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ABSTRACT

Posters

BSH24-PO01 | Synergy of ruxolitinib and carfilzomib targeting PAX5::JAK2: Potential therapeutic advantage for Ph-like acute lymphoblastic leukaemia

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Introduction: PAX5::JAK2, a fusion driving 12% of Philadelphia-like acute lymphoblastic leukaemia (Ph-like ALL), confers aggressive disease, poor prognosis and poor treatment responses. Targeted therapy is urgently required to improve outcomes. We evaluated the efficacy of JAK inhibitor ruxolitinib (RUX) and proteosome inhibitors carfilzomib (CFZ) and bortezomib (BTZ) as monotherapy and in combination against PAX5::JAK2 transfected Ba/F3 cells. RUX and proteosome inhibitors both reduce STAT3 phosphorylation. Given that PAX5::JAK2 results in increased STAT3 phosphorylation driving proliferation, it was proposed that combining proteosome inhibitors with RUX would demonstrate synergy.
Methods: Mouse-derived Ba/F3 cells, an IL-3-dependent B-ALL model, were transfected with the PAX5::JAK2 fusion and demonstrated IL-3 independence. Differing concentrations of RUX and the proteosome inhibitors CFZ and BTZ were applied singly to PAX5::JAK2 transfected Ba/F3 cells and two controls—IL-3-dependent empty vector Ba/F3 and KG1a myeloid cells. Differing concentrations of CFZ and 200 nM RUX were then applied in combination. Inhibitors were applied for 72 h then cell viability at each concentration was ascertained by flow cytometry. Phosphoflow assessed STAT5 and STAT3 activation in basal state and in response to treatment.
Results: RUX, CFZ and BTZ were effective against PAX5::JAK2 Ba/F3 cells with a median lethal dose (LD50) of 514 nM for RUX, 38 nM for CFZ and 19 nM for BTZ. CFZ had a lesser effect, and RUX had a variable effect on JAK/STAT-activated empty vector controls. KG1a cells were unaffected. BTZ had a significant effect on both controls, predicting off-target toxicity and consequently was not applied in combination with RUX. RUX/CFZ in combination demonstrated an LD50 of 21 nM, which is significantly lower than LD50s for the monotherapies. Combination index for RUX and CFZ at 50 nM was 0.49, suggesting moderate synergy. Phosphoflow demonstrated reduced pSTAT5 with the application of RUX/CFZ to PAX5::JAK2 Ba/F3 cells, with mean fluorescence intensity (MFI) reducing from 351 to 285 in inhibitor-treated cells, and STAT3 MFI reducing from 396 to 249. There was no effect on controls. Consequently, the mechanism for growth inhibition is pSTAT3 and pSTAT5 reduction.
Conclusions: RUX, CFZ and BTZ are potent against the high-risk PAX5::JAK2 fusion. The RUX/CFZ combination, drugs widely available in clinical practice, is particularly promising given the synergy in limiting leukaemic cell growth. RUX/CFZ warrant clinical trials for management of the poor prognostic group of Ph-like ALL with PAX5::JAK2, given that they may enhance efficacy and lessen toxicity.

BSH24-PO05 | Physical isolation of tumour associated ctDNA fragments for novel AML liquid biopsy

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Introduction: We describe a novel method for ctDNA analysis in which circulating cell free CTCF-DNA nucleoproteins (cfCTCF-DNA) of tumour origin are chemically isolated from non-tumour nucleoproteins comprising cfDNA of the same sequences by chromatin immunoprecipitation (ChIP). This facilitates a simple, low cost rapid ctDNA analysis method that obviates cfDNA library preparation, next-generation sequencing (NGS) and bioinformatics.
Methods: We developed a ChIP method for isolating cfCTCF-DNA from plasma. Anti-CTCF ChIP-Seq was performed on four patients diagnosed with AML, five patients with inflammatory conditions and five healthy volunteers. We identified 29 cfCTCF-DNA cancer associated gain of occupancy binding site sequences that were present in the ChIP isolates of cancer patients, but not present in isolates from healthy subjects or subjects with inflammatory conditions (where the sequences occur as nucleosomes and had been removed). We developed qPCR assays for 10 CTCF binding site gain of occupancy sequences selectively occupied in cancer.

The 10 qPCR assays were investigated as liquid biopsy assays for detection of AML in a preliminary proof-of-concept study. ChIP isolates from plasma samples obtained from AML patients ($n = 31$) and from control subjects that were either healthy ($n = 35$), or had an inflammatory condition ($n = 15$) were tested for the presence of the 10 CTCF binding site sequences selectively occupied in cancer.

Results: The 10 qPCR assays for cfCTCF-DNA gain of occupancy biomarkers were effective for detection of AML. Using a simple qPCR cut-off, a single qPCR assay detected 19 of 31 AML cases (61%) with one false positive result among 50 control samples (98% specificity). Addition of a second qPCR assay to make a two-member qPCR panel, where a result exceeding cut-off in either or both assays was classified as positive, resulted in the detection of 23 of 31 AML cases (74%) with two false positive results (96% specificity).

Interestingly, the cfCTCF-DNA occupancy biomarkers derived from discovery using AML samples were also effective for the detection of solid cancers including the detection of four of nine stage I cancer cases (44%). Different biomarkers showed selectivity for different solid cancers.

Conclusions: cfCTCF-DNA occupancy biomarkers represent a new class of untapped cancer biomarkers for AML and solid cancers. ChIP/PCR of plasma nucleoproteins is rapid, low cost, suitable for automation and may provide a useful novel liquid biopsy method. Clinical studies to ascertain the clinical accuracy of the method are required.

BSH24-PO09 | Updated UK AML Working Group consensus recommendations for induction treatment of adult acute myeloid leukaemia

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Background: Increasing genomic stratification coupled with an evolving therapeutic landscape present challenges in the choice of optimal induction therapy in adults with acute myeloid leukaemia (AML). We have pioneered an innovative algorithmic approach, combining drug eligibility criteria and genetic risk stratification, which facilitates the development of consensus recommendations for front-line intensive AML therapy in the UK (Coats et al, BJH 2021). In light of the publication of the revised ELN 2022 AML guidelines (Dohner et al, Blood 2022) we have repeated these analyses.

Methodology: 1000 in silico AML cases were generated to cover the spectrum of clinical and genetic features, but updated to include information on FLT3-TKD and TP53 mutation status. The eligibility criteria for each NHS-funded intensive treatment and the ELN2022 (including an additional TP53mut and complex karyotype [CK] adverse risk category) were converted into a digital format. These criteria and classifications were used to assign the in silico cases to distinct clinical scenarios based on the combination of ELN risk group and the choice(s) of available funded treatments.

A representative case from each scenario was independently reviewed by 11 members of the UK AML Working Group seeking their preferred induction treatment in a fit 40- and a 65-year-old patient over two rounds of Delphi consensus. For consensus, 75% of respondents needed to agree.

Frequency of each clinical scenario, as a percentage of all cases, was estimated from UK AML trial data.

Results: 1000 cases were assigned to 24 different clinical scenarios using our digital algorithm. This compared to 22 scenarios in our previous consensus guidance and reflected changes in the ELN 2022 which included changes in the prognostic impact of FLT3-ITD, FLT3-TKD and TP53mut + CK adverse risk group. Delphi consensus was undertaken for the 24 scenarios to ascertain whether clinical practice would change in line with the new classification.

For the patient aged 40, a consensus was reached for 15/24 scenarios representing 96.7% of cases. For the patient aged 65, a consensus was reached for 15/24 scenarios representing 95.8% of cases. The recommendations from the previous consensus changed in 5.2% of cases.

Conclusions: We have confirmed that our methodology is effective for generating consensus UK treatment recommendations reflecting changes in the ELN 2022 treatment recommendations. This is available as a webapp https://amlconsensus.er.kcl.ac.uk. The presented methodology has the potential to generate consensus treatment guidelines for patients with other blood cancers and solid tumours.

BSH24-PO11 | STAT3 and STAT5 inhibition overcomes treatment resistance in an in vitro model of Ph-like ALL

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Introduction: Philadelphia-like acute lymphoblastic leukaemia (Ph-like ALL) comprises approximately 15% of ALL, and the JAK/STAT class confers particularly poor prognosis. Emerging treatments targeting JAK2 fusions and mutations are promising and undergoing large phase 3 clinical trials. However, with the widespread use of JAK2 inhibitors, treatment-resistant mutations will inevitably develop. The JAK2 p.G993a mutation has been

demonstrated in vitro to confer resistance even to high-dose JAK2 inhibitors such as ruxolitinib. STAT3 and STAT5 are downstream products of the JAK/STAT pathway, which drive cell proliferation in Ph-like ALL. We postulated that direct inhibition of STAT3 and STAT5 may overcome resistance, given that the treatment mechanism is not reliant on inhibitors binding to JAK2. SH4-54 is an experimental direct STAT3 and STAT5 inhibitor. Pimozide is an anti-psychotic that, as part of its mechanism of action, demonstrates similar STAT3 and STAT5 inhibition. We propose that both inhibitors would overcome treatment resistance secondary to the p.G993a mutation in JAK/STAT-activated Ph-like ALL.

Methods: Mouse-derived Ba/F3 cells, an IL-3-dependent B-ALL model, were transfected with ETV6::JAK2 with a p.G993a mutation and demonstrated IL-3 independence and ruxolitinib resistance. Differing concentrations of SH4-54 and pimozide were applied singly to ETV6::JAK2 p.G993a cells and two control cell lines, empty vector Ba/F3 cells and Kg1a myeloid cells, for 72 h. Flow cytometry using Annexin V and Aqua Fixed Live/Dead Cell Stain ascertained cell viability.

Results: SH4-54 and pimozide were effective against ETV6::JAK2 p.G993a cells with median lethal doses (LD50) of 296 nM for SH4-54 and 455 nM for pimozide. Both drugs demonstrated a lesser effect on empty vector Ba/F3 cells, with an LD50 of 371 nM for SH4-54 and 596 nM for pimozide. This is not unexpected given that empty vector Ba/F3 cells still exhibit JAK/STAT activation. Neither drug demonstrated any effect on Kg1a myeloid cells, which do not demonstrate JAK/STAT activation.

Conclusions: SH4-54 and pimozide both overcome treatment resistance in our in vitro model of JAK/STAT Ph-like ALL with a mutation conferring resistance to JAK2 inhibitors. While SH4-54 demonstrates greater potency than pimozide, pimozide may be a more clinically viable option given that an acceptable safety profile has been demonstrated in humans. SH4-54 will require mouse trials before human clinical trials. Direct STAT3 and STAT5 inhibition may be an effective approach for overcoming inevitable JAK2 inhibitor resistance conferring mutations in patients with the poor prognostic subtype of JAK/STAT class Ph-like ALL.

BSH24-PO12 | Venetoclax+azacitidine delays deterioration of health-related quality of life in patients with AML: VIALE-A Long-Term Follow-up

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Patients (pts) with acute myeloid leukaemia (AML) experience reduced health-related quality of life (HRQoL), including reduced physical (PF) and emotional (EF) function. Many AML treatments may be associated with negative impacts on HRQoL, such as high transfusion needs and hospitalization. Objective measurements of HRQoL are important when evaluating the long-term benefits of AML treatments. To characterize HRQoL, particularly delay in deterioration, of pts with AML receiving venetoclax (VEN) + azacitidine (AZA) or placebo (PBO) + AZA in the long-term follow-up (LTFU) of phase 3 trial, VIALE-A (NCT02993523).

Treatment-naïve adults ineligible for intensive chemotherapy were randomized 2:1 to receive VEN + AZA or PBO + AZA. Pt-reported outcomes (PRO) included: EORTC QLQ-C30 global health status (GHS/QoL), PF and EF subscales; PROMIS Cancer Fatigue Short Form 7a (fatigue); and EQ-5D-5L health status visual analogue scale (EQ-5D-VAS). PRO data were collected on Day 1 of Cycle 1 and all subsequent cycles. Time to deterioration (TTD) was calculated as the number of days from baseline to the first documented worsening (from baseline) of ≥1 pre-established PRO-specific meaningful clinical threshold (MCT). Association between patient characteristics and PROs was assessed, and within-group level of change in each score was expressed as a standardized effect size (SES) and magnitude of responsiveness.

VIALE-A LTFU analysis identified extended TTD for all PROs for patients treated with VEN + AZA, which was significantly longer in the VEN + AZA versus PBO + AZA group for EF, PF and EQ-5D-VAS. Pts treated with VEN + AZA (vs. PBO + AZA) consistently had at least numerically longer TTD across most PROs in key subgroups, including age

<75 years, ECOG score >2, achievement of complete response (CR) or CR with incomplete blood cell recovery (CR + CRi), measurable residual disease (MRD) negativity and post-baseline transfusion independence (TI). For PF subscale, pts who achieved CR, CR/CRi, TI and/or had an ECOG score >2 had SES that were overall moderate (0.5–0.79), with the magnitude of SES tending to increase from Cycle 3 to Cycle 33. Among those who achieved CR/CRi and MRD negativity, they tended towards consistently moderate to large SES across PROs, while small to no PRO improvement was observed in those who did not additionally achieve MRD negativity. Patients who achieved CR/CRi early by Cycle 2 achieved HRQoL improvement at earlier cycles.

The longer preservation of PROs such as PF, EF and fatigue, including significantly longer TTD in PF, EF and EQ-5D-VAS observed with VEN + AZA versus PBO + AZA, suggests that VEN positively impacts the HRQoL of elderly AML pts.

BSH24-PO13 | Venetoclax–azacitidine salvage chemotherapy in relapsed refractory acute myeloid leukaemia and myelodysplastic syndrome: Single-centre experience

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Venetoclax–azacitidine chemotherapy have revolutionised the management of previously untreated acute myeloid leukaemia (AML); however, there is insufficient evidence supporting this regimen in relapsed refractory disease.

We present 15 patients with relapsed and/or refractory AML and four patients with high-risk myelodysplastic syndrome (MDS) treated with venetoclax–azacitidine as salvage therapy from September 2021 to February 2023 at the Queen Elizabeth Hospital Birmingham.

The median age was 64 years (range 18–77 years) with a male to female ratio of 1.1:1. Eleven patients relapsed postallogeneic stem cell transplant (57.8%), two relapsed following consolidation chemotherapy and six had primary refractory disease (32%). Ten patients (66.6%) had adverse risk disease, three with TP53 mutation and five with complex karyotype. One out of the four intermediate-risk patients (26.6%) had NPM1 mutation with FLT3 ITD and one patient (6.6%) had favourable-risk disease with NPM1 mutation.

Prior to venetoclax–azacitidine chemotherapy, 12 AML patients (80%) received one line of chemotherapy, whereas three patients (20%) had two lines including FLAG-Ida salvage. Two MDS patients achieved remission with Azacitidine, one required FLAG-Ida salvage. No patients were previously exposed to venetoclax.

The median number of delivered venetoclax–azacitidine cycles was two. Four patients (20%) received 28 days of venetoclax, the remaining patients had 14–21 days. Almost all patients developed at least grade three neutropenia, 10 patients (52.6%) were admitted with neutropenic fevers during or after the first cycle. Red cell and platelet transfusion support were required in 13 and eight patients, respectively, with a median of seven red cell units (range 1–16) and 11 platelet units (range 2–23).

Fifteen patients (78.9%) achieved complete remission (CR/CRi) post venetoclax–azacitidine chemotherapy, including the NPM1 mutated patient who achieved molecular remission. Seven patients (36%) underwent consolidation with allogeneic stem cell transplant and six patients (31.5%) received donor lymphocyte infusion (DLI). The median overall survival (OS) for this group is 13.2 months. One patient had detectable molecular disease after two cycles and was refractory to gilteritinib. Four patients (20%) were refractory to venetoclax–azacitidine chemotherapy, two of them had TP53 mutation, the remaining two had t(3;3) and complex karyotype respectively. Twelve patients (63%) are alive and remain in remission. The median OS for the entire cohort is 11.3 months.

Venetoclax–azacitidine can be considered a bridge to transplant or DLI in relapsed refractory AML and high-risk MDS with significantly less toxicity profile, hospital stay and transfusion requirements compared to intensive chemotherapy.

BSH24-PO14 | A UK survey of VENAZA for AML: Variable practice highlights prospective evaluation is warranted

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Venetoclax and azacitidine (VENAZA) is the new standard of care for newly diagnosed acute myeloid leukaemia (AML) patients ineligible for intensive chemotherapy. However, VENAZA is toxic; the commonest adverse events being myelosuppression and febrile neutropenia. Unanswered key questions in routine practice include (1) optimal dose schedule of VENAZA; (2) duration of therapy; (3) whether patients, especially those achieving deep flow cytometric negative complete remissions, could discontinue therapy; (4) whether patients off treatment could be successfully re-treated if disease burden increased.

To support the development of a prospective national clinical trial to address these questions, we surveyed UK haematologists treating AML to establish current UK practice. Fifty-six online surveys were completed by UK health practitioners equally split between teaching ($n = 28$) and district general ($n = 28$) hospitals.

Our survey highlighted variability in practice. Thirty-six (64%) of respondents reported routinely administering 28 days of venetoclax in Cycle 1 as per the summary of product characteristics (SPC); 15 (27%) and 5 (9%) respondents were giving 21 and 14 days respectively. In a move away from the VIALE-A protocol, all respondents gave a strong CYP3A inhibitor azole (typically posaconazole) for fungal prophylaxis alongside venetoclax; venetoclax dosing in Cycle 1 was 100 mg in most cases ($n = 49$, 88%); 400 mg ($n = 1$); 70 mg ($n = 2$) or 50 mg ($n = 4$). Notably, the dose of venetoclax with concurrent use of a strong CYP3A inhibitor azole in the VIALE-A trial was 50 mg, (per SPC, 100 mg or less).

From Cycle 2 onwards, practice was variable, despite a lack of prospective evidence to support decisions. Venetoclax was given for 28 days (19%), 21 days (21%) and 14 days (60%). Many physicians reported lack of data to support decision-making (1) on timing of measure residual disease (MRD) to guide treatment and (2) optimal number of cycles to administer. Sixty-eight per cent of respondents routinely measured MRD; however, 91% of respondents expressed that access to prospective MRD data in VENAZA patients would significantly change their practice. Forty-one per cent of respondents were confident about how long they should continue treatment (most opted to continue indefinitely), whereas 59% expressed a lack of confidence. Many recognised the significant impact of continuing therapy indefinitely on patient/family quality of life.

In conclusion, this survey supports the need for a prospective study to evaluate treatment attenuation in VENAZA patients, and a study proposal is being developed. Particular areas ripe for modification include (1) assessing the non-inferiority of dose-attenuated VENAZA and (2) utilising MRD to guide treatment cessation.

BSH24-PO15 | Targeting KDM4A 9-gene signature products with repurposed drugs combined with DDR inhibitors in AML

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Acute myeloid leukaemia (AML) is a rapidly fatal haematological malignancy characterised by abnormal proliferation/block in differentiation of myeloid lineage cells. Given AML's molecular heterogeneity, discovery of new targets hence moving clinical practice towards personalised medicine is necessary to improve patient outcomes.

Aberrant trimethylation of chromatin histone 3 lysine 9, that is H3K9me3, is associated with AML aetiology. The histone demethylase, KDM4A regulates H3K9me3 to direct leukaemogenesis. Notably, KDM4A overexpression abrogates 53BP1 recruitment to DNA damage sites, leading to error-prone DNA damage repair (DDR), and ultimately genomic instability. KDM4A itself is not easily 'druggable'. Our lab has defined a KDM4A dependent 9-gene signature as a robust predictor of poorer patient outcomes.

Among KDM4A 9-gene signature, SLC29A2 encodes the solute carrier, equilibrative nucleoside transporter 2 (ENT2). In addition to facilitating membrane transport of nucleosides and nucleobases, ENT2 mediates the transport of nucleoside-derived anti-cancer drugs. Playing a key role in signalling pathways and cell cycle progression, high expression of SLC29A2 is a hallmark of advanced cancer, yet it is expressed at low levels in normal lymphoid and myeloid progenitor cells. We hypothesised that inhibition of KDM4A 9-gene signature products, such as ENT2, combined with inhibition of the DDR pathway (e.g. olaparib), could be 'synthetically lethal' to AML cells.

With the direct molecular approach of knocking down SLC29A2 with siRNA before treating with olaparib, apoptosis assay showed a decrease in MLL-AF9 KDM4Ahigh THP-1 cell viability in combination group (49.4 ± 6.0% combination vs. 30.3 ± 2.6% olaparib; $p = 0.0207$). Combination Index (CI) by Bliss Independence indicated a synergistic effect of this combination (CI: 0.96), while RT-qPCR demonstrated a significant downregulation of SLC29A2 (combination fold change 0.324; $p = 0.0681$). Imatinib is considered as a moderate inhibitor of ENT2. Unexpectedly, the pharmacological inhibition of ENT2 with imatinib combined with olaparib augmented THP-1 cell survival and attenuated the pro-apoptotic effects of olaparib alone in vitro, against our hypothesis (%live cells by resazurin at 72 h with imatinib [1 μM] 105.3 ± 2.5%; olaparib [3 μM] 77.3 ± 10.4%; combination 97.8 ± 6.5%). Bulk RNA sequencing was performed to fully understand the transcriptional changes thus exploring putative pro-survival mechanisms, that is new target elucidation. From gene set enrichment analysis (GSEA) and KEGG pathway mapping, genes involved in steroid biosynthesis were upregulated with the combination (NES:2.19; FDR < 0.25), revealing farnesyl-diphosphate farnesyltransferase 1, encoded by FDFT1 gene, as a potential novel target. In conclusion, our results suggest our KDM4A 9-gene signature that includes SLC29A2 (ENT2), contains promising targets to develop further for AML treatment.

BSH24-PO16 | UK cohort of paediatric myelodysplastic syndromes: Interim results from a national observational study 2015–2023

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Paediatric myelodysplastic syndromes (MDS) are stem cell clonal disorders characterised by ineffective haematopoiesis, presenting as chronic cytopenias and an increased risk of progression to acute myeloid leukaemia (AML). Interestingly, 10%–30% of children with paediatric MDS have pathogenic germline predisposition to AML and may present with multisystem syndromic anomalies. In the absence of a pathogenic molecular abnormality, many children with cytopenias remain without a unifying diagnosis or management plan. In order to address this area of unmet clinical need, we established a national study, also supported by a BSH cohort grant, in order to: 1. document the true incidence of these conditions in children in the UK; 2. capture their clinical characteristics and response to treatment; and 3. perform genomic characterisation of these patients in order to identify the molecular drivers for this heterogeneous rare cohort of patients.

Methods/Project Description: Paediatric patients with suspected MDS were recruited through the UK paediatric MDS-JMML study, open in 18 tertiary paediatric haematology centres. Patients with a new diagnosis were prospectively recruited to the study and serial clinical data and samples from diagnosis to relapse were collected. A targeted next-generation sequencing (NGS) panel was used for the detection of known disease-driver mutations and, in selected cases, whole-genome sequencing (WGS) was also utilised, following appropriate parental consent.

Results: One hundred and twenty-four children, with a diagnosis of suspected MDS were recruited to the study from 2015 to date. Following central review of the diagnostic investigations, 47 cases (38%) were identified to have de novo MDS; 12/124 (9.7%) cases presented with AML on the background of MDS; 5/124 cases developed dysplasia on the background of an inherited BM failure syndrome (4%); and 2/124 cases presented as secondary MDS. Four cases presenting as suspected MDS eventually received other diagnoses: Pearson's syndrome ($n = 2$), XIAP deficiency ($n = 1$) and Wiskott–Aldrich syndrome ($n = 1$). The remaining 54/124 children (43.5%) were identified to have sustained cytopenias, BM dysplasia, requiring frequent supportive care such as transfusions, with no MDS associated mutations identified through NGS.

Conclusion: These data show that almost half of paediatric MDS cases in the UK currently have no molecular diagnosis despite systematic use of targeted NGS panels and that access to advanced diagnostic high-throughput sequencing technology is likely to be required to further characterise the molecular drivers for childhood MDS. Children without known pathogenic mutations will populate a future discovery cohort for further genomic analyses correlated with phenotypic characteristics.

BSH24-PO18 | Variants in development of pure red cell aplasia & treatment approaches: Single-centre study in UK

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Introduction: Pure red cell aplasia (PRCA) is characterised by anaemia and reticulocytopenia with depletion of erythroid precursors in an otherwise normal bone marrow. Congenital PRCA in Diamond Blackfan Syndrome usually presents in childhood. Acquired PRCA can occur at any age and can be secondary to drug or toxin exposure, autoimmune conditions, infections such as parvovirus-B19 infection, solid malignancies (thymoma), pregnancy or ABO-incompatible haematopoietic stem cell transplantation. Haematological malignancies/clonal disorders, for example chronic lymphocytic leukaemia, myelodysplastic syndrome and T-large granulocytic leukaemia, are also known to be associated with PRCA. It can also prelude the development of aplastic anaemia. Despite the heterogeneity in aetiology and pathophysiology, the cornerstone of treatment is immunosuppression with steroids and/or ciclosporin. We report herein our single-centre experience in a large cohort of UK patients with PRCA over a 10-year period.

Methods: Patients with pure red cell aplasia referred to the Department of Haematological Medicine at King's College Hospital, London were identified with Electronic Patient Record (EPR) and pathology systems. Patients who developed PRCA postallogeneic stem cell transplant were excluded.

Results: This study encompassed 75 patients diagnosed with pure red cell aplasia (PRCA), for whom both pathological confirmation and clinical data were available. Among these patients, 31 (41.3%) were female, and the median age was 51 years (range 9–84). The majority of individuals presented with underlying conditions known to be linked to PRCA, with the highest prevalence observed in association with myelodysplastic syndrome (MDS).Within our cohort of 75 patients, 82% (61/75) necessitated treatment for PRCA, and 57% (43/75) required two or more lines of therapy. Initial treatment involved corticosteroids in 25.3% (19/75) of cases, with a response rate of 75% and 50% achieving a complete response.

Additional therapeutic modalities included intravenous immunoglobulin (IVIG), erythropoietin and disease-directed therapy such as lenalidomide for MDS with 5q and thymectomy.

Discussion: In this extensive study of 10 years, our findings reveal a reduced occurrence of idiopathic PRCA, a lower median age, despite a substantial representation of myelodysplastic syndrome (MDS), and an elevated incidence among males compared to existing literature. Patients with idiopathic PRCA exhibited favourable response to initial therapy. Notably, we identified STAT3 mutations in two patients, highlighting the significance of molecular testing and the importance of maintaining a comprehensive differential diagnosis when confronted with this uncommon condition.

BSH24-PO19 | Venetoclax–azacitadine as first-line treatment for AML—Real-world data from a multicentre study

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Background: Venetoclax–azacitidine (Ven/aza) was initially licensed in UK for newly diagnosed acute myeloid leukaemia (AML) in 2020 to reduce treatment intensity and hospital stay for patients (pts) with AML during the COVID-19 pandemic. It then obtained ongoing licence in newly diagnosed cases where intensive treatment is unsuitable. Subsequently it is often used as induction chemotherapy for adult pts who are not fit enough to receive intensive induction. Here we report the real-world outcomes from hospitals across Wessex, population of 2.7 million.
Methods: This is a retrospective analysis across eight hospitals in Wessex from May 2020 until November 2023. Pts included were those who received Ven/Aza as induction therapy for AML. Pts who received Ven/Aza as salvage for relapsed/ refractory disease were excluded. We reviewed the median overall survival (OS) and progression-free survival (PFS) for different subgroups. Subgroup analysis to review risk factors including age and P53 mutation status was done. Survival analysis and Kaplan–Meier survival curves were analysed by Prism v10.
Results: A total of 121 pts, with median age of 73 years (range 54–91 years) were treated. The median follow-up was 8 months (range 0 to 42 months) and the median number of cycles across the whole cohort was 4, there was no difference in the median number of treatment cycles for pts < 75 years compared to >75 years.
Risk stratification using ELN cytogenetics criteria demonstrated 36% ($n = 44$) being adverse risk, 48% ($n = 58$) being intermediate risk and 15% ($n = 18$) being low risk.
Median OS for the whole cohort was 15.57 months. The median PFS for the entire cohort was 12.73 months. The median OS for Pts <75 years was 16.93 months vs. 13.77 months for older pts (p-value 0.26). In the TP53 subgroup, there were 19 who had a pathogenic TP53 mutation and 102 had wildtype. The median number of cycles were 2 and 4 respectively. In the former, the median PFS was 3.17 months, and the median OS was 4.5 months versus 16.93 months for pts with no pathogenic P53 variant identified (p-value is <0.0001).
Conclusion: This analysis of real-world data highlights the efficacy of low-intensity treatment in a very challenging subgroup of patients, in keeping with published data. Our subgroup analysis shows that there is little advantage in TP53-mutated patients. Therefore, there is a clinically unmet need in those pts who are diagnosed with P53-mutated AML.

BSH24-PO20 | Elucidating the S100A4-mediated mechanisms promoting AML blast proliferation and survival

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AML is characterized by the uncontrolled proliferation of myeloid precursor cells in the bone marrow. Our previous study identified S100A4 as overexpression in the nuclei of AML blasts (>83%), with an average 5.5-fold increase compared to normal CD34+ nuclei. S100A4 is a calcium-binding protein that regulates cell proliferation and survival; however, its role in AML was not well defined. In this study, we aimed to elucidate the effects of S100A4 on AML cell growth and survival through genetic knockdown and transcriptomic analysis.
Lentiviral vectors expressing short hairpin RNAs targeting S100A4 were used to knockdown S100A4 expression in AML cell lines THP-1, NOMO-1, TF-1 and OCI-AML2. Infection efficiencies exceeding 95% were achieved, with cells remaining viable. Knockdown of S100A4 protein expression was confirmed by Western blot. S100A4 protein expression was significantly reduced by >90% in AML cell lines. The effect of S100A4 KD on AML cell line survival and proliferation was evaluated by flow cytometry, Ki67 and ToPro-3. The proliferation rates of AML cell lines were significantly decreased following S100A4 KD transduction compared to scramble control. However, no effects were seen in KG.1a cells, which have undetectable S100A4 expression.
To understand the effects of whether S100A4 plays a functional role in AML cell proliferation, survival, cell cycle

progression and apoptosis, the annexin V assay and cell cycle assay were performed. The percentage of cells undergoing early apoptosis is consistently higher in the KD S100A4 condition compared to the control condition at each time point measured. The data suggest that the downregulation of S100A4 reduces AML cell proliferation and promotes cell apoptosis. The downregulated levels of S100A4 in AML cells induce G2 arrest in the cell cycle. The results suggest that transfection of AML cells with S100A4 KD caused a delay or arrest of cells in the G1 phase, which led to a decrease or absence of cells in the G2 phase. To understand the mechanisms underlying S100A4's effects, mRNA sequencing was performed to compare the transcriptomes of S100A4 knockdown cells versus controls. This provides a global view of the pathways regulated by S100A4 in AML. High-quality RNA has been extracted and assayed to confirm suitability for sequencing. Bioinformatic analysis identifies differentially expressed genes and affected pathways.

In summary, the genetic knockdown of S100A4 significantly reduced AML cell proliferation, and survival and promoted cell apoptosis, indicating it may be a promising therapeutic target. Transcriptomic profiling will elucidate the molecular mechanisms through which S100A4 exerts its oncogenic effects in AML.

BSH24-PO21 | Transfusion camp—the UK experience and outcomes

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Introduction: Clinicians from all specialties prescribe blood transfusions. Studies have demonstrated gaps in the knowledge of transfusion medicine among trainees in many specialties, including haematology. To address this, Transfusion Camp was established in Toronto in 2012. It is a structured programme, teaching the practical aspects of transfusion medicine. It is offered to trainees in haematology, anaesthetics, ITU, emergency medicine and obstetrics. The course consists of 22 centralised didactic lectures and seven locally delivered interactive seminars that have been delivered online since the COVID-19 pandemic. Each seminar consists of several clinical scenarios, with multiple-choice questions that stimulate discussion and allow consolidation of the material delivered in the lectures. In 2015, Transfusion Camp was offered to trainees in Oxford for the first time, and has since expanded to four sites in the UK. Here, we report the UK experience of delivering Transfusion Camp and the outcome data.

Methods: Transfusion knowledge was assessed before and after the course using the validated 20-question BEST-test. Data are only available for Oxford from 2016 to 2020.

Results: Twenty-three haematology trainees, 23 anaesthetics/ICU trainees and four other trainees attended Transfusion Camp in Oxford between 2016 and 2020. The increase in the performance in the precourse and postcourse tests was 2/20 for haematology trainees and 3.6/20 for non-haematology trainees. The average score was higher for haematology trainees at both the beginning (12/20 vs. 10.4/20) and end (14/20 vs. 13.7/20) of the course. Before the course, 55% of respondents rated their confidence in dealing with transfusion-related patient issues as 'fair'. At the end, 93% of respondents rated their confidence at 'good' or 'very good'.

Discussion: We have demonstrated that the model used for Transfusion Camp in Canada can be rolled out in another country with similar improvement in transfusion knowledge in both haematology and non-haematology trainees. We have anecdotal evidence of improvement in practice, but this needs confirmation by further studies.

The feedback from participants has been excellent, and facilitators feel that the materials provided are easy to use. The knowledge included in Transfusion Camp is complementary to knowledge provided on other transfusion courses in the UK, such as those provided by NHS Blood and Transplant. We recommend that Transfusion Camp is rolled out to more sites across the UK in order to improve transfusion knowledge nationally.

BSH24-PO22 | The benefit of nurse led group end of treatment summary sessions for patients

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People with a haematological cancer often wish they felt better prepared for life after treatment ends. It can bring a mix of emotions as adjusting to life after treatment can be challenging. Discussing the end of treatment summary plan with a person who has had treatment supports self-management and awareness of signs and symptoms of disease recurrence. This approach can also alert people to the late effects of their treatment. It can highlight psychological and emotional problems such as depression and anxiety, which can also occur after treatment. End of treatment summaries are part of Personalised Care and Support Planning, which supports the NHS Long-Term Plan for Cancer, ensuring that every person diagnosed with cancer will have access to personalised care.

Starting in January 2023 the Clinical Nurse Specialist (CNS) team devised and delivered a group face-to-face session that focused on a holistic approach including a copy of their End of Treatment Summary (EOTS). The session includes a face-to-face presentation that covers.

- Why do we have an End of Treatment Summary?
- Late Effects of Treatments.
- Recurrence of disease.
- Common Challenges (physical and mental).
- Self-help.
- Accessing help.
- When and who to contact.

The CNS's initially thought that the sessions would be poorly attended, as historically invites to group sessions held on Teams during the COVID-19 pandemic proved to be unpopular. However, when the CNS's evaluated the sessions in July 2023 and December 2023, the data demonstrated that the Haematology Team went from zero EOTS's in 2022 to 73% of patients that have completed a course of chemotherapy, accepting, and attending a face-to-face EOTS session. On completion of the session, 100% of patients understood signs of recurrence and 100% understood services available to them. In conclusion the sessions proved popular and informative for patients as 100% of patients stated they would recommend the session to other patients. In addition, as the sessions were a group, this saved the CNS time and individual clinic slots by enabling more patients to be seen in fewer sessions. Furthermore, this model promotes self-management and empowerment for patients.

BSH24-PO23 | Every minute counts: PCC delays reported to SHOT especially in patients with intracranial haemorrhage

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Introduction: Pro-thrombin complex concentrates (PCC) are important treatments for immediate reversal of vitamin K antagonists and some other oral anti-coagulants. PCC should ideally be given within an hour once the decision is made, particularly in patients with intracranial haemorrhage (ICH) (NICE 2015). Delays or omissions in administration can result in serious morbidity (such as expansion of an ICH) or death (Sweidan et al., 2020). Such delays prompted publication of a CAS national alert, with actions for hospitals including review of their policies and procedures (SHOT 2022).
Method: The Serious Hazards of Transfusion (SHOT) database was reviewed for all PCC-related cases reported for the 5 years 2018–2022 focusing particularly on delayed administration when the patient had suffered an ICH.
Results: During this period, 81 reports involved PCC, and 51/81 (63.0%) were delays in administration. In 26/51 (50.9%) cases, the patient had an ICH. The median age was 82 years. Of these, there were 8/26 (30.7%) deaths, 2/8 (25.0%) where the death was possibly related to the delay and 6/8 (75.0%) not related. Of the patients that died, the median age was 84 years. There was 1/26 (3.8%) case of major morbidity due to expansion of ICH. Length of delay from time of decision to administer PCC to administration ranged from 1 to 12 h with a median of 4 h.
Among patients with ICH, 7/26 (26.9%) delays in treatment were caused by the patient being transferred from emergency department to a ward before the PCC was given. There were 6/26 (23.1%) delays caused by lack of knowledge including staff not knowing what PCC was, its location, what dose and how to reconstitute and administer it. Other delays were caused by errors in prescribing 5/26 (19.2%), delays in collecting PCC from transfusion laboratory 3/26 (11.5%) mostly due to staff shortages, lack of onsite PCC stock 2/26 (7.7%), delayed diagnosis 2/26 (7.7%) and 1/26 (3.8%) pager failure. Information technology (IT) issues accounted for 3/26 (11.5%) cases including pager failure and incorrect use of IT systems.
Conclusion: Medical and nursing staff working in emergency departments, and other areas where PCC may be prescribed, should be trained in prescription and administration, and be able to locate protocols for use of PCC with clear instructions for dose, reconstitution and administration.
PCC a is an emergency treatment and should be started within an hour of the decision being made and before the patient is transferred to other wards or departments. All organisations must ensure compliance with the recommendations in the CAS alert.

BSH24-PO24 | Theme of the week: Using a clinical reasoning puzzle to teach anaemia

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Introduction: Many medical students do not have a dedicated haematology block, meaning this important area may be neglected in the clinical years. The investigation and management of haematological disease requires understanding of biomedical science, laboratory investigations and clinical presentations—lending itself to integrated learning. Formal teaching delivered by clinical staff is time intensive and can be challenging to deliver in the current climate. We have developed a programme of self-directed educational activities to tackle these challenges.
Objective: To evaluate the effectiveness of anaemia-themed educational activities—consisting of an 'investigator task', multiple-choice question (MCQ)-based quiz and clinical reasoning puzzle—in developing confidence of fourth-year medical students in the assessment of anaemia.
Methods: A qualitative analysis was conducted of the perceived confidence of fourth-year medical students in the assessment of patients with anaemia before and after the completion of educational tasks. The tasks were completed by two groups—33 fourth-year medical students in the first

group, and 34 in the second. Both completed an investigator task (involving seeking a patient with anaemia and answering directed questions about them) and a clinical reasoning puzzle. The second group also completed a formative five-question MCQ-based quiz. Questionnaires before and after the tasks assessed change in perceived confidence in the topic of anaemia.

Results: In the first group of 33 students, 15 (45.5%) completed the end of week questionnaire. In the second block of 34 students, 19 (55.9%) completed the end of week questionnaire. Of these, 79.4% felt that the investigator task helped them to learn about the topic of anaemia during the week. In the second block, 73.7% of students felt that the additional quiz helped them to feel more confident with anaemia. 97.1% of the students felt that the clinical reasoning puzzle helped consolidate their learning, and was engaging and fun. Overall, the educational activities improved confidence in anaemia—at the beginning of the week, 52.9% of students felt confident in the topic, compared to 73.7% at the end of the week.

Conclusions: The use of educational tasks during clinical placement can increase confidence in assessment of anaemia and direct learning on the wards. Students enjoyed the use of clinical reasoning puzzles to integrate academic knowledge with clinical scenarios. This is of relevance in the context of increasing numbers of medical students, as the tasks are mostly self-directed and require few trained members of staff.

BSH24-PO25 | Carbon footprint of red blood cell transfusion: The journey from donor to recipient

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Introduction: The NHS is estimated to account for 4% of UK CO_2 emissions and aims to reach net zero by 2040. Over 2 million blood components are issued by UK blood services each year, providing life-saving transfusions for patients in hospitals. A review of the blood supply chain determined the carbon footprint of each standard red cell concentrate (RCC) supplied and identified opportunities to make significant reductions in CO_2 emissions.

Methods: This lifecycle analysis considered the path from the donation of whole blood (WB) to the transfusion of a standard RCC, incorporating transportation of the donor, the WB donation and the RCC, and the testing, manufacturing, stockholding and hospital transfusion activities. Primary data included the energy use of machinery, consumables used and transport information for donors and deliveries. Secondary data included carbon content estimates for UK electricity and carbon emissions from transportation. Delivery and disposal of consumables and the construction, supply of machinery and other infrastructure were excluded from the scope.

Results: Each unit of RCC transfused is estimated to produce 7.82 kg CO_2eq (Table 1). Annually, red cell transfusions in England generate 10.6 million tonnes of CO_2eq. Hospital transfusion (primarily refrigeration) and transportation were the major contributors to this total. Further refinement is in progress for the transfusion refrigeration footprint, as consumption estimates were used in the calculations, which were based on one hospital trust and extrapolated.

TABLE 1 Carbon footprint of each subprocess in the RCC supply chain.

Subprocess	CO_2 eq/unit (kg)	Proportion (%)
Transportation	2.75	35
Donation	1.55	19.8
Testing	0.35	4.5
Manufacturing	0.58	7.4
Stockholding	0.09	1.2
Hospital Transfusion	1.94	24.8
Disposal	0.57	7.3
Total	7.82	100

Conclusions: Transportation, refrigeration and donation are identified as the primary contributory activities. Potential measures include more efficient refrigeration options, improved blood service logistics and donor transportation to sessions. Incorporate alternative plastics in blood packs, and the use of renewable energy sources. This model can be adapted to investigate the environmental impact of alternative transfusion strategies and other blood components such as Fresh Frozen Plasma and Platelet Concentrates.

BSH24-PO26 | Simulation of haematological emergencies in the regional induction programme for new ST3 registrars

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Background: New haematology registrars may have limited familiarity with several important conditions and clinical scenarios. ST3 registrars will usually join the on-call rota during their first months of training, and inductions may help increase their confidence and ability in recognising and managing key haematological emergencies. This is important in maintaining high standards of patient care.

High-fidelity simulation has previously been used in other settings and specialties to aid induction of new trainees, but is less commonly utilised in haematology registrar training.
Methods: An innovative simulation training day was developed as part of the East of England deanery's regional training programme for newly recruited haematology ST3's in September 2023. All five ST3's participated in simulation exercises held in the dedicated simulation suite at West Suffolk Hospital. The simulation facilitators contained a mix of haematology consultants and senior haematology registrars, who wrote original scenarios and ran the sessions with the simulation suite support staff. Each facilitator additionally led prescenario and postscenario discussion-based teaching with the whole group. Simulation scenarios centred on acquired haemophilia, acute chest crisis in sickle cell, thrombotic thrombocytopenic purpura, new presentation of high-grade lymphoma and acute pro-myelocytic leukaemia. The scenarios and subsequent teaching covered core knowledge about diagnosis and management of these conditions, as well as practical aspects of managing the emergencies on-call. This included handling a microscope and reviewing blood film morphology, reconstitution of coagulation factor concentrate using dummy factor vials and liaison with the laboratory, intensive care and external tertiary centres as appropriate.
Findings: Feedback was collected from all five ST3 trainees, which was overall positive. The participants were asked to rate their confidence before and after the sessions in a number of domains. The average confidence rating improved in every domain after the simulation training.
Conclusions: Simulation may be a valuable tool to improve the confidence and competence of new ST3 haematology registrars in managing emergencies when on-call. This regional session for all new trainees may also help provide a consistent induction experience for those in different hospitals with varying exposure to certain conditions. It also provides a valid face-to-face teaching modality to aid networking for new trainees in different sites across a large geographic region.

