or QoL is less well supported. Understanding clinical drivers of improvements in QoL and fatigue during complement C5i therapy is vital for developing appropriate management strategies for PNH.

This study assessed the relationship between clinical outcomes and fatigue and QoL, as measured by Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-Fatigue) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire—Core 30 Global Health (EORTC QLQ-C30 GH), in patients with PNH receiving C5i therapy.

Post hoc analyses were performed using data from a 26-week data cut of a randomised phase 3 study (NCT02946463) that assessed ravulizumab and eculizumab in complement inhibitor-naïve patients with PNH and high disease activity (defined as a lactate dehydrogenase [LDH] level ≥1.5 × upper limit of normal [ULN; 246 U/l] and ≥1 sign or symptom of PNH at screening). The PRO measures (PROMs) used were FACIT-Fatigue and EORTC QLQ-C30 GH. Clinical variables included LDH, haemoglobin (Hb), bone marrow disorders, transfusions and haematological parameters (reticulocyte, platelet and neutrophil counts). Multivariable regressions were performed separately for each PROM to assess the effect of clinical variables on PROM score changes from baseline to day 183, controlling for demographical characteristics and baseline PROM scores. Multicollinearity between covariates was tested in each regression model and removed when present.

Data for 121 and 125 patients with PNH treated with eculizumab or ravulizumab were included respectively. A reduction in LDH levels at day 183 was associated with improvements in FACIT-Fatigue in both treatment groups; however, no equivalent association was observed with Hb levels. In the regression analyses, significant predictors of FACIT-Fatigue improvement included reductions in LDH levels from baseline to day 183 ($p = 0.0024$) and the interaction of both achieving a LDH level ≤1.5 × ULN by day 183, and improvements in Hb from baseline ($p = 0.0285$). Significant predictors of EORTC QLQ-C30 GH improvement also included reductions in LDH levels from baseline to day 183 ($p < 0.0001$) and an increase in Hb from baseline to day 183 after receiving a transfusion during the study period ($p = 0.02$). However, Hb as a main effect, whether as an improvement in Hb levels from baseline to day 183, or Hb values at baseline, were not statistically significant predictors of improvement in either PROM at day 183.

When multiple clinical variables were considered, reductions in LDH were one of the strongest predictors of improvements in fatigue and QoL. Increases in Hb levels from baseline were only a significant predictor of improvement in FACIT-Fatigue for patients who had attained LDH level ≤1.5 × ULN at day 183, highlighting the importance of controlling IVH in patients with PNH. Finally, these results suggest that Hb alone is not a strong predictor of improvements of fatigue and QoL in PNH.

Disclosure of Interest: H. Schrezenmeier Conflict with: HS has received travel support, honoraria and research support (all to University of Ulm) from Alexion Pharmaceuticals, Inc. and Roche, A. Kulasekararaj Conflict with: AK has received honoraria, travel support and consulting fees from Alexion, AstraZeneca Rare Disease., L. Mitchell Conflict with: LM has received honoraria from Alexion, AstraZeneca Rare Disease., R. Peffault de Latour Conflict with: RPdL has received research grant from Alexion, AstraZeneca Rare Disease, Amgen, Pfizer, and Novartis, honoraria, travel support, consulting fees, and has served as a member of an advisory board for Alexion, AstraZeneca Rare Disease, Novartis and Pfizer, T. Devos Conflict with: TD has served as a member of an advisory board for Alexion, AstraZeneca Rare Disease, Celgene/Bristol Myers Squibb, Novartis and AbbVie., S. Okamoto Conflict with: SO has received honoraria and research funding from Alexion, AstraZeneca Rare Disease., R. Wells Conflict with: RW has received honoraria and research funding from Alexion, AstraZeneca Rare Disease, Celgene, and Novartis and consulting fees from Alexion, AstraZeneca Rare Disease., E. Popoff Conflict with: EP is a full-time employee of Broadstreet HEOR, A. Cheung Conflict with: AC is a full time employee of Broadstreet HEOR, K. Johnston Conflict with: KJ is a full time employee of Broadstreet HEOR, J. Wang Conflict with: JW is a full time employee of Alexion, AstraZeneca Rare Disease., P. Gustovic Conflict with: PG is a full time employee of Alexion, AstraZeneca Rare Disease., A. Wang Conflict with: AW is a full time employee of Alexion, AstraZeneca Rare Disease., I. Tomazos Conflict with: IT is a full time employee of Alexion, AstraZeneca Rare Disease., Y. Patel Conflict with: YP is a full time employee of Alexion, AstraZeneca Rare Disease., J. W. Lee Conflict with: JWL has received grants and honoraria from Alexion, AstraZeneca Rare Disease and has served as a member of an advisory board for Alexion, AstraZeneca Rare Disease.

BSH22-PO92 | Molecular characterisation of Congenital Erythrocytosis and Idiopathic Erythrocytosis analysed by Next-Generation Sequencing

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Abstract Content: Erythrocytosis is a pathology characterised by a significant increase in erythrocyte mass (>125%) as well as an increase in haemoglobin and haematocrit levels to reference values according to age and sex. Erythrocytosis can be congenital (CE) or acquired. According to pathophysiological mechanisms and based on the levels of erythropoietin (Epo), they can be classified as primary or secondary. Primary erythrocytosis is caused by an intrinsic defect in the erythroid precursors and, therefore, independent of Epo levels, the congenital form is molecularly characterised by pathogenic variants in the *EPOR* and *SH2B3* genes and the acquired form, Polycythaemia Vera, by somatic pathogenic variants in *JAK2* gene. Variants in these genes lead to constant activation of the erythropoietin receptor after being stimulated by Epo. Secondary CE results from up-regulation of EPO transcription, which can be caused by defects in the components of the oxygen-sensing pathway, molecularly characterised by pathogenic variants in the *VHL, EPO, EGLN1* and *EPAS1*, or with origin in haemoglobin with high oxygen affinity, due to pathogenic variants in the globin genes (*HBB, HBA1, HBA2*), or in the *BPGM* and *PKLR*. Secondary acquired erythrocytosis results from external factors that induce tissue hypoxia, by a physiological factor that causes a decrease in blood plasma volume, or by tumours that induce higher Epo production. (*EPOR, SH2B3, VHL*, *EPO*, *EGLN1*, *EPAS1, HBB*, *HBA1*, *HBA2, BPGM* e *PKLR)*. However, approximately 60% of patients still do not have an identified molecular aetiology, being designated as having idiopathic erythrocytosis (IE). Next-Generation Sequencing (NGS) studies are essential to identify new pathogenic variants in genes already described or in candidate genes that can clarify the origin of the pathology.

Design and Methodology: In this study, 77 samples of patients with IE, followed up at the Unidade de Eritropatologia e Metabolismo do Ferro, do Laboratório de Hematologia Molecular—Centro Hospitalar e Universitário de Coimbra, were analysed. Laboratory tests were guided by clinical and family history and Epo levels, using NGS and Sanger sequencing, with a NGS panel of genes dedicated to erythrocytosis to find pathogenic variations which justify the presented phenotype.

Results and Discussion: The study carried out allowed the identification of variants in 28 of the 77 individuals studied. In five patients, four pathogenic variants that were already described as associated with CE were detected in the *SH2B3, HBB* and *VHL* genes. In 15 patients, 13 new variants in *EPOR, JAK2, SH2B3, EGLN1, EPAS1, EPO, PKLR* and *VHL* genes were detected. In eight patients, we found six new variants in candidate genes, *EGLN2, EGLN3, HIF1α*, *HIF3α* and *PIEZO1*. The degree of pathogenicity of the variants found was evaluated using *in silico* tools. Of the 18 variants analysed: six were classified as Pathogenic, one as Likely Pathogenic and four as Variants of Uncertain Significance. The remaining seven variants were classified as Benign or Likely Benign. It will be necessary to confirm the pathogenicity of these variants with family and functional studies. When verifying that they are pathogenic variants, the study carried out allowed the identification of the molecular cause responsible for CE in 11 of the 18 samples studied by *in silico* tools.

Key Words: congenital erythrocytosis, erythropoietin, hypoxia, idiopathic erythrocytosis, Next-Generation Sequencing (NGS), Sanger

Disclosure of Interest: None Declared.

BSH22-PO93 | A retrospective comparative study of the effect of automated exchange transfusion *versus* other treatment modalities on vaso-occlusive crisis admission rates in patients with sickle cell disease

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Abstract Content: Backgrond: Regular transfusion is an important treatment option for the management of sickle cell disease (SCD) but there is a lack of consensus as to who should be treated and how to transfuse. A 2014 NICE guideline recommended patients have access to automated red cell exchange transfusion (ARCET), citing limited evidence of favourable outcomes compared to manual exchange transfusion (MET) but no evidence of comparisons

with simple transfusion or hydroxyurea (HU) therapy. Vaso-occlusive crises (VOC) are the commonest cause of acute hospital admission and many specialists recommend ARCET for the management of recurrent VOCs where hydroxyurea has failed, or has not been accepted or tolerated by a patient.

Methods: At The Royal London Hospital (RLH) an ARCET programme was started in 2016. To evaluate VOC outcomes on ARCET compared with other disease-modifying therapies (DMT), we selected patients who had been followed continuously in our service during the period 1/1/10 to 31/6/19, and treated with ARCET for at least 6 months. We determined duration of therapies and VOC rate. Definition of VOC was acute pain, acute chest, dactylitis, acute splenic or hepatic sequestration or priapism requiring admission to hospital. Duration of each therapy and VOC episodes for each patient were extracted from the RLH SCD clinical database. Annualised VOC rates were calculated while receiving each of the following: Simple transfusion (ST), manual red cell exchange transfusion (MRCET), ARCET, Hydroxyurea (HU) or no disease-modifying therapy. The difference in annualised VOC rates between ARCET and other modalities were compared by the Wilcoxen test.

Results: There were 69 patients meeting inclusion criteria. The mean (range) age at start of ARCET was 24.5 (10.5–56.8) years. Thirty-two (46%) were female and all were HbSS genotype. Indications for ARCET were: Neurological 18, recurrent VOC 35, avascular necrosis of hip 3, acute chest syndrome 2, anaemia 1, cardiac disease 1, chronic pain 4, pulmonary hypertension 1, priapism 2, renal transplant 2.

The patients had different treatment histories prior to ARCET. Thirty had been treated with MRCET for a mean (range) 3.6 (0.5–6.5) years, 48 with ST for 4.6 (0.6–8.6) years, 13 with HU for 4.2 (0.6–8.3) years and 26 had received no DMT for 4 (0.3–8.5) years. Some patients received more than one treatment modality prior to ARCET.

The average annualised VOC rate for each treatment and difference in annualised rate compared to ARCET are shown in the table.

The results show that VOC rate was significantly reduced in patients who switched from MRCET to ARCET. There was no significant change in VOC rate overall when switched from simple transfusion or HU to ARCET. These differences were unchanged when restricted to those treated with ARCET for pain.

Conclusions: Overall there are patients that see a reduction in VOC when they switch to ARCET from MRCET and no disease-modifying treatment. There are other benefits of ARCET compared with ST that may mean that it is a better treatment for those patients as well. We noticed that there was a subset of patients who had progressive admissions for pain over time while on disease-modifying treatment who will likely benefit from other interventions to manage the pain episodes.

Abstract Table:

Treatments	Annualised VOC rate Median, (range)	Difference In annualised VOC rate compared to ARCET Median (range)	*p value*
ARCET	0 (0–22)		
MRCET	1 (0–18)	0.99	<0.05
STT	0.38 (0–7.4)	0.13	NS
HU	1.7 (0–7.3)	−0.6	NS
No DMT	0.88	0.4	<0.05

Disclosure of Interest: F. Oyesanya: None Declared, V. Gorur: None Declared, E. Awe: None Declared, F. Barroso: None Declared, S. Bennett: None Declared, B. Kaya: None Declared, C.-A. De Michele: None Declared, K. Newell: None Declared, I. Amoh: None Declared, R. Oloruntobi: None Declared, D. Boodoo: None Declared, P. Telfer Conflict with: GBT and Bluebird Bio.

BSH22-PO94 | Breakthrough Haemolysis Rates Among Patients With Paroxysmal Nocturnal Haemoglobinuria Who Switched From Eculizumab to Ravulizumab Treatment: A Real-World Analysis

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Abstract Content: Paroxysmal Nocturnal Haemoglobinuria (PNH) is a rare and potentially life-threatening disease characterised by complement-mediated haemolysis and thrombosis. Breakthrough haemolysis (BTH), or the return of intravascular or extravascular haemolysis (IVH, EVH), is a hallmark of incomplete complement control in patients with PNH and manifests with the reappearance of PNH symptoms. Two previous phase 3 studies with the C5-inhibitors (C5i) ravulizumab (RAV) and eculizumab (ECU) demonstrated that RAV was noninferior to ECU for the reduction in BTH events among patients with PNH who switched from ECU to RAV. To corroborate these findings, we performed a retrospective analysis of BTH rates among patients with PNH who switched from ECU to RAV with data from a US-based electronic medical record (EMR) network. Several definitions for BTH were used given the lack in consensus in the literature for BTH criteria.

Data were extracted from patients with PNH aged ≥12 years seen between 2010 and 2021 within the TriNetX Dataworks USA Network, a federated EMR network of >68 million de-identified patients. Patients were required to have a visit recorded ≥6 months prior to their first C5i treatment, a PNH diagnosis based on the International Classification of Diseases 9th or 10th Revision Clinical Modification code, a

record of a treatment switch from ECU to RAV (defined as any RAV treatment following ECU treatment as recorded in the EMR data), and no record of atypical haemolytic uraemic syndrome, myasthenia gravis or neuromyelitis optica spectrum disorder. Three definitions of BTH using expert consensus from the literature were used for analysis: (1) ≥1 new symptom or sign of IVH (fatigue, haemoglobinuria, abdominal pain, dyspnoea, anaemia [haemoglobin <10 g/dl], major adverse vascular event [including thrombosis], dysphagia or erectile dysfunction) within 1, 3 or 7 days of LDH elevated ≥2 × upper limit of normal (ULN; ≥2 × ULN = 480 U/l), (2) elevated LDH (LDH ≥2 × ULN) alone regardless of other signs/symptoms and (3) elevated LDH (≥50% increase from baseline) and decreased haemoglobin (Hb; ≥2 g/dl from baseline) within 1 week of one another and measured within ≥4 months after index. BTH events were analysed after 4, 6 and 12 months of C5i treatment. Days between BTH and last C5i treatment were only evaluated during time on C5i treatment and represent the number of days between the patients' first instance of BTH and the previous C5i record closest to the BTH event.

Data were available for 24 and 18 patients who met inclusion criteria and had switched from ECU to RAV for a period of 6 or 12 months respectively (Table). When defining BTH as new signs or symptoms of haemolysis ±7 days relative to an elevated LDH value, one patient in each of the 6- and 12-month treatment periods after switch cohorts met the criteria for BTH. Analysis of BTH defined as elevated LDH alone demonstrated that 20.8% (n = 5) and 16.7% (n = 3) of patients who switched from ECU to RAV demonstrated BTH within 6 or 12 months after switch respectively. When defining BTH as a concurrent increase in LDH and decrease in Hb, 10.0% (n = 2) of patients experienced BTH within 4 months after treatment switch.

These real-world analyses suggest that BTH rates among patients with PNH who switched from ECU to RAV are higher than previously reported in clinical studies and highlight the benefits of real-world analyses using a comprehensive set of definitions for BTH, which may approximate true haemolysis rates more closely.

Disclosure of Interest: J. Fishman Conflict with: Apellis Pharmaceuticals, Inc. (current employment and current equity holder in publicly traded company), S. Kuranz Conflict with: Payments from Apellis Pharmaceuticals to my institution TriNetX, M. Yeh Conflict with: Apellis Pharmaceuticals, Inc. (current employment and equity holder), K. Brzozowski Conflict with: Payments from Apellis Pharmaceuticals to my institution TriNetX, H. Chen Conflict with: Payments from Apellis Pharmaceuticals to my institution TriNetX.

Abstract Table:

	Treatment period after switch[a]	
Patients switched from Eculizumab to Ravulizumab	**6 months** ***N*** **= 24**	**12 months** ***N*** **= 18**
BTH defined as symptoms ± 7 days[b] from elevated LDH[c]		
Patients with BTH, *n* (%)	1 (4.2)	1 (5.6)
Days between BTH and last C5i, mean ± SD	56.0 ± NA	42.0 ± NA
BTH defined only as elevated LDH[d]		
Patients with BTH, *n* (%)	5 (20.8)	3 (16.7)
Days between BTH and last C5i, mean ± SD	113.6 ± 88.4	137.3 ± 198.9
	Treatment period after switch	
BTH defined as elevated LDH and a large Hb decrease[e]	**4 months,** ***N*** **= 20**	
Patients with BTH, *n* (%)	2 (10.0)	
Days between BTH and last C5i, mean (±SD)	212.5 ± 217.1	

Abbreviations: BTH, breakthrough haemolysis; Hb, haemoglobin; LDH, lactate dehydrogenase; NA, not applicable.
[a]Total patient Ns are different between treatment periods due to differences in data availability at 6 and 12 months.
[b]Same results are obtained when using symptoms ±1, 3 or 7 days from elevated LDH.
[c]BTH is defined as at least one new symptom or sign of intravascular haemolysis (fatigue, haemoglobinuria, abdominal pain, dyspnoea, anaemia [haemoglobin <10 g/dl], major adverse vascular event [MAVE, including thrombosis], dysphagia, or erectile dysfunction) within 1, 3 or 7 days of elevated LDH ≥2 x upper limit of normal (480 U/l).
[d]BTH is defined as elevated LDH ≥2 x upper limit of normal (480 U/l) regardless of signs and symptoms.
[e]BTH is defined as a 50% increase in LDH from baseline and Hb decrease in ≥2 g/dl from baseline; both measured at least 4 months after index; LDH and Hb records must have occurred within 1 week of one another.

