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ABSTRACT

e-Posters

BSH24-EP01 | Characterisation of acute promyelocytic leukaemia: Follow-up study at a tertiary care centre

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This original research article seeks to systematically classify acute promyelocytic leukaemia (APL) through comprehensive analysis of morphological, immunophenotypic and molecular characteristics. The primary aim is to establish correlations between these distinctive features and the subsequent therapeutic response.

A prospective study was conducted at the Haematology Department, Armed Forces Institute of Pathology (AFIP), from January 2019 till August 2023, which encompassed individuals newly diagnosed with APL, with meticulous follow-up protocols instituted from the point of diagnosis until the current reporting period.

Results: Among the cohort of 123 recently diagnosed APL patients, male predominance was observed, reflected in a male-to-female ratio of 2.7:1. Age stratification revealed that 20.3% of cases pertained to individuals under 18 years, exhibiting a median age of 7 years, while 79.7% pertained to adult category (median age: 39 years). The prevailing clinical presentation manifested as fever in 92.7% of cases, with concurrent physical examination that revealed bruising in 33.3% of patients. The morphological analysis of bone marrow specimens at the time of diagnosis identified 78% of cases as the hypergranular variant, 9.8% as the hypogranular variant, 9.8% as hyperbasophilic and 3.2% as zinc finger/retinoic acid receptor-α (M3r). On immunophenotyping, 74% patients had the triad of CD117 positive, CD34 and HLA DR negative phenotype. Aberrant expressions of HLA DR, CD7 and CD56 was commonly found. The PML-RARA fusion gene was identified in 93% of cases, predominantly presenting as the BCR1 isoform (43%) while in 2% cases ZBTB16::RARA fusion was found. Additionally, 5% of patients exhibit molecular aberrations, including NPM1, FLT3-ITD or both, along with WT1. Cytogenetic testing revealed further complexities, with abnormalities such as del7q, i(17q), del9q and tetraploid documented in 14.6% of cases. Tragically, 14% of patients were lost to follow-up, and 10.6% succumbed before the commencement of induction therapy. Treatment modalities included induction with ATRA-IDA for high risk and ATRA-ATO for low and intermediate risk patients. Post-induction bone marrow biopsy underscored therapeutic efficacy, with 90.6% of patients demonstrating morphological remission. MRD was done at 3, 6, 12 and 18 months interval.

Conclusion: In consonance with the paradigmatic success observed in chronic myeloid leukaemia (CML), the intricate exploration of molecular and cytogenetic landscapes in APL has significantly propelled diagnostic precision and therapeutic strategies. This evolutionary trajectory not only signifies a triumph in APL management but also serves as a benchmark for the broader landscape of cancer diagnostics and the implementation of molecularly targeted therapeutic approaches.

BSH24-EP02 | c-MYC gene expression in haematological malignancies: Diagnostic and prognostic value

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Introduction: Haematological malignancies refers to a group of neoplastic conditions of lymphoid and haematopoietic tissues, which results in leukaemia, lymphoma and myelomas. The important role of gene expressions in haematological malignancies and cancers in general has become an area of interest in view of diagnosis and prognosis. Nuclear oncogenes that are an essential part of cell differentiation, often being pivotal genes in developmental and cell cycle regulation, are also implicated in cancer progression. c-MYC plays a vital role in the regulation of cell proliferation and also has been well-associated with tumorigenesis. This study was aimed at comparing c-MYC expression in haematological malignancies and apparently healthy subjects as well as assess its diagnostic and prognostic role.

Methods: A total of 32 newly diagnosed haematological malignancy patients presenting at the Haematology Daycare Clinic of the University of Calabar Teaching Hospital, Calabar, Nigeria were sampled for the analysis of c-MYC gene expression and immunohistochemistry. Twelve apparently healthy control subjects were randomly enrolled. Plasma c-MYC expression was determined by quantitative real time PCR using EVA Green chemistry and the cluster of differentiation markers, analysed by immunocytochemistry.

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Result: Plasma c-MYC was higher in subjects with haematological malignancies (8.8 ± 1.1) when compared with apparently healthy controls (4.5 ± 0.5). A screening cut-off c-MYC ratio value of 9.42 with a sensitivity and specificity of 65.5% and 100%, respectively, were obtained using the receiver operator characteristic curve analysis. Plasma c-MYC was found to have no prognostic value using the Kaplan–Meier analysis.
Conclusion: Plasma c-MYC ratio showed promising screening/diagnostic values for haematological malignancies.
Keywords: c-MYC, cancer, cancer diagnosis, cancer screening, diagnosis, haematological malignancies, plasma c-MYCprognosis, q-PCR.

BSH24-EP03 | Relationship of endogenous cytokines TNF, TGFβ1 in acute myeloblastic leukaemia with severity of cytopenia

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The dominance of a certain type of cytopenia may depend on the variant of acute myeloblastic leukaemia (AML) and on the secretory properties of blasts that produce cytokines, antagonists, TNF and TGFβ1. However, the final role of these molecules in the occurrence of cytopenia is not sufficiently understood.
A comparative analysis was conducted and the correlations of the TNF, TGFβ1 level and hemogram in AML were characterised. According to the WHO classification of anaemias, the AML patients (pts) ($n = 36$) were divided into groups, depending on the severity of anaemia. The severity of anaemia was correlated with thrombocytopenia ($r = 0.80$). In the group of pts with life-threatening anaemia, the highest content of TNF in the plasma was determined, and a strong inverse correlation of its value with the level of Hb was established ($r = -0.72$). The presence of an inverse correlation dependence of average strength between the level of TNF in the supernatant (Sp) of the blasts and Hb ($r = -0.48$) of the patients with life-threatening anaemia was established. It was found that the concentration of TGFβ1 in the Sp was directly correlated with the number of erythrocytes ($r = 0.89$) and platelets ($r = 0.38$).
On the basis of a significant difference ($p < 0.05$) in platelet levels, a study of TNF, TGFβ1 was conducted in AML patients with thrombocytopenia complicated by haemorrhagic syndrome and in AML patients with thrombocytopenia without of haemorrhagic syndrome. In the patients with haemorrhagic syndrome, a significantly lower content of TGFβ1 in the Sp ($p < 0.05$), and a significantly higher ($p < 0.05$) level of TNF in plasma were found. An inverse correlation was established ($r = -0.60$) between the concentration of TNF and the level of platelets. No correlation between the level of cytokines, TNF, TGFβ1 and the number of blasts was found in the compared groups of AML patients.
The obtained results indicated a relationship between the level of TNF and TGFβ1 and the severity of cytopenia, especially in AML patients with life-threatening anaemia and in pts with haemorrhagic syndrome. This provided the reason to consider the development of cytopenia in AML not only as a result of mechanical displacement of normal haematopoietic cells by blasts but also as a consequence of the cytotoxic dose-dependent effect of TNF and TGFβ1 on myelopoiesis.

BSH24-EP04 | How does chemotherapy affect elderly AML patients?

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Background: Acute myeloid leukaemia (AML) incidence increases with advancing age. Patients' age, fitness, comorbidities and treatment tolerance are factors influencing the choice of therapy in this age group.
Methods: This is a retrospective single centre study of 226 elderly (≥60 years) patients newly diagnosed with AML at Oncology Centre Mansoura University. The median age was 67 years: 128 were males and 98 were females. Eighty-two patients received standard induction (7 + 3), 85 patients received reduced intensity treatment, for example low dose cytarabine or hypomethylating agents, while 59 patients were fit only for cytoreductive therapy + transfusion support. Adverse events secondary to therapeutic agents were collected and documented according to WHO toxicity grades.
Results: Low intensity treated AML patients had a lower complete remission (CR) rate (4.7%) and slightly higher induction death rate (34.1%) than patients who received standard intensity regimens. There was a significant difference in CR and treatment failure rates between the intensive therapy and low-intensity therapy AML groups ($p < 0.0001$). Serious haematological adverse events (grade 3–4 severe toxicity) were reported in 108/167 (64.7%), 112/167 (67.81%) and 141/167 (84.4%) patients as regard anaemia, neutropenia and thrombocytopenia, respectively. Pulmonary disorders were significantly associated with induction death in patients treated by standard induction protocols in comparison to those treated by other lower intensity regimens (p 0.043).

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Conclusion: Intensive therapy in elderly AML patients is associated with better CR and lower treatment failure rates than low-intensity treatment. We should not depend on age alone in deciding treatment for this subgroup of AML. Comorbidities should be carefully assessed at baseline, and prompt management of adverse events is highly required in this age group.

Keywords: adverse events, comorbidity, elderly AML.

BSH24-EP05 | Acute myeloid leukaemia in adolescents and young adults: A distinct entity?

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Background: As acute myeloid leukaemia (AML) is generally a disease of older age; limited information exists regarding the features and outcomes of adolescents and young adults (AYAs) with AML.

Methods: In this retrospective cohort study, all patients between the ages of 15 and 39 diagnosed with AML at our institution through the years of 2013–2023 were included in the analysis. Moreover, through the utilisation of propensity score matching, a control group of intensively treated older adults (OAs) diagnosed with AML during the same period was generated for comparison.

Results: A total of 105 patients were included in the analysis with 52 (49.5%) in the AYA group and 53 (50.5%) in the OA group. Median follow-up time was 20 months (range 1–109). The median age of diagnosis was 27.5 (range 16.0–39.0) in the AYA group compared to 63.0 (range 51.0–72.0) in the OA group ($p < 0.001$). The distribution of cytogenetic profiles was significantly different between groups ($p = 0.007$); with a higher incidence of complex cytogenetic profiles among OAs (26.4% vs. 5.8%) while AYAs had a higher incidence of CBFB, KMT2A, and RUNX1 rearrangements. Interestingly, there were no significant differences in the incidence of NPM1 (32.7% vs. 34.0%) and FLT3-ITD (28.8% vs. 26.4%) mutations among AYAs and OAs. OAs had a higher incidence of myelodysplasia-related genetic mutations and cytogenetic abnormalities ($p = 0.027$). Utilising the ELN 2022 AML risk stratification score, a significantly higher percentage of AYAs exhibited favourable genetic risk profiles (50.0% vs. 26.4%, $p = 0.045$), whereas a significantly greater number of OAs displayed adverse genetic risk profiles (43.4% vs 28.8%, $p = 0.045$). Overall-survival (OS) was significantly different between the groups, with a 3-year OS of 48.2% [95% CI 34.3–62.1] for AYAs versus 23.9% [95% CI 10.4–37.4] for OAs ($p = 0.007$). The 3-year leukaemia-free survival (LFS) rate was also significantly higher for AYAs when compared to OAs [44.1% (95% CI 30.4–57.8) vs. 21.5% (95% CI 9.2–33.8), $p = 0.003$]. At multivariate analysis, favourable ELN risk grouping, complete remission after induction, and minimal residual disease negativity during consolidation were associated with superior OS and LFS; while not undergoing allogeneic haematopoietic stem cell transplantation was associated with inferior OS and LFS.

Conclusions: Our study has demonstrated that AYAs possess distinct biological and genomic disease characteristics along with superior OS and LFS when compared to their adult counterparts. Larger multicentre prospective trials are required to further evaluate the differences in genomic profiles and outcomes among AYAs and OAs.

BSH24-EP08 | Real-world data on venetoclax-based non-intensive chemotherapy for AML in an elderly, rural population

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Background: Older acute myeloid leukaemia (AML) patients have a bleak prognosis, but venetoclax with azacitidine (Ven-Aza) or low-dose cytarabine (Ven-LDAC) has been shown to have good response rates with tolerable safety in patients otherwise unfit for chemotherapy. Our centre in Cornwall serves an older, lower-income population than average, spread across a large, rural area. Some patients travel long distances for multiple days per cycle. We admit patients for week 1, cycle 1 to manage potential adverse events.

Methods: Data were retrospectively analysed for all patients who received at least one cycle of Ven-Aza or Ven-LDAC for untreated AML up to November 2023. Fifteen patients were included (13 Ven-Aza, 2 Ven-LDAC). The primary outcome was the response rate. Secondary outcomes included the need for dose reductions or delays, and serious adverse events leading to hospitalisation or death.

Results: Median patient age was 76.6 years. All patients were unfit for intensive chemotherapy. Eight had adverse risk genetics as per ELN guidelines, and six intermediate risk.

The overall response rate was 87%, with 13 patients achieving a complete or partial response. Best response could not be determined for the remaining two patients, who died before repeat bone marrow assessment. Eleven patients achieved a complete response (CR) or complete response with incomplete count recovery (CRi). Median follow-up time was 7 months. Longer follow-up is required to comment on overall survival.

The median number of cycles received was 3.5 (range 1–16). Three patients received only 1 cycle of treatment. During treatment, reduced dose-durations were required for venetoclax (11 patients) and azacitidine (6 patients). Eleven patients experienced cycle delays. Overall, all of the 12 patients who received more than 1 cycle of chemotherapy required reductions or delays in treatment due to cytopenias.

Infection was the dominant serious adverse event requiring hospitalisation, with 10 patients treated for infection in Cycle 1 and 3 in later cycles. Six patients died during follow-up:

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Three due to AML, two due to infection and one due to relapse of pre-existing MDS.

Conclusion: Our data shows that venetoclax-based non-intensive chemotherapy is a well-tolerated and effective treatment option in this population, despite significant time and travel commitments. Our response rates reflect those shown in other trials, however, nearly all patients required dose reductions or delays. Infection was the foremost serious adverse event, particularly in Cycle 1, supporting our practice to admit patients for Cycle 1 with a low threshold for longer inpatient monitoring.

BSH24-EP09 | Precise FISH panels guided by population prevalence may assist pragmatic diagnosis of Ph-like ALL

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Introduction: Diagnosis of Philadelphia chromosome like ALL (Ph-like ALL) in the real-world remains challenging because of definitional complexities, the diverse diagnostic techniques available and the cost, skill and time involved. We summarise evidence for diagnosis of Ph-like ALL using fluorescent in-situ hybridization (FISH) targeting only clinically important and actionable lesions, an accessible and cost-effective diagnostic technique.

Methods: Electronic databases were interrogated using broad MESH terms for articles reporting a detailed FISH strategy for diagnosis of Ph-like ALL published since 2014, yielding 653 full text articles and abstracts. We searched the National Library of Medicine Databases including PubMed, Medline, Embase, Cochrane and relevant abstracts. We included studies with a primary aim of determining the utility of FISH for Ph-like ALL diagnosis and studies with broader aims demonstrating Ph-like ALL diagnostic algorithms which partially involved FISH.

Results: Nineteen studies met inclusion criteria. Evidence for FISH to detect CRLF2 rearrangements in Ph-like ALL is strongly established and evidence for FISH to detect non-CRLF2 lesions is evolving rapidly. We documented 1620 non-CRLF2 Ph-like diagnostic FISH published results. Confirmatory side-by-side methods were applied in six studies (246 samples), four of which demonstrated 100% concordance of FISH results with alternative methods, while two studies demonstrated over 70% sensitivity and specificity. Additional studies demonstrated wide utilisation of FISH in Ph-like ALL classification across diverse geographies and ethnicities, with contrasting prevalence, implicating a need for targeted FISH strategies.

Conclusion: In real-world cohorts, it may be clinically useful to prioritise limited early FISH in B-ALL diagnostic algorithms to identify Ph-like abnormalities that respond to locally available kinase inhibitors to promote and prioritise broad access to effective targeted treatment. Additional studies are required to provide adequately powered validations and verifications of targeted Ph-like FISH panels to confirm sensitivity and specificity against side-by-side gold standard methods, and to define optimal local approaches.

BSH24-EP10 | Identifying low risk AML patients on azacitidine and venetoclax that do not require inpatient monitoring

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Tumour lysis syndrome (TLS) is a condition that is characterised by metabolic abnormalities that can lead to life threatening complications. Acute myeloid leukaemia (AML) patients starting on azacitidine and venetoclax combination chemotherapy have been shown to have a 1% risk of developing TLS during the first 3 days of ramp up dosing for venetoclax. These patients are therefore monitored as inpatients. This analysis aims to identify a cohort of low-risk patients that do not require inpatient monitoring by stratifying TLS risk.

Data were collected from electronic and paper records from AML patients that started on azacitidine and venetoclax for a period of approximately 3 years from 2020. The data were analysed and patients were stratified into risk categories derived from Cairo et al. (2010) and the summary of product characteristics for venetoclax. Low TLS risk was classified as LDH <2 the upper limit of normal, WCC <25, BM blasts <90% and creatinine clearance >30 mL/min.

A total of 18 patients were identified which included: 12 males, six females and the median age was 75.5 years. All patients received allopurinol prophylaxis and oral hydration pre-treatment. Of these, 15 patients were categorised as low risk for TLS. Of the three patients who were high risk, only one developed laboratory signs of TLS during treatment. This patient was treated with IV hydration and rasburicase with complete resolution of TLS.

All 15 low risk patients received monitoring and management that could have been delivered in the day unit setting. This analysis showed that all patients spent at least 8 days as an inpatient (despite the fact they could be transitioned to the day unit from Day 4 onwards). This was due to logistical and capacity difficulties of changing patients over to the day unit setting midway through treatment. If all low risk patients were managed in the day unit, this would have potentially saved 120 inpatient days (an approximate cost saving of £48 000). These inpatient beds could be used to treat other patients with more urgent needs as well as avoiding putting patients at risk of hospital associated infections.

In conclusion, this analysis shows that a personalised risk based approach to TLS monitoring can be taken for AML patient starting on azacitidine and venetoclax and low risk patients do not need to be monitored as inpatients.

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BSH24-EP11 | An observational study of AML patients treated with vyxeos chemotherapy—A single centre

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CPX-351 (Vyxeos) is a liposomal formation of daunorubicin and cytarabine. It is licensed for use in therapy related AML and AML with myelodysplasia related cytogenetic/molecular changes.

The aim of this study was to evaluate the rate of complete morphological remission (post induction and consolidation), median survival and number of patients reaching allogenic stem cell transplant in the Blackpool Victoria Hospital cohort of patients (over the age of 18 years) treated with Vyxeos.

Retrospective data were collected from patient records who received at least one cycle of CPX as induction therapy and their subsequent consolidation therapy (if administered). All patients given Vyxeos were treated with the aim of reaching allogenic stem cell transplant.

A total of 27 patients received Vyxeos as induction therapy. The ICC classifications were as follows; 8/27 patients had a diagnosis of AML with myelodysplasia-related gene mutations, 5/27 had AML with myelodysplasia-related cytogenetic abnormalities, 4/27 had CMML (Chronic Myelomonocytic Leukaemia) and 10/27 with other individual molecular or cytogenetic defining mutations. 9 patients (33%) were aged <60. Median overall survival from this study was 20 months for all patients.

The treatment related mortality in induction (cycle 1) was 1 patient (4%). Of the 25 patients with data available, 18 (72%) patients achieved complete morphological remission (CMR), 1 (4%) partial remission, 5 (20%) refractory disease and 1 (4%) aplasia. Seventeen patients who achieved CMR received ≥2 cycles as consolidation. Seven of these were dosed using Summary of Product Characteristics (SPC) and 10 received dosing as per the AML-18 Trial.

Seventeen patients (65%) received two or more cycles of Vyxeos. Five patients (20%) received one cycle as induction and a different consolidation chemotherapy. Two patients (8%) were transplanted after one cycle and one patient (4%) is still awaited.

Twenty-five patients were considered for allogenic transplant. Eighteen (72%) of patients underwent the transplant. A substantial proportion of patients therefore reached potentially curative therapy.

In summary, of the total 27 patients studied, 26 survived cycle one of Vyxeos induction. Also, 18/26 patients (69%) achieved complete morphological remission post the first induction cycle. Of 26 patients with data available, 18 patients (69%) reached transplant. In addition, 7/17 (41%) patients who received Cycle 2 of Vyxeos received the SPC dose, 10/17 (59%) were dosed as per AML-18 trial dosing. In order to rectify this, changes were made to prescribing of Vyxeos on iQemo, including a clearly stated dose and timelines for administration during the induction and consolidation cycles.

BSH24-EP12 | Long term outcomes of stem-cell-transplant in older patients with AML treated with venetoclax HMA therapies

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Allogeneic haematopoietic stem cell transplantation (SCT) remains the most effective curative treatment for patients with intermediate- and poor-risk acute myeloid leukaemia (AML); however, patients who are ineligible to receive intensive chemotherapy (IC) due to age or comorbidities have typically not been candidates. Venetoclax (Ven) in combination with hypomethylating agents (HMAs) leads to rapid and durable remissions in newly diagnosed (ND) patients with AML who are ineligible for IC.

To evaluate the long-term clinical outcomes of SCT after Ven + HMA treatment in this patient population.

Patients with ND AML ineligible for IC who received Ven + HMA and proceeded to SCT on the phase 1b, open-label (NCT02203773) trial of Ven plus decitabine (Dec) or azacitidine (Aza) and the phase 3 VIALE-A trial (NCT02993523) of placebo + Aza versus Ven + Aza were included.

Patients in the phase 1b trial received Ven daily (400, 800, or 1200 mg) with either 20 mg/m^2 intravenous (IV) Dec on days 1–5 or 75 mg/m^2 subcutaneous (SC) or IV Aza on days 1–7 of 28-day cycles. Patients in VIALE-A received Ven daily (400 mg) with 75 mg/m^2 SC or IV Aza on days 1–7 of 28-day cycles. Patients were evaluated for efficacy outcomes before and after SCT.

Thirty-three patients were included in this analysis (31 from the phase 1b trial, 2 treated with Ven + Aza from VIALE-A). Patients had a median age of 69 years, the median time

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on Ven before SCT was 4.18 months (range, 0.9–31.8), and the median time from last dose of Ven + HMA to SCT was 1.22 months (range, 0.4–10.3).
Before SCT, 27 patients achieved a best response of complete remission (CR)/CR with incomplete haematological recovery (CRi), 3 achieved morphologic leukaemia-free state (MLFS), and 3 had resistant disease. Median time to CR/CRi was 1.9 months (range, 0.8–7.1), 9 patients had a measurable residual disease (MRD) response of $<10^{-3}$. Median OS after SCT was 29.9 months (95% CI, 15.8–NR), with a 69% 12-monts post-SCT OS rate.
In patients with MRD responses before SCT, the 12-months-post-SCT OS rate was 76%. In 18 patients with adverse ELN risk disease, median OS was 15.8 mo (95% CI, 4.5–29.9), and the 12-mo-post-SCT survival rate was 56%.
Ven + HMA can lead to rapid and deep responses in patients with ND AML ineligible for IC. Most patients were alive ≥12 months after SCT, including approximately half of those with adverse ELN risk disease. These results suggest that Ven + HMA can enable receiving SCT and long-term disease-free states in patients who are ineligible for IC.

BSH24-EP13 | A multiomic, single-cell measurable residual disease (SCMRD) assay for phasing DNA mutations and surface immunophenotypes

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Background: The small population of cancerous cells that remain following treatment, known as measurable residual disease (MRD), is a strong predictor of relapse in acute myeloid leukaemia (AML). Often, these refractory cells have gained additional resistance mutations or changed their surface immunophenotypes in ways that preclude detection or discrimination from preleukemic clones by current gold standard flow cytometry or bulk NGS assays. For this reason, a multi-omic single cell MRD assay could offer a more comprehensive indicator of relapse and the potential for faster response.
Aims: Here, we present a new single-cell MRD (scMRD) assay with a 0.01% limit of detection, while also giving single cell clonal architecture and immunophenotyping to not only identify residual leukaemia cells, but also identify putative DNA or protein targets for salvage therapy.
Methods: The assay enables rare-cell detection on a standard Mission Bio Tapestri run by adding: (i) an upfront bead-based protocol to enrich for blast cells, (ii) a DNA and protein panel specifically designed for AML MRD diagnosis and treatment in alignment with both ICC and ELN guidelines, and (iii) a new automated analysis pipeline to evaluate single cell multiomics output. In addition, the multiplexing of up to three patient samples combined in one run via germline identification further reduces per sample costs and increases throughput.
Results: Through the use of Mission Bio's technology for detecting DNA variants in single-cells, this pipeline leverages variant-specific error modelling and single-cell co-occurrence to sensitively detect de novo variants, reducing false positive rates to achieve an LOD that meets and exceeds the recommended 0.1% cut-off for MRD-positivity by flow cytometry. It furthermore reconstructs the phylogenetic tree of the detected MRD cells, presents their surface protein signature and arm-level copy number changes. To demonstrate these features on MRD down to 0.01%, we present data from samples constructed by titrating diseased cells into healthy bone marrow cells before processing them with the scMRD assay.
Conclusion: Combining high sensitivity with multi-omics, this assay offers a potential scalable solution for comprehensive AML MRD detection and guiding therapeutic decision-making.

BSH24-EP14 | Morbidity and mortality outcomes in acute myeloid leukaemia patients treated with venetoclax and azacitidine chemotherapy

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Background: Venetoclax and azacitidine chemotherapy has been shown to be an efficacious regime for older patients with acute myeloid leukaemia (AML) that are not fit for intensive treatment. The aim of this study was to assess survival outcomes and morbidity in our patients during their first cycle of treatment, which we currently deliver as an inpatient at our district general hospital.
Methods: From 2020 to 2023; 15 patients were treated with venetoclax and azacitidine and 1 patient was treated with venetoclax and cytarabine. Retrospective data collection on demographics, cytogenetic risk group, presenting blood counts, period of neutropenia, infection rates, complications associated with treatment, blood transfusion requirements, outcomes and readmission was obtained for these patients.
Results: Sixteen patients were included in this study. The age range of patients was 71–85, with an average age of 78. Also, 10/16 (63%) patients had myelodysplasia associated AML, 3/16 (19%) patients had disease associated with prior myeloproliferative neoplasm and 3/16 (19%) patients had AML with recurrent genetic abnormality. The mean duration of admission was 41 days and patients were deemed fit for discharge once their neutrophil count $>0.5\times10^9$/L. 6/16 (38%) patients presented with a haemoglobin <80 g/L and 3/16 (19%) patients presented with a platelet count $<20\times10^9$/L, whereas 9/16 (56%) patients were already neutropenic at presentation. The mean duration of neutropenia was 38 days, one patient did not recover their count. 15/16 (94%) patients required red cells, with a mean of 7 units transfused during the admission, 11/16 (69%) patients required platelets, with a mean of 3 units transfused during the admission. 10/16

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(63%) patients are still alive, the longest survival is currently 1 year and 11 months. There were four readmissions within 6 months of discharge.

Conclusions: Although the mean period of neutropenia was 38 days, it did not appear to correlate with an increased rate of infection and only one patient in our cohort had an isolated causative organism identified in relation to fever. Transfusion burden was high in this group of patients. However, readmission rate remains low. Cytopenia was a frequent reason for treatment cessation in addition to disease progression.

Overall this remains a well-tolerated regime for older patients with AML that would have otherwise had very limited treatment options previously.

BSH24-EP15 | Palliative haematology clinic for patients with bone marrow failure syndromes and acute myeloid leukaemia

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With the rapid advances in haematology treatments, more patients are surviving longer with incurable diseases and receiving palliative chemotherapy. These patients are often older with complex medical needs. There is an increasing body of evidence that these patients benefit from early integration with palliative care, resulting in improved quality of life with better control of physical and psychological symptoms. In September 2022 at East Kent Hospitals University NHS Foundation Trust I established a Palliative Haematology clinic designed for patients with bone marrow failure syndromes or acute myeloid leukaemia thought to be in the last year of their life. The clinic is run by a haematology consultant and a haematology clinical specialist nurse (CNS) both with an interest in palliative care. Patients were invited by their primary clinician and contacted by the CNS prior to the clinic to ensure they were fully informed about the clinic and given written information about topics discussed. The aim of the clinic is to discuss current symptoms, disease progression, symptoms and signs of dying and preferred place of death. In addition, a treatment escalation plan (TEP) is created and resuscitation status discussed. Patient are typically reviewed once in clinic with an hour appointment then followed up virtually. To date 21 patients have been referred to the clinic, 18 patients have been reviewed in the clinic (4 acute myeloid leukaemia, 2 myelofibrosis, 3 lymphoma, 7 myelodysplastic syndrome, 2 myeloma). All patients completed TEP and do not attempt resuscitation paperwork. Three patients died prior to attending clinic. Since attending clinic 7 patient have died, 5 died in their preferred place of death. After attending clinic 13 patients provided feedback. The feedback was very positive 92% of patients felt the clinic meet their needs and expectations, 100% of patient felt all their questions were answered and their concerns we listened to. Overall patients gave the clinic a score of 9.3/10. Patients reported a difficult topic was discussed with compassion and found the clinic useful and informative. This clinic has been well received by patients and made a positive impact in providing more holistic care for patients. Unfortunately, three patients died before attending clinic. To help increase capacity the aim is to extend to clinic to across all hospital sites with three clinics a month. The ambition for the future is to run the clinics in the local hospices to help further bridge the gap with palliative care.

BSH24-EP16 | Review of the acute leukaemia services at a district general hospital

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The Acute Leukaemia services had re-opened in 2021 at the West Hertfordshire Hospitals Trust. This involved immediate diagnosis and management at our centre.

In this audit, we aim to determine the performances of our Acute Leukaemia services, focusing on diagnosis and management of our elderly population, and scope for use of Frailty Scales in stratifying patients and their treatment options.

Since 2021, 48 patients were diagnosed with Acute Leukaemia. We identified 46 patients suitable for auditing, collecting data that includes:

Patient age, ECOG (Eastern Cooperative Oncology Group) status, cytogenetics and molecular analysis, location/intent of treatment, date of diagnosis, MDT discussion, treatment induction/duration, reasons for cessation, and PFS (progression-free survival).

26/46 patients were 65 yo+, mean age = 77.4 years. 16/46 patients had an ECOG of 2+.

APML (Acute Promyelocytic Leukaemia) and ALL (Acute Lymphoblastic Leukaemia) patients (1 and 7 respectively) were immediately transferred to tertiary centre for treatment. Of the remaining AML (Acute Myeloid Leukaemia) patients, 17/38 were transferred to a tertiary centre at some point in management. 21/38 patients were managed locally, all 70yo+. 15/21 were started on curative treatment, 6/21 for non-curative.

Chemotherapy provided locally:

Venetoclax-Azazytidine—14/15.
Venetoclax-Cytarabine—1/15.
Azacytidine + Hydroxyurea—1/6.
No treatment—5/6.

Outcome of treated patients: 3/16 remained stable/in remission, 4/16 stopped treatment due to unrelated comorbidities, 6/16 stopped treatment due to chemotherapy-related adverse effects, and 3/16 stopped treatment due to progression of disease.

Transfer of patients to tertiary centres limits the experience and exposure of district general hospitals to acute leukaemia

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patients, which detriments the expertise of treating staff. Improving links with the tertiary centre, acute leukaemia MDT, and involvement in national clinical trials, would provide us with the specialist expertise to improve treatment outcomes and develop the skills of the staff, to provide the highest quality of care for our local population.

Upgrading our hospital pathways will allow us to expand capacity to treat acute leukaemia patients. This would include 24/7 availability of the chemotherapy pharmacy, and direct admitting rights to the haematology ward.

Our evidence indicates room for improvement in treatment of elderly patients with acute leukaemia. Guidelines advocating the use of geriatric assessment tools can help predict shorter overall survival and prevent adverse outcomes in those who would likely not benefit from certain treatments. Inclusion of palliative care and care of the elderly team to the local MDT can facilitate these decisions and discussions.

BSH24-EP17 | Real-world experience of venetoclax with azacitidine or cytarabine for the treatment of acute myeloid leukaemia

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Acute myeloid leukaemia (AML) is the most common acute leukaemia in the adult population, with greatest incidence rates in elderly patients. Older patients diagnosed with AML are frequently not candidates for intensive treatment options due to existing co-morbidities, genomic features, and frailty, leading to limited treatment options and subsequent poorer outcomes. In this challenging patient population finding effective treatment options for AML is difficult. Venetoclax in combination with azacitidine or cytarabine are reported to be good treatment options for elderly patients with AML in clinical trials and literature. This report aims at investigating and document our 'real world' experience of venetoclax in combination with azacitidine or cytarabine in the treatment of AML at Sunderland Royal Hospital.

Thirteen patients who were diagnosed with AML at Sunderland and South Tyneside NHS foundation Trust between the period of May 2020 and August 2022 were reviewed. Twelve patients received venetoclax and azacitidine therapy and one patient received venetoclax and cytarabine. Patients' co-morbidities, cytogenetics, FLT3 and NPM1 status, and overall response was considered as part of this review, as well as the significance of cytopenia as a side effect of therapy and inpatient/outpatient visits to hospital. Each cycle was reviewed up until at least ten cycles had been given, August 2022 or the patient's death.

Our experience showed that 81% of patients treated with venetoclax plus azacitidine or cytarabine survived 6 months and 67% of patients survived one year after their diagnosis of AML. We feel that these are very good outcomes for patients who otherwise would have a poor outlook.

Cytopenia is a common side effect of chemotherapy, and 53.8% of patients required dose and frequency titrations of therapy due to cytopenia.

As with any patient cohort, it is important to not only consider the chance of remission with treatment as well as the side effect burden but also the effect of treatment on the quality of life of our patients. We found that in our patient cohort, patients can expect an average of 34.8 days as an inpatient, mainly in the first cycle of therapy. Outpatient visits averaged 34.4 across a pateint's treatment course.

We will present our experience at Sunderland Royal Hospital managing AML in a challenging patient population with venetoclax and azacitidine/cytarabine which provides improved disease control, aims at disease remission, is tolerable and can return extended quality of life in those that respond.

BSH24-EP18 | High survival rate in haematology patients admitted to ICU in a tertiary referral centre

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Patients with haematological conditions, particularly those undergoing intensive systemic therapy allogeneic stem cell transplant (alloSCT) and immune effector cells (IECs), are at risk of becoming critically unwell and requiring intensive care unit (ICU) admission for organ support. The aim of this study was to review reasons for admission to ICU admission and outcomes of patients with underlying haematological disease admitted to ICU in our centre.

A retrospective electronic and paper case note review was performed of all patients, age 16 or over, with a haematological diagnosis admitted to ICU between April 2022 and April 2023 at a tertiary level 3 centre, including patients with non-malignant conditions, malignancies undergoing systemic anti-cancer therapy including autologous and allogenic SCT and IECs.

There were 43 admissions to ICU (including 1 patient admitted twice): 23 were female and 20 male. The median age was 63 (range 19–75) at the time of admission, with median age of 67 in those who died on ICU. Most (93%) had haematological malignancies (HM) and 7% had sickle cell disease. Of those with HM: 43% had acute leukaemia, 35% high-grade lymphoma, 5% low-grade lymphoma, 5% multiple myeloma and 5% myelodysplastic syndrome. In the patients with HM: 40% were undergoing chemotherapy, 27.5% had received an alloSCT, 2.5% an autoSCT, 22.5% had received IECs and 7.5% were not undergoing active treatment. The primary reason for ICU admission was sepsis in 16 (37%), immune effector-cell associated syndrome/cytokine release syndrome in 7 (12%) respiratory failure in 6 (14%), reduced GCS in 3 (7.0%) and other causes seen in the remaining 11 (26%). At least one level of organ support was needed in 20 patients

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(47%): intubation in 23%, renal replacement therapy (RRT) in 23% and cardiovascular support in 26%. Non-ventilation respiratory support (positive airway pressure therapy or high-flow nasal oxygen) was required in 19%. ICU survival was 79% with a median ICU stay of 4 days (including those that died). Survival to hospital discharge was 69% (82% in those not requiring organ support in ICU compared to 55% in those needing some level of organ support) with a median of 22 days spent in hospital.

The survival rate for patients requiring ICU admission was high (69% at hospital discharge). Careful discussion with ICU teams and consideration of appropriateness for admission may contribute to this. Further research will review the patients referred, but not accepted, for admission to ICU and the timeliness of assessment.

BSH24-EP19 | Real-world outcomes for patients with acute myeloid leukaemia treated with venetoclax-azacytidine in north of England

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Background: Venetoclax and azacytidine (ven-aza) has been shown to be a useful regimen in treating AML; better tolerated than more intensive therapy and an option for patients who would not previously have been considered candidates for intensive therapy. We present outcome data for a real-world population-based cohort.

Method: A retrospective analysis was undertaken of outcome for all patients with newly diagnosed AML treated with ven-aza at our regional centre 1/2/20–1/9/23. Follow-up was to 1/12/23. The unit serves a population of 1.5 million people and four regional hospital trusts. Baseline characteristics including demographics, karyotype, FLT3 and NPM1 mutation status were recorded. Response data were collected alongside overall survival (OS).

Results: Forty-seven patients (16 female and 31 male) with non-APL AML were treated with ven-aza: 12 patients aged 60–70 years and 35 aged over 70 years. The number of patients treated each year with ven-aza is increasing with 3, 7, 19 and 18 treated each calendar year—note 2023 includes only 8 months of data. The number of patients aged over 60 and treated intensively were 5, 11, 7 and 5 in the same time periods. No patients in the ven-aza cohort moved to allogeneic transplant.

Median follow-up was 15.3 months. The median OS was 16.9 months (range 0–33.5 months), 2 year OS was 30%. Median OS of patients with complex karyotypes was 4 months and for non-complex karyotypes was 18.6 months ($p = 0.001$). Our data showed no survivors with a complex karyotype at 2 years, median 2 year OS for those with non-complex karyotype was 40%. In our population, NPM1 and FLT3 mutations status were not significantly associated with OS. Median time to relapse, for the cohort as a whole, was 7.2 months. Three patients died less than 30 days from treatment commencement: one due to pulmonary haemorrhage, two were sepsis-related. MRD was inconsistently measured but use was increasing over time.

Conclusion: Population-based data from our region 2007–2011 (McGregor et al., *Leuk Lymphoma* 2016;57:1575–84) demonstrated 2 year OS of 31% for intensively treated patients over 60 years old and 5% for those treated non-intensively. The present study of a chronologically older cohort, demonstrates encouraging results with a 2 year OS equivalent to the historic intensively-treated cohort. Outcomes for patients with complex karyotype remain very poor.

BSH24-EP20 | IKZF1 deletion in acute lymphoblastic leukaemia: A single-centre experience in Thailand

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Genetic deletions of IKZF1 have been extensively studied and associated with unfavourable prognosis outcomes in B-cell ALL. However, there is less clarity about the distribution and prognosis significance of the restricted IKZF1 deletion and concomitant IKZF1 deletion with CDKN2A/B, PAX5, and PAR1, so-called IKZF1plus deletion patterns in B-cell ALL. Here, we performed the MLPA assay to analyse IKZF1 deletion and common gain/loss of genes frequently observed in acute lymphoblastic leukaemia. Among 62 B-cell ALL (28 adults, 22 children, 2 adolescents and 10 infants), IKZF1 deletion was observed in 30.6% (19/62) and associated with shorter overall survival compared with patients who had no IKZF1 deletion ($p = 0.047$). Moreover, patients with IKZF1plus have shorter overall survival than those with IKZF1 alone and without IKZF1 deletion ($p = 0.0483$). Remarkably, patients with concomitant deletion of IKZF1 and BCR::ABL1 p190 positive exhibited shorter overall survival than patients with IKZF1 deletion alone and negative for IKZF1 deletion ($p = 0.0234$). In summary, we revealed the association between IKZF1 deletions and survival outcomes of patients with B-cell ALL. Without age-matched and therapeutic intervention comparisons, our data demonstrated

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that patients with IKZF1 and IKZF1plus have shorter overall survival than those without IKZF1 deletion, regardless of considering other genetic alteration backgrounds.