BSH24-PO27 | Audit of nurse led bone marrow biopsy service

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Aims and Objectives: To assess the effectiveness and safety profile of a specialist nurse led bone marrow biopsy service with a focus on the quality of the samples and impact on diagnosis and subsequent management of haematological conditions. We also wanted to obtain patient feedback on their experience of the service/procedure.
Methods: We designed a bespoke audit template and patient experience questionnaire to capture information regarding the above aims.
Sample size $n = 52$ bone marrow procedures.
Similar data were collected simultaneously for procedures performed by medical staff. Comparison was made against bone marrow biopsies undertaken by medical staff as a benchmark.
Results: Twenty-two doctor led bone marrow and 30 nurse led bone marrow procedures were randomly compared. Thirty-one patient experience survey's were completed for the nurse led procedures only.
Nurse Led bone marrow procedures obtained samples that gave a diagnosis in 93% of cases. In 7% a definitive conclusion could not be reached.
Positive feedback from patients—scoring 95% or above.
Overall, patients had a positive experience and the benefits of the nurse led service is demonstrated by both patient feedback and results from samples.
Conclusion: The above data demonstrates that the current nurse led service is delivering a safe and effective service with a good patient experience.

BSH24-PO28 | Favourable outcomes from TKI dose reduction and cessation in patients with chronic myeloid leukaemia

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Introduction: The mainstay of treatment in chronic-phase CML is continuous tyrosine kinase inhibitor (TKI) therapy. Treatment goals include the achievement of major molecular response (MMR) (BCR-ABL ≤0.1%/MR3) and treatment-free remission (TFR). Clinical concerns exist about TKI-related morbidity, which is often dose dependent. This may be mitigated by dose reduction but potentially compromise efficacy.
Methods: We performed a retrospective 'real-world practice' review of patients with chronic-phase CML diagnosed between 2000 and 2023 ($n = 96$) in Aneurin Bevan Health Board (ABUHB).
Our aim was to examine if low dose (LD) TKI regimens can safely maintain patients in MMR, improve tolerability and if our TFR rates reflect the data from published clinical trials. LD was defined as any dose below the recommended level specified in the TKI Summary of Product Characteristics. Reflecting clinical practice, LD nilotinib was defined as <600 mg/24 h.
Results: 42/96 (43.8%) of patients received a LDTKI during their treatment (Imatinib 28.6%, dasatinib 38.1%, nilotinib 16.7%, asciminib 2.4%, bosutinib 14.3%), with a median follow-up of 343 days (11.4 months). Of those currently on a LDTKI, most patients 16/25 (64%) were dose reduced due to intolerance of their current or previous TKI. 25/42 (59.5%)

of patients who have trialled a LDTKI remain on a LDTKI, while 6/42 (14.3%) have gone onto a successful TFR. Only a small proportion of patients (11/42) have increased to full-dose TKI either due to loss of MMR (6/11) or due to side effects (5/11). In those patients who remain on a LDTKI, the vast majority, 22/25 (88%), have maintained MMR at a median follow-up of 472 days (15.7 months).

17/96 (17.7%) of patients underwent TFR (Imatinib 64.7%, dasatinib 23.5%, nilotinib 11.8%). Of these patients, 11/17 (64.7%) remain in TFR, while 6/17 (35.3%) have suffered a molecular relapse, that is loss of MMR. Those maintaining TFR have done so for a median of 1430 days (3.9 years), with 6/11 (54.5%) having TKI dose reduction prior to TFR for a median of 1165 days (3.2 years).

Conclusion: Our real-world data shows LDTKIs are effective in improving tolerability while maintaining efficacy in our chronic-phase CML patients. Our maintained TFR rate of 64.7% at 3.9-year follow-up is higher than the published data. Although our sample size is small and follow-up short, this higher rate may be explained by dose reduction prior to TFR, supporting this approach.

BSH24-PO29 | Incidence of herpes zoster in a range of immunocompromised populations—A SLR in Europe

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Objectives: Herpes zoster (HZ) is known to be more prevalent in older age groups, affecting one in three people over 50 years of age, with painful and difficult-to-manage post-herpetic neuralgia (PHN) occurring in three in 10 affected people over 50 years. The increased risk of HZ is also well recognized in some immunocompromised (IC) patients, such as cancer and transplant patients. The objective was to summarize the incidence of HZ in a broad range of 14 IC populations.

Methods: A systematic literature review (SLR) of observational studies (in Medline and Embase, published in 2002–2022) was performed, to identify HZ incidence rates (IR) in a broad range of IC populations in the European Union/European Economic Area, Switzerland and the UK.

Results: Out of 776 titles screened, 24 studies were included that reported HZ IR per 1000 person-years. IC populations with the highest IR were stem cell transplant (SCT, 37.2–56.1) and solid organ transplant (SOT) recipients (12.1–78.8). This was also observed in three studies that included a range of IC populations. There was considerable heterogeneity across studies, due to differences in study design (time period, case definitions) or study population characteristics (subgroups of IC patients with a higher risk of HZ due to age, sex, greater IC severity or specific immunosuppressive medication used).

Conclusions: A systematic review of HZ incidence in non-IC patients reported IR of 2.0–4.6 per 1000 person-years across Europe, thus HZ incidence appears to be increased in multiple IC populations versus non-IC patients. High IR were found in several IC populations such as SCT/SOT recipients, varying by disease severity, sex and age. Future studies should focus on getting stratified IR by IC population subgroup to better inform policy decision-makers.

Funding: GlaxoSmithKline Biologicals SA.

BSH24-PO30 | Exploring perceptions in management and treatment of polycythaemia vera (PV) in the UK: PV-PINPOINT study

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This study sought to understand the current UK management and landscape for polycythaemia vera (PV). From July to October 2023, 57 healthcare professionals ($n = 37$ consultants, $n = 20$ nurses or pharmacists) across the UK completed a survey with Novartis Medical Science Liaisons. Results were analysed descriptively.

The most influential guidelines are BSH 20181 and most respondents (68%) cited diagnosis in line with these. At diagnosis, next-generation sequencing is also requested by 54% of consultants for at least some patients. Complex and high-risk patients are discussed by the Multidisciplinary Team, although not all patients are discussed routinely.

Key treatment goals are to reduce thrombosis and haemorrhage risk, and control haematocrit (HCT) and symptoms. Most patients (68%) are on cytoreductive therapy (1st, 2nd, >2nd line is 52%, 12%, 4% respectively), while anti-platelets/venesection alone (28%) are less common (low risk/patient choice). Venesection frequency is variable; 36% cited >2-month frequency (11% >1-month) for controlled disease.

Monitoring of stable patients occurs on a 3-monthly basis, mainly via telephone (68%), increasing to monthly when uncontrolled, mainly in-person (54%). Nurses play a key role, often leading PV clinics (65%) and managing stable patients (54%). Ongoing management of cardiovascular (CV) risk is performed by a general practitioner (GP, 56%); although only 16% cited being 'extremely confident' that a GP will act on a referral for CV assessment. Sequential testing of JAKV617F allele burden is not widely used (9%).

All respondents actively monitor symptoms, although specific symptoms monitored vary and only 19% utilise MPN10 at every clinic visit. Intervention occurs for most, if not all patients with HCT >0.45 (pragmatic approach is taken considering other factors). Suboptimal control is also

commonly defined by a worsening of symptoms; 32% cited that 21%–40% of their patients are switched for this reason. Signs of hydroxycarbamide (HC) resistance/intolerance are reviewed at every clinic (81%); with most common indicators being presence of ulcers, neutropenia and venesection need. Identification of resistance and intolerance was also cited as the greatest educational need (58%).

While this study suggests diagnosis and management of PV is largely aligned with current recommendations, it also suggests areas of improvement remain, including consistency in approach to symptom monitoring and confidence in CV risk assessment. Areas of high unmet need in PV were lack of truly disease-modifying treatments and symptom control. Educational needs highlighted by respondents included identifying HC resistance/intolerance, service design and guideline updates.

BSH24-PO31 | Service evaluation of R90 bleeding disorder and platelet panel in thrombocytopenia cases

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Introduction: Thrombocytopenia is a symptom of a heterogeneous group of disorders with varying clinical implications. Immune Thrombocytopenia (ITP), an autoimmune platelet consumption disorder, is classically described as a diagnosis of exclusion. However, genetic testing is not routinely done at presentation. The R90 panel tests for F5; F11; MYH9; ENG; ACVRL1; F7; F8; F9; F10 and VWF MLPA or equivalent. This study aimed to evaluate the diagnostic capability of the R90 gene panel and identify patient characteristics associated with positive genetic yield.

Methods: A retrospective, single-centre service evaluation looking at patients who underwent the R90 genetic panel at the North West Genomic Laboratory Hub (NWGLH), Manchester, UK was conducted in June 2023. Inclusion criteria were patients who presented with thrombocytopenia since the inception of data collection in 2021. For patients from Royal Manchester Children's Hospital (RMCH) and Manchester Royal Infirmary (MRI), additional patient data was collated; including bleeding history, ethnicity, age, family history and thrombocytopenia characteristics such as length of thrombocytopenia and response to previous treatment.

Results: Three hundred and thirty-one patients had undergone the R90 panel at the NWGLH with a positive result in 32.3% (107). Of those with clinical data from RMCH and MRI, a positive genetic result was identified in 41.7% (25 out of 60), and 36.7% (22 out of 60) had an ITP diagnosis. A significant correlation emerged between positive genetic findings and the duration of thrombocytopenia exceeding 12 months (95% CI = 19.0, 191.0; $p < 0.01$). Positive genetic yield by age (≤16 vs. >16 years), platelet count (≤50 vs. $>50 \times 10^9$/L), gender, ethnicity and response to ITP treatment did not demonstrate any significant associations.

Discussion: The findings regarding the R90 panel's diagnostics yield align with those reported by a similar study. The increased yield at RMCH and MRI of 41.7% compared to the overall average of 32.3% suggests current criteria for testing have good specificity. Significantly, thrombocytopenia lasting over 12 months showed a higher likelihood of genetic causation ($p < 0.01$), indicating prolonged duration as a potential referral criterion for genetic testing. No significant correlations were found with age, gender or ethnicity.

Conclusion: The study reaffirms the role of the R90 panel in thrombocytopenia cases. It suggests that prolonged thrombocytopenia duration is an indicator for genetic testing. These insights advocate for a nuanced approach to genetic testing in thrombocytopenia, enhancing diagnosis and patient management.

BSH24-PO32 | Prevalence of reduced bone mineral density in indolent systemic mastocytosis: UK single-centre retrospective review

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Indolent systemic mastocytosis (ISM) is a rare haematological neoplasm and secondary cause of osteopenia or osteoporosis in 24% and 39% of adult patients respectively. The interplay between mast cell mediators, osteoblasts and osteoclasts is complex but generally results in bone resorption. To date, dual energy x-ray absorptiometry (DEXA) scanning frequency and management of reduced bone mineral density (BMD) in ISM have not been formally reviewed.

We performed a retrospective analysis of all adults with a diagnosis of ISM seen in a UK centre of excellence between 2009 and 2023. Baseline demographics, serum tryptase, marrow disease bulk (% mast cells, MCs) and serial BMD data were analysed.

We identified 168 patients with ISM within our cohort. The majority were female (103/168; 61%). The median age at diagnosis was 49 and 50 years for males and females respectively (range 3–80 years). The mean tryptase level at initial DEXA was 42.8 ng/mL (range 5–227 ng/mL) with variable mast cell disease burden; 39% < 5%, 35% 10%–30%, 18%, 5%–9% and 8% > 30% MCs in trephine.

BMD changes were evenly distributed. Thirty-six per cent had normal scans, 36% osteopenia and 28% osteoporosis. Patients with normal scans were younger than those with osteopenia or osteoporosis (median age 42 [19–71] vs. 53 [28–79] vs. 53.5 [18–78] years respectively).

Gender distribution was equivalent in patients with osteopenia/osteoporosis (34% Females [57/168] vs. 30% Males [50/168]) and as expected, reduced BMD was more prevalent in postmenopausal women (defined as >51 years) compared to premenopausal (71% vs. 43%).
In ISM, we found no statistically significant correlation between tryptase levels and osteopenia/osteoporosis ($p = 0.78$). Current guidelines recommend all patients have DEXA scans every 3 years. Within our cohort, 35% (58/168) had follow-up scans available of which 24% (14/58) had an initial normal DEXA, 48% (28/58) osteopenia and 28% (16/58) osteoporosis. In patients with normal baseline scans, 29% (4/14) progressed to osteopenia, while 21% (6/28) with baseline osteopenia progressed to osteoporosis.
Treatment generally followed national guidance with combined calcium/vitamin D tablets and recommendation to follow a healthy lifestyle in osteopenia with additional bisphosphonates in osteoporosis. In the latter group, 69% (11/16) showed improvement in BMD.
Our findings corroborate previous work highlighting a significantly increased risk of osteopenia/osteoporosis in ISM patients. Despite limitations, including omission of other risk factors, our data highlights the necessity of regular screening. Importantly, early intervention and collaboration with metabolic bone disorders teams is essential to optimize the management of these patients.

BSH24-PO33 | Rare MPIG6B gene mutation cause of refractory severe thrombocytopenia with myelofibrosis in adolescent

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Severe thrombocytopenia with myelofibrosis in adolescent is not commonly observed. A rare MPIG6B gene mutation can be responsible, this gene is a regulator of platelet homeostasis, and loss-of-function of G6b-B can cause thrombocytopenia, myelofibrosis and anaemia in both humans and mice. We are hereby reporting a case of 26-year-old male patient presented first time as a teenager with thrombocytopenia, investigated and managed as immune thrombocytopenic purpura-ITP for years in multiple centres with no response to steroids, immunosuppressive agent and thrombopoietin receptor agonists (TPO) treatment. Bone marrow trephine biopsy showed diffuse areas of grade 2 fibrosis and atypical megakaryocyte maturation and no definite features of myelodysplasia or myeloproliferative neoplasm. Normal myeloid NGS panel on molecular testing A whole-exome sequence confirmed a homozygous loss-of-function mutation in MPIG6B: NM_025260.3:c.383_384dup p.(Cys129Ilefs*17). Only a very small number of cases of disease due to this gene have been reported.

BSH24-PO34 | Are standards being met during the consent process for the treatment of haematological cancers?

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Background: Anti-cancer therapies are associated with complex risks, and the benefit–risk balance differs among patients (1). Therefore, patients must have a clear understanding of the benefits and potential risks involved with treatment. To ensure this, patients receiving anti-cancer therapies require valid consent, which involves patients being provided with appropriate information and having an optimal environment for consent. Additionally, advanced care planning (ACP) is necessary to consider. ACP is becoming increasingly complex as treatment lines increase both in number and complexity. The British Committee for Standards in Haematology (BCSH) (2) and Cancer Research UK (1) provide guidance on gaining consent for anti-cancer treatments.
Based on this guidance, our aims are as follows:

1. Determine if patients have an optimal environment for consenting, including adequate time and written information.
2. Check if consent forms contain all relevant information regarding the treatment, encompassing treatment intent, short-term and long-term side effects, mortality, alternatives and the potential need for blood product transfusion.
3. Investigate if future care planning was initiated around the time of consent.

Method: We analysed consent forms from 42 patients undergoing systemic anti-cancer therapies (SACT) between 2020 and 2023. The consent forms were completed by six clinicians. The consent forms were evaluated using guidance from the BCSH and Cancer Research UK standards of care for consenting to chemotherapy.
Results: Compliance for each standard:
The patient was given written information (48%).
Patients were given enough time (>24 h) to consent (33%).
Treatment intention was outlined (98%).
Alternatives were discussed (24%).
Common side effects were discussed (83%).
Long-term adverse effects on fertility and secondary malignancies were included (40%).
Mortality was discussed (40%).
The necessity for blood product transfusions was discussed (31%).
Clear evidence of advance care planning (ACP) documented (14%).
A treatment escalation plan (TEP) was completed at the time of consent (16%).
Conclusion: Our results show low compliance with the majority of the national guidance standards. Further analysis will also

be performed to show the outcome of using an interactive electronic patient record (EPR) standard interactive consent form template and how this has impacted adherence to guidance.

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BSH24-PO35 | Momelotinib versus best available therapy/continued ruxolitinib in myelofibrosis: SIMPLIFY-2 subgroup analysis in transfusion-requiring patients

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To evaluate outcomes in pts who switched to MMB versus continuing RUX or best available therapy (BAT) despite transfusion requirement, we present a descriptive subgroup analysis of pts enrolled in SIMPLIFY-2 (NCT02101268) who were considered transfusion dependent (TD; ≥4 units of RBC transfusions in the previous 8 weeks or haemoglobin [Hb] level < 8 g/dL) or transfusion requiring (TR; receiving transfusions but not meeting TD criteria) at baseline (BL).
In SIMPLIFY-2 pts ($N = 156$) were randomized 2:1 to receive open-label MMB or BAT, which was RUX in 88.5% of pts. The primary end-point was spleen volume reduction ≥35% (SVR35). Total Symptom Score (TSS) response rate (≥50% reduction; TSS50) and transfusion-independence response (TI-R; no RBC transfusions for ≥12 weeks immediately before the end of Week 24, with all Hb levels ≥8 g/dL) were key secondary end-points.
In SIMPLIFY-2, 72 of 104 pts (69%) in the MMB arm and 33 of 52 pts (63%) in the BAT arm were non-TI at BL, and BL characteristics were balanced between both patient groups.
In BL non-TI patients, at Week 24 SVR35 was observed in 7 of 72 pts (10%) treated with MMB and 1 of 33 pts (3%) treated with BAT. TSS50 was achieved in 21 of 72 pts (29%) treated with MMB, but there were no responses in the BAT arm. Additionally, TI-R was achieved in 25 of 72 pts (35%) treated with MMB compared with 1 of 33 (3%) treated in the BAT arm on RUX. Many responders with MMB achieved two or all three end-points (16 of 36 responders [44%]); there were no dual or triple responses in the BAT arm. Of the five pts in the BAT arm who received ESAs, one pt each (different pts per response) achieved SVR35, TSS50 or TI. Safety outcomes were consistent with intent-to-treat (ITT) population.
In RUX/BAT-treated pts with MF who required RBC transfusions, continued treatment with RUX/BAT in most pts resulted in poor treatment outcomes compared with MMB. Specifically, treatment with MMB demonstrated an ability to deliver higher SVR, TI and TSS response rates. The lower SVR35 rate in both arms, similar to the overall ITT population, was likely a result of lack of washout from prior JAK inhibitor treatment. While pt numbers were limited, similar findings were observed compared with pts who received ESAs. Overall, these data support MMB as a potential alternative treatment option for pts with MF who require RBC transfusions.

BSH24-PO36 | 'Application of prognostic scoring in advanced systemic mastocytosis patients and the impact of novel therapies'

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Background: Advanced systemic mastocytosis (AdvSM) is a rare disorder of neoplastic mast cells resulting in multisystem end organ damage and a reduced life expectancy. AdvSM can be challenging to manage and prognostic scores developed could guide treatment strategies.
We previously reported our large single-centre experience in 2021; since then, there has been an increasing range of novel therapies. Here we present an update based on these recent developments.
Methods: We performed a retrospective study of 62 patients diagnosed with AdvSM between 2009 and 2023 including demographics, clinical data and next-generation sequencing (NGS)-based myeloid gene panels where available. Prognosis for all patients was calculated based on International

Prognostic score (IPSM 1–4; 1 = Low risk) (Sperr et al. [2019]) and Mutation-Adjusted Risk Score (MARS; Low vs. High risk) scores (Jawhar et al. [2019]).

Results: There was no gender bias in our cohort with 32 (52%) males and 30 (48%) females; mean age at diagnosis was 65 years (range 5–86). Majority of patients (48/62;77%) had an associated haematological neoplasm (SM-AHN), 11/62 (18%) aggressive SM (ASM) and 4/62 (6%) mast cell leukaemia (MCL). The most frequent AHN subtype was CMML (22/62; 35%). Median tryptase at diagnosis was 155ug/L (range 10–1551) and 59/62 (95%) had KIT D816V mutation.

On applying the IPSM score, largest proportion were AdvSM-3 (42/62; 68%). Survival outcome was higher in the AdvSM-1 group with no deaths recorded, while there were 4/9 (44%) deaths in AdvSM-4 group.

On application of MARS score most patients categorised as low risk (21/62, 34%), 17/62 (27%) intermediate risk and 20/62 (32%) high risk. Survival outcome was higher in the low-risk group compared to the intermediate- and high-risk groups, with 5-year OS of 95% vs. 43% and 47% respectively. 22/62 (35%) had progressive disease (PD) with four transforming to acute myeloid leukaemia (AML). Majority of deaths observed were due to AHN progression (12/22; 55%). There was a notable discrepancy between the IPSM and MARS scores as the latter includes the presence of S/A/R mutations. Four patients with high-risk disease achieved complete response (CR) with two receiving bezuclastinib and the other two avapritinib.

Conclusion: Application of the IPSM and MARS prognostic scores to our data reflects findings of other groups with better outcomes seen in low-risk compared to high-risk patients. Although our cohort is small, adverse risk factors could be overcome through recent advances in targeted treatments and consolidation with stem cell transplant in those with AHN progression.

BSH24-PO39 | Characterisation of disease phenotype and outcomes in young adult patients with myeloproliferative neoplasms

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Myeloproliferative neoplasms (MPNs) are commonly diagnosed in the 6th decade or later, although up to 20% of patients are diagnosed <40 years.

We present a retrospective analysis of 107 MPN adolescent and young adult (AYA) patients diagnosed <40 years, representing 19.6% of the total MPN cohort at UCLH. Median follow-up was 78 months. Median age at diagnosis was 32 years (range 13–40). The majority (66%) were female; 65.4% had a diagnosis of ET, 23.4% PV, 4.7% PMF and 2.8% MPN-U. 3.7% of patients had transformed to post-PV or post-ET myelofibrosis (PPV/PET-MF). There were no transformations to AML. The most common driver mutation was JAK2 V617F (59.8%), followed by CALR (15.0%); 19.6% of patients were classified as triple negative (TN). Additional pathogenic mutations were identified, including TET2 (2.8%), CSF3R (2.8%), RUNX1 (1.9%) and ASXL1 (1.9%).

We observed a thrombosis rate of 19.6%; this was the heralding event in 81.8% of cases. The majority were venous compared to arterial events (14.0% vs. 6.5% respectively). There was a disproportionate number of venous thromboses at unusual sites including cerebral venous sinus and splanchnic venous thromboses, representing 27.3% and 22.7% of events respectively. Thrombotic events were observed in 23.4% of JAK2V617F mutations, 20.0% TN and 5.9% of CALR-mutated patients. Haemorrhagic events were reported in 8.4%; 3.7% had grade 3 or 4 bleeding complications.

Hypertension and type 2 diabetes were present in 13.0% and 6.5% of all patients respectively. 25.2% of patients were current or ex-cigarette smokers. A QRISK3 score to estimate the 10-year risk of cardiovascular events showed a mean risk of 0.88% in all MPN patients; subgroup analysis revealed a mean QRISK3 score of 1.7% (PV) and 0.9% (ET). 30.8% of patients reported pregnancies; of these, 24.2% of patients reported antenatal or perinatal medical complications.

51.4% of patients were commenced on cytoreduction, including pegylated interferon in 24.3% and hydroxycarbamide in 22.4%. Commonest indications for commencing cytoreduction included control of blood parameters (41.8%) and prior thrombosis (34.5%). Eighty-six per cent patients were treated with an anti-platelet agent, and 8.4% were on an anti-coagulant.

AYA MPN patients have unique characteristics and heterogeneous clinico-biological features. Our data highlights a female preponderance and high incidence of venous thrombosis. While traditionally younger patients are considered to have 'low-risk' disease, this real-world study highlights a significant thrombosis rate of ~20%, which may have associated morbidity considering the relatively longer duration of disease course and need for cytoreductive therapy.

BSH24-PO40 | An audit of corticosteroid use in ITP at King's College Hospital NHS Trust

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Corticosteroids are used first line in the management of immune thrombocytopenia (ITP) and are associated with numerous side effects. The updated international consensus report on the investigation and management of ITP advises limiting exposure to corticosteroids with a dose cap of 80 mg prednisolone and stopping within 6–8 weeks (with a faster taper if no response). An audit involving a retrospective

case-note review to examine corticosteroid use in ITP was undertaken at King's College Hospital NHS Trust.

The project was divided into three phases: (i) the 'rescue' phase to identify patients who have been on corticosteroids for >8 weeks, (ii) the 'steroid use' phase to evaluate steroid use in acute ITP and (iii) the 'unified approach' phase to standardise corticosteroid use and monitoring.

As of July 2023, there were 99 patients with ITP under active follow-up at King's College Hospital NHS Trust. Seventeen patients were identified as having been on steroids for >8 weeks (7 had primary ITP and 10 secondary ITP). 8/17 remained on steroids for their underlying rheumatological disorder. The remaining nine were identified as the 'rescue' group. Of these nine patients, three have since stopped steroids, four had a clear plan to taper (with a view to stopping) but two continued steroids.

The use of steroids in managing acute ITP was then evaluated in 47 patients. The median platelet count at presentation was 7 (IQR 3.5–16). The median prednisolone starting dose was 0.8 mg/kg (range 0.3–1.2 mg/kg). Three patients had a starting dose of >80 mg, and one patient was treated with dexamethasone. Response rate (defined as platelets maintained >50) was seen in 31/47 (66%). 6/47 (13%) patients had a partial response (initial response not maintained necessitating second-line therapy). 9/47 (19%) had no response. The outcome was unclear for one patient. A variety of steroid tapering regimens were observed with a median duration of 12 weeks (range 5–39 weeks). Documented baseline monitoring was suboptimal with five (11%) patients having documented BP, 40 (85%) body weight, 7 (15%) HbA1c and 15 (32%) blood glucose. Forty-five (96%) patients were prescribed GI protection and 10 (21%) bone protection. All patients received an emergency steroid card from pharmacy.

The 'unified approach' phase is underway. A proforma is being devised to standardise tapering regimens, monitoring and use of adjunctive medication with the involvement of relevant specialties. A dedicated ITP nurse/pharmacist clinic is being set up to facilitate patient monitoring and support for patients on steroids.

BSH24-PO41 | Diagnosis and treatment patterns in European patients with systemic mastocytosis

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Objective: Systemic mastocytosis (SM) is a group of rare, clonal haematological neoplasm primarily driven by the KIT D816V mutation and characterized by unpredictable and debilitating skin, gastrointestinal, musculoskeletal and systemic symptoms impacting quality of life, ability to work and survival. The Perceptions Realities and Insights on Systemic Mastocytosis (PRISM) survey study sought to examine the experiences of SM patients, as well as gain perspectives from HCPs treating SM in Europe. Interim data from PRISM from HCPs in Germany, UK and Austria and their perspectives on the impact of SM on patients are reported.

Methods: PRISM included two independent studies: a patient survey (eligibility based on self-reported SM diagnosis) and a healthcare providers (HCPs) survey (eligibility based on self-reported SM patient management). The HCP survey (103 questions) queried HCPs on care approaches for patients with SM. Descriptive statistics were generated for each survey for three countries (UK, Germany, Austria).

Results: A total of 296 HCP responses were collected as part of the PRISM survey, from Germany, the UK and Austria. HCP respondents included haematologists/oncologists ($n = 87$), general practitioners ($n = 87$), dermatologists ($n = 35$) and allergist/immunologists ($n = 28$); the largest number of HCP responders were from Germany ($n = 123$). HCP perceptions of time to diagnosis of non-advanced SM averaged around 17.2 months. However, note the time to diagnosis reported accounts only for individual HCP experience and does not include time with other HCPs the patient may have seen previously. Most HCPs perceived significant SM impact on patient QoL and employment opportunities, with 68.2% reporting SM affected patients' lives 'quite a bit' or 'a great deal'; 59% reported patients lost employment opportunities due to SM. Across all countries, HCPs reported their top primary goals for treatment were focused on better QoL (all SM) and improved survival (advanced SM).

Conclusions: A variety of healthcare specialties diagnose and manage SM patients. HCPs perceive SM to have a considerable negative impact on patients' QoL and ability to work. Improving QoL and survival were the primary treatment goals of HCPs for their patients.

BSH24-PO42 | Burden of systemic mastocytosis in Europe and the UK: Interim results from PRISM patient survey

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Objective: Systemic mastocytosis (SM) is a rare, clonal mast cell disease primarily driven by the KIT D816V mutation, characterized by unpredictable and debilitating symptoms including skin, gastrointestinal, neurocognitive, musculoskeletal and other organ systems. These can have a significant impact on the quality of life (QoL) in SM patients. The Perceptions Realities and Insights on Systemic Mastocytosis (PRISM) survey study sought to examine the experiences of SM patients in Europe. Interim data from PRISM on the impact of indolent SM (ISM) on patients from the UK (UK), Germany and Austria are reported.

Methods: Patients reporting an SM diagnosis were eligible to participate in PRISM. The 119-item online survey queried SM type (if known: advanced, non-advanced including ISM), symptom burden (via a validated ISM symptom assessment form [ISM-SAF] generating a Total Symptom Score [TSS]) and QoL via the 12-item Short Form Health Survey (SF-12), EuroQoL five-dimension (EQ-5D), EuroQoL visual analogue scale (EQ VAS) and work productivity and activity impairment questionnaire (WPAI).

Results: Interim PRISM data from 210 SM patients from the UK ($n=101$), Germany ($n=83$) and Austria ($n=26$) showed that approximately half self-reported as ISM. Most ISM patients were female, with a mean age of 52.7 years. Mean TSS (41.2) indicated high patient symptom burden consistent with moderate to severe ISM (TSS ≥ 28); reduced physical functioning and mental health due to ISM were reported, with skin and gastrointestinal-related symptoms as most bothersome (28.6% and 13.3% respectively); a large subset of ISM patients experienced anaphylaxis (19.4%). Polypharmacy was high, with anti-histamines the most common non-prescription medication. Patients reported that ISM impacted their ability to work, with a many having to reduce their hours (31.6%), voluntarily quit their job (15.3%), take medical disability (14.3%), discontinue work entirely (12.2%) or take early retirement (10.2%).

Conclusions: Interim results from the PRISM survey indicated that ISM patients have a high burden of disease, poor QoL and reduced ability to work despite multiple symptom-targeted medications. Improved treatment options that effectively reduce symptom burden long term and polypharmacy are needed for these patients.

BSH24-PO43 | A single-site audit of treatment-free remission identification and monitoring in chronic myeloid leukaemia patients

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Patients with chronic-phase chronic myeloid leukaemia (CML) with sustained deep molecular remission (DMR) may be eligible for de-escalation of their tyrosine kinase inhibitor (TKI). Approximately 40%–50% of patients stopping their TKI will maintain DMR, without medication side effects/interactions, increased cardiovascular risk (up to 8%)[1] and reducing treatment cost. Strict monitoring of blood parameters during de-escalation/cessation of TKI therapy is crucial for early detection of disease recurrence.[2]

This single-site audit sought to assess identification of eligible patients and compliance with guidelines on monitoring of full blood count (FBC) and BCR-ABL during treatment de-escalation/treatment-free remission (TFR). Patients were identified from a local database. The eligibility guidelines were the European LeukemiaNet 2020 recommendations for CML management,[3] and South West Regional Myeloproliferative Neoplasm Forum guidance on monitoring frequency during dose reduction.

Of 33 eligible patients: 63% had started TFR, 12% had declined and 24% had never been approached. Analysis of monitoring compliance included 18 patients (3 excluded as TFR predated guideline). During 50% dose reduction, 83% of patients had a FBC and 61% had a BCR-ABL measured 2-monthly. After dose reduction 77.7% maintained their DMR and fully discontinued treatment, and although two of four that lost DMR had inconsistent BCR-ABL measurements, all maintained MR3. After treatment cessation 50% (of 12 patients) had both monitoring tests monthly for the first 6 months, 43% (of 7 patients) had both monitoring tests 2-monthly during months 7–12 and 66% (of 3 patients) had both monitoring tests 3-monthly at >12 months. A cost analysis found savings of up to £79 706 for the eight eligible patients not yet approached about TFR, and risk of adverse cardiac events would also be reduced.

Actions: a robust system for timely identification of eligible patients is required, led by the local laboratory or a clinical or administrative team member. Patient empowerment to manage monitoring tests should be encouraged, and reducing clinic appointments to only reviewing abnormal results.

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BSH24-PO44 | Single-centre audit of symptom burden in indolent systemic mastocytosis patients: UK centre of excellence

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Indolent systemic mastocytosis (ISM) is a rare, clonal haematological neoplasm, in most cases driven by the KIT D816V mutation. Mast cell mediator release results in a debilitating and unpredictable symptom burden. To date, there are no approved targeted therapies for ISM in the UK and no published UK data evaluating symptom burden. The Indolent Systemic Mastocytosis Symptom Assessment Form (ISM-SAF©) is a validated tool evaluating 11 symptoms over a 24-h recall period.

All adult ISM patients who had a routine outpatient consultation between May 2022 and May 2023 were invited to complete the ISM-SAF©. Additionally we collected data on demographics, anti-mediator therapy and anaphylaxis history.

Ninety-five patients with ISM were identified within our database, of which 76 consented to take part. There was a slight female predominance (41% male; 59% female) and the median age at diagnosis was 46 years (21–78). Median time since diagnosis was 4.6 years (0.5–18.5). Median serum tryptase was 35 mcg/L (9–632). Sixty-six patients (88%) were confirmed KIT D816V mutated (6% D816V negative, 6% not available). The median Total Symptom Score (TSS) was 24 (0–110). The highest scoring symptoms were fatigue (mean 4.66), skin spots (3.97), brain fog (3.43) and itch (2.83). Thirty-three (43%) had a TSS ≥28, which is the threshold determined by psychometric analysis for moderate to severe symptoms, and is used for screening in clinical trials. Forty-six (61%) were prescribed ≥2 anti-mediator therapies; at the time of the study, current therapies included H1 anti-histamines ($n = 64$), H2 anti-histamines ($n = 28$), proton pump inhibitors ($n = 20$), sodium cromoglycate ($n = 18$), montelukast ($n = 12$), corticosteroid ($n = 5$) and omalizumab ($n = 1$). Twelve (16%) were on a bisphosphonate. Twenty-seven (36%) had a TSS ≥28 and were taking ≥2 anti-mediator therapies. Thirty (39%) reported a history of anaphylaxis at least once in their lifetime while nine (12%) had used an adrenaline autoinjector within the last year. There was no statistically significant correlation between TSS and tryptase (Pearson correlation coefficient $r = -0.08$, $p = 0.48$).

Our data demonstrate a significant real-world symptom burden among the ISM patient cohort within the UK Mastocytosis Centre of Excellence, reflecting the findings of other centres. The ISM-SAF© is an effective tool for capturing a snapshot of symptom severity and has utility in the outpatient setting. Importantly, we found over one third of patients had a TSS ≥28 and were on ≥2 anti-mediator therapies, meaning they could potentially be eligible to access tyrosine kinase inhibitors within the clinical trial setting.

BSH24-PO45 | ACKR1/DARC-associated neutropenia (ADAN) is easily overlooked as a cause for unexplained asymptomatic neutropenia

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Background: Neutropenia is a common reason for haematology referral. Diagnostic workups can be challenging and may include invasive or complex tests such as bone marrow biopsies or germline genetic panel testing. ACKR1/DARC-associated neutropenia (ADAN, previously termed 'benign ethnic neutropenia') is a common cause of asymptomatic neutropenia, and confirming this enables patients to be reassured while avoiding more complex or invasive tests, but testing for this can be overlooked.

Methods: Patient lists for the adult benign general haematology clinic at the Bristol Haematology and Oncology Centre (University Hospitals Bristol and Weston NHS Foundation Trust, UHBW) during August–November 2023 were scrutinised to identify patients under follow-up for unexplained asymptomatic neutropenia who had not been tested for ADAN. Clinical notes and laboratory records were reviewed for details of diagnostic workup to identify potential reasons why Duffy phenotyping had not been performed.

Patients were then offered Duffy phenotyping at their clinic visit. This was performed on peripheral blood in the UHBW Blood Transfusion laboratory. Patients found to be Fy(a) negative and Fy(b) negative (Duffy-null) had samples sent to the IBGRL for confirmatory genotyping.

Results: We identified seven patients meeting the study criteria (5/7 female; median age 30 years [range; 21–47 years]). The self-declared ethnicities for the seven patients were 'African' (4/7), 'other White background' (2/7) and 'British' (1/7).

The median duration of follow-up in UHBW was 18 months (range; 9–48 months). Four patients had undergone bone marrow biopsy during diagnostic work-up performed at UHBW (1/7) or other centres (3/7). Review of the clinical notes identified factors that contributed to ADAN not being suspected including previous comprehensive investigation in other centres (3/7), neutrophil count perceived to be too low (2/7), neutrophil count intermittently within normal range (2/7).

All seven patients underwent Duffy phenotyping; five were confirmed Duffy-null, consistent with ADAN mean neutrophil count 0.49×10^9/L, SD 0.22. Four patients were reassured and discharged from further haematology follow-up. The remaining patient has both ADAN (with fluctuating mild neutropenia) and refractory autoimmune haemolytic anaemia and remains under haematology care.

Discussion: This work emphasises the importance of considering ADAN in all individuals with asymptomatic neutropenia, including those investigated previously with no cause found, and those with moderate as well as mild neutropenia. The approach to retrospectively identify individuals with ADAN is being applied to the other UHBW general haematology clinics, alongside prospective testing of all new patients referred with asymptomatic isolated neutropenia.

BSH24-PO46 | Comprehensive frailty assessment in older patients with myeloproliferative neoplasms

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Introduction: Patients with myeloproliferative neoplasms (MPNs) have a median age of onset of 65–68 years with increased risk of frailty associated with this age group. Frailty is predictive of adverse health outcomes such as falls, hospitalisation and increased mortality.

Aim: This study focused on investigating and managing frailty in older adults diagnosed with MPNs and exploring its implications on quality of life.

Methods: Patients completed an 18-point frailty questionnaire with binary responses focusing on frailty-related characteristics. A score of 7 or above is recognised as meeting criteria to suggest frailty. Patients meeting this threshold were referred to the Geriatric Oncology Liaison Development (GOLD) clinic for further assessment and management. Patients attending the GOLD clinic were reviewed via telephone to provide feedback on their experience. The feedback and ratings obtained from patients during follow-up were compiled and patterns in patient feedback were identified to gauge the effectiveness and patient satisfaction with their GOLD clinic appointment in the MPN patient population.

Results: Forty-two participants were included between the ages 69 and 89 with median age 77 years. Participants had a median frailty score of 4.00 (range 0–12), with 30.95% meeting criteria for referral with score >7.

Of note, there was no correlation between increasing age and frailty ($r = 0.13$, $p = 0.41$). There was no significant difference in frailty between patients with essential thrombocythaemia (mean frailty score 4.3) and polycythaemia vera (5.5, $p = 0.33$). Frailty did not significantly differ between genders. Noteworthy frailty characteristics included fatigue in 64% (27), urinary urgency/incontinence in 57% (24), difficulty with activities in 55% (23) and depression in 40% (17). Out of the participants, 30.95% were eligible for referral to the GOLD clinic, primarily due to mobility issues. Post-GOLD clinic, 72.7% experienced pharmacological changes with 36.4% of patients having a reduction in polypharmacy. 36.36% of patients were referred for physiotherapy, and an additional 36.36% were referred for additional investigations. 57.1% rated their experience with an optimal score of 5/5. The mean satisfaction score was 4.57 (4–5). Positive feedback emphasised effective pain management advice and feeling supported by the GOLD team.

Discussion: Comparisons with general population studies suggest increased prevalence of frailty in MPN patients. Our findings emphasise the need for integrating frailty assessments into MPN clinics for a more holistic and personalised approach to patient management. Future research should explore defining a universal frailty definition and consider long-term surveillance to assess the survival benefits of managing frailty in MPN patients.

BSH24-PO47 | Cognitive impairment in patients with immune thrombocytopenia (ITP)

Miss Camelia Vladescu[1,2], Dr Alice Hart[1,2], Ms. Deena Paul[1], Dr Christine Ademokun[1], Ms. Ariam Teklemichael[1], Miss Bridget Chivers[1], Ms. Vashti Ragoonanan[1], Ms. Sandra Sigudu[1], Dr Anastastia Gontsarova[1], Dr Richard Szydlo[2], Prof. Adam Waldman[2,3], Prof. Nichola Cooper[1,2]
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Introduction: Immune thrombocytopenia (ITP) is an autoimmune condition characterised by a low platelet count ($<100 \times 10^9$/L). Patients with ITP have an increased risk of bruising and bleeding (mainly skin and mucosal). A study by Cooper et al published in 2020 showed that 43% of adult ITP patients have occult cerebral microbleeds (CMBs) on susceptibility-weighted magnetic resonance imaging (SW-MRI). The clinical and prognostic significance of CMBs has not been established, but some studies have shown they are associated with cognitive impairment. ITP was believed to

be an isolated blood disease, but more recent studies demonstrate impaired quality of life with symptoms including fatigue, memory and concentration problems. This may be suggestive of cognitive impairment.

Aims: To determine the prevalence of cognitive impairment in patients with ITP and explore any connections between CMBs, ITP parameters and cognitive impairment.

Methods: Patients with primary ITP and a nadir platelet count $\leq 30 \times 10^9$/L were recruited from Hammersmith Hospital. Patients underwent cognitive testing using an automated neuropsychological test battery (CANTAB), completion of SMOG (skin, mucosal, organs) bleeding questionnaire and cerebral SW-MRI to identify CMBs. Five key cognitive domains (episodic memory, executive function, processing speed, working memory and attention) were assessed.

Results: A total of 68 patients completed CANTAB cognitive testing and MRI. The median age was 40 years (range 19–88), median age at diagnosis was 31 years (range 4–83), median duration of disease was 67.5 months (range 5–535), median nadir platelet count was 5×10^9/L (range 0–30), median platelet count at time of test was 95×10^9/L (range 4–653) and median number of ITP treatments received was 4 (range 0–14). Fifty per cent of patients were receiving ITP treatment at the time of cognitive testing.

Thirty-three of the 68 patients tested (48.5%) (95% CI [37, 62]) had at least one impaired cognitive domain, with 23% in episodic memory, 18% in executive function, 16% in processing speed, 12% in working memory and 3% in attention. Twenty-two of the 68 patients (32%) had at least one CMB on the SW-MRI. However, no statistically significant associations were found between CMB presence, ITP parameters and impaired cognition.