BSH22-PO95 | Management of autoimmune haemolytic anaemia during pregnancy or postpartum: A single centre experience

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Abstract Content: Autoimmune haemolytic anaemia (AIHA) during pregnancy is a rare finding, and little is known about maternal and foetal outcomes. AIHA may either develop or relapse during gestation and postpartum or be an issue in a patient on active therapy who becomes pregnant. Furthermore, AIHA management during pregnancy and lactation is not standardised and drug use is often limited by safety concerns.

We conducted a retrospective cohort study of 156 female AIHA patients followed at our Institution and individuated 15 pregnancies occurring in 12 women from 1997 to 2021. We included all patients who had a previous AIHA history or who developed/exacerbated their AIHA during gestation or postpartum. AIHA was classified according to the direct antiglobulin test (DAT) and we focussed on disease severity, treatment requirement and maternal and foetal outcome.

As shown in Table 1, we registered four warm AIHA (1 IgG+ and 3 IgG + C3d+), one cold agglutinin disease, three mixed and four atypical forms. Evans syndrome (i.e. the association of AIHA and immune thrombocytopenia or neutropenia) was present in three patients. The median age at AIHA diagnosis was 25 years (range 8–37).

AIHA diagnosis predated pregnancy in six women and had required at least one therapy line in all of them, and two or more in five (rituximab, $N = 2$, cytotoxic immunosuppressants $N = 4$, splenectomy $N = 4$). Among these six patients, one had a relapse during pregnancy, one during postpartum and one was on active treatment with prednisone and azathioprine at the time of pregnancy (the latter stopped after positive pregnancy test). Further 3 patients had an AIHA onset during gestation and three during postpartum.

In the eight patients experiencing AIHA during pregnancy, median haemoglobin and lactate dehydrogenase levels were 6.4 g/dl (range 5.4–7.7) and 520 UI/l (range 275–1631) respectively. Management generally consisted in blood transfusions ($N = 7$) and prompt establishment of steroid therapy ($N = 8$), all with response (complete $N = 5$, partial $N = 3$). Anti-thrombotic prophylaxis was given in one patient and ciclosporin was added in one patient after delivery.

Abstract Table:

Mean age at AIHA diagnosis (years)	26
N° of observed pregnancies	15
AIHA type	
Warm	1
Cold	1
Warm IgG + C	3
Mixed	3
Atypical	4
Maternal complications	
Pre-eclampsia	2
Placental detachment	1
Biliary colic	1
Foetal complications	
AIHA of the newborn	1
Death	1
Other	1
AIHA therapies	
Steroids	9
Blood transfusions	7
Immunoglobulins injection	1
Ciclosporin (postpartum)	1
Antithrombotic prophylaxis	3 (1 for AIHA, 1 after Caesarean delivery, 1 FIVET)

Abbreviations: AIHA, autoimmune haemolytic anaemia; C, complement; FIVET, fertilisation in vitro and embryo transfer.

Overall, we observed four obstetric complications, including a biliary colic, a placental detachment and two pre-eclampsia, the latter two in patients with active haemolysis. Although overall foetal outcome was good, we observed a transitory respiratory distress of the newborn 48 h after delivery in a mother with active AIHA, and two major foetal complications. The first was a foetal growth restriction requiring urgent caesarean section. The newborn had neonatal jaundice, detectable cold agglutinins and required intravenous immunoglobulins, blood transfusions and plasma exchange. His mother had had an AIHA relapse during pregnancy treated with steroids and antithrombotic prophylaxis. The second was a severe foetal distress with perinatal death in a woman with a severe warm IgG + C3d + AIHA with onset during pregnancy. The patient had been treated with transfusions and steroids but experienced a premature massive placental detachment.

Our experience shows that AIHA developing/reactivating during pregnancy or postpartum is rare (about 12/156, 7%) and may have a good outcome if promptly diagnosed/correctly monitored. However, most patients had a severe AIHA requiring steroid therapy and transfusions, and severe maternal and foetal complications were observed in a fraction of cases, mainly associated with active disease,

pinpointing the importance of maintaining a high level of awareness.

Disclosure of Interest: None Declared.

BSH22-PO96 | Clinically Important Difference for the FACIT-Fatigue Scale in Paroxysmal Nocturnal Haemoglobinuria: A Derivation From International PNH Registry Patient Data

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Abstract Content: Fatigue is a common symptom of paroxysmal nocturnal haemoglobinuria (PNH). Eculizumab, a C5 inhibitor approved for treatment of PNH, has been shown to reduce scores on the validated Functional Assessment of Chronic Illness Therapy-Fatigue scale (FACIT-Fatigue), which ranges from 0 to 52 (higher scores indicate less fatigue). In patients with cancer, the FACIT-Fatigue clinically important difference (CID) is estimated to be an increase in 3–5 points; this CID is often applied in PNH studies where no disease-specific CID for PNH currently exists. A PNH-specific CID would be useful in evaluating treatment efficacy. This analysis sought to determine the FACIT-Fatigue CID for patients with PNH using distribution- and anchor-based approaches and real-world data from the International PNH Registry.

Adults who initiated eculizumab within 28 days of enrolment in the PNH Registry as of January 2021 with non-missing baseline FACIT-Fatigue scores were included; scores were assessed at baseline and 6, 12, 24 and 36 months. Two distribution-based CID estimates were calculated using: (1) 0.5 × SD and (2) standard error of measurement (SEM). SEM was calculated as SD – sqrt (1–α), where α represents the internal consistency measurement Cronbach's alpha; α was calculated from the 13 FACIT-Fatigue subscales. Anchor-based estimates considered two continuous patient-reported outcome variables: European Organization for Research and Treatment of Cancer (EORTC) Global Health Status Quality of Life (QoL) summary score (quartiles; higher scores indicate better quality of life); and EORTC Global Health Status Fatigue Subscale score (quartiles; lower scores indicate less fatigue). Baseline FACIT-Fatigue score was calculated for each predefined categorisation of the anchors; the mean of differences in scores between adjacent categories was calculated and referenced as the anchor-based CID. Changes in anchors and high disease activity (HDA) shift from baseline to each follow-up visit were then assessed by FACIT-Fatigue score change (≤1 CID, no change, or ≥1 CID). HDA was defined as lactate dehydrogenase ratio ≥1.5 × upper limit of normal and ≥1 of the following: history of a major adverse vascular event (including a thrombotic event); anaemia or physician-reported abdominal pain, dyspnoea, dysphagia, fatigue, haemoglobinuria or erectile dysfunction.

Overall, 423 patients were included. Most (84%) patients were Caucasian; 3% were of Hispanic or Latino ethnicity. At baseline, 93% of patients had documented fatigue in their medical history (mean FACIT-Fatigue score, 29.4). The distribution-based CIDs were seven using 0.5 × SD and five using SEM; internal consistency was high (α = 0.87). For anchor-based measurements, the CID was eight using the EORTC QoL score and 10 using the EORTC fatigue subscale score. The percentage of patients who changed from having HDA at baseline to no HDA at eculizumab-treated follow-up visits increased over time. Using the SEM as the referent CID, the majority of these patients experienced >1 CID in FACIT-Fatigue that was sustained through 36 months. Results were similar when 0.5 × SD was used.

These results support the use of 5 points as the CID for FACIT-Fatigue in patients with PNH. This CID is much smaller than the mean FACIT-Fatigue improvement of 10 points achieved with long-term eculizumab treatment in the Phase 3 TRIUMPH study. The results of this analysis support use of the distribution-based CID in future efforts to determine the PNH-specific minimum CID.

Disclosure of Interest: D. Cella Conflict with: DC is the President of FACIT.org., P. Johansson: None Declared, Y. Ueda Conflict with: YU has served as a consultant and received honoraria from Alexion, Sanofi, Chugai, and Novartis, and research funding from Chugai, I. Tomazos Conflict with: IT is a full time employee of Alexion, AstraZeneca Rare Disease., P. Gustovic Conflict with: PG is a full time employee of Alexion, AstraZeneca Rare Disease., A. Wang Conflict with: AW is a full time employee of Alexion, AstraZeneca Rare Disease., A. S. Patel Conflict with: ASP is a full time employee of Alexion, AstraZeneca Rare Disease., H. Schrezenmeier Conflict with: HS has received travel support, honoraria, and research support (all to University of Ulm) from Alexion Pharmaceuticals, Inc. and Roche.

BSH22-PO97 | Difference in Exosomal Content of Transferrin Receptors 1 and 2 Post Erythropoietin Administration in Murine Models

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Abstract Content: The role of transferrin receptor (TFRC) in iron uptake to the cell has long been established. TFRC can be found in several forms: as a full-length membrane-bound protein or in a cleaved form which is soluble in the plasma. Its full-length form is also one of the most abundant proteins found in Exosomes—small secretory vesicles that are released from cells and circulate in the plasma. However, little is known regarding a similar, related protein—Transferrin receptor 2 (TFR2). TFR2's role in iron uptake has not been confirmed, nor has its removal mechanism from the maturing erythroblasts. TFR2's importance however has been well documented as its mutation causes a rare form of Hereditary Haemochromatosis (Type 3 Haemochromatosis). In our study, we evaluated the expression of TFRC and TFR2 mRNA in spleens and bone marrow of controls *versus* EPO-treated mice, as well as the protein content of TFRC and TFR2 in exosomes. Interestingly, TFRC and TFR2 mRNA expression seem to have similar dynamic profiles, increasing in the spleen by an order of magnitude at 24 and 48 h and decreasing after 96 h. This increase in expression is attributed to an overall larger number of erythroblasts in the spleen following EPO administration. However, the exosomal protein content of TFRC increased significantly after EPO, in striking contrast to TFR2 which was not detected in control or EPO-treated mice. This suggests that TFR2 removal via exosomes could be in undetectable levels, or that it has a different removal pathway altogether.
Disclosure of Interest: None Declared.

Thrombosis and Haemostasis

BSH22-PO98 | Mapping the Prothrombin Binding Site of Pseutarin C by Site-directed PEGylation

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Abstract Content: The prothrombinase complex processes prothrombin to thrombin through sequential cleavage at Arg320 followed by Arg271 when cofactor, factor (f) Va, protease, fXa, and substrate, prothrombin, are all bound to the same membrane surface. In the absence of the membrane or cofactor, cleavage occurs in the opposite order. For the less favourable cleavage site at Arg320 to be cleaved first, it is thought that prothrombin docks on fVa in a way that presents Arg320 and hides Arg271 from the active site of fXa. Based on the crystal structure of the prothrombinase complex from the venom of the Australian eastern brown snake, Pseutarin C, we modelled an initial prothrombin docking mode which involved an interaction with discrete portions of the A1 and A2 domains of fV and the loop connecting the two domains, known as the a1-loop. Here we interrogate the proposed interface by site-directed PEGylation and by swapping the a1-loop in Pseutarin C to that of human fV and fVIII, and measuring the effect on rate and pathway of thrombin generation. PEGylation of residues within our proposed binding site greatly reduced the rate of thrombin generation, without affecting the pathway, while those outside the proposed interface had no effect. PEGylation of residues within the a1-loop also reduced the rate of thrombin generation. Swapping the a1-loop for that of hfVIII reduced the rate by 6.6-fold, whereas swapping the a1-loop for that of hfV increased the rate by 3.6-fold, and channelled processing exclusively through the meizothrombin intermediate, with no evidence of prethrombin-2. The sequence of the a1-loop was found to play a critical role in prothrombin binding and in the presentation of Arg320 for initial cleavage.
Disclosure of Interest: None Declared.

BSH22-PO99 | Efficacy of thrombopoietin receptor agonists in Evans syndrome: An international multicentre experience

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Abstract Content: Evans syndrome (ES) is defined as the presence of two autoimmune cytopenias, typically autoimmune haemolytic anaemia and immune thrombocytopenia (ITP). It can be primary or secondary to various conditions. ES onset may be severe, while its clinical course is usually chronic and refractory/relapsing. First-line therapy is based on steroids ± intravenous immunoglobulins (IVIG), followed by rituximab, immunosuppressants or splenectomy (when feasible) in refractory/relapsing cases. Concerning ITP, thrombopoietin receptors agonists (TPO-RAs), are commonly used with high efficacy and our aim is to evaluate the efficacy and safety of TPO-RAs in ES patients.

Baseline haematological parameters, associated conditions, previous and concomitant treatments to TPO-RA were registered. The time from diagnosis to first TPO-RA was collected. Response rates were evaluated at 1, 3, 6 and 12 months, and classified as partial (PR) or complete (CR), for platelets >30 × 10^9/l or >100 × 10^9/l respectively. Treatment-emergent adverse events (TAEs) were registered and graded.

Twenty-two ES patients treated with TPO-RAs at eight European haematological centres have been evaluated, nine of whom secondary (40%). Almost all patients had received steroids ± IVIG, and the majority at least one further line. The median time to TPO-RA start was 25,74 months (1–1390). Response rates to the first TPO-RA (16 EPAG and 6 ROMI) were, respectively, 82%, 84%, 83% and 93% at each time-point. Eight patients started TPO-RA within 1 year from ES diagnosis displaying significantly lower platelets (p = 0.01) as compared to others, however response rates were comparable. Seventy-three of patients required concurrent therapies, including steroids ± IVIG (N = 13), danazol (N = 2), rituximab (N = 3) and immunosuppressants (N = 3). Seven patients required rescue therapies to control ITP (steroids ± IVIG N = 4, rituximab N = 1, danazol N = 1, daratumumab N = 1, immunosuppressants N = 2, parsaclisib N = 1), particularly in secondary ES (63% vs. 33%). The latters less frequently showed increased bone marrow megakaryocytes (67% vs. 92%) but had higher dysplasia (50% vs. 33%). Five subjects switched to the alternative TPO-RA (3 ROMI to EPAG and 2 vice versa), two because of no response (NR), and three for relapses. Three subjects responded but required additional therapies, including splenectomy, steroids ± IVIG, or platelet transfusions. Ten patients developed at least one TEAE: G1 thrombocytosis (N = 1), G2 bone marrow fibrosis (N = 1), G3/4 thrombosis (3 venous and 2 arterial: 1 pulmonary embolism, 1 cerebral vein thrombosis CVT and 1 splanchnic thrombosis, 1 atrial thrombus and 1 acute myocardial infarction in the same APS patient experiencing CVT). Thrombosis was associated with the presence of secondary ES (p = 0.03).

Abstract Table:

Number of patients	22
Median age, years (range)	65 (31–92)
Male/female	12/10
Associated conditions, *N* (%)	9 (40%)
Lymphoproliferative syndromes, *N* (%)	2 (22,3%)
Primary immunodeficiencies, *N* (%)	2 (22,3%)
Anti-phospholipid syndrome, *N* (%)	2 (22,3%)
Connective tissue disease, *N* (%)	1 (11%)
Haematopoietic stem cell transplant, *N* (%)	1 (11%)
Heart transplant, *N* (%)	1 (11%)
Time to TPO-RA, median (range)	25.74 months (1–1390)
Previous therapy lines, median (range)	6 (0–8)
Steroids ± Intravenous immunoglobulins (IVIG), *N* (%)	21 (95%)
IVIG, *N* (%)	18 (81%)
Rituximab, *N* (%)	13 (59%)
Splenectomy, *N* (%)	6 (27%)
Cytotoxic immunosuppressive therapy, *N* (%)	8 (36%)
Danazol, *N* (%)	3 (14%)
Hyperplastic megakaryocytes	92% (primary ES) 67% (secondary ES)
Megakaryocytes dysplasya	33% (primary ES) 50% (secondary ES)

Five patients are still receiving TPO-RA, while the others stopped because of persistent CR (N = 12), thrombosis (N = 3), increase in bone marrow reticulin fibrosis (N = 1), or death for infectious complication.

TPO-RAs were effective in more than 80% of ES patients, even heavily pretreated. However, TPO-RAs use was complicated by a high occurrence of thrombotic events that may be also favoured by the underlying conditions. Additionally, TPO-RAs required a concomitant therapy in the majority of patients, suggesting that in ES autoimmune platelet destruction cannot be completely overcome by bone marrow stimulation.

Disclosure of Interest: N. Cecchi: None Declared, J. A. Giannotta: None Declared, A. Patriarca Conflict with: Takeda, Incyte, Argenix, Pfizer, Amgen, Novartis, A. Glenthøj Conflict with: Agios, bluebird bio, Bristol Myers Squibb, Novartis, Conflict with: lexion, Saniona, Sanofi, Conflict with: Novo Nordisk, M. E. Mingot-Castellano: None Declared, F. Chen: None Declared, S. Cantoni: None Declared, D. Lund Hansen Conflict with: Alexion, Novartis, M. Capecchi: None Declared, H. Frederiksen Conflict with: Gilead; Alexion; Novartis; Janssen Pharmaceuticals; Abbvie, T. J. Gonzalez-Lopez Conflict with: Novartis; Amgen, Conflict with: Sobi; Amgen; Novartis; Grifols, W. Barcellini Conflict with: Agios, Conflict with: Novartis; Agios; Alexion Pharmaceuticals; Incyte; Bioverativ, B. Fattizzo Conflict with: Annexon, Conflict with: Novartis; Apellis; Momenta; Alexion; Amgen; Kira:

BSH22-PO100 | Discrepant results for ADAMTS13 assays with different activity assays. Artefact or cause for concern?

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Abstract Content: ADAMTS13 is a plasma metalloprotease which regulates the multimeric size of VWF by cleaving the protein at Tyr1605-Met1606. ADAMTS13 deficiency (acquired or congenital) occurs in thrombotic thrombocytopenic purpura (TTP). This disease primarily requires a clinical diagnosis, but ADAMTS13 assays can provide confirmation, help characterise the phenotype of the deficiency, may be useful in monitoring treatment, and can be used to identify family members with ADAMTS13 deficiency.

Different assay methodologies are available for measurement of ADAMTS13 activity. We describe here data from a series of proficiency testing exercises for ADAMTS13 assays in 2020 and 2021, in which an average 25 UK and International centres performed assays on lyophilised plasma samples. All samples were obtained through plasma exchange from patients with suspected or confirmed TTP. Samples 2103 and 2104 were prepared from plasma from a patient with acquired TTP, to which normal plasma had been added.