Keywords: BCR::ABL1 p190 positive, IKZF1, IKZF1plus, MLPA.

BSH24-EP22 | Targeting NOX2 overexpression in acute myeloid leukaemia using in vitro models

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Development of treatments that minimise treatment-resistance and prevent relapse are a priority in AML as event-free survival remains challenging. We have previously identified the overproduction of extracellular reactive oxygen species (ROS) by blasts from the majority of AML patients (>60%). ROS play an important role, not only in immune defence, but also regulate intracellular signalling and are contributing factors in several cancer models. In AML, ROS are generated by NADPH oxidase (NOX) proteins, specifically NOX2. However, the genetic basis of ROS heterogeneity in AML and its role in cell survival has not been characterised. This study aims to characterise NOX2-dependent ROS production in AML and how deletion of NOX2 or inhibition of NOX2 impacts cell survival and proliferation.

Initially, we investigated extracellular ROS production in AML patient blasts using luminol based chemiluminescence and found higher ROS levels to be associated with more differentiated AML subtypes. There was no significant association with specific molecular abnormalities though the sample size is low ($n=16$). ROS producing AML patient blasts were treated with the NOX2 specific inhibitor GSK279503 (3 μM) for up to 18 days, while ROS production was inhibited by 2.6–56-fold, cell proliferation and cell viability was not impacted using ToPro-3 and flow cytometry. To explore this further, CRISPR-CAS9 was used to knockout (KO) NOX2 (CYBB), validated by NOX2 protein expression using flow cytometry in two AML cell lines. NOMO-1 and THP-1 KO lines produced 500-fold and 2-fold less ROS than controls, respectively. ROS production was inhibited in these cell lines by 3 and 7-fold respectively, using GSK279503 (3 μM). The impact of NOX2 KO or GSK279503 NOX2 inhibition on AML cell line survival and proliferation was assessed by proliferation and viability monitoring or colony assay. No significant change was found in any of the conditions tested. However, co-culture assays with a ROS producing line (NOMO-1) and a non-ROS producing line (U937) increased proliferation of U937 cells by 2-fold; an effect lost when co-culturing U937 cells with NOX2 KO NOMO-1.

In summary, directly targeting NOX2-driven ROS in AML in vitro alone did not suggest that ROS is a useful individual therapeutic target in AML. However, combination therapy may be necessary to capitalise on the high ROS present in most AML patient blasts. The work presented here has laid the foundation to identifying whether new targets can be identified with synthetic lethality with inhibition of NOX2-dependent ROS.

BSH24-EP23 | Phase 3b design: Comparing treatment preference between oral decitabine/cedazuridine and azacitidine in patients with leukaemias

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Introduction: There is uncertainty about how choice of therapy in myelodysplasia (MDS), low-blast count acute myeloid leukaemia (LB-AML) or chronic myelomonocytic leukaemia (CMML) is made by patients, physicians and carers when >1 treatment type is available. This study's primary objective is to compare patients' treatment preference using the patient 'treatment preference in myelodysplasia questionnaire' (pTPMQ). Secondary objectives include evaluation of preference by carers (cTPMQ), and clinicians (mTPMQ).

Methods: This phase 3b, open-label, multi-centre study (NCT05883956), with sites in Australia and New Zealand, will compare preference between oral decitabine/cedazuridine (Treatment A) and subcutaneous azacitidine (Treatment B). The study design includes 28 days of screening, four continuous 28-day cycles of study treatment, and a follow-up period with two 28-day cycles of continued therapy. Patients ($N=42$) will be randomised to two balanced treatment sequences: ABBA or BAAB. Patients will express a preference twice in the study, first after completing Cycle 2, then after completing Cycle 4. This will be assessed via the patient treatment preference in myelodysplasia questionnaire. Clinician and carer preference will also be assessed. Inclusion criteria are age ≥18 years, diagnosed with International Prognostic Scoring System (IPSS) Int-2, IPSS High-Risk MDS, IPSS revised int-MDS, LB-AML or CMML, Eastern Cooperative Oncology Group (ECOG) 0–2 and life

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expectancy ≥6 months. Exclusion criteria are known hypersensitivity to study treatments, advanced malignant hepatic tumours, severe renal impairment (creatinine clearance <30 mL/min) severe cardiac disease and previous hypomethylating agent treatment.

Results: Trial to be activated in Australia and New Zealand, with first patient recruited in December 2023. We will describe the primary and secondary objectives. Exploratory objectives including treatment discontinuation rates, quality of life and safety of subcutaneous azacitidine and oral decitabine/cedazuridine will also be described.

Conclusions: This study aims to address an evidence gap in the comparison of patients', carers' and clinician's preference between an oral and a parenteral treatment, preference strength, and the reasons for it.

BSH24-EP24 | Outcomes of venetoclax based therapy for AML patients—A UK DGH real world experience

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Since March 2020 venetoclax in combination with azacytidine or low dose cytarabine (LDAC) has been funded through national commissioning and available as an option for treatment of patients with acute myeloid leukaemia (AML) who are ineligible for intensive chemotherapy. We report on a series of consecutive AML patients treated with venetoclax based therapies.

Musgrove Park Hospital is a large UK District General Hospital covering a population of approximately 500 000. Data from patients treated with venetoclax based therapies according to the national guidance was collected. Twenty patients were identified from February 2021 to November 2023. Patients age ranged from 56 to 83 with median of 75 years. There was a 7:3 male preponderance. 74% patients were categorised as poor risk disease based on genetic and molecular profiling. Nearly all patients were treated with azacytidine 95% rather than LDAC 5%.

Patients were treated with 21 days of venetoclax prior to bone marrow assessment. The main side effects included neutropenia fever (14) including sepsis related mortality (4), prolonged cytopenias >49 days (5), renal impairment including tumour lysis (4). Five patients had no significant side effects documented. Outcomes after the initial course showed 55%, 30% and 15% achieved remission, had refractory disease or treatment related mortality respectively. Thirteen patients received a second course and were treated with 100 mg of venetoclax given for 7, 14, 21 and 28 days to 1, 6, 2 and 4 patients respectively. The time between first and second course ranged from 28 to 86 days with a median length of 43 days. There were fewer side effects post course 2 but included neutropenic fevers (3), prolonged neutropenia (6) and no significant side effects (6). Eleven patients proceeded to Course 3 with dosing schedules of 14, 21 and 28 days of venetoclax for six, three and two patients. The total number of courses for each patient ranged from 1 to 13 with median of three courses. No patients proceeded to allograft consolidation. At time of censoring 40% patients were alive with length of survival ranging from 33 to 543 days. Ten patients survived longer than 6 months and 6 longer than 9 months.

These results highlight several points: relatively high remission rates in a cohort of patients with poor risk disease; significant rates of side effects especially during course 1 highlighting the need to have close supervision of these patients; significant and variable development of cytopenias requiring the need for aggressive dose reduction.

BSH24-EP25 | How much is too much? Audit of routine biochemistry requests for AML inpatients on chemotherapy

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Introduction: AML (acute myeloid leukaemia) patients undergoing inpatient chemotherapy regimens require repeated blood investigations to monitor expected haematological and biochemical abnormalities and guide their correction. However, staff often fall into the trap of requesting additional biochemical investigations that are not indicated alongside the daily full blood count (FBC) and urea and electrolytes (U&E) blood tests 'just in case'. Unfortunately, these extra tests add little value to patient management, add to the costs of health care and often lead to further investigations and overtreatment.

This audit set out measure how often LFTs (liver function tests), CRP (C-reactive protein), Calcium and phosphate blood tests were done for AML in patients undergoing chemotherapy and frequency of abnormal results.

Methods: Laboratory records of patients admitted on the haematology ward of a London Hospital, for chemotherapy with daunorubicin/cytarabine, single agent cytarabine, venetoclax/azacytadine and FLAG (fludarabine, cytarabine, G-CSF) regimens between May to October 2023 were examined for results of the following parameters: CRP, calcium, phosphate and LFTs (aspartate aminotransferase [AST], alanine transaminase [ALT] and total bilirubin). Data were recorded and analysed with Microsoft Excel.

Results: Nine patients were admitted during this period with 21 admission episodes. Total inpatients days was 625. LFTs were requested on 95.2% of inpatient days, CRP—77.92%, Calcium—81.76%, phosphate—80.64%. Bilirubin was elevated in 9.91% of requested tests, ALT—39.50%, CRP—83.37%. Abnormal calcium and phosphate results were 5.48% and 32.47% respectively.

Conclusion: The NHS is a healthcare system under financial strain, eliminating routine biochemical tests that do not add to patient management is one way to cut wastage and ensure scarce resources are effectively utilised. Having clear

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guidelines on what blood tests should be routinely requested and educating staff on the rationale for such guidelines are suggested interventions to reduce unnecessary blood tests. The service would then be re-audited to measure compliance with the set guidelines.

BSH24-EP26 | Management of acute leukaemia and pregnancy outcomes in patients with current or previous leukaemia

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Acute leukaemia (AL) diagnosed in pregnancy is a catastrophic clinical scenario with management based upon low quality evidence. There is also an absence of data on reproductive outcomes in previously treated AL women.

This observational study recorded the treatment and pregnancy outcomes of two groups: patients diagnosed with AL during pregnancy (current AL group; CALG) and previously treated AL patients who became pregnant (previous AL group; PALG). Cases from August 2009 to July 2022 were identified from eight UK units.

Of 39 screened cases, 12 CALG and 21 PALG cases were analysed. One woman belonged to both groups. In CALG, 12 pregnancies resulted in 10 deliveries (2 vaginal, 8 operative) of 10 infants, 1 induced abortion and 1 unknown outcome. Pregnancy complications occurred in one woman. 6/10 delivered prior to chemotherapy, two received chemotherapy both antenatally and postnatally and in two information was not available. At delivery, median Hb ($n = 10$) was 97 g/L and median Plt ($n = 10$) was 84.5×10^9/L. 1/10 infants was extremely preterm, two were very preterm and seven were moderate to late preterm. For seven infants, median birthweight was 1757 g, median centile 24.5. 8/12 women were alive at 2-year follow-up, three deceased and one had unknown survival status. All 10 infants were alive 28 days post-delivery.

The PALG comprised 25 pregnancies with 23 deliveries (14 vaginal, 7 operative, two unknown), one miscarriage and one with unknown outcomes. 3/25 infants were extremely preterm, one was very preterm, two were moderate to late preterm, 16 were full term with no information available for three. Pregnancy complications were reported in four women: breech presentation; haemorrhage and HELLP syndrome in two. At delivery, median Hb ($n = 16$) was 115 g/L and median PLT ($n = 14$) was 177.5×10^9/L. Seventeen infants were born at term. In 20 infants, median birthweight was 3257.5 g, higher than in CALG ($p = 0.011$, Mann–Whitney U test), median birthweight centile 32.5. 19/21 were alive 2-years post-delivery with two of unknown status. Also, 24/25 infants were alive 28 days after delivery with one unknown status.

AL diagnosed during pregnancy was generally managed with expedited delivery. Neonates from CALG had low birthweights and were premature. Most PALG neonates had normal birthweight with no medical complications. Our research would support expedited neonatal delivery where possible in CALG. For PALG, pregnancy outcomes appear to be in line with those for the general population.

BSH24-EP27 | Deciphering the puzzle: Acute leukaemias of ambiguous lineage

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Introduction: Classification of acute leukaemia involves assigning lineage by resemblance to normal progenitor cells. Acute leukaemias of ambiguous lineage (ALAL) are a heterogenous group of diseases that according to the 5th edition of WHO classification of Haematolymphoid tumours are arranged into two families: ALAL with defining genetic abnormalities and ALAL, immunophenotypically defined. ALALs include immature haematopoietic neoplasms that show no distinct evidence of specific lineage differentiation (i.e. acute undifferentiated leukaemia [AUL]), as well as those which express markers of more than one lineage (mixed phenotypic acute leukaemias [MPAL]). The objective of this study is to evaluate and refine diagnostic modalities for ALAL, aiming to enhance precision and accuracy in identifying this complex subtype in a developing country.

Methods: This is a retrospective study performed at Haematology Dept, Armed Forces Institute of Pathology, Rawalpindi from January 2019 till December 2023. All patients who were newly diagnosed as MPAL and AUL were included.

Results: Among the cohort of 23 diagnosed ALAL patients, male predominance was observed, reflected in a male-to-female ratio of 2.7:1. The median age was 27 ± 18.2 years. Fever was most common presenting complaint. Eighteen cases fulfilled the definition of MPAL and 5 cases as AUL. Molecular and FISH study revealed seven cases to be classified as ALAL with defining genetic abnormalities out of which four had BCR::ABL1 Fusion and three had KMT2A rearrangement. Additional molecular abnormalities included TP53 and WT1 mutations. Eighty-nine percent cases were immunophenotypically defined. Forty-five percent cases were B/Myeloid, 36% cases were T/myeloid and 3% cases were B/T lymphoid. Sixteen percent cases were diagnosed as AUL. Cytogenetics revealed trisomy 4, del(6p),

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del (5q), structural abnormalities of chromosome 7 and complex karyotype. Seventy-six cases were given ALL like induction protocol and 17% had additional TKIs. The median progression-free survival (PFS) was 120 days, and the median overall survival (OS) was 160 days.

Conclusion: The investigation illuminates the intricate terrain of ALAL, delineating its diagnostic challenges and prognostic intricacies. The results underscore the heightened susceptibility of ALAL patients to inferior outcomes and increased incidence of induction failure in contrast to individuals diagnosed with clearly defined acute leukaemia subtypes.

BSH24-EP28 | Are CCL19 and CCL21 the keys to unlocking dendritic cell function in paediatric B-ALL?

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Despite the accumulation of genetic mutations likely to generate antigenic neoepitopes, acute lymphoblastic leukaemia (ALL) cells are poor at eliciting anti-tumour immune responses. Similarly to dendritic cells (DCs), B cells have antigen presenting capacity. In B cell ALL (B-ALL), blast expression of co-stimulatory molecules is down regulated while endogenous (tumour) antigens are presented through MHC class I and II, thus mimicking the DC peripheral tolerance mechanism. This leads to antigen specific anergy in naïve T cells capable of recognising the malignant cells and an anti-tumour immune response is not mounted. Within the patient, a robust DC response presenting tumour antigens alongside co-stimulation should be sufficient to overcome this. However, several studies have reported deficiencies in DC number and function in patients with B-ALL. This suggests that B-ALL cells or leukaemia derived factors, may inhibit DC development.

We identified that plasma CCL21 is increased in paediatric B-ALL patients at diagnosis, but levels decrease rapidly during induction chemotherapy becoming undetectable by day 29. This coincides with both the rapid reduction in the number of blast cells and the recovery of DC populations in patients. To determine whether increased CCL21 expression may inhibit DC development we generated human DCs in vitro from THP-1 and HL-60 cell lines in the presence and absence of CCL21, or its sister molecule, CCL19. We measured expression of molecules associated with DC phenotype including; CD14, CD40, CD80, CD86, CCR7 and DC-SIGN to determine the effects of both chemokines on DC differentiation. Further, we measured expression of molecules associated with the functional capacity of DCs in terms of the uptake and presentation of antigens, including decalectin and FCγ receptors following CCL21 or CCL19 stimulation.

Based on results from murine studies, CCL19 and CCL21 may have important roles in mediating immune tolerance to malignant diseases and in modulating DCs during an immune response. In paediatric B-ALL, since the re-establishment of bone marrow DCs occurs concordantly to the reduction of CCL21 we investigated whether over-expression of CCL21 may contribute to DC suppression in the context of paediatric B-ALL.

BSH24-EP29 | Audit of blood component requisition forms received at a private superspecialty hospital in South India

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Background and Aim: Delivering safe blood and adequate transfusion to patients are critically dependent on sound communication of information to the blood bank, which ultimately helps the blood bank technologist to identify appropriate blood products. In 2008, the World Health Organisation (WHO) recommended that each institution should use a blood transfusion request form (BRFs) for effective communication of the patient information to the hospital blood bank. The current study was conducted as a part of the quality assurance activity to analyse BRFs sent by clinicians in a Private Super Specialty hospital for the transfusion service to ascertain their completeness and also to take necessary steps to improve the compliance of healthcare personnel with regard to sending completely filled BRF.

Methodology: This was a retrospective, observational study conducted in the Department of Transfusion Medicine at a Private Super Specialty Hospital from January 2023 to June 2023. An audit of all the Blood component requisition forms for assessing the completeness of various parameters present in the forms, was performed. The request form was evaluated for the fullness of the data requested therein: patient details (name, UHID Number), diagnosis, nature of request (routine/urgent/emergency), indication for transfusion, type of blood components with a number of blood components required, lab parameters, previous history of transfusions; Date of requirement, and referring doctor's name and signature. Percentage of each parameter, which remained incomplete on the requisition forms, was analysed.

Results: A total of 2141 consecutive BRFs were submitted to the blood transfusion services during the study period were compiled and reviewed. Parameters of BRF that remained incomplete were: Patient details (name, UHID Number): 0.05%; diagnosis: 25.41%; nature of request (routine/urgent/emergency): 2.52%; indication for transfusion: 24.1%; type of blood components with the number of blood components required: 0%, laboratory parameters: 5.37%; previous history of transfusions: 5.98%; date of requirement: 2.57%; and referring doctor's name and signature: 9.53%.

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Conclusion: The current study provides evidence that the rate of completion of BRFs at the current study site is not appropriate, particularly for the parameters like diagnosis and indication for transfusion. Incomplete blood transfusion request forms create difficulties for the blood bank staff in comprehending the requests, which may compromise patient safety and also the efficiency of blood transfusion services. The Hospital Transfusion Committee can play a key role in solving this problem and thus improving the standards of patient blood management.

BSH24-EP30 | Relationship between early diagnosis/treatment of suspected HLH (haemophagocytic lymphohistiocytosis) on patient survival outcomes

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Background/Aim: Haemophagocytic Lymphohistiocytosis (HLH) is a rare, immune mediated disorder that results in widespread activation of cytotoxic lymphocytes/macrophages and sustained cytokine release. Death is the result of multi organ failure. Our retrospective analysis focusses on secondary HLH; causes include rheumatic disease, haematological malignancy or infection. The primary aim is to determine if early diagnosis and treatment correlate with survival outcomes.
Method: We collected retrospective data from 10 patients who had been treated for HLH, at one Kent NHS Trust between 2020 and 2023. The HScore for reactive HLH (Fardet et al., 2014) was calculated at diagnosis. Ferritin levels are noted to be highly specific for HLH diagnosis. Therefore, time taken for diagnosis was calculated as the number of days from ferritin levels exceeding 2000 μg/L (the minimum value in the HScore) to treatment commencement. Standard local practice invokes both the HLH 2004 protocol and University College London Hospitals NHS Trust (UCLH) Anakinra protocol.
Results: The patient average age was 57 years, with seven male and three female. Co-morbidities included haematological malignancy, immunosuppressive therapy for organ transplant and COVID-19 infection. The average time taken to diagnose was 7 days from ferritin level >2000 μg/L. At diagnosis, all patients had at least two lines of cytopenias and deranged liver function tests (AST >30 U/L). Seven patients had anakinra and all patients received steroid therapy (including dexamethasone in the COVID-19 cases). Two patients received etoposide. The mortality rate was 70%. Of the three surviving patients, one had HLH treatment initiated within 24 h of admission and two patients had treatment initiated within 7 days.
Discussion: Given the high mortality rate of HLH, it is essential that clinicians are confident to enact timely, proportionate interventions. Surviving patients are those who had HLH treatment protocols commenced relatively early (within 1 week) and received methylprednisolone/dexamethasone and anakinra (minimum dose 100 mg BD). One patient received etoposide within 24 h. One patient did not survive despite early treatment. This is in context of severe sepsis, advanced age and complex comorbidities.
The HScore for nine patients was higher at diagnosis (197) compared to initial presentation (153). This reiterates the importance of regular re-calculation of the HScore, and clinical suspicion to guide treatment initiation. Eighty-percent patients had a bone marrow aspirate performed; 24% of these showed evidence of haemophagocytosis. Therefore, absence of this should not be considered as exclusion criteria for HLH diagnosis.

BSH24-EP31 | Preventative information (regarding mucositis) given to paediatric patients awaiting bone marrow transplants: A QI project

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Background: Haematopoietic cell transplantation (known as bone marrow transplantation) is a potentially lifesaving treatment for patients suffering from both acquired and congenital diseases. Despite high success rates, there are many side effects that can affect the patients quality of life. These include an increased risk of infection (with the risk of septicaemia), pneumonia, nausea and vomiting; however, oral side effects are one of the most common problems patients face. 70.0%–86.8% of bone marrow transplant (BMT) patients report oral mucositis as the single most debilitating side effect. Patients are referred from a specialist paediatric haematology, blood and marrow transplantation unit for a dental assessment prior to the transplant. This includes as assessment of their teeth and the provision of preventative advice.
Aims and Objectives: This Quality Improvement Project aims to determine the level of education patients, and their parents/guardians, are being provided with regarding oral mucositis and to identify areas of improvement.
Methods: All patients referred for a pre-BMT dental assessment within an 18-month period were identified. Their parents/guardians were called and given the opportunity to answer questions relating to their level of knowledge of oral mucositis. Information recorded included whether the parent was aware of what mucositis is, their knowledge of the link between oral hygiene and mucositis and what format they would prefer information given to them in (digital versus paper). This was to determine any potential improvements to the service.
Result: The most common haematological diagnosis was Diamond Blackfan Anaemia and Beta Thalassaemia Major: these were followed by sickle cell disease, aplastic anaemia and congenital dyserythropoietic anaemia. Also, 73.3% of parents had no knowledge of mucositis and that their child would be at a high risk of developing it. Of the parents that were aware

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of mucositis, 75% also knew the link between oral hygiene and mucositis. Also, 33.3% of parents preferred having information provided on paper leaflets and 26.7% would have liked information provided both, on paper and electronically. The remaining patients preferred it given solely electronically.

Conclusion: Patients undergoing bone marrow transplants suffer from a wide range of oral side effects. These can have a detrimental effect on their quality of life. Appropriate preventative education and instruction can play a significant role in aiding patients to manage their oral symptoms more effectively and in a timely manner. An electronic patient information leaflet is being developed to facilitate the dissemination of the advice and improve the service.

BSH24-EP32 | Referrals to a haematology day unit: Has the quality improved with a new electronic system?

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Background: The haematology day unit (HDU) at Guy's hospital serves a range of haematological diagnoses and varying levels of acuity. Patients are referred for a medical review electronically. There are also unplanned medical reviews for nurse-led attendances. The medical team identified the quality of referrals as a major limiting step in meeting the demands of the service. This quality improvement project was designed to understand if the quality of referrals was influenced with the intervention of a new trust-wide electronic system, EPIC.

Methodology: The medical team identified five key issues in the quality of referrals. These are: inclusion of the patient's haematological diagnosis, count targets for relevant patients, a named senior to discuss the patient with, a clear referral and the appropriateness of the referral. A case control study was conducted for each variable with the introduction of the new electronic system. The odds ratio and confidence interval were then calculated as well as the *p* value using the Fisher test.

Results and Conclusion: A total of 55 patients had medical reviews in the week pre-EPIC and 63 post-EPIC. 7% of these patients were categorised as red (high acuity) pre-EPIC and 13% post-EPIC. In total there were four admissions pre-EPIC and five post-EPIC. After reviewing the notes, both six patients pre and post-EPIC avoided admission due to care given on HDU. Seven patients avoided A+E attendance pre-EPIC and 11 post-EPIC. There was a significant difference in the number of patients having their count targets included in their referral, this worsened post-EPIC (OR 0.32, CI [0.14, 0.76], $p=0.0117$). This was a hard-stop in the pre-intervention electronic referral system. Referrals post-EPIC were more likely to lack clarity, although not statistically significant. Inclusion of diagnosis, named senior to discuss and appropriateness of referral improved in the week post-EPIC although these results were not statistically significant. The appropriateness of the referral most strongly improved.

The medical team would suggest the EPIC referral system having a hard stop for blood count guidance, whether that's for transfusion or a baseline that has implications for treatment. We also recommend it being updated to incorporate an SBAR structure. We would also suggest two hot referral slots a day to account for red reviews with an additional verbal handover.

BSH24-EP34 | Basic to brilliance: A haematology podcast for trainees

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In response to the distinct challenges faced by intermediate-level trainees (IMT/SHO) transitioning to ST3 in haematology, our collaborative podcast with the British Society of Haematology (BSH) offers a practical and engaging solution. Haematology registrars answer queries from internal and external sources, requiring specific knowledge about treating, managing, and investigating clotting, malignant, and non-malignant conditions. The process of accumulating this practical knowledge while working in internal medicine or at ST3 is daunting and time-consuming; the paucity of resource modality in this area is what this podcast aims to redress, providing tailored episodes to meet the unique time constraints of trainees, especially during long commutes.

The podcast is released bi-weekly, in an approximately 1-h format, covering the curriculum of the FRCPath part 1; for example, ITP or CLL; including pathophysiology, investigations, management, trials, and future directions of research. Each podcast is conducted on Zoom, with audio output edited using Apple GarageBand. The bespoke intro and outro music, composed and recorded in-house.

Employing a loosely scripted approach, the podcast structures its content around a question and answer system to ensure comprehensive coverage of each topic. The conversational tone is complemented by the clarity provided by the Senior House Officer (SHO), who serves as the voice of the listener, ensuring content is pitched at the learners' level. This Socratic method of dialogue is intended to enhance engagement and promote deeper conceptual understanding, crucial for long-term memory storage and retrieval.

The Podcast is poised to engage the community through social media, specifically X (Twitter), allowing listeners to pose questions anonymously. The 'Ask the Expert' sessions give listeners an opportunity to ask questions they would feel uncomfortable communicating in a clinical setting. Positive feedback from regional haematology meetings has sparked collaboration offers from allied health professionals, emphasising the podcast's role in fostering community engagement.

In an attempt to expand the digital resources available to SHO level or ST3 haematology trainees, this podcast provides accessible, well-resourced, and up-to-date information aimed to provide practical, useful knowledge in a time-considerate format and can be accessed at the user's convenience.

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BSH24-EP35 | Bilateral retrobulbar haemorrhage causing spontaneous globe subluxation in a paediatric patient with factor XIII deficiency

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Introduction: Factor XIII deficiency (FXIIID) is a rare inherited bleeding disorder, and its diverse clinical presentation often complicates diagnosis and management. We present a unique case of a 5-year-old female child with FXIIID, emphasising the importance of prompt intervention in the context of its diverse clinical manifestations.

Case Presentation: A 5-year-old female child presented to a tertiary care hospital with bilateral eye protrusion and scalp swelling, 1 day following alleged head trauma during play. She had a history of recurrent non-projectile vomiting, headache, and prolonged bleeding after minor injuries. Born to second-degree consanguineous parents, she experienced prolonged umbilical bleeding post-birth. Ocular examination showed axial proptosis, ecchymosis, chemosis and corneal stromal haze. CT brain revealed bilateral retrobulbar haemorrhage and localised scalp hematoma. A bleeding disorder was suspected, and investigations revealed normal haemoglobin, platelet and coagulation parameters. Factor XIII deficiency was confirmed through quantitative assays. Surgical intervention was performed to manage retrobulbar bleeding and exposure keratopathy. The procedure involved lateral canthotomy and cantholysis to release the right lower eyelid, facilitating access. Subconjunctival fluid was drained through a small incision in the inferior bulbar conjunctiva using tenotomy scissors and a spatula. Chemosis was gently reduced, and temporary tarsorrhaphy was performed by suturing the upper and lower eyelids together. The same procedure was replicated for the other eye. The child was followed up with re-suturing for suture tension-related issues. With meticulous management, the child's hemodynamics stabilised, proptosis reduced, extra-ocular movements improved and vision was enhanced. Although intensive lubrication was maintained due to corneal scarring, overall outcomes were favourable. At 36 months of follow-up the child showed appropriate developmental milestones and improved vision.

Discussion: This case underscores the rarity and diverse clinical presentation of FXIIID, highlighting the importance of early diagnosis and intervention. The severe congenital factor deficiencies like FXIIID7 can manifest in various ways, making timely recognition crucial. FXIIID has been associated with debilitating central nervous system (CNS) haemorrhages, which are a significant cause of morbidity and mortality. This report presents the first-ever case of bilateral retrobulbar haemorrhage in a paediatric patient with FXIIID, thereby expanding the spectrum of clinical manifestations associated with this condition.

BSH24-EP37 | Rosai-Dorfman disease—A single centre experience of a rare histiocytic disorder

Dr Menna Shamma[1], Dr Harry Apperley[1], Dr Robin Dowse[1], Dr Ayad Atra[2], Dr Pilar Gurrera-Garcia[3], Dr Sanjay Tewari[1]
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Background: Rosai-Dorfman disease (RDD) is a rare histiocytic disorder presents with painless massive lymphadenopathy. Pathologically, lymph nodes show accumulation of histiocytes and lymphocytes. Emperipolesis in histiocytes that express S100 is considered diagnostic. It is usually self-limiting, however, it may be associated with a chronic course characterised by episodic exacerbation and remission. Treatment is indicated if there is vital organ compromise, otherwise watch and wait is reasonable.

Aims: Describe current variation in practice regarding management histioproliferative disorder, and describe disparities in presentation, treatment, and outcomes.

Methods: A retrospective and descriptive review of RDD paediatric cases at the Royal Marsden Hospital, between 2012 and 2022. Data regarding age, symptoms, nodal/extranodal involvement, treatment and outcome were collected.

Results: Five patients were identified and followed up; four males and one female. Age range was 23 months to 15 years, with a mean age of 7 years and 9 months. Three had solely cervical node involvement, two had extranodal disease, subcutaneous and bony deposition respectively.

All patients had elevated gamma delta T-cells. No evidence of autoimmune lymphoproliferative syndrome (ALPS) presented in any of the cases. Next Generation Sequencing (NGS) was performed on the biopsy in two patients, with no targetable mutations identified.

Three patients required surveillance only. One had surgical resection of the cervical node and one had curettage of isolated calcaneal lesion with complete symptomatic resolution.

One had a background of undifferentiated immunodeficiency, and chronic suppurative lung disease was treated with steroids and Sirolimus. Clinical course included waxing and waning of painful lymphadenopathy episodes lasting 3–4 days each month. Prednisolone rendered symptomatic improvement, but PET CT illustrated disease progression. Biopsy showed no transformation to lymphoma. Sirolimus was commenced, with significant symptomatic improvement, reassessment PET CT showed good response.

Summary: RDD generally runs an indolent course. Treatment is only indicated if there is vital organ dysfunction. there is significant variation in practice if response to steroids is inadequate or surgery is not feasible. RDD can be seen as a presenting feature of autoimmune lymphoproliferative disorder, and part of the workup of new cases should be exclusion of underlying immune dysregulation. Identification of somatic MAP-ERK mutations in RDD have led to its addition to the group of histiocytic neoplasms in

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the most recent revision of the WHO classification of haematolymphoid tumours. Lesional tissue should be assessed by NGS for such mutations, which may be targetable by small molecules, such as MEK-inhibitors, for cases which fail to respond to conventional therapies.

BSH24-EP38 | Adhering to best practice in a nurse led myeloproliferative clinic

Miss Emma Whitham[1], Miss Roxy Spencer[1]
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After managing the myeloproliferative nurse led clinic for some time, I recognised that there was no consistency in the way patients were followed up and the quantity of venesections that seemed to be required.
The main issues were:

- No documentation of desired haematocrit level.
- No documentation of venesection frequency.
- Limited Consultant review.
- No consistency in follow up times.
- No regular checking of iron levels.

Best practice guidelines suggest regular monitoring of iron deficiency, reducing the number of venesections per year, in particular if patients are on hydroxycarbamide to reduce risk of thrombosis and to ensure that there are clearly documented haematocrit levels.
This formed the basis of a service review audit looking at patients over a year in the myeloproliferative clinic undergoing venesection for polycythaemia with the aim of implementing a new system of working, to improve the service we provide and ensure adherence to best practice guidelines.
Based on the outcome of the audit, I confirmed that the current service was not adhering to best practice guidelines. Therefore, the service underwent a full review and has now been completely changed.
The reason for doing this poster is to hopefully share best practice with other nursing teams, especially as the majority of these patients will be seen and managed in a nurse led setting. Quantitative data will be shared on the poster, currently being collated by the Audit Team.

BSH24-EP39 | Dark web deception: Using laboratory haematology to resolve a case of unexplained coagulopathy

Dr Eleanor Sheppard[1], Dr Danielle Monteil[1], Dr David Simcox[1], Mr. Colin Downey[1], Ms. Ashley Lawrenson[1]
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A 47-year-old man presented to the Emergency Department in August 2023 with infected skin ulcers over his lower limbs. Admission blood tests showed an extremely elevated prothrombin time (PT) 262.3, international normalised ratio (INR) >19 and activated partial thromboplastin time (APTT) 64.5 s. Fibrinogen was preserved at 3.55 g/L and haemoglobin, at 114 g/L, was comparable with historic results.
The patient denied taking anticoagulant or non-prescribed medications. His medical history included prior intravenous drug use, alcohol-related liver disease, treated Hepatitis C infection, cirrhosis and portal hypertension. A recent clotting profile revealed a mild PT elevation (18 s) and a normal APTT.
A repeat sample was immediately taken to ascertain validity of the presenting results, which confirmed the extremely prolonged PT and APTT. Subsequent mixing studies, with 80:20 and 50:50 patient: standard plasma mixes, showed full correction of the PT and APTT. A lupus insensitive APTT assay confirmed a prolonged APTT of 81.3 seconds.
Individual factor assays showed diminished vitamin K-dependent clotting factors: Factor II (16%), Factor VII (1.2%), Factor IX (14.4%) and Factor X (8.7%). Notably, Factor V levels were within normal range. The results suggested use of a vitamin K antagonist. However, the patient emphatically denied this and maintained abstinence from non-prescribed oral medications. He did however admit to smoking cannabis regularly.
The patient's blood cultures were positive for Group A Beta haemolytic *Streptococcus* and he was admitted to the Infectious Diseases (ID) ward for treatment of his infected leg ulcers. We suggested a trial of vitamin K 10 mg once daily for the coagulopathy, with consideration of prothrombin complex concentrate (PCC) in the event of clinically-significant bleeding. The prolonged PT and APTT results rapidly corrected over a few days with vitamin K supplementation only. The patient never became haemorrhagic, and his haemoglobin remained stable throughout the admission.
By discharge, his coagulopathy was restored to his baseline. At follow-up several months later, he admitted to taking diazepam, purchased on the darknet, in the days prior to his admission. We considered that this might have been contaminated with a vitamin K antagonist such as warfarin. The patient was counselled and cautioned about online purchase of unregulated substances.

BSH24-EP40 | Interesting case report: Acute thrombocytopenia following an overseas renal transplant

Dr Aoife Dervin[1], Dr Jay Parekh[1], Dr James Croft[1], Dr Simon Stern[1], Dr Jenny Bosworth[1], Dr Corinne De Lord[1], Dr Stella Appiah-Cubi[1], Dr Fatin Sammour[1], Dr Sneha Muthalali[1], Dr S. Deoraj[1], Dr A. Abbas[1], Ms. C. Cook[1], Ms. S. Brown[1], Dr A. Salama[1], Dr M. Phanish[1], Dr Caroline Ebdon[1]
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Thrombocytopenia post renal transplantation is a common complication, and is reported in up to 66% of patients. There is a wide differential, and although drug toxicity and

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thrombotic microangiopathy (TMA) are important considerations, other causes such as viral infections and immune-mediated reactions are also reported. We report a case of a 39 year old female with known Alport's disease, who presented with thrombocytopenia after receiving a living unrelated donor renal transplant in Nigeria in January 2023.

The patient received anti-thymocyte globulin (ATG) and methylprednisolone induction, and was initiated on tacrolimus, prednisolone and mycophenolate. In the early post-transplant period, she developed TMA, which was treated with two courses of plasma exchange and immunosuppression was switched from tacrolimus to everolimus. On return to the UK she was found to have graft dysfunction, anaemia and thrombocytopenia. Percutaneous transplant renal biopsy showed extensive glomerular TMA, with strong peritubular capillary C4D staining. She was treated with a further six sessions of plasma exchange and three doses of intravenous methyl prednisolone. As donor HLA typing was not known it was not possible to ascertain if the HLA antibodies that she had in her serum were donor specific antibodies. Serum complement levels were normal, anti-glomerular basement membrane (GBM) antibodies were negative. Transplant renal doppler ultrasound scan was unremarkable. She was switched to Cyclosporine from Everolimus and discharged from hospital for ongoing outpatient follow up.

A month later, she represented generally unwell with muscle aches and low-grade fever. There was no obvious source of infection. Bloods showed an elevated CRP, anaemia and thrombocytopenia, and a normal coagulation screen. She was given broad spectrum antibiotics and a blood film was examined to look for evidence of a microangiopathic process. The peripheral blood film revealed malarial parasites (ring form trophozoites). Reference laboratory confirmed *Plasmodium falciparum* with parasitaemia of 8%. She was initiated on intravenous Artesunate therapy. Her transplant kidney function improved and thrombocytopenia resolved.

This case serves as a reminder that thrombocytopenia following transplant is not always the thrombotic microangiopathy of acute antibody mediated rejection (AMR) or calcineurin inhibitor toxicity, and highlights the importance of blood film examination. In this case, the anaemia and thrombocytopenia was secondary to the haemolytic process of malarial erythrocyte phase. It also illustrates that malaria presentation can be delayed and, following return from foreign travel, infection must be considered in all patients, particularly those with immune suppression even if the presentation is after several weeks.

BSH24-EP41 | Peri-operative anaemia optimisation since the covid pandemic—A service evaluation

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Introduction: Peri-operative anaemia is associated with morbidity.[1] Optimisation of iron deficiency is recommended[1] but questions remain regarding treatment benefits.[2] At our centre, a treatment algorithm based on guidance recommends intravenous (IV) iron for patients unsuitable for oral iron or in functional deficiency.[1] We aimed to evaluate how referrals to our pre-operative iron service have changed since 2020.