Conclusion: This is the first study to objectively measure cognitive impairment in patients with ITP and the results suggest that ITP is not just a 'low platelet' disease. Association between presence of CMBs, ITP disease parameters and impaired cognition requires further investigation in a larger cohort.

BSH24-PO48 | Overview of erythrocytosis and thrombocytosis referrals within general haematology clinics—Streamlining the MPN service

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Background: Growing pressures on the myeloproliferative neoplasm (MPN) services, as with all subspecialities, have resulted in prolonged waits, delayed investigations and increased patient anxiety. Compounded by the COVID-19 pandemic, it is now more challenging to review complex patients alongside tertiary referrals in a timely manner.

To address this, we developed a pathway to streamline primary care referrals of erythrocytosis or thrombocytosis. Strict criteria were set to identify high-risk patients who warranted urgent intervention or those with other features suggesting an MPN.

Aim: A prospective audit was completed examining all primary care referrals reviewed in the general haematology clinic between 1st June 2023 and 20th December 2023. Baseline demographics along with blood results, molecular markers and final diagnosis were analysed.

Results: Overall, 32 patients were reviewed. 21/32 (66%) were referred with erythrocytosis and 11/32 (34%) with thrombocytosis. In the erythrocytosis cohort, mean age was 58 years (range 34–72 years) with 14/21 (67%) males. The average haematocrit was 52.0% (range 47–59%) while haemoglobin was 173 g/L (range 152–192 g/L). JAK2V617F was only detected in 2/21 (10%) patients with VAF 0.98% and 38%. Within the thrombocytosis cohort, the majority were females (9/11; 81%) with mean age 48 years (range 19–75 years). The average platelet count was 615×10^9/L (range $423–973 \times 10^9$/L). 7/20 (35%) had molecular markers sent, all of which were negative.

Only 4/32 (13%; 3/21 with erythrocytosis, 1/11 with thrombocytosis) proceeded for bone marrow biopsy for suspected MPN. The rest had identifiable secondary causes with 79% (22/28) of those diagnosed at first visit.

In the erythrocytosis cohort, secondary causes included smoking (9/21; 42%), sleep apnoea (2/21; 10%) and medications (4/21; 19%). In the thrombocytosis cohort, patients had iron deficiency (8/11; 73%) or underlying inflammatory disorders (2/11; 18%).

Notably, of the erythrocytosis and thrombocytosis cohorts, respectively, 11/21 (52%) and 2/11 (18%) did not meet 2019 BCSH initial criteria for referral and diagnosis (PCV >52% in males, >48% in females for erythrocytosis; platelet count $>450 \times 10^9$/L for thrombocytosis).

Conclusion: Overall, although a small cohort, this highlights the efficacy of our referral pathway. Importantly, most patients had identifiable secondary causes with only a small number requiring further appointments or invasive investigations.

The fact that 40% of patients did not meet BSCH referral criteria raises the question whether patients could be further assessed in the community, perhaps virtually or prescreened. Additional work is needed to support the primary sector, aiming to reduce pressures on haematology services and improve patient care.

BSH24-PO49 | An audit: Prevention of glucocorticoid-induced osteoporosis in patients with ITP/WAIHA receiving steroids

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Background: Glucocorticoid-induced osteoporosis (GCIOP) and fragility fractures present challenges in the treatment of immune thrombocytopenia (ITP) and warm autoimmune haemolytic anaemia (WAIHA), affecting 30%–50% of adults on long-term glucocorticoid therapy. The British Committee for Standards in Haematology (BCSH) recommends discussing bone health, identifying additional risk factors for fracture and using preventative interventions early.
Aim: We designed an audit to evaluate compliance with the BCSH guidelines on GCIOP in patients with ITP and WAIHA treatment regimens at our centre.
Method: Electronic records of 49 patients, aged 10–98 years, undergoing glucocorticoid treatment for WAIHA and ITP were analysed.
Results: The demographics show a higher proportion of females (63%; 31/49) compared to males (37%; 18/49). Sixty-five per cent of females were postmenopausal. Nearly half of the patients received steroids for over 6 weeks (49%; 24/49), and over half (55%; 27/49) received a cumulative prednisolone dose exceeding 1000 mg. Calcium levels were routinely checked in 96% (47/49) of the patients, while vitamin D levels were measured in 51% (25/49). The majority of patients did not receive calcium (80%; 39/49) or vitamin D (73%; 36/49). Four per cent (2/49) of patients sustained fractures while on steroids and were not prescribed bone protection. The majority of patients had no documentation of a FRAX score (98%; 48/49) and had not undergone a DEXA scan (92%; 45/49). However, incomplete electronic records could have been a limiting factor as not all low-risk FRAX scores may have been documented. Only 10% (5/49) of patients received bisphosphonates. These numbers were similar in patients over 70 years of age. The majority of postmenopausal women did not receive calcium (70%; 14/20), vitamin D (60%; 12/20) or bisphosphonates (85%; 17/20).
Conclusion: Despite the increasing awareness of GCIOP among healthcare professionals, management of this condition remains suboptimal. It is encouraging that just over half of steroid courses were completed within 6 weeks. Compliance with BCSH guidelines in patients on long-term steroids requires improvement at our centre, and we have implemented measures to improve awareness and compliance. In the future, comprehensive training, automated electronic alerts, educational posters for immune clinics can be incorporated.

BSH24-PO50 | Improvements in health-related quality of life after exagamglogene autotemcel in patients with sickle cell disease

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Background: Severe sickle cell disease (SCD) has substantial negative impact on health-related quality of life (HRQoL). Exagamglogene autotemcel (exa-cel) is a one-time, non-viral, ex vivo CRISPR/Cas9 gene-edited cell therapy shown to eliminate VOCs in patients with SCD. We report HRQoL data from the exa-cel CLIMB SCD-121 study.
Methods: CLIMB SCD-121 is an ongoing phase 3 trial of exa-cel in patients ages 12–35 years with SCD. Changes in patient-reported outcomes measures EuroQol 5 Dimensions 5 Levels of severity (EQ-5D-5L, including descriptive system and visual analogue scale [VAS]), Functional Assessment of Cancer Therapy Bone Marrow Transplant (FACT-BMT, including FACT-General [FACT-G] and bone marrow transplant subscale [BMTS]), Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me) and the 11-point pain Numerical Rating Scale (NRS) were assessed as a secondary end-point.
Results: As of 14 June 2023, 24 adults (18–35 years) followed for ≥16 months were evaluated for changes in HRQOL. At baseline, the EQ-5D-5L health utility US index ($n = 23$; mean [SD]: 0.78 [0.23]) and EQ VAS ($n = 24$; 68.8 [22.7]) scores were lower than the US general population norm and similar to baseline scores reported for adults with SCD with recurrent VOCs. By month 6, both EQ-5D-5L health utility US index score and EQ VAS score substantially improved, which were maintained through month 24 (mean changes [SD] at month 24 [$n = 17$]: 0.13 [0.19]; MCID 0.078 and 26.9 [22.6]; MCID 7–10 respectively). FACT-G Total Score improved from baseline at month 24 (mean [SD] change [$n = 17$]: 21.0 [18.1]; MCID 3–7), with improvements in all four subscales (physical, social/family, emotional and functional well-being). BMTS score improved by month 6 and was sustained through month 24 (mean [SD] change at month 24 [$n = 17$]: 3.9 [5.3]; MCID 2–3). Most ASCQ-Me subscales, including emotional (mean [SD] change [$n = 16$] 10.3 [10.9]), social (16.4 [11.0]) and stiffness impacts (6.6 [10.5]; MCID 5 for all), demonstrated clinically meaningful improvements from baseline through month 24. For the ASCQ-Me pain-related subscales, the largest improvement was observed in pain

episode frequency (mean [SD] change at month 24 [$n = 17$]: −21.0 [7.7]; MCID -5). Improvements in the pain NRS were observed by month 12 and sustained through month 24 (mean [SD] change at month 24 [$n = 17$]: −1.7 [2.5]; MCID -1).
Conclusion: Adults infused with exa-cel reported sustained and clinically meaningful improvements in their HRQoL, demonstrating the broad clinical benefits of exa-cel in patients with SCD.

BSH24-PO51 | Improvements in health-related quality of life after exagamglogene autotemcel in patients with transfusion-dependent beta thalassaemia

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Background: Transfusion-dependent β-thalassaemia (TDT) has a substantial negative impact on health-related qualify of life (HRQoL). Exagamglogene autotemcel (exa-cel) is a one-time, non-viral, ex vivo CRISPR-Cas9 gene-edited cell therapy that has been shown to eliminate the need for red blood cell (RBC) transfusions in patients with TDT. We report HRQoL data from the exa-cel CLIMB TDT-111 study.
Methods: CLIMB TDT-111 is an ongoing, 24-month, phase 3 trial of exa-cel in patients aged 12–35 years with TDT. Changes in patient-reported outcome measures EuroQol Scale 5 Dimensions 5 Levels of severity (EQ-5D-5L, including descriptive system and visual analogue scale [VAS]) and Functional Assessment of Cancer Therapy Bone Marrow Transplant (FACT-BMT, including FACT-General [FACT-G] and bone marrow transplant subscale [BMTS]) for adults and the EuroQol Quality of Life Scale 5 dimensions youth (EQ-5D-Y) and Pediatric Quality of Life Inventory (PedsQL) for adolescents were assessed as a secondary end-point.
Results: As of 16 April 2023, 29 adults (≥18 to ≤35 years) and 13 adolescents (≥12 to <18 years) followed for ≥16 months were evaluated for changes in HRQOL. At baseline, mean EQ-5D-5L health utility US index score ($n = 29$, mean [SD]: 0.87 [0.17]) was near the general population norm and in line with baseline scores reported for adults with TDT. By month 24, EQ-5D-5L health utility US index and EQ VAS scores improved (mean [SD] changes [$n = 19$]: 0.06 [0.28] and 10.7 [18.6] points; MCIDs 0.078 and 7–10 respectively). FACT-G Total Score improved from baseline by month 12 and was sustained through month 24 (mean [SD] change at month 24 [$n = 19$] 8.3 [16.9] points; MCID 3–7), with improvements in all four subscales (physical, social/family, emotional and functional well-being). BMTS score improved by month 12 and was sustained through month 24 (mean [SD] change at month 24 [$n = 19$] 5.6 [5.6] points; MCID 2–3).
For adolescents, EQ VAS scores improved through month 12 (mean [SD] change [$n = 13$] 7.9 [18.7] points). Total PedsQL score improved by month 6 and was sustained through month 18 (mean [SD] change at month 18 [$n = 10$] 11.5 [12.4] points; MCID 4.36). Physical functioning and psychosocial health scores, subcomponents of PedsQL, showed sustained improvement through month 18 (mean [SD] change [$n = 10$] 15.0 [16.6] and 9.6 [11.5] points; MCID 6.66 and 5.30 points respectively).
Conclusion: Adults and adolescents infused with exa-cel reported sustained and clinically meaningful improvements in their HRQoL, demonstrating the broad clinical benefits of exa-cel.

BSH24-PO52 | Clonal expansion during asciminib treatment may be associated with resistance in CML

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Asciminib is a novel BCR::ABL1 inhibitor effective in the treatment of chronic myeloid leukaemia (CML). It differs from existing tyrosine kinase inhibitors (TKIs) because it targets the myristoyl pocket of ABL1, rather than the ATP-pocket targeted by other TKIs. This innovative mechanism predicts for fewer off-target toxicities, with the potential to circumvent ATP-pocket tyrosine kinase domain mutations (TKDM). TKDMs have typically been identified by Sanger sequencing, but next-generation sequencing (NGS) offers greater sensitivity, and wider coverage of the BCR::ABL1, which important when using drugs that have effects outside the kinase domain, such as asciminib. NGS also provides a quantitation of the variant allele frequency, allowing tracking of expansion or regression of variant-harbouring clones over time.
To determine the impact of BCR::ABL1 mutations in patients receiving asciminib, we undertook NGS-TKDM screening for single-nucleotide variants (SNV) resulting in amino acid substitutions (amino acid 220–509), termed BCR::ABL1-SNV (BSNV). In a cohort who had received asciminib as part of a managed access programme from Novarits, we screened samples immediately prior to asciminib initiation in 34 patients, then again at cessation in 10 patients (eight of whom had stopped for resistance and two for intolerance),

and in ongoing treatment samples in 16 patients (10 of whom were in MMR, 3 in CCyR).

In this heavily pretreated group (median number of prior TKIs 4 [2–5]), we identified BSNV in baselines samples of 11 patients (32%). T315I patients received escalated doses of asciminib, and there was no difference in response rates between those harbouring a T315I-BSNV or not (CCyR 43% vs. 73%, $p = 0.116$, MMR 43% vs. 63%, $p = 0.335$). In contrast, those with a detectable non-T315I-BSVN had lower rates of response (CCyR 14% vs. 81%, $p = 0.001$, MMR 14% vs. 70%, $p = 0.007$). Additionally, we identified two distinct patterns of clonal evolution of BSNV-harbouring populations during treatment with asciminib. One group had maintained or expanded clonal dominance that was associated with overt treatment failure or loss of response, while another showed evidence of clonal dominance but with maintained or deepening BCR::ABL1-qPCR responses. These data provide evidence that some BSNV are associated with resistance to asciminib. It also provides evidence of clonal dominance in the context of treatment response, suggesting that asciminib exerts selective pressure on some BSNV-harbour populations. The encouraging responses to escalated doses asciminib in patients with T315I raises the question of the role of dose escalations in patients with non-T315I-BSNV.

BSH24-PO53 | Cognitive impairment in patients with immune thrombocytopenia (ITP)

Miss Camelia Vladescu[1,2], Dr Alice Hart[1,2], Ms. Deena Paul[1], Dr Christine Ademokun[1], Miss Ariam Teklemichael[1], Miss Bridget Chivers[1,2], Ms. Vashti Ragoonanan[1], Ms. Sandra Sigudu[1], Dr Anastasia Gontsarova[1], Dr Richard Szydlo[2], Prof. Adam Waldman[2,3], Prof. Nichola Cooper[1,2]

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Introduction: Immune thrombocytopenia (ITP) is an autoimmune condition characterised by a low platelet count ($<100 \times 10^9$/L). Patients with ITP have an increased risk of bruising and bleeding (mainly skin and mucosal). A study by Cooper et al published in 2020 showed that 43% of adult ITP patients have occult cerebral microbleeds (CMBs) on susceptibility-weighted magnetic resonance imaging (SW-MRI). The clinical and prognostic significance of CMBs has not been established, but some studies have shown they are associated with cognitive impairment. ITP was believed to be an isolated blood disease, but more recent studies demonstrate impaired quality of life with symptoms including fatigue, memory and concentration problems. This may be suggestive of cognitive impairment.

Aims: To determine the prevalence of cognitive impairment in patients with ITP and explore any connections between CMBs, ITP disease parameters and cognitive impairment.

Methods: Patients with primary ITP and a nadir platelet count $\leq 30 \times 10^9$/L were recruited from Hammersmith Hospital, London. Patients underwent cognitive testing using an automated neuropsychological test battery (CANTAB), completion of SMOG (skin, mucosal, organs) bleeding questionnaire and cerebral SW-MRI to identify CMBs. Five key cognitive domains (episodic memory, executive function, processing speed, working memory and attention) were assessed.

Results: A total of 68 patients completed CANTAB cognitive testing and MRI. The median age was 40 years (range 19–88), median age at diagnosis was 31 years (range 4–83), median duration of disease was 67.5 months (range 5–535), median nadir platelet count was 5×10^9/L (range 0–30), median platelet count at time of test was 95×10^9/L (range 4–653) and median number of ITP treatments received was 4 (range 0–14). Fifty per cent of patients were receiving ITP treatment at the time of cognitive testing.

Thirty-three of the 68 patients tested (48.5%) (95% CI [37, 62]) had at least one impaired cognitive domain, with 23% in episodic memory, 18% in executive function, 16% in processing speed, 12% in working memory and 3% in attention. Twenty-two of the 68 patients (32%) had at least one CMB on the SW-MRI. However, no statistically significant associations were found between CMB presence, ITP parameters and impaired cognition.

Conclusion: This is the first study to objectively measure cognitive impairment in patients with ITP, and the results suggest that ITP is not just a 'low platelet' disease. The association between the presence of CMBs, ITP disease parameters and impaired cognition requires further investigation in a larger cohort.

BSH24-PO54 | Early recovery of immune effector cells in myelofibrosis patients treated with momelotinib after ruxolitinib

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Introduction: Momelotinib (MMB), a novel oral JAK1, JAK2 inhibitor (JAKi) and Activin A receptor Type 1 inhibitor, has been shown to improve symptoms, anaemia and splenomegaly in myelofibrosis (MF). Established JAKi therapy with ruxolitinib (RUX) is associated with significant immune suppression, partly due to reduced cellular immunity, increasing risk for opportunistic infections and skin cancer.

The effects of MMB on immune effector cells have not been previously described.

Aim: To evaluate MMB efficacy in a 'real-world' setting and compare its effects on immune effector cell frequencies after switching from RUX.

Methods: Patients were monitored for a 12-week period after MMB initiation. Peripheral blood mononuclear cells from 25 patients were analysed to assess immune effector cell frequency at baseline while on RUX, at 6 weeks ($n = 15$), and 12 weeks ($n = 12$) post-treatment initiation. Ten healthy subjects were used as controls (HC).

Results: Twenty-five MF patients, starting MMB at either 200 mg ($n = 22$) or 100 mg ($n = 3$) daily dose, following prior RUX resistance/intolerance, were included (primary MF $n = 9$, secondary MF $n = 16$). The median age was 71 years, with 1:1 female: male ratio.

Twenty-two patients were monitored for ≥12 weeks after MMB initiation to assess haematological response, with 82% ($n = 18$) requiring regular transfusions at baseline. Of these, 15 patients (83%) achieved transfusion independence by 12 weeks, which some maintained for the entire period. The mean Hb from the 16 patients who remained transfusion independent after starting MMB was 85.9 g/L at baseline versus 99.2 g/L 12 weeks post-treatment ($p < 0.0001$).

Patients showed significantly reduced frequencies of CD3+, CD4+, CD8+ and NK cells at baseline while on RUX compared to HC ($p < 0.01$). There was, however, a significant increase in total lymphocytes, CD3+ and CD4+ T cells, B cells and NK cells after 6 weeks of MMB therapy vs. baseline ($p = 0.01$, 0.03, 0.01, 0.02 and 0.01 respectively), which persisted at 12 weeks post-MMB initiation for total lymphocytes, CD3+ and CD4+ T cells ($p = 0.03$, 0.02, 0.02).

Discussion: We observed a reduced frequency of immune effector cells following initial RUX treatment, as expected, likely due to JAK inhibition of lymphocyte differentiation. However, a significant increase in immune effector cells was observed after 6 weeks of MMB therapy, which was sustained at the 12-week follow-up for total lymphocytes, CD3+ and CD4+ T cells. Additionally, we found that MMB showed a notable benefit in improving anaemia. Continued follow-up and further studies are necessary to assess MMB's mechanistic impact on immune cell proliferation and recovery.

BSH24-PO55 | MyMPNVoice—The new MPN app for patient-reported outcomes and biometric data monitoring

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Introduction: Symptom burden in MPN patients is strongly associated with quality of life, helps determine selection of therapies and can be used as a marker of disease progression. As such, accurate assessment is an important part of routine clinical evaluation. The MPN-10 tool assesses 10 of the most clinically relevant symptoms in MPN. It has been previously shown that self-reporting of patient-reported outcomes (PRO) in cancer can have a benefit on survival.

Wearable technology and mobile applications provide the opportunity for constant patient monitoring. Digital web-based mobile-friendly tools that capture information are currently being successfully implemented; however, the need to include PRO is paramount as these offer the opportunity for more active participation of patients, who are key partners, owners, and drivers of evidence generation.

Aim: To improve monitoring of PRO in MPN patients through development of an app, to better understand relevance for clinical outcomes.

Methods: We initially performed a feasibility patient survey to assess the utility of app development in our patient population. Six hundred and ninety-nine patients were included, with 86% of respondents confirming that they would use an app to track symptoms, monitor treatment response and as a link to patient information. This included 100% of patients under 25 years of age, 93% of 26–59 year olds and 81% of those >60.

In recognition of the above, we have created the MyMPNVoice app in collaboration with the biotech company Sanius. Among other features, this will allow patients to record MPN-10 TSS and other PRO. A single-visit observational study (IRAS 332286) will be conducted to further evaluate its impact. Participants across the UK will be able to enrol by self-referring onto the study through MPNvoice or other social media platforms. Eligibility criteria include age over 18, residence in the UK with access to a smartphone and a confirmed diagnosis of MPN. Participants will consent remotely and undergo a digital 'onboarding' process. This will include the completion of a Subject Access Request (SAR) application, to give permission to request data from the participant's medical records. Participants in the substudy will receive a smartwatch (Withings Scan-Watch), which will record biometric data that will link to the app, to provide information on variables including activity, sleep scores, heart rate and oxygen saturation.

Conclusion: With limited insight into QoL and PROs in MPN currently, this study will deliver critical real-world evidence to act as a valuable tool in patient management and accelerate clinical research in future.

BSH24-PO56 | Exploring prognostic factors in myeloproliferative neoplasms-associated splanchnic vein thrombosis

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Introduction: Myeloproliferative neoplasms (MPN) represent the main underlying cause of splanchnic vein thrombosis (SVT), leading to significant morbidity and mortality. The clinical course is heterogeneous, and as a result, the impact of SVT on MPN patient's survival remains debated.

Methods: A total of 85 patients diagnosed with MPN-SVT referred to Guy's Hospital were retrospectively analysed in this study, and 171 MPNs were used as controls, matched for the MPN subtype. Demographic, clinical and outcome data were collected and reported.

Results: Eighty-five patients with MPN-SVT were analysed with a median follow-up of 7.7 years (range 0.3–30). Female patients (50/85, 58.8%) were prevalent with a median age at MPN diagnosis of 44 years (range, 13–70). MPN and SVT diagnoses were coincident in 56 patients (65.9%), and in 21 (24.7%), an SVT index event occurred after the diagnosis of MPN by a median of 4 years (range, 0.3–14.7). The most common site of thrombosis (70.6%) was the portal vein (PT), followed by splenic thrombosis (ST) in 26% and mesenteric vein (MT) in 23.5%. At MPN diagnosis, MPN-SVT patients had lower Hb ($p < 0.001$), platelet count ($p = 0.004$) and WBC count ($p = 0.019$) compared to the controls. The incidence of recurrent thrombosis was 16.5%, with a median time to recurrence of 4.5 years (range, 0.2–16.5). Controversy, major haemorrhages were experienced in 20% of patients. Overall, 13/85 (15.3%) and 3/85 (3.5%) progressed to secondary myelofibrosis and acute leukaemia respectively. Patients who had not progressed (69/85, 81.2%) had a lower median age at MPN diagnosis (41, range 13–70) than patients who experienced disease progression (49, range 36–69) ($p = 0.006$). The overall survival (OS) at last follow-up was 89.4%. The most frequent cause of death resulted from acute leukaemia transformation in four patients. Finally, the univariate Cox models confirmed a negative influence of age at diagnosis (HR 1.08, 95% CI 1.01–1.16, $p = 0.025$) and history of previous thrombosis (OR 4.46, 95% CI 1.1–18, $p = 0.036$). The median OS of MPN-SVT (358 months) was shorter than controls (not reached, $p < 0.049$).

Conclusion: We confirmed a consistent association between SVT and a specific MPN phenotype, mainly affecting young females diagnosed with PV. This rare entity remains challenging to manage clinically due to the considerable risk of subsequent vascular events. Furthermore, we revealed that the outcomes for MPN-SVT patients are influenced by their history of previous thrombosis and age at diagnosis. In the future, gaining a more comprehensive understanding of MPN-SVT is crucial for enhanced risk stratification.

BSH24-PO57 | Clinical features of triple-negative essential thrombocythaemia at London Tertiary Centre

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Patients with 'triple-negative' (TN) essential thrombocythaemia (ET) demonstrate the clinical and laboratory features (including characteristic bone marrow appearances) of ET, but lack the three driver mutations associated with the disease (JAK2 V617F, CALR, MPL exon 10). We aimed to characterise the clinical features and disease course of this subset of ET patients. Data on consecutive patients, referred to a London tertiary centre between 2001 and 2021, were analysed. Eighteen patients fulfilling the diagnostic criteria for TN ET were identified, of whom most (13/18 = 72.2%) were female, with a median age of 44.5 years (range 29–82), and a median Hb and neutrophil count of 134 g/L (range 111–155 g/L) and 4×10^9/L ($2.5–8.3 \times 10^9$/L) respectively. The spleen size was normal in all patients. Over a median follow-up of 66 months, two patients developed arterial thromboses, both in the presence of other risk factors. Nine of the 18 patients received cytoreduction therapy with hydroxycarbamide, with a median age of 48.5 (range 29–82). Two patients received cytoreduction with anagrelide, and one with pegylated interferon. No patients progressed to develop acute myeloid leukaemia (AML) or myelofibrosis. Myeloid next-generation sequencing (NGS) was performed on PB or BM of all patients but did not identify any mutations of significance. This small dataset confirms other studies suggesting that patients with TN ET are typically younger, more likely to be female and have a relatively benign natural history compared with classical (driver-mutation positive) ET, and contributes to the growing appreciation of TN ET as a separate clinicopathological entity.

BSH24-PO58 | Elucidation of early signalling pathways in an essential thrombocythaemia model during ruxolitinib inhibition

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Essential thrombocythaemia (ET) is a rare chronic myeloproliferative neoplasm characterised by platelet hyperproliferation that is associated with an increased risk of thrombotic and haemorrhagic events. There is no cure for ET and current treatment methods aim to alleviate symptoms for more effective management of the condition however, they do not reduce the risk of disease progression to myelofibrosis (MF) and/or acute myeloid leukaemia. Despite advances in understanding the pathogenesis of ET, the underlying aetiological mechanisms remain unknown. A driver of the disorder is the somatic JAK2 V617F mutation, which is harboured in 50%–60% of patients. The V617F mutation results in the constitutive activation of the JAK–STAT signalling pathway and upregulation of signal transducer and activator of transcription factor (STAT) proteins which promote cell proliferation and survival. The aetiological mechanisms which influence this pathway remain unknown requiring targeted pathway analysis.

This study utilised the novel method of bioorthogonal non-canonical amino acid tagging (BONCAT) along with 'click' chemistry in a targeted analysis to identify newly synthesised proteins in an ET cell model (SET-2) in response to a JAK2 inhibitor, ruxolitinib. Newly synthesised proteins were tagged with a methionine analogue, azidohomoalanine (AHA), extracted using 'click' chemistry on DBCO-agarose beads, released from the beads and quantified using high-resolution mass spectrometry on a 6600 TripleTOF mass spectrometer (AB Sciex, UK) and an Eksigent 1D+ Nano LC systems (Eksigent, CA). Three biological triplicates of each condition (±ruxolitinib) were processed at a 1% FDR for protein identification and quantification (Mascot Daemon and Distiller software). MarkerView and Perseus software were utilised for data filtering and analysis. Three thousand and forty-two proteins were identified, 107 were significant by either Welches *t*-test (p-value <0.05) or presence/absence. Bioinformatic analysis showed that 45.3% of significantly downregulated genes were involved in biological regulation, metabolic process and immune system process. Negative regulators of the JAK–STAT pathway, such as PTPN2, were found to be downregulated in the presence of ruxolitinib. Additionally, we found that the cytokine-mediated signalling pathway and interferon-mediated signalling pathway were downregulated in the presence of the JAK2 inhibitor. This functional proteomic study allows us to gain new insights into the molecular pathways that drive essential thrombocythaemia.

BSH24-PO61 | Immature platelet fraction in ITP is inversely proportional to platelet counts during thrombocytopenic episodes

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Immature platelets are increased when there is peripheral platelet consumption associated with increased bone marrow production and premature release into circulating blood. They can be identified by their large size and high RNA concentration. Immature platelet fraction (IPF) represents the total number of immature platelets to the total number of platelets, expressed as a percentage (%-IPF). Many automated analysers report %-IPF, and a recent study validated normal reference ranges for men and women. There is a general agreement that %-IPF is a reliable index to discriminate platelet hyperconsumption/hyperdestruction from hypoproduction. However, the evidence for its clinical utility in immune thrombocytopenia (ITP) is lacking.

We conducted a single-centre analysis of a selected number of ITP patients using data from the Sysmex-XN20, correlated with their platelet counts.

Twenty-seven (12 M; 15F) patients with primary ITP for which we had a least one %-IPF result were identified. Median age (range) of patients was 41.5 (23–96) years. A total of 260%-IPF results were available for the 27 patients. 58/260%-IPF results were for platelet counts less than 40×10^9/L (range; $0–37 \times 10^9$/L) and %-IPF ranged from 2.7% to 51.4%. Using the validated normal reference ranges for %-IPF in men (1.8–10%) and women (1.5–10.1%), all 58 results, with the exception of one had a %-IPF above the reference range. The one patient with a low %-IPF presented with acute ITP, and 5 days after starting prednisolone the %-IPF had increased to 23.8%. Of the 27 patients, 21 patients normalised their %-IPF when platelets rose above 150×10^9/L. The six patients that still had high %-IPF's, were chronic ITP patients with frequent relapses, which may be the cause of the persistently raised %-IPF.

Longitudinal analysis of these patients demonstrated a dynamic inverse correlation between %-IPF and rising platelet counts following treatment. A Pearson's correlation coefficient of $r = -0.455$ was calculated ($p < 0.0005$).

Our data showed a clear dynamic inverse correlation between platelet counts and %-IPF in ITP. We confirm that an elevated %-IPF is a useful indicator of peripheral platelet consumption in ITP and could be used for early monitoring of treatment.

BSH24-PO63 | SHOT-reportable acute transfusion reactions—A Single-centre 5-year experience

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The risk of acute transfusion reactions (ATR), occurring within 24 h of transfusion, is up to 1 in 7378 blood transfusion components issued in the UK. Annual ATR data are collected by the Serious Hazards of Transfusion (SHOT) national haemovigilance scheme. Here we present 5-year data (2019–2023) regarding SHOT-reportable ATRs at our centre. Of 282 potential reactions reported by clinical teams, 62 were SHOT reportable (i.e. at least moderate severity by International Society of Blood Transfusion/BSH criteria); 12 were excluded due to incomplete/duplicate data.

The median age was 47 years (range 1–91); 30 (60%) were female, and 49 (98%) had underlying medical comorbidities. Twenty-two (44%) ATRs were moderate allergic/febrile non-haemolytic, 17 (34%) severe allergy/anaphylaxis, 10 (20%) TACO and one (2%) non-ABO acute haemolysis. No ABO-mismatched haemolysis, transfusion-transmitted infection, transfusion-associated acute lung injury or transfusion-associated dyspnoea were reported. Packed red blood cells (PRBC), platelet, fresh frozen plasma (FFP) and cryoprecipitate were implicated in 29 (58%), 18 (36%), two (4%) and one (2%) reactions respectively.

The indication for transfusion met those provided by the National Institute for Health and Care Excellence guideline for Blood Transfusion [NG24] in 35 (70%) of patients. 16/35 (46%) had transfusion for chronic anaemia, 13/35 (37%) for prophylaxis and 6/35 (17%) for acute haemorrhage. Fifteen (30%) reactions occurred at night. Thirty-five (70%) occurred in a specialist haemato-oncology clinical area. ATRs were treated with paracetamol (19; 38%), anti-histamine (28; 56%), corticosteroid (30; 60%), adrenaline (11; 22%), supplemental oxygen (30; 60%), inhaled beta-2 agonist (11; 22%) and diuretic (9; 18%). Transfusion was delayed in two (4%) and discontinued in 34 (68%).

On review of TACO cases, the median age was 74 years (range 54–91). Nine (90%) were following PRBC transfusion. There was a history of renal, cardiac, hepatic and respiratory compromise in 3 (30%), 4 (40%), 0 and 2 (20%) respectively. Two (20%) received more than one unit of PRBC; haemoglobin was not tested between units in either case. The median duration of PRBC transfusion was 3 h. TACO assessment was performed prior to transfusion in one case (10%). There were five admissions to ITU and one death secondary to TACO.

Our experience broadly reflects the data reported by SHOT, and further describes the current state of clinical practice regarding ATRs and identifies opportunities to improve patient blood management, by application of the TACO checklist and education on managing ATR including appropriate use of supportive medications such as corticosteroids.

BSH24-PO64 | Deaths attributable to transfusion-associated circulatory overload: 10-year review of serious hazards of transfusion (SHOT) data

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Transfusion-associated circulatory overload (TACO) remains the leading cause of transfusion-related deaths for the last decade, and the second most common cause of transfusion-related major morbidity. Serious Hazards of Transfusion (SHOT) has recommended strategies to mitigate TACO risks. The pretransfusion TACO risk assessment was launched in 2016, and the TACO incident structured investigation tool followed in 2021, with a national patient safety alert planned for 2024. Evaluating progress is complex due to incomplete data, varying case imputability and small datasets; 10 years of SHOT data on TACO-related deaths were analysed based on available data.

Ninety-three TACO-related deaths were reported between July 2013 and June 2023, 95% (88/93) of which had an identifiable TACO risk factor. No risk factors were identified in five cases; two lacked information, two probably had undocumented cardiac risks, leaving one case where, despite good quality information, no TACO risk factors could be identified. The most frequently present TACO risk factors were intravenous fluids in the preceding 24 h (62%), and significantly positive fluid balance (59%).

There were 54 assessable deaths following the introduction of the TACO risk assessment, with evidence of its use in 37% (20/54) of cases, a figure that has not improved over time. Nine TACO risk assessments had no documented mitigations, five had suboptimal mitigations, one had planned mitigations that were not followed and only five cases had ostensibly adequate mitigations.

There was evidence of structural review in 61% (57/93) of TACO-related deaths, informal reviews in 29% (27/93), leaving 10% (9/93) apparently un-reviewed. Twenty-two per cent (20/93) prompted changes in transfusion policies, primarily concerning either the implementation or functionality of the TACO risk assessment. Use of the SHOT TACO incident investigation tool was assessed in 20 cases, where it was utilised in 30% (6/20) of total cases, rising to nearly 60% (4/7) of cases from January to June 2023.

TACO deaths, as reported to SHOT, are rarely seen in the absence of risk factors identified on the pretransfusion TACO risk assessment. This safety check appears to be underutilised and often inaccurately completed, leading to

inadequate mitigation strategies. It is encouraging to see structured reviews following TACO-related mortality, and use of the incident investigation tool is improving rapidly. Organisational changes to enhance safety are not consistently evident. While TACO may not be completely preventable, every case is an opportunity to improve practice and reduce risk for other patients. Organisations are urged to implement SHOT recommendations.

BSH24-PO65 | Clinical and cost-effectiveness of cell salvage use in complex spinal surgery

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Intraoperative cell salvage is the process of collecting, processing and safely returning blood lost during surgery as an autologous red cell transfusion. This can provide an alternative or adjunct to conventional allogeneic red cell transfusion. Cell salvage is recommended by anaesthetic guidelines when it can be expected to reduce the need for allogeneic transfusion.

We reviewed intraoperative blood loss and the use of cell salvage during 57 major spinal surgeries performed at the RVI Newcastle between May and September 2022. Average intraoperative blood loss was 659 mL, which was higher in surgeries for malignant conditions (1033 mL) than non-malignant (614 mL). There were differences in the rate of cell salvage usage between adult and paediatric populations (50% vs. 62%), and between malignant and non-malignant indications for surgery (17% vs. 61%). On average, patients for whom cell salvage was used received 270 mL of blood back, equivalent to approximately one unit of packed red cells.

In surgeries with large-volume blood loss, cell salvage is unlikely to avoid the need for allogeneic red cell transfusion, but can reduce the volume of transfusion required. In cases of smaller volume blood loss, cell salvage may remove need for allogeneic transfusion entirely, eliminating exposure to allogeneic blood. We identified cases in our review where cell salvage may have avoided the need for any intraoperative transfusion if it had been utilised. Particularly in children and adolescents this has implications for avoiding alloimmunisation early in life. The cost of the disposables used in cell salvage was £160 per surgery, comparable to the cost of a single unit red cell transfusion, making cell salvage a cost-effective treatment.

Barriers to higher rate of usage of cell salvage included awareness of its use and benefits by surgeons, and training of anaesthetists and nursing staff to increase their familiarity with its use.

BSH24-PO66 | Survey of the use of cytomegalovirus-negative blood components in allogeneic stem cell transplant patients

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Cytomegalovirus (CMV) infection remains a challenge during allogeneic stem cell transplantation (aSCT). Following the UK's adoption of universal leucocyte reduction in 1999, the risk of transfusion-transmitted CMV infection (TTI-CMV) decreased. Subsequently, the committee for the Safety of Blood, Tissues and Organs (SABTO) recommended using CMV-unselected, rather than CMV-negative components for aSCT patients. However, a 2015 survey revealed that 22.7% of aSCT centres continue to use CMV-negative blood components, prompting the publication of a British Society of Haematology good practice paper addressing concerns about pretransplant CMV serological testing.

A continued preference for CMV-negative blood carries implications for blood services, hospitals and patients. Blood services manage a more diverse inventory with increased wastage, increased time demand on the laboratory and higher rates of donor testing and costs. Hospitals incur extra costs through the higher price of screened units and often additional delivery costs. Consequently, patients may experience delays to transfusion.

We have re-surveyed aSCT centres in England to determine whether, after more than a decade of using CMV-unselected blood components, practice has changed, and to identify ongoing barriers to adoption of the current guidance.

Of the 32 eligible aSCT centres, we received responses from 28, and demonstrated that 25/28 (89%) centres use CMV-unselected blood for all aSCT patients. Of the 25 centres using CMV-unselected blood, three provided qualifications, with two centres using CMV-negative blood prior to CMV serology being resolved, and another using CMV-negative blood for cord aSCTs. Two of the three centres not using CMV-unselected blood described their reasoning; one stating that CMV disease is a never event and therefore all mitigation strategies should be employed, the other highlighting that they predominantly transplant patients with primary immunodeficiency syndromes where the consequences of CMV disease are more significant. The three centres using CMV-negative blood intend to continue with the practice. 19/28 (68%) centres have had at least one case of equivocal pretransplant CMV serology in the past 5 years, with seven centres (25%) seeing more than five cases. Two centres reported cases of possible TTI-CMV.

These results show that while the use of CMV-negative blood in aSCT patients continues to fall, a small pocket of use remains, with the consequences of CMV disease, particularly

in patients with primary immunodeficiency, being a key factor driving this decision.

BSH24-PO67 | An analysis of platelet usage at University College London Hospitals

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Background: NHS Blood and Transplant provides the UK with almost 250 000 units of donor platelets each year and University College London Hospitals NHS Foundation Trust (UCLH) is the largest institutional user of these components. UCLH's demand for this resource has increased steadily over 5 years, in line with an expansion of our services. We examined local patterns of platelet use, to gain greater understanding of local demand, improve compliance with national guidance and reduce waste.

Methods: We conducted a retrospective audit of platelet usage across our clinical sites over a 3-month period. The clinical notes and laboratory results of patients issued with platelet units during this time were reviewed. The requesting specialty and setting of each unit were identified, and each transfusion matched to the closest indication on the National Blood Transfusion Committee (NBTC) 2020 audit tool. Instances where transfusion deviated from guidance of the British Society of Haematology (BSH) or the National Institute for Health and Clinical Excellence (NICE) were highlighted.

Results: Between July and September 2022, 2839 platelet units were issued to 408 patients—85% were transfused into the designated individual, 12% returned and re-allocated to another recipient and 3% ultimately wasted. One-fifth of requests came from outpatient/ambulatory care settings.

Adult haematology accounted for 87% of platelet demands, the vast majority of which were for haemato-oncology. By contrast, other adult specialties acted as primary requestor in 6% of cases, and paediatrics 7%. Of transfused units: 76% were indicated for prophylaxis; 7% prior to invasive procedures; 10% for treating bleeding; and 6% in specific platelet dysfunctions (e.g. use in immune thrombocytopenia/platelet function disorders or while on anti-platelet medication).

Verbatim adherence to BSH/NICE guidance was observed in 81% of transfusions, with periprocedural use and platelet dysfunction attracting proportionally more deviations (30% and 34% respectively of guideline non-conformity). Inappropriate prophylaxis remained the largest burden by absolute number, with up to 182 potentially avoidable transfusions during the audit period (10% of prophylactic prescriptions).

Conclusion: Demand for platelet transfusions in UCLH is driven by an expanding haematology service, particularly in adult leukaemia and transplant patients. Despite this, we maintained a level of component wastage comparable to the national average. This audit highlights diverse settings and indications for platelet usage, much of which falls in line with national guidance. The results point to sources of potentially avoidable transfusions, and have informed efforts in education, enforcement and the making of decision support tools.

BSH24-PO68 | Alloimmunisation in sickle cell disease: A 3-year retrospective study in a tertiary haemoglobinopathy treatment Centre

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Introduction: Patients with sickle cell disease are at higher risk of developing red cell alloantibodies compared with other patient populations, contributing to increased morbidity and mortality. Predisposing factors include recipient-donor antigen mismatch, particularly RH genetic diversity, and the chronic inflammatory state present in sickle cell disease.

Aims: We sought to characterise new cases of red cell alloimmunisation in our sickle cell cohort over a 3-year period and to correlate this with laboratory and clinical parameters.

Methods: We retrospectively identified patients with sickle cell disease who developed a new red cell alloantibody between November 2019 and November 2022, through the hospital laboratory information system, selecting for positive antibody screens and referrals to NHSBT reference laboratory. Clinical information was retrieved from the hospital electronic patient record system.

Results: Thirty episodes of new red cell alloantibody formation were identified in 29 patients. Age range was 6–68 years: 7% (2) <20 years, 38% (11) 20–39 years, 55% (16) ≥40 years. Seventy-six per cent (22) were female and 24% (7) male. One patient was pregnant at the time of alloimmunisation. Anti-C, anti-S, anti-Fya and anti-Kpa were the most frequently identified alloantibodies. Forty-three per cent (13) had previous documented antibody formation and in the remaining 57% (17) patients this represented the first documented antibody formation. One had a history of DHTR, without a previous alloantibody identified. Forty-three per cent (13) of patients were on disease-modifying therapy at the time of presumed alloimmunisation (EBT = 7, hydroxycarbamide = 3, routine top-up = 2, Voxelotor = 1). Transfusions prior to alloantibody detection were given in the acute setting in 60% (18) of cases, in the routine setting in 30% (9) of cases and in unknown circumstances in 10% (3) cases (information not held in

local records). For the transfusion episode that triggered an alloantibody: EBT patients received median 8.4 units (range 8–10), and for other indications median 1.4 units (range 1–2). Six episodes of delayed haemolytic transfusion reaction (DHTR) developed in five patients following new antibody formation. All patients developing DHTR/hyperhaemolysis (HH) were transfused in a clinically acute state, five episodes of which required immunomodulatory treatment for hyperhaemolysis. No deaths resulted.

Conclusions: Antibodies against Rh, MNS, Kell and Fy antigen groups were the most likely to be detected. Approximately half of patients had a previously documented alloantibody and patients often developed multiple antibodies. Consistent with previous findings, sensitising transfusion events happened in an acute pro-inflammatory state in most cases.