Results from eight samples are shown in Table 1. In samples with normal levels of ADAMTS13 activity, there was good agreement between results obtained by FRET, ELISA and chemiluminescence immunoassays (CLIA). For samples from donors with acquired TTP, and low levels of ADAMTS13 activity, results obtained by FRET-based assay methods were significantly higher than those obtained by ELISA and CLIA methods.

It remains unclear whether these findings are a consequence of plasma collection following plasma exchange, sample processing, related to the presence of ADAMTS13 antibodies in the samples, or reflect a genuine difference in results obtained with these different methods. Further studies are required to elucidate the clinical relevance of these findings.

Disclosure of Interest: None Declared.

Abstract Table:

Table 1 sample no.	Survey #	Median activity ELISA methods (u/ml) (n = 10)	Median activity CLIA methods (u/ml) (n = 9)	Median activity FRET methods (u/ml) (n = 3)	Inhibitor level
2001	8	60.3	—	56.5	4 u/ml (neg)
2002	8	1.4	—	4.0	45 u/ml (pos)
2003	9	1.1	0.6	12.0	50 u/ml (pos)
2004	9	1.2	0.6	11.9	49 u/ml (pos)
2101	10	66.0	66.0	66.1	3.0 u/ml (neg)
2102	10	65.0	62.6	72.7	3.3 u/ml (neg)
2103	11	2.7	1.2	15.6	41.5 u/ml (pos)
2104	11	1.0	0.75	11.6	44.7 u/ml (pos)

BSH22-PO101 | Postdischarge complications and mortality of hospitalised patients with COVID-19 in East London Hospitals

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Abstract Content: COVID-19 infection is associated with a hypercoagulable state; critically ill COVID-19 patients have a high incidence of in-hospital venous and arterial thromboembolic events (VTE and ATE). It remains unclear whether there is an increased rate of postdischarge thromboembolism or bleeding beyond the known increased risk following hospitalisation for any other acute illness, how to define any increased risk, and whether extended thromboprophylaxis is efficacious or safe. This is reflected in the variability of recommendations in existing and prior iterations of national and international guidance.

We aim to examine bleeding, VTE, ATE and all-cause mortality (ACM) in cohorts who received and did not receive extended thromboprophylaxis following an inpatient admission with COVID-19.

At the four hospitals comprising Barts Health NHS Trust, we offered 14 days of apixaban 2.5 mg twice a day or enoxaparin at a prophylactic weight-based dose to non-pregnant adults on discharge after an inpatient admission with PCR-positive COVID-19 infection who met the following criteria: they remained clinically unwell; bleeding and thrombotic criteria for inpatient thromboprophylaxis were met; there was an anticipated reduction in mobility on discharge and there was no alternative indication for or contra-indication to anticoagulants.

We retrospectively reviewed the electronic records of all eligible patients discharged between 1st August and 31st October 2020 to audit concordance to our guideline, and to determine the incidence of major bleeding (MB) as defined by ISTH criteria within 30 days and VTE, ATE and ACM within 90 days of discharge. We calculated the IMPROVE-DD score for each patient, which has been used to stratify patients with COVID-19 for inpatient and extended thromboprophylaxis.

286 discharges were assessed (58% male; median age of 55 years). 45/286 (15.7%) of discharges received extended VTE prophylaxis. 43/45 patients received apixaban and 2/45 patients received enoxaparin. In these patients, no MB or VTE complications were reported. There was one ATE and one death, of metastatic cancer. Of these patients, 15 (33%) had an IMPROVE-DD score ≥4. The one patient with ATE had an IMPROVE-DD score ≥4.

Among 241 discharges without extended thromboprophylaxis, 227 were concordant to the Trust guideline. Of the 227 patients, MB occurred in one patient (haemorrhagic stroke), VTE, ATE and death occurred in one, two and seven (3.1%) patients respectively. Eleven out of 227 (5%) of patients had an IMPROVE-DD score ≥4, of whom none had a VTE or ATE.

14 discharges met the criteria for, but were discharged without, extended thromboprophylaxis. In this group, there was zero MB, one VTE, two ATE and three deaths. There were two patients with an IMPROVE-DD score ≥4, of whom neither had a VTE or ATE.

Patients discharged with extended prophylaxis were more likely to have an IMPROVE-DD score ≥4 (33% vs. 5%).

To conclude, our data suggest that the risk of postdischarge thrombotic events and major bleeding after COVID-19 infection is low, irrespective of extended thromboprophylaxis.

We have shown that the guideline we adopted to define patients for extended thromboprophylaxis, that was in keeping with national guidelines at that time, was less restrictive than a score-based approach to patient selection using an IMPROVE-DD ≥4. However, patients with VTE in our cohort did not have an IMPROVE-DD ≥4. This data therefore does not support a score-based approach for patient selection for thromboprophylaxis.

Disclosure of Interest: None Declared.

BSH22-PO102 | Drug-induced thrombotic thrombocytopenic purpura (TTP): Review of European and North American pharmacovigilance report data

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Abstract Content: Thrombotic thrombocytopenic purpura (TTP) is a rare but life-threatening condition caused by deficiency of ADAMTS13. Medications have historically been reported to be the trigger for up to 15% of all cases of TTP. However much of the data on the association between drugs and TTP is inconclusive or incomplete. In particular, much of the data dates from before ADAMTS13 activity assays were used to define TTP and in many cases may represent drug-induced thrombotic microangiopathies, rather than confirmed TTP.

In this review of pharmacovigilance report data, our primary aim was to identify which drugs and drug classes have been commonly reported to pharmacovigilance agencies as potential causes of TTP.

We reviewed the number of cases reported to the UK Medicines and Healthcare Regulatory Agency (MHRA), European Medicines Agency (EMA), US Food and Drug Administration (FDA) and Health Canada (HC) to identify drugs and drug classes reported to be associated with TTP. Data from the MHRA and EMA were provided on request. Data from the FDA and Health Canada was obtained from online databases (FDA Adverse Reporting System Public Dashboard; HC Vigilance Adverse Reaction Online Database) using search terms "TTP" and "thrombotic thrombocytopenic purpura" in adverse reaction reports. TTP was defined by those reporting data and there was not a consistent definition for TTP or for its association with medications.

We included all reports of TTP that had been reported as a suspected adverse reaction to a drug in the analysis. Concomitant drugs that were not suspected to be causative were excluded. We assessed the consistency of reports between the different health agencies.

There were 13 700 adverse event reports, of which 4626 were reports of TTP as an adverse event related to a drug. Due to the differing time periods of the reports from each pharmacovigilance agency (MHRA 1964 to 2020; $n = 203$, FDA 2009 to 2020; $n = 647$, HC 1966 to 2020; $n = 161$, EMA 2012 to 2021; $n = 3615$), health agencies were analysed separately. Overall, 881 separate drugs had been reported to be potentially associated with TTP. There was little congruity between the drugs most commonly reported to each pharmacovigilance agency. Only clopidogrel was among the ten most reported drugs in all four health agencies. Antiarrhythmic/antihypertensives, antibiotics and monoclonal antibodies were among the five most commonly reported drug classes in the MHRA, EMA and HC data, though none of these were among the five most commonly reported drug classes in FDA data.

Data were available for demographics from 109 cases from HC. In the HC data, drug-induced TTP was reported more in women (66/109, 61%) than men (43/109, 39%), and the frequency of reports has increased over time, more than doubling in recent decades (mean 2.9 ± standard deviation 0.93] annual reports 2001 to 2010 rising to 6.1 [±2.92] annual reports 2011 to 2020), with the highest number of reports recorded in 2019 (11 reports). There was little consistency in the drugs reported as potential triggers for TTP to each pharmacovigilance agency.

Assessment of the relationship between medications and TTP is hampered by the quality of the data and causality cannot be assessed on the basis of these data from pharmacovigilance agencies. No standardised definition of TTP was used for reporting, nor for assessment of the likelihood of causality. Prospective data will be required to formally assess causality.

Disclosure of Interest: None Declared.

BSH22-PO103 | Safety and Efficacy of Apixaban as Thromboprophylaxis in Multiple Myeloma Patients Receiving Chemotherapy: A Prospective Cohort Study

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Abstract Content: Apixaban 2.5 mg twice-daily replaced low-molecular-weight-heparin as thromboprophylaxis (TP) for multiple myeloma (MM) patients receiving outpatient-based chemotherapy considered to be high-risk of venous thromboembolism (VTE) on 1st November 2019 in our regional centre.

This prospective cohort study aimed to assess the safety and efficacy of apixaban as thromboprophylaxis in high-thrombotic risk patients with MM.

Data were systematically collected from the electronic noting system for service evaluation, retrospectively for the historic cohort (1st Nov 2018–1st Nov 2019) prior to the introduction of the novel thromboprophylactic strategy, and prospectively (1st Nov 2019–1st Nov 2020) following the change of local guidelines to include apixaban as TP in high-thrombotic risk patients with MM. Exclusion criteria included antithrombotic treatment other than thromboprophylaxis or contraindication to thromboprophylaxis such as thrombocytopenia or doxorubicin use (due to possible drug–drug interaction with apixaban leading to reduced levels). Data collected included previous VTE history, thromboprophylactic agent, thrombosis and bleeding events while on chemotherapy. Primary outcomes included thrombotic and bleeding events.

Table 1 demonstrates patient characteristics and results. There were 102 MM patients in the historic and 147 in the prospective cohort. VTE prophylaxis was prescribed in 82 out of 102 (80%) of the historic cohort and 114 out of 147 (78%) of the prospective cohort. In patients not prescribed thromboprophylaxis, the chemotherapy regimen contained Daratumumab in 65% in the historic and 76% in the prospective cohort. After the introduction of the amended thromboprophylactic strategy, prescriptions of apixaban increased from 22out of 82 (27%) to 60 out of 114 (53%), while aspirin prescriptions fell from 51out of 82 (62%) to 47 out of 114 (41%).

After the introduction of apixaban as recommended thromboprophylaxis for high thrombotic risk patients, thrombotic events reduced from 3% (3/102) to 1.4% (2/147). All thrombotic events (two deep vein thrombosis [DVT], one pulmonary embolism) in the historic cohort occurred despite aspirin as thromboprophylaxis and on a pomalidomide-containing regimen. In the prospective cohort, the thrombotic events were a proximal DVT while on aspirin TP and a peripherally inserted central catheter (PICC)-associated thrombosis occurring on no TP. There were no thrombotic events in patients receiving prophylactic apixaban in either cohort.

There were five bleeding events in the historic cohort. This included one major bleeding event of a traumatic subdural haematoma (on apixaban TP). There were two clinically relevant non-major bleeding (CRNMB): an episode of frank haematuria and a per rectum bleed secondary to haemorrhoids (aspirin as TP), and two minor bleeds.

In the prospective cohort, there was one major bleeding event which was a gastrointestinal bleed requiring a two-unit blood transfusion (aspirin as TP). One CRNMB event included haemoptysis secondary to COVID-19 (apixaban as TP) and eight minor bleeding events, two of which occurred on no TP. Overall, major bleeding occurred in 1.2% (1/82) and CRNMB in 1.2% (1/82) patients on prophylactic apixaban across both cohorts.

These data add further support to the use of apixaban rather than LMWH as thromboprophylaxis for myeloma patients

Abstract Table 1: Baseline Characteristics

Category	1st Nov 2018–2019	1st Nov 2019–2020
Characteristic	*n* = 102	*n* = 147
Gender		
Female, *n* (%)	47 (46%)	62 (41%)
Median age on C1D1, years (range)	67 (33–86)	63 (28–86)
Weight (kg)		
<50	6 (6%)	7 (5%)
50–120	95 (93%)	139 (95%)
>120	1 (1%)	1 (1%)
Previous VTE		
Yes	6 (6%)	5 (3%)
VTE prophylaxis		
Yes	82 (80%)	114 (78%)
Line of chemotherapy		
1	15 (15%)	28 (19%)
2	25 (25%)	40 (27%)
3+	62 (61%)	79 (54%)
Thromboprophylactic agent prescribed	**(*n* = 82)**	**(*n* = 114)**
Aspirin	51 (62%)	47 (41%)
Apixaban 2.5 mg	22 (27%)	60 (53%)
pLMWH	8 (10%)	6 (5%)
Clopidogrel	1 (1%)	1 (1%)
Thrombotic and bleeding events		
Venous thrombotic events, *n* (%)	3 (3%)	2 (1.4%)
PD (on aspirin)	2	0
Pom (on aspirin)	1	0
DVD (on aspirin)	0	1
Dara-VRD (no TP)	0	1
Bleeding events, *n* (%)	5 (5%)	10 (7%)
Major (agent)	1 (Apixaban)	1 (Aspirin)
CRNMB (agent)	2 (Aspirin x2)	1 (Apixaban)
Minor (agent)	2 (Aspirin x1, Apixaban x1)	8^

Abbreviations: C1D1: Cycle 1 Day1 of chemotherapy, CRD: cyclophosphamide-lenalidomide-dexamethasone, CRNMB: clinically relevant non-major bleed, DD: daratumumab-dexamethasone, DVCD: daratumumab-Velcade®(*bortezomib)*-cyclophosphamide-dexamethasone, DVD: daratumumab-Velcade ®(*bortezomib)*-dexamethasone, DVRD: daratumumab-Velcade®(*bortezomib)*-lenalidomide-dexamethasone, IRD: ixazomib-lenalidomide-dexamethasone, KCD: carfilzomib-cyclophosphamide-dexamethasone, kg: kilogram, pLMWH: prophylactic low-molecular-weight-heparin, PCD: pomalidomide-cyclophosphamide-dexamethasone, PD: pomalidomide-dexamethasone, Pom: pomalidomide monotherapy, TP: thromboprophylaxis, VCD: Velcade ®(*bortezomib)*-cyclophosphamide-dexamethasone, VCP: Velcade ®(*bortezomib)*-cyclophosphamide-prednisolone, VD: Velcade ®(*bortezomib)*-dexamethasone, VTD: Velcade ®(*bortezomib)*-thalidomide-dexamethasone, VTE: venous thromboembolism, ^ two on no TP, one on aspirin, five on prophylactic apixaban.

is considered to be at high thrombotic risk, with very low rates of thrombosis and acceptably low rates of major and CRNMB.

Disclosure of Interest: None Declared.

BSH22-PO104 | Direct Oral Anti-Coagulant (DOAC) external quality assessment (EQA) scheme assay results and interpretations from UKNEQAS BC DOAC Survey 192 021

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Abstract Content: DOAC EQA scheme requires participants to perform DOAC assays and results are performance assessed. The assay interpretation is a recent addition to the NEQAS BC programme with clinical and laboratory staff being asked to provide interpretations.

Data were collected as part of the DOAC exercise survey 19. Participants were asked to provide interpretations from below level of detection, anticoagulant present at sub-therapeutic level, anticoagulant detected, unable to state if therapeutic, anticoagulant present at therapeutic level or anticoagulant present at supra-therapeutic level. The clinical scenario associated with Survey 19 stated that the patient had taken dose of anticoagulant 3 h before medical assessment.

The interpretations for the DOAC assays were either from anticoagulant nurses (2%), biomedical scientists (34%) and clinicians (33%) or clinical scientists (9%). Twenty-two percent of participants did not provide an interpretation.

From the interpretative data returned on Survey 19, none of the participants interpreted the assays results as below the level of detection. The majority of interpretations returned for dabigatran, apixaban and edoxaban indicated that levels of the drug were at a therapeutic level. The returns for rivaroxaban interpretation included 45% of participants who had indicated that the drug was at a level above the therapeutic range.

In clinical scenarios that state the level of drug remains unknown, an interpretation of 'anticoagulant detected, unable to state if therapeutic' might stimulate the requesting clinician to review the time and dosage administered to the patient.

DOAC monitoring is not required for the vast majority of patients receiving these anticoagulants. However measuring DOAC levels is indicated in some settings including but not exclusively: bleeding risk; thrombotic risk; compliance and or accurate interpretation of other laboratory assays. Our data indicate that there is currently substantial variability in how the same levels of DOACs are interpreted.

Disclosure of Interest: None Declared.

Abstract Table:

Overall interpretation (answers)	Dabigatran 21:05 (*n*) (% of returns)	Rivaroxaban 21:06 (*n*) (% of returns)	Apixaban 21:07 (*n*) (% of returns)	Edoxaban 21:08 (*n*) (% of returns)
DOAC sample				
Below level of detection	—	—	—	—
Anticoagulant present at subtherapeutic level *Range ng*/ml	3 (4%) Median 152 ng/ml *115.1–161*	—	21 (21%) Median 84 ng/ml *59.1–106.2*	3 (5%) Median 145 ng/ml *144.1–165.9*
Anticoagulant detected, unable to state if therapeutic *Range ng*/ml	13 (19%) Median 154 ng/ml *132–210*	23 (22%) Median 394 ng/ml *284–447.1*	25 (25%) Median 92.4 ng/ml *74–106.0.6*	13 (22%) Median 164 ng/ml *138–174.2*
Anticoagulant present at therapeutic level *Range ng*/ml	53 (77%) Median 154 ng/ml *114–193*	34 (33%) Median 393 ng/ml *301–441*	56 (55%) Median 95.68 ng/ml *46–115.9*	41 (71%) Median 157 ng/ml *141.5–190*
Anticoagulant present at supra-therapeutic level *Range ng*/ml	—	47 (45%) Median 417 ng/ml *363–476.8*	—	1 (2%) Median 159 ng/ml *159*

BSH22-PO105 | Platelet function abnormalities are common among women with menorrhagia referred for surgical intervention

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Abstract Content: Menorrhagia may be the first presenting symptom for women with a bleeding disorder. In a prospective study, we sought to establish the prevalence of bleeding disorders among women who have failed conservative treatment and were referred for surgical management of menorrhagia. The role of the International Society on Thrombosis and Haemostasis Bleeding Assessment Tool (ISTH-BAT) as a screening measure to identify those warranting haemostatic investigation was also examined.