Methods: The local Audit and Quality Improvement (QI) panel approved this evaluation. Using the electronic patient record (EPR), a time series was conducted from January 2020 to May 2023. Referral patterns were analysed. Further data was collected on 11 patients per year, including post-operative haemoglobin, length of stay, blood transfusions and reactions to iron. Data was analysed in Excel.

Results: 1116 patients were referred during the period. General surgery, Gynaecology and Orthopaedics made most referrals. Median days from referral to planned surgery increased. Mean referral haemoglobin (Hb) has increased. Fluctuation in referrals was noted in 2020. The deeper analysis from 2021 to 2023 revealed approximately 20% had peri-operative blood transfusions. There was inconsistent data in the EPR for the deeper analysis of 2020. Mean post-operative Hb varied from 124 to 99 g/L. Median length of stay varied and was longest in 2023 at 13 days. There were no documented adverse reactions to IV iron.

Discussion and Conclusion: We describe the temporal effect on our established iron clinic. Increased days from referral to surgery reflect QI efforts improving workflow resulting in increased time for anaemia optimisation. Median Hb has trended up over time, but this is unlikely to have significance. The number of patients requiring transfusions has remained static, further work should be done to determine the significance of this. The impact of Covid-19 is noted with a referral peak in the second half of 2020, reflecting the backlog. Inconsistent data in the EPR in 2020 may be explained by the disruption to usual processes during Covid-19.

Ongoing work will ensure that our service continues to follow national guidance and adapts to the changing demands since the pandemic.

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BSH24-EP42 | Phase 3 randomised double-blind study evaluating selinexor, an XPO1 inhibitor, plus ruxolitinib in JAKi-naïve myelofibrosis

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Background: Myelofibrosis (MF) is a myeloproliferative neoplasm with common somatic gene driver mutations in JAK2, CALR, and MPL. Selinexor, an investigational oral XPO1 inhibitor, may inhibit MF-relevant JAK/STAT and non-JAK/STAT pathways and preclinical studies have shown potential synergy with ruxolitinib treatment. In the phase 1 portion of XPORT-MF-034 evaluating the combination of selinexor and ruxolitinib in JAKi-naïve patients with MF, the most common AEs in the 60 mg cohort were nausea (79%), anaemia (64%), thrombocytopenia (64%), and fatigue (57%); treatment-related AEs leading to treatment discontinuation were thrombocytopenia ($n = 1$) and neuropathy ($n = 1$). SVR35 and TSS50 were achieved by 79% and 58% of the 60 mg cohort intent-to-treat population at week 24, respectively. These data provide strong support to further evaluate selinexor (60 mg) and ruxolitinib in patients with JAKi-naïve MF.
Methods: The XPORT-MF-034 (NCT04562389) trial includes a global, phase 3 randomised, double-blind, placebo-controlled study designed to evaluate selinexor and ruxolitinib. JAKi-naïve patients with MF will be randomised 2:1 to receive oral selinexor 60 mg or placebo once weekly (28-day cycle) and twice daily ruxolitinib. Randomization will be stratified by DIPSS risk category (intermediate-1 vs. intermediate-2 or high-risk), spleen volume (<1800 cm^3 vs. >1800 cm^3 by MRI/CT scan), and baseline platelet counts (100–200 × 10^9/L vs. >200 × 10^9/L). Dual anti-emetics for nausea prophylaxis will be required for the first two cycles. Select eligibility criteria include ≥18 years of age, spleen volume ≥ 450 cm^3 by MRI or CT, DIPSS (intermediate-1, intermediate-2 or high-risk), active symptoms of MF (MFSAF v4.0), currently not eligible for stem cell transplantation, ECOG ≤2 and platelet count ≥100 × 10^9/L. Select exclusion criteria include >10% blasts in peripheral blood or bone marrow; previous treatment with JAKi for MF, or previous treatment with selinexor or other XPO1 inhibitors. The co-primary study endpoints are SVR35 and TSS50 at week 24 tested hierarchically. The key secondary endpoint is anaemia response at week 24 per the IWG-MRT and ELN criteria.
Results: The XPORT-MF-034 phase 3 trial is currently open for enrollment; a total of 306 JAKi-naïve MF patients will be enrolled and the study was initiated on June 28, 2023.

BSH24-EP43 | The burden of anaemia in a primary care population in UK: What is haematology's role?

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Background: Anaemia is a global health problem, contributing to poor quality of life, increased morbidity and mortality, and substantial economic costs. Anaemia has consequences for many areas of medical, surgical, and obstetric practices. The enduring burden of anaemia, despite available treatment, suggests uncertainty around existing approaches to diagnosis and management. This study aimed to describe the epidemiology of anaemia and patterns of diagnostic investigations across a primary care population in the United Kingdom. We report initial results on anaemia prevalence by age, sex, and ethnicity.
Methods: Retrospective cohort study using data from 13.9 million patients registered in General Practices within the Clinical Practice Research Datalink from 2017 to 2022.
Outcomes: Prevalence, type of anaemia and patterns of testing. Anaemia was defined using World Health Organisation's age-specific haemoglobin thresholds.
Results:
There is a high prevalence of anaemia in females of reproductive age, males over 76 years and females from Asian or Black ethnicities. These populations had the highest rates of haemoglobin testing. Rates of haemoglobin testing increased with age, and in females of reproductive age.
Discussion: A concerted effort is needed to address the burden of anaemia in the community. Anaemia in hospitals represents only one element of the pathway for many patients. There is a need to better integrate services for testing and management across areas of medical, surgical and obstetric practices.

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TABLE 1. Prevalence of low haemoglobin (Hb) in all patients (2019).

	Males			Females		
	Total	Low Hb	%	Total	Low Hb	%
All	6900829	231414	3.4	6963021	403454	5.8
Age group						
5–11 Years	631882	4766	0.8	603583	4834	0.8
12–14 Years	256456	921	0.4	245563	2985	1.2
15-49 Years	3645347	19525	0.5	3607736	166926	4.6
50–65 Years	1314333	40050	3.0	1262417	58269	4.6
66-75 Years	601209	54375	9.0	634424	52657	8.3
76–80 Years	194841	34639	27.9	225627	32451	14.4
>80 Years	256761	77138	30.0	383671	85332	22.2
Ethnicity						
Asian, Asian British	606624	20025	3.3	595326	62191	10.4
Black, Black British, Caribbean, African	286710	11345	4.0	296184	32615	11.0
Mixed	123924	2327	1.9	134359	7678	5.7
Other	120244	2002	1.7	113001	6705	5.9
White: British	3817092	159190	4.2	4093259	224437	5.5
White: Gypsy or Irish Traveller, Roma	551881	7527	1.4	609838	22970	3.8
White: Irish	52063	2661	5.1	54698	3605	6.6
Missing	1342291	26337	2.0	1066356	43253	4.1

BSH24-EP44 | Exceptionally high prevalence of iron deficiency anaemia in children residing in rural areas in Pakistan

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Introduction: Despite a reduction in the global prevalence of anaemia over the past three decades (from 28.2% to 24.3%), anaemia in children aged ≤15 years remains a major public health challenge in sub-Saharan Africa and south Asia. In these regions, there is substantial variation in anaemia burden by age, sex, and socioeconomic status—the highest prevalence is observed in children aged ≤5 years and females. The condition is attributed to a complex interplay of several interconnected causes, including nutritional deficiencies (i.e., iron, vitamin B12, folate), poor and/or cultural child feeding practices, parasitic infections, high birth rates, and short birth intervals. We examined children presenting with signs/symptoms of anaemia at SHINE Humanity primary healthcare clinics in rural settings in the Sindh province, Pakistan, to ascertain the prevalence of anaemia in children aged ≤15 years to inform the development of targeted interventions to reduce the associated morbidity—(e.g. impaired development, years lived with disability [YLDs]) and premature mortality.

Methods: All children aged ≤15 years, presenting with pallor and complaints from parents of weakness, fatigue, and decreased concentration were subject to laboratory investigation for complete blood count examination. A haemoglobin (Hb) level of ≤11.4 g/dL was considered diagnostic for anaemia. Informed consent was obtained from all parents.

Results: During the study period (July–November 2023), a total of 593 children aged ≤15 years (45.9% males, 54.1% females) were examined for anaemia—of these, 74.4% ($n = 441$) were diagnosed with anaemia (mean Hb 10.3 g/dL; standard deviation = 1.8; range, 4.7–15.0). The prevalence of anaemia was 73.5% in males and 75.1% in females. With regard to age, the highest prevalence (86.5%, 64/74) was observed in children aged ≤5 years (mean Hb 9.7 g/dL; standard deviation = 1.7; range, 6.3–13.6), followed by 75.8% (266/351) in those aged 6–10 years and 66.1% (111/168) in those aged 11–15 years.

Conclusion: Compared with the World Health Organization (WHO) Global Anaemia estimates (2021 Edition) for South-East Asia, this is the highest recorded prevalence of anaemia in children (86.5% in those aged ≤5 years) in the region. Considering the morbidity (e.g. poor cognitive and motor development) associated with the duration and severity of anaemia and subsequent YLDs, this study informs formulation of targeted multifaceted interventions, including early diagnosis, combating iron and nutrient deficiencies, promoting hygiene, and health education to reduce the burden of anaemia in children residing in rural areas in Pakistan.

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BSH24-EP45 | VAMPIRC: Venesection audit in the Midlands for secondary polycythaemia investigating thrombotic complications

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Secondary polycythaemia is rare and there is no randomised evidence to inform its management. The British Society of Haematology (BSH) recommend optimising risk factors, and considering venesection in selected cases, with a target haematocrit (Hct) of 0.45–0.55 in different situations (McMullin, 2018). Although venesection may theoretically reduce thrombosis risk, it reduces oxygen carrying capacity and confers a burden on patients and the healthcare system. We are carrying out a retrospective audit in the West Midlands of patients with polycythaemia, negative for JAK2 V617F and exon 12 mutations, who were diagnosed between 2014 and 2018. We are collecting details of diagnosis, investigations performed, and management including risk factor modification and venesection. Additionally we are recording thrombosis risk factors and thrombotic events, to inform the feasibility of a randomised trial of venesection.

As of January 2023, data has been collected on 85 patients with a first diagnosis of JAK2-negative polycythaemia. Of these, 55 (65%) were male, with a median Hct of 0.50 in women, and 0.53 in men. There was a history of prior arterial or venous thrombosis in 14 (16%), and 16 (19%) were taking an antiplatelet or anticoagulant. Venesection was initially planned in 23 patients (27%), and of these, 14 had a documented venesection target Hct. The median target was 0.47 (range 0.44–0.60). During the 5 year follow-up period, 28 patients (33%) underwent at least one venesection, and 11 (13%) underwent ≥4 venesections. Despite this low rate of venesection, the median Hct fell within 6 months of diagnosis and remained lower than baseline at 5 years (for men, 0.50 by 6 months and 0.49 at 5 years; for women, 0.49 by 6 months and 0.45 at 5 years). Current smoking was documented in 42 (49%) patients and 41 of these received smoking cessation advice. Thrombosis in the 5 years after diagnosis was uncommon, with six cases (7%) having an arterial event and three (4%) a venous thrombosis. We aim to collect 200 cases from our two large hospital trusts. Data collection is ongoing and complete results will be presented at the meeting.

BSH24-EP46 | Outcome of bone marrow examinations in children with isolated thrombocytopenia: Experience from LMIC

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Background: Immune thrombocytopenia (ITP) is diagnosed by exclusion of an alternative aetiology for isolated thrombocytopenia. Standard international guidelines do not recommend bone marrow examinations (BME) prior to initiating treatment in children with ITP. However, BME are still carried out especially in the paediatric population of lower middle-income countries (LMIC) to rule out acute leukaemia.

Objective: The aim of the study was to analyse the findings of BME performed in children with isolated thrombocytopenia at Lady Ridgeway Hospital for children, Sri Lanka.

Methods: A record based retrospective study carried out of all BME performed in children with isolated thrombocytopenia from May 2018 to April 2023. Request forms and biopsy reports were reviewed to extract the data. Permission was obtained from relevant authorities to conduct the study. Data was analysed using SPSS version 22.

Results: A total of 131 BME were performed in children with isolated thrombocytopenia during the study period. The male to female ratio was 1.29:1. The proportion of children less than 5 years of age was 50.4%. Majority (98.5%) were referred by paediatric specialists. Among the children who underwent BME, 82 (62.6%) presented with bleeding manifestations, 4 (3%) had pyrexia of unknown origin and 3 (2.3%) had joint symptoms. Of the total bone marrow examinations, 120 (91.6%) were consistent with ITP. In the remaining group only one (0.8%) had a malignancy, who was later found to have a mediastinal mass. Other findings in BME are inherited bone marrow disorders (5.3%) and reactive marrow (2.3%).

Conclusion: BME confirmed the diagnosis of ITP in the majority of children with isolated thrombocytopenia and clinical suspicion. Malignancy was rare and was associated with atypical clinical findings.

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BSH24-EP47 | Hyperhaemolysis syndrome in a young patient with autoimmune haemolytic anaemia

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Background: Hyperhaemolysis syndrome (HHS) is a rare complication of blood transfusion which results in the destruction of transfused red cells as well as patient's own red cells. Although most of the cases of HHS are reported in patients with sickle cell disease (SCD), this can occur in patients with other haematological disorders as well. As this is a potential life-threatening complication, prompt diagnosis and treatment are essential.

Case Report: We report a case of a 19-year-old male, who was transferred from a peripheral hospital to a tertiary care hospital for the management of severe anaemia. This patient was investigated for anaemia 4 months back and was diagnosed as having mixed type autoimmune haemolytic anaemia in the presence of some bone marrow pathology and β-Thalassaemia trait. He had several red cell transfusions for last 4 months duration. When he was transferred to the tertiary care hospital his haemoglobin (Hb) level was 3.6 g/dL, for which he has received 2 units of crossmatch compatible leuco-reduced red cell concentrates (LRRC). Following these transfusions, his anaemia symptoms worsened with dropping Hb to 2.2 g/dL. He developed icterus with rising total and indirect bilirubin levels and rising lactate dehydrogenase (LDH). As he developed type II myocardial infarction, he was transfused with another unit of LRRC under intravenous immunoglobulin (IVIG) and steroid cover. But his Hb further dropped to 1.7 g/dL with reticulocytopenia and high serum ferritin levels. His direct antiglobulin test was positive for both IgG and C3d and no underlying allo-antibodies were identified. He was treated with 2 g/kg IVIG and IV Methylprednisolone for possible HHS. As he was severely symptomatic, 2 units of LRRC as a lifesaving treatment option. Two days after completion of IVIG regime, the patient's Hb started to rise with reticulocytosis. With off red cell transfusions for 1 week time, his clinical and laboratory parameters improved and was transferred back to the peripheral hospital after arranging further clinic follow up.

Conclusion: Even though HHS is commonly seen in patients with SCD, this must be suspected in other patients with lower post-transfusion Hb when compared to pre-transfusion Hb level with worsening clinical features. Prompt treatment with IVIG and steroids is the most important aspect of management of HHS. Although further transfusions can exacerbate the haemolysis, red cell transfusion can be given as a life-saving treatment option in patients with severe life-threatening haemolysis.

BSH24-EP48 | Quality improvement and resource optimisation—Subcutaneous immunoglobulin for secondary immunodeficiency associated with haematological disorders

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Immunoglobulin (Ig) is used as replacement therapy (IgRT) in patients with secondary immunodeficiency (SID) to prevent infections, administered intravenously (IVIG) or subcutaneously (SCIG). The supply and demand of plasma derived Ig is in fine balance and shortages occur if demand outpaces supply or supply chains are disrupted. In 2019, a scarcity of IVIG resulted in local shortages, resulting in significant implications for patients. Consequently, subregional immunoglobulin assessment panels (SRIAPs) were established to ensure appropriate patient access.

Following the establishment of the East of England Immunoglobulin Assessment Panel (EOEIAP), three cohorts of patients with haematological disorders and SID receiving IVIG across the Mid and South Essex NHS Foundation Trust were reviewed before switching to SCIG pre-filled syringes (PFS). Here, we present the findings of switching from IVIG to SCIG PFS following EOEIAP review in one of the three cohorts, located at Broomfield hospital (a similar study is currently in process at a second site [Basildon] and will be implemented shortly at a third site).

In total, nine patients underwent review by EOEIAP. Six patients were deemed eligible for SCIG PFS, while three patients had IgRT discontinued. Of the six patients eligible for SCIG PFS, three had their SCIG dose optimised, and one patient was unable to switch due to visual impairment. The five patients who switched to SCIG PFS were trained in-house to self-administer and received SCIG via the pharmacy. The patients were routinely monitored to ensure correct administration before being transferred to homecare.

The introduction of EOEIAP led to improvements in both clinical and service outcomes. Changes in clinical outcomes following switching to SCIG PFS included improved patient satisfaction and quality of life, as well as improved infection rates. Regular (3-month) reviews of infection history and trough Ig levels resulted in more optimal dose regimes. Improvements in service outcomes associated with switching from IVIG to SCIG PFS included an annual saving of 336 h of day therapy chair capacity, an annual re-distribution of 126 h of nursing time, an annual saving of 600 g of Ig, no hospital transport costs, and reduced costs of in-house training compared with external training. In addition, there was an annual saving of 14 h prescribing and 42 h pharmacy time. In conclusion, this study highlights the importance of SRIAPs to ensure appropriate Ig use and demonstrates switching from IVIG to SCIG PFS is associated with improved patient outcomes and hospital cost and time savings.

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BSH24-EP49 | Use of low dose naltrexone and hydroxycarbamide for mast cell disorders (SM, MCAS and HaT)

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Mast cells, in addition to their presence in bone marrow, are ubiquitous, lining the gut, lungs, uterus, bladder as well as the brain, and can release more than 1000 mediators, causing multiple symptomologies which may result in difficulties in symptom control in mast cell disorders.

We describe use of Low Dose Naltrexone (LDN) together with hydroxycarbamide (HC) in two cases of indolent systemic mastocytosis (ISM), two patients with hereditary alpha tryptasemia (HαT) and one with mast cell activation syndrome (MCAS).

LDN is as it sounds, very low dose compared to standard dose Naltrexone; it is a 50:50 mixture of Left and Right isomers, with the left blocking opiate receptors and right blocking receptors on immune cells, including TLRs. It is used in multiple auto-immune conditions in the USA and Europe, as well as for mast cell disorders.

Hydroxycarbamide is an old and well known drug in the treatment of MPNs and Sickle cell disease, and is associated with reduction in cell load in the former, and pain reduction in latter.

Two female patients with c-kit positive ISM had bone pain which responded to LDN (4.5 mg od), in one case with HC in addition (1 g od). In addition GI symptoms improved in both cases. Another two female patients with HαT with similar symptoms again improved on the combined treatments.

A further patient with MCAS received a combination of both drugs, and had significant improvement in symptoms, both in bone pain, fatigue, gut and skin symptoms. A large group of patients with MCAS (40) reported improvements on LDN alone in their MCAS symptoms, while another 20 patients did not tolerate this medication. All patients were also on mast cell stabilisers and antihistamines prior to commencing these treatments, and had regular blood tests in view of HC usage.

While LDN is an unfamiliar drug in most hospitals the UK, due to the overall positive effects in our patients, we have stocked it in our pharmacy, while some patients receive their LDN prescriptions directly from a Glasgow chemist which specialises in its production and advice on use.

As patients with mast cell disorders often have difficult-to-manage symptomology we recommend consideration of this drug combination.

BSH24-EP50 | Investigation of isolated neutropenia in childhood: Aetiology and outcomes

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Introduction: Neutropenia in childhood is a common referral to the paediatric haematology clinic. While there are small case series describing the aetiology and outcomes of isolated neutropenia in children, evidence is lacking. The aim of this study was to analyse the investigation and outcome of isolated neutropenia in childhood.

Methods: We performed a retrospective chart review of referrals to a tertiary paediatric haematology outpatient clinic with isolated neutropenia over 5 years from 2018 to 2022. We excluded patients with reduced haemoglobin or platelets, except clear iron deficiency or thalassaemia trait. Ethical approval was granted by our institutions research ethics committee. Given the retrospective nature and anonymised data, individual patient consent was waived.

Results: We identified 170 children investigated for isolated neutropenia. We noticed a bimodal peak in age, with infants below age one and adolescents being most common. The majority (80%) had chronic neutropenia. Neutropenia was mild in 49%, moderate in 30%, and severe in 21%. Frequency of bacterial infections was associated with severity, reported in 4.9% with mild neutropenia, 8% with moderate neutropenia, and 38% with severe neutropenia.

The most frequent diagnoses were transient neutropenia (45%), Duffy Appropriate Neutrophil Count (DANC) (14%), autoimmune neutropenia (14%), chronic idiopathic neutropenia (12%), congenital neutropenia (6%). At time of analysis, neutropenia was persistent in 40.5%, and resolved in 56.6%. Median duration of transient neutropenia was 1.1 years. Treatments included GCSF (5.3%) and prophylactic antibiotics (1.8%).

Transient neutropenia in children aged between 1 and 12 months was particularly common ($N = 28$). We noted that 13/28 (46%) had a reduced IgG level, so would be considered to have transient hypogammaglobulinemia of infancy. This resolved in all evaluable cases (11/13), with median duration of 6 months (range 3–19 months), without clinical sequelae.

While chronic idiopathic neutropenia was the final diagnosis in 28% of adolescents, it was rarely diagnosed in those aged >2 to <12 (10%) and never in those under 2.

Conclusion: We report the frequencies of various diagnostic categories in children with isolated neutropenia, along with outcomes. We found a novel association between transient neutropenia in infants and transient hypogammaglobulinemia. We demonstrate that chronic idiopathic neutropenia is unusual in early childhood and more common in adolescence, which would suggest that chronic unexplained neutropenia before adolescence should be treated with a high index of suspicion for an underlying cause. This study provides valuable information to inform workup of neutropenia in childhood and provides information regarding clinical outcomes.

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BSH24-EP51 | Treatment free remission in CML patients on TKIs: An audit from a London DGH

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Treatment free remission (TFR) is now a realistic goal for chronic myeloid leukaemia (CML) patients on treatment with tyrosine kinase inhibitors (TKIs). BSH and European LeukemiaNet Guidelines suggest considering TFR in patients who have achieved a deep molecular response (DMR) as measured by BCR-ABL1 (IS) transcript levels for at least a 3 year period. There are other strict criteria that need to be met before considering TFR based on the experience from clinical trials. Despite multiple clinical trials on TFR, there remains a paucity of real world data on TFR. We conducted an audit to review our BCSH level 2b centre's performance on TFR.

Fourty-one patients were identified with CML on TKI treatment over a 5 year period. Twenty were eligible for TFR based on DMR and BSH guideline criteria. Sixteen eligible patients were offered TFR and 14 went on to discontinue treatment. The mean time from DMR to treatment discontinuation was 50.6 months. Six patients remained in TFR at the time of the study (42.9%). Fifty percent of patients had TFR >6 months and 35% had TFR >24 months.

Our results show real world evidence that TFR can be offered and achieved successfully in an NHS district general hospital setting. Our data is in keeping with large clinical trial data including the EURO-SKI trial. In EURO-SKI, 61% of 755 patients were relapse free at 6 months. While the EURO-SKI study suggested duration of DMR correlated to success of TFR, this was not evident in our study.

In conclusion, TFR is a realistic and achievable treatment goal for patients with CML in the real world district general hospital setting. Stopping treatment has a number of benefits for patients, improving their quality of life and reducing the clinical and financial burden on healthcare providers. Further research is needed to assess dose reduction strategies and second attempts at TFR after relapse.

BSH24-EP52 | Two years of the genomic haematology clinic: Outcomes from a new service for South-West England

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Background: University Hospitals Bristol and Weston NHS Foundation Trust (UHBW) provides specialist haematology services for patients across South-West England. In response to the rapid expansion of NHS genomic testing for haematological disorders, the region's first Genomic Haematology clinic was established at UHBW in January 2022 with the following aims:

- To offer patients with suspected inherited haematological disorders not already served by specialist clinics a streamlined care pathway including access to genetic testing, specialist follow up and relevant research studies, registries or clinical trials.
- To ensure clinical genetic testing is performed within the framework of the National Genomic Test Directory and thereby adheres to national standards.
- To offer support in the application of genomic investigations to haematologists working in other subspecialty areas.

It was planned to review the performance of the service after 24 months of activity.

Methods: A database was designed to prospectively capture data from the Genomic Haematology clinic, including reason for patient referral, nature of genetic testing performed, results of genetic testing and research participation. Summary data were extracted after the clinic had been running for 24 months.

Results: Between January 2022 and December 2023, 63 individual patients were seen (49 index cases [IC], 9 affected and 5 unaffected family members). Sixty-three new patient (40 min) and 111 follow up (20 min) appointments were completed over 40 clinics. The most common reasons for referral were suspected heritable thrombocytopenia (16/49 IC), neutropenia (12/49 IC) and erythrocytosis (8/49 IC).

A genetic diagnosis was confirmed in 29/49 IC who had (likely) pathogenic variants in relevant genes detected using NHS testing, including confirmatory testing following research findings in six IC. The highest rates of genetic diagnosis were in patients with hereditary haemorrhagic telangiectasia (HHT, 7/7 IC), hereditary haemolytic anaemia (2/3 IC) and suspected heritable thrombocytopenia (9/16 IC). Patients with syndromic disorders (including Fanconi anaemia, GATA2-deficiency, HHT) have been referred to additional specialities for specialist care following their diagnosis. One patient has had a previous clinical diagnosis of Gitelman syndrome rescinded.

Also, 29/63 patients participated in research studies including the NIHR BioResource for Rare Diseases, Severe Congenital Neutropenia International Registry and local investigator-led studies.

Discussion: The Genomic Haematology clinic is running efficiently and has facilitated genetic diagnosis, research participation and appropriate follow-up for patients with suspected heritable haematological disorders. The plan for 2024 includes developing and implementing a bespoke patient feedback tool to guide opportunities to improve patient experience.

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BSH24-EP54 | Pegylated interferon in myelodysplastic syndrome/myeloproliferative neoplasm with ringed sideroblasts and marked thrombocytosis: Single-centre case series

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Myelodysplastic syndrome/myeloproliferative neoplasm with ringed sideroblasts and marked thrombocytosis (MDS/MPN-RS-T) is characterised by dysplasia, clonal thrombocytosis and the coexistence of SF3B1 and JAK2 or other MPN specific mutations. It has a median survival that is better than myelodysplastic syndrome with ringed sideroblasts (MDS-RS) but worse than essential thrombocythaemia (ET). The rate of thrombotic events is similar to ET. Around 50% of patients are blood transfusion dependent. Commonly used treatment approaches include cytoreduction with hydroxycarbamide that cause anaemia requiring Erythropoiesis Stimulating Agents and/or transfusion support. There are no data on the use of pegylated Interferon (PEG-IFN) in this patient group.

Methods: Patients with MDS/MPN-RS-T under follow up in myeloproliferative neoplasms (MPN) clinic who were started on PEG-IFN were identified. PEG-IFN was offered to patients with anaemia or who were at high risk of anaemia or not suitable for or failed to respond to hydroxycarbamide. Starting dose of PEG-IFN was 45 μg every 2 weeks that was gradually increased to control platelet count <400. Once achieved dose was reduced gradually to most effective lowest dose.

Results: Six patients (five males, one female) with MDS/MPN-RS-T received PEG-IFN between January 2022 and December 2023. Patients' ages ranged between 69 and 89 years. PEG-IFN was initiated to control platelets count in the presence of anaemia and or blood transfusion dependence in 83% of patients. Five patients had Hb <125 g/L, two patients were transfusion dependent and one patient had splenomegaly at initiation of PEG-IFN. Median duration of follow up was 19.5 months. Overall response rate (ORR) was 100% including 33.33% Complete Responses (CR). There was significant reduction in platelets count (943 vs. 388; p 0.01). The observed reduction in WBC (11.98 vs. 7.88; p 0.14) and neutrophils (8.17 vs. 5.4; p 0.222) did not reach statistical significance. The patient with splenic enlargement showed reduction in spleen size. One patient became transfusion independent and second showed reduction in blood transfusion needs with an increase in reticulocytes count from a mean of 59.55 before treatment to 153 after.

Conclusion: PEG-IFN in low doses was well tolerated with no significant toxicities and all patients remained on PEG-IFN at the date of data collection. PEG-IFN showed high response rates and tolerability in a single-centre cohort with MDS/MPN-RS-T. These findings are novel and represent the first report of PEG-IFN in this patients group. We recommend further exploration of the role of PEG-IFN in the management of MDS/MPN-RS-T in larger studies.

BSH24-EP55 | Safety and efficacy of low dose pegylated interferon (PEG-IFN) in myeloproliferative neoplasms: Real world data

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Introduction: Patients with myeloproliferative neoplasms (MPN) require cytoreduction to normalise the elevated counts to reduce the risk of thrombosis. We present real world data from a single centre in the UK in patients with MPN who were commenced on PEG-IFN between January 2014 to December 2022.

Methods: Starting dose of PEG IFN was 45 μg every 1–2 weeks, dose was increased gradually to achieve complete haematological response (CHR) over 12 months. Once achieved dose was reduced to a minimum effective dose to as low as 45 μg every 6 weeks.

Results: The study has accrued 214 patients with MPN who commenced PEGIFN from January 2014 to December 2022. Median duration of follow-up was 60 m (range 12–120 months); 94 patients were males and 120 females; 91 patients had polycythaemia vera, 101 essential thrombocythaemia and 22 had myelofibrosis.

JAK2 mutation was present in 155 patients, CAL-R in 41, MPL in 3, whereas 14 were triple negative.

PEG IFN was chosen as first line (n = 91) due to young age or choice and at a subsequent line (n = 123). Twenty-four patients on venesections were offered PEG-IFN due to leucocytosis (n = 5) thrombocytosis (n = 12) or severe iron deficiency (n = 7). Ninety-nine patients were switched from hydroxycarbamide (HC) due to young age (n = 20), ineffective/intolerant (n = 46) or contraindicated due to leg ulcers/recurrent skin cancers/fever (n = 33).

Overall response rate was achieved in 91%, CHR in 50% at 12 months, JAK2 allele burden fell in 60%. Complete molecular response was seen in five patients at a median of 51 months. Deeper sustained responses were associated with earlier use of PEG-IFN in the course of disease, younger patients as first line as compared to it being used at second or subsequent line (74% vs. 63%).

PEG IFN was discontinued in 45 patients (ineffective 14, intolerant 15, unrelated 12 and disease progression/transformation 2). Thrombotic events were seen in 14 patients (11 arterial, 3 venous) unrelated to control of blood counts.

Only 15 patients came off PEGIFN due to adverse events as majority (n = 65) were grade 1–2 and managed with reduction

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or temporary suspension of PEG IFN and recommencing at a lower dose and frequency.
Conclusion: PEG-IFN is a safe and effective cytoreductive alternative to HC in patients with MPN. Low dose and slower increments avoid adverse events and discontinuation. It is least restrictive in terms of quality of life such as family and holiday planning and may modify disease course.

BSH24-EP56 | Detection and management of iron deficiency in pregnant women who had a major obstetric haemorrhage

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Background: Patient blood management in obstetrics aims to optimise haemoglobin levels and minimise bleeding for improved clinical outcomes, especially in the context of obstetric haemorrhage, a leading cause of maternal mortality. A key aspect includes prompt detection and treatment of iron deficiency early in pregnancy as it confers an increased risk of postpartum haemorrhage.
Methods: Here, we describe a case note review of electronic patient records, assessing the prevalence of pre-delivery iron deficiency and management among pregnant women with major obstetric haemorrhage (MOH) at University College Hospital between April and June 2022. Our cohort consisting of pregnant women who had a MOH was identified through a database and forms from our local transfusion lab.
Results: Fifty women with MOH were identified. One patient who had MOH from an early miscarriage was excluded. Median age was 33 years (range, 21–52). There were two twin pregnancies (4.1%). 16.3% (8/49) had normal vaginal delivery, 28.6% (14/49) had instrumental delivery while 74.1% (27/49) had Caesarian section. 95.9% (47/49) had ferritin screened for iron deficiency with 78.2% (37/47) being iron-deficient (ferritin <30). Among these 37, 48.7% (18/37) had oral iron, 5.4% (2/37) had intravenous iron while the remaining 46.0% (17/37) did not have iron replacement. Two women (4.1%) had iron deficiency anaemia during the antenatal period where only one patient was treated with oral iron.
The mean estimated blood loss was 1975 mL (range 1500–4000 mL). A total of 83 units of packed red cells (PRC), 30 units of fresh frozen plasma (FFP) and two pools of platelets were issued. In addition, 31/83 units of PRC and 13/30 units of FFP were administered. Sixteen MOH calls (32.7%) required administration of PRCs. Among the 16 women, 62.5% (10/16) were iron-deficient. Only one patient was anaemic who had coagulopathy secondary to cirrhosis. During the postpartum period, 55.1% (27/49) were anaemic. 18.4% (9/49) had PRC transfusion after delivery where a total of 12 units were administered. All patients with postpartum anaemia had iron replacement treatment with 70.4% (19/27) having intravenous iron and 29.6% (8/27) receiving oral iron only.
Conclusion: Iron deficiency is prevalent antenatally in our cohort of MOH women. Thus, prompt diagnosis and treatment is vital in the presence or absence of anaemia. This may mitigate the risk of obstetric haemorrhage, minimising the need for transfusions. In our local setting, there is scope for further improvement in treating iron deficiency during pregnancy through development of clear pathways and education measures.

BSH24-EP58 | More than just a number: Impact of ITP on psychosocial QoL in paediatric patients

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Introduction: Immune thrombocytopenia, characterised by low platelet counts due to immune system dysfunction, poses unique challenges for children and their families due to risk of serious bleed. It is one of the long-term conditions affecting multiple aspects of an individual's life which ultimately leads to a lower QoL. Though not an uncommon scenario in haematology clinics, the data showing impact of ITP on a patient's life from a physician's perspective is scarce. Since the exact aetiology is unknown, the management options are very limited while working in a resource restricted setting. Lack of awareness or inaccessibility, unaffordability being the major reasons influencing the management of ITP. This study will contribute to the global discourse on the psychosocial aspects of chronic illnesses in paediatric populations, with specific relevance to the unique socio-cultural context of Pakistan.
Objectives:

- Assess the impact of ITP on psychosocial quality of life
- Evaluate the clinical and demographic spectrum of childhood ITP

Methods: Descriptive, cross-sectional study was conducted at the Haematology Clinic LUMHS, Jamshoro.
A detailed predesigned, pre-structured questionnaire was filled by the physician in OPD, history taken from the patient or next of kin who came for follow-up. Specific investigations were added where available.
The questionnaire comprised five sections and collected information on demographics and diagnosis, symptoms of ITP, QoL (psychosocial) associated with ITP in patient, impact of ITP on parents' life, treatment received.
Results: Total 46 ITP patients were considered, and median age was 5.8 years (1.5–16 years), and mean platelet count was 17×10^9/L. (range 3–61) $\times 10^9$/L. Platelet transfusion history was positive in 77%. Overall QoL was low with limited access to school, outdoor activities, travel and sports. Children with visible bruises experienced negative social attention.

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Sixty-eight parents reported discontinuing therapy at some point due to economic reasons.

Conclusion: Though a benign disorder with a wait and watch approach in most patients, ITP does pose an undue pressure on the child as well as parents, limiting their overall exposure to the common challenges of life. Limited treatment modalities, non-responding to steroids often leads to main reliance on transfusion of platelet concentrates leaving the patient exposed to various transfusion related infections.

Keywords: bleeding, immune thrombocytopenia, paediatric, psychosocial, quality of life, transfusion

BSH24-EP59 | Myeloproliferative neoplasms and thrombosis—A single centre retrospective cohort study of 111 cases

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Myeloproliferative neoplasms (MPNs) are associated with an increased risk of arterial and venous thrombosis, representing a major cause of morbidity and mortality. We hereby present a UK single tertiary centre retrospective cohort of 111 patients with MPN thrombosis yielding insights into thrombosis characteristics and clinical practice.

Out of 485 registered MPN patients, 111 (22.8%) had a recorded thrombosis as of January 2023. Median age at the time of thrombosis was 56 years (range *r*, 14–84). A total of 55/111 (50%) patients were female and the majority were Caucasian (85/111, 76.7%). The underlying MPN was essential thrombocythaemia (ET) in 61/107 (57%), polycythaemia vera (PV) in 34 (31.8%) and myelofibrosis in 6 (5.6%). Cardiovascular risk factors were identified in 38/111 (34.2%). Regarding smoking status, 15/79 (19.0%) were current smokers and 27/79 (34.2%) were ex-smokers.

In cases where the dates of the MPN and thrombosis diagnosis were known, the MPN was diagnosed first (>100 days prior to thrombosis) in 28/84 (33.3%), the thrombosis first (>100 days prior to MPN) in 33/84 cases (39.3%) and simultaneous diagnosis (±100 days) in 23/84 (27.4%).

In this cohort, JAK2 V617F was the most common mutation (89/111, 80.2%) followed by CALR (8/111, 7.2%). No mutation was detected in 7/111 (6.3%). Eight percent of patients had additional mutations, most commonly DNMT3A ($n=3$) and TET2 ($n=2$).

At thrombosis, median haemoglobin was 136 g/L (*r*, 89-189 g/L), platelet count 483×10^9/L (*r*, 215–1206×10^9/L), white blood cell count 8.06×10^9/L (*r*, 4.28–26.01×10^9/L), haematocrit 0.40 (*r*, 0.28–0.59). Sixteen patients were taking cytoreduction at time of thrombosis, of whom 8 (50%) did not have fully optimised blood counts.

Also, 48/111 patients had two or more thrombotic events; there were 156 total thrombotic events. Venous thromboses accounted for 70/156 (44.9%), most commonly DVT ($n=24$) and PE ($n=18$). Atypical site thrombosis comprising cerebral venous sinus thrombosis and splanchnic vein thrombosis accounted for 13 (18.6%) and 9 (12.9%) of venous thromboses respectively. Arterial thrombosis accounted for 86/156 (55.1%) events, most commonly CVA (50/86 [58.1%]) and MI (23/86 [26.7%]). There were 16 significant haemorrhages.

Our data provide a real-world insight into the clinical challenges posed by MPN-thrombosis such as the incidence of atypical site thrombosis and stress importance of cardiovascular risk factor management.

We propose to extend this study via a multi-centre national retrospective cohort and subsequently to a prospective national registry of MPN thrombosis to gain vital insights into optimal management strategies for these patients and potentially inform future interventional clinical trials.

BSH24-EP60 | Real-world, single-centre experience of pregnancy in patients with Philadelphia negative myeloproliferative neoplasms

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Pregnancy in myeloproliferative neoplasms (MPN) can be associated with maternal and foetal complications due to increased risk of haemorrhagic and thromboembolic events and placental dysfunction. UK incidence of pregnancy in MPN is estimated to be 32/100 000 maternities per year. We hereby present obstetric outcomes of MPN patients attending University College London Hospital (UCLH), between 2015 and 2024.