BSH24-PO69 | Beyond binary: Necessity for updated transfusion guidelines for transgender and gender-diverse patients

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Transgender and gender-diverse (TGD) individuals, constituting 0.5% of the England and Wales population (262 000 individuals) according to the 2021 Census, have gender identities that differ from their assigned birth sex. TGD people can change their name, title and gender on their medical records at any time, including if they have not yet changed their legal gender via the Gender Recognition Act (GRA). Changing one's gender generates a new medical record with a new NHS number. The GRA safeguards gender recognition information, prohibiting its disclosure without the person's explicit consent.

In the Trans Lives Survey 2021, 70% of respondents reported being impacted by transphobia when accessing healthcare. Inclusive healthcare for TGD individuals requires acknowledgment of their identified gender in medical records. However, this results in complexity in many aspects of healthcare. Screening programmes rely on recorded gender, leading to exclusions (for example, trans males are not routinely invited for cervical screening). Some blood tests report results against normal ranges which differ between biological males and females (for example, haemoglobin and haematocrit). There is a unique risk for TGD patients requiring blood transfusion, where their childbearing potential and historical transfusion records may not be known. Blood transfusion is particularly affected, in part due to guidelines which are binary by sex. They are written to protect 'females of childbearing potential' from the risk of haemolytic disease of the fetus and newborn, but overlook trans males retaining childbearing potential.

Incidents and near misses within our transfusion laboratory exposed a lack of national guidance on providing transfusion services to TGD individuals safely, to the same standards as cisgender people, and while working within the GRA. We surveyed transfusion laboratories across North West England to establish regional practice. Most Trusts (8 of 10 responses) had no TGD policy or, if they did, had a policy which provided no guidance on clinical aspects of care. While several Trusts (3 of 10) reported incidents, none reported any formalised policy or procedure to prevent recurrence.

This anecdotal evidence highlights that we are not providing the same level of care to TGD patients; this can pose significant clinical risk, as well as being discriminatory. Given the large number of people this affects, and the significance of potential problems which can result, we hope that urgent conversations within the transfusion community can lead to robust and comprehensive guidance, to improve the care we provide to all patients.

BSH24-PO70 | The conundrum of red cell matching in haemoglobinopathies—how has the updated evidence informed guidelines?

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Patients with sickle cell disease (SCD) and thalassaemia commonly receive repeated red blood cell (RBC) transfusions. To mitigate against the risk of alloimmunization, the ICTMG 2018 guideline recommends ABO, DCcEe and K-matched transfusions. Many transfusion providers offer matching

of RBC antigens beyond ABO and D. Internationally, antigen matching varies and is likely dependent on donor blood pool, patient cohort and available resources.

We present an updated systematic literature review to inform new guidelines, developed by a multidisciplinary international team of transfusion experts and patient representatives, following on from previous ICTMG guideline (Transfusion 2018;58:1555–66). The objective of the review was to determine whether previous recommendations were still appropriate and relevant to the current clinical practice and literature.

This systematic review was conducted in accordance with 2020 PRISMA guidelines. Meta-analysis was not conducted due to heterogeneity across studies. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool was used to grade the certainty of evidence and to develop recommendations.

Five new observational studies (three prospective and two retrospective), conducted in three countries, were included in this updated systematic review, in addition to the 12 studies identified in the previous review. The five new studies enrolled 902 patients in total with sample sizes ranging from 18 to 476 patients. Studies were heterogenous and utilised varying degrees of RBC matching, but all reported on alloimmunization as an outcome. The overall rate of alloimmunization using extended matching was 6.2% (56/902) vs. 13.1% (119/902) using limited matching. One hundred and twenty-eight patients were alloimmunized before study entry. The overall risk of bias across studies was moderate to serious.

The international panel reviewed the overall evidence. The limitations of the evidence precluded any strong recommendations. The panel continues to recommend that ABO, DCcEe and K-matched RBCs are selected for individuals with SCD and thalassaemia, even in the absence of alloantibodies, to reduce the risk of alloimmunization. In patients with SCD and thalassaemia who have developed clinically significant alloantibody(ies), selection of RBCs antigen negative to the alloantibody is recommended. The panel recognised the importance of research in several areas, such as the feasibility and benefit of matching for additional RBC antigens, or using DNA-based methods to guide donor selection, in patients with existing alloantibodies.

The evidence base to inform optimal matching strategies in SCD and thalassaemia is limited. Large research databases and clinical studies are needed to better understand the (cost-)effectiveness of different approaches to RBC matching.

BSH24-PO71 | Single-centre experience of multidisciplinary, patient-centred patient blood management in abnormally invasive placenta

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Abnormally invasive placenta (AIP) describes a spectrum of obstetric disorders whereby placental implantation into the endometrium is dysfunctional. This leads to disordered separation of the placenta during the third stage of labour, with associated major obstetric haemorrhage.

AIP is rare, with an estimated incidence of <0.2% live births. As such, evidence is lacking regarding effective patient blood management (PBM) strategies at the time of delivery.

Here we describe the clinical characteristics and outcomes of AIP at our centre over a 5-year period, with a focus on PBM.

Thirty-four women with AIP underwent delivery from January 2019 to November 2023. At delivery, the median age was 37 years (range 25–52), gestational age 36 weeks (range 29–39). Two (6%) were multiple pregnancies. Thirty-three (97%) had a history of previous caesarean section (CS); median para 2 (range 1–9).

All deliveries were coordinated using a multidisciplinary approach (obstetrics, midwifery, haematology). Individualised care by the transfusion practitioner included creation of a patient-centred transfusion plan for each delivery, ensuring pretransfusion testing was complete, and appropriate blood components were available at the time of delivery; and where possible, attending the delivery in-person to coordinate transfusion/red cell salvage (RCS) and liaise with haematology/laboratory.

All deliveries were by CS (category 1 [3; 9%], 2 [4; 12%], 3 [5; 15%], 4 [22; 64%]). Nineteen (56%) experienced antepartum haemorrhage. All patients were consented for blood transfusion and 33 (97%) had valid pretransfusion testing prior to delivery. Median estimated blood loss was 4.7 litres (range 0.7–14). Thirty-two (94%) received packed red blood cells (median 6 units, range 0–23), 17 (50%) platelets (median 1 unit, range 0–4), 25 (74%) fresh frozen plasma (median 4 units, range 0–14), 20 (59%) cryoprecipitate/lyophilised fibrinogen (median 0 units/2 g; range 0–4/0–7) and 33 (97%) received tranexamic acid (median 2 g, range 0–4) periprocedurally or intraprocedurally. Intraoperative RCS was performed in 29 (85%; median 470 mL, IQR 320–700).

There were no maternal or neonatal deaths. Seventeen (50%) underwent hysterectomy. Seventeen (50%) required ITU admission. There was no maternal red cell alloimmunisation or acute transfusion reactions.

Our data supports the role of effective PBM for AIP. The multidisciplinary approach taken at our centre suggests that early, active input by transfusion specialists may be an

important determinant of the favourable management of the profound haemorrhagic complication associated with this rare condition.

BSH24-PO72 | The economic evaluation of the provision of blood transfusion to treat patients: A systematic review

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Blood transfusions involve significant clinical and economic implications, marked by usage variations and a complex mix of risks and costs. This necessitates detailed economic evaluations for guiding resource management effectively and efficiently.

This study systematically reviews health economic evaluations of blood transfusion practices across various clinical fields in the UK and OECD countries from 2015 to 2022. It aims to assess their effectiveness in resource utilisation and their potential to shape policy guidelines.

A systematic review was conducted following the PRISMA guidelines. Multiple databases were searched for studies on economic evaluations of blood transfusions, including MEDLINE, Embase, The Cochrane Library, EconLit, Health Technology Assessment, the Cost-Effectiveness Analysis Registry and others. A quality assessment was performed using Drummond's checklist, and its applicability to the UK NHS was evaluated using NICE's Economic Evaluation Methodology Checklist. The review focused on primary, full economic analyses related to blood transfusions in OECD countries, published in English from January 2010 to September 2022. The economic data were standardised to 2022 GBP values for a contextually relevant synthesis.

Out of 7106 references, 27 economic studies met the inclusion criteria. Interventions covered various transfusion products, including erythropoietin (1), intravenous iron (2), tranexamic acid (TXA) (2), cell salvage (3), red blood cells (2), whole blood (1), fresh frozen plasma (1) and haemostatic products (3). Additionally, 6/27 studies were on patient blood management (PBM), comparing blood transfusions with alternatives in anaemia, surgery, trauma and obstetric interventions. Economic evaluations included 10 Cost-Effectiveness Analysis (CEA), 10 Cost-Utility Analysis (CUA), four Cost-minimisation Analysis (CMA) and three Cost–Benefit Analysis (CBA). These evaluations used different models, often incorporating subgroup analysis.

The key studies demonstrating cost-effectiveness and relevance to the UK setting included the use of TXA for traumatic brain injury (TBI), which proved to be highly cost-effective, the adoption of a 1:1:1 transfusion ratio in trauma care and the erythropoiesis-stimulating agents (ESAs) for cancer-induced anaemia. These interventions align with and could potentially influence updates to NICE guidelines. Additionally, the cost-saving implementation of pre-operative anaemia screening and the effective use of TXA in surgical procedures were highlighted, suggesting areas for guideline refinement. Our results also highlighted the lack of cost-effectiveness studies for many blood transfusion interventions.

This review highlights the economic significance of transfusion strategies, supporting current guidelines and pinpointing areas needing more research. It stresses the necessity for evidence-based, intervention-related approaches in healthcare to optimise blood resource usage, enhance patient outcomes and maintain economic sustainability.

BSH24-PO73 | Large cell transformation of mycosis fungoides: Patterns of care and patient outcomes

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Objective: Large cell transformation of mycosis fungoides (LCTMF) is rare, and often associated with a more aggressive clinical course and inferior survival than classical MF. LCTMF is neither recognised as an independent entity in the International Classification of Diseases nor part of the current staging systems for MF. Reflecting the paucity of published data to guide management, LCTMF is frequently omitted from clinical guidelines. Herein, we describe patient characteristics, management and outcomes of LCTMF, from Australia's only quaternary cancer service for the management of cutaneous lymphomas.

Methods: Eligibility required clinicopathological diagnosis of LCTMF between 1/1/1990 and 1/10/2021, at Peter MacCallum Cancer Centre. Demographic, clinicopathological and treatment data were retrospectively reviewed.

Results: Eighty-three patients were eligible: 53 (64%) male, median age 67 (range, 37–87) years. Median time from diagnosis of MF to LCTMF was 2.1 (range, 0–27.2) years. At the time of LCTMF, 23 (28%) patients had early-stage MF (IA-IIA). Cutaneous-only LCTMF was seen in 63 (76%) patients, of these, 31 (49%) were uni-lesional at time of diagnosis. CD30 expression was positive (defined as >10% atypical lymphocytes) in 47 (57%) patients. Median follow-up from time of LCTMF was 8 (95% CI: 6, 11) years.

After diagnosis of LCTMF, seven treatment regimens were used in the first-line setting, including skin-directed therapies (localised radiotherapy [48%], phototherapy [2%]) and systemic therapies (multiagent chemotherapy [23%], single-agent chemotherapy [10%], interferon [8%], monoclonal antibody-based monotherapy [4%] and histone deacetylase inhibitors [2%]). Most patients (84%) required >1 line of therapy during their treatment journey with LCTMF (median 3; range 0–11).

Median overall survival (OS) was 3.5 years (95% CI: 2.23, 8.20), with 5- and 10-year survival probabilities of 41% (95% CI: 32, 54) and 31% (95% CI: 21, 46) respectively. Of the 54 deceased patients, causes of death were: MF related, 40 (74%); unrelated causes/competing comorbidities, six (11%); treatment related, three (6%); unknown, five (9%).

In multivariate analyses, age (>55 years) and extra-cutaneous LCTMF were both independent adverse prognostic factors: hazard ratios, 2.18 (95% CI 1.05–4.54) and 2.37 (95% CI 1.07–5.24) respectively.

Conclusion: In this study, we report a median OS of 3.5 years for patients with LCTMF, and 10-year survival probability of 31%. Unfavourable prognostic factors were age >55 years and extra-cutaneous disease at time of LCTMF diagnosis. Given the differences in pathology, behaviour, management and outcomes of LCTMF and MF, further research is required to identify patients at highest risk of LCTMF, and for development of risk-based treatment protocols for patients diagnosed with LCTMF.

BSH24-PO74 | Outcomes ≥1 year after transitioning from treatment with ibrutinib in the ASPEN study to zanubrutinib

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Introduction: ASPEN (NCT03053440) compared Bruton tyrosine kinase inhibitors (BTKi), zanubrutinib and ibrutinib in patients with MYD88–mutated Waldenström macroglobulinaemia (WM). LTE1 (NCT04170283) is a zanubrutinib long-term extension study. We report clinical outcomes ≥1 year after transition from ibrutinib in ASPEN to zanubrutinib in LTE1.

Methods: Upon LTE1 enrolment, ibrutinib-treated patients from ASPEN began zanubrutinib at 320 mg/day. Disease response was assessed every 6 months using modified Owen criteria or 'no evidence of progressive disease' at investigator discretion. Safety and efficacy outcomes were analysed ad hoc.

Results: Between 26/06/2020 and 23/06/2022, 47 ibrutinib-treated patients from ASPEN enrolled in LTE1; most (79%) had relapsed/refractory WM prior to ASPEN participation. At LTE1 enrolment, median age was 73 years; median time from ASPEN discontinuation to zanubrutinib initiation was 0.07 months.

As of 23/06/2023, 40 patients (85%) remained on study treatment. Median treatment duration was 50.4 months for ibrutinib prior to transition, and 15.3 for zanubrutinib. During LTE1, grade≥3/serious treatment-emergent adverse events (TEAEs) occurred in 23%/13% of patients; infections (6.4%; all COVID-19) were the only grade≥3 TEAEs affecting >2 patients; no serious TEAEs affected >2 patients. Most ibrutinib TEAEs of interest for BTKi treatment did not continue or worsen following transition to zanubrutinib (exceptions: infections [$n = 3$, all due to COVID-19], anaemia [$n = 1$] and neutropenia [$n = 1$]). Six of seven patients who experienced cardiovascular AEs (8 events) in LTE1 had experienced at least one ibrutinib-emergent cardiovascular AE during ASPEN. No worsening or new hypertension occurred following transition to zanubrutinib. There was no recurrence

or worsening of atrial fibrillation/flutter; one new case of atrial fibrillation occurred (LTE1 Day 12) in a patient with extensive cardiovascular history and concurrent pericarditis (LTE1 Day 10). No cardiovascular TEAE led to death in LTE1. Two deaths occurred, both due to COVID-19. Best overall response (BOR) in LTE1 was unchanged in 34 (72%) and improved in 10 patients (21%) from last response assessment in ASPEN. Median (IgM) change was −36 mg/dL, and (IgM) was stable/decreased in 29 patients (73%) from last response assessment in ASPEN to BOR in LTE1.

Conclusions: Following transition to zanubrutinib, at median ibrutinib treatment duration of 50.4 months, most ibrutinib-emergent TEAEs of interest for BTKis did not recur or worsen at 15 months median zanubrutinib treatment duration. Response was maintained or improved in 96% ($n = 44/46$) of efficacy-evaluable patients. Although limited, these data suggest that transitioning ibrutinib-tolerant WM patients to zanubrutinib does not compromise safety or efficacy; long-term follow-up is ongoing.

BSH24-PO75 | Zanubrutinib in Acalabrutinib-Intolerant Patients with B-Cell Malignancies

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Introduction: Adverse events (AEs) may limit use of Bruton tyrosine kinase inhibitors (BTKis) in patients with B-cell malignancies. The next-generation BTKi zanubrutinib was designed to maximize tolerability by minimizing off-target binding. Results from the ongoing phase 2 study BGB-3111-215 (NCT04116437) showed that zanubrutinib was well tolerated in patients intolerant of ibrutinib and/or acalabrutinib. Here, updated tolerability and efficacy results in the acalabrutinib-intolerant population are reported.

Methods: Eligible patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), Waldenström macroglobulinemia (WM), mantle cell lymphoma (MCL), or marginal zone lymphoma (MZL) with protocol-defined acalabrutinib intolerance received zanubrutinib 160 mg twice daily or 320 mg once daily. Patients whose disease progressed with prior BTKi therapy were excluded. Safety and efficacy, including recurrence of acalabrutinib-intolerance events, were evaluated.

Results: As of May 15, 2023, 27 patients had received zanubrutinib (CLL/SLL, n=19; WM, n=4; MCL, n=2; MZL, n=2). Median age was 73 years (range, 51-87), median treatment duration was 11.4 months (range, 0.5-32.2), and median follow-up was 12.4 months (range, 1.6-32.2). Median number of prior therapies was 2 (range, 1-6), and 13 patients (48%) had received prior ibrutinib and acalabrutinib. Median cumulative acalabrutinib exposure was 5.4 months (range, 0.5-33.7). Seven patients discontinued zanubrutinib (AE, n=2; physician decision, n=2; withdrawal by patient, n=2; progressive disease, n=1); 20 remained on treatment. Forty acalabrutinib-intolerance events occurred in 27 patients, most commonly arthralgia (n=6 events), headache (n=5), myalgia (n=5), diarrhea (n=3), and rash (n=3). Twenty-eight acalabrutinib-intolerance events (70%) in 17 patients (63%) did not recur with zanubrutinib. Twelve events (30%) recurred (lower grade, n=5; same grade, n=7; higher grade, n=0). Two patients discontinued due to recurrence (myalgia and diarrhea; both same grade). Of 3 patients who experienced the same intolerance event with ibrutinib and acalabrutinib, 2 (atrial fibrillation, n=1; pain in extremity, n=1) did not experience recurrence with zanubrutinib, and 1 (diarrhea: grade 3 [ibrutinib]; grade 2 [acalabrutinib]) experienced grade 1 recurrence with zanubrutinib. Of 25 efficacy-evaluable patients receiving zanubrutinib, 24 (96%) maintained or improved responses from baseline, with 16 (64%) achieving a minor response or better.

Conclusions: With a median zanubrutinib exposure 6 months longer than the cumulative acalabrutinib exposure before discontinuation (11.4 months vs 5.4 months, respectively), 17 patients (63%) did not experience recurrence of acalabrutinib-intolerance events, and disease was controlled in 24 of 25 efficacy-evaluable patients, suggesting that acalabrutinib-intolerant patients may maintain or improve on the clinical benefit by switching to zanubrutinib. Enrollment and follow-up are ongoing.

BSH24-PO76 | Updated results of the safety run-in of the phase 3 LOTIS-5 trial

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Context: Loncastuximab tesirine (loncastuximab tesirine-lpyl; Lonca) is an antibody–drug conjugate comprising an anti-CD19 monoclonal antibody conjugated to a pyrrolobenzodiazepine dimer toxin, indicated for relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) after ≥2 systemic treatments.

Objective: To characterize the safety and efficacy of Lonca + rituximab (Lonca-R) in patients with R/R DLBCL.

Design: LOTIS-5 (NCT04384484): a phase 3 randomized, open-label, multicentre, two-part, two-arm study, with a primary outcome measure of progression-free survival. Preliminary results presented at SOHO 2022 were updated with new safety/efficacy data collected in part 1.

Patients: Part 1 enrolled 20 patients in a nonrandomized safety run-in; part 2 will randomly assign approximately 330 patients to receive Lonca-R or rituximab–gemcitabine–oxaliplatin. Key inclusion criteria include ≥18 years; DLBCL (including transformed from indolent lymphoma) or high-grade B-cell lymphoma with MYC, BCL2 and/or BLC6 rearrangements; ≥1 line of prior therapy; not a candidate for stem cell transplantation; and measurable disease per 2014 Lugano classification.

Interventions: Patients received 0.15 mg/kg Lonca +375 mg/m^2 rituximab every 3 weeks for 2 cycles, then 0.075 mg/kg Lonca +375 mg/m^2 rituximab every 3 weeks for up to six additional cycles.

Results: Part 1: patients had median age of 74.5 years and received median of five cycles of Lonca-R and 1 previous therapy; seven patients completed treatment, and five continue in follow-up. As of 10 April 2023, 11 (55%) patients had grade ≥3 TEAEs. The most common grade ≥3 TEAEs were increased gammaglutamyltransferase (5 patients [25%]) and neutropenia (3 patients [15%]). The overall response rate by central review was 16/20 (80%) patients; 10/20 (50%) and 6/20 (30%) attained complete and partial response respectively. The median duration of response was 8.0 months (95% CI: 3.2, –); the median progression-free survival was 8.3 months (95% CI: 4.5, –).

Conclusions: Lonca-R demonstrated no new safety signals and showed encouraging anti-tumour activity in patients with R/R DLBCL. Initial signs of durability are promising. Lonca-R has a fixed treatment duration, making it an appealing alternative to continuous therapies. Part 2 of LOTIS-5 commenced in January 2022; recruitment is ongoing.

Funding: ADC Therapeutics SA; medical writing: CiTRUS Health Group.

BSH24-PO77 | How often does interim scanning affect treatment decisions in DLBCL? A single-centre audit

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Introduction: Patients with diffuse large B-cell lymphoma (DLBCL) routinely undergo positron emission tomography (PET) at diagnosis and following treatment. However, variation exists in interim scanning practice between the use of interim PET (iPET) and contrast enhanced (CE), computerised tomography (CT). iPET results are predictive of outcome with an iPET4 (after 4 cycles) considered the optimal timing with many centres performing this. Conversely, the Pan-London Haemato-Oncology Clinical Guideline for the management of DLBCL suggests that interim imaging can be omitted when response to treatment can be assessed clinically.

The aim of our study was to assess the utility of iPET in patients with DLBCL with palpable disease.

Methods: Data was collected for patients diagnosed with DLBCL at our centre (April 2015–December 2022). Information collected included baseline characteristics, revised international prognostic index (R-IPI), treatment regimen, presence of palpable disease, clinical and radiological response to therapy and impact of interim imaging on management decisions.

Results and discussion.

Two hundred and two patients (114 male, 88 female) were included, with median age at diagnosis of 70 years (range 28–96). Ninety-one patients had palpable disease, of which 50.5% had an R-IPI ≥3. Of those with palpable disease, 70.3% ($n = 64$) received rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone chemotherapy (R-CHOP). In R-CHOP-treated patients 70.3% had iPET, 28.1% had interim CECT and 1.5% had no interval imaging.

In the iPET subgroup, of patients with a reduction in palpable disease, 69.2% demonstrated a complete metabolic response (CMR, Deauville 1–3). In the interim CECT subgroup, 15.6%

had a complete response (CR), 81.2% had partial response (PR) and 3.1% had stable disease.

Across both subgroups with improving palpable disease, 93.2% (69/74), continued the same chemotherapy regimen after interval imaging. Two patients (2.7%) with low R-IPI, limited-stage disease had treatment de-escalation following a CMR on iPET.

Three patients (4%) had a discrepancy between clinical and radiological findings, with reduction in palpable disease but an unfavourable interim scan result (Deauville 4 or PR) causing chemotherapy intensification. Two of these patients received heavily modified chemotherapy at diagnosis due to poor performance status. The third patient received R-CHOP first line, with progressive disease on iPET resulting in therapy intensification.

Our data suggest that interim scanning may be avoidable in advanced DLBCL, with improving palpable disease who receive full-dose first-line therapy, leading to reduced costs and radiation exposure, although undertaking interim scanning may be psychologically beneficial to patients. Routine iPET remains important in low-risk, limited-stage DLBCL to allow treatment de-escalation.

BSH24-PO78 | A national census of the lymphoma clinical nurse specialist role

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With emerging advanced nursing roles within Haematology, the traditional role of the Clinical Nurse Specialist (CNS) is changing. To help provide clarity for CNSs looking after people with Lymphoma, the Lymphoma Action Charity supported three nurses to carry out a national audit of Lymphoma CNSs across the nation.

Fifty Lymphoma CNSs responded from across England, Scotland and Wales. The census demonstrated disparity in role titles, grading and skills across regions. There were 10 different role titles, grading went from band 6 to band 8a. Besides the core key working and supportive aspects of the role, many also had higher skills such as prescribing, clinical examination and consultation skills. A smaller proportion were also doing additional higher-level skills such as bone marrow aspirations and intravenous access skills. Many were very experienced, averaging of over 10 years of experience, with a small proportion having over 20 years of experience. Most CNSs were of retirement age or within 10 years of it. Most were working in teams rather than lone workers, suggesting a degree of service planning. Almost all CNSs also had a large education and training role for colleagues and junior staff.

The census demonstrated that CNSs are working at a higher level of practice, have advanced skills and autonomous roles. There were variations in CNS skill sets across the nation, suggesting that they are a group of nurses who are able to be flexible to the demands of their individual regional services. The census also demonstrated a heavily involvement in the training of future haematology nurses, which is perhaps one of the CNSs most under recognised role.

The census suggests many avenues of further exploration especially the lack of governance framework in comparison to more modern role of the Advanced Clinical Practitioner.

BSH24-PO79 | Staging bone marrow aspirate and trephine for stage 1 low-grade orbital non-Hodgkin lymphomas

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Introduction: Low-grade orbital lymphoma is rare and represents 1% of NHL. BSH advises that staging BMAT can be avoided if it will not alter management for follicular lymphoma patients. ESMO highly recommends BMAT for extra-nodal marginal zone lymphomas, particularly in non-gastric lymphoma and when only local treatment is planned. We conducted a locoregional audit to assess:

1. if staging BMAT was performed;
2. whether staging BMAT result changed management;
3. response following radical and palliative radiotherapy schedules.

Methods: All patients with de novo clinical/radiological stage 1 low-grade orbital NHL treated at four radiotherapy centres between 01/2009 and 05/2023 were included.

Patient lists were captured via radiotherapy information systems using diagnostic codes for lymphoma and 'eye' or 'orbit' treatment sites. Dose fractionation, date of radiotherapy and re-irradiation data were collected.

Local patient information systems were used to collect data on histological diagnosis, BMAT date and result, staging and post-treatment imaging. Clinic letters were accessed to capture information on clinical response and disease relapse.

Results: Of the 52 patients identified, 51 had radiotherapy. Eighty-one per cent had marginal zone lymphoma. Staging BMAT was performed in 52%. Of those who underwent staging BMAT, 30% were positive and 7% were equivocal.

All 17 patients with negative BMATs were treated radically (88.2% with 24Gy/12#; 5.9% with 20Gy/10#; 5.9% with 30Gy/15#). Seventy-six per cent had complete/partial response; 11.8% had local progression of disease; 5.9% had stable disease; response not known for 5.9%.

Of those with positive/equivocal BMATs, 50% were treated radically (24Gy/12#) and all had a complete/partial response; 30% were treated palliatively (4Gy/2#) and had a complete/

partial response; and 20% were treated palliatively (4Gy/2#) with stable appearances but with no local progression following re-irradiation.

Discussion: In our cohort, radiotherapy dose was changed from 24Gy/12# to 4Gy/2# in 50% of patients with positive staging BMAT.

The FoRT trial (Hoskin et al. Lancet Oncol. 2021;22(3):332–340) demonstrated 5-year progression-free survival of 70% (4Gy/2#) and 90% (24Gy/12#). While 24Gy/12# is preferred for durable control, 4Gy/2# is a reasonable alternative, especially for frailer patients. 24Gy/12# has greater acute and late radiotoxicity and financial implications compared to 4Gy/2#, which is associated with negligible toxicity and significantly fewer outpatient appointments.

Conclusion: Staging BMAT altered management in 50% of cases, and therefore it would be reasonable to discuss BMAT with patients prior to committing to 24Gy/12#. However, if 4Gy/2# will be recommended regardless of the BMAT result, then this procedure could be avoided.

BSH24-PO80 | From fragility to strength: Improving bone health in lymphoma patients

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Introduction: Advances in B-cell lymphoma treatment has resulted in improved progression-free survival for these patients. There is greater focus on minimising treatment toxicity and its late effects. Glucocorticoid therapy, which decreases bone mineral density, forms an important component of lymphoma chemotherapy regimens with data demonstrating patients with lymphoma have significant bone loss compared to the general population. This results in an increased risk of osteoporosis and fragility fractures.

Our aim was to review our practice in assessing and managing bone health in patients with lymphoma across at our centre.

Methods: We analysed electronic patient records for 125 patients treated for diffuse large B-cell lymphoma between January 2016 and March 2022, at our Trust.

Data on treatment regimen, baseline vitamin D, the correction of vitamin D deficiency, documentation of Fracture Risk Assessment (FRAX) scores and identifying patients at risk of fracture who may benefit from bisphosphonate therapy, as well as fracture events was collected.

Results: All patients received corticosteroids as part of their treatment, with the commonest regimens being R-CHOP (71%) followed by R-CVP (19%). Only 45% of patients had a vitamin D level checked prior to or during lymphoma treatment. Of these, 55% had low levels (defined by ≤50 nmol/L) and 22% were deficient (defined ≤25 nmol/L); however, only 37% of these patients were started on replacement.

There was no documentation of FRAX score in any of the patients. Only five patients had documentation of their osteoporosis risk, of which three had their vitamin D checked and all were offered bisphosphonates.

Thirteen patients out of 125 (10.4%) developed a fracture during treatment, of which only nine patients had had their vitamin D checked. Two of these patients were vitamin D deficient with no replacement prescribed.

Conclusion: Our findings identified a need for improved management of bone health in lymphoma patients treated with steroid-containing regimens. Following the presentation of this data at local and sector-wide level, we have designed and implemented a patient questionnaire and physician checklist to be given to patients at diagnosis, prior to commencing treatment. Questionnaires are returned to the treating clinician or nurse specialist at subsequent clinical review. This document, which includes FRAX score parameters, identifies patients who will benefit from vitamin D replacement with or without bisphosphonate therapy based upon their FRAX score, enabling a more proactive practice in optimising the management of bone health in lymphoma patients embarking upon glucocorticoid-containing therapy.

BSH24-PO81 | Comparing the in vitro activity of CD20xCD3-bispecific antibodies in diffuse large B-cell lymphoma

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Background: Diffuse large B-cell lymphoma (DLBCL) represents the most common non-Hodgkin lymphoma. Although first-line R-CHOP is curative for most, up to one third of patients exhibit relapsed or refractory (R/R) disease. CD20xCD3 bispecific antibodies (BsAbs)—including glofitamab (Roche), epcoritamab (AbbVie), odronextamab (Regeneron) and mosunetuzumab (Genentech)—have demonstrated transformational activity in R/R DLBCL. However, no study to date has directly compared the efficacy of these constructs, highlighting a need for new evidence to inform the choice of BsAb in the clinic. We aimed to assess the in vitro activity of glofitamab, epcoritamab, odronextamab and mosunetuzumab head-to-head against a panel of DLBCL cell lines, in order to investigate differences between BsAb constructs and individual cell line response.

Methods: BsAb activity was assessed using a flow cytometry-based cytotoxicity assay. DLBCL, NOS cell lines with varying levels of CD20 expression—SU-DHL-10 (highest), UoL-RAD, K1718 and UoL-AME (lowest)—were treated with 0.01–10000pM BsAb biosimilar (Proteogenix) for 24 h, using healthy volunteer peripheral blood mononuclear cells as effector cells. B-cell depletion (BCD) was calculated by

comparing live target cell counts with a no drug control. Effector T and natural killer (NK) cell activity was determined by the expression of CD69 (early activation), CD25 (late activation) and CD107a (degranulation). Absolute EC50 values were estimated using a four-parameter log-logistic regression model.

Results: CD20xCD3 constructs demonstrated dose-dependent killing against UoL-RAD and SUDHL10, with simultaneous activation and degranulation of T cells, but not NK cells. Against UoL-RAD and SU-DHL-10 respectively, glofitamab demonstrated the highest maximal killing (glofitamab: 95% and 74%, epcoritamab: 85% and 65%, odronextamab: 87% and 70%, mosunetuzumab: 80% and 35%) with significantly lower EC50 values (glofitamab: 2pM and 81pM, epcoritamab 68pM and 428pM, odronextamab 173pM and 586pM, mosunetuzumab 203pM and >10000pM). Despite its minimal CD20 expression, UoL-AME was sensitive to glofitamab (BCDmax: 62%, EC50: 802pM), albeit with lower T-cell activation. Conversely, K1718 demonstrated a poor response to all four BsAbs (BCDmax: 17%–34%), despite high levels of T-cell activation and degranulation, suggesting an intrinsic mechanism of resistance.

Conclusions: These experiments suggest that, in vitro, glofitamab has superior efficacy against DLBCL compared to other CD20xCD3 constructs, which may be due its unique 2:1 (CD20:CD3) binding configuration. Whether this finding translates to the clinic remains uncertain. Interestingly, significant responses to glofitamab were observed in vitro for UoL-AME, despite low CD20 expression. Further studies are needed to characterise tumour-intrinsic determinants of response in this setting.

BSH24-PO82 | Successful treatment with daratumumab in a case of R-CHOP resistant CD38+ EBV-driven post-transplant lymphoproliferative disorder

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Introduction: Post-transplant lymphoproliferative disorder (PTLD) poses a significant risk following solid organ transplantation and haematopoietic stem cell transplantation (HSCT). The incidence of PTLD after HSCT is 1%, rising to over 10% in profound T-cell depletion. The introduction of rituximab has significantly improved survival rates, yet PTLD remains one of the most formidable complications of HSCT. This case report highlights the challenges of PTLD and the use of novel targeted therapies such as daratumumab.

Case Presentation: Case X, an 11-year-old female with a background of severe aplastic anaemia, was referred in July 2021 to our centre. She underwent a 10/10 matched unrelated donor allogenic stem cell transplant as per the British Society for Haematology guidelines in September 2021.

Transient engraftment occurred on Days 13 and 18 of neutrophils and platelets respectively.

However, at Day 31 post-transplant, there was a precipitous drop in blood counts in keeping with poor graft function, despite a chimerism on Day 16 of 100% donor. She had sustained profound pancytopenia, and an urgent second transplant was being considered for immune-mediated graft rejection. Imaging showed progressive pulmonary changes on Day 84, while EBV was detected for the first time in peripheral blood simultaneously. Subsequently, a right lung biopsy at Day 90 showed non-destructive PTLD and plasmacytic hyperplasia with kappa restriction. CD 20 negative, with CD38 staining the plasma cell. EBER-ISH positive and troposim studies demonstrated EBV-infected T cells. Biochemical markers of haemophagocytic lymphohistocytosis (HLH) were detected and rising.

Rituximab was initiated along with the discontinuation of immunosupression in early December, and CHOP therapy (cyclophosphamide, doxorubicin hydrochloride, vincristine sulphate and the steroid hormone prednisone) was commenced. CHOP resulted in transient lysis. However, there was a rapid resurgence in HLH markers. Limited therapeutic options were available; thus, daratumumab was initiated based on the identification of CD38+. After three doses, the patient achieved a complete response to PTLD, HLH and EBV.

Subsequent chimerism revealed 100% recipient cells, a second transplant was warranted. The second transplant proceeded relatively uncomplicatedly with prophylactic donor-derived EBV-specific cytotoxic T lymphocytes (CTLs) administered, and the patient is currently well 2 years post-BMT.

Conclusion: In conclusion, this experience underscores the critical role of histopathological diagnosis in confirming and characterising a diagnostically challenging case of PTLD, emphasising the pivotal role of tailored therapy such as daratumumab. To the best of our knowledge, this signified the first sustained response in the HSCT setting of PTLD with daratumumab.

BSH24-PO83 | Phase 2 trial of nanatinostat and valganciclovir in patients with EBV-positive (EBV+) relapsed/refractory lymphomas (NAVAL-1)

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Epstein–Barr virus-positive (EBV+) lymphomas are a heterogeneous group of malignancies that harbour latent EBV within the lymphoma cells, and are associated with variable clinical features, treatments and prognoses. Outcomes in EBV+ lymphoma patients are typically inferior compared to EBV– lymphomas of the same subtype. There are no approved targeted treatments specific for EBV+ lymphomas, therefore this is an area of unmet medical need. The oral combination of nanatinostat (Nstat), a potent Class I HDACi, and valganciclovir (VGCV), a pro-drug of ganciclovir (GCV), is a novel mechanism to kill EBV+ tumour cells through inducing the expression of the lytic BGLF4 protein kinase to activate the nucleoside analogue GCV via phosphorylation, resulting in termination of DNA replication and apoptosis. The combination of Nstat plus VGCV was well tolerated and showed promising preliminary activity in a phase 1b/2 study of patients with R/R EBV+ lymphoma ($n = 55$) (NCT03397706), with an ORR of 40% (17/43) (CR 19%) in efficacy-evaluable patients. Patients with T/NK-NHL ($n = 15$) had an ORR/CR of 60%/27%; in EBV+ DLBCL, NOS ($n = 6$), the ORR/CR was 67%/33% (both CRs were patients refractory to first-line R-CHOP). The degree of EBER-ISH positivity (%) was not related to the clinical response, with the majority of patients having a baseline EBER-ISH below 50% (Haverkos 2021).

NAVAL-1 is an international, open-label, multicentre, single-arm, basket design trial (Simon, 1989). The following cohorts of R/R EBV+ lymphomas are included: EBV+ DLBCL, PTCL, PTLD and EBV+ lymphoproliferative disorders other than the subtypes mentioned previously, including extranodal NK/T-cell lymphoma (ENKTL). Eligible patients have R/R EBV+ lymphoma after ≥1 prior systemic therapies, with no curative therapy available, measurable disease according to Lugano 2007 and adequate haematopoietic, hepatic and renal function. Patients will receive Nstat 20 mg orally once daily, 4 days weekly with VGCV 900 mg orally once daily, 7 days weekly. End-points include: Primary: ORR. Secondary: OS and PFS, TTP, safety and pharmacokinetic parameters.

As of the data cut-off date of 30 June 2023, initial results from the first five patients with R/R EBV+ PTCL treated with Nana-val showed an overall response rate (ORR) and complete response rate (CRR) of 40%. The EBV+ PTCL cohort met the efficacy threshold for expansion into Stage 2 of the study, which was based upon achieving two objective responses within the first five of 10 patients enrolled in Stage 1 of the study. Median duration of response (DoR) has not been reached. Enrolment began in May 2021.

BSH24-PO84 | Detecting early relapse of high-grade B-cell lymphoma in the era of telemedicine

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Prompt detection of relapsing high-grade B-cell lymphoma provides patients with the best opportunity to access second-line therapies, including novel treatments such as CAR T therapy. Current UK guidance recommends outpatient follow-up for a 2- or 3-year period after completion of therapy. Current evidence does not support the use of routine surveillance imaging. The use of telemedicine has risen since the start of the SARS-CoV-2 pandemic in 2020; however, the efficacy of telemedicine consultations in the detection of lymphoma relapse is unknown. We performed a two-centre retrospective study of patients treated for high-grade B-cell lymphoma to evaluate disease relapse characteristics and assess for the potential impact of changes in follow-up practice. We retrospectively reviewed all patients diagnosed with high-grade B-cell lymphoma between 1st January 2017 and 31st December 2020 at haematology departments in two university teaching hospitals. Baseline demographics, disease characteristics, treatment regimens and end of treatment response data was collated for patients commenced on first-line chemo-immunotherapy. Clinic and radiology attendances and episodes of disease relapse occurring within a 2-year period following completion of therapy were evaluated.

Two hundred and forty-two patients commenced first-line chemo-immunotherapy (R-CHOP, R-miniCHOP, R-DA-EPOCH, R-GemCVP, R-CODOX-M-R-IVAC), with a median age of 71 years (range, 34–89 years). One hundred and ninety-five patients (80.6%) responded to therapy and commenced clinical monitoring, of whom 25 patients (12.8%) relapsed within 2 years. Relapse was detected due to lymphadenopathy or 'B' symptoms in 10 patients, abnormal laboratory results in two patients, incidental imaging findings in two patients and atypical symptoms in 11 patients (including neurological, abdominal and cutaneous symptoms). The use of telemedicine consultations increased over time when

comparing patients diagnosed in 2017/18 with those diagnosed in 2019/20. Patients presenting with relapse within these two periods were equally likely to present acutely requiring inpatient admission (50% vs. 45%), and the timepoint of relapse detection was unchanged (9 vs. 8.8 months). Our experience suggests that the increasing use of telemedicine consultations in this patient group did not affect the timepoint or clinical setting of relapse detection. Our data support previous publications that highlight the importance of patient-reported symptoms during follow-up. A significant proportion of patients with relapsed disease presented with atypical symptoms, emphasising the importance of robust patient education and direct patient access to haematology services. The significant proportion of patients who were diagnosed with relapse during an acute inpatient admission demonstrates the unmet need for a cost-effective modality of monitoring disease status after therapy.

BSH24-PO85 | Pirtobrutinib, a highly selective, non-covalent (reversible) BTK inhibitor in relapsed/refractory follicular lymphoma

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Background: Covalent Bruton tyrosine kinase inhibitors (cBTKi) have transformed the management of B-cell malignancies. Pirtobrutinib is a highly selective, non-covalent (reversible) BTKi. Here, we report the safety and efficacy of pirtobrutinib in a cohort of patients with relapsed/refractory (R/R) follicular lymphoma (FL) from the BRUIN study (NCT03740529).
Methods: Patients with previously treated B-cell malignancies were eligible for treatment with pirtobrutinib monotherapy in the phase 1/2 BRUIN study. FL diagnosis required pathological review of an adequate biopsy. Key efficacy and safety end-points were evaluated.
Results: As of 05 May 2023, among the 48 patients with FL, 45 patients received the recommended phase 2 dose of pirtobrutinib (200 mg once daily) as their starting dose. Patients had a median age of 64.5 years (range, 37.0–85.0) were mostly male (60%), and had a median of 3 (range, 1–12) prior lines of therapy. Most patients (81%) had Ann Arbor stage III/IV disease. The FLIPI risk in the patient population was: low (0–1) in 19%, intermediate (2) in 27%, high (3–5) in 48% and missing in 6%. These patients had previously received: chemotherapy plus an anti-CD20 antibody (90%), PI3K inhibitor (35%), lenalidomide (29%), autologous stem cell transplant (13%) and CAR T-cell therapy (8%). Of the four patients who had received a prior cBTKi, three discontinued due to disease progression and one for intolerance. The ORR was 50.0% (95% CI, 35.2–64.8). With a median follow-up of 18.4 months (IQR, 10.1–21.0) among 24 responding patients, median DOR was 5.5 months (95% CI, 3.7– NE), median PFS was 5.8 months (95% CI, 3.8–8.1) and median OS was NE. At 18 months follow-up, the estimated rates were: 41.0% (95% CI, 20.1–60.9) for DOR, 32.3% (95% CI, 19.1–46.2) for PFS and 78.3% (95% CI, 62.1–88.1) for OS. The median time on treatment was 7.6 months (range, 0.6–42.2), with 29.2% patients still receiving pirtobrutinib. The most common TEAEs were: diarrhoea (29.2%), fatigue (25.0%) and nausea (22.9%). TEAEs of haemorrhage/haematoma (6.3%), hypertension (4.2%) and atrial fibrillation/flutter (2.1%) were infrequent. The most frequent grade ≥3 TEAEs were infection (18.8%) and neutropenia (14.6%). Only one patient had a TEAE (rash) that led to pirtobrutinib discontinuation.
Conclusions: In this cohort of heavily pretreated R/R FL patients, pirtobrutinib showed potential efficacy and was well tolerated, including in high-risk FLIPI patients.