Women aged ≥18 referred for hysterectomy or endometrial ablation for treatment of menorrhagia at our institution, a tertiary gynaecology and Haemophilia Comprehensive Care Centre, were eligible for inclusion. Exclusion criteria included a prior bleeding disorder diagnosis, pelvic malignancy or current antithrombotic therapy. A structured medical history applying the ISTH-BAT was obtained. Laboratory testing comprised a coagulation screen, Clauss fibrinogen, von Willebrand disease (vWD) screen, PFA-100 and platelet function testing using lumiaggregometry. Whole blood impedance aggregometry was also tested with the Multiplate® analyser (Roche). Women for whom an abnormality was detected were referred to a haematologist for further evaluation. Fifty patients were recruited and underwent testing between 2016 and 18. Fifteen patients (30%) had abnormal results warranting further haematological assessment. Eight women (16%) had a reproducible abnormality on platelet function testing with lumiaggregometry. Of these eight patients, three were categorised as having a storage pool disorder and in another three cases concomitant medication use was a possible contributor. No further clinically relevant abnormalities were detected.

The mean ISTH-BAT score overall was 6.2 (range 4–12). Among those with abnormal lumiaggregometry, this was higher at 7.1 (range 4–10) in contrast with 6 (range 4–12) among those with normal platelet function.

Out of the eight patients with abnormal platelet function, all proceeded to surgical intervention. Three were given DDAVP and tranexamic acid (TXA) preoperatively (2 endometrial ablation, 1 laparoscopic hysterectomy), four were managed with TXA alone (3 ablation, 1 laparoscopic hysterectomy) and one patient was given no additional haemostatic cover for their ablation. Neuraxial anaesthesia was avoided in all and no patient in this group experienced excess bleeding or other peri-operative complications. Of the six patients treated with ablation, only half reported symptomatic improvement with no need for further treatment; one patient required subsequent hysterectomy.

In summary, a high prevalence of platelet function abnormalities was identified within this cohort of women referred for surgical intervention of menorrhagia. The ISTH-BAT was not discriminatory in separating patients with abnormal platelet function from those without a haemostatic abnormality and alternative strategies for screening and diagnosis of bleeding disorders need to be considered in women with severe menorrhagia.

Disclosure of Interest: A. Delaney Conflict with: Previously received consultancy fees from Novo Nordisk (not in relation to this study), R. Maclean: None Declared, M. Makris: None Declared, K. Horner: None Declared, S. Kitchen: None Declared, J. Sedcole: None Declared, T. Baxter: None Declared, C. Samuelson Conflict with: Grant awarded by the Platelet Charity to fund research into platelet function disorders.

BSH22-PO106 | Laboratory assays for patients receiving Argatroban therapy or normal plasma spiked with Argatroban: A review of UK NEQAS (Blood Coagulation) External Quality Assessment Scheme exercises 2021

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Abstract Content: Measurement of fibrinogen with the Clauss assay is a thrombin time-based method that can be affected by Direct Thrombin Inhibitors. Argatroban a direct thrombin inhibitor is used in patients being treated for HIT and VITT. The current guidelines recommend using the APTT to monitor the argatroban levels for patient management.

A supplementary exercise for argatroban was distributed to 32 laboratories in spring 2021. Samples containing argatroban from a pool of treated patients and from a spiked normal plasma were distributed and participants requested to return APTT, argatroban and fibrinogen assay results. The data were analysed as ratio of test/mid point of APTT, argatroban and fibrinogen assay results.

Samples distributed as part of an argatroban exercise (A21:01–05) are detailed in Table 1.

Commercial reagents for fibrinogen quantitation have a range of thrombin concentrations and it is clear that the level of argatroban in patient or spiked samples can interfere with the measurement of fibrinogen. The data highlight the fibrinogen underestimation with some assays in samples with levels of argatroban at therapeutic levels. Information also collected from the exercise indicated that participants were using 1.5–3.0 times the baseline APTT as their therapeutic target for argatroban For argatroban the kits employed in this exercise a therapeutic target of between 0.4 and 2.0 µg/ml was in use. There was a total of six sets of results for APTT that did not fall between 1.5 and 3 times the baseline APTT out of a total 90 APTT ratio results.

Disclosure of Interest: None Declared.

Abstract Table:

	A21:01 Normal ~0 µg/ml	A21:02 Patient ~1.0 µg/ml	A21:03 Patient ~1.5 µg/ml	A21:04 Spiked ~0.6 µg/ml	A21:05 Spiked ~0.9 µg/ml
Argatroban IIa µg/ml					
Hyphen Hemoclot kit					
median conc	0.05	1.02	1.58	0.63	0.99
Hemosil DTI kit					
median conc	0	0.84	1.43	0.61	0.85
STA ECAII kit					
median conc	0.07	0.95	1.4	0.63	0.95
Clauss fibrinogen g/l					
Fibrinogen assay Thrombin conc 100NIH					
median conc	2.19	4.21	3.5	2.95	2.89
Fibrinogen assay Thrombin conc 35NIH					
median conc	2.5	0.4	0.4	1.38	0.4
APTT ratio					
Actin FS					
median APTTr	1.19	1.96	2.92	2.33	2.69
Synthasil					
median APTTr	1.22	1.53	1.96	2.20	2.46
Cephascreen					
median APTTr	1.2	2.07	3.42	2.18	2.46
Trinity APTT					
median APTTr	1.28	1.75	No result	2.19	No result

BSH22-PO107 | The advantages of using expansion microscopy to visualise single platelets and aggregates

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Abstract Content: Platelets are small anucleate cells circulating in the blood, which can undergo a dramatic shape change upon activation. Whenever they encounter a blood vessel injury, a coagulation cascade is triggered, which leads to platelet aggregation and clot formation. However, platelet activation in some cases leads to strokes or myocardial infarction.
It is challenging to obtain super-resolved images of platelets as there are very small cells, with a diameter of 2–3 µm. In addition, the membrane receptors of interest are highly abundant. The high receptor density makes platelets challenging for super-resolution microscopy methods, such as dSTORM. In order to overcome these challenges, we have chosen expansion microscopy (ExM), a new, affordable and easy-to-use protocol to obtain super-resolution images using a conventional microscope that allows the isotropical expansion of the sample 4 or 10 times. In principle, two different expansion protocols that vary on when the immunolabelling is performed were described.
We found that the pregelational labelling protocol allows the expansion of the platelets 4 and 10 times, however comes at the cost of diminished signal when Fab-fragments (and not IgGs) were used. As shown on the quantification of the fluorescence intensity of each step, we conclude that the signal loss happens during the digestion process. This problem was overcome by using another version of the ExM protocol, Using this different protocol, the expansion and the labelling with both full-length antibodies as wells as with Fab-fragments was successful.
In addition, using the ExM protocol we are able to perform the expansion of not only single platelets but also platelet aggregates, allowing us to single platelets within our super-resolved images of platelets aggregates.
Disclosure of Interest: None Declared.

BSH22-PO108 | Tranexamic Acid use to improve outcomes in Meningioma Surgery

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Abstract Content: Introduction: Meningioma surgery is associated with intraoperative bleeding and large transfusion requirement. Tranexamic Acid (TXA) has been used in medical and surgical practice to reduce haemorrhage. This review aimed to evaluate the effect of TXA use on operative and postoperative outcomes.
Methods: A systematic review and meta-analysis was conducted in accordance with the PRISMA statement and registered in PROSPERO (CRD42021292157). Six databases were searched up to November 2021 for phase 2–4 clinical trials and multiple arm cohort studies. Random effects meta-analysis were performed to delineate operative (e.g intraoperative blood loss) and postoperative outcomes (e.g. postoperative complications).
Results: Four studies (181 patients) were included. TXA use significantly reduced intraoperative blood loss (mean difference 315.69 mls [95% CI -532.94 to −98.54]) and transfusion requirement (OR 0.52 [95% CI 0.27–0.98]). Factors not affected by TXA use were operation time (mean difference = −0.11 [CI 95% -0.27 to 0.05]), postoperative seizures (OR = 0.87 [CI 95% 0.31, 2.49]), hospital stay (OR = -1.24 [CI 95% -3.38 to 0.90]) and disability after surgery (OR = 0.53 [CI 95% 0.26, 1.04]).
Conclusions: TXA use reduces blood loss and transfusion requirement in meningioma surgery, but not postoperative complications, or disability after surgery. Larger trials are required to investigate the impact of TXA on patient-focussed postoperative outcomes.
Disclosure of Interest: None Declared.

BSH22-PO109 | Internal and external validation of venous thromboembolism predictive model in haematological malignancies

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Abstract Content: Venous thromboembolism (VTE) is a frequent complication in haematological malignancies (HM) with a significant impact on morbidity and mortality, having and incidence similar to that observed in solid tumours at high thrombotic risk. Although several well-validated scores stratify VTE risk in solid tumours, HM are underrepresented in these models. The aim of this study was to develop an internal and external validation of a logistic regression model based on demographic, clinical and laboratory variables for predicting the risk of VTE in hospitalised patients with HM.
We conducted an internal and external validation of existing VTE predictive model using 496 data-based prospective

case–control study, hospitalised patients with a diagnosis of HM between December 2010 and December 2020, at Arnaldo Milián University Hospital, Santa Clara, Cuba. The predictive model, designed with a data of 285 HM patients (94 with VTE/191 without VTE) includes five predictive factors according to multivariate logistic regression: hypercholesterolaemia, tumoral activity, use of thrombogenic drugs, diabetes mellitus and immobilisation. Predictive score system was constructed based on the regression β coefficient. Patients were divided into two risk groups according to low and high risk. The model was internally validated using a bootstrap analysis over 1000 repetitions. The external validation was realised to test the real predictive power of the model in a prospective external dataset of 211 hospitalised patients (59 with VTE/152 without VTE) with diagnosis of HM. Informed consent was obtained and the study was approved by a medical ethics committee complying with the Declaration of Helsinki.

The incidence of VTE in the study was 30.9%. The HM that contributed the highest number of VTE were: acute leukaemias (6.8% acute myeloid leukaemia and 2.6% acute lymphoid leukaemia), lymphomas (6.6%), myeloproliferative neoplasms (5.8%) and multiple myeloma (5%).Most patients (57.5%) were in relapse or progression of HM at time of VTE. The predictive model had 76.4% of negative predictive value (NPV), 81.7% of positive predictive value (PPV), 58.6% of a sensitivity and 90.8% of specificity in the bootstrapping internal validation. There were no significant differences between the Area Under Receiver Operating Characteristic (AUROC) curve in the derivation set (0.853) and bootstrapping validation sets (0.838). The proportion of patients correctly classified into each risk category was similar with an accuracy of 80.1% and 82.9% in the internal and external validation sets respectively. In the external validation cohort, the model produced 82.9% of accuracy, 89.7% of NPV, 67.7% of PPV, 74.6% of sensitivity and 86.2% of specificity. The AUC in the external validation performance was 0.900. The bootstrapping validation results show the stability of the model and the external validation highlight its relevance to predict the risk of VTE with good accuracy. The VTE predictive model is a reproducible and simple tool with good accuracy and discrimination.

Disclosure of Interest: None Declared.

BSH22-PO110 | Thromboembolism in COVID-19 patients on ECMO

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Abstract Content: Venous thromboembolism (VTE) is a common complication of COVID-19 (coronavirus disease 2019), which often leads to sudden deterioration and death. There are multiple mechanisms contributing to this phenomenon. Endothelial injury from COVID-19 triggers platelet activation and adhesion, leucocyte aggregation, cytokine storm and complement activation. Cytokine storm triggers coagulation activation and thrombin generation. Complement activation is also thought to trigger the formation of systemic thrombus through recruiting inflammatory cytokines and possible complement-mediated thrombotic microangiopathy.

Patients on extracorporeal membrane oxygenation (ECMO) are at risk of developing thromboembolism. Thrombus formation within the extracorporeal circuit is the main reason for systemic thromboembolism. Possibly that by contacting blood and nonendothelial surfaces, ECMO triggers activation of coagulation pathway and inflammatory response.

Thromboembolic prophylaxis is critical in managing COVID-19 patients on ECMO. Anticoagulation is recommended to all hospitalised COVID-19 patients unless there are contraindications. However, patients are still found to develop VTE while on anticoagulation and the prevalence of VTE in COVID-19 patients on ECMO is still unclear. We aim to investigate the VTE incidence and contribute to anticoagulation strategy and management in this specific population.

We retrospectively reviewed the data of 23 patients who were diagnosed with COVID-19 and managed with ECMO. All patients received thromboembolic prophylaxis since admission. We report our findings of the incidences of thromboembolism.

Twenty-three adult patients who were diagnosed with COVID-19 received ECMO support. Sixteen patients were

Abstract Table: Complications during hospitalisation and comparison to the previous study

	VTE	DVT	PE	Stroke	MI	HIT	Clotted circuit	ECMO
Our study	8/23 (34.7%)	6/23 (26%)	2/23 (8.7%)	0	0	0	4 (17.4%)	23 (100%)
Jenner's study	996/2928 (34%)	431/2671 (16.1%)	325/2580 (12.6%)	52/1736 (3.0%)	137/1736 (8.0%)		13/48 (27.1%)	529 (18%)
Odds ratio	1.03 (0.44, 2.45)	1.03 (0.44, 2.45)	0.66 (0.15, 2.83)					

Odds ratio calculation and Fisher exact test were performed in R (version 4.1.2) using the package 'epiR'. $p < 0.05$ is considered statistically significant.

minorities, and seven patients were Caucasians. The mean age of patients was 44.8-year old. Seventeen patients were males, and 11 patients had at least one of the following pre-ECMO comorbidity: ten (43.5%) patients had hypertension, 11 (47.8%) patients had type 2 diabetes and four (17.3%) patients had hyperlipidaemia. None of the patients were active smokers or had chronic lung disease.

During the hospital course, all patients received heparin for thromboembolic prophylaxis. The overall VTE rate was 34.7%. Six patients developed deep vein thrombosis (DVT) (26%) with lower extremities induration. Two patients were found to have pulmonary embolism (PE) (8.7%). Four patients had clotted circuit that requiring exchange. No stroke or myocardial infarction (MI) was diagnosed in these patients. Heparin-induced thrombocytopenia (HIT) was excluded in all cases.

Based on our study, the overall VTE rate of COVID-19 patients on ECMO was 34.7% with 26% incidence of DVT and 8.7% incidence of PE. According to Jenner's recent systemic review of 28 studies, 34% of 2928 ICU-managed COVID-19 patients developed VTE. PE was found in 12.6% of patients and DVT was detected in 16.1% of patients. 529 patients (18.0%) received ECMO in the cohort. When compared with our study, there were no statistically significant differences of the incidences of VTE, DVT or PE between these two studies, although all our patients were on ECMO support. Further investigation into the prevalence, implications and management of thromboembolism in COVID-19 patients on ECMO will lead to significantly improved outcomes for this specific patient population.

Disclosure of Interest: None Declared.

BSH22-PO111 | Vaccine-Induced Immune Thrombocytopenia and Thrombosis Syndrome post second dose of ChAdOx1 nCov-19 vaccine: Case Presentation

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Abstract Content: We present the case of a 39-year-old female who presented to University Hospitals of Leicester 14 days after the second dose of ChAdOx1 nCov-19 vaccine. Her presenting symptoms included skin rash, nausea, intermittent abdominal pain and occasional episodes of dizziness. Her past medical history included Type 2 Diabetes Mellitus and hidradenitis suppurativa. The first dose of ChAdOx1 nCov-19 vaccine had been administered on 27th February 2021, following which the patient reported flu like symptoms that resolved after four days and did not require further medical input. Following this, a preplanned surgical procedure to incise and drain a vulval abscess was performed on 17th May 2021. Preoperative testing performed on 13th May 2021 showed a normal platelet count of 219 × 10^9/l. The second dose of ChAdOx1 nCov-19 vaccine was subsequently administered on 23rd May 2021.

On presentation, examination revealed mild epigastric tenderness and features of classical thrombocytopenic rash affecting all limbs with no other associated bleeding. Initial blood results confirmed thrombocytopenia of 11 × 10^9/l, with D-Dimer 14.26 µg/ml and fibrinogen 2.1 g/l. Blood film microscopy revealed an occasional schistocyte and microangiopathic haemolysis was considered. Treatment with plasmapheresis of 1.5 x plasma volume using Octaplas was administered. Subsequent abdominal computed topography imaging identified extensive thrombotic events. This included bilateral pulmonary embolism, superior mesenteric vein non-occlusive thrombus and multiple soft atheromas lining the abdominal aorta causing moderate infrarenal stenosis. In view of the recent history, vaccine associated thrombosis and thrombocytopenia (VITT) was considered. Subsequent testing showed a normal ADAMTS13 level. Treatment for VITT with intravenous immunoglobulin along with oral steroids and anticoagulation using Argatroban was commenced in line with national guidance. Anti-PF4 antibody, tested using the Asserachrom HPIA ELISA assay, was positive at a level of 1.298 OD units confirming the diagnosis of VITT; the first case we are aware of in the UK following second dose administration. Given high-risk presentation, Rituximab therapy was given as an inpatient with good clinical response. Prior to discharge, anticoagulation was switched to oral apixaban with a platelet count on discharge of 170 × 10^9/l. Subsequent follow-up has shown ongoing clinical remission with consistently negative Anti-PF4 antibody titres. This report outlines the first known definite case of VITT identified following administration of the second dose of ChAdOx1 nCov-19 vaccine in the United Kingdom. The subsequent clinical course was similar to those of patients presenting after their first dose but the atypical presentation mimicking that of Thrombotic Thrombocytopenia is noted.

Disclosure of Interest: None Declared.

BSH22-PO113 | The effect of lockdown and media coverage following vaccine rollout on Deep Vein Thrombosis (DVT) clinic activity during the first year of the COVID-19 pandemic—a single-centre experience

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Abstract Content: An explosion of research has occurred since the advent of the COVID-19 pandemic relating to its effect on the NHS, health consciousness and vaccine side effects, such as vaccine-induced thrombocytopenia and thrombosis (VITT). This project sought to establish the effects of the UK's national lockdowns and media coverage of VITT on the rate of referrals and outcomes of DVT clinic appointments at our hospital. There was a suspicion among

nurses running the DVT clinic that referrals were lower, but rates of positive scans higher, during the first national lockdown and that the reverse was true following media reporting of the first cases of VITT, with large numbers of patients testing negative for DVT.