Twenty-three patients were identified with a median age at MPN diagnosis of 33 years (range (*r*), 13–46). 82.6% (19/23) had a diagnosis of essential thrombocythaemia (ET) or triple-negative thrombocytosis, 8.7% (2/23) polycythaemia vera (PV) and 8.7% (2/23) secondary-myelofibrosis. In 64.5% (40/62) of pregnancies, diagnosis was known at conception. Regarding mutational status, JAK2V617F was present in 47.8% (11/23) patients, CALR in 21.7% (5/23) and MPL in 4.3% (1/23). The remaining 26.1% (6/23) patients were triple negative.

The cohort collectively experienced 62 pregnancies, 43 of which were managed at UCLH. Accounting for two ongoing pregnancies, the live-birth rates were 70.0% (42/60) and 80.5% (33/41) respectively. Focusing on pregnancies managed at our centre, median age at pregnancy was 35 (*r*, 22–47). Eight (18.6%) pregnancies necessitated assisted conception and demonstrated a higher median age of 38.5 years

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(*r*, 35–47). Where gestation at delivery was known, 92.9% (26/28) of live-births delivered at >37 weeks. Caesarean rate was 39.4% (13/33), of which 53.8% were emergency sections. Eleven (47.8%) patients (ET [*n* = 8, 72.7%] and PV [*n* = 3, 27.3%]) experienced foetal loss. Fifteen (24.2%, 15/62) miscarriages were recorded; 6 (14.0%, 6/43) in those managed at UCLH. Median maternal age was 32 (*r* 21–43) and median gestation 8 weeks (*r*, 5–24). One patient experienced four miscarriages and demonstrated a heterozygous prothrombin G20210A mutation in addition to ET.

Nine (39.1%) patients collectively experienced 11 haemorrhagic events. The majority (72.7%, 8/11) were post-partum haemorrhage, 50.0% of which were classified as major. With regards to thrombosis, one patient with undiagnosed ET experienced a cerebral venous sinus thrombosis at 11 weeks gestation. One patient experienced hypertensive complications necessitating an emergency delivery via caesarean section at 35 weeks.

Our data highlights promising live-birth rates in patients with MPN, although there is an increased risk of foetal loss and obstetric complications. There remain inconsistencies in the management of pregnancy in MPN and, although we adopt an individualised, patient-centred approach, there is an unmet need for further study and development of evidence-based treatment algorithms.

BSH24-EP61 | Chronic myelogenous leukaemia presenting with Morel Lavallee lesion—Case report

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Chronic myelogenous leukaemia (CML), is one of the myeloproliferative neoplasms, defined by dysregulated and uncontrolled proliferation of mature and maturing granulocytes with a uniform distribution. It is associated with the fusion of BCR (on chromosome 22) and ABL1 (on chromosome 9) resulting in a BCR: ABL1 fusion gene. This fusion gene produces BCR: ABL1 protein which causes the constitutive activation of Tyrosine kinase, implicated in the pathogenesis of chronic myelogenous leukaemia.

The clinical manifestation of CML is variable depending on the stage of the disease at diagnosis. 20%–50% of patients are asymptotic at the time of diagnosis, and 85% of patients are diagnosed in the chronic phase. systemic symptoms such as fatigue (34%), malaise (3%), weight loss (20%), drenched sweating (15%), abdominal fullness (15%), and bleeding episodes due to platelet dysfunction (21%) are the commonest manifestations.

The Morel Lavallee lesion is a closed soft tissue degloving injury resulting from the separation of the hypodermis from the underlying fascia, which in turn leads to hematoma collection between the layers. It is a rare manifestation of chronic myelogenous leukaemia (CML). Platelet dysfunction, acquired Glanzmann's thrombasthenia, and acquired Von Willebrand deficiency, are the main proposed mechanisms of Morel Lavallee lesion.

In this report, we describe a 50-year-old female who presented with right abdominal swelling, associated with easy fatigability, and significant weight loss of 1-month duration. Bone marrow aspiration revealed myeloid hyperplasia (with myeloid to erythroid ratio of 15:1). Neutrophils and bands 68%, metamyelocytes 6%, promyelocytes 8%, blasts 3% suggestive of CML-chronic phase. The diagnosis of CML was confirmed after RT-PCR (reverse transcription polymerase chain reaction) was positive for BCR/ABL1.

The patient was started on hydroxyurea, allopurinol and hydration. Imatinib 400 mg p.o/day was begun after cytoreduction. She received conservative care for the haematoma accumulation and was discharged with appointments to the general surgical and haematology clinics. She has significant clinical and laboratory improvement within 2 weeks of treatment.

BSH24-EP62 | Use of new third-line therapy for myeloproliferative neoplasm with concurrent BCR-ABL1 translocations and JAK2-V617F mutation

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Myeloproliferative neoplasms (MPNs) are clonal haematopoietic stem cell disorders characterised by overproduction and abnormal functioning of red and white blood cells and platelets. These chronic conditions affect various age groups and are present in various forms: chronic myeloid leukaemia (CML), polycythemia vera, essential thrombocythaemia and primary myelofibrosis (PMF).

Genetic mutations, notably JAK2, CALR, and MPL play a role in MPN development. The classification into BCR/ABL1-positive CMLs and BCR/ABL1-negative MPNs depends on the presence or absence of BCR/ABL1 translocation and is usually considered mutually exclusive (Ho Yi & Kim, 2019). Herein, we report the case of a patient diagnosed with PMF JAK-2 positive in 1997, subsequently developing concurrent BCR/ABL1-positive CML.

A 49-year-old female diagnosed with myelofibrosis in 1997 underwent Interferon treatment and was confirmed to be JAK-2 positive in Nov 2007. Her disease progression was monitored during this time, revealing splenomegaly in June 2010. In 2016, bone marrow analysis indicated a JAK2 V617F allele burden of 67% and demonstrated fibrosis (reticulin grade 2–3). Despite cytogenetic challenges, rRuxolitinib (JAK2 inhibitor) was started with the patient's DIPPS+ risk score calculated as intermediate 1. Interferon was held due to MPN10 symptom persistence.

With rising WCC, hydroxycarbamide was commenced in May 2022. By this time the patient was transfusion-dependent and bone marrow aspirate showed no leukaemic transformation with ASXL1 (34%), PHF6 (48%) JAK2 (48%). Surprisingly, a concurrent diagnosis of CML (chronic phase)

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with classical BCR-ABL-positive (42%) profile emerged in the following year. Imatinib was initially administered but no response was observed in subsequent bone marrow monitoring. The patient was switched to bosutinib with ruxolitinib maintenance again with response failure.

With no response to the above treatment, the patient was started on asciminib, a new third-line treatment option for CML (Yeung, Shanmuganathan & Hughes, 2022). Our patient's WCC results have remarkably improved to just above borderline abnormal by cycle 1, the third week of treatment. Treatment remains ongoing.

Limited case reports make the treatment of concurrent JAK2-positive MPNs and BCR-ABL-positive CML challenging. Previous reports have noted response to kinase inhibitors in patients with dual mutations; here the patient failed in treatment response until third-line therapy asciminib. Occurrence of this double diagnosis remains uncommon and increased awareness of this dual presentation may lead to improved clinical outcomes and inform future treatment strategies, especially as genetic diagnosis and treatment options expand.

BSH24-EP63 | A real-world patient experiences and quality of life insights snapshot in cold agglutinin disease (CAD)

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Background and Aim: Cold agglutinin disease (CAD) is a rare chronic haemolytic disorder characterised by a clonal lymphoproliferative disease with a range of clinical manifestations and treatments. Our aim was to determine the characteristics of CAD symptoms and to explore quality of life (QoL) issues across a small cohort.

Methods: Patients with CAD managed at a treatment centre, University College London Hospitals, were invited to complete an online survey regarding disease, treatment, hospitalisations, QoL, symptoms and unmet needs.

Results: Twelve patients completed the online survey. The median age of patients was 71 (range 51–88) years, and the majority of patients were female (8/12, 67%). 8/12 were White, 3/12 Asian, 1/12 Black.

Forty-two percent (5/12) had received complement inhibitors, while 25% (3/12) reported receiving chemotherapy or immunotherapy. No patients were hospitalised at the time of the survey and 33% (4/12) had been in the 6 months prior. All hospitalisations were reported to have been related to CAD or infection.

Regarding quality of life, median scores for the patient cohort were 0.756 (IQR 0.186) for the EQ-5D-5L Index Score, 5.5 (IQR 3.0) for 'Health State' (10/10 being patient-perceived 'best health'), 6.5 (IQR 2.3) for 'Fatigue' (10/10 being the most severe), and 7.0 (IQR 3.0) for 'Psychological/Mood' (10/10 being the best). 'Pain/discomfort' was the most highly scored EQ-5D-5L domain in terms of severity at a median of 2/5, while 'self-care' was the least severely scored domain at 1/5.

Blue extremities in response to the cold was the most common symptom, with 83% of patients reporting this either 'often' or 'always', in comparison to 42% for shortness of breath, 17% for dizziness, and 8% for sweatiness outside of exercise. All patients reported some form of shortness of breath, while 33% of patients experienced no sweatiness outside of exercise. Free-text capture of patients' unmet needs highlighted a better understanding of the disease and its management as the most common theme (2/12 patients, 17%). 92% (11/12) were interested in a digital health solution that could support their day-to-day function.

Conclusions: In this real-world snapshot of QoL, 'pain/discomfort' was the most severely affected EQ-5D-5L domain. Future work will focus on further expanding the cohort and including digital tracking to support the monitoring of disease.

BSH24-EP64 | Real-world electronic data in a haematology centre to better understand patient and care activity

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Background and Objectives: We report on the use of real-world data capturing patient activity and services at a single site. Our aim is to develop a continuous data structure for a better understanding service activity change over time. This will inform allocation of resources and act as a vehicle for practice improvement for better patient care. Exemplar data are described for myeloma practice, but myeloid service and use of blood components will also be discussed.

Methods: We developed scripts and programmatic notebooks to connect multiple information systems and extract relevant data. We initially focused on two data sources: chemotherapy prescribing system (ARIA MedONC) and Oxford University Hospital's internal data warehouse, which provides our electronic patient record (EPR) system Oracle Millennium. We used well-established free and open source languages and software, python libraries including pyodbc, psycopg2, pandas, numpy, jupyter and matplotlib, and the database postgreSQL to generate descriptive analyses, including for drivers of service activity in the haematology Day Treatment Unit (DTU).

Results: As a first example, we analysed the change in prescription numbers of fully oral myeloma treatment regimens versus those including intravenous/subcutaneous components/DTU activity, over the past 7 years. We found fully oral myeloma regimens (for example

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lenalidomide dexamethasone [LD] and ixazomib, lenalidomide and dexamethasone) (IRD, approved for CDF roll-out in 2017) increased dramatically in usage (>5-fold) from 2021 onwards, during the COVID pandemic. However, 2023 oral prescription numbers then fell slightly, accompanying a change to include more cycles on the same prescription to reduce staff workloads. In comparison, the number of all haematology prescriptions rose 2.6-fold between 2010 and 2023, with fully oral regimen prescriptions increasing 3.4-fold and iv-inclusive regimens increasing 1.9-fold. Display of prospective transfusion data generated feedback information on usage, by comparison to standards.

Conclusions: We have established proof-of-concept for use of routine electronic data to analyse practice and areas where density of activity is changing, enabling prediction of resource shortfalls or reallocation requirements. In the future, new NICE approvals (such as that to allow broader use of fully-oral IRD for myeloma during COVID) may significantly change prescribing habits over only a few months, which can now be more readily monitored. We anticipate another change with the recent approval of daratumumab lenalidomide dexamethasone for non-transplant eligible induction therapy, bringing a new set of patients from fully oral to DTU-requiring regimens. Further applications include more efficient quality improvement initiatives, rather than resource-intensive manual audits, with potential cost-savings.

BSH24-EP65 | Stopping TKI-therapy in CML as per the BSH guidelines, an audit from a DGH practice

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Introduction: The overall survival of chronic myeloid leukaemia (CML) patients has remarkably improved after tyrosine kinase inhibitors (TKI). TKI therapy was initially thought to be indefinite. To date around 3000 trial patients have discontinued TKI treatment safely. In the UK DESTINY study, eligible patients underwent de-escalating therapy for 12 months with half-dose, before withdrawing completely. These patients have shown a particularly high recurrence-free survival rate (RFS) of 76% at 24 months for those patients in stable MR4.

The BSH 2020 guidelines recommend considering stopping TKI in patients who are on approved TKI therapy for at least 3 years (preferably 5 years), who have sustained molecular response of MR4 (molecular response <0.01%)/deep molecular response (DMR) by BCR-ABL1 measurement for the last 2 years. 50% dose reduction for 12 months prior to discontinuation is recommended, with monthly monitoring.

Methods: An audit was conducted in a district general hospital (NGH) to assess the total number of the eligible patients with CML–chronic phase (CML-CP) who can stop TKI as per the guidelines.

Patients on first line TKI therapy for CML-CP were identified. Eligible patients were included based on duration of DMR. Clinic letters were reviewed to see if they were offered to stop TKI as per the guidelines. Patients with prior history of accelerated phase or blast crisis, previous resistance to any TKI, previous detection of a BCR-ABL1 KD mutation, patients on an approved TKI therapy for less than 3 years were excluded.

Results: We had 45 patients on TKI therapy, 18 of them were eligible to stop TKI based on the BSH guidelines recommendation. Eleven patients were on imatinib, four on nilotinib and three on dasatinib. Only nine eligible patients had stopped for various reasons including intolerance. Also, 50% of the eligible patients were not offered to stop. Average duration of DMR for eligible patients was 5 years 2 months.

This audit was presented in the department meeting and was re-audited in 6 months. Subsequently, three patients had reduced dose/stopped TKI therapy, three were referred to MDT, 1 declined (patient choice) and two were not offered.

Conclusion: Re-audit showed there was a better recognition of the patients eligible for stopping TKI. Stopping treatment safely would reduce cost, improve quality of life and allow younger patients to conceive safely. However, we should recognise that stopping TKIs can be a difficult decision especially for the patients who have been tolerating it without any side effects.

BSH24-EP66 | Refining Ph-MPN diagnostic pathways: Insights from an audit of Wales' Medical Genomics Service

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Background: The All Wales Medical Genomics Service (AWMGS) is the sole NHS provider of cancer genomic testing in Wales, serving a population of 3 million people. The AWMGS accepts referrals for Philadelphia chromosome negative myeloproliferative neoplasm (Ph-MPN) investigations from GPs and specialist healthcare providers across Wales. Ph-MPNs, specifically polycythaemia vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (PMF) constitute approximately 11% of haematological malignancies in the UK.[1] These disorders are distinguished by mutations occurring in a limited set of genes, namely JAK2, CALR, and MPL, with JAK2 V617F analysis being a first genetic line test. Ph-MPN referrals constitute approximately 40% of those received for haematological malignancies at the AWMGS, with 50%–60% of these requests received for JAK2 testing alone. This is disproportionately high in the context of UK haematological malignancy incidence rates. As part of a continuous improvement initiative, an audit was planned to review Ph-MPN referrals received from across Wales.

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Methods: Data was extracted from the AWMGS database on JAK2, CALR and MPL requests received over a 12-month period from August 2021 to August 2022. This information was used to evaluate the JAK2 diagnostic yield of referring hospitals and GPs. Subsequent to this, 3 months' worth of data was sent to Clinical Haematology to align the genetics results and clinical presentation for each request. Upon reviewing of the data, the clinical team provided a final consensus on whether each request was consistent with the 2016 World Health Organisation (WHO) criteria for Ph-MPNs. Data were analysed with an aim to understand trends in diagnostic yields and compliance with the WHO criteria.
Results: These investigations demonstrated that there is a significantly reduced diagnostic yield for GP referrals, as compared with that of specialist referrers (2% and 14% respectively). The JAK2 pickup rate varied across the NHS Wales health boards, which may be a reflection a differing adherence to the WHO criteria. Results presented will include a breakdown of diagnostic yields for all Ph-MPN associated investigations, an assessment of the type of specialties referring, and an evaluation of compliance with the WHO criteria.
Conclusion: These data evidence the need to review the referral guidance that is provided for Ph-MPN investigations across Wales.

Reference

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BSH24-EP68 | Case study presentation ITTP and JW treated without plasma exchange (PEX) and blood products

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We report the successful treatment of a Jehovah's Witness patient with immune TTP (iTTP) without PEX. The patient was treated with immunosuppression and caplacizumab.
Thrombotic thrombocytopenic purpura (TTP) is a rare and life-threatening thrombotic microangiopathy characterised by microangiopathic haemolytic anaemia, severe thrombocytopenia, and organ ischemia linked to disseminated microvascular platelet rich-thrombi.
TTP is specifically related to a severe deficiency in ADAMTS13 (a disintegrin and metalloprotease with thrombospondin type 1 repeats, member 13). The first-line therapy for acute TTP is based on daily therapeutic plasma exchange supplying deficient ADAMTS13, with or without steroids. Additional immune modulators are steroids and the humanised anti-CD20 monoclonal antibody rituximab. Caplacizumab is also utilised in the management of TTP.
This is a case study of a patient treated in our hospital who was admitted with immune thrombotic thrombocytopenic purpura (iTTP).
The patient was a 47-year-old female. Her past medical history was as follows: Recurrent venous thromboembolism with anti phospholipid syndrome, lymphocytic interstitial pneumonia (LIP)—secondary to SLE—ITP, CVA October 2021, Uterine fibroid—hysterectomy—B12 deficiency and fibromyalgia.
Diagnosis showed TTP but complicated by fact that patient will not accept blood products including FFP/octoplas.
The prescribed treatment was as follows: STAT 1 g IV methylpred then OD for 3/7 total with PPI cover, 10 mg STAT caplacizumab IV followed by SC dose 4 h later, aranesp 300 µg STAT, folic acid 5 mg OD and rituximab 375 mg per $m^2 \times 4$.
Outcome: The patient made excellent clinical and laboratory evidence of remission: the patients acute treatment period was unremarkable and uncomplicated. The patient respond to immunosuppression and caplacizumab without the need for PEX or blood products. This case study further support the treatment of acute ITTP without PEX as successful standard of care.
As part of a review, we also systematically searched for previous published reports of TTP in Jehovah's witness patients. There were 14 results in Medline, 29 in Embase and five in Emcare. Altogether there were 30 results once the duplicates were removed.
Conclusion: This case study links in with the myari study that is currently in recruitment within our directorate which looks to explore standard first line treatment of acute iTTP with subcutaneous caplacizumab. This case study will add to the body of knowledge and help with the further treatment of ITTP Jehovah's Witness. It is important that case studies like this are presented into the public arena to further support patient safety and care.

BSH24-EP69 | Patient experience, quality of life and unmet need in UK CML community

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Introduction: With the introduction of tyrosine kinase inhibitor (TKI) therapy, patients with chronic myeloid leukaemia (CML) have a life expectancy close to that of the general population.
Considering the impact of long-term treatment on quality of life (QoL) is critical to improve healthcare quality and optimise outcomes. Patient reported outcomes (PROs) provide the unique patient perspective and their use has demonstrated benefits on overall and progression free survival in cancer. Furthermore, understanding patients' unmet real-world needs is paramount to improving service-provision, new therapies and patient outcomes.
Smartphone applications, wearable technology and associated digital health technological innovation provide an

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opportunity for continuous patient monitoring, as well as greater engagement, autonomy, and responsibility for managing health. In this study, we aimed to investigate QoL, symptom burden and unmet need within the UK CML community, including acceptability of potential digital healthcare solutions.

Methods: In partnership with CML patient support groups, we created an electronic patient questionnaire. Alongside demographic and treatment parameters, QoL and symptom burden were assessed via EORTC QLQ-CML24. Uptake and acceptability of the smartphone application 'My CML' was assessed. Patients were also asked about unmet needs, challenges and what could improve outcomes.

Results: A total of 54 patients responded, aged 29 to 77 years (median 55). Twenty-six percent were male ($n = 14$), 70% female ($n = 38$), 2% ($n = 1$) non-binary and 2% ($n = 1$) preferred not to say. Current treatment included imatinib ($n = 18$), nilotinib ($n = 11$), dasatinib ($n = 9$), bosutinib ($n = 6$), ponatinib ($n = 1$) and asciminib ($n = 4$), with 29 (54%) in first-line setting and 25 (46%) beyond first-line. Five patients had achieved a treatment-free remission (treatment discontinued).

Fifty-one patients (94%) reported living with side effects (any grade), the most common being muscle and joint aches/pains (77%), skin problems (72%), and drowsiness (69%). Common concerns included worrying about future health (81%) and risk of infection (70%). Unmet needs included mental health support, management of pain, fatigue and healthcare professionals not understanding the impact on QoL.

Thirty patients (55%) had used the 'My CML' app, with the most helpful features being tracking blood results, recording/tracking symptoms, and a drug interaction checker.

Fourty-two patients (77%) were keen to support their CML management with a wearable device.

Conclusions: Despite significant advances in the management of CML, most patients live with side effects which impact on their QoL. Capturing PRO data can optimise therapy and drive crucial real-world evidence generation. Biometric monitoring is an unmet need in the CML population.

BSH24-EP71 | Navigating the storm: Adherence and management of polycythaemia vera through the COVID-19 pandemic

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Introduction: We sought to investigate the adherence of physicians to the 2018 British Society for Haematology (BSH) guidelines on the diagnosis, risk stratification and management of polycythaemia vera (PV) patients and the impact of the pandemic on routine haematological investigation/management of a common problem erythrocytosis and PV. The groundwork of our investigation was established through a pre-pandemic audit at GSTT in June 2019, highlighting lack of consistency in investigations for suspected PV. Subsequently, we followed this with a repeat analysis during the pandemic when patients frequently underwent telephone assessment.

Methods: A cohort of 41 patients who were diagnosed with PV from 2019 to 2023 and managed in the clinic were randomly selected. Guidelines for the stage 1 investigations of suspected PV include a full blood count (FBC), serum ferritin, serum erythropoietin (EPO), carboxyhaemoglobin (CoHb) and JAK2 V617F mutational analysis. The patients' case should also be discussed in a multidisciplinary team meeting (MDT) and an assessment for cardiovascular risk (CV) factors. The guidelines stratify thrombotic risk based on age >65 years and history of thrombosis. Standard treatment for all low-risk and high-risk patients involves aspirin therapy and venesection to target haematocrit of less than 0.45. Cytoreductive therapy is indicated in all patients with high-risk disease and a few low-risk patients with persistent disease, symptoms, or leucocytosis despite venesection and aspirin therapy.

Results: Compared to the first audit, the use of FBC and JAK2V617F mutational analysis remained at 100%. Serum ferritin and MDT compliance had marginal changes within 10% of pre-pandemic levels. There was a significant improvement in the use of CoHb from 12.5% pre-pandemic to 43% post-pandemic while a decrease in the use of serum EPO from 75% to 61%. However, in clinical practice, a high haematocrit and positive JAK2V617F mutation satisfies the positive primary PV diagnosis criteria. In addition, all patients were accurately screened for thrombotic risk and cardiovascular risk was assessed in 76% of patients. Treatment based on thrombotic risk considering aspirin, venesection and cytoreductive therapy was 100% compliant with guidelines. Finally, 66.7% of patients had their pruritis treated according to the guidelines.

Conclusion: Despite additional strain on healthcare resources, adherence to BSH guidelines remained strong, demonstrating the resilience of the haematology service delivery through the pandemic. Furthermore, we found a maintenance of most and improvement in particular use of CoHb compared to pre-pandemic rates management standards were not compromised by remote assessments.

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BSH24-EP72 | PACIFICA: A randomised, phase 3 study of pacritinib versus physician's choice in patients with myelofibrosis

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Background: As the treatment landscape continues to evolve in myelofibrosis, there remains an unmet need for patients with cytopenic myelofibrosis who have thrombocytopenia, leukopenia, and/or anaemia (Palandri et al. *Cancer* 2023). Pacritinib is an oral JAK2/IRAK1/ACVR1 inhibitor with demonstrated clinical activity in myelofibrosis in two Phase 3 studies and a phase 2 dose-finding study, all inclusive of patients with severe thrombocytopenia and anaemia. The PACIFICA trial (NCT03165734) is designed to confirm the efficacy and safety of pacritinib 200 mg twice daily (BID) versus physician's choice therapy in patients with myelofibrosis and severe thrombocytopenia.

Study Design: PACIFICA is an international, multicenter, randomised, controlled phase 3 trial of pacritinib versus physician's choice (P/C) in adults with myelofibrosis (primary or secondary) with DIPSS intermediate- or high-risk disease, ECOG performance status 0–2, platelet counts $<50\times10^9$/L, who are not candidates for stem cell transplant and can be either JAK2 inhibitor naïve or have had prior JAK2 inhibitor therapy.

Patients with prior ruxolitinib exposure may enrol provided that the daily dose did not exceed 10 mg in 90 of the 120 days prior to Day 1. Patients with other (non-ruxolitinib) prior JAK2 inhibitor exposure may enrol provided that the total duration of therapy was <90 days. Patients may not have had exposure to >1 prior JAK2 inhibitor. Additional exclusion criteria include recent grade ≥2 cardiac or hemorrhagic events, left ventricular ejection fraction <50%, QTcF >450 ms, or use of medications that increase risk of haemorrhage or QTc prolongation.

Patients are randomised 2:1 to continuous pacritinib 200 mg BID or P/C (low-dose ruxolitinib [≤10 mg/day], danazol, corticosteroids or hydroxyurea). The study has co primary endpoints: the proportion of patients achieving a ≥35% spleen volume reduction and the proportion achieving a ≥50% reduction in total symptom score (version 2.0, excluding tiredness) from baseline at week 24. A sample size of 399 provides 85% power to meet both primary endpoints. Secondary objectives include overall survival, patient global impression of change response at week 24, and safety. Tertiary endpoints include leukaemia-free survival, haematological improvement, fatigue improvement, changes in biomarkers and gene expression, and proportion of patients who experience a major adverse cardiac event (MACE). PACIFICA is enrolling at approximately 100 sites globally (excluding the USA).

BSH24-EP73 | An audit of use of intravenous immunoglobulin therapy in haemato-oncology patients

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Acquired hypogammaglobinaemia is common in haematological malignancies; this can be driven by the disease pathogenesis or therapeutic agents employed. There remains an inconsistent approach in how these patients are managed, in particular with regards to the use of intravenous immunoglobulin (IVIG). Here we present a retrospective case notes review of haemato-oncology patients in receipt of IVIG at University College London Hospital over a 12-month period (1/1/2022 to 31/12/2022).

We identified 86 patients who received a total of 382 doses: an average of 4.4 doses per patient (range 1–13). The median age was 63 years (range 11–84), the majority (67%) were male. The commonest underlying diagnoses were low grade lymphomas (L-GL) (21/86, 24%), high grade lymphoma (17/86, 20%), multiple myeloma (MM) (14/86, 16%), acute leukaemia (AL) (11/86, 13%), chronic lymphocytic leukaemia (7/86, 8%), and Waldenstrom macrobulinemia (6/86, 7%).

The indications for IVIG were secondary immunodeficiency (54/86 [63%]), post allogenic bone marrow transplant (BMT) (19/86 [22%]), secondary ITP (7/86 [8%]) and cancer associated HLH (6/86 [7%]). With regards to dosing, 66/73 (90%) received 0.4 g/kg, 5/73 (7%), 0.5 g/kg and 2/73 (3%) 0.6 g/kg. In terms of frequency, the majority (65/73, 89%) were treated monthly. 71/73 (97%) patients had immunoglobulin through levels performed prior to each infusion. IVIG was well tolerated, however, 27/86 (35%) patients experienced a mild reaction. 3/86 (9%) patients discontinued treatment due to a severe adverse event.

In our cohort, MM patients required IVIG later in their treatment pathway. The majority (11/13 [85%]) had received at least four lines of MM therapy. Of these, 5/13 (38%) were treated with bispecific antibodies. Regarding lymphoma patients, 12/38 (32%) had only one line of therapy, before requiring intervention with IVIG. However, heavily pretreated patients were also observed, including 8/38 (21%) who underwent CAR-T therapy. In the post allogenic BMT subgroup, the commonest underlying diagnoses were AL (6/19, 33%) and L-GL (5/19, 26%).

In conclusion, our findings highlight the increasing use of IVIG in haemato-oncology patients. This is most likely in part driven by the rise of immunotherapy and novel agents such as bispecific antibodies. IVIG was well tolerated, with low rates of discontinuation due to reactions. We observed good practice in terms of dosing, frequency of administration and monitoring of immunoglobulin through levels pre-treatment.

With the expansion of CAR-T therapy and bispecific antibodies, there is an unmet need for high-quality trials to establish the optimal strategy for management of acquired hypogammaglobulinemia in haemato-oncology patients.

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BSH24-EP75 | Evidence of relevant anaemia response in myelofibrosis patients with impaired renal function treated with momelotinib

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Introduction: Anaemia is a common finding in patients with myelofibrosis (MF), is a marker of more aggressive disease, and remains an area of unmet need despite the introduction of JAK inhibitors such as ruxolitinib and fedratinib, which may worsen anaemia despite their wider benefits. Momelotinib (MMB) a novel oral JAK1, JAK2 inhibitor (JAKi), and activin A receptor Type 1 inhibitor has been shown to reduce associated symptoms, improve anaemia and reduce spleen size in MF. A common cause of anaemia is chronic kidney disease (CKD) which is prevalent among patients with MF, in prior MMB studies SIMPLY 1, SIMPLIFY 2 and MOMENTUM patients with eGFR,30 mL/min (CKD stage IV) were excluded.
Aim: To evaluate MMB efficacy in a 'real-world' setting with a particular focus upon patients with difficult to treat co-morbidities especially CKD.
Methods: Access to MMB is available in the UK via a compassionate use scheme. MF patients receiving this treatment were monitored via our service at Guy's and St Thomas' NHS Foundation Trust. CKD-EPI equation was used to calculate eGFR. Subjects with Stage-IIIB and Stage-IV CKD are identified as moderate to severe or severe CKD. Clinical assessment was performed at 2, 4, 6 and 12 weeks with full blood count, renal and liver function tests.
Results: There were 18% ($n=4$) with eGFR >90, 45% ($n=10$) with Stage-II, 22% ($n=5$) with Stage-IIIa, 4.5% ($n=1$) and 9% ($n=2$) with Stage-IIIb and IV CKD were respectively at baseline. Two patients had Stage-IV CKD. Both were male aged 71 and 83 with transfusion dependence (12 and 6 units over the 12 weeks pre-baseline). MMB was initiated at 200 mg OD then down-titrated to 100 mg OD in one patient, with the other patient starting at 100 mg OD. They subsequently remained transfusion free between 2 and 5 weeks, respectively. There were no reports of significant signs of toxicity apart from Grade 1 fatigue ($n=2$), Grade 1 lightheadedness ($n=1$).
Discussion: Despite Stage-IV CKD patients were excluded from clinical trials with MMB, our results demonstrated that MMB is safe and efficient in these patients with minimal side effects when lower dose is used. Further data are required to evaluate the place of MMB in a real-world setting.

BSH24-EP76 | Randomised, open-label phase 3 study of the lysine-specific demethylase 1 inhibitor bomedemstat for essential thrombocythaemia

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Essential thrombocythaemia (ET) is a myeloproliferative neoplasm (MPN) characterised by thrombocytosis and megakaryocyte hyperplasia and commonly associated with driver mutations in JAK2, CALR and MPL. Current treatments prevent thrombotic complications but do not substantially alter the natural history of ET. The lysine-specific demethylase 1 (LSD1) enzyme regulates haematopoietic stem and progenitor cell proliferation and is overexpressed in MPNs. Bomedemstat is an irreversible inhibitor of LSD1 that, in a phase 2 study, improved symptoms, durably reduced platelet and white blood cell counts, and reduced mutation burden in patients with ET. This randomised, open-label, phase 3 study (NCT06079879) is designed to evaluate bomedemstat versus best available therapy in patients with ET who had an inadequate response to or were intolerant of hydroxyurea. Eligible patients are ≥18 years of age; have a diagnosis of ET per World Health Organization 2016 diagnostic criteria and have a bone marrow fibrosis score of grade 0 or 1, a platelet count of $>450\times10^9$/L, an absolute neutrophil count of $\geq0.75\times10^9$/L, and a history of inadequate response to or intolerance of hydroxyurea. Approximately 300 patients will be randomly assigned 1:1 to receive bomedemstat at a starting dose of 50 mg/day PO or investigator's choice of best available therapy (anagrelide, busulfan, interferon alfa/pegylated interferon alpha or ruxolitinib) for up to 52 weeks. The dose of bomedemstat will be titrated for each patient to a target platelet count of ≥150 to $\leq350\times10^9$/L. After 52 weeks, patients in the bomedemstat arm can continue treatment, and patients in the best available therapy arm can cross over to bomedemstat for a maximum of 156 weeks on study. Randomization will be stratified by hydroxyurea history (inadequate response vs. intolerance) and Myelofibrosis Symptom Assessment Form, version 4.0 (MFSAF v4.0) baseline score (≥4 vs. <4). Clinic visits will occur every 2 weeks until week 12 and monthly thereafter. Adverse events will be monitored up to 30 days after treatment end and will be graded per NCI CTCAE, version 5.0, criteria. The primary end point is durable clinicohaematologicalal response rate by week 52 per modified European LeukemiaNet criteria. Secondary end points are duration of clinicohaematologic response and haematologic remission, change in fatigue and total symptom score per MFSAF v4.0, change in total fatigue score per the Patient-Reported Outcomes Measurement Information System Fatigue SF-7a scale, incidence of thrombotic or major haemorrhagic events, disease progression to post-ET myelofibrosis

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or myelodysplastic syndrome/acute myeloid leukaemia, event-free survival, and safety and tolerability.

BSH24-EP77 | Parathyroid hormone in *Plasmodium berghei* infection

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Background: Malaria infects approximately 250 million and kills over 600 000 people per year. The *Plasmodium berghei* murine model is used to study the effect of malaria on haematopoietic stem cells (HSCs). Parathyroid hormone (PTH) can avoid HSC proliferation by protecting osteolinage cells in the bone marrow (BM). This study evaluates haematopoietic stem and progenitor cell (HSPCs) number and their localisation in the BM during *P. berghei* infection and PTH therapy via microscopy.
Methods: A cKit, lineage and DAPI immunofluorescent staining panel was employed to identify HSPCs via microscopy. Four mice were used to study the effects of *P. berghei* and PTH, with one section of femur bone marrow from each PBS/PTH and infected/control mouse analysed. HSPCs and HSPC clusters (≥3 HSPCs less than 20 μm from each other) were counted manually. Cell-to-cell and cluster-to-cluster distances were evaluated using ImageJ and compared to that of similar numbers of randomly distributed dots within the same sections, the FigureJ plugin created figures. Welch's *t*-tests and Kolmogorov–Smirnov tests assessed the significance of differences between groups. $p < 0.05$ was considered significant.
Preliminary Results: HSPC and cluster frequencies were greatest in PTH-treated control mice (35 HSPCs and four clusters $1 \times 10^6\,\mu m^2$). HSPCs and clusters were significantly further apart in the PTH-treated infected compared to both PTH-treated control ($p < 0.0001$ and $p = 0.0061$ respectively) and placebo-treated infected mice ($p < 0.0001$ and $p = 0.0441$ respectively). HSPCs showed no significant difference in cell-to-cell and cluster-to-cluster difference between the observed cells and a computer-generated random distribution.
Discussions: Previous literature reports HSPC proliferation in PTH-treated infected mice is markedly lower than in PTH-treated control and placebo-treated infected, and the observation of the present study align with this. However, the lack of a significant difference in cell-to-cell and cluster-to-cluster distances between the observed distribution and computer-generated distribution on cells in the PTH-treated infected mice suggests, PTH alone may be insufficient to control HSCPs; similar to *N*-acetyl-l-cysteine (NAC) in prior studies. Cohort differences in cellular distances were identical to differences in proliferation rates reported in previous literature indicated that these distances could be used a metric for proliferation rate.
Conclusions: PTH and *P. berghei* infection have significant effects on HSPCs organisation in the BM microenvironment. However, further studies, including PTH-NAC treatment combination and ki67 as a marker of proliferation, are needed to validate the utility of PTH as a regulator of HSPCs in malaria infection and the effect of infection on the localisation of HSPCs in the bone marrow.

BSH24-EP79 | Prevalence of ABO and RhD blood group system among blood donors in blood centre Batticaloa

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Introduction. Major blood group systems in human which significantly affect the transfusion are ABO and Rh blood group systems. The prevalence and distribution of these blood group systems vary across the worldwide. ABO system was discovered by Dr Karl Landsteiner in 1901 (A, B, O) and AB was discovered later in 1902 by Landsteiner association. It is the most important blood group system in humans and there are four major phenotypes A, B, AB, O. Apart from these four major phenotypes there is another phenotype with clinical significance; Bombay O. Rh system is the second most important blood group system after ABO system. It is the most complex blood group system and was discovered in 1940 by Landsteiner and Wiener. RhD antigen is highly immunogenic among other antigens in Rh system.
Aims: To determine the prevalence of ABO and RhD blood group system among voluntary blood donors in Regional Blood Centre Teaching Hospital Batticaloa, SriLanka.
Methods: Retrospective study was conducted among 4408 voluntary blood donors who donated in Regional Blood Centre Teaching Hospital Batticaloa from 1 May 2023 to 30 September 2023. ABO and RhD typing were done by using tube agglutination method. Grouping discrepancies were confirmed by the National Immunohematology Reference Laboratory.
Results: During this period 4408 voluntary blood donors were analysed. All the donors were between age of 19 and 60 years and have fulfilled the donor selection criteria to donate. Among total number of donors, majority of them were male donors ($n = 2999$; 68%) whereas 32% ($n = 1409$) were female donors. Regarding ABO system, 43.9% ($n = 1935$) of donors were Group O, 28.99% ($n = 1278$) of donors were Group B, 22.05% ($n = 972$) of donors were Group A, and 5.01% ($n = 221$) of donors were belong to group AB. There were 2 (0.05%) donors whose blood group was Bombay O; which is a very rare phenotype of ABO blood group system. 94.33% ($n = 4158$) of donors were RhD Positive whereas 5.62% ($n = 248$) of donors were RhD Negative. Among 4408 donors, 2 (0.05%) donors were RhD variant.
Summary and Conclusions: Overall majority of the donors had blood group O and second highest group was Group B in ABO blood group system. In this study population we were

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able identify Bombay O donors which is a rare phenotype of ABO blood group system. Vast majority of donors were RhD positive where as there were few donors with RhD variants.