BSH24-PO86 | Pirtobrutinib in prior cBTKi R/R MCL: Phase 1/2 BRUIN study updates including high-risk subgroup analyses

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Background: Despite covalent (c) Bruton tyrosine kinase inhibitors (BTKi) efficacy in relapsed/refractory (R/R) mantle cell lymphoma (MCL), disease relapse arises. Pirtobrutinib, a highly selective, non-covalent (reversible) BTKi, is approved in the USA to treat R/R MCL after at least two lines of systemic therapy, including a prior cBTKi. Here, we report updated results of pirtobrutinib therapy in patients with a median survival follow-up of 24.2 months (range, 18.2–29.8) from the multicentre phase 1/2 BRUIN study (NCT03740529).
Methods: Patients with R/R MCL received pirtobrutinib monotherapy (25–300 mg/day), with 93% ($n = 141$) receiving ≥1 FDA-approved dose of 200 mg/day. Efficacy was assessed in cBTKi-pretreated ($n = 152$) and naïve ($n = 14$) patients.
Results: As of 05 May 2023, among the cBTKi-pretreated patients, the median age was 70 years (range, 46–88) and the median prior lines of therapy were 3 (range, 1–9). The percentage of patients determined to be intermediate and high risk by sMIPI scores were 52% and 28.3% respectively. Among patients with high-risk biomarker data available, 30/60 (50%) had TP53 mutations, and 45/63 (71%) had a ≥30% Ki-67 index. ORR for cBTKi-pretreated patients was 49.3% (95% CI, 41.1–57.6), including 15.8% complete responses ($n = 24$) and 33.6% partial responses ($n = 51$). ORR for naïve patients was 85.7% (95% CI, 57.2–98.2). ORR among patients who discontinued a prior cBTKi due to progressive disease ($n = 128$) or toxicity/other reasons ($n = 21$) was 43.0% and 90.5% respectively. Median DoR for the 75 responding cBTKi-pretreated patients was 21.6 months (95% CI, 9.2–27.2). DOR rates at 18 and 24 months were 51.9% (95% CI, 37–64.8) and 38.9% (95% CI, 22.7–54.8) for cBTKi-pretreated patients respectively. DOR rates at 18 and 24 months among 12 responding cBTKi naïve pts were both 90.0% (95% CI, 47.3–98.5). Median PFS was 5.6 months (95% CI, 5.3–9.2) and OS was 23.5 months (95% CI, 17.1-NE) for cBTKi-pretreated patients. In the MCL

cohort ($n = 166$), the most frequent TEAEs were fatigue (31.9%), diarrhoea (22.3%) and dyspnoea (17.5%). Among grade ≥3 TEAEs, neutropenia/neutrophil count decreased (13.3%) was most common, the infection rate was 19.9%, and haemorrhage/haematoma (2.4%) along with all-grade atrial fibrillation/flutter (3.6%) were infrequent. Treatment-related AEs resulted in eight patient (5%) dose reductions and five patient (3%) discontinuations.

Conclusions: Pirtobrutinib continues to demonstrate durable efficacy and a favourable safety profile in heavily pretreated R/R MCL patients with prior cBTKi therapy. High ORRs were observed in patients who progressed on a prior cBTKi, as well as in patients with high-risk biomarkers, including elevated Ki-67 index and TP53 mutations.

BSH24-PO87 | Sonrotoclax (BGB-11417) monotherapy in patients with relapsed/refractory marginal zone lymphoma: An ongoing phase 1 study

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Background: Sonrotoclax (BGB-11417) inhibits BCL2 with a potency >10× that of venetoclax in biochemical assays. BGB-11417-101 (NCT04277637) is an ongoing, first-in-human, phase 1/2 dose escalation/expansion in patients with B-cell malignancies. Data are presented for the relapsed/refractory marginal zone lymphoma (MZL) cohort.

Methods: Patients received one of the following sonrotoclax target doses: 40/80/160/320/640 mg QD; a 3-day ramp-up was used; expansions at 640 mg and 320 mg followed. Dose-limiting toxicities (DLTs) at the intended dose were evaluated. The primary end-point was safety; a secondary end-point for expansion was ORR. Responses were assessed per Lugano 2014 criteria. Tumour lysis syndrome (TLS) was assessed per Howard (2011) criteria.

Results: As of 24 April 2023, 13 patients received sonrotoclax across groups (40 mg, $n = 1$; 160 mg, $n = 2$; 640 mg, $n = 10$). Of 4 patients with progression on Bruton tyrosine kinase inhibitors (BTKi), three had BTKi as their last prior therapy. The maximum tolerated dose was not achieved with doses ≤640 mg. One DLT occurred (febrile neutropenia, 160 mg group), which resolved after 2 days without dose modification. The recommended phase 2 dose after dose expansion was 640 mg. Median follow-up was 7.8 months (range, 2.6–36.6). Treatment-emergent AEs (TEAEs) in ≥20% of patients were nausea (39%) and pyrexia, diarrhoea and constipation (31% each). The most common grade ≥3 TEAEs were neutropenia, febrile neutropenia/neutropenic sepsis and TLS (15% each). Five patients discontinued treatment ($n = 3$, progressive disease; $n = 1$, AE [infection]; $n = 1$, withdrawal); no TEAEs led to death. Two patients (640 mg group) experienced laboratory TLS following the initial ramp-up dose. The first patient had elevated potassium, phosphate and urate after a 160 mg dose, which resolved within 24 h with intravenous hydration and supportive care without sequela or dose modification. After protocol amendment, patients with circulating tumour cells received an additional 3-day ramp-up starting at 40 mg. A second patient had elevated phosphate and urate after initial 40 mg and 80 mg doses. Both episodes resolved within 24 h without sequela or dosing change. In 12 assessed patients, the ORR was 67% ($n = 8$), including four (33%) CR. Nine evaluable patients treated at 640 mg had an ORR of 78% ($n = 7$), including four (44%) CR. All patients with previous progression on BTKi had CR ($n = 3$) or PR ($n = 1$).

Conclusions: Sonrotoclax monotherapy was tolerable across tested doses and had encouraging anti-tumour activity in patients with MZL. Two patients had laboratory TLS following initial dosing that resolved. No clinical TLS was observed, indicating that TLS can be mitigated with current measures, including revised ramp-up. An exploratory 320 mg group is currently enrolling.

BSH24-PO88 | Infectious complications of bispecific antibody treatment in patients with lymphoproliferative disorders

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Bispecific antibody (BiAb) treatments have demonstrated efficacy in patients with relapsed/refractory lymphoproliferative disorders (R/R LPD) who previously had few treatment options. We present a retrospective analysis of a pooled dataset of patients treated with BiAbs for R/R LPDs at a single centre between May 2019 and January 2024.

Twenty-eight patients were treated during this time, of whom 10 (38%) were female and 18 (62%) were male. The median age at the start of treatment was 71 years (range 51–82). Nine patients had follicular lymphoma (FL), three high-grade transformation of FL, 10 diffuse large B-cell lymphoma (DLBCL) and one each had chronic lymphocytic leukaemia and mantle cell lymphoma. The median number of prior treatment lines was 2 (range 1–6). Ten out of 28

(36%) patients did not undergo response assessment due to the early progression of disease. Of 18 assessable patients, 13 achieved a complete response, three a partial response and one stable disease. The median OS of the whole cohort was 918 days.

The most common reason to stop treatment was progressive disease (13/28 patients); however, of those who responded, 10 stopped for other reasons. The most common of these was infections, in 6/10 after a median of 14 cycles (range 3–29), of which three were COVID-19 related and three due to non-COVID-19 (hepatitis E infection, influenza A, pneumonia). Other reasons for stopping included planned autoSCT, MDS, Hodgkin lymphoma and rash.

16/28 (57%) patients required admission for infection, and 15 (54%) had at least one treatment delay due to infection. Seven (25%) patients developed symptomatic COVID-19 while on treatment, with three patients admitted to hospital; three patients also experienced a prolonged infection lasting at least 4 months, which in one case resulted in death. The mean lymphocyte count at the time of first treatment was 1.0×10^9/L; however, in those patient's subsequently admitted for infection, it was 0.7×10^9/L and 1.3×10^9/L in those not admitted.

Of the six patients that stopped treatment due to infection, one died of COVID-19 and five remain in remission at a median of 186 days following cessation.

This demonstrates the efficacy of BiAb treatment in patients with R/R LPD. Infective complications are, however, a source of morbidity, resulting in admission and treatment delays for the majority of patients. COVID-19 remains a significant contributor to this, despite advances in vaccination and management. Further work to optimise BiAb treatment is required, including the duration of treatment and prophylaxis measures.

BSH24-PO89 | Indirect comparison of epcoritamab versus Tisa-cel in R/R LBCL CAR T-naive and CAR T-eligible patients

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Background: Epcoritamab is a subcutaneous, off-the-shelf, bispecific antibody (bsAb) recently approved for the treatment of adults with different types of relapsed/refractory (R/R) large B-cell lymphoma after ≥2 lines of systemic treatment in various regions, including the US, Europe and Japan. In the absence of head-to-head data comparing chimeric antigen receptor T-cell therapy (CAR T) with T cell-engaging bsAbs, we conducted an indirect treatment comparison between CAR T-naive patients treated with epcoritamab in EPCORE NHL-1, including a subgroup of CAR T-eligible patients, identified according to ZUMA-1 eligibility criteria and patients treated with tisagenlecleucel (tisa-cel) in the JULIET trial.

Methods: Published data on overall response rate (ORR), complete response (CR) rate, progression-free survival (PFS) and overall survival (OS) for tisa-cel from JULIET publications were used in MAIC versus individual patient-level data of CAR T-naive and CAR T-eligible patients from EPCORE NHL-1. Analyses were adjusted for baseline characteristics and imbalances between cohorts. Kaplan–Meier methodology estimated survival.

Results: Overall, 96 CAR T-naive patients from EPCORE NHL-1 were included, with an effective sample size of 33 CAR T-naive patients after adjustment. The CAR T-eligible subgroup included 57 patients, with an effective sample size of 21 patients after adjustment. After adjustment, there was a significant difference in ORR for epcoritamab versus tisa-cel (77.9% vs. 53.0%, respectively; difference [95% confidence interval (CI)]: 24.8% [9.5, 40.2]; $p = 0.002$) in the CAR T-naive cohort, and in CR rate (52.3% vs. 39.1%, respectively; difference [95% CI]: 13.2% [5.9, 32.3]; $p = 0.174$). Also, in the CAR T-naive cohort, there was a trend towards PFS benefit for epcoritamab versus tisa-cel after adjustment (hazard ratio [HR]: 0.725; 95% CI: 0.447, 1.177; $p = 0.194$) and OS (HR: 0.611; 95% CI: 0.356, 1.049; $p = 0.074$). In the CAR T-eligible subgroup, there was a significant difference in ORR (80.8% vs. 53.0%, respectively; difference [95% CI]: 27.7% [11.0, 44.4]; $p = 0.001$) and CR rate (61.9% vs. 39.1%, respectively; difference [95% CI]: 22.8% [1.5, 44.1]; $p = 0.036$) for epcoritamab versus tisa-cel after adjustment. There was a statistically significant survival benefit for OS (HR: 0.450; 95% CI: 0.227, 0.891; $p = 0.022$) and a numerical trend towards benefit for PFS (HR: 0.548; 95% CI: 0.300, 1.003; $p = 0.051$) in epcoritamab versus tisa-cel after adjustment.

Conclusion: This MAIC of the R/R LBCL CAR T-naive cohort and the eligible subgroup treated with epcoritamab versus tisa-cel demonstrated improved response rates and survival outcomes for epcoritamab, indicating the potential for this novel, subcutaneous, off-the-shelf, T cell-engaging bispecific to be a core therapy.

BSH24-PO91 | A single-centre retrospective cohort study comparing the tolerability/safety profile of Pola-R-CHP versus R-CHOP in the UK

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The POLARIX study demonstrated superior progression-free survival with Pola-R-CHP 76.7% compared to R-CHOP 70.2%, although no significant difference in overall survival (OS) was identified. The safety profile was similar between each cohort, although febrile neutropenia (FN) was more prominent in the experimental arm. 1.

We conducted a retrospective audit of patients treated with Pola-R-CHP in 2023 versus R-CHOP in 2022 to compare their efficacy and safety profiles. Patients with an IPI <2 were excluded. Variables collected included performance status, comorbidities, the number of cycles given and the use of G-CSF prophylaxis. Rates of G3 infection, total number of days patients required IV antibiotics and hospital admission were collected. The CTCAE scoring system was used to record grades of neutropenia and peripheral neuropathy (PN). Complete response (CR), overall response (OR) and OS were also calculated. Cell of origin (GCB vs. non-GCB) was also recorded.

Eighty-three patients were included, with 42 and 41 in the Pola-R-CHP versus R-CHOP groups respectively. Both groups were similar in terms of patient characteristics and disease status. OR and CR appeared slightly higher in the Pola-R-CHP group (100% vs. 89% and 89% vs. 76%); however, as in the pivotal trial, these results were not statistically significant ($p=0.31$ and $p=0.25$ respectively). Rates of FN were 38% vs. 27% ($p=0.61$) and G3 infection were 23% vs. 18% ($p=0.65$) in the Pola-R-CHP versus R-CHOP groups respectively. The mean number of days in hospital was greater in the R-CHOP group (17 vs. 7 days) ($p=0.03$), as was the mean number of days on IV antibiotics (8 vs. 4 days) ($p<0.10$) respectively. The rate of PN in all grades was significantly higher in the R-CHOP versus Pola-R-CHP group, 68% vs. 28% OR 5.50 ($p<0.0001$).

Our results demonstrate that the efficacy and safety of Pola-R-CHP in the real-world setting are comparable to those of the POLARIX study. Despite our data suggesting an improvement in OR and CR with Pola-R-CHP, this is not statistically significant. As only 64% of the Pola-R-CHP group completed six cycles, longer follow-up is required to further investigate this. Comparable with the trial, rates of G3 infection, FN and hospitalisation appear similar between each cohort; however, PN and hospital admission days are significantly higher in the R-CHOP cohort, but the latter results could be skewed by one anomalous result and small sample size. A UK-wide study is needed to better understand if other factors (e.g. GCB vs. non-GCB) significantly affect outcomes in the real-world setting.

BSH24-PO92 | Mitigating the risk of cytokine release syndrome: EPCORE NHL-1 DLBCL Cycle 1 optimization cohort results

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Background: Epcoritamab, a subcutaneous CD3xCD20 bispecific antibody, is approved for the treatment of adults with different types of relapsed or refractory (R/R) large B-cell lymphoma (LBCL) after ≥2 lines of systemic treatment in various geographies, including the US, Europe and Japan. In patients with R/R LBCL in the expansion portion of the phase 1/2 EPCORE™ NHL-1 trial (NCT03625037), epcoritamab monotherapy demonstrated deep, durable responses with a manageable safety profile, characterized by low-grade, predictable CRS events, the majority of which occurred following the first full dose. We present the first data disclosure from a diffuse LBCL (DLBCL) cycle (C) 1 optimization cohort of the EPCORE NHL 1 trial, further investigating CRS risk mitigation in patients treated with epcoritamab monotherapy.

Methods: Adult patients with R/R CD20+ DLBCL and ≥2 prior treatment lines received epcoritamab (0.16/0.8-mg step-up and 48-mg full doses) in 28-day Cs (QW, C1–3;

Q2W, C4–9; Q4W, C ≥10 until progressive disease or unacceptable toxicity). To further mitigate CRS, patients received dexamethasone 15 mg, diphenhydramine and acetaminophen premedication (D1, D8, D15, D22) and dexamethasone prophylaxis (D2–4, D9–11, D16–18, D23–25) in C1. C1 recommendations included adequate hydration, holding anti-hypertensives 24 h prior to treatment and temperature self-monitoring. Hospitalization and inpatient observation were not mandated. The primary end-point was CRS rate (grade [G] ≥2 and overall).

Results: As of 17 July 2023 (median follow-up, 1.7 months), 60 patients were treated in this C1 optimization cohort (median age, 66 years; median prior lines of treatment, 3; primary refractory, 60%; prior CAR T, 55%); 70% of patients remained on treatment. CRS (23%), fatigue (20%) and pyrexia (17%) were the most common treatment-emergent AEs (TEAEs); 32% of patients experienced infections. Among the CRS-evaluable population ($n = 36$), CRS incidence was 22%. CRS events were low grade (G1, 14%; G2, 8%) and predictable, mostly occurring after the first full dose (C1D15); none led to treatment discontinuation, and all resolved (median time to resolution, 2.5 days). No patients had clinical tumour lysis syndrome or fatal TEAEs; one patient had ICANS (G1). At C1D16, median circulating IL-6 level was lower in the C1 optimization cohort versus the expansion cohort. Optimization had no impact on T-cell activation or B-cell depletion. Preliminary efficacy was comparable to the expansion cohort.

Conclusions: Encouraging preliminary data from this DLBCL optimization cohort demonstrate that C1 prophylactic dexamethasone and hydration effectively decreased rates and severity of CRS, with no impact on efficacy.

BSH24-PO94 | The effect of intermittent fasting on patients with sickle cell disease, a single-centre experience

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Sickle cell disease is a genetic disorder that frequently presents with vaso-occlusive crisis (VOC). Most patients with sickle cell disease in Qatar are Muslims; hence, they practice intermittent fasting during the holy month of Ramadan. However, there is a paucity of literature describing the effect of intermittent fasting on the occurrence of severe VOC. As a result, there is a lack of guidelines or standardized protocols that can help physicians advise patients with sickle cell disease who wish to practice intermittent fasting. Therefore, this study's aim was to investigate the effect of intermittent fasting on the clinical and haematological parameters of individuals with sickle cell disease.

After obtaining approval from the ethical committee at Hamad Medical Corporation, we conducted a retrospective study for 52 Muslim patients with sickle cell disease in Qatar aged 18 years or more who were confirmed to be fasting during the holy month of Ramadan during any of the years 2019–2021. The confirmation of fasting status was done through a telephone script. The difference in the occurrence of severe VOC, haemolytic crisis and other clinical, haematological and metabolic parameters were studied 1 month before, during and 1 month after the intermittent fasting of Ramadan using the patients' medical records. Mean (SD), median (IQR) and frequency (%) described the data. One-way with repeated measures ANOVA with a Greenhouse–Geisser correction and Friedman tests were used at alpha level 0.05.

The study participants' (mean ± SD) age was 31.1 ± 9.2 years; 51.9% were males, and 48.1% were females. Roughly 70% of the participants were of Arab ethnicity, while the rest were either African or Asian. Most of the patients were homozygotes (SS) (90.4%). The median number of severe VOC ($p = 0.7$) and haemolytic crisis ($p = 0.5$) was not found to be significantly different before, during or after Ramadan. Significant differences, however, were found in platelet count ($p = 0.003$), reticulocyte count ($p < 0.001$) and creatinine level ($p = 0.038$) with intermittent fasting.

In this preliminary study, intermittent fasting does not seem to influence the rate of occurrence of severe vaso-occlusive crisis or haemolytic crisis in patients with sickle cell disease; however, it was found to be associated with differences in platelet count, reticulocytes count and creatinine level. The statistical and clinical significance of these findings needs to be confirmed in studies with a larger sample size.

BSH24-PO95 | Multiprofessional simulation learning to improve management of sickle cell crisis

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Individuals living with sickle cell disorders are at risk of acute and life-threatening complications of their condition. Patients often present to busy emergency departments (EDs) with emergent pathologies, including acute chest syndrome, painful crisis or sepsis. It is imperative that patients receive evidence-guided urgent care, and that severe complications carrying a high mortality risk are diagnosed and managed in a timely manner. The need for multidisciplinary, collaborative training between the Haematology and Emergency medicine departments was recognised, to improve the

management of patients presenting to the ED with acute complications of sickle cell disease in our trust.

A portfolio of measures to improve patient experience and outcomes have been introduced. These include the provision of an accessible folder of sickle cell guidelines and individualised care plans, held in the resuscitation area of the ED. A role of Link Nurse for sickle cell disease was appointed to within the ED, with responsibilities for disseminating training and supporting best practice. Most recently, an interdepartmental simulation training and teaching session was facilitated for ED staff.

Simulation training is a recognised tool for experiential learning, with scope for both technical and non-technical learning through open, facilitated discussion during the debrief session. We felt this was the best tool to aid in the discussion of shortcomings and challenges that may be faced during the initial management of patients presenting with complications of sickle cell disease to the ED.

A collaborative simulation session was delivered around the case of a young patient presenting with acute chest syndrome. A trainee was used to play the patient to allow real-time feedback of pain management and communication. During the scenario, equipment from the trust simulation centre was used to feed in observations and investigations, including chest radiography and blood gases. Attendees included junior ED nurses, junior doctors and emergency medicine higher specialty trainees, with additional observers. Faculty running the session included an emergency medicine nurse, consultant, registrar and a haematology registrar.

The initial session of collaborative learning was highly successful, as evidenced by consistently positive feedback collated from participants and observers. A summary of key lessons learnt were subsequently circulated to all ED staff via a monthly newsletter and educational messaging group. This initiative is expected to translate into better experiences and improved early management for our sickle cell patients and such a programme is recommended for other hospital trusts in which the ED forms part of the patient presentation pathway.

BSH24-PO96 | Long-term data for danicopan add-on therapy in patients with PNH and clinically significant extra-vascular haemolysis

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Introduction: The efficacy and safety of the first-in-class oral factor D inhibitor danicopan (ALXN2040) as an add-on treatment to ravulizumab or eculizumab for patients with paroxysmal nocturnal haemoglobinuria (PNH) and clinically significant extra-vascular haemolysis (cs-EVH) were assessed in a phase 3 randomized, double-blind, placebo-controlled superiority clinical trial (ALPHA, NCT04469465). Open-label 24-week and ongoing long-term extension (LTE) data are presented.

Methods: Adult patients with PNH and cs-EVH (haemoglobin [Hgb] ≤9.5 g/dL; absolute reticulocyte count [ARC] ≥120 × 109/L) on ravulizumab/eculizumab for >6 months were randomized 2:1 to danicopan or placebo add-on therapy for 12 weeks (previously reported). At Week 12, placebo-treated patients switched to danicopan (Pbo-Dan), and danicopan-treated patients continued (Dan-Dan) for another 12 weeks, followed by a 1-year LTE in which all patients received danicopan add-on therapy. The primary end-point was change from baseline in Hgb at Week 12. Safety assessments included treatment-emergent adverse events (TEAEs) and laboratory abnormalities throughout the study.

Results: As of 20 September 2022, 86 patients were randomized; 60 completed Weeks 12–24 (danicopan $n = 40$;

placebo $n = 20$). At Week 24, mean Hgb level was maintained in the Dan-Dan arm and increased from Week 12 in the Pbo-Dan arm. ARC was maintained in the Dan-Dan arm and improved in Pbo-Dan arm at Week 24. From Weeks 12–24, the proportion of patients with Hgb increase of ≥2 g/dL in the absence of transfusion was maintained in the Dan-Dan arm and improved in the Pbo-Dan arm. Transfusion avoidance was maintained in the Dan-Dan arm (83.3% and 78.0%) and increased in the Pbo-Dan arm (38.1% and 90.0%, respectively), from Weeks 12–24. Mean lactate dehydrogenase levels were maintained from Weeks 12–24 and were near normal in both arms. Compared with placebo add-on alone, transfusions decreased in the Pbo-Dan arm (mean, 2.2 vs. 0.1 respectively).

The safety analysis included the 80 patients exposed to danicopan during the trial.

Through data cut-off, 90% of patients had ≥1 TEAE. Serious AEs related to danicopan were reported in two patients (gastrointestinal disorders/increased blood bilirubin; headache). Six events (four patients) led to the withdrawal of study drug; four events were reported as breakthrough haemolysis. There were no deaths, meningococcal infections or discontinuations due to haemolysis.

Conclusion: Danicopan as an add-on to ravulizumab/eculizumab significantly improved Hgb and ARC levels and reduced the need for transfusion by addressing cs-EVH while maintaining control of IVH through 48 weeks of treatment. Danicopan demonstrated a favourable benefit–risk profile.

BSH24-PO97 | Awareness, knowledge and acceptance of bone marrow transplantation for beta thalassaemia major in Sri Lanka

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Background: Bone marrow transplantation (BMT) is identified as an effective management option for children diagnosed with transfusion-dependent beta thalassaemia major (BTM). However, lack of awareness and knowledge on BMT identified as a major drawback in the low acceptance rate of BMT by parents/caregivers.

Objective: This study was conducted to assess the awareness and knowledge, and acceptance of BMT among the parents/caregivers of children diagnosed with BTM.

Methodology: A cross-sectional study was conducted among a sample of 125 parents/caregivers of children diagnosed with BTM at paediatric units in the National Hospital Kandy and Teaching Hospital Kurunegala in Sri Lanka. An interviewer-administered questionnaire was used to assess awareness, knowledge and acceptance status on BMT. Chi-square test at 0.05 is used to identify associated factors for BMT at 0.05 significance level.

Results: Majority of caregivers (91.2%) were heard about BMT, among them 85.1% were heard about BMT as treatment option for BTM. However, haematologist or paediatrician had discussed the role of BMT only in 13.2%. Mean (SD)age of the discussion was 4.0 (1.6) years. Nearly 78% had satisfactory awareness status on BMT. Only 45.6% of caregivers/parents had satisfactory knowledge on BMT. The acceptance rate of BMT was 56.0%. Among parent/caregivers ($n = 55$) who did not ready to accept BMT, majority (34.5%) was due to not yet decided followed by cost (21.8%), fear of complications (16.4%). Sinhalese parents/caregivers ($p = 0.001$) and parents/caregivers with satisfactory education level ($p < 0.001$) were more likely to have satisfactory awareness status on BMT. Parents/caregivers not having children with comorbidities other than present child with thalassaemia ($p = 0.026$) were more likely to have satisfactory knowledge status on BMT. Parents/caregivers who are employed (<0.05) and having satisfactory education level (<0.05) were more likely to have higher acceptance on BMT. Interestingly, parents/caregivers had satisfactory awareness status ($p < 0.001$) on BMT and satisfactory knowledge status ($p = 0.003$) on BMT were more likely to have higher acceptance status.

Conclusion and Recommendations: Awareness on BMT was at satisfactory level, but knowledge on BMT was poor. Acceptance rate on BMT is also up to substandard level. As awareness and knowledge status on BMT had identified two important factors in acceptance status, the study recommends health education and health promotion interventions to improve the acceptance rate for BMT by the parents/caregivers of children diagnosed with beta thalassaemia major.

Keywords: awareness, knowledge, acceptance, bone marrow transplantation.

BSH24-PO98 | Renal status of children with SCA in steady state at Rivers State University Teaching Hospital, Nigeria

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Background: Sickle cell anaemia (SCA) is the leading genetic disorder among children in Nigeria and can present with kidney-related complications. About one in five SCA-related deaths are attributed to progression of chronic kidney disease from sickle cell nephropathy (SCN). In resource-limited settings, identifying early markers of renal disease could enable targeted interventions to reduce morbidity and

limit disease progression. This study aimed to determine the prevalence of microalbuminuria and hyperfiltration among children with SCA in a steady state attending the Haemato-oncology clinic of the Department of Paediatrics, Rivers State University Teaching Hospital, Nigeria.

Methodology: A comparative cross-sectional study was conducted with 60 SCA (HBSS) cases and 60 age- and sex-matched controls (HbAA). A questionnaire was used to obtain socio-demographic, clinical and anthropometric data. Urine and blood samples were collected, and the urine was assayed for microalbuminuria by fluoro-immunoassay, and urine creatinine using a semi-automated chemistry analyser. Microalbuminuria was defined as a urine albumin–creatinine ratio of 30 to <300 mg/mmol, and hyperfiltration was defined as an estimated glomerular filtration rate of >140 mL/min/1.73 m^2. Data were analysed.

Results: Of the 120 children recruited, 62 (51.7%) were males. The mean age of participants was 9.36 ± 4.06 years. The indicators of renal dysfunction were significantly higher in the cases compared to the controls: microalbuminuria (HBSS 16.7% vs. HbAA 3.3%; $p = 0.015$) and hyperfiltration (HBSS 25.0% and HbAA 6.7%, $p = 0.002$). Logistic regression revealed that the SCA patients were five times (AOR: 5.80; 95% CI: 1.29–26.03) and four times (AOR: 4.67; 95% CI: 1.44–15.04) more likely to have microalbuminuria and hyperfiltration respectively, compared to the controls. There was a significantly higher prevalence of hypertension among controls compared to cases (HBSS 1.7% vs. HBAA 16.7%; $p = 0.004$).

Conclusion: The prevalence of biomarkers indicative of sickle cell nephropathy among SCA children in 'steady-state' Port Harcourt is high. Surprisingly, we found microalbuminuria and a higher prevalence of hypertension among children in the control group as well. This underscores the importance of routine blood pressure checks and screening for kidney disease in both the SCA and the general paediatric population.

BSH24-PO99 | Neuroimaging & neurological complications in patients with sickle cell disease in the Thames Valley

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Introduction: Patients with sickle cell disease (SCD) have a high rate of neurological complications. Up to one in two adults will have had a cerebral infarct, either with (stroke) or without (SCI—silent cerebral infarct) neurological symptoms, by the age of 30 (1). This compares with <20% of the Caucasian population over the age of 75 having experienced the same (2).

The rate of intracranial aneurysms (ICAs) in SCD is 4%–12% (3,4), compared to <2% in the general population (2).

The use of screening MRI/MRA to look for SCIs and ICAs is not validated, and is not currently recommended by the BSH; however, a single MRI in adults is recommended by the American Society of Haematology (5).

We aimed to examine the rates of neuroimaging and neurological complications in our patients, and compare these with the existing literature.

Methods: We performed a retrospective review of the medical records of 279 patients with SCD, registered with the Thames Valley Specialist Haemoglobinopathy Team, to identify those who had experienced a neurological event or undergone MRI neuroimaging.

Results: Of our 279 patients, 55 (20%) had undergone MR neuroimaging at some point. Of these, 14 (5%) also underwent MRA, and four (1.5%) also underwent MRV. Fifty-eight per cent of MRIs showed a significant abnormality.

Nineteen patients (7%) were found to have had an ischaemic event—six had strokes in childhood, while in adulthood, six had strokes, two had TIAs and five had SCIs. Excluding those occurring in childhood, the median age of event was 44, and most patients (64%) are HbSS genotype. Three (23%) were on treatment with hydroxycarbamide at the time of event, seven (54%) were not on treatment at the time of the event, and data was not available for the remaining three patients. None were on exchange transfusions at the time of event.

Seven patients (2.5%) were found to have an ICA, of whom four presented with a subarachnoid haemorrhage. The median age of presentation was 41, and patients were predominantly (6 of 7) HbSS genotype. Five of seven patients were offered intervention on their aneurysm(s).

Four patients were found to have early-onset small vessel disease, with a median age of 56.

Conclusions: Our population was found to have a high rate of neurological complications of SCD—prospective studies are required to validate whether the use of screening neuroimaging in asymptomatic patients would offer benefit.

BSH24-PO100 | Paroxysmal nocturnal haemoglobinuria in pregnancy: A systematic review

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Paroxysmal nocturnal haemoglobinuria (PNH) is a rare, acquired, clonal disorder of haematopoietic stem cells, characterised by complement-mediated intravascular haemolysis and thrombosis. The co-occurrence of PNH and pregnancy

has been associated with poor feto-maternal outcomes. Eculizumab, a terminal complement inhibitor, is used in pregnant patients with PNH, but the drug is not available worldwide. We therefore present the first comprehensive systematic review of outcomes in 190 pregnancies from 135 PNH patients, comparing those receiving eculizumab and those not.

The MEDLINE database was searched for studies reporting primary data on pregnancy outcomes in the context of PNH. Thirty-five papers were selected for inclusion (published 1968–2021). The majority were small case series or case reports. There were two larger retrospective studies on 45 and 75 pregnancies respectively, and one small ($n = 15$) prospective study.

Eculizumab was used in 131 pregnancies (69%). There was one maternal death in a woman not receiving eculizumab. The risk of fetal loss was lower in pregnancies where eculizumab was used than those where it was not (24% vs. 32.2%, OR 0.45, 95% CI 0.2–0.9, $p = 0.03$). Where eculizumab was used, 45% of women required eculizumab dose increases to optimise PNH disease control. Antenatal thromboprophylaxis was administered in 76% of pregnancies (90% of eculizumab pregnancies, 50% non-eculizumab). Of these patients around 2/3 received prophylactic dose, 1/4 received treatment dose (typically indicated due to previous thrombotic event(s), but in several cases the regimen was instituted prophylactically) and a small number received intermediate doses. Thrombosis complicated 6% of pregnancies, with no thrombotic events in women receiving treatment dose anti-coagulation. Bleeding events were over twice as common (14%) as thrombosis. The incidence of thrombotic and bleeding events did not significantly differ between eculizumab and non-eculizumab pregnancies. The incidence of pre-eclampsia was high in this population, with a trend towards a reduced incidence of pre-eclampsia in eculizumab pregnancies (9% vs. 15.2%), but this did not reach statistical significance. No Neisserial infections were observed in patients treated with eculizumab. Fetal structural anomalies occurred in three cases, none of which had been exposed to eculizumab, suggesting the drug is not significantly teratogenic. Premature birth (<37 weeks' gestation) was observed in 32% of eculizumab pregnancies and 44% of non-eculizumab pregnancies. Mean birth weight did not significantly differ between the two groups.

This study is the only comprehensive systematic review of pregnancy outcomes in PNH to date and supports the safety and efficacy of eculizumab in pregnant patients with PNH.

BSH24-PO101 | Evaluate and improve the quality of care provided to patients with sickle cell disease

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This study, conducted at Nottingham University Hospitals (NUH), aims to enhance the care of individuals with sickle cell disease (SCD) by focusing on the screening, prevention and treatment of sickle cell nephropathy (SCN). The objectives include evaluating current practices against the standards set by the Sickle Cell Society in 2018. This assessment involves a comprehensive review of SCD patient management, specifically addressing renal complications.

The guidelines from the Sickle Cell Society highlight the importance of collaborative management with renal physicians, particularly for patients experiencing acute renal failure or declining renal function. Key recommendations include annual monitoring for renal disease symptoms, hypertension, and markers like albuminuria, proteinuria and declining renal function. The Investigations for new-onset haematuria are crucial, and patients with proteinuria exceeding 50 mg/mmol should be considered for ACE inhibitors, angiotensin receptor blockers (ARBs) and potentially hydroxycarbamide therapy. Moreover, patients with end-stage kidney disease (ESKD) should be evaluated for renal replacement therapy options, including transplantation.

The study encompasses 100 patients with confirmed SCD under the care of NUH Clinical Haematology. Evaluated parameters include demographic data, genotype, glomerular filtration rate (GFR), proteinuria levels, UP: UC ratio, renal follow-up status, renal transplant history, chronic kidney disease (CKD) status, biopsy results, immunology, virus serology, myeloma screening and renal tract ultrasound findings.

Preliminary data analysis reveals no current cases of acute renal failure, with one patient lacking renal function test records. Three patients show a significant decline in GFR, with one having concurrent proteinuria, yet not receiving ARB/ACEI treatment or under renal follow-up. A substantial number of patients exhibit proteinuria exceeding 30 mg/L, with many surpassing 50 mg/L. The UP: UC ratio is notably high in a majority of patients. Only a small fraction is receiving appropriate medication or under renal follow-up, and there is a lack of comprehensive data for new-onset haematuria. Although annual screening for urine protein, haematuria and renal function is offered, no patients with end-stage kidney disease were identified.

The study underscores the need for enhanced monitoring and adherence to the Sickle Cell Society's guidelines at NUH. Recommendations include incorporating new-onset haematuria into the annual sickle cell review proforma, considering renal referral for patients with proteinuria, and thorough evaluation of patients exhibiting declining renal

function. These steps are crucial for improving the management of SCN in SCD patients.

BSH24-PO102 | Circulating MiRNAs as new biomarkers for detecting haemolysis in the non-acute phase of G6PD deficiency

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Glucose-6-phosphate dehydrogenase (G6PD) deficiency is one of the most common enzymopathies worldwide. Patients with G6PD deficiency are usually asymptomatic throughout their lives, but can develop acute haemolysis after exposure to free radicals or certain medications. Several studies have shown that circulating microRNAs (miRNAs) can be used as prognostic biomarkers in various types of haemolytic anaemias. However, the impact of G6PD deficiency on circulating miRNA profiles is largely unknown. This study aimed to assess serum miRNAs as biomarkers for detecting haemolysis in the non-acute phase G6PD deficiency. Patients with severe, moderate G6PD Viangchan (871G>A) deficiency and normal G6PD subjects were enrolled in this study. The research protocol was approved by the ethical review committee for research involving human subjects at Chulalongkorn University (COA no. 200/65 and COA no. 196/66) and the International University of Health and Welfare (22-Ifh-050) in accordance with the ethical standards of the Helsinki Declaration. Our findings show that biochemical haemolysis indices were normal in the three groups. The levels of serum miR-451a, miR-16 and miR-155 were significantly increased in patients with severe G6PD deficiency ($p < 0.05$). In addition, a set of three miRNAs differentiated G6PD-deficient individuals from normal G6PD individuals through 3D analysis. These findings suggest that a set of three miRNAs (miR-451a, miR-16 and miR-155) may serve as a potential biomarker for patients in the non-haemolytic phase of G6PD deficiency. Taken together, circulating miRNAs can be utilised as additional biomarkers to detect haemolysis in non-acute phase G6PD deficiency.

BSH24-PO103 | Klebsiella liver abscesses in Paediatric haemoglobinopathy patients on transfusion-chelation regimen

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We present four cases of Klebsiella Pneumonia liver abscesses in paediatric haemoglobinopathy patients on transfusion-chelation regimens at Royal London Hospital (UK). Our cases highlight diagnostic and management challenges, heightened during COVID-19 pandemic, while reporting for the first time an association between deferasirox and invasive Klebsiella infections.

Our tertiary centre retrospective case-note review identified four haemoglobinopathy patients (age < 18) treated for pyogenic liver abscesses between 2006 and 2021. The mean diagnostic age was 12 years (range 10–15), with male–female distribution of 3:1. Most children had HbSS (75%) and were ethnically Black African (75%). One patient had bronchiectasis and ulcerative colitis managed with azathioprine and sulfasalazine. Presenting symptoms included fever in all cases, and abdominal pain, vomiting and body aches in 50%. All patients had USS-confirmed liver abscesses, further visualised with CT-imaging. Management in all patients required PICU admission, broad-spectrum IV antibiotics, nurse-controlled analgesia and drain insertion. Drains remained in situ for a mean of 12 days (range 7–18 days), and removal followed concerns regarding drain-related sepsis in one, and upon sufficient abscess resolution in the remainder.

All cases grew Klebsiella and were managed initially with broad-spectrum IV antibiotics. Pus sampling importantly allowed antibiotic choice to be guided by culture sensitivities in three cases.

In summary, our report documents two cases of Klebsiella abscesses in patients on regular deferasirox, highlighting the need for further insight into this novel chelator's role in propagating ferrophilic infections. Several challenges in diagnosing liver abscesses in this group are highlighted, owing to non-specific clinical manifestations, raising crucial learning points:

1. Not all pain is vaso-occlusion related
2. Abdominal imaging is essential in transfusion-chelation patients with a PUO
3. Highlighted by the COVID-19 pandemic, in complex immunocompromised patients like those with haemoglobinopathies, and the source of hyper inflammation and sepsis must be aggressively sought and treated.

Liver abscess management in our patients, and in other case reports has focused on prolonged sensitivity-guided antimicrobial management, along with surgical or interventional abscess drainage. Pus culture was most successful in

identifying causative organisms; however, success in abscess resolution following drain insertion remains variable. We emphasise that risks must be considered and management optimised using MDT expertise including paediatric haematologists, hepatologists, radiologists and surgeons.

BSH24-PO104 | Transcranial Doppler screening of children with sickle cell disease in the HOPE Kids 2 trial

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Background: Transcranial Doppler (TCD) ultrasound is an effective screening tool for identifying children with sickle cell disease (SCD) who are at high risk of stroke. Implementing TCD screening for the purpose of stroke prevention in resource-constrained settings remains challenging. HOPE Kids 2 (NCT04218084) is an ongoing, phase 3, multicentre, double-blind, placebo-controlled trial of voxelotor in children with SCD and conditional TCD velocities at screening.
Objective: To describe the findings from successful implementation of a standardized TCD screening protocol that was conducted in a multinational setting.
Methods: In HOPE Kids 2, children aged 2 to <15 years with SCD (HbSS/HbSβ^0) were screened after local sonographers were trained and certified on standardized TCD examination protocol and equipment. TCD assessments underwent central quality review and interpretation by two independent reviewers. STOP criteria were used to classify stroke risk using time-averaged maximum of the mean velocity (TAMMV): normal, <170 cm/s; conditional, 170 to <200 cm/s; or abnormal, ≥200 cm/s.[1] Baseline characteristics were measured during screening.
Results: Between November 2020 and February 2023, 708 participants consented at 29 sites in Nigeria ($n = 250$), Kenya ($n = 241$), Egypt ($n = 145$), Ghana ($n = 28$), the US ($n = 17$), Italy ($n = 9$), Oman ($n = 9$), Saudi Arabia ($n = 8$) and the UK ($n = 1$). Of these patients, 92.1% (652/708) completed TCD screening examinations (mean [SD] age 7.6 [3.24] years; range 2.0–14.0 years; 50.8% male; 23.0% receiving hydroxycarbamide). Among TCD screening completers, the mean (SD) TAMMV was 163.0 (31.3) cm/s, and 47.1% (307/652) had conditional TCD at baseline. The main reason for screen failure was index TAMMV outside of conditional range (abnormal, $n = 39$ [6.0%]; normal, $n = 306$ [46.9%]). Elevated TAMMV on screening TCD was more common in younger children (2 to ≤8 years vs. >8 to <15 years); patients aged 2 to ≤8 years comprised 66.8% and 82.1% of the conditional and abnormal TCD categories respectively. Adjudication was required for 39 assessments; nine were deemed unreadable. Of all patients screened, 36.2% (236/652) fulfilled eligibility criteria for randomization. The mean (SD) haemoglobin level and TAMMV at screening for randomly assigned patients was 7.7 (1.1) g/dL and 182.7 (7.5) cm/s respectively.
Conclusion: Clinical sites for the HOPE Kids 2 study successfully implemented a standardized, local TCD screening protocol supported by central quality review. For a large interventional trial aimed at reducing the risk of stroke in children with SCD, African and Middle Eastern sites presented relatively few limitations with respect to participant screening.

[1]. Adams, N Engl J Med, 1998.