We report the findings of a retrospective, observational case–control study of 3550 patients presenting to Norfolk and Norwich University Hospital outpatient DVT clinic from any referral source (usually GP or A + E) between 2/3/2020 and 10/5/2021. Data from 2015 to 2019 were also obtained, providing 5-year averages for comparison. Outcomes were classified as positive (for DVT), negative (including those where Doppler ultrasound scan was not indicated due to low Wells score and negative D-dimer) and DNA (did not attend).

Chi-squared (χ^2) analyses were undertaken to determine heterogeneity of weekly referrals during specific periods of the pandemic. With 2 degrees of freedom (2df), a χ^2 result above 5.9 suggests heterogeneity. *T*-tests were run to compare the outcomes driving the χ^2 results with the data from the preceding 5 years.

Compared to the non-lockdown period, there was a significant reduction in the number of referrals seen during the dates of the 1st national lockdown ($\chi^2 = 20.01$, 2df, $p = <0.01$). This was primarily due to a reduction in the number of patients subsequently found to be negative for DVT (31.0 vs. 45.4, $p = <0.01$). The difference was less marked and did not reach statistical significance during the 2nd and 3rd lockdowns.

A significant increase in total weekly referrals was observed during the period immediately following media reporting of the first cases of VITT related to the AstraZenaca COVID-19 vaccine (55.1 vs. 73.1, $p = <0.01$). This was driven by an increase in patients subsequently found to be negative for DVT (39.2 vs. 57.2 $p = <0.01$). The weekly number of positive patients during this time was not significantly higher than the preceding 5-year average for the same dates (9.7 vs. 10.2, $p = 0.30$).

Comparison with 5-year averages confirmed that the pattern seen in different parts of the pandemic year described above did not follow the usual pattern of referrals across the year.

Finally, throughout the observed period, there was a below average rate of DNA outcomes when compared to the preceding 5-year average.

These findings suggest several phenomena unique to the COVID-19 pandemic. First, measures to prevent the spread of COVID-19 were associated with fewer patients without DVT being referred to the DVT clinic. Second, media reporting of VITT was associated with a higher rate of referral of patients without a DVT to the DVT clinic without any change in the number of positive patients compared to the preceding 5 years. Third, during the COVD-19 pandemic, there were fewer patients failing to attend their clinic appointment, which we hypothesise is as a result of increased awareness of the need not to waste NHS resources.

Disclosure of Interest: None Declared.

Transplantation, Gene & Cellular Immunotherapies

BSH22-PO114 | Patient-Reported Outcomes in ZUMA-7, a Phase 3, Randomised, Open-Label Study Evaluating the Efficacy of Axicabtagene Ciloleucel (Axi-Cel) *Versus* Standard-of-Care Therapy in Relapsed/Refractory Large B-Cell Lymphoma

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Abstract Content: Background: Outcomes are poor for patients with large B-cell lymphoma (LBCL) who relapse early or are refractory to first-line therapy. Furthermore, patients receiving second-line standard-of-care (SOC) therapy

often report poor health-related quality of life (QoL; Lin V, et al. J Clin Oncol. 2020;38:e20070). In the pivotal Phase 3 ZUMA-7 study, we conducted the first comparative analysis of patient-reported outcomes (PROs) with axi-cel, an autologous anti-CD19 chimeric antigen receptor T-cell therapy, *versus* standard of care (SOC) as second-line treatment in relapsed/refractory (R/R) large B-cell lymphoma (LBCL).

Methods: PRO instruments, including the European Organisation For Research And Treatment of Cancer (EORTC) QLQ-C30 (cancer-specific 30-item survey) and the EQ-5D-5L (general survey with 5 quality-of-life [QoL] domains and a global assessment), were given at baseline (before treatment), Day 50, 100, 150, Month 9 and every 3 months from randomisation until 24 months or an event-free survival (EFS) event (i.e. disease progression, death from any cause, or new lymphoma therapy), whichever occurred first. Patients who had a baseline PRO and ≥1 measure completed at Day 50, 100 or 150 were assessed. Prespecified hypotheses for 3 PRO domains (EORTC QLQ-C30 Physical Functioning, EORTC QLQ-C30 Global Health Status/QoL and EQ-5D-5L visual analog scale [VAS]) were tested. False discovery rate adjusted the p values across key endpoints; sensitivity analyses controlled for covariates and patterns of missingness. A clinically meaningful change was defined as 10 points for each EORTC QLQ-C30 score and 7 points for EQ-5D-5L VAS score.

Results: Of 359 enrolled ZUMA-7 patients, 296 (165 axi-cel, 131 SOC) were included for analysis: 70% had primary refractory disease, 42% had high second-line age-adjusted International Prognostic Index (2–3) and 30% were ≥ 65 years. There was a statistically significant ($p < 0.0001$) and clinically meaningful difference in mean change of scores from baseline at Day 100 in favour of axi-cel on all prespecified PRO domains. Sensitivity analyses showed similar results with retained significance at Day 100. Scores significantly favoured axi-cel over SOC for EORTC QLQ-C30 Global Health Status/QoL ($p = 0.0124$) and EQ-5D-5L VAS ($p = 0.0004$) at Day 150. For prespecified end-points, the mean estimated scores for the axi-cel arm had numerically returned to or exceeded scores at baseline by Day 150 *versus* on or after Month 9 for the SOC arm. After Month 9, attrition (eg, an EFS event) in the QoL analysis set was substantial, particularly in the SOC arm. Analyses of additional PRO end-points demonstrated similar trends.

Conclusion: ZUMA-7, the first randomised, global, multicentre Phase 3 study of axi-cel *versus* SOC in second-line R/R LBCL, showed that treatment with axi-cel results in clinically meaningful improvement in QoL over SOC at Day 100 as measured by multiple validated PRO instruments. Score comparisons at later timepoints warrant cautious interpretation, particularly in the SOC arm, as attrition due to EFS events may select patients with the best outcomes. The data also suggest faster recovery to pretreatment QoL with axi-cel compared with SOC. The superior clinical outcomes and patient experience with axi-cel over SOC should help inform treatment choices in second-line R/R LBCL.

These data are reported on behalf of all ZUMA-7 investigators and contributing Kite members.

Disclosure of Interest: K. Cwynarski Conflict with: consultancy or advisory role for Kite, a Gilead Company, Roche, Takeda, Celgene, Atara, Gilead, Janssen, Incyte; speakers' bureau for Roche, Takeda, Kite, a Gilead Company, Gilead, Incyte; and travel support from Roche, Takeda, Kite, a Gilead Company, Janssen, BMS/Celgene, M. Elsawy Conflict with: honoraria from Kite, a Gilead Company, BMS, Novartis, Pfizer, Janssen; and consulting or advisory role with Kite, a Gilead Company, BMS, Novartis, Pfizer, Janssen, J. C. Chavez Conflict with: consultancy fees for Kite, a Gilead Company, Abbvie, Janssen, ADC Therapeutics, Karyopharm, Kymera, GenMab, Novartis; speakers' bureau participation for Morphosys, Epyzime, BMS, BeiGene, AstraZeneca; research funding from AstraZeneca, Merck, ADC Therapeutics, Adaptive, I. Avivi Conflict with: speakers' bureau participation for Kite, a Gilead Company and Novartis., J.-F. Larouche: None Declared, L. Wannesson Conflict with: consultancy or advisory role for Novartis, MSD, BMS, AstraZeneca and Roche; research funding from Roche; and expert testimony from AstraZeneca and Novartis, K. Osman Conflict with: honoraria from Kite, a Gilead Company; and consultancy or advisory role for Kite, a Gilead Company., K. Davison Conflict with: consulting or advisory role for Merck, AstraZeneca, Janssen, Novartis, Gilead, Abbvie, Celegene, J. D. Rudzki Conflict with: consultancy or advisory role with Kite, a Gilead Company, Novartis, Amgen, MSD, Roche and BMS-Celgene; speakers' bureau for Kite, a Gilead Company, Novartis and Roche; and research funding from Kite, a Gilead Company and Novartis, S. Dahiya Conflict with: consultancy or advisory role for Kite, a Gilead Company, Atara Biotherapeutics, BMS; research funding from Jazz Pharmaceuticals and Miltenyi Biotech, K. Dorritie Conflict with: research funding from Kite, a Gilead Company, Juno/BMS, Hoffman-LaRoche, Janssen, and Genmab, S. Jaglowski Conflict with: consultancy or advisory role for Kite, a Gilead Company, Novartis, BMS, Takeda, CRISPR; research funding from Kite, a Gilead Company, Novartis, BMS, and Caribou, J. Radford Conflict with: stock or other ownership in ADC Therapeutics and AstraZeneca; honoraria from Takeda, ADCT and BMS; consultancy or advisory role for Takeda, ADCT, BMS and Novartis; speakers' bureau from Takeda, ADCT; research funding from Takeda; and expert testimony from Takeda and ADCT, F. Morschhauser Conflict with: consultancy or advisory role for Roche, BMS, Gilead Science, Epizyme, GenMab, Novartis and Abbvie; speakers' bureau participation from Roche; expert testimony from Roche and Genentech, D. Cunningham Conflict with: research funding from MedImmune, AstraZeneca, Clovis, Eli Lilly, 4SC, Bayer, Celgene and Roche, A. M. Garcia-Sancho Conflict with: honoraria from Roche, Celgene, Janssen, Servier, Gilead; consulting or advisory role with Roche, Celgene/BMS, Morphosys, Kyowa Kirin, Clinigen, Eusa Pharma, Novartis, Gilead, Servier, Incyte; research funding from Janssen; expert testimony from

Gilead; and travel support Roche, Celgene, Servier, Kern Pharma, D. Tzachanis Conflict with: consultancy or advisory role for EUSA, Takeda, Partner, BMS; research funding from BMS, M. L. Ulrickson: None Declared, R. Karmali Conflict with: consulting or advisory role with BeiGene, Kite, a Gilead Company, Morphosys, Karyopharm, BMS/Celegene, Genentech, Roche, Janssen, Pharmacyclics; speakers bureau from astraZeneca, BeiGene, Kite, a Gilead Company, Morphosys; research funding from Kite, a Gilead Company, BMS/Celgene, Takeda, N. Kekre Conflict with: honoraria from Gilead, Novartis, and Celgene; and consultancy or advisory role for Gilead, Novartis, and Celgene, C. Thieblemont Conflict with: honoraria from BMS/Celgene, Abbvie, Takeda, Novartis, Roche, Kite, a Gilead Company and Incyte; consultancy or advisory role for BMS/Celgene, Abbvie, Takeda, Roche, Novartis, Kite, a Gilead Company and Incyte; and travel support from BMS/Celgene, Takeda, Roche, Novartis, and Kite, a Gilead Company, G. Enblad Conflict with: consultancy or advisory role with Kite, a Gilead Company and Gilead Sciences, P. Dreger Conflict with: consulting or advisory role for AbbVie, AstraZeneca, Bluebird Bio, BMS, Gilead Sciences, Janssen, Novartis; and research funding from Riemser, R. Malladi Conflict with: honoraria from Gilead; consultancy or advisory role Gilead Science; and travel support from Gilead, N. Joshi Conflict with: employment with Open Health; consulting or advisory role and research funding from Kite, a Gilead Company and various clients via employment, W.-J. Wang Conflict with: consultancy or advisory role for Kite, a Gilead Company and additional companies through employment with OPEN Health; research funding from Kite, a Gilead Company and additional companies through employment with OPEN Health, C. T. Solem Conflict with: employment with OPEN Health, consultancy or advisory role for Kite, a Gilead Company through employment at OPEN Health; research funding from multiple clients through employment at OPEN Health, J. T. Snider Conflict with: employment with Kite, a Gilead Company; stock or other ownership in Gilead and research funding from life science companies through PrecisionHEOR, C. To Conflict with: employment with Kite, a Gilead Company; stock or other ownership in Gilead Sciences, M. J. Kersten Conflict with: honoraria from Kite, a Gilead Company, Novartis, and Miltenyi Biotech, Roche and BMS/Celgene; consultancy or advisory role for Kite, a Gilead Company, Roche, BMS/Celgene, Novartis and Miltenyi Biotech; research funding from Kite, a Gilead Company, Roche, Takeda and Celgene and travel support from Kite, a Gilead Company, Roche, Novartis and Miltenyi Biotech.

BSH22-PO115 | Excellent outcome with FB4 conditioning regimen in patients affected with myeloid malignancies older than 55 and with HCTI-score <2. A new insight for raising the upper limit for myeloablation in fit patients and high-risk diseases

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Abstract Content: Allogeneic haematopoietic stem cell transplant (HSCT) is considered a curative strategy for acute myeloid leukaemia (AML) and myelodysplastic syndrome (MDS) with excess of blasts or complex/adverse cytogenetic. The evaluation of comorbidities with HCT-CI score and the upper limit of 55 years for administering myeloablative conditioning (MAC) are common strategies to minimise HSCT non-relapse mortality (NRM). Despite multiple studies performed previously, this remains an area of uncertainty and precise data guiding MAC selection are still needed.

Herein we report the outcome of patients affected with AML and MDS conditioned with MAC.

HSCT was performed with GCSF mobilised peripheral blood stem cells. Conditioning protocol was with fludarabine 30 mg/m^2 days −7, −6, −5, −4, −3 busulfan 3.2 mg/Kg days −6, −5, −4, −3 (FB4); graft versus host disease (GVHD) prophylaxis consisted of thymoglobulin (ATG 5 mg/Kg) or Campath 60 mg (27 and 94 patients respectively) and single-agent ciclosporin 3 mg/Kg (therapeutic level of 150–200) until d + 56 and then tapered in absence of GVHD. A median of 5.5 × 10^6 CD34+/Kg was infused (3.1–8). Donors were as follows: 21 full-matched siblings, 76 full matched unrelated donors and 24 mismatched unrelated donors.

Between January 2016 and November 2020, 121 patients (77 AML, 44 MDS) with a median age of 56 (19–73) had FB4 conditioning. Patients aged >55 were 64 (53%). HCT-CI score <2 and ≥2 was present in 48 and 73 patients respectively.

Two years overall survival (OS) was 55% with a median OS of 42 months. No septic death before engraftment or primary graft failure was noted. The median time to neutrophils ≥1000/ml was 12 days (10–18), and 10 days (8–48) to platelets ≥20.000/ml. The median CD3 and CD15 chimerism at day 365 were 98% and 100%. The incidence of acute GVHD was 60% (grade III-IV 9%); overall chronic GVHD rate was 33% (moderate 14%, severe 7%). The incidence of venous occlusive disease (VOD) was 7%, no VOD-deaths were recorded. The cumulative incidence of relapse was 20%. Flow cytometry minimal residual disease (MRD) was positive in 28 patients at the time of HSCT and did not affect the OS. There was no significant difference in OS when patients were stratified according to age (Figure 1B)

even if there is a non-significant trend for patients younger than 55.
Age at HSCT did not influence NRM but was higher in patients with higher HCT-CI: 10% vs. 43% if HCT-CI was <2 and ≥2 respectively (p 0.04). Two years OS for patients aged ≥55 and with HCTI-CI <2 and for those with HCTI-CI ≥2 were 63% (median OS not reached in this group) and 45% respectively. Three years OS was 57% and 42% respectively. Two years GRFS for patients aged ≥55 and with HCTI-CI <2 and for those with HCTI-CI ≥2 were 46% and 20% respectively.
This analysis supports the feasibility of FB4 conditioning in patients affected with AML and MDS regardless of age. The decision for myeloablation should rely on comorbidities and disease characteristics rather than chronological age, especially for those with positive MRD at time of HSCT.
Disclosure of Interest: None Declared.

BSH22-PO116 | Use of a foamy-virus vector system to produce an 'off-the-shelf' anti-CD19 CAR T-cell product

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Abstract Content: Introduction: Anti-CD19 chimeric antigen receptor (CAR) T cells have transformed the field of cancer immunotherapy. Current CAR T cell trials use autologous cells, with several limitations (prolonged production time, costly, manufacturing failure), whereas the Lentiviral vectors (LV), used for commercial products, are endowed with extra limitations (packaging limits and mutagenesis risk). Our group has developed an in-house anti-CD19 CAR-T cell product, using a safer to LV, foamy virus vector (FV).
Materials and Methods: We constructed FV vectors expressing the anti-CD19 CAR and eGFP from an EFP1 and IRES2 promoter respectively. second-generation LV vector backbones were purchased from a commercial vendor. Peripheral blood from healthy individuals and cord blood (CB) were used as T-cell sources. T cells were activated by anti-CD3/CD28 beads and transduced with antiCD19 CAR-T, LV or FV vectors. Transduction efficiency was assayed by flow cytometry (FCM) using either an anti-protein L antibody or recombinant CD19 protein. FV and LV CAR-T cells were expanded with a modified Rapid Expansion Protocol (REP). Immunophenotypic analysis of CAR T cells was performed by flow cytometry. Their cytotoxic effect was evaluated against the CD19+ Raji and Daudi cell lines and against the CD19-cell line, HL60. Cytotoxicity was assessed by flow cytometry and calculated as: [1-live targets (sample)/live targets (control)] × 100. CAR-T cell activation was also assayed by INF-γ ELISA.
Results: LV and FV vector titres were between 3–5 × 10^5 TU/ml and 4–5 × 10^5 TU/ml, respectively, regardless of the presence of the eGFP cassette. Transduction efficiency ranged from 45 to 83% at MOI 3–5 with FV vectors and was comparable to the transduction efficiency of LV vectors at a much higher MOI (10–20). Following REP, the vast majority of cells consisted of CAR T cells, regardless of the vector used or the T-cell source and isolation method. Immunophenotypic analysis of CAR T cells revealed a central memory phenotype (CD45RO+/CD45RA-/CCR7+), (>99% cells). For cytotoxicity assays, CAR T cells were incubated with CFSE-labelled Raji and/or Daudi cells at different ratios (5:1, 10:1) for 18 h. At the end of the incubation period, the % cell lysis was 87.3 (SD 6.38) and 92.4 (SD 3.2) at 5:1 and 10:1 ratio respectively (n = 3). Similar results were obtained for LV vectors. When CD19- HL60 cells were used as targets, no/minimal lysis was noted, indicating a specific anti-CD19 cytolytic effect of CAR T cells. IFN-γ levels were measured at the end of the co-culture period in the supernatant to assess CAR T-cell activation. Results showed a significant increase both in the FV- and LV- CAR T cells, compared to untransduced cells (mean 890.2 and 3141 pg/ml and 1553 and 2225 pg/ml for FV- and LV- CAR T cells, in ratios 5:1 and 10:1 respectively).
Conclusion: Our group has developed for the first time a FV vector for anti-CD19 CAR T cell production, with an efficient gene transfer to human T cells and with potent *in vitro* cytotoxic properties, similar to their LV-derived counterpart. Overall, we provide a proof of concept that allogeneic, in-house CAR T cells derived from a non-patented viral backbone such as the FV, could be a safe, efficient and affordable alternative to LV-derived vectors for immunotherapy.
Disclosure of Interest: None Declared.