BSH24-EP80 | Influencing change in transfusion information technology systems—The SCRIPT survey and collaborative working project

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SCRIPT is the SHOT Collaborative Reviewing and reforming IT Processes in Transfusion working group. The group was formed in 2019 following identification in SHOT reports of increasing numbers of IT-related errors during the transfusion pathway. SCRIPT aimed to enhance transfusion safety by identifying areas for improvement and provide resources to bridge gaps identified in IT processes. An initial survey of all registered SHOT reporters in late 2020 helped understand the current status of IT implementation across the NHS, and identify gaps and challenges faced by teams across the UK. The user survey identified key challenges with IT:

1. Barriers to implementing IT systems, including lack of funding, resources, and engagement from Trust/Health Board, particularly relating to electronic blood management systems (EBMS)
2. Lack of IT expertise, training and allocated time for implementation, development, and maintenance of systems
3. A need for national guidelines and templates for procurement, validation, and implementation
4. Deficiencies in laboratory information management systems (LIMS), particularly relating to algorithms for appropriate selection of blood components where patients have specific requirements

The key challenges identified were reviewed by a collaborative group including representatives from key transfusion stakeholders. Processes for addressing each of the key challenges were agreed and taken forward by the group.
To address gaps in funding the survey results were presented to NHS England. This enabled provision of a funding stream for hospitals in England to implement IT systems for transfusion.
Lack of IT expertise and training was addressed by the provision of IT related educational resources on the SCRIPT page of the SHOT website.
The need for national guidelines and templates was addressed by provision of resources on the SCRIPT page of the SHOT website, including support for business cases for procurement.
A LIMS supplier survey was performed in late 2021 to address specific issues identified in the initial user survey. Survey results are available on the SCRIPT page of the SHOT website and an article relating to LIMS has been published.
The SCRIPT user survey has effected tangible changes in supporting transfusion IT systems, including release of funding and provision of many useful resources freely accessible to all organisations. SCRIPT continue to build on this work, including plans for further discussions with LIMS providers, an e-learning module to support training for IT experts in transfusion and more useful resources. The SCRIPT project highlights the power of surveys and collaborative working to influence positive change.

BSH24-EP81 | Role of therapeutic plasma exchange in a child with secondary haemophagocytic lymphohistiocytosis

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Background: Haemophagocytic lymphohistiocytosis (HLH) is an immune mediated life-threatening disease caused by excessive inflammation and tissue destruction due to abnormal immune activation. It can be either primary or secondary. Macrophage activating syndrome (MAS) is classified among secondary forms of HLH which is usually associated with autoimmune disease conditions. Therapeutic plasma exchange (TPE) suppresses hyperinflammatory syndrome and removes toxic substances as a result of organ failure in patients with HLH. Even though HLH is a category III indication for therapeutic plasma exchange (TPE) according to American Society for Apheresis (ASFA) 2019 guideline, herewith we report a case of a child MAS associated with systemic onset juvenile idiopathic arthritis (SOJIA) being successfully treated with TPE.
Case Report: An 8 year old, previously well girl presented with high grade fever for 6 days duration, which was associated with multiple joint pain, evanescent salmon pink rash and colicky abdominal pain. Her vitals were normal with GCS of 15/15 on admission and her condition deteriorated during hospital stay, over the period of 2 months. She underwent multiple investigations for the diagnosis and multiple treatment regimen in parallel, including intravenous immunoglobulins (IVIG), IV methyl prednisolone followed by oral steroids, etoposide, cyclosporin, cyclophosphamide and multiple intravenous antibiotics. Ultimately, she was diagnosed as having SOJIA and MAS. At the time, she was referred to the Department of Transfusion Medicine for TPE, she lost her vision and was delirious. Her serum ferritin level was 42 027 ng/mL and fibrinogen level was 4.181 g/dL with dropping white blood cell count (41.7×10^9/L to 3.7×10^9/L), platelet count (325×10^9/L to 126×10^9/L) and haemoglobin levels (9.4 to 7.1 g/dL). She also had hypertriglyceridaemia with mildly deranged liver

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functions. Hepatosplenomegaly was noted in the contrast-enhanced computed tomography (CECT)-abdomen.
Five cycles of TPE were performed using continuous flow centrifugation plasmapheresis system. One volume plasma exchange was performed every other day using 5% albumin as the replacement fluid. There was marked clinical improvement and reduction in serum ferritin level (42 027 to 11 000 ng/mL) following the first two cycles of TPE. After completion of five TPE procedures, the patient's clinical and laboratory parameters became normal, and she was discharged after 1 month of hospital stay after arranging weekly clinical follow up.
Conclusion: This case highlights the importance of TPE as a lifesaving procedure in patients with HLH, even though it is categorised as a category III indication according to ASFA 2019 guidelines.

BSH24-EP82 | Audit on the usage of O RhD-negative red cells in emergencies in a tertiary hospital

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Background: O RhD-negative red cells are considered to be a 'universal' blood component. They can be transfused in emergencies where a patient's blood group is unknown, and in instances where group specific stock is unavailable. Balance between its supply and demand remains a challenge for almost every blood service. The National Blood Transfusion Committee (NBTC) commissioned an audit on the use of O RhD-negative red cells in 2008 and published guidelines for the appropriate use of group O RhD-negative red cells following the audit. The national audit recommended hospitals should regularly review the usage of O RhD-negative red cells in emergencies.
Aim: To evaluate the usage of O RhD-negative red cells in emergencies and its appropriateness in Ninewells Hospital according to NBTC recommendations.
Method: A 6-month retrospective audit of all O RhD-negative red cells transfused between 1 December 2022 and 31 May 2023 was conducted. Major Haemorrhage Protocol (MHP) activation was identified and the usage of O RhD-negative red cells in MHP were evaluated.
Results: Total 53 activation of MHP were identified and 433 units of O RhD-negative red cells were transfused. Fifty-four units (12.5%) of O RhD-negative red cells were transfused in MHP while 379 units (87.5%) were transfused in non-MHP. In MHP, there were 19 units (35.2%) of O RhD-negative red cells transfused to O RhD-negative patients, 7 units (12.9%) to non-O RhD-negative patients, and 28 units (51.9%) to RhD-positive patients. There were 31 units (57.4%) of red cells were transfused to adult males, and females >50 year-old. There were no O RhD-negative red cells transfused to avoid time expiry and the median time to expiry was 21.6 (4.1–29.4) days. In non-MHP, 312 units (82.3%) of O RhD-negative were transfused to RhD-negative patients, 11 units (2.9%) to neonates, and 56 units (14.8%) to RhD-positive patients as a substitution.
Conclusion: Although O RhD-negative red cells are considered appropriate to be transfused to all blood groups in MHP, there were 31 units (57.4%) of O RhD-negative red cells transfused could have been potentially replaced by O RhD-positive red cells to conserve O RhD-negative red cells stocks in the hospital if a policy for supplying O Rh-D positive red cells in emergencies was introduced. Discussion at the local Hospital Transfusion Committee (HTC) led to further gap analysis surveys to identify barriers and learning gaps in order to implement using O RhD-positive red cells for adult males in emergencies.

BSH24-EP83 | Haematological predictors of no-reflow in patients undergoing primary PCI for STEMI

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Background: Primary percutaneous coronary intervention (PPCI) is the recommended treatment for acute ST-elevation myocardial infarction (STEMI). No-reflow phenomenon (NRP) refers to incomplete myocardial reperfusion in absence of infarcted related arterial obstruction and is associated with higher major adverse cardiac events (MACE) including extension of infarction, mortality, reduced left ventricular function and arrhythmia.
Objectives: To address the neutrophil/lymphocyte (N/L) ratio and mean platelet volume (MPV) as haematological predictors for NRP that can be assessed from a simple complete blood count (CBC) done for patients with STMI presenting for primary PCI.
Patients and Methods: This observational study included 950 patients with STEMI treated with primary PCI at Ain Shams University Hospitals. Seven hundred seventy-one patients attained TIMI 3 flow post PCI and was labelled as group I (Optimum flow group) and 179 patients attained TIMI flow of less than 3 and was labelled as group II (no-reflow group; NRP). In the emergency department all patients illegible for the study were screened for haematological disorders and then a CBC was withdrawn as a part of the routine tests before proceeding to fast track for primary PCI.
Results: The no-reflow group (II) had a significantly higher post stent balloon dilatation ($p = 0.031$), significantly lower predischarge left ventricular EF ($p = 0.044$). Group II had a significantly higher N/L ratio ($p = 0.001$) and MPV ($p = 0.001$) in comparison to group I. Regression analysis showed that post stent balloon dilatation, N/L ratio and MPV were predictors of NRP in STEMI patients treated with primary PCI.

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Conclusion: N/L ratio and MPV are simple and readily available markers in the admission CBC of STEMI patients that can strongly predict no-reflow in these group of high-risk patients.
Keywords: mean platelet volume, neutrophil-to-lymphocyte ratio, no-reflow phenomenon, Primary PCI, STEMI.

BSH24-EP84 | DNA extracted from cultured cells as a source of survey material for molecular haemoglobinopathy EQA

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UKNEQAS Haematology provides a comprehensive range of external quality assessment (EQA) programmes designed to support the quality assurance needs of laboratories in the UK and overseas. The DNA Diagnostics for Haemoglobinopathies programme supports specialist laboratories offering molecular haemoglobinopathy testing, aiming to assess their proficiency in identifying mutations of the alpha- and beta-globin genes. Accurate molecular diagnosis is vital for haemoglobinopathies, especially in patients where antenatal risk assessment and prenatal diagnosis are required.

The programme has approximately 50 participants, the majority based overseas. Since the programme's inception, survey material has been prepared from patient DNA material surplus to testing from haemoglobinopathy patients at the Leiden University Medical Centre (LUMC). While this source of material has been sufficient thus far, it has its limitations. The DNA can vary in quality, and there is a limited quantity, imposing a cap on the number of participants that can be registered for this programme.

UKNEQAS, in collaboration with Manchester Cell Bank, is working to establish a library of cases that can be used as a long-term source of survey material. Blood taken from haemoglobinopathy patients and obligate carriers can be cultured to establish a cell line, serving as an infinite source of material suitable for use in an EQA programme. DNA extracted from cultured cells is of higher quality and quantity than that of routine diagnostic blood specimens. Building a library of cases will benefit the programme in the long term by ensuring continuous access to high-quality survey material. It would also remove the cap on the number of participants that could register for the programme.

Currently, there are 24 cases in the library. Eight have been transformed and DNA has been extracted, and 16 remain in storage. Three have been used successfully as survey material. One of the challenges of donor recruitment is the tight timeframe within which specimens must be taken and transported to the cell bank to establish a cell line successfully. UKNEQAS is relying on the assistance of haematology specialists across the field to recruit donors for this project. The aim is to build a library of at least 50 cases covering a range of genetic mutations that give rise to different haemoglobin variants, alpha and beta thalassaemias. Donors with a wide range of different haemoglobinopathy states are sought to test the proficiency of molecular haemoglobinopathy laboratories worldwide.

BSH24-EP85 | Evolving caseload of adult bone marrow biopsies in a specialist integrated haematological malignancy diagnostic service

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Background: Diagnostic haematopathology has been transformed by an increased understanding of the molecular pathogenesis of haematological malignancies, followed by new assays that supplement traditional morphological assessment. These tests can provide more accurate diagnosis, prognosis and options for sensitive disease monitoring and targeted treatment. In the UK, tests are coordinated within Specialist Integrated Haematological Malignancy Diagnostic Services (SIHMDS). Recent changes in laboratory services, particularly genomics, and therapeutic developments for diseases such as acute myeloid leukaemia (AML) have had significant impacts on SIHMDS practice.

Aims: To investigate changes in SIHMDS provision between 2017 and 2022, specifically, numbers of bone marrow samples received, clinical indications and diagnoses of cases referred, and the nature of additional testing on individual bone marrow samples.

Methods: Service evaluation comprising electronic medical record review of 1556 adult bone marrow aspirates, received at a single SIHMDS with nine referring NHS Trusts, during equivalent three-month periods in 2017 and 2022.

Results: Sample numbers increased by 3.9% between 2017 and 2022, with no changes in age or blood count abnormalities for which patients were investigated. Numbers of samples investigating for a new diagnosis did not increase whereas samples following up a known haematological diagnosis increased by 17.6%, largely accounted by an increase in samples showing acute leukaemia in remission (6.3% of samples in 2017, 20.4% of samples in 2022, $p < 0.0001$).

Mean number of additional testing modalities performed on each aspirate (out of: flow cytometry; fluorescence in situ hybridisation; single nucleotide polymorphism/SNP array; karyotype; standalone molecular studies; next-generation sequencing/NGS gene panel; chimerism; sendaway molecular tests) increased from 1.41 in 2017 to 1.82 in 2022 ($p < 0.0001$). Total additional tests increased by 34.5%,

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particularly affecting NGS panels (9.6-fold increase), acute leukaemia flow cytometry panels (34.5% increase), SNP array/karyotype (30.6% increase) and sendaway molecular tests (2.3-fold increase). These increases were associated with fewer samples being deemed non-diagnostic (27.5% in 2017, 18.4% in 2022, $p < 0.0001$) or inadequate (8.3%–2.5%, $p < 0.0001$) and an increase in those diagnostic for chronic myeloid neoplasia (13.4%–17.5%, $p = 0.023$).

Conclusions: Over 5 years bone marrow caseload has increased, largely reflecting demand for acute leukaemia monitoring that parallels developments in treatment. Our data suggest that greater uptake of additional tests, particularly genomics, benefits patients—with fewer inconclusive biopsies and increased confident diagnoses of chronic myeloid disease. These additional tests increase the complexity of integrated haematopathology reporting, which should be accounted for in the resourcing of SIHMDS and genomics laboratories.

BSH24-EP86 | Patient consent for blood transfusion: An audit

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Introduction: It is an accepted principle that a patient should give valid consent before receiving medical treatment, including receiving a transfusion of blood and blood components (such as fresh frozen plasma and platelets).

In 2020, the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) updated its guidelines on Patient Consent for Blood Transfusions stipulating the specific information that medical professionals should give to patients prior to receiving a transfusion in order to allow them to make an informed decision. This information should contain details of the type[s] of component transfused, benefits of transfusion and any adverse events associated with the transfusion including risk of transfusion transmitted infections (TTIs). Furthermore, this should be documented in the patient's clinical record.

Objectives: The primary objective of this audit is to evaluate the compliance of medical professionals in obtaining valid consent for blood transfusions in a hospital. Our secondary objective is to improve the current practices through improvement measures and re-audit.

Methods: A retrospective study involving data collection from transfusion record sheets completed over 1 month and associated patient electronic record. Analysis is focused on assessing compliance of SaBTO guidelines, in particular: Consent gained, risks/benefits explained, and reason for transfusion documented. Improvement measures were made in between audit cycles.

Results: Findings indicate overall poor compliance with SaBTO guidelines with only 52% of patients having consent for transfusion documented and 36% having benefits/risks explained. After implementation of tick boxes for consent and benefits/risks on the transfusion record sheets, a minor improvement has been seen in compliance to 57% and 44% respectively. There has been a significant decrease in documenting reason for transfusion on record sheets from 2021 to 2022, from 89% to 57% respectively; however, this is thought to be due to interpreter bias during data collection.

Conclusion: Blood transfusion is a large part of daily practice as a medical professional in a hospital. However, the results of this audit suggest that further work should be done to improve clinical practice around consent for blood transfusion. With implementation of education on this topic we hope the next data collection shows improvement in our practice with the ultimate goal of enhancing patient autonomy, shared decision-making and safety.

BSH24-EP87 | The CD47-blocking immune checkpoint inhibitor maplirpacept does not interfere with blood transfusion compatibility testing

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The transmembrane glycoprotein CD47 delivers an anti-phagocytic ("do-not-eat") signal by binding to signal regulatory protein α (SIRPα) on macrophages. Tumours express high levels of CD47 to escape macrophage-mediated immune surveillance, and blockade of the CD47-SIRPα pathway has emerged as a novel therapeutic strategy demonstrating preclinical and clinical activity. Maplirpacept (PF-07901801, TTI-622), a human SIRPα-Fc fusion protein with an IgG4 domain, is an innate immune checkpoint inhibitor that binds to CD47 to promote phagocytosis of malignant cells and antitumor activity. Maplirpacept is currently in clinical development to treat patients with acute myeloid leukaemia, lymphoma, myeloma and ovarian cancer.

CD47 is also expressed on red blood cells (RBCs) and plays a role in the natural clearance of aged RBCs. CD47 expression on RBCs has been shown to interfere with pre-transfusion laboratory testing in patients treated with the anti-CD47 mAb, Hu5F9-G4. Unlike anti-CD47 mAbs, minimal binding to human RBCs is observed with maplirpacept; therefore, this study investigated whether the minimal binding of maplirpacept to human RBCs precludes interference with routine pre-transfusion laboratory tests.

Using RBCs from healthy donors representing the eight major ABO-Rh blood groups, we demonstrated that the addition of maplirpacept (0.6, 1.2 or 2.0 mg/mL) does not cause agglutination of test RBCs and produces the expected blood typing result with standard blood typing protocols. No interference was observed at all concentrations tested. However, addition of an anti-CD47 mAb (clone: Hu5F9-G4, 0.1 mg/mL), caused pan-agglutination, as well as false positive blood typing results. In a standard indirect

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antiglobulin test (IAT) that mimics the in vitro compatibility crossmatching test performed prior to a blood transfusion, the anti-CD47 mAb gave false positive results while maplirpacept produced results identical to the control serum condition. This data is consistent with a previous study demonstrating interference by Hu5F9-G4 in routine pre-transfusion blood testing. Additionally, no interference was observed when maplirpacept was added to conditions which produced agglutination in a standard IAT across a range of blood types.

Interference with RBC panel testing has important consequences in transfusion medicine as the presence of irregular antibodies can complicate the selection of suitable RBC units for treated patients. In this study we demonstrate that interference with blood compatibility testing is dependent upon CD47-blocking agent type. Maplirpacept, unlike anti-CD47 mAbs, does not interfere with blood group serological testing, which may confer a significant clinical advantage by negating the need for approaches to prevent interference.

BSH24-EP88 | Pathology portal: Developing a novel, interactive education portal for transfusion medicine

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Background: Transfusion is essential for patient care with ~2 million units of blood and components per annum administered across the UK. There are significant concerns around current transfusion education with a lack of integration between clinical and laboratory services that can lead to ineffective blood management and patient safety concerns as highlighted by the Serious Hazards of Transfusion (SHOT) UK Haemovigilance scheme. Recent national feedback from trainees has highlighted key gaps including decreased exposure of trainees to laboratory transfusion.

The Pathology Portal is an innovative award-winning learning resource for pathology trainees and consultants, launched in August 2022 by The Royal College of Pathologists (RCPath) and Health Education England (HEE). Published content includes >4000 modules with phased rollout covering 17 pathology specialties, that have been collectively accessed >100 000 times since the Portal launch (www.rcpath.org/profession/pathology-Portal.html).

Methods: We are now developing educational resources for transfusion medicine for the Portal promoting greater consistency and efficiency in training. We have identified key transfusion learning objectives from the curricula for haematology trainees and higher specialist scientists in training (HSST). This has been coupled with a comprehensive review of a wide range of educational resources available, identifying key gaps where development is needed. We have recruited clinical and scientific representatives in transfusion medicine from professional organisations across the four UK nations and the International Society of Blood Transfusion (ISBT) to support content development and provide editorial oversight.

Results: We have collated >400 transfusion learning resources from several sources including BSH Guidelines, SHOT, British Blood Transfusion Society, UK Blood services and ISBT, aiming to cover all aspects of curricular, management and additional topics. Hosting links with permissions to high-quality material from trusted resources will aid learners to access content easily. We are now also developing novel material with a focus on case-based teaching greatly valued by learners. Management training has been identified as a key learning gap and we are recording webinars addressing real-world examples of lab management issues. User engagement including new and return users will be tracked. Quantitative and qualitative feedback, via a diverse focus-group of volunteers, will inform modifications to support more effective learning.

Conclusion: We have designed transfusion medicine educational resources for the Pathology Portal as a sustainable learning platform, freely available to trainees and other healthcare professionals. A particular challenge is updating and ensuring continuity of resources to maintain accuracy, which will require ongoing input.

BSH24-EP90 | Insights on erythrocyte alloimmunization and auto-immunisation in children from North India

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Background: Erythrocyte alloantibodies and autoantibodies can create complications during blood transfusions. However, there has not been an estimation of the prevalence of erythrocyte alloimmunisation and auto-immunisation in the northern paediatric population of India. Our goal was to use this information to develop a transfusion management policy for children that is reasonable and safe.

Methods: We included 1086 paediatric inpatients admitted to our tertiary hospital in northern India between July 2023 and December 2023. We carried out antibody screening using a 3-cell panel through column agglutination technology. Samples with positive screening were further analysed for antibody specificity using an 11-cell identification panel (Ortho Clinical Diagnostics Pvt Ltd, Mumbai, India). We also collected clinical details of patients, including the number of red blood cell (RBC) unit transfusions, to determine any association with antibody formation.

Results: The average age of the children involved was 7.6 years, ranging from 6 months to 17 years, with a male-to-female ratio of 4:3. The rate of alloimmunization was 0.55% ($n = 6/1087$ cases) affected, while the auto-immunisation rate

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was 0.36% ($n = 4/1086$ cases) affected. Alloantibodies made up 60% of the antibodies present, with the most common being anti-M (50%) and a combination of anti-C + anti-E + anti-K (10%) in one case. Autoantibodies made up the remaining 40% of the antibodies. Factors such as age, gender, location, ABO blood group and diagnosis were found to be independent risk factors for the development of antibodies. The formation of allo-antibodies was more common in individuals who had received an average of 5 units of RBC transfusions, compared to those who had an average of 3 transfusions and had developed autoantibodies. The odds ratio, which measures the association between previous exposure to RBC transfusion and the development of allo or auto-immunisation, was 12.9 ($p = 0.0172$).

Conclusion: It is unnecessary to repeat pre-transfusion testing for newborns who are under 4 months old as their immune systems are not fully developed yet. Among children, MNS system antibodies, specifically anti-M, are more commonly observed at a younger age. Our institutional extended phenotype-matched blood donor registry has enabled us to provide antigen-negative RBC units to children who have already developed alloimmunisation.

BSH24-EP91 | CDK1 inhibitor RO-3306 enhances BTKi potency in diffuse large B-cell lymphoma by suppressing JAK2/STAT3 signalling

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Objective: To elucidate the principal genes influencing BTK inhibitor (BTKi) sensitivity in diffuse large B-cell lymphoma (DLBCL) and to delineate the underlying mechanism.

Methods: Utilising the microarray dataset GSE138126 extracted from the Gene Expression Omnibus (GEO) database, we conducted a comprehensive analysis to identify differentially expressed genes (DEGs) between BTKi-resistant and BTKi-sensitive cells, employing the "limma" tool. Subsequently, a network of 30 hub genes exhibiting significant connectivity was curated, with CDK1 emerging as the predominant gene. The potential impact of targeting CDK1 using its specific inhibitor, RO-3306, was examined in DLBCL through various methods, including CCK-8 and flow cytometry assays. The efficacy of RO-3306 in augmenting BTKi sensitivity in DLBCL was scrutinised both in cellular models and in mouse xenografts. Further, the mechanistic action of RO-3306 was investigated using RNA-seq and substantiated through qRT-PCR and western blot analyses.

Results: The study pinpointed CDK1 as the central gene influencing BTKi sensitivity in DLBCL cells. The application of RO-3306 effectively thwarted growth and heightened apoptosis rates of DLBCL cells. Furthermore, RO-3306 was observed to amplify the susceptibility of DLBCL cells to BTKi, both in vitro and in xenograft experimental models. RNA-seq analyses suggested the potential modulation of the JAK2/STAT3 signalling cascade by RO-3306, a notion further confirmed by the diminished phosphorylation documented in western blot assessments.

Conclusion: This study pioneers in unveiling pivotal insights into the mechanisms governing BTKi sensitivity in DLBCL, potentially heralding new avenues for targeted therapeutic strategies.

BSH24-EP92 | Type 1 cryoglobulinemic vasculitis associated with marginal zone lymphoma successfully treated with bendamustine and rituximab

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Cryoglobulins are proteins that precipitate from an individual's serum or plasma at temperatures lower than 37°C, which can deposit in medium and large-sized blood vessels throughout the body, causing endothelial injury and end-organ damage known as cryoglobulinemia. This is subclassified into subgroups based on their immunoglobulin (Ig) composition. Marginal zone lymphoma (MZL) is commonly associated with mixed cryoglobulinemia or Type II cryoglobulinemia defined as a mixture of monoclonal IgM (or IgG or IgA) with rheumatoid factor (RF) activity and polyclonal Ig, rarely with Type 1 Cryoglobulinemia noted with expression of monoclonal Igs without RF activity.

A 71-year male presented with chief complaints of a 15-pound weight loss, anorexia, and early satiety. He denied nausea, vomiting, fevers, chills, night sweats, or abdominal pain. Initial investigation was pertinent for normocytic anaemia with Haemoglobin (Hgb) of 9.8 mg/dL. Computerised Tomography of Abdomen and Pelvis notable for splenomegaly of 20.3 cm craniocaudal. Investigations included negative hepatitis studies, normal immunoglobulin levels, and a normal echocardiogram. Further testing included bone marrow biopsy positive for low-grade B-cell lymphoma, involving approximately 30% of a normocellular marrow, flow cytometry analysis of bone marrow aspirate revealed 33% kappa-light chain restricted monotypic B-cells and fluorescence in situ hybridization (FISH) positive for MALT1 (19%) confirming MZL. Unfortunately, despite being started on Rituximab, he developed bilateral necrotic leg ulcers that raised suspicion of vasculitis. Skin biopsy revealed an abundance of neutrophils but was negative for infection. Detection of positive cryoglobulins with monoclonal IgM Kappa expression, and absence of RF activity led to the diagnosis of Type 1 cryoglobulinemia. He was initiated on steroids, treatment was modified to include Bendamustine with Rituximab. After 12 weeks of treatment, symptoms along with skin lesions had resolved, subsequent cryoglobulin levels tested negative.

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MZL is a subtype of non-Hodgkin lymphoma (NHL) often associated with Type II Cryoglobulinemia, characterised by low-grade lymphoproliferation, and a frequent connection to Hepatitis C Virus infection. Although Type 1 cryoglobulinemia has been associated with B cell NHL, it has been infrequent and rare. A high degree of suspicion is required in patients presenting with symptoms of vasculitis, especially in patients with negative Hepatitis C. Biopsy and extensive testing for cryoglobulinemia should be pursued. It is crucial to differentiate the sub-type of cryoglobulinemia as it may dictate therapeutic strategies. In addition, in case of disease progression or refractory symptoms with Rituximab, inclusion of an alkylating agent should be considered.

BSH24-EP93 | "Modified DHAP" salvage therapy for refractory and/or relapsed classic Hodgkin's (CHL) and non-Hodgkin's lymphomas (NHL)

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Background: The combination of dexamethasone, high-dose cytarabine and cisplatin (DHAP) is an established salvage regimen for lymphoma patients. Novel approaches have been tried to modify this standard regimen to overcome its toxicities while maintaining its efficacy.
Aim and Study Design: This is a prospective cohort study intended to detect the efficacy, outcomes, and toxicity profile of modified DHAP protocol (mDHAP) in the treatment of relapsed/refractory (R/R) CHL and NHLs. Fifty-one R/R patients (34 NHLs [diffuse large B-cell, or follicular, mantle-cell, peripheral T-cell, T-cell B-cell rich] and 17 CHLs); were included and followed from January 2020 to March 2022 at the Oncology Centre at Mansoura University (OCMU).
Patients and Methods: The mean age was 45.7 (±12.3 SD) years, M/F: 28/23 (54.9%/45.1%). Most patients had advanced stages (III–IV) at the time of enrollment (32 [94.1%] NHL and 11 [64.7%] HL). At the end of the study, 46 (90.2%) were alive. All patients received mDHAP regimen (Days 1–4: dexamethasone 40 mg 15 min iv infusion, cytarabine 0.5 g/m^2/12 h 1 h iv infusion, cisplatin 25 mg/m^2 3 h iv infusion).
Results: In total, 127 treatment cycles were administrated. Severe neutropenia was the main toxicity occurring in 60.8% of the total lymphoma patients, followed by thrombocytopenia in 37.3% of the patients. Febrile neutropenia occurred in <40%. Three patients died from COVID-19 infection. Nephrotoxicity did not exceed CTC grade 3, which occurred in eight cycles (6.3%). Complete (CR) or partial (PR) responses after mDHAP were documented in 52% and 16.6% (overall response rate "ORR" 68.6%). Five patients proceeded to autologous stem-cell transplantation. The median overall survival was 7 and 8 months for HL and NHL, respectively. The log-rank test did not show a significant difference in OS between the two subgroups of lymphoma ($p = 0.81$).
Conclusion: An ORR 68.6%, manageable haematological toxicity, and reduced renal impairment suggest the efficacy and feasibility of this salvage regimen, however further investigation on a larger sample size or multicenter studies are required for this protocol validation.
Keywords: HL, mDHAP, NHL, ORR, OS.

BSH24-EP94 | Identification of plasma lncRNA for bone marrow infiltration and staging in diffuse large B-cell lymphoma

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Background: Diffuse large B-cell lymphoma (DLBCL), the most common non-Hodgkin lymphoma (NHL), exhibits significant heterogeneity, complicating diagnosis, and prognosis. Long non-coding RNAs (lncRNAs) have emerged as critical regulators in cellular processes and cancer, including DLBCL. We investigated the potential of five circulating lncRNAs (HOTAIR, MALAT-1, XIST, SNHG15, and H19) as non-invasive biomarkers in DLBCL patients.
Methods: Real-time quantitative PCR (qRT-PCR) was used to measure lncRNA expression in newly diagnosed adult DLBCL patients ($n = 65$) and healthy controls.
Results: HOTAIR was significantly upregulated in DLBCL patients compared to controls, while SNHG15 showed strong downregulation. Both lncRNAs displayed remarkable discriminatory power for DLBCL diagnosis, with AUC values exceeding 69%. H19 expression specifically correlated with early-stage (stage I) disease. Upregulated HOTAIR was associated with poor prognosis, whereas increased SNHG15 appeared protective against mortality.
Conclusions: Circulating lncRNAs, particularly HOTAIR, SNHG15, and H19, offer promising avenues for non-invasive DLBCL diagnosis, staging, and prognostication. Further studies are required to validate these findings, elucidate long-term survival associations, and explore potential interactions with other genetic and pathological features.
Keywords: DLBCL, HOTAIR, lncRNAs, SNHG15, survival.

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BSH24-EP95 | Diffuse B-large cell non-Hodgkin's lymphoma (DBCL) associated with hepatitis B virus (HBV), clinical characteristics, therapy, and prognosis

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Billion people in the world are infected with hepatitis B virus. There are studies showing the etiopathogenetic role of HBV in the development of B-cell lymphomas. While the risk of HBV reactivation in patients with non-Hodgkin's lymphoma receiving immunochemotherapy (IHT) is well known, its significance as a potential oncogenic factor in the development of DBCL needs to be investigated.

To evaluate clinical, laboratory characteristics and therapy results of patients with HBV+ DBCL and HBV– DBCL.

The study included 23 HBV+ DBCL (G1) and 46 HBV– DBCL (G2) patients receiving ICT from 2016 to 2023 at four centers. Median age was G1—51 years, G2—63 years 19 (83%) ($p = 0.03$), male/female: G1—4/19 (17%/83%), G2–20/26 (43%/57%) ($p = 0.003$). Disseminated stages III–IV in G1—21 (91%), in G2—31 (67%) ($p = 0.005$). Extranodal lesions in patients in G1—18 (78%), in G2—26 (57%) ($p = 0.005$). In G1 patients were most frequently involved: spleen 16 (70%), liver 10 (40%), bones 5 (20%), in G2—gastric lesions 10 (20%) spleen 7 (13%). Liver cirrhosis was only in 4 (17%) G1 patients.

In the blood of G1 patients, platelet level was decreased in 10 (40%), haemoglobin was decreased in 8 (32%), and in G2 platelet level was decreased in 4 (8%). Elevation of transaminases were only in G1—ALT 60%, AST 56%, GGTP and/or alkaline phosphate 42%. LDH was elevated in G1 in 65% of patients and in G2—46% ($p = 0.005$) G1 patients had a history of HBV infection more than 10 years before to DBCL. HBV DNA levels ranged from 1.2×10^3–1×10^8 copies/mL (median 3.6×10^5). Atypical nucleoside therapy (AVT) was treatment to 16 patients 2 weeks before the initiation of ICT and completed 6 months after the end of antitumor treatment. In seven patients AVT was started only after transaminases level increase. All patients underwent IGT according to the R-CHOP program. Remissions of lymphoma in G1/G2 were achieved in 68% and 72% ($p = 0.2$), respectively. The 3-year relapse-free survival rates were in G1—69% and in G2—77%. During ICT, significant hepatotoxicity developed in 30% of only G1 patients who did not receive AVT. Virologic remission was achieved in only 10 (43%) G1. Twelve patients in this group received AVT with interferon (INF) at standard dose for up to 24 months. None of these patients had a relapse of lymphoma during the follow-up time period.

HBV+ DVKL patients are characterised by younger age, advanced stages of the disease, frequent extranodal lesions, and severe hepatotoxicity. Further accumulation of material will allow to optimise AVT and IHT of patients with HBV+ DVKL.

BSH24-EP96 | A retrospective regional case series of grey zone lymphoma: Treatment approaches and clinical outcomes

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Background: Grey zone lymphoma (GZL) is a rare and aggressive subtype of non-Hodgkin lymphoma with intersecting features between classical Hodgkin lymphoma (cHL) and diffuse large B-cell lymphoma (DLBCL). In 2022, the World Health Organisation updated the diagnostic criteria defining GZL as an intermediate between cHL and primary mediastinal B-cell lymphoma (PMBL) reflecting the differences between mediastinal (MGZL) and non-mediastinal GZL (NMGZL). Treatment approaches mirror those seen in PMBL and cHL with poorer outcomes. With limited data, no treatment guidelines exist and the benefit of intensifying first-line treatment is unclear.

Methods: Retrospective analysis of adults diagnosed with GZL after specialist haematopathologist review in the Northeast of England from 01/01/2015 to 01/12/2023. Demographics, first-line treatment, radiotherapy, autologous stem cell transplant (ASCT), clinical outcomes, and toxicity data were reviewed.

Results: Twenty-three adults were diagnosed with GZL (median age 46 years), 15/23 MGZL and 8/23 NMGZL. First-line treatments were R-CHOP 10/23, R-DHAP 3/23, DA-R-EPOCH, EscBEACOPP, GDP, R-CEOP, R-ABVD, R-IVE each 1/23, palliative regimens 3/23 (CVP, GCVP), and 1/23 declined treatment.

Median follow-up was 50.4 months with OS 47.8%. Causes of death were progressive lymphoma (7), infection (2), secondary malignancy (1), and non-treatment-related (2) with EFS at 24 months of 48.2% (events included PD, death, or new lymphoma treatment).

All patients treated with palliative regimens were refractory and died within 23 months. In first-line treatment, 5/23 patients received high-dose 'salvage' regimens (R-IVE, R-DHAP, GDP) and were planned for ASCT. Three were refractory so only two underwent ASCT, both remaining in remission at 93 and 61 months.

In this study, 13/23 patients had standard-dose treatment (R-CHOP, R-ABVD, escBEACOPP) without ASCT, three were refractory, two relapsed at 12 and 53 months, one developed AML and died, seven in remission (median follow-up 67.6 months). Three patients had ASCT in the relapsed/refractory setting, all achieving remission.

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10/23 patients had consolidation radiotherapy as first-line treatment, four had partial response (PR) pre-radiotherapy and six had complete metabolic response (CMR). Of the patients with PR, three had further lines of treatment within 6 months, while one went on to ASCT and CMR after.

Discussion: In this small series, high-dose chemotherapy consolidated with ASCT first-line was not superior to standard-dose treatment without ASCT. While in the relapsed/refractory setting, high-dose chemotherapy and ASCT was effective. The benefit of consolidation radiotherapy was unclear. With a rare disease, reporting small cohorts of treatment and outcome data is important. National and international collaboration may provide clarity on optimal treatment pathways.

BSH24-EP97 | Prognostic Significance of β2-Microglobulin in Diffuse Large B-cell Lymphoma Patients: A Meta-analysis

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Objective: Over the past 25 years, the International Prognostic Index (IPI) has proven to be a valuable tool for prognosticating aggressive non-Hodgkin lymphoma. However, the prognostic significance of isolated β2-microglobulin (β2-MG) for patients with diffuse large cell B-cell lymphoma (DLBCL) remains under investigated. Thus, the objective of this research was to assess the prognostic significance of β2-MG on the overall survival (OS) of patients with DLBCL by meta-analyses.

Methods: The hazard ratios (HRs) of multivariate analysis for OS between the normal β2-MG and the increased β2-MG group were obtained by searching pertinent literature in the PubMed, EMbase, Science Direct, and OVID databases from inception to December 2023. The results were then combined using a fixed or random effect model as per heterogeneity among the included studies. Using RevMan 5.4 software, the generic inverse variance was chosen, and log (HR) and Standard Error (log (HR)) were entered to do OS analysis. The Q test was used to examine heterogeneity. For statistical significance, a p-value of less than 0.05 was used. Forest plots were used to depict the combined HRs.

Results: Nine qualifying publications totaling 5774 DLBCL cases were included in the total. The analysis revealed heterogeneity among set of studies (P < 0.00001, I square = 85%). The pooled results showed that elevated β2-MG was a significant indicator for poor overall survival (OS) (HR = 2.52, 95% CI = 1.76–3.59, p<0.00001). The total effect analysis produced a statistically significant result (Z = 5.08, P < 0.00001). All pati

Conclusion: In conclusion, β2-MG strongly correlated with worse OS in DLBCL patients based on the meta-analysis. The increased β2-MG level as an independent risk factor for the prognosis of DLBCL was evident. β2-MG might be suggested as a low-cost prognostic biomarker in DLBCL.

BSH24-EP98 | DAAA therapy in patients with hepatitis C associated indolent non-Hodgkin lymphomas (HCV+ INHL) results of prospective study

Dr Sergey Lepkov[1], Prof. Gayne Tumian[2], Dr Oleg Kolomietsev[2], Dr Svetlana Lunina[2], Dr Oleg Zaharov[3], Prof. Nataliy Chernova[3], Dr Eleonora Makunina[3], Dr Svetlana Borisovskay[1,4], Dr Nataliy Gavrilina[1,4], Prof. Igor Nikitin[1]
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Large-scale epidemiologic studies including 48 systematic reviews and more than 5000 patients ($n = 5542$) found a median frequency of infection with the virus.

HCV infection rate of 13%, and it was shown that the prevalence of HCV was much higher in patients with B-NHL compared to healthy population: 17% versus 1.5% (Zhang, 2023). The most frequent association of HCV with INL DAAS has created an opportunity for rapid eradication of HCV. However, the antitumour effect (AT) and duration of DAAS in HCV+ INHL remains a subject of debate and discussion.