BSH24-PO105 | Over 4 years of safety and efficacy with voxelotor in patients with sickle cell disease

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Introduction: In patients with sickle cell disease (SCD), polymerization of sickle haemoglobin (HbS) results in red blood cell sickling and leads to haemolysis, chronic anaemia and vaso-occlusive crises. Voxelotor, a first-in-class HbS polymerization inhibitor, is approved in the UK for the treatment of haemolytic anaemia due to SCD in patients aged ≥12 years. To assess the safety and efficacy of long-term voxelotor use, we report an updated interim analysis of an open-label extension (OLE) of the HOPE phase 3 trial (NCT03036813).
Methods: Patients who completed the HOPE trial were eligible to enrol in the multicentre, global OLE study (NCT03573882) and receive ongoing treatment with once daily voxelotor 1500 mg if they continued to derive clinical benefit. Adverse event (AE) data were collected

through 28 days after voxelotor discontinuation, and measurements of haemoglobin and clinical markers of haemolysis were summarised through 168 weeks of treatment in the OLE. Data are based on an interim data cut (31 December 2022).

Results: Of 199 patients who completed the HOPE trial, 178 (89.4%) were enrolled and dosed in the OLE. Median age at enrolment was 25 years. The median duration of voxelotor exposure in the OLE was 124.0 weeks, and 81 patients were treated for ≥168 weeks. Of these, 52 had received voxelotor in the HOPE trial, for a combined duration of exposure of ≥240 weeks. Patients previously treated with placebo in the HOPE trial had a mean (SD) haemoglobin change from baseline (start of OLE) of 1.1 (1.51) g/dL at Week 168. The mean (SD) haemoglobin change from baseline for patients who previously received voxelotor 1500 mg was 0.5 (1.49) g/dL ($n = 18$), indicating durability of response with continued treatment. Markers of haemolysis (indirect bilirubin, reticulocyte percentage) improved in patients who received placebo in the HOPE trial and were stable for patients who previously received 1500 mg voxelotor in the HOPE trial. Non-SCD-related treatment-emergent AEs (TEAEs) were reported in 88.2% of patients; no new safety signals were identified. Most TEAEs were grade 1 or 2 in severity. Eight deaths occurred, none deemed related to voxelotor treatment.

Conclusions: In this updated analysis from the HOPE OLE, long-term use of voxelotor was effective at maintaining reductions in anaemia and haemolysis in patients with SCD. The safety profile in the OLE was consistent with findings from the HOPE trial, and no new safety signals were identified with exposure through a combined 240 weeks of treatment.

BSH24-PO106 | Ravulizumab provides long-term control of intravascular haemolysis and improves survival in patients with PNH

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Introduction: Long-term treatment outcomes with ravulizumab (up to 6 years) in complement component 5 (C5) inhibitor-naïve patients with paroxysmal nocturnal haemoglobinuria (PNH) from study 301 (NCT02946463) are reported and survival rates were compared with untreated patients from the International PNH Registry (NCT01374360).

Methods: C5 inhibitor-naïve patients with PNH and high-disease activity (HDA; lactate dehydrogenase [LDH] level ≥ 1.5 × the upper limit of normal [ULN] and at least one sign or symptom of PNH; $N = 246$) were randomized to receive ravulizumab or eculizumab. After the primary evaluation period (26 weeks), patients received ravulizumab for the 5-year open-label extension (OLE) period. LDH level change from baseline, the proportion of patients experiencing major adverse vascular events (MAVEs) and transfusion avoidance were evaluated. Cox proportional hazards regression analyses compared survival of ravulizumab-treated patients with untreated patients with HDA and clone size ≥5% at PNH Registry enrolment. Transfusion history ($p = 0.05$), age at PNH diagnosis and gender were included in the final adjusted model.

Results: Ravulizumab treatment data were available for 244/246 patients (median follow-up: 46.8 months). At baseline, all 246 patients had LDH levels >1.5 × ULN; at 26 weeks,

87.1% of patients achieved LDH levels ≤1.5 × ULN, which was maintained in 79.3% of patients at last follow-up. At baseline, 17.1% of patients had a history of MAVEs (MAVE rate: 3.4/100 patient years [PYs]). MAVE rate in ravulizumab-treated patients was low throughout the study ($n = 11$MAVE rate: 1.4/100 PYs), with nine patients (3.7%) reporting MAVEs during the OLE (1.3/100 PYs). Prior to randomization, 24.8% of patients did not need transfusions; at 26 weeks, this increased to 73.6% and was maintained in 53.9% of patients throughout the OLE. Units transfused reduced from 1019 prior to randomization to 110 during the final 6 months of the OLE. Overall, 33 patients (13.4%) discontinued ravulizumab treatment during the entire study period. When compared with 413 untreated patients, ravulizumab was associated with an adjusted survival probability (95% confidence interval [CI]) of 84.1% (77.4, 91.3) at 4 years (hazard ratio [95% CI]: 0.14 (0.06, 0.32), $p < 0.001$), and mortality was 3.5-fold lower than in untreated patients in the PNH Registry.

Conclusions: This study reports the longest duration of ravulizumab treatment exposure in C5 inhibitor-naïve patients with PNH (925.7 PYs) to date. For up to 6 years, ravulizumab provided effective long-term control of IVH. No new safety signals were identified and ravulizumab improved survival compared with untreated patients in the PNH Registry.

BSH24-PO107 | Exploring the relationship between fucosyltransferase VII (FUT7) levels and disease severity in sickle cell disease

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Background: Sickle cell disease (SCD) is a hereditary haemoglobinopathy associated with morphological distortion of red blood cells, haemolysis and vaso-occlusive events. Various clinical markers have been used to assess disease severity in affected individuals with limited diagnostic performances, hence the need to explore other alternatives. Fucosyltransferase VII (FUT7) has been implicated in the process of leukocyte adhesion and inflammation, suggesting a possible link to the severity of SCD, and may serve as a target for intervention. This study aims to investigate the potential role of FUT7 as a marker for assessing SCD severity.

Methodology: In this hospital-based study, researchers analysed SCD patients in a stable state at the Haematology Clinic of the University of Nigeria Teaching Hospital, Enugu. The participants were divided into mild, moderate and severe groups based on a severity scoring system. Blood samples were collected to measure the levels of FUT7 using an enzyme-linked immunosorbent assay (ELISA). The study used statistical tests like the Kruskal–Wallis Test to compare the median of the severity categories and the Spearman's rank correlation to examine the relationship between FUT7 levels and the severity of SCD. The analysis was done using SPSS version 25, and a p-value less than 0.05 was considered statistically significant.

Result: In a study of 37 participants with SCD, 32.4% ($n = 12$) had mild disease, 35.2% ($n = 13$) had moderate disease and 32.4% ($n = 12$) had severe disease. The median serum FUT7 levels (±Interquartile range) were 19.58 (±0.378) ng/mL, 20.23 (±0.378) ng/mL and 17.08 (±0.378) ng/mL respectively (p-value = 0.749). After adjusting for possible confounders, serum FUT7 has no significant correlation ($r = 0.007$; p-value = 0.968) with the severity of sickle cell disease in the study group.

Conclusion: This study found no significant relationship between FUT7 levels and the severity of SCD. Therefore, FUT7 may not be a reliable marker for disease severity in the study population. Further research with larger sample sizes and exploration of alternative biomarkers is necessary to assess SCD severity accurately.

BSH24-PO108 | Real-world patient awareness around emerging gene therapies: Implications for barriers to access

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Background/Aim: Recent approval of gene therapy for the treatment of sickle cell disease (SCD) has been groundbreaking for patients and their clinicians. Our study aim was to generate a better understanding of patient awareness and their interest in gene therapy, specifically CRISPR-Cas9 gene editing with exagamglogene autotemcel (exa-cel) as curative treatment for SCD.

Methods: An online survey with questions around patients' characteristics, awareness of therapies, information sources, concerns surrounding gene therapies and access barriers was conducted in November 2023. In total, 94 SCD patients completed the survey.

Results: The majority of patients were between 24 and 34 years old (27%). The most common genotype was HbSS (76%), followed by HbSC (20%).

Most patients reported 'limited' awareness of gene editing (37%), 16% reporting 'extensive' and 12% 'no' awareness. Few patients were aware of gene therapy clinical trials (26%), and 23% were aware of exa-cel ($n = 22$). Thirty-seven patients (40%) had considered or knew someone who had considered this treatment.

Most patients relied on healthcare professionals (66%) for information about medical advancements such as gene therapy. In those <35 years of age, 'Social Media' was the second most common source (60%), in comparison to 'Online Resources' (57%) for those ≥35 years.

Over half of patients felt that access to treatments like gene editing was 'very important' (54%). However, 56% of patients felt inadequately informed about risks/benefits. Thirty six per cent were 'not comfortable' undergoing gene therapy given its newness, with 36% being 'slightly comfortable'. While 23% of patients reported no reservations, others highlighted safety as the most common concern (26%), including side effects, complications and adverse events.

First-hand experiences shared by past patients were flagged as beneficial evidence to support decision-making (22%), in addition to 'general statistics' (16%) and 'scientific evidence from studies/research' (13%) demonstrating long-term safety, efficacy and outcomes. The most common impact patients hoped to see was the reduction of crises/pain (24%), followed by a complete cure for SCD (18%), better quality of life (14%) and a reduction in complications/mortality (12%).

The cost of treatment and the securing of funding to support its availability was flagged by 53% as a critical barrier to accessing gene therapies.

Conclusions: Our survey results explore the current understanding of SCD patients regarding gene editing as a novel therapy. Treatment safety formed a recurring theme. Many patients felt inadequately informed about the risks/benefits. This highlights the need for sufficient accessible information to support shared decision-making for gene therapy.

BSH24-PO109 | Serum soluble VCAM-1 is not associated with severity of SCD in adult Ghanaian patients

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Background: Sickle cell disease (SCD) is a monogenic disorder under polygenic and environmental influence. It is a multisystem condition that is phenotypically variable, making it challenging to define what 'severe disease' means. There is a predictive model of disease severity for SCD that considers demographic information, laboratory tests and clinical events and is accessible online as a 'Sickle Cell Disease Severity Calculator'.

Soluble vascular cell adhesion molecule-1 (sVCAM-1), a 90-kDa glycoprotein that is inducible and predominantly expressed at low levels on the luminal surface of endothelial cells, has been demonstrated as a marker related to disease severity in SCD, as evidenced by its association with early mortality and organ dysfunction. Thus, the potential utility of plasma levels of sVCAM-1 to identify high-risk patients merits further investigation.

Aim: To determine the association between sVCAM-1 level and disease severity in adult SCD patients.

Methods: This cross-sectional study enrolled 75 SCD patients (≥18 years) in their steady state from the Ghana Institute of Clinical Genetics and 75 voluntary donors from the Ghana Southern Area Blood Centre donor clinics as controls. Demographic and medical information were obtained using questionnaires, followed by clinical measurements of blood pressure, weight and height. Blood samples were taken for the analysis of full blood count, reticulocyte count, lactate dehydrogenase, liver function, haemoglobin phenotype and sVCAM-1.

Data were analysed using SPSS version 23. Continuous variables were summarized as means and standard deviations, and associations were determined through correlations. Categorical variables were summarized as frequencies, proportions, percentages and associations determined through the Chi-square test and Fischer's exact test. Severity was computed using the online severity calculator.

Results: Based on the scores, 20.0% (15/75) of the SCD participants had severe disease, 60.0% (9/15) aged >40 years. None of the participants with HbSC had severe disease. Neither male nor female gender was associated with a mild or severe phenotype ($p = 0.221$). There was a statistically significant difference between the mean concentrations of sVCAM-1 of the SCD participants and controls ($p < 0.001$), with SCD participants having a higher mean concentration (878.8 ± 220.3 pg/mL), compared to controls (507.8 ± 221.2 pg/mL). There was no association found between the severity of SCD and the levels of sVCAM-1.

Conclusion: This study reported severe disease in a fifth of the SCD participants, with most being ≥40 years and all having HbSS disease. However, there was no association between the levels of sVCAM-1 and the severity of SCD.

BSH24-PO110 | Does prehydroxycarbamide neutrophil count influence treatment response for paediatric sickle cell patients?

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Background: Neutrophils play an important role in the pathophysiology of sickle cell disease (SCD), and mild neutropenia is considered a therapeutic outcome of hydroxycarbamide, with a recommended neutrophil target range of $2–3 \times 10^9$/L on treatment. This study explores the impact of baseline prehydroxycarbamide neutrophil counts on clinical and haematological outcomes after achieving the maximum tolerated dose (MTD).
Methodology: In this retrospective observational study, data were gathered from electronic patient records and our hydroxycarbamide database, including all paediatric SCD patients on hydroxycarbamide for at least 6 months as of December 2023. The 3×10^9/L threshold was used to define our 'lower' ($<3 \times 10^9$/L) and 'higher' ($>3 \times 10^9$/L) baseline neutrophil groups for comparative analysis.
Results: The study included 61 patients (33 female), with a mean age at hydroxycarbamide initiation of 6.9 ± 4.2 years and a mean treatment duration of 3.1 ± 1.8 years. MTD escalation was achieved in 79% of patients, with a mean MTD dose of 28 ± 3.9 mg/kg. Mean baseline neutrophil count was $5.7 \pm 3 \times 10^9$/L (IQR $3.3–7.4 \times 10^9$/L), and mean baseline HbF was 9.5 ± 5.5% (IQR 5.9–12.7%). Patients initiating hydroxycarbamide due to sickle-related complications exhibited a higher baseline neutrophil count than those with an asymptomatic clinical background (6.7×10^9/L vs. 5.1×10^9/L, $p = 0.03$). Patients in the lower baseline neutrophil count group, experienced more treatment interruptions due to myelosuppression, lower MTD dose (28.7 mg/kg vs. 25.9 mg/kg, $p = 0.04$), lower neutrophil count (2.9×10^9/L vs. 4.4×10^9/L, $p = 0.025$) at MTD, higher HbF% (27% vs. 20%, $p = 0.04$) at MTD and a greater reduction in hospitalizations for vaso-occlusive crises compared to those in the higher baseline neutrophil count group. Although not statistically significant, the mean age of hydroxycarbamide initiation was lower in the lower neutrophil group (5.1 years) than the higher neutrophil group (7.1 years).
In conclusion, although patients with lower neutrophil counts prior to starting hydroxycarbamide may exhibit a more favourable laboratory response, they are more prone to increased treatment interruptions, achieve lower MTD levels, and experience smaller reductions in hospitalizations. Larger prospective studies are essential to further investigate and validate these observations and their significance in clinical practice.

BSH24-PO111 | IVC filters—5-year service evaluation

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Introduction: The BSH guideline covering inferior vena cava (IVC) filters is 18 years old. It recommends IVC filter insertion to prevent pulmonary embolism (PE) in patients with deep vein thrombosis (DVT) and a contraindication to anti-coagulation.
A more recent guideline has been published by the Society of Interventional Radiology (SIR), which increases the number of recommended 'indications', despite no evidence to support them.
In previous audits, compliance with BSH guidance at Norfolk and Norwich University Hospital (NNUH) has been high, following the introduction of a service designed to track all cases.
Here we present a review of compliance with BSH guidance in the last 5 years and compare this with compliance with newer SIR guidance.
Outcome: Between January 2017 and December 2022, 102 retrievable IVC filters were inserted. At the time of insertion, 18 filters (18%) were intended to be permanent, 82 filters (80%) were intended to be temporary and in two cases the intention was not stated.
Fifty-four patients were female (53%). Median age was 74 years (range 24–94). Median dwelling time of IVC filters was 90 days (range 3–730 days).
Indications for IVC filters that complied with both BSH and SIR guidelines were: DVT with contraindication to anti-coagulation (21 cases, 21%) and preoperative insertion in patients with recent thrombosis (16 cases, 16%).
Indications only compliant with SIR guidance were: acute PE with contraindication to anti-coagulation (52 cases, 51%), prethrombectomy for DVT (1 case, 1%) and prethrombolysis for PE (1 case, 1%).
One insertion occurred for DVT prophylaxis (1%) that was not compliant with either guideline.
DVT recurred in nine patients (9%), one patient (1%) experienced a PE and filter thrombus was reported in five cases (5%).
Follow-up rate was 95%. Removal was attempted in 46 patients, including four filters initially inserted with permanent intention. Twenty patients died before temporary filter removal (predominantly of cancer), and five patients with temporary filters were lost to follow-up. Eleven temporary filters were made permanent. Five patients are awaiting removal.
Removal was successful in 39/46 cases (success rate 85%).
Conclusion: The NNUH filter service has high follow-up rates and compliance with SIR guidance. BSH guidelines are in need of updating as a decrease in compliance with the BSH indications was observed (45%, previously 97%), which is attributable to an impression they have been superseded

by SIR guidance, which is more permissive, despite the level of evidence for additional indications in SIR guidelines being poor.

BSH24-PO112 | Efanesoctocog alfa prophylaxis outcomes in European patients from the XTEND-1 trial

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Introduction: Once weekly, fixed-dose efanesoctocog alfa prophylaxis allowed patients in the XTEND-1 trial to achieve mean factor VIII (FVIII) activity levels in the non-haemophilic range (>40%) for most of the week as well as superior bleed protection when compared with their prestudy FVIII prophylaxis. We present here a subanalysis of prophylaxis outcomes for European patients from XTEND-1.

Methods: XTEND-1 (NCT04161495) was an open-label, multinational, phase 3 trial evaluating the safety, efficacy and pharmacokinetics of efanesoctocog alfa (50 iu/kg) in previously treated patients ≥12 years of age with severe (<1%) haemophilia A. Data are presented on European patients enrolled in Arm A from Belgium, Bulgaria, France, Germany, Greece, Hungary, Italy, Netherlands, Spain and the UK. In Arm A, patients received prophylaxis with efanesoctocog alfa once weekly for 52 weeks. A subset of patients was included in an observational prestudy. The primary end-point in Arm A was annualised bleed rate (ABR). Secondary end-points included bleed treatment, quality of life (Haem-A-QoL physical health domain score, PROMIS Pain Intensity 3a T-score), joint health (Haemophilia Joint Health Score – Total score), consumption, safety and an intraparticipant comparison of prestudy versus on-study ABRs.

Results: In total, 67 European patients (mean age 34 years) received prophylaxis in Arm A. Model-based mean ABR (95% CI) was 0.56 (0.35; 0.89). Median ABR (IQR) was 0.0 (0.0; 1.0). Forty-seven patients (70%) had zero bleeds. Most bleeding episodes (32/34 [94%]) were resolved with one injection of efanesoctocog alfa. Improvements in physical health (mean change [SD]: −3.04 [14.94], $n = 51$), pain (−1.99 [8.14], $n = 60$) and joint health (−1.1 [5.8], $n = 53$) were observed between baseline and Week 52. For 42 patients with ≥6 months follow-up in both the prestudy and XTEND-1, the switch from prestudy FVIII prophylaxis to efanesoctocog alfa prophylaxis decreased the model-based mean ABR from 3.11 to 0.52 (rate ratio [95% CI]: 0.17 [0.10; 0.30], $p < 0.0001$). Mean (SD) weekly on-study consumption was 50.7 (2.5) iu/kg ($n = 42$). Efanesoctocog alfa was well tolerated, and inhibitor development was not detected.

Conclusion: In European patients, efanesoctocog alfa improved bleed protection versus prestudy prophylaxis. Results were consistent with the XTEND-1 primary analysis.

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BSH24-PO113 | Audit and quality improvement project looking at venous thromboembolism risk assessment and thromboprophylaxis prescribing

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Since 2010 all patients admitted to hospital in England need to have a venous thrombosis (VTE) risk assessment (RA) and then to be prescribed chemical, mechanical or a combination of both as prophylaxis (TP) to reduce VTE risk.

Guideline from National Institute for health and Care Excellence NG 89 provides timescales for completing RA and TP. For RA this should be as soon as possible or by the time of the first consultant review using an appropriate tool. For TP prescribing also as soon as possible and within 14 h of admission. The clock starts on hospital admission and not any time spent in the emergency department. Historically this was not an issue as 95% of patients were admitted or discharged within 4 h. Recently, patients spend longer awaiting admission with 12 h waits increasing. We looked at RA in the medical admissions unit (MAU) and time for first administration of TP to see if NICE guidance was followed.

We audited 54 patients in August 2023. Of these 53 had a RA but only 31 (57%) had this fully completed as there was an issue that partly completed forms were accepted by the system. Average time to completion was 515 min. TP was not indicated in four persons. Forty six per cent (23/50) received TP within 14 h (average 825 min range 0–4320 min).

After speaking with the MAU team, the reaudit looked at 26 patients with 21 RA but none fully completed average time 282 min. Twenty patients prescribed TP 12 within 14 h average 7394 min range 0–103 680.

Following an IT change which meant RA had to be fully completed we reaudited 50 patients between November and December 2023. Of these 38/50 were completed in full, average time 778 min. No TP was indicated in 11 persons. Of the

39 TP-indicated persons 28 received TP within 14 h (average 400 min range 0–2895).
Overall, 26 patients started TP in ED prior to admission.
This quality improvement study showed to change practice verbal approach had a poor result and an electronic approach needed to improve RA. Overall of patients needing TP 63/109 (58%) received this within 14 h. We plan to follow-up at 3 months to identify new VTE cases. This small quality improvement study shows importance of robust systems to collect VTE RA data but also TP can be prescribed in the absence of a completed RA.

BSH24-PO114 | Overview of the effect of anti-coagulants on heavy menstrual bleeding in women with thrombosis

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Introduction: Heavy menstrual bleeding (HMB) in menstruating women on anti-coagulants is a frequently encountered but often overlooked problem in clinical practice. It is essential to educate all menstruating women about the potential impact of anti-coagulants on their menstrual bleeding when they commence treatment. The ramifications of excessive menstrual bleeding should be systematically assessed and managed. In urgent situations, the decision to discontinue anti-coagulation therapy is determined by the balance between patient's risk of developing thrombosis and the severity of the bleeding.
Method: The local database at a teaching hospital was used to identify women in the reproductive age group, with history of thrombosis and anti-coagulated, experiencing HMB. Detailed data were collected on the indication, type and dose of anti-coagulant.
The HMB analysis including frequency, haemoglobin, ferritin levels, passage of clots, hospital admission, tranexamic acid use, blood transfusion, Iron infusion or oral supplements, Gynaecology referral, Pelvis ultrasound, Surgical or hormonal treatment and Quality of life measures such as absence from school/work or fatigue were reviewed.
Results: A total of 266 women in the reproductive age group between 12 and 55 years with history of thrombosis and on anti-coagulation were included in this analysis. Out of 266 patients, 65 (24.4%) experienced HMB.
Out of 65 (13.8%) patients, 9/65 were on rivaroxaban 20 mg, 4/65 (6%) on rivaroxaban 10 mg, 28/65 (43%) on apixaban 5 mg, 13/65 (20%) on apixaban 2.5 mg, 1/65 (1.5%) on edoxaban 60 mg, 7/65 (11%) on vitamin K antagonists and 3/65 (4.6%) on therapeutic Low molecular weight heparin (LMWH).
Out of the 65 patients with HMB, 13/65 (20%) received tranexamic acid, 12/65 (18%) required hospital admission, 11/65 (16.9%) needed blood transfusion, 15/65 (26%) required iron infusion and 37/65 (53.8%) received oral iron. Additionally, 40/65 (61.6%) received gynaecological input, 47/65 (72.3%) underwent pelvic ultrasound, 38/65 (68.5%) received hormonal treatment and 17/65 (26.2%) underwent surgical intervention. It is worth noting that there was documentation of quality of life (QOL) for 6/65 (9.2%) patients which is suboptimal.
Conclusion: The prevalence of high morbidity among women on anti-coagulation with HMB in the UK is largely attributed to the lack of timely multispecialty reviews. It is suggested that the establishment of a joint gynaecology–haematology clinic will further improve the current care of this population, as evidenced by the data presented. These in turn improve the patient experience by minimising multiple clinic visits and waiting time.

BSH24-PO115 | UK insights on managing heavy menstrual bleeding on anti-coagulation: It is time for clinical trials

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Introduction: Heavy menstrual bleeding (HMB) is a prevalent and challenging complication in patients on anti-coagulation, negatively impacting their health and quality of life.
Methods and Aims: We conducted a survey through the HaemSTAR network to understand current practice in managing HMB in patients on anti-coagulation for acute venous thromboembolism (VTE). The survey was distributed to UK consultants running haemostasis and thrombosis (H&T) clinics and/or providing haemostasis advice.
Results: Respondents included 98 haematology consultants, of which10 specialised in paediatric haematology, and three consultant clinical pharmacists. Among the 102 respondents, 74.5% run H&T clinics, while 25.5% only provide liaison advice. Fifty-six per cent of participants reported managing at least 10 cases of HMB on anti-coagulation annually. Apixaban was the favoured choice for 68.6% of the respondents, followed by LMWH and dabigatran, 2.7% stated that HMB will not influence their anti-coagulation choice. In terms of pausing anti-coagulation in HMB, 95% reported they rarely or never pause anti-coagulation for patients with recent VTE. Practice varied widely in the timing of tranexamic acid (TXA) for HMB post-VTE with 35% administering it at any time, 20.6% waiting 4 weeks post-VTE and 11.8% waiting 3 months, while 7.8% do not use TXA at all. Regarding the choice of oral contraceptive pills, 47.1% advise to stop oestrogen-containing pills, and 64.7% would

not recommend it for controlling HMB despite ongoing anti-coagulation.

In addition to exploring clinical practice variations, the survey aimed to assess clinicians' willingness to participate in the RCT (Randomised controlled trial) proposed by HaemSTAR/Haemtrial network, evaluating TXA use in HMB in patients on anti-coagulation for acute VTE. The majority of respondents agreed that the existing evidence does not sufficiently demonstrate an increased risk of VTE with TXA use in patients with recent VTE, on anti-coagulation. Additionally, none reported observing thromboembolic events due to TXA use in such cases. Despite this consensus: only 34.3% of respondents were strongly willing to enrol patients, 50% would consider and 4.9% were unwilling to participate. 30.4% reported having some concerns about the RCT in the context of acute VTE and 5.9% believed the risks of TXA in this setting outweighed the benefits. Interestingly, two respondents opposed participation not due to safety concerns, but for ethical considerations particularly due to the limited treatment options for patients in the placebo arm.

Conclusion: The Variation in HMB management in anti-coagulated patients and the ongoing uncertainty around TXA use indicate the need for a RCT to establish evidence-based standardisation.

BSH24-PO116 | Pregnancy outcomes in patients with anti-thrombin and protein C deficiencies

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Background: Inherited thrombophilias induce a hypercoagulable state, which predisposes to venous thromboembolism (VTE) and has been associated with poor pregnancy outcomes. Thus far, studies have pooled data from inherited thrombophilias, with a paucity of data for rarer deficiencies of endogenous anti-coagulants, which has impeded our ability to delineate the impact of specific thrombophilias on patient outcomes. Protein C (PC) and anti-thrombin-III (AT) are two such endogenous anti-coagulants, and the impact of their respective inherited deficiencies on pregnant mothers and their fetuses remains unclear.

Aims: This study sought to determine maternal and neonatal outcomes in patients with inherited AT and PC deficiencies.

Methods: Sixty nine patients with AT/PC deficiency were identified via the UK Obstetric Surveillance System (UKOSS) between 1st July 2019 and 30th June 2022. Data were gathered using a standardised collection form.

Results: The average age of participants was 33 (20–49). Thirty one (45%) had AT deficiency, 25 (36%) had PC deficiency and 13 were unspecified between AT/PC deficiency. Previous obstetric events included 32 (46%) patients with previous miscarriages, with 7/32 having ≥3 miscarriages (10% of total participants). Of those with previous miscarriage, 15/32 (47%) were diagnosed with PC deficiency, 9/32 (28%) with AT deficiency and 8/32 (25%) with AT/PC deficiency that was unspecified. Average newborn weight was 3350 g (1175–4170 g) and was comparable between deficiencies.

Management of the index pregnancies included low molecular weight heparin (LMWH) in 58 patients, aspirin and LMWH in six, aspirin only in three and two received no thromboprophylaxis. Twenty-six (84%) AT-deficient patients had anti-Xa monitoring, requiring dose escalation in all. Ten (32%) AT-deficient patients received AT concentrate at delivery when levels fell <20 iu/mL.

Overall, 64 live births were recorded. Of these, six were preterm (all pre-36 weeks, two ≤32 weeks) with neonates <2500 g. There were two miscarriages and two intrauterine deaths (IUD) (both PC deficiency), one with multiple thrombi on placental histology. Five patients suffered VTE in pregnancy (four AT deficiency and one PC deficiency). Average est. blood loss at delivery was 615 mL (100–3000). Twelve patients had postpartum haemorrhage (PPH) >1000 mL (two retained placenta, four uterine atony, two perineal trauma, one placenta praevia and three unknown). Three patients developed pre-eclampsia, one with HELLP syndrome. One patient with PC deficiency had placental abruption. Fifty-three (77%) patients continued anti-coagulation postpartum.

Conclusion: Although UKOSS endeavours to collect prospective data on all patients in the study demographic, it is still vulnerable to positive reporting bias. Nevertheless, this study reveals a strikingly high prevalence of early and recurrent miscarriage, late pregnancy complications, thrombosis and PPH in women with inherited AT and PC deficiencies.

BSH24-PO117 | Renal vein thromboses: A 10-year review of a tertiary paediatric centre

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Background: Renal vein thrombosis (RVT) is a rare diagnosis predominantly affecting neonates. Although uncommon, there is a long-term risk of hypertension (HTN) and chronic kidney disease (CKD). RVT tends to be unilateral (70% of cases), but extension of thrombosis is common (52% of cases). There are many risk factors predisposing to RVT, including genetic thrombophilia mutations, whose contributions are uncertain.

Methodology: We carried out a retrospective review of RVT cases over the past 10 years in a tertiary paediatric centre involving paediatric haematology and nephrology.

Results: Eighteen patients were screened, with 14 patients eligible for inclusion. All patients identified were neonates, diagnosed with RVT at a median age of 3 days, except for one child diagnosed at 2 years of age. More than 30% presented with haematuria, renal mass, deranged renal function and sepsis. The presence of central venous catheter (71%) with prematurity and sepsis (28%–35%) were the risk factors noted. Our review found a higher proportion of cases having bilateral RVT (57%) compared to unilateral (43%), with associated other thromboses occurring in 71% of cases. Eighty-six per cent of cases received anti-coagulation initially with low molecular weight heparin (LMWH)/enoxaparin (50%), unfractionated heparin (42%) or alteplase (8%). Long-term anti-coagulation was predominantly LMWH (62.5%), with others receiving warfarin (25%), and one case receiving rivaroxaban. The duration of anti-coagulation varied between 1 week and 6 months. Most children (79%) were investigated with a thrombophilia screen, and 45% of those investigated had a heterozygous gene mutation identified (two with prothrombin mutation, one with factor V Leiden mutation and one with both).

Mortality was high (21%), with long-term outcomes of HTN (50% of cases) and CKD (43% of cases) being common at 3- and 6-month follow-up. None of the patients alive are known to have recurrent thrombosis.

Conclusion: Our review, although small, highlighted the variability in RVT presentation and management. Most cases received anti-coagulation, but we recognise the variation in practice and length of therapy. Current recommendation is in line with our findings that thrombophilia testing should only be considered in an unprovoked RVT. Thrombophilia testing does not give extra benefit in management of RVT, though it may give an estimation of recurrence. Thus, larger international studies or an RVT registry on long-term outcomes and management of RVT with inherited thrombophilia are needed.

BSH24-PO118 | APTT sensitivity to mild bleeding defects data from the UK NEQAS BC programme 2023

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For the investigation of haemostatic disorders, some centres increasingly rely on the APTT test to detect mild, moderate or severe bleeding phenotypes, despite evidence that the ISTH BAT score is more appropriate. Data collected from a number of UK NEQAS BC exercises in 2023 highlight that the interpretation by APTT alone was unreliable when Factor IX levels of 22 iu/dL and 14 iu/dL were distributed to participants in the UK NEQAS BC APTT programme.

Sample 23:13 (22 iu/dL).

Reagent details and median APTTRatio—Interpretation % Normal/Borderline/Abnormal.

Actin FS Median APTTR 1.19—48.3/22.5/29.2.

Synthasil Median APTTR 1.12—88.5/8.3/3.3.

Cephascreen Median APTTR 1.14–81.6/7.9/10.5.

All APTT's Median 1.14—69.3/14.1/16.7.

Sample 23:40 (14 iu/d L).

Actin FS Median APTTR 1.20—32.4/28.4/39.2.

Synthasil Median APTTR 1.09—96.2/1.9/1.9.

Triniclot Median APTTR 1.14—79.5/11.4/9.1.

All APTT's Median 1.14—68.3/13/18.7.

The WFH guideline* recommends that an APTT within the reference range cannot be used to rule out mild haemophilia A and B. The reagents selected for the tables 1 and 2 are those APTT reagents used most widely by Sysmex/Siemens, IL Werfen and Stago users in two NEQAS BC surveys for 2023. It is evident that an APTT is unsuitable to screen for mild bleeding disorders and to manage patients with bleeding disorders. One-stage and chromogenic factor assays should be used instead. These exercises highlighted that participants returned a normal interpretation of 69.3% for Survey 23:13 (F!X 22 iu/dL) and 68.3% for survey 23:40 (FIX 14 iu/dL) based on APTT.

The data in both the tables for all APTT reagents is a salient reminder for clinical and laboratory staff that screening for mild haemophilia B with an APTT test as part of a coagulation screen is relatively insensitive to FIX levels seen in mild haemophilia B.

*Kitchen, S et al. 'Laboratory diagnosis and monitoring.' WFH Guidelines for the Management of Hemophilia, 3rd Edition. Haemophilia 26.Suppl 6 (2020): 29–54.

BSH24-PO119 | INR measurement data from the UK National External Quality Assessment for Blood Coagulation programme 2023

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Introduction: Measurement of INR in patients to monitor vitamin K antagonists is a routine test carried out both by laboratory and point of care testing platforms. The UK NEQAS BC data have highlighted that there are differences between the INR measurement across the PT reagents from Sysmex/Siemens, Werfen and the Stago group. The samples distributed in both of these exercises had INRs calculated by participants and submitted to the UK NEQAS BC portal. Samples were prepared using plasma form patients on VKA therapy.

Sample 23/38:

Reagent details median INR value/ % Underdosed (U)/ Adequately dosed (A)/Overdosed (O).

Recombiplastin 2G median INR 2.9 U/A/O % 0.7/81.6/17.7.

Innovin median INR 2.4 U/A/O % 4.6/92.7/2.7.

Thromborel S median INR 2.69 U/A/O % 2.4/90.2/7.3.

Neoplastine R median INR 2.83 U/A/O % 0.0/89.2/10.8.
Neoptimal median INR 2.87 U/A/O % 0.0/76.6/23.4.
Sample 23/19:
Recombiplastin 2G median INR 3.33 U/A/O % 0.7/19.9/79.4.
Innovin median INR 2.87 U/A/O % 0.0/85.0/15.0.
Thromborel S median INR 2.81 U/A/O % 0.0/80.0/20.0.
Neoplastine R median INR 3.40 U/A/O % 0.0/24.5/75.5.
Neoptimal median INR 3.49 U/A/O % 2.1/19.1/78.7.
The difference in the INRs calculated by the alternative PT reagents from Werfen, Sysmex, Siemens and Stago is not unique to the samples distributed by UK NEQAS BC. The local commutability study using individual patient samples found that UK NEQAS BC-lyophilized samples and samples from warfarin patients had similar INR discrepancies to those seen in these two distributions. The apparent INR difference between the reagents from the Sysmex/Siemens group and the Werfen/Stago group is not at a level to predict any adverse effect on the clinical management of patients on warfarin.
Although at a clinical cut-off, interpretations can vary between reagent groups, it is difficult to predict if this would alter the warfarin dosage prescribed.

BSH24-PO120 | UFH measurement with Anti-Xa assays from the UK National External Quality assessment Blood Coagulation 2023

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Monitoring or measuring unfractionated heparin (UFH) in patients can be undertaken by APTT ratios (APTTR), anti-Xa assays or point of care devices. NEQAS BC data have highlighted that there are differences between the UFH Xa measurement across the Hyphen, Werfen and Stago groups. The samples distributed in both of these exercises were constructed by addition of UFH to normal plasma. We received APTTR and UFH Xa results from participants. The Xa assays are calibrated with unicalibrators or multicalibrators. Both the Hyphen Xa and Werfen Xa kits have dextran sulphate, which is absent from the Stago Xa kit. Local study on individual non-lyophilised patient samples showed a similar pattern of results with the three kits, thereby confirming that NEQAS BC samples were commutable to patient samples (data not shown).
The therapeutic range for UFH for an anti-Xa assay is 0.3–0.7 iu/mL. Results in Table 1 suggest that the median values returned for kits with and without Dextran Sulphate are within the therapeutic range. There was one outlier below and four outliers above the therapeutic window of 0.3–0.7 iu/mL.
Sample 23/22 0.5 iu/mL UFH.
Reagent details median Xa value/Reagent details APTTR median Underdosed (U)/Adequately dosed (A)/Overdosed (O).
Hyphen LRT UFH Xa median 0.61/Actin FS APTTR median 2.4 U/A/O % 2.0/77.6/20.4.
Werfen UFH Xa median 0.51/Synthasil APTTR median 3.43 U/A/O % 2.0/18.3/79.7.
Stago UFH Xa median 0.38/Cephascreen APTTR median 2.2 U/A/O % 1.6/89.1/9.4.
Overall UFH Xa median 0.51 95.5% A/Overall APTTR median 3.02 U/A/O % 1.7/46.9/51.4.
Sample 22/49 0.2 iu/mL UFH.
Hyphen LRT UFH Xa median 0.21/Actin FS APTTR median 1.23 U/A/O % 88.2/7.4/4.4.
Werfen UFH Xa median 0.15/Synthasil APTTR median 1.39 U/A/O % 88.5/9.8/1.7.
Stago UFH Xa median 0.10/Cephascreen APTTR median 1.26 U/A/O % 88.9/2.8/8.3.
Overall UFH Xa median 0.15100% U/Overall APTTR median 1.3 U/A/O % 86.2/10.2/3.7.
The anti-Xa assay overall medians of 0.51 (23/22) and 0.15 (22/49) iu/mL, with and without dextran sulphate in the kit, have much better interpretation consensus of 95% and 100% respectively. The interpretation of APTT ratios for the sample with 0.5 iu/mL UFH varied more according to the reagent used.
UK participants registered for Heparin Dosage Assessment by APTT ratio/UFH Xa is a split of 81%/19%.
Despite some kit-related differences in the presence or absence of dextran sulphate in reagents, there was more consensus among anti-Xa users than APTTR users in the interpretation of heparin dosage.

BSH24-PO121 | Factor V and VII assay discrepancies in the UK NEQAS blood coagulation (BC) programme

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The International Society on Thrombosis and Haemostasis (ISTH) SSC plasma standard, calibrated for a range of haemostatic parameters, is primarily available to diagnostic manufacturers to aid in labelling commercial plasma. It is also available to external quality assessment (EQA) providers for proficiency testing purposes, either to troubleshoot apparent calibration issues for individual centres or as an EQA sample in routine surveys. Successive UK NEQAS BC exercises had demonstrated discrepant results between users of different reagent sources for FV and FVII assays. Independent confirmation of such discrepancies with the SSC plasma standard may help clarify the source of discrepancy.
SSC plasma standard lot #5 was distributed to 241 centres performing FV and FVII assays in September 2023. Results were analysed by reagent, deficient plasma and reference plasma sources. The pattern of results was also compared

to previously distributed UK NEQAS BC samples in earlier exercises.

With the SSC plasma standard, median FV assay results with reagent B (97 iu/dL, $n = 44$) were significantly higher than those for reagent A (81.5 iu/dL, $n = 64$) and reagent C (86.0 iu/dL, $n = 23$, $p < 0.001$). The same pattern was observed for reference plasmas and also for deficient plasmas from the same sources. These findings were almost identical to those for a previously distributed NEQAS sample with a median value of 76.0 iu/dL. Median FVII assay results with the SSC plasma standard again were significantly higher with reagent B (108 iu/dL, $n = 45$) than reagents A (97.8 iu/dL, $n = 92$) and C (99.6 iu/dL, $n = 23$, $p < 0.001$). However, previous NEQAS plasma samples with levels of 23.0 and 36.7 iu/dL showed results with reagents B and C to be in better agreement. The large majority of centres employ reagent, deficient plasma and reference plasma from the same commercial source, making it difficult to identify the source of these discrepancies. Compared to the values assigned to the SSC plasma standard through the calibration process, the overall median results in the NEQAS exercise for FV assays (assigned value 87 iu/dL, NEQAS all-method median 85.9 iu/dL) and FVII assays (assigned value 100 iu/dL, NEQAS all-method median 100 iu/dL) were in good agreement. Exercises such as this can help confirm between-method issues with these assays.

BSH24-PO122 | Exacerbation of chronic obstructive pulmonary disease-associated pro-thrombotic phenotype and linkage with cardiovascular disease

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Exacerbations of chronic obstructive pulmonary disease (COPD) are associated with an increased risk of cardiovascular and thrombotic events. The upregulation of procoagulant pathways during exacerbation, driven by factors such as hypoxia and inflammation, could be implicated in this increase.

We aimed to assess the impact of community-treated COPD exacerbation on the pro-thrombotic phenotype in a cohort of patients during community-treated exacerbation, compared to their baseline. A subgroup was also evaluated during exacerbation recovery (2 and 6 weeks postonset). Thrombin generation (TG) was measured using calibrated automated thrombography (CAT) at each time point. The association of change in TG at exacerbation with clinical parameters, including lung function, comorbidities, exacerbation symptoms and markers of inflammation, was assessed. Sensitivity analysis was used to correct for multiple exacerbations in the same patient.

Between 2021 and 2023, 64 exacerbations in 42 patients were included. The mean age was 74.1 ± 7.8 years, and 54.8% were male. Both overall TG as measured by endogenous thrombin potential (ETP) (1147.5 vs. 1226 nM/min, $p = 0.0004$) and peak-thrombin (236.5 vs. 242.4 nM, $p = 0.0003$) increased at exacerbation compared to baseline. This remained significant in sensitivity analysis and normalised by 2-week follow-up. There was no difference in the lag time or time to peak TG (TTP).

In the sensitivity analysis group ($n = 42$), those with cardiac comorbidities had a greater percentage increase in ETP from baseline to exacerbation (20.2% vs. 0.8%, $p = 0.03$) and percentage increase in peak-thrombin (46.3% vs. 6.4%, $p = 0.01$) compared to those without cardiac comorbidities. Similarly, patients with atherosclerotic disease showed greater percentage increases in ETP (19.4% vs. 0.8%, $p = 0.04$) and peak-thrombin (38.4% vs. 6.4%, $p = 0.04$) compared to patients without atherosclerotic disease. This occurred despite appropriate anti-coagulation or anti-platelet therapy. Greater lung function impairment (reduced diffusion capacity [KCO]) at baseline correlated to markers of increased TG (KCO vs peak-thrombin [$R = -0.3$, $p = 0.05$], TTP [$R = 0.4$, $p = 0.01$]).