BSH22-PO117 | Burden of Cardiac Late Effects Following Stem Cell Transplantation—Real-World Data from the South Wales Blood and Marrow Transplantation Programme

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Abstract Content: Cardiovascular (CV) complications post stem cell transplantation (SCT) are a well-recognised entity worldwide. Many of these complications present late on post SCT when some irreversible damage may have occurred. International consensus guidelines (BBMT 2012) recommend screening for high-risk patients at baseline prior to SCT, to allow for earlier diagnosis, intervention and improved outcomes. To assess the number of patients at risk of developing CV complications, we retrospectively analysed data from a single centre (University Hospital of Wales,

Abstract Table:

	Allogenic SCT *N* = (%)	Autologous SCT *N* = (%)
Total number (*N* = 178)	108	70
Median age at Day 0 (range)	52 (68–20)	57 (73–19)
Sex (male/female)	55/53	47/23
Disease Group		
Myeloid neoplasms	62 (57%)	1 (1%)
Lymphoid neoplasms	39 (36%)	31 (44%)
Plasma cell disorder	2 (2%)	38 (54%)
Others	5 (5%)	0 (0%)
Cardiovascular risk factors	26 (24%)	28 (40%)
Prior Anthracycline	84 (78%)	30 (43%)
Radiotherapy (mediastinal/TBI)	26 (24%)	11 (16%)
Median EF pre-SCT	55%	55%
Median EF post-SCT	50%	50%
Median time to repeat echo post-SCT (Range)	1.5 (0.5–7) Years	4 (1–7) Years
Borderline or Impaired EF pre-SCT	33 (31%)	16 (23%)
EF > 50% pre-SCT	75 (69%)	54 (77%)
Patient survived to post transplant with repeat Echo with drop in EF < 50%	9/46 (20%)	5/29 (17%)
Symptomatic patients required Cardiology referral:		
In normal EF pre-SCT	6/9 (67%)	8/10 (80%)
In impaired EF pre-SCT	4/9 (44%)	5/9 (56%)

Cardiff), between 2011 and 2013, which included 178 SCT recipients (allogenic and autologous).

Pretreatment CV risk factors assessed included hypertension, diabetes and dyslipidaemia. Among the allogeneic (allo) and autologous (auto) groups, 24% and 40%, respectively, had one or more risk factors prior to SCT. It is established that anthracycline therapy and chest radiation are major risk factors for CV complications post SCT. We found, (allo vs. auto 78 vs. 43%) had prior anthracycline therapy, while (24% vs. 16%) had prior radiotherapy (mediastinal or TBI). The median age at SCT across both groups (52 years vs. 57 years). Within the allo-SCT group 33 out of 108 (31%) had borderline or impaired EF prior to SCT. Of the 33, nine (27%) had an impaired EF (defined as EF <50%), of which only five survived to 1-year post SCT and four out of nine had a fall in EF causing symptoms requiring cardiology input. Similarly, nine out of 46 (20%) of those with a normal EF prior to SCT and who survived to 1-year post-SCT had a drop in EF to <50%. Of these nine, six became symptomatic requiring cardiology input. This highlights the importance of regular CV imaging during and post-SCT. The median time for repeat echo post-allo-SCT was 1.5 (0.5–7) years (Table 1).

Within the auto group, a borderline or impaired EF noted in 16/70 (23%) prior to SCT. Of these 16, nine survived to have a follow-up echo (median time 4 [1–7] years) Table 1, five became symptomatic requiring cardiology input. A normal EF pre-SCT was observed in 54/70 (77%) auto patients, 29 out of 54 (54%) had repeat echo post-transplant with 10 (34%) showing a drop in EF (5 had EF <50%), and five patients developed arrhythmias or valvular disease. Eight (80%) patients become symptomatic and required cardiac intervention.

In conclusion, this retrospective analysis reports a high burden of CV complications in both allo- and auto-transplant recipients. We highlight the importance of a structured, robust late effects follow-up for all transplant recipients to recognise and promptly manage cardiovascular complications particularly in those with recognised risk factors. Furthermore, local studies are ongoing to evaluate alternative measures of cardiac function to better predict patients who require early intervention or may benefit from protective cardiac medication. Newer imaging techniques within echocardiography which are more accurate and reproducible such as 3d volume measurement and GLS (Global Longitudinal Strain) which have been utilised in emerging subspecialty of cardio-oncology may show benefit in future.

Disclosure of Interest: None Declared.

NURSING

BSH22-PO118 | The future of Outpatient Haematology: Self Supported Follow-up (SSFU) for patients with Chronic Lymphocytic Leukaemia (CLL) and Monoclonal Gammopathy of Undetermined Significance (MGUS)—An online Portal audit

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Abstract Content: The primary aim of face to face follow-up is to recognise early disease relapse or progression and to identify physical or psychological concerns, the latter often being overlooked during increasingly busy clinics. Due to advances in diagnostics and treatments, current follow-up models are proving unsustainable, with most haematological conditions now requiring long-term follow-up.

St Helens & Knowsley NHS Trust (STHK) became a pilot site to utilise 'My Medical Records' (MMR) within haematology, having already proved successful across other solid tumour sites. MMR is an online portal that can be accessed by both patients and the haematology team. Patients with Stage A CLL and MGUS were identified and enrolled onto the online portal after attending an initial education workshop. The workshop aims to empower patients to self-manage; emphasis is

placed on self-examination with the need to report any red flag symptoms and psychological concerns via an online health questionnaire. When a patient raises a concern, either physical or psychological, they are contacted by a haematology cancer support worker. After attending phlebotomy patients are able log on to MMR to access their own blood results and can message the team with any concerns. Blood results are checked for evidence of progression by a haematology clinical nurse specialist. If no concerns are identified then the patient remains on SSFU without the need to attend hospital, in turn freeing up a consultant-led clinic slot. If there is any suspicion of disease progression patients are invited to attend a face to face clinic appointment in a consultant or nurse clinician led clinic.

An audit was undertaken 12 months post implementation of SSFU at STHK, to assess the safety and effectiveness of the model. In addition, patient experience and satisfaction were assessed using patient surveys and interviews. Within the audited 12 months 258 patients had been enrolled to SSFU. During this time there were 17 patients suspended from SSFU and moved back to consultant led care due to suspected disease progression. All of the suspensions were appropriate with no missed opportunities and with no delays to diagnostics or treatment. Seven patients died during the audited timeframe, but none of these were due to their underlying haematological condition.

From the surveys and interviews, patients concluded that SSFU is an acceptable form of follow-up, saving them time off work and hospital parking fees. Users reported confidence in being able to access the haematology team when they had a concern.

In conclusion, our audit into the use of SSFU and MMR has proven to be a safe and effective follow-up model in patients with both CLL and MGUS. Patients can successfully report symptoms suggestive of disease progression and self-supported follow-up can free up valuable face to face clinic slots for clinicians. In addition to saving face to face clinic slots, the model promotes self-management and empowerment for patients. The online health questionnaire provides additional regular holistic needs assessment, something that is often overlooked in a busy clinic setting.

With cancer numbers predicted to increase significantly over the next couple of decades SSFU is a model that can help with capacity and demand issues. We believe that there is potential for this model to be rolled out to other conditions such as ITP and Lymphoma.

Disclosure of Interest: None Declared.

BSH22-PO119 | Developing the first pan-UK multiprofessional guideline for perioperative management of anaemia

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Abstract Content: A third of people undergoing major surgery have anaemia. Patients with anaemia have worse outcomes from surgery.[1] Anaemia is often diagnosed late in the surgical pathway and management is inconsistent. Where patients are optimised for surgery, they have fewer complications, a shorter length of stay and higher satisfaction.

Many patients do not get a gold standard approach despite a decade of literature on Patient Blood Management (PBM). Many published guidelines are specialty specific. The Centre for Perioperative Care (CPOC) aimed to create a new multiprofessional guideline for perioperative patients (from the moment an operation is contemplated until full recovery).

A wide-ranging working group was convened with representation from nursing, operating department practitioners, surgery, anaesthesia, pharmacy, obstetrics, haematology and patients. This crystallised core concepts, allowing a guideline to be produced covering all surgery, including emergency and elective surgery and for all ages from neonates to advanced years. A literature review was undertaken. Other standards and examples of good practice, including international, were collated. For patients undergoing surgery with a risk of blood loss of over 500 ml or 10% of blood volume, an active PBM plan is recommended. For others, general health optimisation advice is given.

Abstract Table:

Useful to:	Example of information in www.cpoc.org.uk perioperative Anaemia guideline
Hospital management	Anaemia should be identified early, its cause diagnosed and management planned.
All staff	In one out of three of men and postmenopausal women with Iron deficiency, a gastrointestinal cause is found—referral to gastroenterology is welcomed [3].
All staff	Functional iron deficiency (associated with chronic disease) is a marker of ill-health and a patient requiring senior clinician input.
All staff	Consider ways to identify and manage anaemia—e.g. nutritional info; if testing renal function before a CT scan also test for anaemia, etc.
Public	Nutritional deficiencies (iron/B12) are common. Supplements contain 14 mg elemental iron (far less than treatment dose).
Preassessment nurses	Patients can buy oral iron treatment (100–200 mg daily) over the counter from pharmacies removing the need for a prescription.
Operating theatre staff	Tranexamic acid and other strategies to minimise blood loss should be considered.
Postop therapy	Mobilise as symptoms allow. Work with prehabilitation services, for preop optimisation.

The CPOC ethos involves pathways, empowering all staff, standardisation and harmonisation wherever possible, agreed expectations and clear red flags where a patient requires individualised care. For some patients, surgery should be delayed to optimise anaemia. For others, preoperative transfusion has a place. Patients with complex medial issues benefit from medical assessment and optimisation. A Shared Decision Making (SDM) approach formalises individual discussion considering Benefits, Risks and Alternatives to surgery and a 'doing Nothing' option (BRAN). At age 65, 50% of UK adults have multiple co-morbidities. Half the patients undergoing an operation requiring anaesthesia and/or admission in the UK are aged 65 or over,[2] in both emergency and elective settings, and most would benefit from medical review and optimisation.

Despite the complexity of the biology of anaemia, it was possible to write clear guidance that can be applied by all staff in all cases, with an educational package. Algorithms developed help all staff plan care. Highlighting the association between functional iron deficiency and long-term disease encourages more intense medical input for such patients.

Defining clear standards, such as the early identification of anaemia, investigation of its cause and delivery of standard treatments, allows individual hospitals to improve services. The guidance includes general concepts and specific detail. The large stakeholder group allowed messages and education to be re-packaged from one discipline to others where they were less well known (examples in Table 1).

The work highlights the poor awareness of anaemia, dietary insufficiencies and absorption problems (such as coeliac disease) among the public and health professionals. Patient-facing information can be used to support staff to empower patients. Coherent messages across pathways and professions should improve general health.

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Disclosure of Interest: S. McNally: None Declared, C. Frank: None Declared, H. R. Qureshi: None Declared, C. R. Evans Conflict with: Prev NIAA/NIHR grant holder for anaemia research., Conflict with: Honoraria Pharmacosmos, Pfizer, S. Evans: None Declared, L. Blood: None Declared, V. Padmanabhan: None Declared, N. Roy: None Declared, J. Tam: None Declared, A. Patel: None Declared, F. Sear: None Declared, M. Donnellon: None Declared, J. Holland: None Declared, N. Bhala: None Declared, J. Dhesi: None Declared.

BSH22-PO120 | Pharmacist and physicians associate led Myeloproliferative neoplasm clinics

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Abstract Content: The myeloproliferative neoplasm (MPN) clinics have traditionally been delivered by medical staff and haematology specialist nurses. However, there have been increased pressures experienced by the medical workforce with 8% locums at the haematology consultant level nationally, increased number of retirements and increased numbers of less than full-time consultants. There have also been improvements in treatment for chronic myeloid leukaemia (CML) and Myeloproliferative neoplasms (MPN). This has led to a large unsustainable number of patients in the MPN medical clinics. To help resolve this issue, Sheffield Teaching Hospital NHS trust have invested in pharmacists and Physicians associates to run CML and MPN clinics independently.

Pharmacists have been utilised to run the CML clinics since 2020. Pharmacist oversee the monitoring of BCR::ABL1 monitoring, Tyrosine kinase inhibitor prescribing and consenting for initiation of Treatment free remission (TFR) in CML. They review patients who have achieved a Major molecular response (MMR) or are in a TFR. The pharmacists have developed standard operating procedures for CML clinics and attend the haematology MDT. The physician associates (PA) have run the MPN clinic since 2019. PA have developed SOPs incorporating the MPN 10 score and arranged venesections independently for PRV and liaise with medical staff for MPN related prescriptions.

At present, there are 82 patients with CML under regular follow-up. Forty-six (56%) are reviewed in the pharmacist-led

clinic. The pharmacy team has also initiated 11 patients for TFR, with only 1 patient losing Major molecular response (MMR). There has been an improvement with respect to patient adherence with medication, monitoring of drug–drug interactions, appropriate initiation of statin in high QRISK three patients and compliance with BCSH CML guidelines. There are 176 patients in the Sheffield MPN clinics, with 63 (35%) reviewed in the PA-led clinic and 46 (26%) patients reviewed in the nurse-led clinic. The PAs have 100% compliance with MPN 10 score evaluations.

The Sheffield MPN and CML service have used a sustainable long-term model of utilising the skills of pharmacists and PAs to deliver clinics safely and efficiently. They adhere to BCSH guidelines and follow SOPs. Greater than 50% of patients are now reviewed by non-medical staff in the MPN and CML clinic. This has resulted in improved patient feedback and allows care to be delivered in a clinical governance-approved framework.

Disclosure of Interest: None Declared.

BSH22-PO121 | 'Just one thing'—what would myeloma patients change about their treatment and care?

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Abstract Content: Ensuring patients with cancer have the best possible experience throughout their treatment and care has long been central to National Health Service (NHS) strategy, with patient-centred services that are responsive to individual needs. The Clinical Service Excellence Programme (CSEP) is a best practice initiative in myeloma, designed to support hospitals in delivering optimum care to myeloma patients. As part of the CSEP assessment process, feedback is gathered from myeloma patients using a patient experience survey which includes the question 'If you could change one thing about your myeloma treatment and care, what would it be?' The responses to this question highlight the areas of improvement that would positively impact patients' experience of care and the process supports hospital teams in seeking feedback and anonymous data gathering. The survey results can positively contribute to resource planning and service development, demonstrating a process that is dynamically responsive to patient feedback. The survey is repeated when a hospital undertakes CSEP reaccreditation, providing a mechanism to measure improvements to patient experience.

Between 2015 and 2021, survey comments were submitted by patients from 38 CSEP accredited hospitals. Of the 585 total comments, 196 gave constructive or negative feedback. Not all respondents answered the free text comment question, and some hospitals only received positive feedback. The 196 comments were thematically organised into nine categories: communication, continuity of care, coordination of care, holistic treatment, hospital facilities, travel, treatment options, waiting time and miscellaneous. These nine themes highlight both systemic logistical problems within the NHS (waiting time, hospital facilities, travel to access treatment and care) and individual concerns of patients over their relationship with healthcare providers (communication) or personal well-being (holistic treatment). One theme (continuity of care) involves both.

This analysis indicates the key areas of change important to patients. Waiting times across different departments were the key concern for patients, reflecting the increased volume of myeloma patients attending clinics as survival rates increase and patients stay on treatment for longer. While most of these comments predate the pandemic, it will be of interest to gauge if remote appointments remain impacted by waiting times. Other common concerns highlight the importance of good communication, continuity of care and being treated holistically; all of which have significance in myeloma, a disease that requires ongoing close management. Collectively these results improve understanding of myeloma patients' overall experience and what matters most to them within their care.

Disclosure of Interest: None Declared.

BSH22-PO122 | Disease Knowledge in Adolescents and Young Adults with Sickle Cell Disease in a Low Resource Setting

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Abstract Content: Sickle cell disease (SCD) is a common form of blood disorder that is found mainly in Africa, the Middle East, and in people of African descent. Many people with sickle cell disease suffer from various complications such as gallstones, acute chest syndrome and high blood pressure, leading to frequent hospitalisations. SCD is a lifelong condition which requires long-term management and care. As children with SCD reach adolescence, they increasingly take responsibility for managing their conditions and thus need to have a good level of knowledge about their condition. The aim of this study was to assess the disease knowledge levels of adolescents and young adults with sickle disease within the context of a low-resource setting and examine its relationship with the number of hospitalisations and sociodemographical factors. A cross-sectional and observational approach was taken for this study. Adolescents and young adults aged 14 to 24 years attending routine consultations at the Integrated Care Centre for Children and Pregnant women with SCD and the Hematology unit of the University Hospital in Benin, were invited to complete a questionnaire. We used a locally developed

questionnaire to assess SCD knowledge. Furthermore, we collected information on, number of annual hospitalisations, healthcare utilisation, frequency of occurrence of painful episodes and sociodemographical factors. Regression analysis was used to examine the relationship between SCD knowledge, number of hospitalisations and socio-demographical characteristics. The study is ongoing, and we aim to include at least 105 adolescents and young adults with SCD. To date, a total of 48 adolescents and young adults with SCD have been recruited for the study. Half of the participants are male (n = 24; 50%). Few participants demonstrated good SCD knowledge (N = 10; 21%) answering correctly over 70 percent of the questions. No associations were found between SCD knowledge and the frequency of hospitalisations. Significant associations however were found between SCD knowledge and age. The disease knowledge levels of adolescents and young adults with SCD is sub optimal. This provides an indication on the need for healthcare practitioners to pay more attention to particularly younger patients. This study provides baseline information upon which future initiatives targeting the overall improvement of the knowledge levels of adolescents and young adults with SCD in a low resource context.