To evaluate the antiviral and antitumour efficacy of DAAS alone or in combination with interferon in primary HCV+ INL patients.

The study included 38 patients with HCV + INL who received therapy from 2016 to 2023 in four centre.

Median age 52 years (31–83 years), male/female ratio was equal (51%/49%), the majority had prevalent III–IV stages (91%), B-symptoms were present in 18 (46%) patients. Extranodal lesions were present in 88%, spleen 92%, liver 62%, bone marrow 89% were most frequently involved. Spleen lesions in 22 patients the size of the organ exceeded 20 cm. Liver cirrhosis was diagnosed in 14 (37%) patients, and in 10 of them tumour lesions of liver were detected. Laboratory parameters revealed decrease in platelet level 30 (80%), haemoglobin level.

Twenty-eight (74%), increased level of transaminases: ALT 80%, AST 76%, GGTP and/or alkaline phosphorus 52%, LDH above normal in 80% patients, decreased albumin level in 39%. HCV RNA at onset in the patients ranged from 1.2×103 to 1×10^6 copies/mL (median 3.6×10^5). Genotype 1 was present in 50%. As sofosbuvir-containing regimens were administered as first-line therapy. DAAS was performed of about 6 months (4–8 months). In absence of complete antitumor (AT) effect, INF was added to DAAs for 12–24 months. Using DAAS virus elimination was obtained in 37 of 38 patients, but AT using was achieved in 14 (37%) patients.

No patient with cirrhosis and splenomegaly could achieve remission. Twenty-four patients ineffective were treated with INF therapy. This allowed to obtain remission in 17 patients with splenomegaly. Thus, at median follow-up of

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42 months, the 4-year progression-free survival was 70% in DAAS-treated patients and 70% in combination treatment DAAS + INF was 82%. Four-year overall survival in the group as a whole was 79%.

Antiviral treatment is preferred option for first-line therapy of patients with HCV+ INHL. The rate of complete virologic response treatment should be started with DAAS. In absence of durable antitumor effect, with significant splenomegaly, the addition of INF + DAAs for 12–24 months is effective.

BSH24-EP99 | Improving bone health in lymphoma—DGH experience

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Background: Patient with Lymphoma are at risk of developing low bone mineral density from use of high dose glucocorticoids. Zoledronic acid is a safe option to prevent osteoporosis in Lymphoma. This project aims to implement a policy locally to improve bone health in Lymphoma patients by use of single prophylactic dose of zoledronic acid in our District General Hospital.

Method: There is currently no policy for bone protection in Lymphoma in our setup. This project was carried out in two audit cycles.

Pre-Implementation Audit Cycle: Retrospective audit cycle spanned from July 2023 to December 2023 during which fourteen patients received high dose steroids as part Osteoporosis risk assessment done for just 5 patients and only 45% of high-risk patients received bone protection.

Implementation: We collaborated with lymphoma team at tertiary centre for development of a bone protection policy. Medical students developed flow chart and checklist to identify high-risk patients. Introduced mandatory checking of vitamin D levels as part of baseline investigations pre-chemotherapy and identify patient at high for bisphosphonate administration. Information about bone health added to consent forms. Routine dental assessment not required unless obvious poor dental health. Single dose of zoledronic acid to be given with second cycle of chemotherapy.

Results: *Post-implementation audit cycle*: Assess all lymphoma patients for a month. Vitamin D levels checked for all patients and all patients had risk assessment for osteoporosis. All patients were at high risk for development of osteoporosis. Three were deficient in Vitamin D and scheduled to receive zometa post Vitamin D loading. All patients received zoledronic or booked to receive with subsequent cycles.

Conclusion: Newly diagnosed lymphoma patient are at high risk of low BMD, which worsens further, with high doses of steroids as part of lymphoma treatment. We successfully implemented the bone protection policy to ensure bisphosphonates is given to prevent bone loss and associated risk of fractures. The implementation of this new policy locally will improve care and quality of life for our lymphoma patients.

BSH24-EP100 | Patient initiated follow-up in lymphoma: Reducing clinic appointments, cost and environmental impact

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Introduction: Patient initiated follow-up (PIFU) allows patients to book appointments when required due to clinical need, as opposed to attending predetermined follow-up clinics. PIFU has been utilised in secondary care for several malignancies, yet there is limited evidence for its use in Haematology. Aneurin Bevan University Health Board (ABUHB) has utilised PIFU for the treatment of lymphoma since 2020. Once under PIFU, if a patient notices any symptoms of concern, they can directly contact the lymphoma team and subsequently attend clinic if required. This audit aims to evaluate the success of PIFU in the context of patients with lymphoma, in particular to assess the proportion of patients that returned to clinic, and the incidence of disease relapse. Additionally, it aims to estimate the number of clinic appointments preserved through the use of PIFU and the consequent environmental impact.

Methods: We collated data on patients enrolled to PIFU between January 2022 and January 2023, with a follow-up period ending in November 2023. We gathered information on baseline characteristics alongside appointments using our online clinical portal. On average, patients were invited to follow-up appointments every 4 months prior to transferral to PIFU; we used this to estimate appointments saved.

Results: Seventy-two patients were analysed, with the majority (55%) having low grade non-Hodgkin Lymphoma. Twenty patients (28%) re-presented to clinic within the follow-up period, most frequently due to noticing a new swelling. Yet only 9 of these 20 were diagnosed with relapse of lymphoma. However, two patients were diagnosed with relapsed disease via inpatient admissions rather than through self-presenting to PIFU.

Patients remained under PIFU for an average of 12 months, saving an estimated 216 clinic appointments. It is estimated that each secondary care appointment costs the NHS between £120–160, and a face-to-face outpatient appointment is predicted to generate 22 kg of carbon dioxide. Therefore, ABUHB PIFU scheme has generated savings between

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£25 920–34 560 and avoided 4752 kg of CO_2 emissions within the analysed 22-month period.
Conclusion: Under the ABUHB PIFU scheme, less than a third of patients re-presented to lymphoma clinic. One in eight PIFU patients developed relapsed disease within the analysed time period. We estimate that the employment of PIFU has saved 216 clinic appointments and consequently obviated CO_2 emissions equivalent to driving a petrol-car for 12 000 miles. Utilising PIFU can therefore provide an appropriate approach to care for this patient group, and additionally reduce the economic and environmental burden of follow-up.

BSH24-EP101 | Night sweats as a referral criterion for suspected lymphoma in the post-COVID era

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Introduction: Night sweats (NS) are a common symptom for referral to haematology for suspected lymphoma. NS are a common feature of many conditions including infection, hormonal changes and drug side effects but can also be seen in malignancy. Two week wait criteria (2WW) do not currently include NS, but NICE guidelines state that this should be considered when referring. Our haematology department noticed an increase in lymphoma referrals compared to pre-COVID19 and scrutinised our service data. We looked at whether there had been a change in referrals with NS since COVID19 era, whether this was predictive of lymphoma and whether other criteria in conjunction with night sweats was predictive.
Methods: We reviewed lymphoma 2WW clinic lists in 2019 (pre-COVID) and 2022. We used Medisec/ICE systems to collect data on referral symptoms, source, results of scans, blood tests and biopsies. We looked at the number of patients referred with NS alone versus that in conjunction with weight loss and lymph node enlargement (LNE), and we compared this to the number of patients who were diagnosed with a lymphoma, splitting this into high- and low-grade.
Results: One hundred and ninety referrals were made in 2022 compared to 120 in 2019. Sixty-nine patients (36%) were referred with NS in 2022 compared to 35 (29%) in 2019. Of these, night sweats alone accounted for 9 referrals (7.5%) in 2019 and 12 (6.3%) in 2022. Two patients with NS (both high-grade) had lymphoma diagnosed in 2019 (3.2% lymphoma diagnoses) and 4 (all low-grade) in 2022 (4.9% lymphoma diagnoses). Overall, in patients diagnosed with lymphoma, 20 (24.3%) suffered with NS in 2022 compared to 15 in 2019 (24.2%). The symptom with the highest likelihood of having a lymphoma was LNE alone (34% overall), and the symptom with the lowest likelihood of having a lymphoma was NS alone (4.2% overall). There was no correlation between symptoms and lymphoma grade.
Discussion: Our results suggest that NS are not predictive of having a lymphoma, and in those who did have a lymphoma, there was no difference between rates of high or low-grade lymphomas. The most predictive symptom is LNE, which reflects the current 2WW criteria. Based on these findings, we suggest that NS are not a reliable indicator of the likelihood of a patient being diagnosed with a lymphoma, and should not form part of the referral criteria.

BSH24-EP102 | A review of a district general hospital lymphoma service before and after the COVID19 pandemic

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Background: Our district general hospital serves a population of >420 000. The clinicians in our Haematology department and radiologists noticed a marked increase in referrals for suspected lymphoma since the COVID19 pandemic. Given the importance of addressing any unmet needs in cancer population and concerns from staff about whether we were meeting the demand adequately, we performed a service evaluation to analyse this.
Methods: We reviewed our clinic list in 2019 (pre-pandemic) and 2022 (post-peak pandemic) for 2 week wait (2WW) referrals for suspected lymphoma. Demographic data for the population were collected. We reviewed the source of referrals and diagnostic methods used and looked at the time from referral to review, diagnosis and treatment in conjunction with cancer governance standards.
Results: In 2019, 120 patients were referred to our 2WW clinic with suspected lymphoma, 70 from GP and 50 from another hospital specialty. In 2022, 190 patients were referred to our 2WW clinic, 120 were referred by GP and 65 were referred by another hospital specialty. Five patients were referred by a lung screening programme introduced since the COVID19 pandemic. This amounts to an overall 58.3% increase in referrals. In 2019, 80 patients (66.7%) required biopsy and 4 patients required >1 biopsy (3.33%). In 2022, 103 patients (54.2%) required biopsy and 16 patients (8.42%) required >1 biopsy. The number of patients diagnosed with lymphoma in 2019 was 62 (51.7%) versus 81 (42.6%) in 2022. Other diagnoses in 2019 included six non-haematopoietic malignancies and in 2022 included four other non-lymphoma haematological malignancies and 10 non-haematopoietic malignancies.
Time from referral to review was median 7 days (IQR 3–8) in 2019 and 8 days (IQR 4–11) in 2022 meeting the national standard of <14 days. Time from referral to diagnosis was median 28 days (IQR 19–39) in 2019 and 38 (IQR 28–63) days in 2022 and our 2022 data would not meet the new faster diagnostic standard (FDS) of 28 days. Time from referral to treatment was median 32 days (IQR 23–40) in 2019 and 48 days (IQR 37–91) in 2022.

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Discussion: These findings are likely explained by the increased in number of patients requiring >1 biopsy for diagnosis in 2022. Reviewing our service and considering how to improve it we have had funding improved for a one stop lymph node biopsy clinic to take place in the 2WW clinic to try to reduce the time from referral to diagnosis.

BSH24-EP103 | Epidemiological analysis of Hodgkin's lymphoma in a developing middle eastern country over 18 years

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Introduction: Despite the remarkable advancements in the treatment of Hodgkin's lymphoma alongside the noted decline in incidence, different trends in incidence and overall survival of the disease are more likely to be encountered in developing countries. Accordingly, thorough evaluation of the epidemiology and overall survival of Hodgkin's lymphoma in a developing middle-eastern country, such as Jordan, is of paramount significance to effectively tackle the imposed health burden.
Methods: Comprehensive data on 3114 individuals, both males and females, of different nationalities residing in Jordan who were diagnosed with Hodgkin's lymphoma during the period of 2000–2018 has been retrieved from the formal cancer epidemiology reporting institution in Jordan, the Jordan Cancer Registry. Statistical analysis, including Kaplan–Meier analysis, was performed to determine the epidemiological characteristics and survival of Hodgkin's lymphoma in Jordan.
Results: A total of 3114 individuals with a mean age of 30.7 ± 16.6 years old with a male predominance of 55.4% were included in the study. Only 445 (14.3%) patients were reported to be smokers at the time of diagnosis. Classical Hodgkin's lymphoma accounted for the vast majority of the cases (73%), with nodular sclerosing subtype being the most prevalent followed by mixed cellularity subtype, which were reported in 41.7% and 15.1% of the patients, respectively. Despite that a substantial portion of the enrolled patients did not have a reported disease's stage (42.6%), only 280 (9%) of the patients had localised disease at the time of diagnosis whereas a considerable and worrisome portion of the patients (30.7%) had systematic and distant spread of disease at the time of diagnosis. No statistically significant increase in the crude incidence of Hodgkin's lymphoma over 18 years was evident with a crude incidence estimated effect of 0.021. The overall survival was 97.6%, 93.4%, 89.3%, 82.2% and 74.5% at 1-year, 2-year, 3-year, 4-year and 5-year interval, respectively.
Conclusion: Over a span of 18 years, Jordan evidently deviates from international trends in the epidemiology of Hodgkin's lymphoma, namely the mean age of diagnosis, smoking status and overall survival. Prominently, the identified 5-year survival of Hodgkin's lymphoma in Jordan varies substantially from the internationally reported 5-year survival rates and thus mandates immediate intervention.

BSH24-EP104 | Epidemiological analysis of non-Hodgkin's lymphoma in a developing Middle Eastern country over 18 years

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Introduction: Non-Hodgkin's lymphoma imposes significant global health and socioeconomic burden not only due to the resultant morbidity and mortality but also due to the increasing incidence worldwide. Therefore, the identification of the epidemiological characteristics and overall survival of non-Hodgkin's lymphoma is of vital importance, especially in developing Middle Eastern countries such as Jordan.
Methods: Extensive data on a total of 5208 individuals of different nationalities residing in Jordan who were diagnosed with non-Hodgkin's lymphoma during the period of 2000–2018 was retrieved from the formal cancer reporting entity in Jordan, the Jordan Cancer Registry. Comprehensive statistical analysis was performed to describe the epidemiological features and overall survival of non-Hodgkin's lymphoma in Jordan over a span of 18 years.
Results: A total of 5208 patients with a mean age of 47.4 ± 20.3 years old and a male predominance of 58.4% were enrolled and subsequently analysed. Despite that the smoking status was unknown in 32.8% of the study population, a significant 50.2% of the enrolled individuals were reported to be smokers. Diffuse large B cell lymphoma was the most prevalent subtype as it was identified in 37.9% of the patients, followed by T-cell lymphoma, follicular lymphoma, and mantle cell lymphoma which were identified in 21.7%, 7.2% and 6.8% of the patients, respectively. An alarming 35.7% of the patients were identified to have widespread distant metastasis at the time of diagnosis, in contrast to only 9.8% having localised disease. The overall survival was 88.7%, 80.2%, 74.5%, 64.6% and 56.1% at 1-year, 2-year, 3-year, 4-year and 5-year interval, respectively. In regard to the incidence, there was no statistically significant increase in the crude incidence of non-Hodgkin lymphoma over 18 years with a crude incidence estimated effect of 0.023.

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Conclusion: Non-Hodgkin's lymphoma in Jordan demonstrates an alarming epidemiological profile over a span of 18 years. Notably, the mean age at diagnosis in Jordan is substantially younger compared to the reported average age in developed countries. More importantly, the 5-year survival rate of non-Hodgkin's lymphoma in Jordan is considerably less than the average rate in developed countries, and thus warranting further investigation and intervention.

BSH24-EP105 | A multiplexed fluorescent immunohistochemical analysis of CXCR4/CXCL12 axis in de novo and CNS B-cell lymphoma

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Positron emission tomography (PET) scans are the standard of care for the staging of lymphoma. However, the PET tracer fluorodeoxyglucose (FDG) has limitations due to high basal uptake especially in the brain, leading to challenges in diagnosing central nervous system spread. Alternate tracers of interest include radiolabeled antagonists of the transmembrane G-protein coupled C-X-C chemokine receptor type 4 (CXCR4), such as 68Ga-pentixafor, as CXCR4 is widely expressed in malignant cells. CXCR4 activates major cellular signalling pathways upon engagement of its natural ligand CXCL12. This axis is known to promote tumour proliferation, modulate immune response to tumour tissue and is overexpressed in >30 tumour types including haematological malignancies. However, the distribution of CXCR4 in diffuse large B-cell lymphoma and especially in central nervous system (CNS) lymphoma is still poorly understood. We therefore designed a multiplex study to evaluate cxcr4 in de-novo and CNS lymphoma along with its ligand CXCL12. We also co-stained for key cells in the immune microenvironment.

Firstly, 152 patients with DLBCL were assessed using multiplexed immunohistochemistry (mIHC) on a tissue microarray (TMA). The percentage of cells within the tumour that were positive (% extent) for CXCR4 was high (cohort mean = 82.5%), though considerably lower for CXCL12 (mean = 12.9%). There was a significant correlation between the staining of mean intensity of CXCR4 and CXCL12 (p-value $2.2e^{-16}$). There was no significant association between the expression of either markers and prognosis or International Prognostic Index (IPI) risk score. The mIHC analysis did uncover a positive correlation between CXCL12% extent and the presence of CD163+ macrophages ($r = 0.237$ $p = 0.006$). Importantly, examining a small cohort consisting of both primary and secondary CNS DLBCL ($n = 34$), we observed that the mean % extent of CXCR4 was higher than the DLBCL cohort (93.9% vs. 82.5%, p-value $= 1.22 \times 10^{-5}$). Taken together, these preliminary results suggest that the CXCR4–CXCL12 axis is active in lymphoma and regulates the immune microenvironment. The proclivity of CNS DLBCL to express CXCR4 implies that radioligands like 68Ga-pentixafor may help with PET based identification of low volume CNS involvement. The correlation between CXCL12 expression and the infiltration of pro-tumour macrophages is of potential biological and therapeutic relevance, and will require further mechanistic studies.

BSH24-EP106 | A child with sporadic Burkitt lymphoma presenting as acute flaccid paralysis and capillary leak syndrome

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Introduction: Burkitt lymphoma (BL) is an extremely aggressive and fast-growing mature B-cell non-Hodgkin lymphoma. Sporadic BL is mainly an extranodal disease. The common presentation is as an abdominal mass while primary spine, liver, kidney and bone involvement is less common.

Case Presentation: A 4-year-old previously healthy boy presented to local hospital with progressive weakness in both lower limbs over 3 days. Examination was documented as symmetrical flaccid paralysis with absent reflexes. Initial nerve conduction study (NCS) showed possible early changes of Guillain-Barre syndrome (GBS). The child was managed as GBS with intravenous immunoglobulin and therapeutic plasma exchange (TPE) with partial response. Course of the illness was complicated with Staphylococcal central venous line infection. A week after the discharge, he presented to us with right side thigh pain and fever and was found to have multiple thigh abscesses, generalised oedema with circulatory collapse and worsening paraplegia. Cerebro-spinal fluid at this time showed lymphocytes of 7/μL with protein of 140 mg/dL and poly-radiculopathy pattern in NCS. Pus and blood cultures isolated *Staphylococcus aureus*. MRI spine revealed thoracic myelitis, arachnoiditis with changes in conus medullaris and existing nerve roots. Further imaging revealed thoracic para vertebral lesions, intra spinal soft tissue lesions in lower thoracic and upper lumbar regions with possible compression of lower spinal cord. Multiple lesions in the skull with bony destruction, a solitary liver lesion, bilateral renal lesions and multiple soft tissue nodules in lungs were also noted. Biopsies from the kidney, bone marrow and liver showed an infiltrate of monomorphic round cells. On immunohistochemistry, the cells were positive for CD20, CD10 and bcl-6 and negative for bcl-2, with a Ki67

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proliferation index of 100%, confirming the diagnosis of BL. The child was transferred for specialist oncology opinion and subsequently succumbed to septic shock.

Discussion: Children with sporadic BL can be presented with atypical clinical features and paediatricians should aware about the uncommon presentations of BL.

BSH24-EP107 | Axicabtagene ciloleucel real-world manufacturing experience in the United Kingdom

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Introduction: Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 chimeric antigen receptor T-cell (CAR-T) therapy, which includes a CD28 costimulatory domain to elicit rapid and robust expansion resulting in target-specific cytotoxicity. Axi-cel is reimbursed across the United Kingdom (UK) for: (1) the third-line or later treatment of adults with relapsed/refractory (R/R) large B-cell lymphoma (LBCL); and (2) patients with LBCL refractory to or who relapse within 12 months after first-line chemoimmunotherapy (England, Wales and Northern Ireland). Reliable manufacturing and timely delivery are important factors for the success of CAR-T therapies, as they can impact patient outcomes. Here, we describe the manufacturing experience for patients with R/R LBCL treated with commercial axi-cel in the UK.

Methods: Patients with R/R LBCL registered on KiteKonnect™ and leukapheresed for axi-cel manufacturing between 01-Jan-2023 and 16-Nov-2023 in the UK were included in the analysis. The manufacturing success rate was defined as the percentage of those patient lots dispositioned as qualified person released or physician released out of the total number of lots dispositioned. Delivery success rate was defined as the percentage of patient lots shipped from the total number of patients leukapheresed. Lots that were withdrawn (either by patients or by physicians for any reason) or were still in process/transit were excluded from the analysis. The turnaround time was defined as the median time from the date of leukapheresis to the date of quality release of final product.

Results: A total of 364 lots were initiated and dispositioned during the pre-defined period and met the study inclusion criteria. The manufacturing success rate was 97.8% (356/364 batches), which included both batches released by quality and by physicians. Of the 348 patients that were leukapheresed, 345 had their dose delivered to treatment centres resulting in a delivery success rate of 99.1%. The median turnaround time between leukapheresis and quality release was 19 days (range, 16–27).

Conclusions: In this analysis, axi-cel demonstrated high and reliable manufacturing and delivery success rates and a short turnaround time in patients LBCL.

BSH24-EP109 | Single centre experience of personalised stratified follow-up for patients with lymphoma treated with curative intent

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The NHS Long Term Plan for Cancer includes personalised stratified follow-up after treatment. To facilitate this, we set up a supported self-management (SSM) pathway for patients with lymphoma. For service evaluation, we reviewed outcomes, satisfaction and quality of life data for patients on the pathway. Anecdotally, there have been concerns from some clinicians about the lack of evidence for this model. We therefore share our experiences.

Sixty patients have to date been recruited onto the SSM follow up pathway since it was set up in June 2021. It has been offered to patients with high grade and classical Hodgkin lymphoma who remain in remission 1 year following first line treatment with curative intent. All patients undergo standard consultant led follow up for the first year following treatment. After one year, SSM is offered if deemed suitable by their consultant. On entry into the pathway, patients attend a consultation with their Lymphoma Clinical Nurse Specialist (CNS) for education on symptoms of relapse, long-term effects and how to access the team, and for health and wellbeing support. They have open access to the lymphoma service but no regular follow up. After a specified period of time, they are discharged back to primary care. We collected data on patient satisfaction and quality of life using a patient questionnaire.

To date, all patients recruited onto the SSM pathway remain in remission. There have been 20 contacts to the CNS team by 13 patients, 3 of which went on to have further imaging. It is estimated that approximately 85 clinic appointments have been saved over the last 12 months because of the pathway.

Twenty-eight responses have been received to the questionnaire. Of these 16 (61%) agreed or strongly agreed that they felt confident in managing their own health, 22 (79%) agreed or strongly agreed they knew how to access the lymphoma team if they had concerns, and 22 (79%) agreed or strongly agreed they were happy with their follow-up arrangements. We also collected patient comments and quality of life data, some of which we plan to present at the BSH ASM.

Our early experience is that personalised stratified follow-up can be successfully set up for patients with lymphoma. As well as advantages for the individual, this has a positive

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impact on the lymphoma service, which is seeing an increased prevalence of patients due to increased lines of therapy and improvements in survival.

BSH24-EP110 | The expression of hepatitis C in patients with Diffuse B-cell large lymphoma (HCV + DBCL): clinic and therapy results

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Epidemiologic studies in the last 10 years have identified that approximately 10% of DBCL cases are infected with hepatitis C virus (HCV+). Patients with HCV+ DBCL demonstrate clinical and immunomorphologic distinct characteristics. The timing of initiation, type and duration of DAAA in HCV+ DBCL remains a matter of debate and discussion.
The aim of the study was to investigate the clinical and immunomorphologic features of HCV+ DBCL, to evaluate the efficacy and safety of DAAA and immunochemotherapy in this category patients.
In this study, 42 primary HCV+ DBCL (G1) and 47 HCV– DBCL (G2) patients were included. They received therapy at five centers from 2018 to 2022. The median age in G1 was 49 years (32–76 years) and in G2, it was 63 years (21–83) ($p = 0.003$): the male/female ratio in G1 and G2 was 1:1.13. Stage III–IV in G1 patients was 91%; in G2, it was—67% ($p = 0.003$). Extranodal lesions were detected in 78% of patients in G1 and 63% in G2. B-symptoms were 68% in G1 patients and 32% ($p = 0.001$) in G2. Among extranodal lesions, the spleen was involved in 70% of G1, and 8% ($p = 0.001$) of G2; the liver was affected in 66% of G1 patients and 21% ($p = 0.001$) of G2; and bone marrow was involved in 29% of G1 patients and 6% ($p = 0.001$) of G2. The expression of MYC+/BCL2+ proteins was determined of tumour in 29% in G1, G2—1% ($p = 0.001$). In blood tests, decreased platelet levels were detected in 41% of G1 patients and 8% in G2; decreased haemoglobin was detected only in 33% of G1 patients. Only in G1 patients, there was an increase in ALT—91%, AST—75% and GGTP—62%. LDH was above normal in 91% in G1 patients and 46% ($p = 0.005$) in G2. HCV RNA in patients ranged from 1.2×10^3 to 1×10^8 copies/mL (median 2.6×10^6), and genotype 1 was in 61%.
Both groups of patients received immunochemotherapy R-CHOP. G1 patients received DAAA therapy 2 weeks before R-CHOP, which was continued for 3–8 months.
The results of therapy were as follows: complete remissions were achieved in 47% in G1 patients and 72% ($p = 0.005$) in G2. Virus elimination was obtained in all G1 patients. There was no significant hepatotoxicity during chemotherapy in both groups. Median progression-free survival was 14 months in G1 and 44 months ($p = 0.001$) in G2; median overall survival was 28 and 67 months, respectively ($p = 0.0003$).
Conclusions: HCV+ DBCL has a different clinical characteristic from the general population: younger age and widespread disease stages with frequent multiple extranodal lesions. Virologic remission has no correlation with antitumor remission. It is necessary to development an effective treatment algorithm for HCV+ DBCL patients.

BSH24-EP111 | Pilot for speeding up the diagnosis of lymphadenopathies

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Lymphadenopathy of unknown cause is a frequent reason for patients' referral to a haematology clinic, but only a third of cases include lymphoma. Optimising the patient pathway and ensuring efficient and timely diagnosis, especially in probable suspected cancer is important for patient experience, clinical outcome and health economics. Patients with groin and internal lymph nodes picked up incidentally by cross-sectional imaging do not have a well-established pathway. The Marsden model of rapid access multidisciplinary lymph node diagnostic clinic, led by an oncologist (Kühnl et al., 2018, BMC Haematology) although first set up in 2000, this system has not been replicated in other hospitals.
In 2022, we launched a 2-year Lymph Node pathway project with a team of two haematology consultants covering two hospitals, a specialist nurse and an MDT administrator; all patients entering the pathway would have imaging of suspected pathological lymphadenopathy.
The trial pathway is accessible for the following:

- Primary care—GPs had no route for efficient referral leading to long delays for patients,
- Secondary care—admissions to AMU with enlarged lymph nodes were frequently difficult to triage by a speciality leading to increased length of stay.
- Rapid diagnostics centres are not able to facilitate biopsies.

Results: We have demonstrated improvement to patient experience and clinical outcomes. The pathway delivers cost reductions through reduced outpatient appointments; for primary care patients, we saved 31 new patients (NP) slots and 31 follow-ups ($n = 31$, over 9 months, an average conservative save of 1NP and 1 FU per patient). We had 68 patients referred from secondary care, 50% of whom were discharged after referral to LNP. For those who remained as inpatients, we have saved at least 3 days per patient from the duration

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of the inpatient stay (102 inpatient stays over 9 months and 34 FU appointments). FDS (faster diagnosis standard) has improved from 66.3 to 26.39 days in primary care and 31.2 to 16.88 days in secondary care, which is within the FDS target; we have helped for quicker discharge in seven patients from AMU and ED.

There is also another new source of patients: gastroenterology, colorectal and urology where the patients are scanned first, which leads to an increased number of incidental findings (from the pilot study, there were 21 patients referred from gastroenterology, nine from urology and seven from colorectal); there is no onward pathway for these patients.

Total referrals were 123, 47 had cancer diagnoses (37 haematological, 10 other), and 32 were reactive.

BSH24-EP112 | Elderly patient with haematological and neurological manifestations of undetermined origin: Diagnostic dilemma of pernicious anaemia

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Background: Pernicious anaemia (PA) is a chronic inflammatory destructive disease of parietal cells of predominantly the gastric fundus. It leads to vitamin B_{12} (cobalamin) deficiency secondary to a deficiency of intrinsic factors. Despite the medical advances nowadays, diagnosing PA can be challenging. It is often unrecognised and probably missed because of the highly variable clinical presentation of the disease and the unavailability of reliable diagnostic tests. PA is a treatable disease; however, the consequences can be devastating if undiagnosed. This report highlights a neglected case of PA with ongoing subacute combined degeneration of the cord (SCDS) in an elderly patient.

Case Presentation: An 86-year-old lady with a past medical history of hypertension, congestive heart failure on a background of ischaemic heart disease, primary pulmonary hypertension and a Stage 3 non-dialysis-dependent chronic kidney disease was referred to the haematology outpatient clinic due to refractory anaemia for the last 2 months. Her general practitioner treated her as a case of anaemia of chronic disease but without improvement.

Her initial clinical assessment revealed haematological and neurological manifestations of undetermined origin, including global weakness, hypertonia, and hyperreflexia with sensory deficits, especially in the lower limbs. On investigation, the haemoglobin level was 9 g/dL with high indirect bilirubinemia and lactate dehydrogenase (LDH). Despite the normal mean corpuscular volume (MCV) and peripheral blood smear, positive anti-intrinsic factor and parietal cell antibodies tests were subsequently reported, suggesting the diagnosis of PA. As a result, she was commenced on lifelong parenteral cobalamin replacement therapy. On follow-up visits of 3 months, she illustrated a clinical recovery in fatigability and paranaesthesia. As expected, the laboratory parameters revealed a rise in the haemoglobin level (11 g/dL) and serum vitamin B_{12} (418 pg/mL). However, she remained bedridden with spastic limbs.

Conclusions: This article highlights a case of pernicious anaemia with an ongoing SCDS. PA is a treatable disease; on the contrary, if it is left undiagnosed, the consequences can range from irreversible neurological complications to death in serious cases. Therefore, clinicians should have a high index of suspicion since PA is a rare disease with variable clinical presentations. The optimal management approach is by a multidisciplinary care team of internists, neurologists, gastroenterologists and haematologists. Those patients must remain on lifelong parenteral B_{12} injections and regular follow-ups.

BSH24-EP113 | Preoperative transfusion in patients with sickle cell disease: Systematic review and meta-analysis

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Surgeries in patients with SCD are associated with a higher rate of perioperative complications, however, clear recommendations on preoperative transfusion in the guidelines are lacking. PubMed and Embase electronic search identified 655 articles (randomised controlled trials and observational studies) about the safety of preoperative transfusion in SCD. After removing duplicates and non-relevant articles 39 articles were evaluated in full text for eligibility, 24 studies were found eligible for inclusion in qualitative analysis, and 16 studies with 3486 participants eligible for inclusion in the quantitative analysis. The assessment of quality and risk of Bias was done using the Cochrane tool for RCTs and ROBBINS-I tool for observational non-randomised studies. The safety outcomes of preoperative transfusion, including acute chest syndrome (ACS), painful crisis, neurological complications, fever, minor or major bleeding, thrombosis, intensive care unit (ICU) admission and all-cause mortality were assessed in comparison to SCD patients undergoing surgeries with conservative transfusion strategy.

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Thirteen studies had the control arm as no transfusion in comparison to preoperative transfusion, while the remaining studies had a conservative strategy guided by the haemoglobin level as a control. Sixteen studies reported ACS among SCD patients who received preoperative transfusion ($n = 1890$) versus conservative transfusion strategy ($n = 1596$) (RR = 0.91, 95% CI 0.58–1.41, $I^2 = 58\%$). Fifteen studies reported painful crisis with preoperative transfusion ($n = 1856$) versus conservative transfusion strategy ($n = 1532$) (RR = 0.94, 95% CI 0.53–1.68, $I^2 = 63\%$). Neurological complications associated with the preoperative transfusion in SCD ($n = 1590$) compared to conservative transfusion strategy ($n = 1250$) were reported in nine studies (RR = 1.38, 95% CI 0.54–3.57, $I^2 = 0\%$). Seven studies reported fever as a postoperative complication following preoperative transfusion in SCD ($n = 1243$) versus conservative transfusion ($n = 922$) (RR = 1.36, 95% CI 0.94–1.97, $I^2 = 51\%$). Six studies reported bleeding following perioperative transfusion in SCD ($n = 847$) versus conservative strategy ($n = 477$) (RR = 4.32, 95% CI 1.75–10.68, $p = 0.002$, $I^2 = 0\%$). Three studies reported thrombotic events following preoperative transfusion in SCD ($n = 885$) versus conservative transfusion ($n = 404$) (RR = 0.59, 95% CI 0.06–5.68, $I^2 = 0\%$). ICU admissions were reported in three studies with perioperative transfusion ($n = 53$) versus conservative transfusion ($n = 147$) (RR = 4.99, 95% CI 0.98–25.48, $I^2 = 0\%$). Mortality was reported in six studies with preoperative transfusion ($n = 1320$) versus conservative transfusion ($n = 977$) (RR = 0.67, 95% CI 0.05–8.75, $I^2 = 71\%$).

According to this systematic review and meta-analysis, preoperative transfusion in SCD resulted in a significantly higher rate of bleeding compared to conservative strategies without affecting other outcomes.

BSH24-EP114 | Causal relations between autoimmune diseases and aplastic anaemia: A bidirectional two-sample Mendelian randomization study

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Numerous observational research avenues have identified a possible correlation between aplastic anaemia (AA) and autoimmune diseases (ADs), rooted in analogous dysfunctional immune responses. Nevertheless, establishing a direct causal link between ADs and AA remains a complex task. This study leveraged summary data from genome-wide association studies (GWAS) pertaining to six prevalent ADs: ulcerative colitis (UC), Crohn's disease (CD), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), celiac disease (CeD) and type 1 diabetes mellitus (T1D), procured from expansive, public GWAS meta-analysis databases. AA-related genetic information was extracted from the UK Biobank. Utilising single nucleotide polymorphisms (SNPs) as genetic instruments—meeting criteria $p < 5 \times 10^{-8}$ and linkage disequilibrium [LD] $r^2 < 0.001$—the study employed Cochran's Q test, the MR–Egger intercept test, and leave-one-out analysis to gauge the sensitivity concerning the impact of ADs on AA. The findings underscore a definitive causal relationship between SLE and AA, as evidenced by the statistics (ORMR–Egger = 1.392, 95% CI 0.925–2.094, $p = 0.188$; ORWM = 1.317, 95% CI 1.101–1.576, $p = 0.003$; ORIVW = 1.193, 95% CI 1.013–1.404, $p = 0.035$). However, the investigation did not denote any significant associations between AA and other ADs, including UC, CD, RA, CeD and T1D. Additionally, the Mendelian randomization analysis reported no evidence of horizontal or directional pleiotropy.

In summary, the study suggests that SLE could serve as a potential risk factor contributing to the onset of AA. To further substantiate this hypothesis, ensuing studies encompassing larger sample sizes are warranted.

BSH24-EP115 | Severe B12 deficiency mimicking HELLP syndrome: A case report

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Introduction: HELLP syndrome is a serious consequence of pre-eclampsia (PET) that results in haemolysis, elevated liver enzymes and low platelets. This is due to peripheral microangiopathy caused by PET. Severe B12 deficiency can also manifest as macrioangiopathic haemolytic anaemia, thrombocytopenia and pancytopaenia, and as well as serious consequences for the foetus, such as neural tube defects, pre-term birth and intrauterine fetal death.

Method: This case report describes an example of severe B12 deficiency causing a similar biochemical profile to HELLP syndrome, without hypertension. Hb of 63 g/L, platelets 36×10^9/L, white cells 3.8×10^9/L, reticulocyte count 17×10^9/L. Grossly elevated LDH 4393 iu/L prompted suspicion of intramedullary destruction rather than peripheral haemolysis as seen in HELLP.

A literature review yielded few similar reported cases.

Conclusion: B12 deficiency is relatively easy to treat, and with the rise in obesity, we are likely to see more severe deficiencies. It forms an important differential in atypical presentations of suspected HELLP and can reduce morbidity from iatrogenic early deliveries particularly where it manifests at early gestations.

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BSH24-EP116 | Use of conventional transfusion thresholds contribute to iron overload in patients with sickle cell disease

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Introduction: Sickle cell disease is characterised by chronic anaemia and recurrent pain episodes. These are sometimes managed with exchange or simple transfusions using packed red blood cells (PRBC). Randomised data are available that support lower transfusion thresholds in non-sickle cell related conditions. Current recommendation is to transfuse at haemoglobin levels less than 7 for patients who are critically ill and at less than 8 for patients undergoing orthopaedic surgery. Due to lack of similar randomised trials in patients with sickle cell disease, recommendations from other trials are often applied to patients with sickle cell diseases. However, this can make pre-existing iron overload states worse.
Methods: The haemoglobin threshold used for giving PRBC's during pain crisis episodes was studied in patients who were getting red blood cell exchanges or simple transfusions for chronic sickle cell related pain. Eight individuals were selected from the cohort of patients with homozygous sickle cell disease who had been receiving elective packed red blood cell exchanges and later just simple transfusions. Patients with ferritin levels persistently remaining above 1000 mg/dL were then evaluated with regard to transfusion thresholds used for simple transfusion support during hospitalisation for pain crisis episodes.
Results: A total of 30 units of packed red blood cells was found to be transfused over the subsequent 6-month period. During this time only one patient in the cohort required an exchange transfusion session. Two out of 30 units were given for a haemoglobin level above 7. The majority, representing 24 out of the total 30 PRBC's were given for a haemoglobin threshold of 6.0. Only 4 units were given at a haemoglobin threshold less than 6. The mean ferritin level before and after the period of simple transfusion support was 6097 and 6076 mg/dL.
Conclusions: Transfusion thresholds used in sickle cell disease appear to be similar to patients without sickle cell disease. Guidelines from studies like TRICC and FOCUS is to transfuse at haemoglobin levels less than 7 or 8 depending on the condition. Studies are ongoing trying to reduce the transfusion threshold even further to a lower haemoglobin level. However, in patients with sickle cell disease, conventional thresholds may not be appropriate since baseline haemoglobin is lower to begin with. These patients also tend to have iron overload, which likely will not improve unless transfusions are limited further. Therefore, applying a lower transfusion threshold would be recommended especially in sickle cell patients with pre-existing iron overload.