ETP and peak-thrombin were associated with systemic inflammation at exacerbation. Changes in peak-thrombin were positively correlated with white cell count ($R = 0.3$, $p = 0.04$), neutrophil count ($R = 0.3$, $p = 0.03$) and fibrinogen ($R = 0.5$ $p = 0.003$), while ETP correlated with fibrinogen ($R = 0.4$, $p = 0.004$) and C-reactive protein ($R = 0.3$, $p = 0.04$). Change in COPD symptom severity scores positively correlated with change in peak-thrombin, though this was not significant (COPD Assessment Tool, $R = 0.25$, $p = 0.1$).

Overall, thrombin generation is upregulated during COPD exacerbations, more so in those with evidence of systemic inflammation, more severe COPD and underlying cardiovascular comorbidity. The impact of this on well-known thromboembolic complications of COPD exacerbation should be further evaluated.

BSH24-PO123 | Use of apixaban for stroke prevention in atrial fibrillation patients with low body weight

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Background: Limited data exists for use of direct oral anticoagulants (DOACS) for stroke prevention in patients with atrial fibrillation (AF) & low body weight. Patients with low body weight were under represented in the landmark DOAC AF clinical trials. Apixaban patients with body weight <50 kg

have approximately 27% higher apixaban exposure than those patients with body weight 65–85 kg. There is a lack of clinical guidelines for anti-coagulation in AF patients with low body weight & clinicians may be reluctant to prescribe DOACs due to concerns of drug accumulation and potentially increased risk of bleeding.

Aims: To determine the effect of low body weight on apixaban 2.5 mg bd on plasma levels, efficacy & safety of apixaban in non-valvular AF patients with low weight (<51 kg) &/or low BMI (<21 kg/m^2).

Methods: Retrospective case series of low body weight (<51 kg)/low BMI (<21 kg/m^2) AF patients prescribed apixaban 2.5 mg BD between 01/02/2017–01/01/23. Patients followed up for 12 months after measuring trough apixaban level to determine efficacy—stroke & systemic embolisation; safety—major bleeding as defined by ISTH.

Results: Nineteen patients (17 women and 2 men) with a median age 85 years, had 23 apixaban levels measured. Median weight 40.5 kg (range 34–51 kg) with a median BMI of 17.3 kg/m^2 (range 14.5–20.3 kg/m^2). Median creatine clearance was 33 mL/min (range 27.4–62 mL/min). Two patients (10%) had an apixaban trough level lower than the 5th centile of the predicted steady-state exposure reported in the apixaban summary of product characteristics (SMPC). Two patients (10%) had apixaban trough levels (191 and 168 ng/mL) above the 95th centile of predicted steady-state exposure reported in the apixaban SMPC. One of these patients subsequently had an ISTH defined Major Bleed within 12 months of the level. In total four patients (21%) had an ISTH defined Major Bleed within 12 months of having an apixaban level taken (all four patients were admitted following a fall and had Hb measured). No patients had an on treatment stroke or systemic embolisation.

Conclusion: Apixaban 2.5 mg bd in this case series of AF patients with low weight (<51 kg)/low BMI (<21 kg/m^2), was effective at preventing stroke and systemic embolisation but was associated with a major bleeding rate of 21% (4/19 patients).

BSH24-PO124 | Service evolution—How do we meet the needs of ITP patients?

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Service Evolution.

How do we meet the needs of ITP patients?

Objective: Recent evidence from the ITP world impact survey (Cooper et al. 2020) put the holistic needs of ITP patients in the spotlight. At a London teaching hospital, ITP services have been consultant led in an outpatient clinic environment. When the ITP services were evaluated, there was a clear gap in the care provision from a multidisciplinary team within the clinic environment and, vitally, access to care and advice outside clinic appointments. We aimed to meet this need by implementing a holistic multidisciplinary ITP service.

Method: A multidisciplinary working group aimed at understanding the needs of our patient population was created in early 2021. This comprised of clinical nurse specialists, pharmacists and haematologists and included a literature review, patient focus groups and consultation with other ITP specialist centres. The working group used these data to plan implementation of a multidisciplinary service to better meet patient needs.

Results: Two main stages of service development were implemented. Phase 1 included nurse and pharmacist training, establishing a patient phone line and email address and the development of patient information resources. The patient information leaflet was developed with patient input and evaluated by the patient focus group. Having access to a clinician outside clinic hours was deemed invaluable to patients. Phase 2 comprised of establishing a multidisciplinary service, and the development of this is ongoing. Clinic appointments with various MDT members have been set up, an audit evaluating steroid use allowed further understanding of the needs of patients with respect to monitoring and support. Clinicians also report increased satisfaction with the holistic care now being provided. Most importantly, initial feedback from patients is extremely positive.

Conclusions: ITP patients benefit from an accessible multidisciplinary service that is responsive to their needs. The creation of the ITP service has also led to developmental opportunities for the clinical nurse specialists and pharmacists involved. We continue to develop the service with patient involvement.

BSH24-PO125 | Five-year single-centre experience on the use of emicizumab prophylaxis in children with severe haemophilia A

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Background: Emicizumab, is a bispecific humanized monoclonal antibody that promotes effective haemostasis in persons with haemophilia A (PwHA) with and without inhibitors. Given its easy administration as a subcutaneous injection, it became the preferred option for prophylaxis in both children and adults PwHA. Primary analyses of clinical trials and real-world data have shown emicizumab safety and efficacy. However, long-term data are limited.

Aim & Methods: We conducted a retrospective study to assess real-world long-term outcomes of paediatric patients on emicizumab in our paediatric haemophilia care centre between the period of 13th February 2018 and 1st September 2023. Data including age at start of emicizumab, duration of emicizumab, inhibitor status, haemophilia joint health score

(HJHS), genetic mutations, surgical/dental interventions and adverse events were gathered.

Results: Among the 78 patients enrolled, five had active inhibitors and 73 had no inhibitors. Eleven (14.1%) were previously untreated patients (PUPs) and eight (10.3%) were minimally treated patients (MTPs). Twenty-three patients (29.5%) were <2 years of age at initiation of treatment with emicizumab and only three out of them had single factor-treated bleeding episode each. One out of five patients with active inhibitors while on emicizumab prophylaxis experienced a single rFVIIa-treated bleeding episode. Twenty-eight (28/78) patients underwent surgical/dental procedures without bleeding complications except for two patients (7.1%) who needed additional doses of rFVIII postoperative. There were 62 factor-treated bleeding episodes among 33 patients with only 11 imaging-confirmed joint/muscle bleeding episodes among eight patients. No major safety concerns were reported in the study and emicizumab was discontinued in five patients (two for anti-drug antibody development, two for joint bleeding and one for non-compliance). There was no significant relation between breakthrough joint/muscle bleeds and intron 22 or non-intron 22 genetic mutations. No deterioration in haemophilia joint health score (HJHS) was recorded among participants. In conclusion, emicizumab prophylaxis maintained low bleed rates in paediatric PwHAs with and without FVIII inhibitors and remained well tolerated, with no new safety concerns.

BSH24-PO126 | Rituximab therapy for immune-mediated TTP—How much, how often?

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Immune-mediated TTP (iTTP) is a disorder caused by a severe deficiency of the von Willebrand factor-cleaving protein ADAMTS13. Acute episodes are associated with ADAMTS13 activity levels of <10 iu/dL; however, iTTP is also acknowledged as a chronic condition with a relapse incidence of 30%–50%. Patients therefore require lifelong follow-up and monitoring of ADAMTS13 activity to prevent clinical relapse. The 2023 British Society of Haematology guidelines advise that elective rituximab/anti-CD20 treatment should be initiated where the ADAMTS13 activity is <20 iu/dL, or at higher levels in the presence of clinical symptoms. Although elective rituximab therapy (ERT) has become the standard of care in iTTP patients, the frequency of treatment required and duration of remission are variable.

This was a retrospective study of patients receiving ERT for iTTP in a UK TTP Specialist centre serving a population of ~7.3 million. Data from iTTP patients ($n = 24$) receiving ERT over the period 01/01/2019–01/01/2024 was collected from pharmacy records and electronic case notes. Data included ADAMTS13 activity pre/post-ERT, treatment length and duration of remission. A course of rituximab was defined as the number of infusions required to achieve an ADAMTS13 >40%.

Over 5 years, 24 patients (66% female, median age 53 years [34–81]) received ERT. The median ADAMTS13 activity of these patients preinitiating ERT was 14% (0%–31%). 13/24 patients required more than one course of ERT during the 5 years, and the total number of courses received was 40. The median number of infusions administered in each course was 4 (3–8). 35/40 courses administered (87.5%) were at standard dose 375 mg/m^2 weekly, while the remaining 5/40 (12.5%) were at a 200 mg reduced flat dose weekly as part of a clinical trial. An ADAMTS13 >40% was achieved in response to 97.5% of ERTP courses in a median of 14 days. Furthermore, 75% of courses achieved a complete remission (ADAMTS13 activity >70%) in a median of 51 days. For patients requiring >1 course of rituximab over the 5-year period, the average duration of remission was 717 days. A partial remission, defined as ADAMTS13 of 40%–70%, resulted in an average treatment-free period of 477 days, while a complete remission (ADAMTS13 >70%) saw an average of 797 days.

Most patients requiring ERT currently receive four doses per course of treatment and achieve a remission ADAMTS 13 activity of >40%, with a durable remission of at least 12 months.

BSH24-PO127 | SHOT data relating to solid organ transplants reveals common themes and the need for guidelines

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Solid organ transplant (SOT) patients may require intensive transfusion support, with specific requirements relating to blood groups and compatibility testing for blood component provision. Recipient's ABO/D group may differ from donor's; incorrect selection and release of blood components can lead to incompatible transfusions. ABO-incompatible (ABOi) transfusions can result in passenger lymphocyte syndrome (PLS), where donor ABO antibodies mount an immune response against the recipient. Serological compatibility testing is required to identify cases where PLS may result in transfusion reactions. D-negative recipients may develop immune anti-D where donor is D-positive. Additional specific requirements may be needed based on underlying diagnosis, component type and previous treatment. Serious Hazards of Transfusion (SHOT), the UK's haemovigilance scheme, analyses reports relating to serious adverse reactions/events in SOT patients.

Review conducted on transfusion incidents relating to SOT accepted by SHOT from 2013 to 2022.

A total of 156 reports were analysed, including kidney ($n=92$), liver ($n=34$), lung ($n=7$), heart ($n=5$), pancreas ($n=2$), bowel ($n=1$), hand ($n=1$), pancreas and kidney ($n=4$), liver and kidney ($n=1$) and multiorgan ($n=2$). In seven cases, the organ transplanted was not reported. Five reports were related to paediatric liver SOT (age ranging from 1 to 16 years old). Adverse events were reported under incorrect blood component transfused (IBCT)-specific requirements not met (SRNM) ($n=109$;70%), IBCT-wrong component transfused (WCT) ($n=28$;18%) and Near Miss (NM) ($n=19$;12%). Common errors included inappropriate provision of non-irradiated blood components ($n=51$ IBCT-SRNM), failure to use serological compatibility testing ($n=15$ IBCT-SRNM) and wrong ABO/D group transfused ($n=26$ IBCT-WCT). One patient recovered and survived from a transfusion reaction following an ABOi transfusion. The error in 33 cases resulted from flags not added/updated or heeded in the Laboratory Information Management System (LIMS). Poor communication and knowledge gaps contributed to the error in 64 cases. Similar events were reported as NM, if these errors had not been identified at the right time, this would have resulted in six non-irradiated components transfused and four transfusions of wrong ABO group.

SHOT has published recommendations for safe transfusions for SOT patients based on reports analysed. SOT patients may be under shared care across multiple organisations and teams. Effective, timely communication, co-ordination and patient/family education help ensure safety. The clinical and laboratory teams should ensure that knowledge gaps are addressed, and educational tools are provided. Laboratory processes should ensure that flags are added to the LIMS in a timely manner. LIMS should support relevant flags that cannot be easily overridden. National transfusion guidelines specific to SOT are needed to reduce transfusion risks in this group of patients.

BSH24-PO129 | Transplant in the elderly: FluBu3 + ATLG is safe and effective in myeloid disease

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The optimal conditioning for older patients with myeloid disease is unclear and several options with varying alkylator and T-cell depletion strategies are used internationally. Balancing toxicity and efficacy is important in this vulnerable patient group, where harnessing the GVL effect is critical. We retrospectively reviewed 175 patients who underwent reduced intensity conditioned allogeneic SCT, with fludarabine (180 mg/m^2), busulfan (8 mg/kg) and ATLG (30–60 mg/kg).

The cumulative incidence (CI) of NRM at 1 and 2 years was 10.4% and 11%, respectively, with high-risk MF (HR: 8.61, $p=0.005$), severe aGVHD (HR: 5.29, $p<0.001$) and invasive fungal disease (HR: 8.0, $p<0.001$) predicting a worse outcome. OS at 1 and 2 years was 80.34% and 72.35%, respectively, worse in CIBMTR-DRI high-risk disease (HR: 1.74, $p=0.03$) and ABO mismatch (HR: 2.34, $p=0.003$) and better after cGVHD (HR: 0.35, $p=0.02$). The CI of relapse was 19.5% and 27% at 1 and 2 years. RFS at 1 and 2 years was 69.95% and 61.73%. Relapse risk was significantly reduced in those with mixed chimerism who received a pre-emptive DLI (HR: 0.33, $p=0.01$), and those who relapsed experienced longer overall survival after salvage DLI (HR: 0.43, $p=0.03$). In those aged 65–74 ($n=27$) there were no NRM events and 1- and 2-year OS was 92.5% and 75.9% (vs. 78% and 71.4% in those <65). The CI of relapse was higher in older patients: 34.5% at 2 years (vs. 25.5% in those <65). RFS, however, was superior at 81.3% and 67.34% at 1 and 2 years (vs. 67.85% and 60.62% in those <65). Major GVHD was less common: grade III–IV acute GVHD occurred in 10% (vs. 15% aged <65) and chronic GVHD in 11.5% (vs. 17%). Immune reconstitution at 6 and 12 months was slightly lower, with a 1-year median CD4 count of 127×10^6/L in those >65 (vs. 167 in those <65), and this effect was most prominent in those >70 years. DLI was well tolerated in those >65 with no aGVHD > grade II, extensive cGVHD or NRM events.

FluBu3 with ATLG demonstrates a robust safety profile, with low NRM, severe aGVHD and extensive chronic GVHD risk. With a 2-year RFS of over 60%, it similarly offers effective disease treatment for older patients with myeloid disease, particularly when combined with judicious use of DLI. Candidate selection is important, and pretransplant frailty optimisation is crucial to success. The regimen is well suited to elderly patients over the age of 65, although improvements in relapse risk and immune reconstitution justify a trial of reduced ATLG dosing.

BSH24-PO130 | Predictive value of haematopoietic progenitor cell count to assess CD34+ cells in mobilised peripheral blood

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Introduction: Monitoring of stem cells in mobilised peripheral blood (PB) is crucial in determining the optimal time of apheresis and is typically done by assessment of CD34+ cells by flow cytometry (turnaround time of ~60 min). This results in lengthy wait times for patients prior to onset of apheresis, and has cost implications for clinical and

laboratory staff. To reduce wait times, we assessed the utility of the haematopoietic progenitor cell (HPC) parameter (turnaround time ~ 5 min) using the XN-stem cells mode on the XN-1000 Sysmex Haematology analyser.

Patients and Methods: A total of 208 mobilised PB samples were assessed from patients undergoing autologous stem cell transplants for plasma cell myeloma ($n = 114$), lymphoma ($n = 74$) and other diseases ($n = 20$). Only samples from Day 1 of apheresis were included for analysis. Correlation between the Sysmex HPC parameter and flow cytometric quantification of CD34+ stem cells in both PB (CD34 precounts) and the peripheral blood stem cell (PBSC) harvest (CD34 harvest counts) was performed. Flow cytometric assessment of CD34+ cell counts was still performed to monitor the apheresis collection efficiency.

Results: A moderate positive correlation was observed between both the HPC parameter and CD34 precounts ($r^2 = 0.56$), and CD34 harvest counts ($r^2 = 0.39$). However, lower HPC values were seen to be less predictive of CD34+ stem cell counts. We typically use a threshold of a CD34+ precount of ≥8 cells/μL in mobilised PB to initiate apheresis. Analysis of data revealed that an HPC cut-off of ≥100 cells/μL correlated with the PB CD34 precount cut-off with a 98.7% accuracy, and 92% of these samples resulted in a CD34 harvest yield of $\geq 0.8 \times 10^6$/kg. Interestingly the accuracy of this HPC threshold increased to 100% in patients with lymphoma. Implementation of this HPC cut-off of ≥100 cells/μL allowed us to introduce a 'straight to harvest' approach where patients with HPC ≥100 cells/μL (seen in ~38% of patients) could proceed straight to apheresis without awaiting assessment of CD34 precounts.

Conclusion: Here we demonstrate the successful implementation of a 'straight to harvest' approach using an HPC threshold of ≥100 cell/μL. This resulted in adequate stem cell yields and allowed more efficient apheresis procedures. Further work will continue to monitor the efficacy of the introduced HPC threshold in the clinical setting.

BSH24-PO131 | Implementing a myeloma service user advisory group into research: A patient and public involvement perspective

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Background: Patient and public involvement (PPI) in research is rarely examined from the patient perspective. Myeloma UK fully engages in PPI, as it empowers people affected by multiple myeloma (MM) to share their views and shape the research that impacts their lives. Our gold standard approach operates as a dual lens; one that allows researchers to view the data through their own lens but filtered through patient and caregiver perspectives. The current research outlines the methods used to deliver, collect and embed PPI into a project investigating diagnosis, treatment and well-being of individuals throughout their cancer journey.

Method: The Myeloma UK Patient and Carer Research Panel reviewed the study prior to ethical approval. A volunteer Service User Advisory Group (SUAG), consisting of MM patients and carers, was recruited via our social media and Volunteer Panels. SUAG meetings took place on Zoom at suitable times. A member of the research team regularly presented at SUAG meetings on the research aims, the methodology (i.e. semi-structured interviews that were analysed using Interpretative Phenomenological Analysis) and the analysis of the data. SUAG members were asked to provide feedback on the study, the emerging themes and whether these reflected their heterogeneous experiences as individuals. Members were asked to provide verbal feedback during meetings (these were recorded) and/or through written feedback via email.

Results: Ten MM patients and carers were recruited to the SUAG. Results consisted of thematic data organized around the objectives of the study. Focusing on treatment, the key themes included: pain management, managing fatigue, mood swings, well-being and experiences of treatment induced neuropathy, alongside other related themes. Generally, SUAG members agreed that the insights from the study were reflective of their own personal experiences. However, members also provided greater context around specific issues including the continued impact of COVID-19 on their lives. Patient feedback in SUAG meetings was key in enhancing specific areas of the research (e.g. the psychological support theme was recontextualized as a critical area of development that should be integrated into treatment pathways in MM). Patients also fed back on their increased sense of helpfulness due to their involvement in the SUAG meetings.

Conclusion: SUAG feedback enriched the analysis process and provided more context on issues that did not emerge during the interviews or initial analyses. This recontextualization of the data enhanced the researchers focus and allowed for deeper insight into the heterogeneity of patient and caregiver experiences.

BSH24-PO132 | Ibrutinib efficacy in ALPINE and ELEVATE-RR trials in relapsed/refractory chronic lymphocytic leukaemia: Matching-adjusted indirect comparison

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Background: Bruton tyrosine kinase inhibitors (BTKis) are widely used for treating chronic lymphocytic leukaemia (CLL). Ibrutinib was the first BTKi approved for CLL, followed by acalabrutinib and, recently, zanubrutinib, a next-generation BTKi. In the ALPINE trial (NCT03734016), zanubrutinib demonstrated superior progression-free survival (PFS) compared with ibrutinib in relapsed/refractory (R/R) CLL (hazard ratio [HR], 0.65), whereas in the ELEVATE-RR trial (NCT02477696) acalabrutinib showed non-inferior PFS versus ibrutinib in R/R CLL with del(17p) or del(11q) (HR, 1). Recent comparisons of ibrutinib efficacy across trials have omitted patient characteristics that are critical for appropriate cross-trial comparisons.

Objective: To assess ibrutinib efficacy across ALPINE and ELEVATE-RR using a comprehensive matching-adjusted indirect comparison (MAIC).

Methods: Individual patient data from the ALPINE ibrutinib arm (median follow-up, 29.6 months) were adjusted to match population-level data from the ELEVATE-RR ibrutinib arm (median follow-up, 40.9 months). To obtain comparable populations for MAIC, an ALPINE patient subgroup was included in the analysis. An unanchored MAIC was conducted to adjust for all relevant treatment effect modifiers (EMs), such as IGHV status, del(17p), del(11q), TP53 status, serum β2-microglobulin, number of prior therapies and Binet stage. Additional prognostic factors (PFs) were adjusted in sensitivity analyses. Adjusted HRs obtained by weighted Cox proportional hazards model were applied to assess PFS (analysed per independent review committee [IRC] and investigator [INV]) and overall survival (OS). As ALPINE, but not ELEVATE-RR, was conducted during the COVID-19 pandemic, ALPINE PFS and OS were adjusted by censoring patients who died due to COVID-19.

Results: The high-risk ALPINE population included 123 ibrutinib-treated patients, matched against 265 ibrutinib-treated patients in ELEVATE-RR. After adjustment, no statistically significant differences were observed between ALPINE and ELEVATE with regard to PFS-IRC (HR, 0.80; 95% CI, 0.49–1.28; $p = 0.3485$), PFS-INV (HR, 1.18; 95% CI, 0.75–1.86; $p = 0.4827$) and OS (HR, 0.91; 95% CI, 0.50–1.65; $p = 0.7539$). Adjustment for COVID-19 and scenarios matching for both EMs and PFs yielded similar results compared with the main analysis.

Conclusions: This MAIC, which used a comprehensive list of matching variables, demonstrated no difference in ibrutinib efficacy across ALPINE and ELEVATE-RR. Analysing common comparator arms (ibrutinib vs. ibrutinib) versus different investigational arms (zanubrutinib vs. acalabrutinib) eliminated some residual confounding inherent to MAICs. Despite the decrease in estimated sample size due to the adjustment, results were consistent across multiple sensitivity analyses. While MAIC provides a basis for evaluating cross-trial treatment efficacy, relative efficacy must ultimately be evaluated within randomized controlled trials.

BSH24-PO133 | Real-world data for the efficacy and safety of acalabrutinib across two centres in East England

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Acalabrutinib is a next-generation covalent Bruton tyrosine kinase inhibitor, approved for chronic lymphocytic leukaemia (CLL). Acalabrutinib has demonstrated good efficacy and tolerability in pivotal registration clinical trials; the ELEVATE-TN and ASCEND trials. However, there are limited studies exploring the outcomes of acalabrutinib using real-world data from large general hospitals serving an unselected rural patient population.

A retrospective study was undertaken between 2020 and 2023 across two university teaching hospitals in East England. Seventy-six CLL patients were treated with acalabrutinib; 27/76 (36%) were female, median age 77 years (range 49–96 years), with a median Cumulative Illness Rating Scale for Geriatrics score of 8 (range 4–20). 37/76 (49%) patients had Rai stage 3 or 4 disease, and in the high and intermediate genetic risk group, 5/76 (7%) patients had a TP53 mutation, 14/76 (18%) had ATM and 15/76 (20%) had trisomy 12. 67/76 (88%) patients were treatment naïve. 75/76 (98%) patients commenced on the recommended 100 mg twice daily dosing.

Median follow-up was 17.4 months (range 1.9–41.0 months). Only one patient (1%) stopped treatment before their last follow-up or death. 15/76 (20%) patients had their dose reduced, and 14/76 (18%) patients had treatment temporarily suspended due to adverse effects. The most common adverse effects were: infection, with 22/76 (29%) grade 1–2 and 5/76 (7%) grade 3–5; headache, 17/76 (22%) all grade 1–2; bruising, 17/76 (22%) all grade 1–2; and fatigue, 17/76 (22%) all grade 1–2. 11/48 (14%) patients experienced a grade 3 or higher adverse effect, with infection the most common.

Infections were mostly of the respiratory tract (25/76, 33%) and urinary tract (4/76, 5%). 12/76 (16%) patients suffered one or more COVID-19, with only one COVID-19-related death. Notably, 3/76 (4%) patients developed atrial fibrillation. At the most recent follow-up, 23/76 (30%) patients had a complete response and 39/76 (51%) had a partial response. Only 6/76 (8%) patients progressed on therapy, and one patient (1%) had Richter transformation. Median progression-free survival (PFS) was not reached during our follow-up period.

In conclusion, our real-world data in unselected patients from peripheral large hospitals demonstrates acalabrutinib to be an effective and well-tolerated drug. There were no new safety concerns reported, and the treatment was safely delivered in a notably more rural population. Furthermore, in our experience, it was safe to use during the COVID-19 pandemic, and only one COVID-19-related death was reported while on acalabrutinib.

BSH24-PO134 | Zanubrutinib versus FCR in fit treatment-naive patients with chronic lymphocytic leukaemia: A matching-adjusted indirect comparison

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Background: Fludarabine, cyclophosphamide and rituximab (FCR) is the standard first-line therapy for fit (physically active, no major health problems and normal renal function) treatment-naive patients with chronic lymphocytic leukaemia (CLL). However, the associated haematotoxicity and infections necessitate more efficacious, safer treatments. Zanubrutinib, a highly specific, potent, small-molecule Bruton tyrosine kinase inhibitor, is approved for treatment-naive patients with CLL. However, the comparative efficacy of zanubrutinib versus FCR in patient with CLL remains uninvestigated.

Objective: To determine the relative treatment effects of zanubrutinib versus FCR in fit treatment-naive patients with CLL.

Methods: The CLL10 trial (NCT00769522) investigated FCR and bendamustine + rituximab (BR), while SEQUOIA (NCT03336333) compared zanubrutinib to BR. An anchored matching-adjusted indirect comparison (MAIC) was conducted, comparing zanubrutinib to FCR, using the BR arms as a common comparator. Propensity score matching using patient-level data from SEQUOIA adjusted for the interpopulation differences, per National Institute for Health and Care Excellence (NICE) MAIC methods. Independent review committee-assessed progression-free survival (PFS) was compared using the matched patient populations. Matching variable selection was based on literature review and expert opinion. Given the BR arm-anchored indirect treatment comparison, solely prognostic patient characteristics did not need to be included. The core model included: immunoglobulin heavy-chain gene mutation, 11q deletion, β2-microglobulin, Binet stage and age. Geographic region, sex, creatinine clearance, Cumulative Illness Rating Scale (CIRS) score, Eastern Cooperative Oncology Group performance status (ECOG-PS) and previous infections underwent sensitivity analyses.

Results: In the core model, zanubrutinib achieved significantly better PFS than FCR (hazard ratio [HR], 0.41; 95% CI, 0.20–0.81; p-value = 0.01). Sensitivity analyses showed significantly improved PFS with zanubrutinib when adding geographic region (HR, 0.43; 95% CI, 0.21–0.90; p-value = 0.03), sex (HR, 0.44; 95% CI, 0.22–0.89; p-value = 0.02), ECOG-PS (HR, 0.30; 95% CI, 0.14–0.64; p-value<0.01) and previous infections (HR, 0.45; 95% CI, 0.22–0.93; p-value = 0.03) to the core model matching variables. A sensitivity analysis incorporating CIRS (HR, 0.45; 95% CI, 0.16–1.24; p-value = 0.12) showed only numerically favourable PFS with zanubrutinib, owing to the expanded model's low effective sample size (ESS). Enriching core model matching variables with creatinine clearance yielded similar results (HR, 0.52; 95% CI, 0.24–1.13; p-value = 0.10). The variable-dependent ESS was 64.05–174.1.

Conclusion: Our findings suggest that zanubrutinib offers clinically meaningful benefits in PFS over FCR in fit treatment-naive patients with CLL. MAICs rely on relevant published patient characteristics. Here, the ZAP-70 methylation and TP53 mutation, two treatment effect modifiers, were not reported in CLL10 and were not accounted for in the propensity model.

BSH24-PO135 | Consensus statements for the introduction of BCMA-bispecific antibodies within the NHS

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Background: Multiple myeloma is a relapsing, debilitating blood cancer tha0074 remains predominantly incurable despite advances in treatments.

Patients typically receive multiple lines of treatment to which they become refractory, thereby limiting treatment options.

BCMA-bispecific antibodies represent a new modality of treatment that has significant efficacy for relapsed refractory patients. However, these need careful consideration prior to implementation in the NHS to optimise patient flow, maintain safety and ensure equitable access.

Objective: To develop consensus statements for the effective implementation of bispecific antibodies for relapsed multiple myeloma patients within the NHS based on clinical experience.

Method: In March 2023, a literature review on the topic of novel treatments for multiple myeloma was performed using the PubMed database. Search terms included but were not limited to: "incidence & prevalence", "patient impact", "societal and health costs", "guideline recommendations" and "BCMA bispecific antibody therapies".

Following the review, a panel of five haematologists, one specialist nurse and two pharmacists met virtually June 2023. Employing a Delphi methodology, guided by an independent facilitator, the panellists identified and agreed five main topics of focus.

These topics were discussed, and 44 statements were agreed and developed into an online survey that was distributed to Consultant Haematologists, Nurse Specialists and Pharmacists working in Level 1, 2 and 3 Haematology Centres in the UK.

Respondents were offered a 4-point Likert scale to indicate their level agreement with each statement. Surveys were collated anonymously and independently analysed. Results were then shared with the expert panel to determine conclusions. Stopping criteria for consensus rounds were defined as a 1-month period to collect responses, a target of 60 responses within the time, and 90% of statements passing the threshold for consensus. The threshold for consensus agreement was set at 75% a priori.

Results: A total of 60 responses were received from all three centre levels. There was representation from all job roles from England, Wales and Scotland.

Consensus was achieved in 42 statements (95%) and was not achieved in two statements. Consensus was achieved in topics including:

- Patient considerations
- Initiation and managing step-up dosing
- Monitoring and ongoing care requirements
- Role of multidisciplinary team

Given the level of agreement and that the stopping criteria were met, it was decided not to undertake further Delphi rounds.

Conclusion: This consensus provides a framework to support the effective introduction of novel treatments for Multiple Myeloma in the NHS.

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BSH24-PO136 | Engaging with the patient voice to shape early clinical trial design

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Patient and public involvement (PPI) and engagement with diverse individuals (EDI) should play a pivotal role in shaping the landscape of clinical trials. However, while trials prioritise the development of curative interventions to increase survival, other aspects of the patient experience are inconsistently considered. Although patient-reported outcome measures are often included in clinical trials, few studies identify measures that are most relevant to patients in advance. This is problematic for long-term chronic conditions such as multiple myeloma (MM), as they may fail to fully capture the impact of novel treatments.

A horizon scanning exercise by the UK Myeloma Research Alliance- Myeloma UK- Concept and Access Research Programme (UKMRA-MUK-CARP) team identified several areas of research that are currently under addressed by clinical trials and highlighted as patient priorities. One key area identified was the management of bone disease in MM—a prevalent complication often causing a significant decrease in the quality of life (QoL) of patients. We sought to investigate patient and carer perceptions of the significance of factors related to bone disease with the intention of integrating these findings into the design, conduct and reporting of our upcoming studies.

In collaboration with Myeloma UK, we organised online workshops involving individuals with lived experiences of MM. These aimed to understand patient priorities in relation to MM and its therapy, such as the management of bone disease, with the intention of ensuring the appropriateness and acceptability of clinical trial end-points and interventions. Understanding the patients' perspective in relation to supportive research trials highlighted insights not typically prioritised by the clinical teams. For example, patients and carers expressed a desire for trials that reduce the overall burden of treatment to patients, go beyond conventional

end-points and focus on outcomes that directly impact daily lives, not just disease burden.

This patient-centred approach has played a vital role in shaping the design of upcoming trials and has led to ongoing adaptations and refinements in our research strategies. These outcomes underscore the importance of continuous collaboration with patients and the embedding of the gold standard of PPI in research. By actively integrating patient voices, we have not only enhanced the relevance of our clinical trials, but also fostered a sense of community engagement and acceptance for studies that depart from the conventional curative-focused approach in MM research, enabling trials to answer those questions deemed most important by the people most affected.

BSH24-PO137 | DREAMM-6 Arm A: Safety and efficacy of belantamab mafodotin, lenalidomide and dexamethasone in relapsed/refractory multiple myeloma

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Introduction: Belantamab mafodotin (belamaf), a first-in-class antibody–drug conjugate targeting B-cell maturation antigen, demonstrated increased clinical activity with pomalidomide in the ALGONQUIN study among triple-class exposed/refractory multiple myeloma (MM) patients, suggesting potential for belamaf-based combinations. Preclinical data support benefits with belamaf combined with immunomodulatory agents, like lenalidomide (Len). Phase I/II DREAMM-6 (NCT03544281) study's Arm A assesses the safety and clinical activity of belamaf with the standard of care (SOC) (Len plus dexamethasone [Dex]) in relapsed/refractory MM (RRMM) patients.

Methods: Eligible patients with ≥1 prior line of therapy (LOT), participated in Part 1 (dose escalation) up to two dose levels (belamaf 1.9 mg/kg Q4W and 2.5 mg/kg Q4W) and alternative schedules in combination with the fixed SOC dose. Part 2 (dose expansion): belamaf at 1.9 mg/kg Q8W, 1.9 mg/kg Q4W, 2.5 mg/kg Q4W or 2.5 mg/kg Q4W split dose. Oral Len 25 mg (10 mg if estimated glomerular filtration rate < 60 mL/min/1.73m^2) and Dex 40 mg (20 mg for patients >75 years old, BMI <18.5 or prior tolerability issues to Dex) were administered on specified days. Part 1 focused on adverse events (AEs) or dose-limiting toxicity, while Part 2 examined safety (AEs and serious AEs) and efficacy (overall response rate [ORR]). Secondary outcomes: pharmacokinetics (PK) and anti-drug antibodies; exploratory end-points: duration of response (DOR), progression-free survival (PFS) and overall survival (OS).

Results: In Parts 1 and 2, 45 patients (age, median [range], 68 [36–80] years) underwent a median (range) prior LOTs of 3 (1–10) at final analysis cut-off (28 February 2023). 26/45 (57.8%) patients were Len-exposed and median (range) follow-up was 23.7 (0.5–51.3) months. Incidence of AEs resulting in permanent discontinuation and dose adjustments was similar but limited by sample size. Common drug-related grade 3+ AEs were keratopathy, visual acuity decline and neutropenia. ORR range was 58%–75%. The greatest depth of response (≥very good partial response [VGPR] 56%, ≥complete response 44%) was in 2.5 mg/kg Q4W cohort. Interpretation of DOR, PFS and OS was limited due to small cohort sizes. PK characteristics were consistent with higher Cycle-1 peak and average concentrations (Cave) at higher doses and lower peak concentrations with split dosing. Len PK were consistent with historical data. No belamaf–Len interaction was observed. A positive trend was observed between belamaf Cycle-1 Cave and the probability of achieving PR or better.

Conclusion: Belamaf with SOC (Len/Dex) demonstrated deep and durable responses with a manageable safety profile in RRMM patients with no belamaf–Len interaction. These findings support belamaf–SOC use in RRMM patients.

BSH24-PO138 | Talquetamab + pomalidamide in relapsed/refractory multiple myeloma: Preliminary results from MonumenTAL-2 (phase 1b)

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Talquetamab, a T-cell-redirecting bispecific antibody (BsAb) targeting GPRC5D, and CD3, demonstrated deep and durable responses, and manageable safety in patients with relapsed/refractory multiple myeloma (RRMM) in the MonumenTAL-1 study. Pomalidomide is an established

immunomodulatory drug (IMiD). Combining pomalidomide with T-cell redirection therapy may lead to synergistic anti-myeloma effects. We report initial results of talquetamab + pomalidomide from the MonumenTAL-2 study (NCT05050097)

Patients received the recommended phase 2 doses of subcutaneous talquetamab 0.4 mg/kg weekly (QW) or 0.8 mg/kg every other week (Q2W), with step-up dosing, + oral pomalidomide 2 mg daily (dose escalation to 4 mg daily permitted) starting in Cycle 2. Patients received ≥2 prior lines of therapy (LOT) including a proteasome inhibitor and an IMiD; prior T-cell redirection therapies along with prior pomalidomide exposure were permitted.

Median follow-up was 11.4 months (range, 1.2–14.9) in the QW cohort ($N = 16$) and 7.7 months (range, 1.6–10.8) in the Q2W cohort ($N = 19$). Median age, 69.5 years (range, 49–78) and 63.0 years (range, 43–76), respectively; 41.7% and 33.3% with high-risk cytogenetics and 12.5% and 10.5% had extramedullary disease respectively. Median prior LOT were 3 in both cohorts; 25.0%, 21.1% triple-class refractory respectively. Prior treatments: CAR T (18.8%, 0%), BsAb (6.3%, 0%) and anti-CD38 Ab (75.0%, 73.7% [56.3%, 36.8% refractory]) in the QW and Q2W cohorts, respectively; 31.3%, 15.8% had prior pomalidomide exposure (18.8%, 5.3% refractory). All patients had ≥1 AE; most common was dysgeusia (77.1%). Grade 3/4 AEs occurred in 88.6% of patients; most common were neutropenia (48.6%), anaemia (25.7%) and thrombocytopenia (20.0%). Nail, skin and rash toxicities occurred in 65.7%, 40.0% and 20.0% of patients (no discontinuations) respectively. ICANS occurred in two patients (both grade 1). Infections occurred in 71.4% of patients (22.9% grade 3/4). AEs led to dose reduction/schedule change of talquetamab in 34.3% of patients and dose reduction of pomalidomide in 31.4% of patients. Two patients (5.7%) in the Q2W cohort discontinued, and one death occurred (not drug related). ORR was 86.7% and 83.3% in the QW and Q2W cohorts, respectively, with ≥CR in 60.0% and 44.4% and ≥ VGPR in 86.7% and 77.8% respectively. Median DOR and PFS were not reached.

Talquetamab + pomalidomide showed rapid, deep responses in patients with RRMM (≥2 prior LOT). The safety profile of the combination was consistent with the individual agents. These results support talquetamab as a versatile combination partner and warrants further evaluation of this regimen.

BSH24-PO139 | A matching-adjusted indirect comparison of acalabrutinib versus zanubrutinib in relapsed/refractory chronic lymphocytic leukaemia

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Background/Aims: The Bruton's tyrosine kinase inhibitor (BTKi) ibrutinib is the standard of care in relapsed or refractory chronic lymphocytic leukaemia (RR CLL) and was compared in head-to-head randomized clinical trials (RCTs) with second-generation BTKis: acalabrutinib in ELEVATE-RR and zanubrutinib in ALPINE. Major differences in these RCT's populations prevent the comparison of acalabrutinib and zanubrutinib. Acalabrutinib was also assessed in the ASCEND RCT, which had a similar population to ALPINE but a different comparator.

We used an unanchored matching-adjusted indirect comparison (MAIC) to compare the efficacy and safety of acalabrutinib versus zanubrutinib.

Methods: Acalabrutinib individual patient data (IPD) from ASCEND were weighted to match zanubrutinib baseline data from ALPINE. This reduced between-study differences that were prognostic/effect-modifying of progression-free survival (PFS) in an exploratory multivariate cox regression analysis of ASCEND. An efficacy analysis assessed investigator-assessed PFS (INV-PFS) in randomized patients with baseline data (acalabrutinib, $n = 149$; zanubrutinib, $n = 327$). Pseudo-IPD for INV-PFS for zanubrutinib were obtained from Kaplan–Meier curves. A safety analysis assessed odds ratios (ORs) of adverse events (AEs) in patients with baseline data (acalabrutinib, $n = 148$; zanubrutinib, $n = 324$). To allow comparison of the incidence of AEs, an artificial data cut-off (21 February 2020) was imposed for acalabrutinib to match zanubrutinib median treatment exposure (both 28.4 months).

Results: After matching, the effective sample size of acalabrutinib was 99 (66.6%; 65% male; median age 66 years). The MAIC hazard ratio (HR) for INV-PFS is similar for acalabrutinib versus zanubrutinib (HR: 0.90, 95% CI: 0.60–1.36). The risk of having a grade ≥3 AE (OR: 0.66, 95% CI: 0.41–1.05), atrial fibrillation (AF; OR: 1.32, 95% CI: 0.56–3.08), grade ≥3 AF/atrial flutter (OR: 0.60, 95% CI: 0.12–2.89), grade ≥3 haemorrhage (OR: 0.61, 95% CI: 0.19–2.03) or an AE leading to discontinuation (OR: 1.14, 95% CI: 0.61–2.13) was similar with acalabrutinib versus zanubrutinib. The risk of having a serious AE (OR: 0.61, 95% CI: 0.39–0.97), hypertension (any grade: OR: 0.18, 95% CI: 0.09–0.37; grade ≥3: OR: 0.22, 95% CI: 0.09–0.54), any grade haemorrhage (OR: 0.54, 95% CI: 0.34–0.87) or AE leading to dose reduction

(OR: 0.30, 95% CI: 0.14–0.67) was lower with acalabrutinib versus zanubrutinib.

Summary/Conclusion: Acalabrutinib and zanubrutinib have similar efficacy in patients with RR CLL. Acalabrutinib had a lower risk of grade ≥3 haemorrhage, any grade/grade ≥3 hypertension and dose reduction due to AEs versus zanubrutinib. Limitations of MAIC analyses mean the results are hypothesis generating.

BSH24-PO140 | Final results: Phase 1b study of subcutaneous isatuximab administration by OBDS plus pomalidomide–dexamethasone in RRMM

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Introduction: Intravenous (IV) administration of isatuximab (Isa) plus pomalidomide–dexamethasone (Pd) is approved for RRMM patients (pts). Subcutaneous (SC) delivery allows a shorter duration of administration, optimizing convenience and enhancing pts comfort. Prior phase 1b investigations, (NCT04045795) determined recommended phase 2 dose (RP2D) for SC Isa at 1400 mg, and showed safety and efficacy for SC Isa + Pd comparable to IV Isa + Pd in the pivotal ICARIA-MM trial in RRMM pts. We now present the final safety and efficacy results.

Methods: This study SC versus IV Isa + Pd in RRMM pts with ≥2 prior treatment lines including lenalidomide and a proteasome inhibitor. Pts were randomized to SC by infusion pump (IP) 1000 mg or IV 10 mg/kg and to IP1400 mg or IV. In the expansion cohort, SC Isa was administered at the RP2D via an on body delivery system (OBDS). Primary end-points: safety and PK; Key secondary end-points: ORR and PFS.