Disclosure of Interest: None Declared.

PAEDIATRIC

BSH22-PO123 | What is the diagnostic yield of bone marrow aspiration to exclude leukaemia prior to systemic treatment in juvenile idiopathic arthritis?

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Abstract Content: Juvenile idiopathic arthritis (JIA) is a common, potentially life-threatening inflammatory disorder of childhood. The clinical symptoms and signs overlap with those of acute leukaemia, and there are reports of acute leukaemia mimicking JIA at presentation. Therefore, clinicians are reluctant to start systemic therapy for JIA without ruling out a diagnosis of leukaemia with a bone marrow aspirate (BMA). There is, however, little evidence available to support a need for routine BMA to rule out leukaemia in children presenting with symptoms of JIA.

To answer this question, we conducted a single-centre retrospective review of all patients attending our hospital with a diagnosis of JIA, over a 5-year period. Of 1174 patients, 52 (4.4%) had a BMA due to a systemic presentation and concerns about possible malignancy. Only one patient was found to have leukaemia. As with previous studies, clinical features not helpful in predicting leukaemia were organomegaly (~54%) and lymphadenopathy (~60%) as these were common in those with JIA. Cytopenias (defined as haemoglobin <100 g/l, white cell count <4 × 10^9/l or neutrophil count <1 × 10^9/l, platelets <100 × 10^9/l) were helpful in differentiating between leukaemia and those with an ultimate diagnosis of JIA. The majority of JIA patients had a single cytopenia (29/48), predominantly anaemia, but only the single patient with leukaemia had pancytopenia. A second BMA was undertaken in ~15% of patients but similarly was of no further utility in detecting leukaemia.

In order to systematically investigate the presenting features of leukaemia when investigated in our hospital for any reason, we also examined all BMAs conducted over a 5-year period (4539 procedures in 1574 patients). We excluded those with an established oncological diagnosis, or a blood film suggestive of leukaemia. Of 357 remaining patients who underwent a BMA. none with a single cytopenia were subsequently diagnosed with leukaemia. However, bicytopenia and pancytopenia enriched for leukaemia: respectively, 9% and 20% of patients investigated for these were ultimately diagnosed with a malignancy. All five out of five patients with intractable bone pain, and 30% of patients with abnormal marrow signal on magnetic resonance imaging (MRI) had an eventual leukaemia diagnosis. No patient (n = 39) whose primary indication for a BMA was to rule-out leukaemia had leukaemia, and the majority (36/39) were found to have a rheumatological diagnosis.

This study is the first to investigate the routine use of BMA in JIA to exclude leukaemia, and to identify features which increase a pretest probability of leukaemia such that a BMA might be indicated. Our data suggest that presenting features of JIA are unlikely to be associated with leukaemia unless the following factors are present: two or more cytopenias, intractable bone pain, or abnormal marrow signal on MRI. Our data, therefore, suggest that BMA should not be routinely performed for symptoms of JIA alone, but should be considered where these additional clinical features are present.

Disclosure of Interest: None Declared.

BSH22-PO124 | Aberrant expression of lncRNA 'leukaemia-induced non-coding activator RNA' predicts poor Outcome in Childhood T-Acute Lymphoblastic Leukaemia

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Abstract Content: Background: T-cell acute lymphoblastic leukaemia (T-ALL) is considered to be one of the most aggressive forms. It accounts for around 15% of all paediatric leukaemia's. Unfortunately, it is associated with unfavourable clinical characteristics, such as central nervous system infiltration and a significant chance of developing

drug resistant. Nowadays, the prognosis for (T-ALL) has improved as a result of both the discovery of new molecular diagnostics and the development of medication that targets specific locations. Of the genetic alterations that have been identified in T-ALL, the NOTCH1 gene mutation is the most significant. Genetic mutations in the NOTCH pathway, are associated with a poorer prognosis in patients with Minimal Residual Disease (MRD). As a result, anti-NOTCH1 immunotherapy has the potential to be effective in the molecular elimination of the disease.

Nucleic acids known as non-coding RNAs (ncRNAs) are ribonucleic acids that do not encode proteins and are produced via transcription from the genome. In this study, it was demonstrated that the leukaemia-induced non-coding activator RNA (LUNAR1) 'long non-coding RNA' responsible for the oncogenic regulation of NOTCH1, which promotes the proliferation of T-ALL cells by elevating the insulin-like growth factor receptor 1 (IGF-1R), which maintains both the expression of mRNA and the transmission of IGF1 signals. In addition, LUNAR1 works as an enhancer of RNA (eRNA) by interacting with the complex mediator on the IGF1-R promoter, triggering the transcription mechanism of the IGF1-R promoter through direct targeting of the NOTCH1 gene, as previously described.

Objectives: On the basis of these data, it has been hypothesised that LUNAR1 plays a critical role in the pathogenesis of T-ALL. However, there has been no investigation of the degree of LUNAR1 expression and its predictive significance in paediatric T-ALL. With this study, we wanted to look at the predictive value of LUNAR1 in paediatric T-ALL, as well as its association with NOTCH1 and IGF-1R.

Methods: The expression of the LUNAR1, NOTCH1 and IGF-IR genes in peripheral blood (PB) samples from l85 children with T-ALL and 40 non-leukaemic samples served as a control group. The results were analysed using RT-PCR.

Results: The expression levels of LUNAR1 and NOTCH1 genes were higher by three folds in T-ALL patient samples; however, IGF-1R showed twofolds' increase. Moreover, higher expression levels were significantly associated with advanced stage and poor disease outcome. The results of a Cox regression analysis revealed that overexpression of LUNAR1, NOTCH1 and IGF-IR was strongly associated with a poor prognosis, a short overall survival time and a short progression-free survival time in cancer patients.

Conclusion: We came to the conclusion that LUNAR1 could be used as an independent predictive biomarker in children with T-ALL. In the current study, we provided evidence that LUNAR1 is an independent predictor of poor outcomes in paediatric T-ALL patients, which was previously unknown.

Disclosure of Interest: None Declared.

BSH22-PO125 | National protocol required for consistent transfusion duration in patients having regular tranfusion? Resulrs from a national survey and recommendations

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Abstract Content: Red cell transfusion administration is a routine and frequent procedure for many paediatric patients with haematological malignancies and haemoglobinopathies. However, frequent transfusion requirements can take several hours and impact the quality of life for patients and disrupt school attendance for paediatric patients. Audit from large adult haematology units have demonstrated that it is safe to administer blood in adult patients without underlying heart condition with the rate of one unit per hour; and this policy is currently adopted in many centres in order to reduce time for transfusion for adult patients.

With this work, we aimed to evaluate the current transfusion practice in tertiary paediatric haematology We designed a national survey which was distributed to all 20 major paediatric haematology tertiary centres. Eligibility criteria for patients included oncology and haemoglobinopathy patients receiving frequent tranfusions. 13 out of 20 centres responded to the survey. Results identified that 60% of centres did give 5 ml/kg/h tranfsusion but nine out of 13 gave a maximum transfusion rate of 150 ml/h with each unit going over a minimum of 2 h. These results showed that despite an adult practice in many centres showing that 5 ml/kg/h tranfusion is safe most paediatric centres were still giving one unit of blood over 2 h, regardless of weight and even in patients over 30 kg. This has implications for those older patients requiring 3 units as the transfusion would take 6 rather than 3 h which has an impact on tme in day care.

Overall, this national paediatric audit demonstrates that a routine red cell transfusion at a rate of 5mls/kg/hr is generally up to 30 kg and a maximum rate of 150 ml/he is given in most centres regardless of weight. However, adult practice has shown that a maximum rate of one unit/hour in patients without a risk of circulatory overload or history of transfusion reaction is a safe practice. This should be adopted in the paediatric setting at a national level in order to reduce the duration in hospital for patients require frequent red cell transfusions.

Disclosure of Interest: None Declared.

BSH22-PO126 | Need to contextualise the fight against sickle cell disease in regions with limited resources: The case of the Democratic Republic of the Congo

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Abstract Content: Background: Sickle cell disease (SCD) is a public health problem resulting from a genetic defect that leads to the body's synthesis of abnormal haemoglobin responsible of erythrocyte dysmorphism and dysfunction. The African continent is full of more than ¾ of the patients counted throughout the world. WHO-recommended control strategies include screening, case management and genetic counselling. The objective of this study was to analyse the level of application of the screening strategy in countries with limited resources and to propose alternative strategies.
Method: A descriptive cross-sectional study was carried out in paediatric hospital setting in the city of Kindu in the Democratic Republic of the Congo. Systematic screening for SCD was performed on all children under five admitted to five targeted health facilities between December 2019 and October 2020. This study was followed by a review of the literature on sickle cell screening.
Result: The cross-sectional study showed that the hospital prevalence of SCD in children under 5 years of age was 31.9% of which 12.7% were in the homozygous form SS and 19.2% were sickle cell trait. The clinical suspicion of SCD before screening was 6% and not consistent with the results of the biological screening (p = 0.31). Certain characteristics of children with SCD were statistically associated with sickle cell status. These are age, family history of SCD, transfusion history, recurrent anaemia, painful manifestations, undernutrition, frontal lumps, conjunctival jaundice, cervical lymphadenopathy, hepatomegaly and splenomegaly.
The literature review that screening of SCD in less well-off countries is not systematic. It is carried out on an ad hoc basis during scientific surveys. The geographical, technical and financial accessibility to standard diagnostic means and the poor knowledge of the disease by health professionals limit the early detection of SCD as wanted by WHO.
Conclusion: The burden of SCD in resource-limited hospitals is underestimated due to the lack of a routine screening programme. This negatively interferes with the optimal care of sick children. Raising awareness among healthcare professionals of the suspicion of SCD, setting up a predictive clinical score for sickle cell status and applying provider-initiated screening to suspected cases are temporary alternatives to be implemented. to increase screening for sickle cell disease pending the concrete systematisation of neonatal screening of SCD in countries with limited resources. Rapid diagnostic tests are the preferred biological means to circumvent the difficulties associated with standard diagnostic means.
Disclosure of Interest: None Declared.

BSH22-PO127 | Appraisal of quality of life and assessment of factors influencing quality of life in transfusion-dependent beta thalassaemia—A cross-sectional study

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Abstract Content: Beta thalassaemia major is one of the most significant inherited disorders of haemoglobin production caused by monogenic defects in the adult beta globin gene. It is more prevalent in the Mediterranean region, Sub-Saharan Africa, South east Asia and Middle eastern countries. However, due to ever increasing globalisation, in recent years, beta thalassaemia has emerged as a significant health problem in western countries including the United Kingdom.
Beta thalassaemia major has become a chronic disease, with the majority of patients being managed with lifelong regular red cell transfusion support and iron chelation therapy, despite the introduction of potentially curative options like stem cell transplantation and gene therapy in recent years.
As with any chronic disease, it has a sizeable impact on all facets of life, including physical, mental, social and academic domains of the affected individual and their family members. In this cross-sectional study, we aim to determine the quality of life and describe the factors that are associated with a poor quality of life in children with transfusion-dependent beta thalassaemia. We also describe the perspective of the patients and their carers on the different treatment options available at present and their major concerns about the modern curative treatment options; namely stem cell transplant and gene therapy.
The study cohort included all transfusion-dependent beta thalassaemia patients aged less than 17 years of age registered in our haemoglobinopathy service. Clinical, demographical and laboratory data were collected using an interviewer administered questionnaire and validated disease-specific quality of life questionnaire, Transfusion-dependent Quality of Life (TranQoL), from both patients and their parents or carers. The data obtained were analysed using SPSS software.
A total of 38 transfusion-dependent thalassaemia patients were recruited into the study. 52% of them were male and the mean age was seven years and 5 months. The overall Quality of Life (QOL) score for the patients and the parents were 88.2% and 77.45% respectively. The study suggests that the academic and professional domains were most affected. The mean quality of life scores of the patients and their parents were significantly lower in the poorly iron chelated group (mean annual ferritin >1500 mcg/l) than the ones with optimal chelation ($p < 0.05$). The other factors that were associated with poor QoL were large family size (greater than 4 members) and the presence of siblings with transfusion-dependent thalassaemia.
31.5% of patients and family prefer stem cell transplantation over a conventional transfusion programme as a potential treatment option. The major concern about stem cell transplantation amongst the rest of the patients was infertility

after the transplant. 10.5% of patients preferred gene therapy over other modalities of treatment.
Overall, appraising quality of life using a validated tool such as this and understanding the factors influencing quality of life can help clinicians to facilitate a holistic care in chronic diseases such as thalassaemia.
Disclosure of Interest: None.

BSH22-PO128 | Combining pharmacokinetics and comprehensive evaluation system to individualise the prophylaxis in paediatric patients with haemophilia A

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Abstract Content: Background: Prophylaxis is the standard treatment for haemophilia A (HA). Due to the inter-individual variability of pharmacokinetics (PK), bleeding phenotype and joint vulnerability, individualised prophylactic protocol are vital to optimise the therapy of HA.
Objective: To investigate the clinical outcomes of the new proposed PK-guided dosing strategy which combined the comprehensive evaluation system for escalation.
Methods: Patients with severe HA and without FVIII inhibitor were enrolled. After a 72 h washout period and a single-dose infusion of 50 IU/kg of their routine used FVIII concentrate, each one received a PK test with a 5-point design. The trough levels were calculated by WAPPS-Hemo. The bleeding rates (ABR, annualised bleeding rate; AJBR, annualised joint bleeding rate) were estimated from 6 months before enrolment to the study exit. The ultrasound and HJHS were used to evaluate the patients' joints (both sides of ankles, knees and elbows) at every 12 months. The escalation criteria depended on joint bleeds, US scores and HJHS scores. Their quality of life was assessed by CHOKLAT sheets. The yearly FVIII consumption and infusions were calculated according to the prophylactic record of patients.
Results: Fifty-eight severe HA boys who had an observational period over 2 years were analysed. Their age and body weight

Abstract Table:

	Baseline	0–6 M	6–12 M	12–18 M	18–24 M
ABR					
Median (interquartile range)	4 (0,8)	2 (0,4)	2 (0,4)	0 (0,4)	0 (0,2)
Mean (range)	5.09 (0–40)	3.02 (0–14)	2.57 (0–16)	1.76 (0–8)	1.1 (0–6)
p value		<0.05	<0.01	<0.0001	<0.0001
AJBR					
Median (interquartile range)	2 (0,4)	0 (0,2)	0 (0,2)	0 (0,2)	0 (0,0.25)
Mean (range)	2.68 (0–26)	1.25 (0–12)	1.13 (0–12)	1.0 (0–8)	0.67 (0–6)
p value		<0.05	<0.01	<0.001	<0.0001
ZBR					
number (proportion)	16 (27.6%)	28 (48.3%)	29 (50%)	35 (60.3%)	40 (69.0%)
ZJBR					
number (proportion)	27 (46.5%)	37 (63.8%)	42 (72.4%)	41 (70.6%)	47 (81.3%)
	Baseline		**12 M**		**24 M**
US scores					
Median (interquartile range)	2 (1,5)		2 (1,5)		1.75 (1,5)
Mean (range)	4.04 (0–22)		3.69 (0–18)		3.39 (0–18)
p value			0.15		<0.05
HJHS scores					
Median (interquartile range)	0.5 (0,4.5)		0 (0,3)		0 (0,2.25)
Mean (range)	2.5 (0–9)		2.03 (0–10)		1.55 (0–10)
p value			0.11		<0.05

Abbreviations: ABR, annualised bleeding rate; AJBR, annualised joint bleeding rate; ZBR, zero bleeding rate; ZJBR, zero joint bleeding rate; US, ultrasound; HJHS, haemophilia joint health score.

was 5.3 (2.8,6.9) years and 21.5 (16,25) kg respectively. At baseline, 34 of them had a trough level of <1 IU/dl and seven target joints were detected according to previous definition. During the study period, 47 escalations were observed. Joint bleeds count the most proportion (48.3%, $N = 28$). Significantly reduced ABR [0 (0,6) vs. 4 (0,8),$p < 0.0001$] and AJBR [0 (0,0.25) vs. 0 (0,2),$p < 0.0001$] was observed at study exit as well as the trend of decreased bleeding rates as the study progressed. Also, 85% (6/7) of the target joints vanished during the study. Statistical improvement of US scores ($p = 0.04$) and HJHS scores ($p = 0.02$) was also reported at the study exit. The median annual weight-adjusted FVIII consumption and infusions were 3500 IU/kg/year and 156 times/year finally.

Conclusion: This newly proposed PK-guided dosing strategy could reduce bleeding rates, eliminate target joints and improve impaired joints, which has the potential to be an optimal prophylactic protocol for more individualised therapy.

Disclosure of Interest: None Declared.

BSH22-PO129 | Thrombopoietin receptor agonists for treatment of new and relapsed immune thrombocytopenia in children—A single-centre experience

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Abstract Content: Immune thrombocytopenia (ITP) is the most common bleeding disorder in paediatrics. ITP is usually a self-limiting disorder; however, it can be associated with significant and life-threatening bleeding. Outside the context of the COVID-19 pandemic, the first-line treatment for newly diagnosed or relapsed ITP is corticosteroids or intravenous immunoglobulin (IVIg). Treatment of ITP in the COVID-19 era became more challenging due to the shortage of IVIg, the continuous fear of immunosuppression, and the need for hospital contact. Because of these additional burdens, NHS England established a rapid policy in February 2021 to aid clinicians in offering the best care and advice to ITP patients. This policy recommended the use of thrombopoietin receptor agonists (TPO RAs) as first-line therapy for new or relapsed ITP in adults and children over the age of 1 year. TPO RAs including eltrombopag and romiplostim have been shown to be safe and effective in chronic ITP in children. Data on its safety and efficacy in acute ITP are limited.