BSH24-EP118 | Methemoglobinemia—A case report

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Methaemoglobinaemia of unknown cause—a case report.
Rationale: Methaemoglobinemia is a rare red cell disorder usually secondary to toxins/drugs and treated with methylene blue and ascorbic acid. When no obvious trigger is identified it can be challenging to diagnose and manage complications of methaemoglobinaemia. In these cases, a poor response to conventional treatment may be seen requiring establishment on exchange transfusions programs to optimise symptoms.
Diagnosis: A 62 gentleman had multiple admissions over several years and was treated as recurrent exacerbations of asthma/COPD before being subsequently diagnosed with symptomatic methaemoglobinaemia during an emergency visit (MtHb% 20% on ABG).
Management: Initially, he was treated with methylene blue and then ascorbic acid and riboflavin. However, he kept deteriorating with decline in quality of life.
Extensive investigations were undertaken (enzyme levels, HPLC and Genetics) and all were negative.
Patient was discussed in regional MDT and started on an exchange transfusion program (8 weekly) which improved his symptoms dramatically.
Outcomes: Met-Hb blood level improved along with patient's quality of life.
Conclusion: A high suspicion of methaemoglobinaemia in adult patients with recurrent admissions of cyanosis and shortness of breath. Exchange transfusions can help in reducing MetHb levels and improve symptoms in methaemoglobinaemia of unknown cause if refractory to conventional therapy.

BSH24-EP119 | Design and implementation of sickle cell disease electronic registry in limited resources setting in Nigeria

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Background: Electronic registry (ER) is a unified system that uses observational study methods to collect uniform data to evaluate specified outcomes for patients and that serves one or more predetermined scientific, clinical or policy purposes. It comprises electronic data collection

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facilities, database, data management mechanism with analysis and reporting templates.

Objective: To design and implement ER for sickle cell disease (SCD) in Ahmadu Bello University Teaching Hospital (ABUTH) in Zaria, Nigeria with the aim of maintaining and promoting collection of reliable data on persons with SCD attending ABUTH clinics.

Methods: The design of the registry was initiated during a staff exchange programme funded by the African Research and Innovative Initiative for Sickle cell Education: Improving Research Capacity for Service Improvement (European Union grant no. 824021—ARISE-H2020-MSCA-RISE-2018/H2020-MSCA-RISE-2018) and in collaboration among researchers from ABUTH and Fondazione per la ricerca farmacologica Gianni Benzi onlus (Italy). Ethical approval and relevant permissions were obtained and then existing hard copy records were retrieved. Microsoft Office Access was used to develop two databases for adults and paediatric ERs. ER design was based on literature analysis, other registries reviews and consultations with clinicians and experts. This is a single centre, retrospective records abstraction of clinic visit details of SCD patients attending ABUTH, implemented as a pilot study to test the feasibility of prospective adoption as part of ARISE mandate of implementing E-health technologies in sub-Saharan Africa.

Results: Data of 2659 sickle cell patients were included in the ER. In this study, 698 (26.3%) were adults and 1961 (73.7%) were children. There were 287 (41%) male among the adults, 404 (58%) female and 7 (1%) patient's gender not recorded. There were 1041 (53.1%) male among the children, 906 (46.2%) female and 14 (0.7) gender not recorded. Also, 142 (20%) adults were married, 513 (74%) single, 8 (1.1%) divorced, 1 (0.1%) widow and 34 (4.8%) did not record their marital status. In addition, 590 (84.5%) adults have phenotype SS, 34 (4.8%) SS + F, 49 (7%) SC, 2 (0.3%) CC and 24 (3.4%) did not record their phenotype. We found that 1493 (76%) children had phenotype SS, 187 (9.5%) SS + F, 31 (1.5%) SC and 250 (13%) did not record their phenotype. The most prevalent SCD related complication documented at adult clinic visits was body pain (18.3%) while in children it was vaso-occlusive crises (42.5%).

Conclusion: It is possible to design SCD ER, train users and implement it in ABUTH for disease management, monitoring, research and training.

Keywords: database, electronic registry, sickle cell disease.

BSH24-EP120 | Minimising alloimmunization: Rethinking blood transfusions in acute chest syndrome management

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Acute chest syndrome (ACS) is a leading cause of morbidity and mortality in patients with sickle cell disease. It is defined by the presence of fever and/or respiratory symptoms with new pulmonary infiltrate on chest X-ray. Current BSCH guidelines for management of ACS acknowledge a lack of random controlled trials regarding transfusion in ACS management, but recommend consideration of top-up transfusion in hypoxic patients and exchange transfusion for severe clinical features or progression despite simple transfusion. Red cell transfusion carries the risk of alloimmunization against Rhesus antigens (CE) to which persons of African and Caribbean origin are particularly prone due to a high prevalence of the R0 genotype. Safely limiting transfusions for acute chest syndrome would reduce this risk.

A prospective observational study was conducted over a six-month period at one tertiary care centre in Trinidad and Tobago where SCD is prevalent to examine clinical features and the use of red cell transfusions managing Acute Chest Syndrome. Seventeen cases were seen at the Eric Williams Medical Sciences Complex in TTO of whom all had HbSS disease. All 17 were hypoxic requiring oxygen treatment.

Of these seventeen cases, seven received top-up red cell transfusion. Of the transfused group, the SpO_2 ranged from 75% to 90% on room air. Four (57%) had Hb 2 g/dL below steady state haemoglobin, and were transfused as per local policy, 3 (43%) were 1 g/dL below documented steady state—but based on additional factors—one pregnant 34 weeks, two use of a re-breathable oxygen mask they received a transfusion. Of this group four (57%) had unilateral consolidations and three (43%) bilateral consolidation on chest X-ray. Only two cases were on disease modifying treatment with hydroxyurea. The average hospital stay was 10.7 days ranging from 5 to 21 days.

Among the ten non-transfused patients, SpO_2 ranged 85%–94%, bilateral consolidation was present in five cases and unilateral in five cases. Hb on presentation ranged from 6.7 to 10.4 g/dL. Haemoglobin on presentation was around their known steady state for all 10 patients. Six (60%) were on hydroxyurea. The average hospital stay was 10.5 days ranging from 6 to 20 days. There were no deaths reported in either group.

The study demonstrates favourable outcomes with judicious top up transfusion in patients with acute chest syndrome. This approach could reduce the need for exchange transfusion and reduce the risk of alloantibody development.

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BSH24-EP121 | Dapsone induced haemolytic anaemia and methemoglobinemia in a paediatric case study

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Introduction: Methemoglobinemia is a potentially life-threatening condition, with serum levels of methaemoglobin over 70% typically resulting in death. Red blood cells usually maintain a methaemoglobin level of 1%, however levels can be raised by exogenous oxidising agents, such as drug metabolites. Alongside local anaesthetics, dapsone is a common cause of methemoglobinemia, with literature suggesting incidences of this side effect ranging from 4% to 23% during use.

Case Presentation: A 3-year-old female attended the emergency department with a 24 h history of yellow skin and hyperpigmented urine. She was otherwise well, denying symptoms such as shortness of breath, rashes, bruising, abdominal pain, weight loss or change in bowel habits. She had no significant family history or history of recent travel. Her only medical history was ongoing severe chronic urticaria: receiving treatment of 30 mg dapsone once daily and 5 mg loratadine four times daily, alongside a recently completed 7-day course of prednisolone under dermatology. Her dose of dapsone had recently been doubled.

A full systems examination discovered low oxygen saturations despite 15 L high flow oxygen but was otherwise unremarkable. A chest x-ray was ordered in view of low saturations, which also showed no obvious abnormalities. However, a blood gas revealed low haemoglobin (97), raised methaemoglobin (16.4) and raised bilirubin (28). Venous blood tests indicated haemolytic anaemia with raised reticulocytes (10.2).

The next steps in management involved a multi-disciplinary approach from haematology, dermatology, toxicology and general paediatrics. IV access was gained, blood cross-matched and 4 h full blood counts were taken to ensure the patient was not acutely significantly haemolysing. Following haematology input, a diagnosis of dapsone induced haemolytic anaemia and methemoglobinemia was made.

Treatment consisted of discontinuing dapsone, oxygen therapy to support clearance of methaemoglobin and a 6-week course of treatment dose folic acid. In this case, methylene blue was not considered necessary. The patient recovered well and was discharged from hospital 2 days later once clinically stable. She received follow-up by dermatology, who initiated ciclosporin and methotrexate as an alternative to dapsone and underwent repeat venous blood tests 5 days later, demonstrating resolution of her haemolytic anaemia and reduction of methaemoglobin levels to 6.7.

Discussion: This case illustrates prompt diagnosis and treatment of dapsone induced haemolytic anaemia and methemoglobinemia leading to optimal patient outcome. Additionally, it encourages clinicians to consider methemoglobinemia as a differential in hypoxemia refractory to supplemental oxygen and the importance of eliciting a drug and toxicology history in such cases.

BSH24-EP122 | Between the extremes … A case report of polycythemia vera post autoimmune haemolytic anaemia

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Background: Autoimmune haemolytic anaemia (AIHA) is characterised by the immune-mediated destruction of red blood cells. In contrast, polycythemia represents an overproduction of red blood cells, leading to increased blood viscosity. This report documents an exceptional case of AIHA that progressed to polycythemia, challenging our understanding of these distinct clinical entities.

Aim: Here I report the clinicopathologic findings and treatment outcome of this unusual presentation of an Egyptian gentleman who was diagnosed initially with autoimmune haemolysis then polycythemia and understanding the relation between the two extremes.

Methods: A case report of a gentleman who attended the haematology clinic in Oncology centre, Mansoura University, Egypt. This includes history taking, physical examination, full blood count, chemistry profile, haemolytic screen, immune profile, Clonal markers evaluation. Besides Bone marrow examination and trephine biopsy along with whole body CT scan.

Results: Our 55 year old non-smoker patient presented in May 2018 with progressive anaemia proved to be autoimmune haemolysis. This was investigated with Positive direct coombs test, high indirect bilirubin level and reticulocyte count. He had high LDH level with low haptoglobin. Secondary causes were excluded by negative immunological markers (ANA, ADNA), normal findings in whole body scans. His bone marrow examination showed hypercellularity (100% cellularity) and marked erythroid hyperplasia with dyserythropoiesis and predominant immature forms. He was started on steroid therapy with adequate response until steroid withdrawal and stoppage. He stayed off steroid for more than 2 years until late 2020 when he presented with isolated erythrocytosis (Haemoglobin level 18.7 g/dL, haematocrit level 53%). Causes of secondary polycythemia were excluded. Re-investigations including JAKII V617F mutation, calreticulin (CALR) were negative. The epoietin level was normal as well. Bone marrow aspiration and trephine biopsy was done and showed slightly hypercellular bone marrow for age (60% cellularity), E-cadherin highlight erythroid series about 30% of overall cellularity. Our patient was started on aspirin 75 mg daily and venesection with lack of control so he was shifted to low dose hydroxyurea which keeps his counts in good response with no related symptoms.

Summary and Conclusion: The progression from AIHA to polycythemia is rare, if not previously unreported. This unique clinical course highlights the complex interplay between the immune system and haematopoiesis and underscores the need for regular follow-ups and thorough investigations in AIHA patients. Further research is required

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to elucidate the potential mechanisms behind such a transition and its implications for management.

BSH24-EP123 | Management of obstetric patients with sickle cell disease—A case series

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Introduction: Pregnancy in women with sickle cell disease (SCD) is associated with increased maternal and fetal morbidity and mortality. In the UK there are 110–200 pregnancies in women with SCD per year. This case series aims to evaluate the management and pregnancy outcomes of women with SCD attending the joint obstetric-haematology antenatal clinic at Queen's Hospital, Barking, Havering and Redbridge Trust.
Method: We retrospectively reviewed the clinical records of pregnant women with SCD attending the clinic between January 2022 and April 2023.
Results: Six women, all of Black Afro-Caribbean ethnicity, had SCD. Their average baseline haemoglobin (Hb) was 86 g/L (IQR 86–92).
All women were first seen in clinic before 20 weeks gestation and reviewed monthly thereafter. Folic acid, aspirin, antibiotic prophylaxis and relevant immunisations were recommended to all. All patients underwent an echocardiogram and eye check antenatally. Three women were initiated on prophylactic thromboprophylaxis in early pregnancy, and automated red cell exchange transfusions (ARCET) from the second trimester. One woman who did not require ARCET had mild phenotype and high percentage of HbF, the other declined treatment but eventually agreed for ARCET from the third trimester. One woman with multiple pregnancy was commenced on 4-weekly prophylactic transfusions from the second trimester. Four women suffered acute SCD crisis in pregnancy, with 1/4 requiring intensive care management. Two women delivered preterm; one with multiple pregnancy at 31 + 6 weeks gestation due to acute SCD crisis and concerns regarding foetal wellbeing, and the other at 35 + 6 weeks gestation secondary to preterm prolonged rupture of membranes. Two women had spontaneous vaginal delivery and four women had caesarean section. The average foetal weight at birth was 2504 g (IQR 1553–3449). One neonate from the twin pregnancy died on day 1 of life due to pulmonary haemorrhage. Good neonatal outcomes were reported in all other cases.
Conclusion: Pregnant women with SCD can be safely managed at local maternity services with appropriate multidisciplinary team input in place. There was great variation in compliance with recommended treatment, with non-compliance associated with increased incidence of crises. This small case series highlights the importance of patient education and individualised care plans for optimal maternal and neonatal outcomes.

BSH24-EP124 | Is umbilical cord blood a better treatment for treating paediatric patient with sickle cell disease

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Background: Sickle cell disease is an inherited red cell disorder which could be in the form of homozygous or heterozygous trait. The disease occurs when thymine is replaced for adenine in the beta globin chain causing valine to be produced instead of glutamine. It is estimated that 300 000 infants are born with SCD in Africa. The United Nations has estimated that 12–15 million of the world's SCD patients are living in Africa. Childhood mortality rate is also highest in children with ages ranging from 6 months and 3 years. So many complications are associated with SCD, but the hallmark of the disease is pain because of vaso-occlusion. Over the years, several treatment inventions have been used in the treatment of SCD but the only known cure is the use of HSCT. Earlier studies have shown promising outcomes using umbilical cord blood for treating SCD and this research study aim to look at the overall survival of paediatric patients who have had umbilical cord blood transplant.
Method: Eleven studies were eligible after thorough selection. Also, 1967 patients with SCD were pooled from the 11 studies with 317 patients out of 1967 had undergone umbilical cord blood transplant and 1650 who have had bone marrow transplant.
Result: OS and haematopoietic recovery time was 92.50% for UCBT, while OS of BM was 96.37%. There was no significant difference in the OS of both interventions although the time of neutrophil and platelet recovery were different.
Conclusion: There was no significant difference between the overall survival although UCB had a better outcome in terms of engraftment especially when related matched cord blood was uses. Less death and event-free survival were also recorded.
Keywords: alemtuzumab (ATG), bone marrow (BM), cord blood, event free survival (EFS), graft versus host disease (GVHD), haematopoietic stem cell transplant (HSCT), overall survival (OS), reduced intensity conditioning (RIC), sickle cell disease (SCD), stem cells, transplantation, umbilical cord blood.

BSH24-EP125 | Treatment of autoimmune hemolytic anaemia in beta thalassaemia major

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Beta Thalassaemia major (BTM) is one of the common and severe inherited hemoglobinopathies resulting from defective beta globin chains. Children suffering from BTM require regular blood transfusions from early childhood to alleviate the symptoms of anaemia. Apart from the need for

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regular transfusions and the associated risks such as iron overload and transfusion-transmissible infections, the simultaneous occurrence of autoimmune haemolysis worsens the anaemia. The data on optimal treatment of autoimmune hemolytic anaemia (AIHA) in children suffering from BTM are limited.

In this study, we included BTM patients suspected of AIHA and tested for AIHA by direct Coomb's test (DCT). Our findings suggest that 20% of the BTM patients had DCT-positive AIHA.

These patients were treated with prednisolone (1–1.5 mg/kg) orally for 3 weeks followed by slow tapering. Only 40% of patients responded to Prednisolone while 60% remained non-responsive or relapsed on tapering doses.

The non-response or relapsed cases were then given rituximab (375 mg/m^2) intravenously weekly for 4 weeks with or without prednisolone. Over 90% of AIHA cases responded to rituximab eliminating the need for frequent blood transfusion and symptomatic relief.

Hence, our findings suggest that both prednisolone and rituximab can be used as treatment options in DCT-positive AIHA in BTM patients. However, rRituximab is superior to prednisolone alone in treating AIHA in BTM if affordable in patients from low and low-middle-income countries.

BSH24-EP126 | Pharmacological intervention for pain management in paediatric sickle cell anaemia patient: A network meta-analysis

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Sickle cell anaemia (SCA) is a hereditary disease that encompasses abnormality in the globin chains of red blood cells, resulting in low blood oxygen levels and organ damage. Due to its hereditary pattern, most SCA patients are children and adolescents. The main treatment of SCA in children and adolescents is pharmacological treatment, including pain management. This study aims to systematically gather randomised controlled trials (RCTs) on pharmaceutical intervention for pain management in SCA in paediatric patients.

Twenty-three studies with 2123 paediatric patients were included, comparing the efficacy of 15 pharmacological treatments in paediatric SCA pain management to placebo. The analysis indicated that hydroxyurea was the most effective pharmacological treatment in decreasing acute chest syndrome (ACS) incidences (Odds ratio [OR] 0.39 95% CI [0.17; 0.90], $p = 0.02$) and hospitalisation (OR 0.32 95% CI [0.16; 0.64], $p = 0.001$), SC411 was superior in preventing vaso-occlusive crisis (VOC) incidence (OR 0.47 95% CI [0.23; 0.97], $p = 0.04$), ketorolac (mean difference [MD] −4.18 95% CI [−5.91; −2.44], $p < 0.0001$) and arginine (MD −2.06 95% CI [−2.48; −1.64], $p < 0.0001$) was effective in decreasing pain intensity in SCA paediatric patients, dexamethasone was efficient in decreasing transfusions (OR 0.19 95% CI [0.05; 0.77], $p = 0.02$) and severe adverse events (SAEs) (OR 0.19 95% CI [0.05; 0.77], $p = 0.02$) in paediatric SCA patients. However, there were no statistically significant treatments in adverse events, but all of the interventions had better outcomes than the placebo arm.

We conducted a frequentist network meta-analysis of RCTs. A literature search was performed on data collected from Cochrane Library, PubMed, and Scopus database. The risk of bias was calculated and analysed using the Cochrane tool RoB 2.0. Network diagrams were constructed for outcomes consisting of pain score, ACS, VOC, AEs, SAEs, hospitalisation and transfusion, and all analyses were performed using a frequentist approach, assuming a random effects model within the RStudio.

This study shows the significant efficacy of various pharmacological treatments in reducing the symptoms of SCA, such as the number of hospitalizations, ACS, VOC, SAEs and pain intensity over the placebo group. However, the interventions were not statistically significant for adverse events but showed a better outcome than the placebo arm.

BSH24-EP128 | Evaluation of some haemostatic parameters in management of HBV infection treatment outcome in Asaba, Nigeria

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Hepatitis B virus (HBV) infection is a viral infection that affects the liver causing acute as well as chronic disease worldwide. Poor diagnosis and prognostic factors remain crucial factors responsible for poor management of the disease despite progress in implementing vaccination programmes and development of new treatment perspectives in the management of hepatitis B virus (HBV) infections. HBV infection remains a major health problem worldwide, contributing considerably to cirrhosis- and hepatocellular carcinoma (HCC)-related mortality of 0.5–1 million per year. Thus, this study was aimed at evaluating HBV infection treatment outcome using viral load and changes in haemostatic variables such as activated partial thromboplastin time, prothrombin time, fibrinogen and D-dimer of HBV positive treatment naïve, on treatment at 3 months and treatment at 6 months subjects attending gastro-enterology clinic in Federal Medical Centre Asaba, Delta State, Nigeria. A total of 115 adults aged 22–64 years were randomly enlisted in the study. The cross sectional study consist of 50 confirmed hepatitis B negative subjects as negative controls whereas, the follow-up study consist 65 treatment naïve HBV positive subjects who were followed-up at 3

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and 6 months on treatment with tenovofir respectively. Four of the participants (two in 3 months post treatment and two 6 months post treatment) dropped-out of the research due to time constrain. The blood samples collected in Ethlyene Diamine Tetra-acetic acid was used for platelet count using Sysmex® Automated Haematology Analyser. Fibrinogen, viral load and D-dimer were analysed using enzyme-linked immunosorbent assay method. Blood was also anticoagulated with 0.109 M trisodium citrate (9:1 v/v) for the measurement of activated partial thromboplastin time and prothrombin time. The levels of platelet count did not differ significantly ($p > 0.05$) for the various groups whereas, the median levels of HBV viral load, fibrinogen, D-dimer, prothrombin time and APTT in the HBV naïve, 3 months on treatment and 6 months on treatment subjects were significantly higher when compared with the control group ($p < 0.05$). Thus, it is possible that the distortions in synthesis of coagulation proteins in the liver which are reflected in prolongation of PT, APTT, increased D-dimer and low fibrinogen concentration plays a crucial role in pathogenesis of HBV infection as such these parameters could be used as co-markers to viral load in monitoring the treatment outcome of HBV infection in Nigeria.

BSH24-EP132 | An audit of laboratory practice conformance with guidelines for antiphospholipid tests

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Since the development of pathology networks, transportation of coagulation samples to central sites for specialist testing has become more prevalent, presenting problems relating to preserving sample integrity for prolonged periods. This issue is particularly relevant to coagulation tests due to its complexity and sensitivity to degradation of cell components. Additionally, in the context of antiphospholipid screening, various tests, and reagents available could pose additional challenges. Guidance has been provided from the British Committee of Standards in Haematology (BCSH), the International Society of Thrombosis and Haemostasis (ISTH) and the Clinical and Laboratory Standards Institute (CLSI), which laboratories should take into consideration when developing an antiphospholipid diagnostic repertoire. The purpose of this audit it to review the commonalties between the guidelines and to develop a framework against which the compliance of the antiphospholipid assays employed by Manchester Royal Infirmary, the central site in the Manchester Foundation Trust Network, can be evaluated and improved.

Audit criteria was derived from assessment of commonalities between the three guidelines. Compliance, or non-compliance, of the processes published in local standard operating procedures for Manchester Royal Infirmary was recorded. Findings were then critically evaluated for the clinical impact with reference to the guidance reviewed and potential improvements are discussed.

Non-conformances emerged that highlighted areas for improvement and an associated corrective action was suggested, including clarification in the laboratory standard operating procedure to guide assessment of suitability of testing patients in certain clinical states. Guidance of pre analytical handling of samples was found to be unclear and corrective actions to clarify this were suggested. There was no evidence to suggest the origin of cut-off values were locally derived, and it was suggested a revised cut-off value be established. There was found to be no interpretive comment advising the clinical team to repeat testing at least 12 weeks after initial investigation.

While guidelines from the three sources reviewed were occasionally contrasting, the interpretation of them covers all areas of laboratory aspects of lupus testing. The audit findings conclude that the local protocol for Lupus anticoagulant is generally compliant with the guidelines set by the BCSH, ISTH and CLSI, though there are opportunities to improve as highlighted in the findings. Independent evidence such as the EQA reports demonstrate a satisfactorily performing test process.

BSH24-EP134 | Hyperhomocysteinemia-associated thrombosis in patients with pernicious anaemia

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Background: Pernicious anaemia (PA) is due to cobalamin deficiency (CD) resulting from cobalamin malabsorption in the ileum, secondary to autoimmune chronic atrophic gastritis (CAG). CD leads to hyperhomocystinemia, a risk factor for thrombosis. However, the clinical presentation and outcomes of PA-related hyperhomocystinemia-associated thrombosis are not fully understood.

Methods: We undertook a literature search using PUBMED and SCOPUS databases using the terms "pernicious anaemia AND thrombosis", "pernicious anaemia AND embolism", "pernicious anaemia AND thromboembolism", "autoimmune gastritis AND thrombosis", "autoimmune gastritis AND embolism", "autoimmune gastritis AND thromboembolism" from inception through July 2023 and reviewed the published literature. We collected data on age/sex, homocysteine and cobalamin levels, types of thrombosis (initial vs. late presentation of PA, thromboses at usual sites vs. unusual sites, arterial vs. venous), positive anti-intrinsic factor (anti-IF) and anti-parietal cell (anti-PC) antibodies, presence of bone marrow (BM) megaloblastosis, and CAG and overall survival (OS). Our main aim was to illustrate the clinical features and outcomes of PA-related hyperhomocysteinemia-associated thrombosis by descriptive statistics.

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Results: Of 19 patients, the median age was 53 years with 58% males. The median serum homocysteine level was 70 µmol/L. We found that 25% of patients developed thromboses at multiple locations while 21% had thromboses at unusual sites. Also, 95% of cases presented with thrombosis before the diagnosis of PA was established. In addition, 42% of patients had co-existing neuropsychiatric symptoms. Also, 78% of patients were positive for anti-intrinsic factor (anti-IF) antibodies. All patients received antithrombotics with a median duration of 6.5 months, and cobalamin replacement. None developed recurrent thromboembolism. BM megaloblastosis was present in those who underwent BM biopsy. Fifteen patients (79%) had macrocytic anaemia while one each presented with normocytic anaemia (5%), and microcytic anaemia (5%). Haemoglobin was normal in two patients (11%). CAG was present in 85% of patients who underwent gastric biopsies. One died of liver failure following intestinal resection and the OS rate was 95%.
Conclusions: This condition, although rare, is associated with high incidence of thromboses at unusual sites, multiple-site thromboses, co-existing neuropsychiatric symptoms and high rate of positive anti-IF antibodies, and very low recurrent thrombosis rate and low mortality rate.

BSH24-EP135 | An audit to assess venous thromboembolism prevention management in pregnant/postpartum hospital inpatients

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Background: Women who are pregnant or in the postpartum period have a four-to five-fold increased risk of venous thromboembolism (VTE) compared with non-pregnant women. Pregnant women have all components of Virchow's triad: venous stasis, hypercoagulability and vessel wall damage. Thrombosis remains the leading direct cause of maternal deaths. VTE risk assessments are important to guide antenatal/postnatal VTE prevention management.
Aim: To establish whether pregnant/postpartum women at risk of VTE have appropriate VTE prevention measures during hospital and on discharge if indicated, and assess compliance to local guidance.
Objectives: To establish if pregnant/postpartum hospitalised inpatients have:

- A VTE risk assessment completed on hospital admission/after birth, to identify thrombosis and bleeding risk factors and prompt appropriate VTE management.
- Appropriate pharmacological thromboprophylaxis during admission/on discharge (based on VTE score), unless contraindicated.
- Appropriate mechanical thromboprophylaxis during admission, unless contraindicated.
- A thrombotic (venous and/or arterial) event during and/or within 30 days of recent admission.

Methods: Retrospective data collection via electronic patient records using Cerner® electronic system.
Two hundred and forty-six patients across two hospital sites (inclusion and exclusion criteria applied) were included in the audit.
Patient demographics, clerking/admission documentation, VTE risk assessment forms, pathology/radiology results, medication chart and discharge summaries were reviewed to assess performance against standards to evaluate VTE prevention management.
Patients were followed up for 30 days to identify any thrombotic (venous and/or arterial) event(s) post discharge.
Results: In total, 100% of inpatients had a completed VTE risk assessment on Cerner system, of which:

- At booking: 60% ($n = 148/246$) patients.
- On hospital admission: 74% ($n = 181/246$) patients.
- After birth: 82% ($n = 202/246$) patients.
- Accurate VTE risk assessment was completed for 55% ($n = 135/246$) of patients at booking, 66% ($n = 162/246$) of patients on hospital admission, and 70% ($n = 171/246$) of patients after birth.
- Seventy-four percent ($n = 182/246$) of patients at booking and 41% ($n = 102/246$) of patients after birth had weight documented.
- Ninety-six percent ($n = 237/246$) of inpatients were prescribed appropriate pharmacological thromboprophylaxis during admission, and 61% ($n = 150/246$) on discharge, unless contraindicated.
- Fourteen percent ($n = 36/246$) of inpatients were prescribed appropriate mechanical thromboprophylaxis.
- No thrombotic (venous and/or arterial) events occurred during admission or 30-day follow-up.

Conclusion: VTE prevention measures are important for maternity inpatients to prevent VTE events during pregnancy and postnatal period. VTE risk assessment supports decision-making before offering thromboprophylaxis. Further education and awareness is required particularly on prescribing mechanical thromboprophylaxis, and the importance of re-weighing women after birth for correct postnatal thromboprophylaxis dosing. Action plan developed to address recommendations.

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BSH24-EP136 | An audit to assess venous thromboembolism prevention management for COVID-19 positive hospital inpatients

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Background: COVID-19 is characterised by a cytokine outburst with hyperinflammation, a hypercoagulable state, platelet activation, endothelial dysfunction, sepsis-induced coagulopathy and immobility. Severe COVID-19, complicated with coagulopathy, is associated with an increased risk of venous thromboembolism (VTE) events and mortality.
Aims: To assess VTE prevention management in COVID-19 positive hospital adult inpatients (excluding maternity), and assess compliance to local and national guidance.
Objectives: To establish:

- VTE risk assessment completion on admission.
- Prescribing of appropriate pharmacological thromboprophylaxis during admission and on discharge, unless contraindicated.
- If critically-ill inpatients prescribed appropriate mechanical thromboprophylaxis during admission, unless contraindicated.
- Thrombotic (venous and/or arterial) event(s) during, within 30 days and/or within 90 days of recent admission.

Methods: Retrospective data collection was conducted via electronic patient records.
Sixty-six COVID-19 positive inpatients across two hospital sites (inclusion and exclusion criteria applied) were included in data analysis.
Patient demographics, admission documentation, VTE risk assessment forms, pathology/radiology results, medication chart and discharge summaries were reviewed to assess performance against standards to evaluate VTE prevention management.
Patients followed up for 30 and 90 days to identify if any thrombotic events occurred following discharge.
Results:

- Eighty-nine percent ($n = 59/66$) of inpatients with completed VTE risk assessment within 14 h and 97% ($n = 64/66$) within 24 h from admission.
- Eighty-four percent ($n = 51/61$) of inpatients were prescribed appropriate pharmacological thromboprophylaxis during admission, unless contraindicated.
- Sixty-seven percent ($n = 4/6$) of COVID-positive critically ill inpatients were prescribed appropriate mechanical thromboprophylaxis.
- Eighty percent ($n = 6/10$) of symptomatic COVID-positive inpatients established on anticoagulation therapy prior to hospital admission were not appropriately switched to alternative anticoagulation.
- Hundred percent ($n = 6/6$) of asymptomatic COVID-positive inpatients established on anticoagulation therapy prior to hospital admission continued on the established anticoagulant agent during admission as appropriate.
- Sixty-three percent ($n = 33/52$) of inpatients were prescribed appropriate thromboprophylaxis on discharge, unless contraindicated.
- Three thrombotic events (venous and/or arterial) occurred during admission, 3 thrombotic events during 30 day follow-up and no thrombotic events occurred within 90 days of recent hospital admission. All patients received appropriate thromboprophylaxis during admission.

Conclusion: COVID-19 patients are at increased risk of VTE. Accurate and timely VTE risk assessment is important to assist clinicians in decision-making on anticoagulation to prevent VTE events, and improve clinical outcomes. It is important to keep abreast of evidence and latest guidance to apply to local clinical practice, with education and awareness so front-line staff aware of appropriate management. VTE management for COVID patients remains an evolving and topical area.

BSH24-EP137 | A review of hospital-associated thrombosis with a shared learning dashboard

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Background: Hospital associated thrombosis (HAT) is defined as any new venous thromboembolism (VTE) event diagnosed during hospital admission or within 90 days of discharge. VTE is one of the leading causes of preventable hospital-associated morbidity and mortality. It is important to identify HATs, which can be a multifactorial process, and perform root cause analysis (RCA) investigation to identify if HAT was potentially preventable, identify contributory factors/any themes, implement actions, and share learning for education and awareness to prevent recurrence.
Aim: To review reported HATs and identify if HATs potentially preventable, themes and contributory factors.
Methods: HATs were identified by local incident reporting system. HAT RCA investigation, using a template proforma, performed to assess VTE risk assessment completion, pharmacological and mechanical thromboprophylaxis prescribing for patients at risk of VTE during admission and/or on discharge (if indicated and no contraindications), and commentary. RCA establishes if the HAT is potentially preventable, identify any contributory factors and implement actions to help prevent recurrence. RCA form is reviewed by VTE leads for quality assurance, and challenge where appropriate.
Results: Twenty-seven HATs reported from April to November 2023 across two hospital sites, within:

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- Medicine: 37% ($n = 10/27$).
- Surgery: 48% ($n = 13/27$).
- Maternity and Gynaecology: 15% ($n = 4/27$).

Eighteen HATs with completed RCA investigations were not potentially preventable. 33% HATs ($n = 9/27$) pending review. *Common themes*:

- Appropriate thromboprophylaxis prescribed and administered with no missed doses.
- Incorrect thromboprophylaxis prescribing in renal impairment patients (outcome not affected as dose subsequently reviewed).
- No written/verbal VTE information offered to patient prior to discharge.

A HAT dashboard, disseminated quarterly, was developed to provide feedback and shared learning on themes, contributory factors, education and awareness with helpful tips and signposting to local guidance, with an aim to prevent recurrence and reduce risk of potential unavoidable harm.

Conclusion: 60% of all VTEs are related to hospital admission. There is no programme to help reduce HATs globally. VTE risk assessment is an important role to guide use of appropriate thromboprophylaxis to help save lives, reduce morbidity, and reduce costs of acute and long-term VTE effects to healthcare systems. It is important patients are involved and educated so aware of VTE signs and symptoms and when to seek urgent medical attention. A robust process is required to identify and report HATs for RCA investigation. Sharing the learning from HATs in a dashboard provided feedback on contributory factors, key messages and actions to ensure patient safety.

BSH24-EP138 | Von Willebrand's disease and gastrointestinal angiodysplasia: A case series from a haemostasis and thrombosis centre

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Background: Gastrointestinal angiodysplasia is seen in patients with normal haemostasis and is estimated to be the cause of 10% of cases of GI bleeding. It is also associated with GI bleeding in patients with both inherited and acquired forms of von Willebrand's disease (VWD). Within the literature it is more commonly associated with the loss of high molecular weight multimers seen in type 2 and type 3 VWD.

Aims: To review the outcomes in our von Willebrand disease patient cohort who have gastrointestinal bleeding associated with angiodysplasia.

Methods: Data from patients with VWD and gastrointestinal angiodysplasia from our centre were retrospectively reviewed.

Results: Five patients were identified who had concurrent VWD and gastrointestinal angiodysplasia. Two patients both of whom were over 70 years old with no prior bleeding diathesis were referred to our centre's gastroenterology team for recurrent GI bleeding in order to perform more detailed examination of the small bowel via endoscopic methods such as capsule endoscopy and push enteroscopy techniques, as conventional endoscopic methods and imaging had not identified bleeding points. During these procedures angiodysplastic lesions were identified within the gastrointestinal tract which prompted retrospective reviews of the patient's clotting screens leading to a diagnosis of acquired VWD in both patients. The remaining three patients had a pre-existing diagnosis of inherited VWD with recurrent GI bleeding secondary to angiodysplasia; these patients had severe anaemia requiring multiple transfusions, use of factor concentrate and recurrent intravenous iron infusions. Capsule endoscopy and push enteroscopy, in particular double balloon enteroscopy (DBE) were used to diagnose and treat lesions which were not seen on oesphagoduodenogastroscopy (OGD). Treatment of the lesions endoscopically led to prolonged periods (months-years) without further bleeding events.

Summary: Patients 1 and 2 demonstrate that clinicians should have a high index of suspicion of acquired VWD in patients presenting with GI bleeding associated with angiodysplasia and it should prompt a review of haemostatic parameters. Patients 3,4 and 5 demonstrate that the use of endoscopic techniques such as capsule endoscopy and push enteroscopy techniques such as DBE are effective in diagnosing and treating angiodysplastic lesions. Therefore, we recommend referring to a centre experienced in these endoscopic techniques for patients with VWD and recurrent GI bleeding. Interestingly, despite the evidence in the literature, we have not seen angiodysplasia in any of our type 3 VWD cohort which likely reflects the complex role of von Willebrand factor in angiogenesis.

BSH24-EP139 | Root cause analyses of deaths associated with hospital-acquired venous thromboses over twelve months

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Through retrospective analysis, we found that 34 out of 89 patients who died of venous thromboembolism (VTE) between October 2021 and October 2022 in the Torbay region

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had experienced a hospital-acquired thrombosis (HAT), which contributed to their death, according to their Medical Certificate of Cause of Death.

Out of the 34 HAT-related deaths, 17 of them received appropriate and satisfactory VTE diagnosis and management, with some having deteriorated due to comorbidities. We found some areas to improve in the other 17—related to VTE assessment and preventative measures.

This included undocumented missed doses of anticoagulation, patient refusal of anticoagulation, and decisions to hold or stop anticoagulation due to bleeding risk. The gaps in thromboprophylaxis might have contributed to adverse outcomes and HAT-related death.

We identified four cases not fitting standard criteria for decision-making, such as an underweight patient, a bleeding patient, an inconclusive CT pulmonary angiogram (CTPA), and a case where CTPA was not performed due to pre-existing evidence of pneumonia.

These cases have raised questions about guideline consensus and individualised treatment. They also raised discussions around pre-test probabilities for ruling in or out VTE, scoring systems' role in aiding decision-making in these complex scenarios, and the high pulmonary embolism number-needed-to-test values that CTPAs yield.

Alternate treatment modalities for VTE were discussed briefly, including the roles of Inferior Vena Cava (IVC) filters, thrombolysis, and heparin infusions.

We highlight the importance of thorough and clear documentation in complex cases, especially when decisions diverge from the standard VTE guidelines. We emphasise the lack of guidelines for borderline cases and the need for better consensus in the medical community—which may be facilitated through means such as, but not limited to, discussions of complex cases in Morbidity and Mortality meetings or educational seminars for junior doctors.

BSH24-EP140 | Evaluation of D-dimer cut-off levels for VTE diagnosis in a tertiary centre

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Introduction: Venous thromboembolism (VTE) requires prompt and accurate diagnosis, with D-dimer serving as a key biomarker. Challenges in applying universal D-dimer cut-offs include varied baseline levels and a lack of standardised measurement methods. Implementing age-adjusted cut-offs has improved diagnostic accuracy and reduced false positives, particularly in emergency settings.