Results: Among 56 randomized pts, 25% (3/12) IV, 25% (3/12) IP1000, 30% (3/10) IP1400 and 32% (7/22) of OBDS pts remained on treatment until 15 April 2023. Median follow-up was 33, 39, 33 and 19 months for IV, IP1000, IP1400 and OBDS cohort respectively. ≥50% pts had ≥3 prior treatment lines. In the IV, IP1000, IP1400 and OBDS cohorts, serious treatment-related AEs occurred in 17%, 25%, 50% and 14% of pts; any ≥G3 infections in 25%, 25%, 30% and 36% of pts including 0%, 8%, 0% and 14% ≥G3 COVID-19 respectively. Median duration of OBDS injections was 10 min (6.6–49.5); all injections were completed without interruption and infusion reactions (IRs). Local tolerability: seven (32%) pts had 10 injection site reactions, all G1, and mainly erythemas. Relative dose intensity of Isa at SC RP2D was ≥90% (97%, 95%, 91% and 93% in IV, IP1000, IP1400 and OBDS cohorts respectively). ORR was 66.7% in both IV, IP1000 and 80% and 72.7% in IP1400, and OBDS cohorts (75% at RP2D) respectively. Median PFS was 22.0, 17.4 months, not reached and 20.6 months respectively (20.6 months at RP2D). Incidence of anti-drug antibodies appeared comparable after Isa SC or IV (9.1% vs. 8.3%).

Conclusions: Final results with SC Isa administration via OBDS at the 1400 mg RP2D + Pd show an efficacy and safety profile consistent with IV administration, with no IRs, and excellent local tolerability. A non-inferiority phase 3 trial (NCT05405166) evaluating SC Isa via OBDS versus IV Isa is ongoing.

BSH24-PO141 | Thirty-minute infusion of isatuximab in newly diagnosed multiple myeloma patients: Results of phase 1b study

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Introduction: Isatuximab is approved in various countries with pomalidomide–dexamethasone for relapsed/refractory multiple myeloma (RRMM) patients with ≥2 prior therapies including lenalidomide and a proteasome inhibitor (ICARIA-MM study) and with carfilzomib-dexamethasone with ≥1 prior therapy (IKEMA study). For convenience, shorter 30-min isatuximab IV infusion was assessed in newly diagnosed MM patients not eligible/with no immediate intent for autologous stem cell transplantation on maintenance therapy in phase 1b trial (NCT02513186), which previously reported efficacy of isatuximab with bortezomib–cyclophosphamide–dexamethasone (VCd)/bortezomib–lenalidomide–dexamethasone (VRd), with manageable safety profiles. Preliminary results with new 30-min isatuximab administration are presented here.

Methods: Patients receiving maintenance treatment were switched to 30-min isatuximab infusion at 10 mg/kg diluted in 250 mL 0.9% sodium chloride infusion bag. First infusion rate was 250 mL/h; if no infusion reactions (IRs), subsequent infusions were at 500 mL/h. Incidence safety and IRs severity during initial two full 30-min infusions were evaluated. The initial, recommended premedication included dexamethasone 20 mg orally (PO) (or equivalent [eq.]), acetaminophen 650–1000 mg PO; ranitidine 50 mg IV (or eq.), diphenhydramine 25–50 mg IV (or eq.) and montelukast 10 mg PO (or eq.). Prior switching, patients received weight-based isatuximab infusion in VCd cohorts and initially in VRd Part-A cohort, followed by fixed-volume isatuximab infusion in VRd Part-A and B (in Part-B, at 200 mL/h from third infusion, ~75-min with no IRs/interruptions).

Results: As of 19 May 2023, 29.4% of Isa-VCd, 48.1% of Isa-VRd Part-A and 60.9% of Isa-VRd Part-B patients remained on treatment. Median follow-up was 71.1, 55.1 and 38.1 months for Isa-VCd, Isa-VRd Part-A and Isa-VRd Part-B cohorts, with median exposure duration of 63.5, 54.1 and 40.8 months respectively. During January–May 2023, 45 patients received 142 infusions: 45 first infusions with intermediate rate; 97, 30-min infusions with median of 3 cycles started by patients (range, 1–5) (44 patients received ≥2 infusions) and median relative isatuximab dose intensity of 99.4% (range, 73.7–105.5%). In all treated patients switching occurred at median of 46 cycles (range, 38–88) and median duration of isatuximab infusion was 32-min, 33-min and 33-min at the second, third and subsequent infusions respectively. Thirty-minute isatuximab infusion was well tolerated, with no IRs and infusion interruptions across cohorts.

Conclusions: A 30-min isatuximab infusion is feasible, well tolerated and convenient administration method for MM patients on isatuximab for several months. This shorter infusion is currently being assessed in the ongoing phase 1–2 UMBRELLA trial of isatuximab with/without dexamethasone and novel agents, RRMM patients (NCT04643002).

BSH24-PO142 | Pooled safety analysis from birtamimab phase 1–3 trials in patients with light chain (AL) amyloidosis

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Introduction: AL amyloidosis is a progressive, fatal disease characterized by organ dysfunction from amyloid fibril deposition. Birtamimab is a humanized monoclonal antibody amyloid depleter being investigated in AL amyloidosis. We present a pooled safety analysis from phase 1 to 3 birtamimab trials.

Methods: Patients with AL amyloidosis received birtamimab up to 24 mg/kg/month in the non-placebo-controlled phase 1/2 trial (NCT01707264) and open-label extension (OLE; NCT02613182), and two randomized controlled trials (RCTs; phase 2 PRONTO [NCT02632786] with OLE [NCT03154047] and phase 3 VITAL [NCT02312206]). In PRONTO, patients with ≥1 previous systemic therapy and cardiac dysfunction received birtamimab or placebo. In VITAL, treatment-naïve patients with cardiac involvement received birtamimab + standard of care (SoC) or placebo + SoC.

Patients who received ≥1 dose of birtamimab were included. For VITAL and PRONTO, pooled rates and severity of adverse events (AEs) were compared between treatment arms. Safety data from non-placebo-controlled trials were summarized.

Results: The median (range) birtamimab exposure among 302 patients was 12.24 (0.03–57.72) months. RCT analysis included 196 birtamimab-treated patients (PRONTO, $n = 66$; VITAL, $n = 130$) and 193 placebo patients (PRONTO, $n = 63$; VITAL, $n = 130$). Rates of serious and grade ≥3 AEs were similar between trial treatment arms and in the pooled analysis set; in the birtamimab and placebo arms, respectively, 29.6% and 34.7% of patients had treatment-related AEs, 58.7% and 61.7% had grade ≥3 AEs, and 52.0% and 54.9% had serious AEs; no treatment-related AEs led to death. Higher rates of AEs were reported in VITAL versus PRONTO, presumably due to the treatment-naïve population and concomitant SoC therapy in VITAL. In the pooled analysis set, the most common AEs with greater frequency in the birtamimab arm in either trial were, respectively, fatigue (36.2%, 34.2%), diarrhoea (33.2%, 33.7%), nausea (31.6%, 30.1%), constipation (31.1%, 31.6%) and dyspnoea (25.0%, 24.9%). Cardiac disorders were the most common (≥5%) serious and grade ≥3 AEs. Infusion-associated AEs were mild to moderate, and rates were low in the pooled birtamimab and placebo arms (5.1% vs. 3.6% respectively). The safety profile in the non-placebo-controlled trials ($n = 106$) was consistent with that of the RCTs.

Conclusions: Birtamimab was well tolerated, with a favourable safety profile as monotherapy and no evidence of additive toxicity with SoC in AL amyloidosis. AE rates in the birtamimab and placebo arms were similar in the RCTs. A confirmatory phase 3 RCT of birtamimab in patients with Mayo Stage IV AL amyloidosis (AFFIRM-AL; NCT04973137) is enrolling.

BSH24-PO143 | First results from a phase 1, first-in-human study BGB-16673 in patients with relapsed/refractory B-cell malignancies

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Introduction: B-cell malignancies that progress on BTK inhibitors (BTKis) often have BTK mutations associated with treatment resistance. BGB-16673 is a heterobifunctional small molecule that binds BTK and E3 ligase, resulting in BTK degradation via ubiquitination. In preclinical models, BGB-16673 degraded wildtype BTK and known covalent and non-covalent BTKi-resistant mutant proteins, leading to tumour suppression.

Methods: In BGB-16673-101 (NCT05006716), eligible patients had B-cell malignancies treated with ≥2 prior therapies (≥1, Richter transformation), including, if approved for their disease, a covalent BTKi (cBTKi). BGB-16673 was administered orally, once daily, in 28-day cycles at five planned dose levels. The primary objectives are to assess safety/tolerability and establish the maximum tolerated dose (MTD) and recommended phase 2 dose. Secondary objectives include evaluation of pharmacokinetics, pharmacodynamics,

dose-limiting toxicities (DLTs) and anti-tumour activity. Responses are assessed per Lugano criteria, except for CLL (iwCLL 2018 criteria) and WM (iwWM-6 criteria).

Results: As of 26 May2023, 26 patients were enrolled (50 mg, $n = 4$; 100 mg, $n = 9$; 200 mg, $n = 9$; 350 mg, $n = 3$; 500 mg, $n = 1$) with a median of 3.5 prior therapies (range, 2–9), including cBTKis ($n = 21$), BCL2 inhibitors ($n = 12$) and non-covalent BTKis (ncBTKis; $n = 4$). del(17p)/TP53 mutation ($n = 8$) and unmutated IGHV ($n = 7$) were frequent in CLL. Median follow-up was 3.5 months (range, 0.2–13.9). MTD was not reached. Treatment-emergent AEs (TEAEs) occurred in 88.5% of patients (grade ≥ 3, 46.2%; serious, 38.5%); the most common were contusion (30.8%; no grade ≥ 3), pyrexia (23.1%; no grade ≥ 3), neutropenia/neutrophil count decreased (23.1%; grade ≥ 3, 15.4%) and lipase increased (23.1%; grade ≥ 3, 3.8%). No hypertension or atrial fibrillation were observed. One patient died (sepsis with possible disease progression). No discontinuations due to AEs occurred. Two patients had dose reductions due to TEAEs (grade 3 haematuria; grade 2 arthralgia). One DLT occurred (200 mg; grade 3 maculopapular rash).

BGB-16673 exposure increased dose dependently. At steady state with doses ≥50 mg daily, BGB-16673 exposure exceeded the calculated half-maximal degradation concentration for WT and C481-mutated BTK for the dosing interval. Preliminary data showed reduced BTK protein levels in peripheral blood and tumour tissue. Most patients with CLL experienced lymphocytosis during the first 3 cycles. Twenty patients (77%) remain on therapy (discontinuations: 4 progressive disease; 2 withdrawal). Of 18 response-evaluable patients, 67% responded (1 CR), including patients with prior cBTKi ($n = 10$) and ncBTKi ($n = 2$).

Conclusions: Preliminary data from this ongoing, first-in-human study of BGB-16673 demonstrate a tolerable safety profile and meaningful clinical responses in heavily pretreated patients with B-cell malignancies, including BTKi-resistant disease.

BSH24-PO144 | Acquired mutations in patients with relapsed/refractory chronic lymphocytic leukaemia that progressed in the ALPINE study

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Introduction: Patients receiving covalent Bruton tyrosine kinase inhibitors (cBTKis) for chronic lymphocytic leukaemia (CLL) can develop drug resistance, leading to progressive disease (PD). cBTKi binding site mutations (C481) are most common. For insights into cBTKi resistance in a randomized CLL patient population, we performed next-generation sequencing (NGS) on samples from patients who progressed on zanubrutinib or ibrutinib in the phase 3 ALPINE study (NCT03734016).

Patients and Methods: PD (Hallek et al, Blood. 2008) was determined by independent review ($n = 139$) and/or investigator ($n = 132$); 57 patients (zanubrutinib, $n = 26$; ibrutinib, $n = 31$) had PD samples (median follow-up: zanubrutinib, 25.4 months; ibrutinib, 28.1 months). Paired blood samples from baseline and at or after PD and prior to subsequent therapy from patients without Richter transformation at PD were included (zanubrutinib, $n = 24$; ibrutinib, $n = 28$). A 106-gene NGS panel, including putative CLL driver genes, was used (BTK and PLCG2 mutations, variant allele frequency [VAF] ≥0.25%; all other genes: pathogenic mutations, VAF ≥1%). Baseline chromosome abnormalities were assessed.

Results: No baseline BTK mutations were detected. Nine patients acquired BTK/PLCG2 mutations: eight in BTK (zanubrutinib, $n = 5$; ibrutinib, $n = 3$); two in PLCG2 (both ibrutinib; 1 in both BTK and PLCG2). Of 18 BTK single-nucleotide variants (SNVs), 77.8% (zanubrutinib, $n = 11$; ibrutinib, $n = 3$) were at C481; 3/24 zanubrutinib patients had non-C481 BTK mutations. Median treatment duration at PD was shorter in patients without (zanubrutinib: $n = 19$, 16.8 months; ibrutinib: $n = 25$; 15.9 months) versus with (zanubrutinib: $n = 5$; 29.7 months; ibrutinib: $n = 3$; 30.8 months) acquired BTK mutations.

Baseline mutations in 18/27 driver genes were observed in 48/52 patients; most frequent: NOTCH1 ($n = 21$), TP53 ($n = 19$), BRAF ($n = 10$), SF3B1 ($n = 8$) and ATM ($n = 8$).

Twenty-three patients had copy number aberrations (CNAs) in 9/27 driver genes; most frequent: CCND2 ($n=10$), ATM ($n=8$), TP53 ($n=6$) and KMT2D ($n=6$). At PD, six patients acquired SNVs (zanubrutinib: TP53 and XPO1 in $n=1$; ibrutinib: TP53, SETD2, SF3B1 [each $n=1$], ASXL1 in $n=2$). Ten patients acquired CNAs in driver genes (most frequent: KRAS [zanubrutinib, $n=3$]; NRAS [ibrutinib, $n=2$]; CDKN1B [zanubrutinib, $n=2$; ibrutinib, $n=1$]; BIRC3 [ibrutinib, $n=2$]). Acquired driver gene mutations were not associated with del(17p), IGHV mutation or complex karyotype status.

Conclusion: Of 52 patients, most (82.6%) did not acquire BTK/PLCG2 mutations. These data suggest BTK and/or PLCG2 mutations are not the sole factors driving PD in this population. Given the low incidence of non-C481 mutations in patients with PD in ALPINE, patients with CLL treated with cBTKis likely remain sensitive to other BTK-targeting therapies.

BSH24-PO145 | Survey scoping the practice of pharmacist prescribers within myeloma outpatient clinics in the UK

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Haematology services are under increasing pressure due to increasing patient numbers, complexity and duration of treatment and difficulties in recruiting haematologists. The British Society of Haematology Annual Scientific meeting 2023 identified these workforce issues and highlighted the use of allied healthcare professionals to deliver models of care to address this. These discussions were the driver for this survey.

Aims: To assess the scope of practice of pharmacist independent prescribers (PIPs) in myeloma outpatient clinics.

Methods: A predefined questionnaire was circulated electronically to pharmacists in the UK in August 2023 via British Oncology Pharmacy Association and UK Myeloma Society. Results were collated and analysed descriptively.

Results: Twenty-seven PIPs responded, several questions were 'select all that apply' and therefore have more than 27 answers.

Respondent Demographics: All worked in NHS trusts within the UK, with varying levels of a haematology service. Nineteen respondents are currently Agenda for Change band 8a (range 8a–8c). The mean time respondents have been working in the myeloma outpatient setting is 3.4 years (range <1–10).

Training: All respondents are qualified PIPs. Additional training undertaken included communication skills six (22%), ordering imaging three (11%), clinical skills two (11%) and in-clinic training 2 (7%).

Clinic Models: Various models have been implemented. Twenty (74%) respondents work in consultant led, eight (30%) in pharmacist-led and two (7%) in joint nurse–pharmacist clinics. Consultation type varied with 26 (96%) undertaking telephone, 24 (89%) face-to-face and two (7%) undertake virtual appointments.

Clinic Capacity: Nineteen (70%) of respondents undertake one clinic per week (range < 1 to >3 per week). The mean number of myeloma patients reviewed in each clinic is 7.1 (range 2–14), some of these were within mixed diagnosis clinics.

Clinical Activity: Nineteen (70%) pharmacists reviewed all patients irrespective of the treatment regimen. Seven reviewed follow-up patients on treatment, 13 reviewed follow-up patients on or off treatment and two (7%) also reviewed new patients. Other roles undertaken included delivering bad news (56%), consenting patients for systemic anti-cancer therapy (SACT) (22%), completing Blueteq requests (30%) treatment break forms (37%), attending MDT (74%) and counselling patients on SACT (93%).

Discussion & Conclusion: Results indicated that pharmacists are routinely working as an integral part of the Myeloma Multidisciplinary Team in the outpatient setting. They are reviewing a wide range of patients using different consultation types and carrying out a range of activities within clinics. This suggests that, with appropriate training and support, pharmacists nationally may be being underutilised resource in addressing capacity challenges.

BSH24-PO146 | Belantamab mafodotin in patients with relapsed/refractory multiple myeloma: Long-term safety and efficacy data from DREAMM-3

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Introduction: DREAMM-3 (NCT04162210) is a randomized study comparing single-agent belantamab mafodotin (belamaf), a first-in-class antibody–drug conjugate targeting B-cell maturation antigen, to a standard of care regimen, pomalidomide plus dexamethasone (Pd). This post hoc analysis evaluated the safety and efficacy of long-term belamaf treatment (≥52 weeks) compared with Pd in adults with relapsed/refractory multiple myeloma at third line of therapy or later, exploring the impact of dose modifications.
Methods: Patients were randomized (2:1) to belamaf 2.5 mg/kg intravenously once every 3 weeks (Q3W; 21-day cycle) or pomalidomide 4 mg orally once daily (Days 1–21) and dexamethasone 40 mg (20 mg if >75 years) orally once weekly (28-day cycle). Ocular exams were performed prior to dosing belamaf Q3W up to Cycle 6, then every 3 months if no significant ocular events were reported. Efficacy responses were assessed Q3W, regardless of treatment delays.
Results: As of 12 September 2022, 50/218 (23%) patients received belamaf for ≥52 weeks. All 50 patients reported AEs. Grade ≥ 3 AEs occurred in 82% ($n = 41$); the most frequent were reduced visual acuity (24%), thrombocytopenia (18%) and neutropenia (16%). The majority of AEs emerged at or before Cycle 17, with minimal new occurrences of most common AEs (>40%, any grade) postcycle 17 (dry eye, reduced visual acuity, eye irritation and thrombocytopenia; one of each reported). Few infections (any grade) occurred after Cycle 17 (COVID-19, $n = 5$; viral infection, $n = 1$; pneumonia influenzal, $n = 1$). No permanent treatment discontinuation occurred due to belamaf-related AEs. Ocular AEs affected 94% ($n = 47$) of patients, mostly ($n = 487$) grade 1 or 2 severity (88%) with no study discontinuations. At data cut-off, 95% patients ($n = 41$) with Grade ≥2 Keratopathy Visual Acuity events recovered prior to the end of study treatment exposure with most patients having dose modification and maintaining efficacy. The clinical benefit rate (≥minimal response) was 90% (45/50), median time to best response was 6.3 months (range 0.8–18.8), and median duration of response was not reached (NR; 95% CI 17.9, NR) in the subset of patients treated for ≥52 weeks. At the data cut-off, 94% ($n = 47$) patients were alive.
Conclusions: In patients with long-term treatment (≥52 weeks), belamaf maintained a consistent safety profile aligning with previous reports. Despite dose delays and reductions, no patients discontinued treatment due to belamaf-related AEs. Clinical responses were maintained or deepened in most cases during dose delays, indicating effective management of emerging AEs through dose modifications while allowing for sustained clinical benefit.

BSH24-PO147 | Comprehensive genetic analysis of multiple myeloma by chromosomal microarray

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Multiple myeloma (MM) is a terminally differentiated plasma cell neoplasm characterized by bone marrow clonal proliferation of malignant plasma cells (PCs). The diversity at the genomic level leads to the heterogeneity of the disease and contributes to distinct phenotypes in patients, including disease progression and the establishment of resistance to available therapies. This study aims to explore genetic abnormalities in newly diagnosed MM using the chromosomal

microarray (CMA) technique. Twenty-four DNA samples were isolated from CD138-enriched PCs and subsequently analysed for genetic abnormalities using CMA. Common genetic abnormalities detected in this study were the following copy number gain in chromosomes 1q, 5, 9, 19, 6p, 15, 3, 7 and 21q and copy number loss in 13q, 14q, 17p, X, 1p, 22q, 6q, 8p, 12q, 4p and 7p respectively. Moreover, copy-neutral loss of heterogeneity (cnLOH) chromosome regions was observed in nine patients (37.5%), including chromosomes 1, 4, 7, 8, 9, 11, 12, 13q, 14q, 16q and 18, which predominantly observed in high-risk patients. CMA could detect more gain and loss of chromosomes than conventional cytogenetic analysis, iFISH and MLPA. In summary, the data suggested that high-resolution CMA could be used together with karyotyping and iFISH to analyse clinically relevant genomic aberrations and additional genetic abnormalities in patients with MM.

BSH24-PO148 | Single-cell multiomic correlation of SNVs, CNV and surface epitopes for clonal profiling of myeloma

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Introduction: Multiple myeloma (MM) is a cancer of plasma cells with approximately 200 000 new diagnoses each year. As myeloma cells expand, clonal genetic differences lead to relapse due to acquired resistance in 100% of patients, mandating regular, long-term surveillance. Existing diagnostic modalities are unable to correlate subclonal genetic changes and putative antibody targets on refractory myeloma cells, leaving the clinician to use their best judgement on salvage therapy, which can lead to unnecessary expense and toxicity to patients due to ineffective treatment. Specifically, knowing actual targets on refractory MM cells would better facilitate precision medicine and potentially improve outcomes.
Methods: Cryopreserved, human MM patient samples were processed on the Mission Bio Tapestri platform, enabling simultaneous single-cell quantification of subclones by single-nucleotide variants (SNV), copy number variants (CNV) and surface protein analysis. These single time point samples were thawed from frozen bone marrow mononuclear cells previously enriched for CD38, stained with a 45-plex antibody-oligo cocktail to label common haeme-specific surface markers for sequencing analysis, and processed with a 733-plex DNA primer panel that combined whole-genome CNV coverage with MM gene hotspots. Sequencing was performed on an Illumina system with the raw data being analysed using Mission Bio proprietary algorithms.
Results: We show complex clonal evolution of MM in individual samples as copy gains and losses that were sequentially acquired and correlated with expression changes of MM markers. Across the cases analysed, complex branching phylogenetic trees were reconstructed with as many as five subclones and clear associated shifts in MM marker expression. When averaged across subclones, each sample had CNV profiles that matched patient bulk genome-wide array records, ranging from a single gene-level copy gain to arm-level gains and losses across the majority. The progression of protein expression within different samples could be mapped together on a single plot and correlated with generally higher MM markers as subclonal genetic variants were acquired, though occasional branches saw reversal. The fraction of other cell phenotypes, such as T cells and those with low viability, decreased within subclones as mutational burden grew.
Conclusions: This high-resolution, single-cell assay offers a potential new modality for the diagnosis and surveillance of patients. We have demonstrated: (1) exceptional results from cryopreserved human specimens, (2) the ability to use genetic lesion profiling to positively identify subclonal MM and, most importantly, (3) correlate cell surface protein expression of potential therapeutic targets with each clonal and subclonal population.

BSH24-PO149 | A Single-centre experience of cardiac transplantation in patients with AL amyloidosis with advanced cardiac involvement

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Systemic light chain (AL) amyloidosis can cause infiltrative cardiomyopathy and heart failure. Median survival of AL amyloidosis is 4.6 years from diagnosis. However, a significant number of patients die within 12 months of diagnosis and cardiac involvement is a major cause of early mortality for patients with AL amyloidosis. In recent years, cardiac transplantation followed by autologous stem cell transplantation (ASCT) has been offered in select centres to improve survival for patients with primary cardiac involvement but limited data on patient outcomes are available.
Data were collected on 21 patients referred for cardiac transplantation at the Queen Elizabeth Hospital Birmingham between January 2008 and May 2023. In total, 17 patients were screened, and six patients underwent cardiac transplantation. Of the patients who were transplanted, the median

age at screening was 49.9 years (range 39.9–59.8 years). Five patients had lambda light chain isotype with average free light chain values of 465, 86.8 and 46.4 mg/L at presentation, pretransplant and post-transplant respectively. One patient had kappa light chain isotype with free light chain values of 434, 141.6 and 346.6 mg/L at presentation, pretransplant and post-transplant respectively. All patients had responded well to clonally directed treatment prior to transplantation. Three patients had extra cardiac manifestations at the time of transplant including renal, splenic and glossal amyloid deposition. Prior to transplantation, two patients received mechanical bridging support with biventricular and left ventricular assist devices. Two patients went on to receive ASCT. The range of postcardiac transplant survival is 0.1–7.7 years. One patient passed away due to postoperative complications 42 days after transplant, one patient survived 7.7 years after transplant and passed away from ciclosporin-induced neuropathy and four patients remain under follow-up at 7.5, 9, 10 months and 7.6 years post-transplantation.

Cardiac transplantation is infrequently performed in patients with AL amyloidosis but can provide an excellent option to improve survival and functional outcomes in selected patients with predominantly isolated advanced cardiac AL amyloidosis and who have achieved a good response to clonally directed treatment. Here, we summarise the experiences of a tertiary care centre in cardiac transplantation ± ASCT for patients with AL amyloidosis.

BSH24-PO150 | Dynamic assessment of a multiple myeloma patient access scheme using real-world data and Bayesian inference

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Background: Treatment options for multiple myeloma (MM) are constantly evolving, with several key therapies recommended by NICE within the last decade. Many of these therapies were initially made available through the Cancer Drugs Fund (CDF), a patient access scheme (PAS) enabling early access to potentially beneficial therapeutics during an evidence-gathering period prior to NICE's final recommendation decision. Leveraging a Bayesian inferential approach when analysing PAS data may allow for early termination of the data collection phase, as interim analysis is not penalised in this framework. Here, we have integrated real-world and trial data within a Bayesian framework to investigate the viability of early decision-making based on assessment of daratumumab monotherapy for relapsed/refractory MM (NICE TA783).

Methods: This retrospective observational study used anonymised electronic health records from patients diagnosed with MM across three NHS trusts. A cohort of patients who received daratumumab through the CDF were compared with a cohort of patients who received standard of care pomalidomide at 4 L with no prior daratumumab exposure was constructed. An exponential Bayesian survival framework was employed to compare overall survival (OS) in these two treatment groups. The prior distribution on the baseline hazard was informed by the median survival observed in an earlier, single-armed, daratumumab trial. Analyses were performed dynamically through time using incrementally updated 3-month data cuts in both treatment groups, with the estimated marginal treatment effect and variance recorded for each analysis. Additional sensitivity analyses increased the variance of the baseline hazard prior.

Results: From a total of 2823 MM patients, 88 patients received daratumumab through CDF, and 27 patients received pomalidomide at 4 L with no prior daratumumab exposure. The marginal probability that daratumumab provides improved OS over pomalidomide exceeded 0.95 by month 6. This result was obtained after only 14.8% of the data collection period that was used in NICE TA783 had elapsed. The posterior distribution of the treatment effect stabilised after 15 months of PAS data was analysed. The same result was observed in sensitivity analyses with a diffuse prior on the baseline hazard, suggesting the estimated treatment benefit is driven by the observed data.

Conclusion: This study found that an OS benefit for daratumumab over pomalidomide could be identified with a shorter data collection period than in NICE TA783, demonstrating the viability of this framework for expedited assessment of treatment benefit in a patient access scheme.

BSH24-PO151 | Pirtobrutinib and venetoclax ± rituximab in relapsed/refractory chronic lymphocytic leukaemia: Updated BRUIN phase 1b results

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Background: Covalent Bruton tyrosine kinase inhibitors (cBTKi) have transformed the management of chronic lymphocytic leukaemia (CLL). Recent studies have shown fixed-duration regimens with venetoclax and cBTKi to be effective; however, use may be limited by toxicity. Pirtobrutinib, a highly selective, non-covalent (reversible) BTKi, has shown promising results in heavily pretreated relapsed/refractory (R/R) CLL patients. Here, we report the safety and efficacy of fixed-duration pirtobrutinib combined with venetoclax ± rituximab in these patients.

Methods: Patients with R/R CLL were eligible for the phase 1b portion of the 1/2 BRUIN study (NCT03740529). Prior cBTKi therapy was allowed, but not prior venetoclax. Twenty-five patients were enrolled to receive either combination pirtobrutinib 200 mg/day + venetoclax (PV, $n = 15$) or PV + rituximab (PVR, $n = 10$). The primary end-point was safety assessed by treatment-emergent adverse events (TEAEs) graded according to CTCAE v5.0. Other key end-points included overall response rate (ORR), progression-free

survival (PFS) and minimal residual disease (MRD). A data cut of 5 May 2023 was utilized.

Results: The median age was 66 years (range, 49–77) with a median number of prior therapies of 1 (range, 1–2) in the PV arm, and 69 years (range, 39–78) with a median number of prior therapies of 2 (range,1–4) in the PVR arm. Most patients had IGHV unmutated CLL (PV = 73%; PVR = 89%) and received prior cBTKi (73%; 60%). Among all patients, the ORR was 96.0%, with 40% achieving complete response (CR). The ORR in the PV arm was 93.3% (95% CI, 68.1–99.8) and 100% (95% CI, 69.2–100.0) in the PVR arm, with 10 complete responses (PV = 7; PVR = 3). Median duration of follow-up for PFS was 22.1 months for both arms, with a 24-month rate of 79.5% (95% CI: 52.0–92.3) for all patients. By Cycle 13, 70.8% of patients had undetectable MRD (uMRD), and 87.5% achieved uMRD at some point during the trial. All but 1 patient maintained uMRD in subsequent assessments. Safety profiles were generally similar between treatment arms with treatment-related adverse events (TRAEs) leading to two discontinuations and three dose reductions. The most common TEAE of any grade included nausea (PV = 60.0%; PVR = 40.0%), fatigue (53.3%; 50.0%) and diarrhoea (46.7%; 60.0%). The most common grade ≥ 3 TEAE was neutropenia/neutrophil count decreased (PV = 46.7%; PVR = 60.0%).

Conclusion: Fixed-duration pirtobrutinib combined with venetoclax ± rituximab was well tolerated and demonstrated promising efficacy to warrant further investigation in patients with R/R CLL. BRUIN CLL-322 phase 3 trial comparing PVR versus VR in pretreated CLL is currently enrolling (NCT04965493).

BSH24-PO152 | Molecular analysis at relapse of ibrutinib and rituximab-treated CLL patients on the NCRI FLAIR study

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The FLAIR trial confirmed ibrutinib+rituximab (IR) improved progression-free survival compared to FCR in front-line CLL. Despite durable responses to Bruton's tyrosine kinase inhibitors (BTKi), acquired resistance mutations in BTK and PLCG2 affect up to 80% of relapsed/refractory pts. We present patterns of clonal evolution in front-line IR-treated pts with progressive disease (PD), integrating next-generation sequencing (NGS) with serial measurable disease monitoring by flow cytometry and tracking BTK mutations (BTKmt) from initial detection to disease progression using digital droplet PCR (ddPCR).

Sixty-one PD IR-treated pts were included. Thirty-three recurrently mutated genes in LPD were sequenced by MiSeq at baseline and progression. ddPCR screening of 57/61 IR-treated PD pts and quantitative serial assessment from initial detection to frank PD were performed to detect four BTK hotspot mutations. Allelic mutation burden was expressed as fractional abundance (FA) adjusted for disease burden determined by flow cytometry.

61/386 IR-treated pts progressed after a median follow-up of 44 months. Of 47/61 IR-treated pts sequenced by MiSeq at baseline and PD, 15 developed new mutations in genes recurrently mutated in CLL. Fifty-six IR-treated PD samples were analysed by ddPCR for BTKmt. BTK was the most frequently mutated gene at PD. Twenty-one per cent had ≥1 mutations at C481 hotspot. 10/12 patients with BTKmt were IGHV unmutated. The majority of patients had >1 BTKmt mutation. No BTKmt detected at PD were detected at baseline by NGS or ddPCR. One had a PLCG2 mutation at PD. Median time to progression for pts with BTKmt was 72 months. Median time to the first BTKmt was 63 months. Six monthly samples during Ibrutinib were studied for BTKmt. The evolutionary dynamics of BTKmt on Ibrutinib, show a steady rise in the FA preceding frank PD in a subset of pts.

In front-line IR-treated CLL pts 15.8% progressed, the majority late. Only 20% of the IR PD cohort had a BTKmt/PLCG2mt, suggesting other non-BTKmt/PLCG2mt factors contributing to PD after initial response in the up-front setting. The majority of IR-treated PD with BTKmt were IGHV 100% homologous to germline, suggesting an inherent higher risk disease profile as a contributing factor for acquiring BTKmt with prolonged BTKi therapy. BTKmt were enriched among late progressors, with 8/12 pts progressing shortly after stopping therapy at 72 months, later than previously reported for relapsed/refractory CLL pts. In pts where the BTK-resistant clone contributed to PD, initial detection of the BTKmt preceded PD by a median of 12 months.

BSH24-PO153 | Barriers and enablers to pharmacist prescribing in myeloma clinics

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Background: There has been a significant increase in the number of new drug approvals in myeloma with the majority of these continued until progression. A key theme at the BSH (British Society of Haematology) 2023 annual symposium was how to plan the future haematology workforce. We conducted a survey to understand the extent of pharmacist prescribing within the myeloma setting.

Methods: Pharmacist independent prescribers (PIPs), working within Myeloma clinics in the UK, were invited to complete an MS (Microsoft™) Forms survey consisting of 31

questions, exploring the scope and nature of their practice including barriers and enablers. Barriers and enablers were predefined, but participants were able to specify additional factors. The survey was reviewed by the UKMS Pharmacy group steering committee and BOPA (British Oncology Pharmacy Association) Research subcommittee. UKMS and BOPA forums were used to distribute the survey. MS Forms collated the data into an excel spreadsheet to enable descriptive analysis.

Results: Twenty-seven PIPs responded, with 13 (48%) PIPs experiencing several barriers (1–5 barriers were cited per PIP) when participating in myeloma clinics.

The most commonly cited barrier was 'lack of room capacity' ($n = 7$) followed by 'no allocated time in job plan' ($n = 6$) and 'no funding to backfill pharmacy role' ($n = 6$). Only two PIPs cited a 'lack of clinical engagement' as a barrier. One respondent identified restrictions to the completion of Prescription Authorisation Forms (PAFs) for immunomodulatory drugs (imids) by PIPs, as an additional barrier. With respect, to level of experience, no significant correlation was identified in respondents in the barriers and no-barriers group.

With regards to enablers, across the whole cohort, the most commonly expressed enablers to undertake myeloma clinic were cited as 'increased job satisfaction' ($n = 18$), 'career progression' ($n = 15$) and 'consultant request' ($n = 13$). 'Increased service demand' ($n = 21$), 'improved skill mix in clinics to benefit patients' ($n = 18$) and 'medical workforce shortage' ($n = 14$) were the most frequently reported service drivers.

Conclusion: Barriers and enablers to the implementation and utilisation of PIPs in this setting are evident. We hypothesised that more experienced pharmacists would encounter fewer barriers, but this was not the case. Further work is required to identify potential strategies to optimise the number of PIPs working in myeloma clinics. Reassuringly, clinician engagement is more commonly an enabler rather than a barrier to PIPs working in clinic. Future areas for research include exploring barriers and enablers for PIPs who are yet to take up roles in clinics.

BSH24-PO154 | MRD targets for CLL treatment cessation in the ibrutinib+venetoclax arm of the FLAIR trial

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Introduction: The optimal target for treatment cessation is not clear with time limited therapies. The iwCLL threshold of bone marrow (BM) undetectable MRD4 (<0.01%) has been demonstrated to be a powerful indicator of improved outcomes. The aim of this analysis is to determine the feasibility of using peripheral blood (PB) MRD analysis to identify patients who have attained BM uMRD4.

Methods: FLAIR is an open-label, randomised, controlled, phase 3 trial comparing ibrutinib plus rituximab (IR) with fludarabine, cyclophosphamide and rituximab (FCR), subsequently amended to compare ibrutinib plus venetoclax (I + V) and ibrutinib alone (I) with FCR. Paired PB & BM samples were scheduled at: (1) response assessment 9 months after randomization in all arms ($n = 1086$); (2) end of treatment after 72 months in the ibrutinib-containing arms ($n = 137$, most I/I + V participants have not reached this timepoint yet); and (3) confirmation of BM uMRD4 for initiation of planned stopping rules in participants with sustained PB uMRD4 defined as <0.01% PB MRD at three timepoints over 6 months ($n = 188$ in the I + V arm). An 8-colour flow cytometry MRD panel comprising core ERIC markers CD19/CD20/CD5/CD43/CD79b/CD81 plus ROR1 and CD200.

Results: Participants receiving FCR had a median 0.54 log higher disease in the BM versus PB (range − 0.78 to 2.1). The difference did not persist in the IR arm but remained during I + V treatment in some cases, with median >0.59 log higher BM versus PB MRD levels in 29/182 participants achieving PB uMRD4 but with detectable BM MRD. In FCR arm, PB uMRD5 (<0.001%) identifies patients with BM uMRD4 in 92% of cases while PB dMRD5 (0.001%–0.01%) identifies BM uMRD4 in only 23.5% of cases. At 9 months, the response to I + V 0.01 log higher MRD in BM versus PB (range − 1.1 to 1.8); Also, PB uMRD5 (<0.001%) identifies patients with BM uMRD4 in 91% of cases while PB dMRD5 (0.001%–0.01%) identifies BM uMRD4 in only 48% of cases.

Conclusions: PB uMRD4 sustained for 6 months is 95% effective in identifying BM uMRD4 for patients receiving I + V. PB uMRD4 at a single time point is not suitable for identifying BM uMRD4 because most patients with PB dMRD5 (0.001%–0.01%) have >0.01% BM MRD. For MRD-guided treatment in future, bone marrow assessment may be replaced with PB monitoring if the uMRD5 (<0.001%)

threshold is applied. The results highlight the use of PB MRD to guide duration of therapy with I + V.

BSH24-PO155 | Impact of immunoglobulin replacement therapy on infections with elranatamab treatment for myeloma: MagnetisMM-3 post hoc analysis

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Patients with RRMM are at increased risk for severe infections due to immunosuppression related to the disease and anti-MM therapies. Management guidelines support anti-infective prophylaxis in high-risk patients, including immunoglobulin (Ig) replacement therapy for hypogammaglobulinaemia. However, sparse data exist showing the impact of Ig replacement on infections in these patients.

A post hoc analysis was conducted in patients with RRMM enrolled in MagnetisMM-3 (NCT04649359), a phase 2 study of SC elranatamab (BCMA/CD3-bispecific monoclonal antibody). Exposure-adjusted infection rates (EAIR) were analysed in patients On versus Off Ig replacement therapy ($n = 187$) and without versus with hypogammaglobulinaemia (in patients with quantitative IgG data available, $n = 137$). Any new (non-continuous) infection event, any increase in grade in a single continuous event, and any event starting in one period and spanning across the entire next period (if ≥30 days) were counted as distinct infection events. 'On Ig' period was defined as time between the administration of Ig replacement therapy +30 days. Hypogammaglobulinaemia was defined as IgG <400 mg/dL. For patients with non-IgG myeloma, quantitative IgG results were used. For patients with IgG myeloma, functional IgG levels were determined by subtracting the M-spike in SPEP from the quantitative IgG result. EAIR were calculated as number of infection events per period divided by total time in months in each period.

A total of 187 patients received elranatamab; median (range) treatment duration was 4.37 (0.03–25.79) months. During the treatment period, 41.2% of patients received Ig replacement. The median (range) time on and off Ig replacement was 3.02 (0.07–25.03) vs. 4.57 (0.16–18.63) months respectively. Monthly EAIR (95% CI) in patients on versus off Ig replacement were 0.22 (0.18–0.27) vs. 0.36 (0.33–0.40) for any grade, and 0.05 (0.03–0.08) vs. 0.14 (0.12–0.16) for Grade ≥ 3 infections respectively. The median time without and with hypogammaglobulinaemia was 4.12 (0.03–20.47) versus 6.34 (0.03–17.71). Monthly EAIR (95% CI) in patients without versus with hypogammaglobulinaemia were 0.23 (0.19–0.27) vs. 0.36 (0.32–0.40) for any grade, and 0.05 (0.03–0.07) vs. 0.14 (0.11–0.17) for Grade ≥ 3 infection respectively. Similar results were observed across infection types (bacterial, fungal, viral).

In this phase 2 study of patients with RRMM treated with elranatamab, IgG levels ≥400 mg/dL or Ig replacement therapy were associated with a decreased infection rate, including Grade ≥ 3 infections. These data support the need for close monitoring of Ig levels during treatment and benefit of Ig replacement therapy in management of patients with RRMM treated with BCMA-directed bispecific antibodies.

BSH24-PO156 | Local cytogenetic testing for risk-stratified therapy in newly diagnosed multiple myeloma: UKMRA RADAR experience

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Background: Recent studies in genetically high-risk (HR) multiple myeloma (MM) have reported high response rates with intensive induction and post-ASCT treatment strategies, providing the rationale for stratified therapy based on genetic risk. While centralised testing in clinical trials offers ready uniformity and quality control, the use of local laboratories paves the way for genetic testing to be available for

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all patients. We designed the UKMRA RADAR study to use local laboratories for cytogenetic testing.

Methods: RADAR is an ongoing national, multicentre, risk-adapted, response-guided multiarm, multistage phase II/III trial for patients with newly diagnosed MM eligible for ASCT. Patients receive induction with RCyBorD (lenalidomide, cyclophosphamide, bortezomib, dexamethasone), followed by ASCT. Post-ASCT, HR patients are randomised to receive isatuximab or not, alongside RBorD/R consolidation/maintenance while standard risk (SR) patients receive MRD-guided regimens. A protocol amendment (2022) included isatuximab for all HR patients within induction treatment.

Testing is undertaken in local cytogenetics laboratories on CD138-selected bone marrow (BM). HR is assigned based on the presence of ≥2 of: t(4;14), t(14;16), t(14:20), del(17p), del(1p32) and gain(1q). Clone size cut-offs are 10% for IgH translocations and 20% for copy number changes. Results are centrally reviewed to assign risk in real-time, overseen by a genomics working group.

Results: As of 15/12/23, 662 patients have been recruited from 88 UK sites. Median age is 60 years, 59.1% male and 83.1% white. Twenty-five local laboratories were used for CGN testing. 75.2% were assigned SR, 16.9% HR, 7.2% undefined. Gain(1q) was most prevalent (33.7%), followed by del(17p)(9.8%), t(4;14)(9.5%), del(1p)(9.1%), t(14;16)(3.2%) and t(14;20)(0.8%).

In 84.3%, risk was assigned from one BM sample. 15.1% required a second sample, with a success rate of 71.0%. The median turnaround time (from D1 induction until site notified of result) is 9 days.

Conclusion: The RADAR study demonstrates that risk-stratified treatment approaches using local laboratories are feasible. The majority of patients have been successfully allocated to a risk-adapted treatment pathway following a first FISH test. The HR protocol amendment requires time-critical risk stratification for addition of isatuximab to induction treatment, and this has proven to be achievable.

The RADAR study enables UK hospitals to access cytogenetic testing via a network model of laboratories with standardisation of testing and clinically relevant turnaround times. This model is applicable internationally and supports the infrastructure for accessible genetic risk stratification for all newly diagnosed MM patients.

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