We conducted a retrospective observational study at Birmingham Children's Hospital between February 2021 and December 2021. The study aimed to assess the response to TPO RAs as first-line therapy in newly diagnosed or relapsed paediatric ITP patients. Eleven paediatric patients were included, nine were acute ITP and two had relapse of chronic ITP. All patients had baseline platelet count less than 10×10^9/l. They presented with either moderate, severe or life-threatening bleeding requiring rescue treatment with steroids and/or IVIG. The 11 patients were commenced on eltrombopag. Two patients did not tolerate dietary restrictions with eltrombopag, and therefore they were switched to romiplostim. Nine out of the 11 patients who continued on TPO RAs had good and sustained response to TPO RAs with a platelet count more than 50×10^9/l. No adverse events to the treatment have been reported during the study period. Four patients stopped treatment after sustained platelet count more than 200×10^9/l, and they are currently off treatment for 4–9 months without rebound thrombocytopenia. Two out of the 11 patients did not respond to TPO RAs. One of them had poor response to romiplostim and hence it was discontinued, after a maximum dose of 10 mcg/Kg. This child then received rituximab and is currently stable with a platelet count of $>50 \times 10^9$/l.

The clinical trials of using TPO RAs in the setting of acute ITP are still ongoing. However, after the current recommendations of their use in acute ITP, we expect TPO RAs to be increasingly brought forward in the management pathway of ITP. Although we are unable to quantify, but this NHS England policy has had a significant positive impact on the need for rescue therapy, hospital admissions, need for IVIG, in this cohort of patients. Further studies would be helpful to confirm these initial observations.

Disclosure of Interest: None Declared.

BSH22-PO130 | DVT prophylaxis in 16 and 17-year-olds and the NICE guidelines—should adult risk assessment tools be used for children?

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Abstract Content: Background: In 2018 NICE produced their guidelines with regards to the prevention of hospital-acquired thrombosis (HAT) which extended the age range to include 16- and 17-years old patients. In contrast to the previous guidelines, NICE now suggests that these patients are risk assessed and receive thromboprophylaxis if indicated. We analysed the incidence of VTE in this age group in our institution over a 7-year period. Our data show that the incidence of VTE in 16- to 17-year-olds is extremely low and often not related to risk factors commonly included in adult risk assessment tools.

Methods: We retrospectively reviewed the data of 13 951 patients aged 16 and 17 years of age in our admission database at the University Hospitals of Leicester (UHL) over a period of 7 years between 2013 and 2019. This was cross-referenced with our imaging database which identified scans carried out for suspected Venous Thromboembolism (VTE) and any positive scans were screened by the trust thrombosis nurse for analysis.

Results: There were 1275 admissions and 12 676-day case attendances over the study period. Of these, 145 patients had scans for suspected VTE. Thirteen patients had positive scans and fulfilled the inclusion criteria. Of the 13 positive scans, 10 were excluded as either they were admitted with VTE (6)

or were mislabelled entries and no VTE was present (4). Of the remaining three positive scans, one patient had suffered a fractured Calcaneus and was treated with a below knee cast but had received VTE prophylaxis. One patient had cancer and a long line associated VTE, and one patient was in a below knee back slab for an osteochondral fracture of the Talus and was taking the Combined Oral Contraceptive Pill (COCP).
Conclusion: This study shows that the risk of developing VTE in the 16- and 17-year-old age group is extremely low in patients attending hospital (0.1% in admitted patients and 0.007% in day attenders and an overall rate of 0.02%). We question whether routine risk assessment for VTE in this age group, especially using existing adult tools, is efficacious. We also note that as the guidance itself acknowledges, the evidence for prescribed drugs is both lacking as well as the prescription for such agents being outside their Licencing Authorisation.
Disclosure of Interest: None Declared.

BSH22-PO131 | A year of coagulation studies in a Paediatric Emergency Department: A service evaluation project

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Abstract Content: Coagulation studies are frequently performed for patients within the paediatric emergency department, but little is known about the indications for this or what is done with the results. Guidelines exist to cover a number of situations, however, it was felt that this did not cover all eventulalities.
All requests for coagulation studies requested from the emergency department of a tertiary paediatric hospital over a 1-year period (Jan–Dec 2020) were identified via the laboratory database. Following this, an analysis of the notes and other available patient data was undertaken to identify the indication(s) for the test, and any subsequent treatment, testing or follow-up which ensued.
A total of 1398 requests were identified:-.

- 47% of these related to 'green' indications (i.e. where a guideline suggested the use of the test in that clinical scenario, e.g. major haemorrhage, known coagulation disorder, paracetamol overdose, non-blanching rash).
- 23% related to patients who were bleeding (or injured and at risk of bleeding), but stable & not requiring transfusion or operation. In many cases, the concern seems to have been that an underlying haemophilia might be missed in a patient who has minor epistaxis, post-tonsillectomy bleeding or similar. There is no current local or national guideline on this scenario.
- 13% related to patients who might go on to require an operation but were not currently bleeding or injured (e.g. abdominal pain). Existing guidance suggests that coagulation tests be undertaken in these patients only where there is a personal or family history suggestive of bleeding disorder—95% of these patients had no such history documented.
- In the remaining 17% of cases there appeared to be no clinical justification for sending the test.

663 of the samples sent (47% of the total) returned an abnormal result. Of these:-.

- nine were known to have clotting disorders and the tests formed part of their acute management.
- 10 patients had coagulation products released from the laboratory for acute coagulopathy (e.g. DIC), and in all cases this was suspected clinically based on the information available at presentation.
- 88 patients underwent further investigations after leaving ED, and 25 were seen in the haematology clinic. Two patients received a new diagnosis of a coagulation disorder as a direct result of testing in the paediatric ED (one mild haemophilia A, one dysfibrinogenaemia)—both of these had been tested for 'green' indications.

These data show that current use of the coagulation screen in our emergency department is poorly focussed, and risks both under and over diagnosis of coagulopathy. A large amount of extra work for staff (and worry for children and parents) is generated by abnormal tests, for little gain. All of the abnormal tests requiring action were sent in patients with "green" indications.
Improvement could be made by sending samples only in situations where guidelines already suggest it (particularly with respect to preoperative samples). Additionally, there is a need for guidelines to advise emergency physicians on testing in the stable child where there is concern for an underlying coagulation disorder.
Disclosure of Interest: None Declared.

BSH22-PO132 | Positive Impact of Covid-19 on Providing Health Care Services: Experience from a Large Haemophilia Comprehensive Care Centre

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Abstract Content: In response to the COVID-19 pandemic and the UK governance restrictions to prevent the spread of the virus, several policies have been adopted to balance the delivery of uninterrupted healthcare services and the risk of COVID-19 exposure. In a very short period, methods of providing healthcare in the UK has changed dramatically and efficiently. At the haemophilia unit (HU) of Birmingham Children's hospital (BCH), most face-to-face consultations were replaced by remote consultations. On the other hand, accessibility of the haemophilia team was increased and improved by the introduction of a dedicated mobile phone and an email address for the HU. In cases of emergencies,

Abstract Table 1:

	Before COVID-19	After COVID-19	Percent reduction	
Outpatient attendance				
Planned	1784	1000	43.95%	$p < 0.001$
Unplanned	464	200	56.90%	$p < 0.001$
Total	2248	1200	46.62%	$p < 0.001$

families were encouraged to contact the HU to discuss injuries/bleeding, and medical advice was given based on remote assessment by either video consultation or reviewing emailed injuries' pictures. Families were supplied at home with extra haemostatic agents to be used in case of breakthrough bleeding events, and their administration was monitored through the Haemtrack system. These approaches not only limited the risk of exposure to the virus, but also saved time and resources of the healthcare system.

We conducted a retrospective study at HU of BCH. The study aimed to compare haemophilia patients' attendance before and after the pandemic. At the same time, patients' satisfaction towards healthcare services was measured in order to identify the effect of decreased attendance and assess the success of the new management approaches. Attendance was categorised into either planned or unplanned. Planned attendances were for treatment/prophylaxis, education, vaccines and regular clinic reviews. Unplanned attendances were either at the HU or the emergency department for management of injuries and breakthrough bleeding events. Patients' satisfaction was measured using a validated questionnaire. The questionnaire was sent to all caregivers of haemophilia patients through a text message.

Baseline attendance (January 2019–January 2020 inclusive, before the pandemic) was compared to those during the pandemic (April 2020–April 2021 inclusive, after lockdown measures legally came into force). Total attendance during the pandemic was reduced by 46.6% compared to total attendances before the pandemic. Also, planned attendances were reduced by 43.9%, and unplanned attendances were reduced by 56.9%. More details are described in (Table 1). No adverse events have been reported because of the decreased number of attendances. On analysing patients' satisfaction questionnaire, 80% of patients reported positive experiences despite reduced attendance, while 20% did not respond to the questionnaire. None of the caregivers reported negative experiences.

Our results highlight that those remote consultations, due to COVID-19 precautions, were effective in reducing attendances with appropriate patients' satisfaction and without major adverse events. There is no doubt that there was a tremendous strain on healthcare services during the peak of the pandemic. However, on the long term, we can conclude that this pandemic has also positively impacted healthcare systems through the introduction of telemedicine and remote consultations. Despite the ease of COVID-19 restrictions, at the HU we continue to use same approaches beyond the pandemic as part of the new normal. Further studies post restrictions ease are essential to obtain robust evidence and create effective service transformation.

Disclosure of Interest: None Declared.

BSH22-PO133 | Single Centre Study on Safety and Efficacy of Rivaroxaban in Paediatric Venous Thromboembolism

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Abstract Content: Venous thromboembolism (VTE) is uncommon in healthy children; however it is an increasing problem in children with underlying primary health conditions such as cancer, dependency and congenital heart disease. Incidence of paediatric hospital-acquired VTE especially catheter related is high causing significant morbidity and mortality. Options of anticoagulation *in paediatrics were limited to warfarin, unfractionated heparin, and low molecular weight heparin until the recent approval of rivaroxaban for treatment of paediatric VTE*. Rivaroxaban is more attractive for children because of its oral formulation, predictable pharmacokinetics and the minimal need for laboratory monitoring. Clinical trial data showed similar efficacy and lower risk of bleeding for rivaroxaban and standard anticoagulation in treatment of paediatric VTE; however, real-world data on its safety and efficacy in the paediatric population has not yet been explored.

We conducted a retrospective study at Birmingham Children's hospital. Thirty-five patients started on rivaroxaban since its license and after establishing our local hospital guidelines in March 2021. All patients received initial parenteral anticoagulation for at least 5 days prior to rivaroxaban initiation. Patients <30 kg received bodyweight-adjusted liquid formulation, while those ≥30 kg received tablets. For all patients, imaging was done initially at diagnosis then repeated after completing the course of anticoagulation either 1.5, 3 or 6 months according to the clinical decision. All the 35 patients were compliant with treatment. Rivaroxaban was used for VTE treatment in 33 patients and for prophylaxis in two. Thrombosis was catheter related in 11 patients, unprovoked in two, while the rest had one or more risk factors that induced VTE. One patient did not tolerate rivaroxaban and therefore it was discontinued and another patient lost follow-up. On assessing response to rivaroxaban, re-imaging

Abstract Table 1:

Patient number	Age in months[1]	Site of thrombosis	Duration	Outcome	Provoking factors	Co-morbidities
1	18	CVT	3 months	Normalised	Severe anaemia	—
2	27.6	CVT	3 months	Improved (minor residual)	Dehydration	—
3	1.2	CVT	3 months	Improved (minor residual)	—	Congenital heart disease
		PVT		Normalised	Umbilical venous catheter	
4	156	Leg DVT	3 months	Improved	—	Autism and immobilisation
5	1.2	Leg DVT	1.5 month	Improved	Catheter related	Congenital heart disease
6	1.2	Leg DVT	1 month[2]	Normalised	Catheter related	HIE
7	109	Neck DVT	3 months	Improved	Mass effect of mediastinal lymphadenopathy	Acute lymphoblastic leukaemia
8	2.4	Bilateral leg DVT	3 months	No relevant change	—	Congenital heart disease
9	3.6	Leg DVT	3 months	Normalised	Catheter related	Cervical lymphatic malformation
10	81.6	Arm DVT	1.5 month	Normalised	Catheter related	Acute lymphoblastic leukaemia
11	67.2	Infra-renal IVC	3 months	Improved	—	—
12	22.8	Leg DVT	3 months	Improved	—	—
13	51.6	Leg DVT	3 months	Normalised	Catheter related	—
14	182.4	Neck DVT	3 months	Normalised	Central venous catheter related	Extensive burns
15	20.4	Leg DVT	3 months	Normalised	Catheter related	Sickle cell anaemia
16	1.2	IVC and bilateral renal vein thrombosis	3 months	Improved	—	Prematurity
17	12	Leg DVT	1.5 month	Uncertain[3]	Catheter related	Congenital heart disease Trisomy 21
18	7.2	Leg DVT Neck DVT	6 months	Normalised Improved	Peri-cardiac arrest post heart surgery	CHARGE syndrome Prematurity Congenital heart disease Seizures
19	69.6	Neck DVT	1.5 months	No relevant change	Central venous catheter related	Autoimmune encephalopathy treated by exchange transfusion
20	75.6	Neck DVT	3 months	Normalised	Central venous catheter related	Congenital heart disease
21	171.6	Arm DVT	1.5 months	Improved	Catheter related	Multiple endocrine disorders
22	175	CVT	3 months	Normalised	Chemotherapy-related thrombosis (L-asparginase	Acute lymphoblastic leukaemia
23	175.2	Leg DVT	3 months 6 months	Improved Normalised	Chemotherapy-related thrombosis (L-asparginase)	Acute lymphoblastic leukaemia

Notes: 1 Age at start of rivaroxaban, 2 previous bridging for 2 weeks.

Abbreviations: CVT, cerebral venous thrombosis; DVT, deep vein thrombosis; HIE, hypoxic ischaemic encephalopathy; IVC, inferior vena cava; PVT, portal vein thrombosis.

was done in 23, details in (Table 1), while eight have not yet completed the course of treatment and therefore re-imaging has not been done. Twelve patients (52.1%) had complete recanalisation after finishing the treatment period, of which one had improvement after 3 months treatment for leg DVT; though imaging normalised after completing 6 months. 10 patients had improvements (partial recanalisation or fewer segments involvement), two of them had minor residual thrombosis. Two patients (8.6%) had the similar extent of the thrombus on re-imaging, but no further deterioration was reported. One patient stopped rivaroxaban after completing 1.5 months of treatment based on clinical improvement without re-imaging. Rivaroxaban was used for prophylaxis in two patients; one was a leukaemia patient and had recurrent cerebral venous sinus thrombosis, while the other was on warfarin prophylaxis after superior mesenteric venous thrombosis and was switched to rivaroxaban prophylaxis. Regarding the eight patients who are currently on rivaroxaban, they showed clinical improvement with no significant side effects and thus, they are continuing on rivaroxaban until further reassessments. None of the patients in our cohort reported either relevant bleeding or symptomatic recurrence of VTE. This study results highlight that rivaroxaban is safe and effective in paediatric patients. Long-term follow-up and further studies including large number of patients are essential to provide valuable clinical insight for the management of paediatric VTE.

Disclosure of Interest: None Declared.

BSH22-PO134 | Impact of levofloxacin-based prophylaxis during the pre-engraftment phase in allogeneic haematopoietic stem cell transplant paediatric recipients: A single-centre retrospective matched analysis

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Abstract Content: Infectious complications are the most common and significant cause of mortality and morbidity after allogeneic haematopoietic stem cell transplantation (HSCT). Bloodstream infections are frequent and life-threatening complications in HSCT recipients, particularly during pre-engraftment and many of these are caused by bacteria. Therefore, prophylactic antibiotics are introduced in the pre-engraftment phase to prevent the onset of infections. To date, the most widely used antibiotics are fluoroquinolones. To our knowledge, no studies compared the outcomes of levofloxacin *versus* ciprofloxacin prophylaxis in allogeneic HSCT paediatric recipients treated for haematological malignancies.

Our retrospective single-centre study aimed to evaluate potential differences in these two prophylaxis regimens. We enrolled all patients under the age of 18 years who underwent allogeneic HSCT for haematological malignancies in our department in the period between January 2005 and July 2020. A total of 180 paediatric HSCT recipients were enrolled: 120 patients received levofloxacin prophylaxis and 60 patients received ciprofloxacin prophylaxis (both intravenous at 10 mg/kg/dose twice daily, maximum 500 mg per dose) from 1 day before their stem cell infusion until recovery from neutropenia.

Within each group, baseline characteristics such as age, gender, primary diagnosis, type of conditioning, donor type, stem cell source and supportive care of the patients were similar. Both prophylaxis regimens demonstrated the same efficacy on the risk of febrile neutropenia (33.3% vs. 36.7%; $p > 0.05$). In contrast to this primary end-point, we found a difference in the incidence of bloodstream infection in favour of levofloxacin prophylaxis (15.0% vs. 28.3%, $p < 0.05$), especially for those caused by Gram-positive organisms (8.3% vs. 20.0%, $p < 0.05$). In addition, we documented a significantly lower incidence of Clostridium difficile-associated diarrhoea in the levofloxacin group (2.5% vs. 15%; $p < 0.05$). While no significant differences were found in the rate of severe sepsis, invasive fungal infection, length of hospital stay, overall mortality and hospital readmission. Levofloxacin prophylaxis was associated with significantly lower cumulative antibiotic exposure. The levofloxacin prophylaxis group demonstrated significant reductions in the use of both Gram-negative and Gram-positive empiric antibiotics.

Our study is the first to compare the effects of primary antibacterial prophylaxis with levofloxacin *versus* ciprofloxacin on serious infectious complications and antibiotic exposure in children undergoing allogeneic HSCT. Although both prophylaxis regimens demonstrated the same efficacy on the risk of febrile neutropenia and severe complications as sepsis, besides to the same rate of overall mortality, hospital readmission and length to stay, levofloxacin prophylaxis led to less exposure to both Gram-positive and Gram-negative-infection-related antibiotics, and a reduction of Clostridium difficile infection.

Disclosure of Interest: None Declared.