Objectives: This study aims to evaluate the effectiveness of a higher D-dimer cut-off (>500 ng/mL) versus the standard (>250 ng/mL) in diagnosing VTE, and explores the potential of age adjustment in determining optimal cut-off values. It also assesses the safety and sensitivity of the higher proposed cut-off.

Methodology: Retrospective study from the Queen Elizabeth Hospital's laboratory and electronic records provided data over a three-month period in 2019. All D-dimer tests conducted during this timeframe were included. Variables such as patient ID, lab number, D-dimer level, date, VTE scan result, scanned status, and age were collected. The HemosIL D-dimer assays on the IL coagulation system, known for their high sensitivity and specificity, were used.

Data Analysis: 1532 cases were evaluated for the diagnostic efficacy of D-dimer in VTE. Of these, 580 cases had D-dimer levels above 500 ng/mL, and 427 in the 250–500 ng/mL range. Notably, 66% of patients were aged 50–100 years. In the 250–500 ng/mL group, 15 patients (3.5%) were diagnosed with VTE. 12/15 (2.8%) had VTE near the D-dimer test date. Of these, 3 (1%) had a low Well's score (<4). Additionally, 37.4% of patients in the >250 ng/mL range were not scanned, highlighting potential diagnostic gaps.

Age-adjusted analysis with a 5× multiplier for those over 50 years identified only one patient beyond the threshold.

Limitations: Conducted at a single tertiary centre, the study's findings may have limited generalisability. The brief duration of the study and variability in Well's score documentation are noted limitations. Additionally, not all potential confounding factors were accounted for in the analysis.

Conclusion: The study confirmed the presence of VTE in patients with D-dimer levels below 500 ng/mL, emphasising the need for a balanced approach to VTE diagnosis and recommending against a uniform rise in the D-dimer cut-off. Implementing age-adjusted cut-offs, particularly for those over 50 years significantly reduced false positives. However, caution is advised due to the potential of missing genuine VTE cases, advocating for a tailored approach based on age and clinical context. Further research is encouraged to validate these findings and explore integrating Well's score with age-adjusted D-dimer in older patients.

BSH24-EP141 | Time-in-therapeutic range (TTR) falls as the target INR range increases in patients on warfarin

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Background and Aims: The time-in-therapeutic range (TTR) is important for predicting the efficacy and safety of anticoagulation with warfarin. National guidelines for anticoagulation in patients with atrial fibrillation consider TTR <65% to indicate poor control. External quality assurance (EQA) surveys show an increased distribution size in participant reported INRs and a much higher percentage of participants who are out with consensus, when the sample INR is above 3.0. This is consistent with the INR performing less well at higher values. We hypothesized that the TTR

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would be lower in patients with higher target INR ranges, independently of the indication for anticoagulation. Our aim is to assess whether TTR changed as a function of INR range.

Methods: The cohort consisted of 6592 patients anticoagulated with warfarin for at least 6months in a single NHS trust between 1996 and 2022. The overall TTR and indication were extracted from DAWN AC anticoagulation software. The TTR reported by DAWN was for the whole of the period that the patient was monitored excluding interruptions, for example for surgery. Patients were grouped into INR ranges 1.5–2.5, 2.0–3.0, 2.5–3.5, 3.0–4.0. We calculated the mean TTR for all patients in the group and the standard error of the mean. We also assessed the group with target INR 3.0–4.5 although this group cannot be directly compared with the others because of the greater interval.

Results: The duration of anticoagulation monitoring in DAWN ranged from 0.5 to 26 years, with a mean length of treatment of 37 months.

For *N* patients in INR range 1.5–2.5 *N* = 89 Average TTR = 68% (SEM 1.9); INR range 2.0–3.0 *N* = 5738 Average TTR = 64% (SEM 0.2); INR range 2.5–3.5 *N* = 405 Average TTR = 56% (SEM 0.8); INR range 3.0–4.0 *N* = 92 Average TTR = 54% (SEM 1.7); INR range 3.0–4.5 *N* = 268 Average TTR = 61% (SEM 1.3); Total *N* = 6592 Average TTR = 61% SEM (0.2).

We found that the mean TTR is lower in patient groups with higher target INR ranges. This correlation remained when patients with the same indication, for example recurrent venous thromboembolism, were compared over different target INR ranges.

Conclusion: In the groups with a target INR interval of 1.0 the mean TTR decreased as the target INR range increased. This suggests that the INR may be less accurate at higher values. Further study is required to determine whether this correlates with clinical outcomes.

BSH24-EP142 | Variation of monitoring for vitamin K antagonist in antiphospholipid syndrome (APS)

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Background: Patients with antiphospholipid syndrome (APS) are treated with Vitamin K antagonists with regular INR monitoring (1). Though point of care (POC) INR monitoring is less reliable yet convenient, correlation between POC INR and venous INR needs attention. To address this, we recruited all patients registered with APS and compared POC and venous INRs at Whipps Cross Hospital (WXH).

Objective:

- To ascertain the discordance of POC versus venous INR in patients with APS and estimate the percent difference in venous and capillary results.
- To establish the antibodies present and their association with venous INR results.

Methods: Total of 35 patients were recruited from the electronic health records of registered patients at WXH. Retrospective data collection from an audit was used from March 2023 to July 2023. Complete dataset of 19 participants was recorded. Average difference in venous versus capillary INR was noted and difference in co-efficient was assessed in patients with INR of <4 and ≥4.

Results: Out of the 19 cases, about half of the patients (47%) had an average difference of more than 20%, whilst 42% had discordance between 10% and 20%, though about 10% cases only had discordance less than 10% for POC and venous sample. Frequency of triple antibodies were in direct correlation with increased difference of POC and venous INR, where five of the nine cases were triple antibody positive. Of the remaining four cases, two cases did not have full antibody screen in the dataset and so may be under reported. In case of discordance of 10%–20% between INR values, only one patient had triple antibody presence, while remaining seven cases had only single antibody present. In terms of the co-efficient difference between POC and venous INR, correlation was more considerable with INR values above 4.

Discussion: Systematic variation exists in APS which requires venous INR monitoring, with correlation of POC and conventional INR testing. (1) Counselling of patients at initiation of therapy for variation in coefficient <0.5 is acceptable by BSH. (2) Regular venous INR checks and individualised choices of anticoagulation may also be considered. (3) Correlation with triple antibody is an alternative explanation for variation in INRs and emphasis of regular venous sample review.

Conclusion: Patients with APS could be managed with POC INRs in selected patients, but venous INRs biannually to annually will help to avoid thrombotic events, improving morbidity. Further larger datasets are needed for regional and national representation.

BSH24-EP143 | Venous thromboembolic events in a Scottish District General Hospital: Variation in management and significant recurrence

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Forth Valley Royal Hospital is a District General Hospital in Scotland. An Advanced Nurse Practitioner (ANP) led Rapid Access Care Unit (RACU) opened in 2022. Guidelines for assessment and management of deep vein thrombosis (DVT) were created by the acute medical team and haematology. No dedicated service currently exists for follow up of unprovoked venous thromboembolism (VTE). Decisions regarding duration of anticoagulation in VTE can be complex and take into account the presence of provoking factors,

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as well as the risk of recurrent VTE balanced with the risk of bleeding.

This retrospective study assessed the frequency of patients diagnosed with VTE in RACU, reviewed treatment plans and communication of anticoagulation decisions to general practice. This information will be used to create a dedicated document proforma and amend guidelines.

Patient records were identified through diagnosis coded on the discharge letter for a period from 1st September 2022 to 30th November 2022. A total of 175 patients were identified. Electronic records were reviewed and excluded if there was no VTE ($n = 102$), event was Superficial Thrombophlebitis ($n = 17$) or review was deemed unsuitable ($n = 1$). Information was collected on age at event, type of event, documentation of provoking factors, recommendation on duration of anticoagulation on discharge letter, ongoing anticoagulation and history of prior VTE or subsequent recurrence.

Fifty-five patient records were identified, 42% female ($n = 23$) and 58% male ($n = 32$). Median age was 60 years (range 21–92 years). 22% ($n = 12$) were recorded as provoked events, 27% ($n = 15$) as unprovoked and 51% ($n = 28$) were not explicitly specified. Ninety-six percent ($n = 53$) contained recommendation for duration of anticoagulation. There was considerable variation in recommendations for anticoagulation, regardless of categorisation as provoked, unprovoked or not specified. Continued prescription of anticoagulation was identified in 53% ($n = 29$), and of these 51% ($n = 18$) had anticoagulation as recommended in the discharge letter. In 40% ($n = 22$) there was history of prior VTE and 7% ($n = 4$) had a recurrent event between diagnosis and data collection. 60% of males >50 years old with unprovoked or unspecified clot presented with a recurrent event or had a subsequent recurrent event.

In conclusion our data shows that our service clearly documents and communicates anticoagulation decisions, albeit with variation in these recommendations. Furthermore, our data highlights a significant frequency of recurrence in our small data cohort. This finding supports development of services to ensure consistency of advice, documentation and informed long term anticoagulation decision making.

BSH24-EP144 | Peak levels of Von Willebrand activity after loading dose of Veyvondi at Manchester Royal Infirmary

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Von Willebrand disease is the most common inherited bleeding disorder. A genetic defect in the Von Willebrand factor causes Von Willebrand disease. Von Willebrand factor plays a pivotal role in Haemostasis helping in platelet aggregation and as a carrier molecule for factor 8. Veyvondi is a recombinant form of the Von Willebrand Factor. Veyvondi has fewer side effects as compared to plasma-derived factor products.

Method: we analysed data from 25 patients Registered with the Haemophilia Centre of Manchester Royal Infirmary Hospital. The primary Aim was to evaluate the rise in Von Willebrand activity after a loading dose of veyvondi based on their body weight and baseline levels.

Among 25 patients 12 (48%) Patients were males, 13 (52%) were females 0.10 patients (40%) were in the age group 20–30 years, 4 patients each (16%) in 30–40 and 40–50 and 3 patients (12%) in age Group 50–60 and 60–70 years. Twelve (48%) patients were Type 1, 5 (20%) Type 2, 6 (24%) Type 3 and 2 (8%) acquired vWB.

Results: Seventeen (68%) patients showed a rise of >100% from baseline levels, 6 (24%) patients had an increase of between 50% and 100% and 2 (8%) patients levels incremented to less than 50%.

These results showed the variability in Von Willebrand activity Peak levels after a Loading dose of Veyvondi. These results suggest that there are factors that might influence the rise in the Von Willebrand activity levels and even with the same product the rise in peak Von Willebrand activity is variable among different patients.

BSH24-EP145 | Magnetic Nanoparticles: the Possibility of Applications in the Technology of Purification of Factor VIII Coagulation

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Background: Isolation, separation and purification of various types of proteins and peptides, especially factor of coagulation, is widely used in biotechnology and medic science. Nanotechnology is one of the most important researches in modern biotechnology.

Magnetic nanoparticles (MNPs) are a special class of nanoparticles that can be controlled using a magnetic field. Such particles usually consist of two components: a magnetic core (iron, nickel or cobalt) and a chemical shell (starch, dextran, silica gel, biomolecules, etc.) that can be designed to obtain affinity to target molecules. By choosing an appropriate method of synthesis and fractionation, the size, shape, surface coverage, and colloidal stability of MNPs can be controlled. The combination of the rich possibilities of chemical shell and the ability to respond to the external magnetic field and makes magnetic materials universal tool for magnetic separations of various types of proteins.

Aim: to investigate the possibility of using MNPs in the technology of isolation and purification of blood coagulation factor VIII (FVIII).

Materials and Methods: In the work were studied: Nanomag-COOH-500; Nanomag-PEG-COOH-300; Nanomag-NH2-250; Nanomag-NH2-130; Nanomag-NH2-80; Nanomag-OH-250. The activity of factors VIII was determined using one-stage clotting methods. For

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fractionation of MNPs a tripod with a constant field neodymium magnet (0.24 T; Sphere Sim, Lviv) was used.

Results: A study of the influence of MNPs on FVIII activity was conducted. The initial concentration of FVIII was 1.0 IU/mL. FVIII activity was determined: (1) after 15 min of incubation and (2) after separation of MNPs on a permanent neodymium magnet (24 h).

The following results were obtained:

The activity of FVIII was established: Nanomag -COOH-500 nm: after 15 min – 1.0 IU/mL, after separation on a permanent neodymium magnet – 1.0 IU/mL; Nanomag -PEG-COOH-300 nm: after 15 min – 1.45 IU/mL, after magnet action – 0.6 IU/mL; Nanomag-NH2-250 nm: after 15 min – 0.5 IU/mL, after the action of the magnet – 0.5 IU/mL; Nanomag-NH2-130 nm: after 15 min – 1.45 IU/mL, after the magnet – 1.0 IU/mL; Nanomag-NH2-80 nm: after 15 min – 1.7 IU/mL, after the magnet – 0.5 IU/mL; Nanomag-OR-250 nm: after 15 min – 1.0 IU/mL, after the magnet – 0.45 IU/mL.

Conclusions: It was established that the activity in the FVIII solution was reduced by two times after the action of the magnet using the following MNPs: Nanomag-PEG-COOH-300; Nanomag-NH2-250; Nanomag-NH2-80 and Nanomag-OH-250.

Keywords: nanotechnology; magnetic nanoparticles (MNPs); factor VIII coagulation (FVIII).

BSH24-EP146 | Audit of comprehensive care of haemophilia B against World Federation of Haemophilia guidelines

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Introduction: *Aim*: To assess the care of haemophilia B at a Comprehensive Care Haemophilia Centre against international guidelines (1).

Methods: A proforma and standards were compiled. A stratified sample was selected, using a random number generator, from the National Haemophilia Database. Data were collected from electronic records following local audit registration.

Results: Fifty-six patients with haemophilia B were identified. Data collection included 19 patients: 7 mild, 5 moderate, 5 severe and 2 carriers from 2018 to 2023.

Prophylaxis: Hundred percent of patients with severe haemophilia B were on prophylaxis. 5/5 switched prophylaxis from standard to extended half-life products (Alprolix, Refixia or Idelvion) due to breakthrough bleeds (4/5) or compliance (1/5). The mean annual bleed rate was 2.2 in 2019, and 0.4 in 2023, comparable with trial data (2).

Three out of five patients with moderate haemophilia had joint bleeds: One out of three was on prophylaxis.

Annual Haematology Assessments: Seventeen out of nineteen patients were under active follow up. Two others were regularly uncontactable, and another declined follow up.

There was evidence of shared decision making in 12/14 patient records.

Ten out of twelve patients under 50 years had genetic counselling. There was evidence of ongoing patient education and comorbidity management in 12/14 patients.

All 14 patients were offered dental care.

Four out of fourteen had promotion of physical activity and 0/14 were encouraged to have adequate calcium and vitamin D intake. One out of fourteen patients had annual blood pressure assessments.

Zero out of five patients with chronic musculoskeletal pain or functional limitations had support networks recommended.

Carriers of Haemophilia with Low Levels: Factor levels were measured prior to procedures or pregnancy. 2/2 received genetic counselling and had a factor IX level assayed in the third trimester.

Recommendations: Areas of strength include use of extended half-life products with high trough levels and a trend towards a reduction in the bleed rate. Excellent evidence of shared decision-making, genetic counselling and dental care.

- Resume follow up for historical discharges.
- Consider prophylaxis with recombinant FIX in moderate haemophilia B with joint bleeds.
- Inhibitor screens with a Bethesda assay (versus mixing studies).
- Written information regarding physical activity, vitamin D, calcium intake and peer support.
- Annual blood pressure measurement.

We will discuss these action points within our audit and multidisciplinary team meetings and then close the audit loop. Audits such as this may assist preparation for peer review and improve the standard of care offered.

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BSH24-EP147 | Antiphospholipid syndrome vasculopathy with severe aortic stenosis

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Antiphospholipid syndrome (APS) is an autoimmune disorder characterised by recurrent thrombosis and/or pregnancy morbidity in the presence of persistently positive antiphospholipid antibodies. Arterial stenotic lesions are well described in APS manifesting as vasculopathy, this can be seen in the renal, cerebral, coeliac, and superior mesenteric arteries. The pathophysiology is poorly understood but could be secondary to endothelial activation and proliferation leading to vessel stenosis. We describe a case series of two patients

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with severe symptomatic infra-renal aortic stenosis associated with APS antibodies.

A 56-year-old previously fit and well, non-smoker gentleman presented with two episodes of deep venous thrombosis (DVT) in 2011 and was put-on long-term Warfarin. APS was diagnosed based on persistently positive IgG anticardiolipin antibodies and borderline positive anti beta 2 glycoprotein antibodies. Around the same time, he was diagnosed with mixed connective tissue disease and cutaneous lupus. Two years later, he was switched to Rivaroxaban and no further thrombotic events were described. Warfarin was recommended again in 2020, however the patient declined. In 2021, he developed bilateral thigh wasting and weakness associated with intermittent claudication. CT abdominal angiogram showed severe focal stenosis at the infrarenal aorta and coeliac axis. Repeat antiphospholipid screen showed a strongly positive lupus anticoagulant, IgG anticardiolipin antibodies and negative anti-B2GP1 antibodies. Surgery was considered risky, and the patient was treated with a combination of Warfarin (target INR 2.5) and Aspirin 75 mg. Symptoms have improved a little over time.

A 25-year-old previously fit and well non-smoker lady presented with a 1-year history of progressive bilateral intermittent claudication with weak femoral pulses on examination and was subsequently started on Clopidogrel. CT abdominal angiogram showed severe infrarenal aortic stenosis with short occlusion and multiple collaterals. She had mild thrombocytopenia with a platelet nadir of 116×10^9/L. She had a history of one uneventful pregnancy with no neonatal or postpartum complications. Lupus anticoagulant was negative, but IgG anti-cardiolipin antibodies and anti-beta 2 glycoprotein antibodies were strongly positive. Clopidogrel was substituted with Aspirin and Warfarin, however, she developed significant menorrhagia requiring interruption of Aspirin and insertion of Mirena coil. Symptoms are currently stable.

Infrarenal aortic stenosis is an extremely rare manifestation of APS vasculopathy with only one publication in the literature in a heavy smoker population group. Surgery or endovascular intervention would risk renal arterial supply and represent a very high risk of complications. We have used Warfarin and Aspirin combination as a non-invasive medical line of therapy.

BSH24-EP148 | Investigating the utility and clinical relevance of thrombin time

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Background: Thrombin time (TT) is a measure of the time taken for fibrin to form following addition of external thrombin to a platelet depleted sample of plasma. Prothrombin time (PT) and activated partial thromboplastin time (APTT) are tests with an identical endpoint of fibrin formation but differ by their starting points in the coagulation cascade. TT is a better indicator of fibrinogen abnormalities due to its occurrence later in the cascade; however, many hospitals no longer perform this test routinely in a standard clotting screen. Instead, it is left to the clinician's discretion to order a further specific fibrinogen assay.

Primary Aim: To investigate how many TTs are simultaneously prolonged with APTT and/or PT in a hospital that still routinely performs the test; to find isolated prolonged TTs and investigate how many were further followed up.

Secondary Aim: To investigate the cost incurred to the trust due to these tests.

Methods: A sample of 517 clotting screens with prolonged TTs during the month of October 2023 from the Kettering General Hospital biochemistry database were studied. Patients using factor II inhibitors, warfarin and unfractionated heparin were excluded. Clotting screens with incomplete data were also excluded. The incidence rates of prolonged APTT and/or PT were calculated.

Results: From a final sample of 509 TT tests, 240 tests (47%) had prolonged APTT and/or PT and 269 tests (53%) had isolated prolonged TTs. The majority of the isolated TTs were within the less significantly raised TT ranges. Seventy-four percent of clotting screens within TT ranges of 19–19.9 s were isolated raised TT results, and 60% of screens within the 20–20.9 s range were isolated results. Furthermore, 52% of clotting screens within the 21–21.9 s ranges were isolated results and 25% of screens within the 22–22.9 s range were isolated results. With more significantly raised TT ranges of 23–23.9, 24–24.9 s and >25 s, 5%, 36% and 10% of screens were isolated raised TT results. From a preliminary subset of 124 isolated TT results, 92% of these were not further followed up.

The cost of the TT test has been requested and will be applied for further cost analysis. A subset sample of isolated prolonged TTs has been generated and the incidence rates of a further fibrinogen test or haematology team knowledge will be calculated.

BSH24-EP149 | Managing pelvic intraperitoneal bleed secondary to ovulation in adolescents with congenital bleeding disorders

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Massive hemoperitoneum due to ovulation is a rare but serious and life-threatening complication for women with coagulation disorders. The rupture of the corpus luteum may occur at all stages of a woman's reproductive life and the bleeding varies from self-limiting haemorrhage to massive hemoperitoneum, causing shock and subsequent emergency surgery. We describe three patients presenting with hemoperitoneum in association with factor V deficiency, Severe Type 1 Von Willebrand Disease and Factor VII deficiency.

The management and prevention of Corpus luteum bleed is based on anecdotal information from case reports, given the

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rarity of these events. Conservative management is crucial for these patients. If surgery cannot be avoided, a conservative surgical approach should be chosen to preserve ovarian function. Prevention of recurrence is desirable to avoid life-threatening bleeds, to preserve fertility and to avoid the potential morbidity caused by loss of ovarian function. Oral contraceptives have shown to be beneficial in avoiding first ovulatory as well recurrent ovulatory bleed. However, this may not be possible in most cases. In this case series, in two of three patients, ovulatory bleeding occurred prior to introduction of an oral contraceptive pill. Conservative management with blood products and factor concentrates support was successful in avoiding surgery in all cases except one, where an explorative laparotomy had to be performed to rule out torsion of an ovary.

Optimum management of corpus luteal bleeding and haemorrhage is more likely to be achieved if knowledge of bleeding issues during ovulation are more widely known and appropriate interventions are instituted in a timely fashion. The role of patient education and engagement is paramount. Further, a close collaboration between haematologists and obstetricians or gynaecologists is prudent towards a favourable outcome. Preservation of ovarian function is possible with a conservative approach and recurrent episodes may be prevented by suppression of ovulation.

BSH24-EP152 | Cost-efficiency of home treatment/early discharge low risk patients with pulmonary embolism in a low-income country

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Introduction: Pulmonary embolism (PE) is the most serious clinical presentation of venous thromboembolism, which patients have been traditionally treated in hospital. Nowadays, as many of them are at low risk of early death, there is sufficient evidence supporting early discharge and outpatient treatment as option if correctly identified patients. One of many advantages includes reduced risk of in hospital complications and cost savings.

Methods: It is a descriptive, single-centre study that included patients admitted from January 2020 to December 2022 to the emergency department of PHI Institute of Cardiology with a diagnosis of PE. Patients were retrospectively assessed by using the Pulmonary Embolism Severity Index (PESI) or simplified PESI (sPESI), HESTIA criteria and the risk of early death using 2018 European Society of Cardiology (ESC) guidelines. The study was performed only on low risk patients (PESI class I/II). Therefore, three groups were created: Group1—none HESTIA criteria and low risk of early death (elective for home treatment)—Group2—none HESTIA criteria and intermediate-low risk of early death (elective for early discharge)—and Group 3—HESTIA criteria ≥1 independent of the early death risk and patient with intermediate-high and high risk independent of HESTIA criteria. Control costs were obtained using the clinical costing system SIAAMS and the costs catalogue of medical services (updated Government decision No. 1020 from 29-12-2011, 1leu = €0.05). For statistical analysis of data was used the SPSS software (version 12, USA).

Results: From 193 patients diagnosed with PE, were selected 81 patient with PESI class I and II. Group 1 included 24 patients (30%) with a mean length stay of 7.9 ± 0.46 days, a median cost of hospitalisation of 9219 lei (interquartile range [IQR]: 7094) and median control costs for outpatient treatment of 7082 lei. Group 2 included 18 patients (23%) which were suitable for early discharge (after 72 h), with a mean length of stay 9.65 ± 0.76 days. The median cost per hospitalisation was 12 080 lei (IQR: 4131) with a minimum of 10 960 lei and a maximum of 18 851 lei, the median recommended control cost was 10 117 lei (IQR: 1702). Thirty-eight patients (47%) were assigned in the group 3, with a mean length of stay 9.02 ± 0.45 and a median cost per hospitalisation of 13 093 lei (IQR: 3900).

Conclusions: Home treatment and early discharge of uncomplicated EP provides effective cost minimization with an estimated cost reduction of 2137 lei per patient for home treatment and 1963 lei for early discharged. This difference underlines the advantage of triage-based home treatment and early discharge of EP low risk patients.

BSH24-EP153 | Healthcare resource utilisation of patients with VWD treated with recombinant Von Willebrand factor: Chart review

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Background: There is a paucity of real-world evidence (RWE) that describes healthcare resource utilisation (HRU) of patients with von Willebrand disease (VWD) who are treated with recombinant von Willebrand factor (rVWF; vonicog alfa).

Aims: To assess HRU in patients with VWD treated with rVWF on demand (OD) or in the prevention and/or treatment of bleeds during surgery.

Methods: A retrospective chart review study was conducted on adults (≥18 years) with congenital VWD from seven UK hospitals. Eligible patients must have received rVWF OD

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to treat ≥1 spontaneous/traumatic bleeds and/or to prevent/treat surgery-related bleeding (date of first rVWF dose [index]: 01/10/2020–30/06/2022). Patients were excluded if they had other bleeding disorders or factor deficiency (including acquired von Willebrand syndrome), VWF neutralising antibodies/inhibitors, or participation in clinical trials during the study period. Those receiving intermittent/long-term VWF-prophylaxis during the study period were eligible for inclusion but have been excluded from this analysis. Data were collected from medical records at index treatment, and 12 months pre- and post-index treatment. VWD-related HRU data included admissions for inpatient and outpatient visits, admission to intensive care (ICU), and length of stay (inpatient and ICU). Patient informed consent and ethical approval was obtained.

Results: The analysis sample totalled 32 patients, 22 (68.8%) were female, with a mean (±SD) age of 48.3 ± 19.5 years. The majority of patients had type 1 ($n = 9$) or type 2 ($n = 21$) VWD. At index, 12 patients were treated with rVWF for spontaneous/traumatic bleeds and 20 patients for surgery. Inpatient and/or outpatient attendances were required by 91.7% of patients treated OD for spontaneous/traumatic bleeds; six (50.0%) had an inpatient attendance, with a mean length of stay of 3.3 days (±1.0), and five (41.7%) patients had an outpatient visit. For surgery-related treatment, 14 (70.0%) patients had an inpatient stay, two of which were admitted to ICU; five (25.0%) patients had an outpatient appointment; and one (5.0%) patient had an inpatient and outpatient attendance. The mean length of stay was 8.2 days (±10.3) for inpatient attendances with 4.5 additional days (±2.1) for those admitted to ICU.

Conclusions: The results presented here are, to our knowledge, the first to report RWE of HRU in UK patients with VWD treated OD to treat spontaneous/traumatic bleeds or to prevent/treat surgical bleeds. More research is required to assess HRU in patients with VWD across treatment centres both within and outside of the UK.

The study was funded by Takeda UK.

BSH24-EP154 | A 13-month audit on adherence and outcomes of bridging therapy at a UK tertiary centre

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Objectives and Study: Determining the adherence of Guy's and St Thomas Hospitals' (GSTT) to the recently published British Society of Haematology (BSH) guidelines on Low Molecular Weight Heparin (LMWH) bridging therapy. Secondary aims involve identifying the number of bleeding and thrombotic complications that occurred perioperatively.

Methods: Review of Electronic Patient Records (EPR) for all patients on long-term warfarin undergoing elective invasive procedures requiring LMWH bridging at GSTT between 01/11/21 and 01/12/22.

Results: Forty-two patients with a mean age of 60.2 ± 12.8 years (35.0–83.0) and a mean BMI of 29.3 ± 7.2 (16.5–43.0). 45.2% were male and 69.0% were white. Comorbidities were recorded in 95% of patients, other 5% only had a mechanical heart valve. All patients had a target INR range between 1.5 and 4.0 (59.5% target INR 2.0–3.0). 54.8% of the procedures had a high bleeding risk. 47.6% patients had a high or very high thrombotic risk. The bridging plan was adhered to in 95.2% of patients. Bleeding complications occurred in 14.3% of patients, 50% of these being major bleeds. Thrombotic complications occurred in 7.1% of patients with 33.3% being arterial thrombotic events. Overall, 19.0% of patients had perioperative complications, with 2.4% patients suffering from both bleeding and thrombotic complications.

Conclusion: 100% of patients were given an appropriate bridging plan. The high bleeding complication rate was likely due to the high percentage of high bleed risk procedures. The high thrombotic complication rate was likely due to the cohort's high thrombotic risk. The audit allowed assessment of collecting necessary data; monitoring compliance with newly published BSH guidelines and provided insight into bridging therapy outcomes.

BSH24-EP155 | The consequences of delayed diagnosis of pulmonary embolism, a comparative study

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Background: Although pulmonary thromboembolism (PE) is usually considered as an acute illness, delayed presentations are fairly common. Moreover, the incidence and the outcomes of PE missed during emergency department (ED) workup are largely unknown.

Objectives: This study aims to investigate delays to presentation/diagnosis, to describe the frequency, demographics, their likely correlation with patients' clinical and radiographic findings and outcomes of patients with delayed diagnosis of PE.

Methods: All cases of PE diagnosed in our hospital between January 2020 and December 2022 were reviewed for the date of symptom onset, the dates of presentation and diagnosis, clinical findings, localization of embolism in pulmonary vascular tree and pleuropulmonary changes. We compared patients diagnosed with PE during ED workup (early diagnosis) with patients diagnosed with PE thereafter (delayed diagnosis). The parameters related to presentation delays were analysed using U test and logistic regression analysis.

Results: Of the 168 patients enrolled, 30.4% presented to hospital 1 week after the start of their symptoms. The onset of symptoms suggestive of PE was on average 10.5 ± 11.4 days' (median 4 days) before hospitalisation, ranging from 1 to 45 days, and about 1/3 of the patients surveyed visited at least one medical institution

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(15%—2 to 3 institutions) prior to hospitalisation. The delay from presentation to diagnosis was 1.9 ± 1.4 days (median 0, range 0–16). Median age of patients with early diagnosis was significantly lower as compared to delayed diagnosis (65 vs. 78.3 years). Main symptoms were dyspnea (70 patients [60%] in early, 22 patients [45%] in delayed diagnosis), chest pain (60 patients [50.1%] in early, 9 patients [18.2%] in delayed diagnosis), and nonspecific complaints (11 patients [9.1%] in early, 15 patients [29.9%] in delayed diagnosis). Patients with hypotension, respiratory rate >20 and atelectasis in CT presented earlier. However, no correlation was found between delays and the level of thromboembolic occlusion in pulmonary artery. In-hospital mortality was 4.6% in early diagnosis and 33.8% in delayed diagnosis.

Conclusion: Pulmonary thromboembolism should be considered not only in an acute setting, but also in patients with prolonged respiratory symptoms, since there was a significant delay to presentation among our patients. Delayed diagnosis of PE carries a worse prognosis than early diagnosis. This discrepancy may arise from either delayed therapy, confounding variables or both. The presence of hypotension and a tachypnea was clearly associated with early presentation. Possible reasons for delayed diagnoses are nonspecific presentations and symptoms overlapping with preexisting conditions.

BSH24-EP156 | Prospective data collection project to facilitate audit in the nurse-led DVT service

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Objective: Practice in the nurse-led ambulatory Deep Vein Thrombosis (DVT) service has evolved over time in response to both local organisational developments and changes in national guidance on the management of Venous Thromboembolism (VTE) (NICE 2020). The DVT service are keen to engage in quality improvement work and audit of changing practice but have recognised several barriers to retrospective data collection and analysis in the way clinical data is currently recorded, necessitating laborious manual searching for additional data. The need has therefore been identified to review data recording processes to facilitate audit and service development going forward.

Method: A project committee with interest in audit was established comprising of a Thrombosis and Haemostasis Consultant, Anticoagulation Pharmacist, Thrombosis Research Nurse and Lead DVT Clinical Nurse Specialist. The goals of the project were stated as creation of a new database for prospective clinical data collection for patients seen in the nurse-led DVT service, to allow efficient recording and retrieval of data and to facilitate future audit of a variety of aspects of care and clinical outcomes. The committee agreed a regular meeting schedule to review progress and have outlined the essential parameters for capture on the database, including demographic data, venous thrombotic event details, results of screening and investigations and patient outcomes. Technological support has been sought from appropriate specialists in other departments to assist with database design and set up.

Evaluation: This project is ongoing and the aim is for data collection to begin in 2024. The project committee will continue to meet regularly and evaluate and refine the database to ensure usefulness and functionality. A number of audits have already been proposed, for example around cancer screening in unprovoked VTE and management of isolated distal DVT. It is hoped that the results will be used to inform practice and can be presented at future meetings.

BSH24-EP157 | VTE associated with N_2O use: No laughing matter

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Recreational use of N_2O is prevalent among 16–24 year olds. The UK Office for National Statistics reported use in 8.7% of 16–24 year-olds (equivalent to approximately 549 000 individuals) in 2019–2020.[1] Vitamin B12 deficiency and the risk of subacute combine degeneration of the spinal cord are recognised complications, but there also appears to be a risk of thrombotic complications. Case reports exist describing the development of thrombosis after N_2O use including venous thromboembolism (VTE), splanchnic vein thrombosis, cerebral venous sinus thrombosis, stroke, myocardial infarction and peripheral artery thromboembolism.[2] Some of these have confounding factors, for example, pregnancy, use of the oral contraceptive pill or a concurrent diagnosis of COVID.

The pathogenesis, however, remains unclear. One explanation relates to hyperhomocysteinaemia associated with B12 deficiency. A systematic review of case reports reported high or high-normal homocysteine levels.[2] However, reducing homocysteine levels has not resulted in lower VTE rates.[3] There may be other mechanisms involved at an endothelial or cellular level.

We present two cases of VTE following recreational N_2O use. The first was a 19-year-old gentleman presenting with numbness of the hands and feet, which progressed to reduced mobility, requiring crutches. He developed subsequent heaviness of the left leg and was diagnosed with a proximal deep vein thrombosis (DVT). Subacute combine degeneration of the cord was confirmed on MRI. He had no personal or family history of VTEs. He was using N_2O on average once every 2 weeks over a period of 10 months. His B12 level at diagnosis was 180, Hb 121 and MCV 90.4 and homocysteine level 9.2.

The second case was another 19-year-old gentleman who presented with shortness of breath, chest pain and right leg swelling. He was found to have bilateral PEs and a right proximal DVT. He had no neurology to suggest subacute combined degeneration of the cord and his mobility was normal at diagnosis. His medical history included chronic seborrheic dermatitis. There was no personal or family history of

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VTE. He had been using N_2O heavily in the 2 days prior to diagnosis and on average 15 times per week over many years. His B12 level at diagnosis was 157, Hb 112, MCV 114 and homocysteine level 47.
These cases support an association between N_2O use and increased thrombotic risk. This and the underlying pathogenesis warrants further study. Reducing N_2O use to prevent these complications should be promoted and awareness of risks highlighted.

BSH24-EP159 | Comparison between CMV viraemia in fully matched and haploidentical stem cell transplants in acute leukaemia

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Background: Cytomegalovirus (CMV) reactivation is a significant post-transplant concern in acute leukaemia patients undergoing haematopoietic stem cell transplantation (HSCT). This study aims to assess the impact of donor type (fully matched sibling [MSD] vs. haploidentical [Haplo-HSCT]), complete remission (CR) status, and conditioning type on CMV viraemia and its subsequent effects on overall survival (OS), relapse, and acute graft-versus-host disease (GvHD). Additionally, the study contrasts the clinical outcomes between post-transplant cyclophosphamide (PTCy) and methotrexate (MTX) groups used for GvHD prophylaxis.
Methods: A retrospective cohort study was performed on 242 acute leukaemia patients from Nasser Institute, Cairo, and OCMU centre, Mansoura University, Egypt. Patients were stratified into 153 MSD and 89 Haplo-HSCT recipients. The study focused on CMV viremia incidence, its correlation with CR status and conditioning type, and its impact on OS, relapse rates, and acute GvHD. Clinical outcomes between PTCy and MTX groups were also compared.
Results: CMV viraemia was substantially higher in the Haplo-HSCT group (31.5%) than in the MSD group (6.5%), with a $p < 0.001$. Acute GvHD incidence was significantly higher in patients with CMV viraemia, ranging from 20% to 28.57% ($p < 0.05$). No significant correlation was observed between CMV viraemia and relapse rates ($p > 0.05$). CMV viraemia severely diminished mean OS, particularly in the MSD group. PTCy was associated with a higher incidence of CMV viraemia compared to MTX ($p < 0.05$). No significant disparities in CMV viraemia were found based on CR status or conditioning type between the two groups ($p > 0.05$).
Conclusions: Haplo-HSCT is linked with a higher incidence of CMV viraemia and acute GvHD compared to MSD transplants. Complete remission status and conditioning type did not significantly influence CMV viraemia incidence. CMV viraemia notably impacts OS, necessitating customised preventive strategies. The study also reveals that PTCy is associated with a higher risk of CMV viraemia compared to MTX, emphasising the need for targeted monitoring and management in these patients.

BSH24-EP160 | Utility of PBSC collection post salvage chemotherapy for relapsed and refractory lymphomas—A single centre study

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Autologous stem cell transplant (ASCT) of Peripheral Blood Stem Cells (PBSCs) is an important treatment option for patients with relapsed and refractory lymphomas. The timing of PBSC collection is less well defined. Some patients do not eventually get a re-infusion of the collected PBSC for a variety of reasons. PBSC collection is a cumbersome and costly process covering the pre-apheresis evaluation, apheresis procedure, cryopreservation, and analysis of circulating CD34 cells among other aspects.
The audit was aimed at determining the utility of collected PBSCs and factors that affect the eventual outcome. The primary objective was to assess the eventual therapy outcomes of patients with relapsed and refractory lymphomas who had PBSCs collected at the Clinical Apheresis Unit (CAU), Glasgow between February 2018 and February 2020.
Data was collected retrospectively for patients with lymphomas referred for PBSC collection between February 2018 and February 2020. A total of 83 patients were referred and had PBSCs collected with the relapsed and refractory cohort accounting for 72.3% (60) of the total. Thirty-six (46.6%) of patients were in their first relapse with 12% being primary refractory. Fourty nine (81.6%) of patients in the relapsed and refractory cohort who had PBSC collected proceeded to receive ASCT. Disease status prior to PBSC collection (ie either complete response CR or partial response PR on imaging) did not influence the eventual outcome with 93.3% of patients in CR proceeding to ASCT compared to 78.8% of patients in PR ($p = 0.262$). More patients in first relapse proceeded to ASCT (91.9%) compared to those in later stages of relapse ($p = 0.004$). Median CD34 cell dose obtained was higher in first relapse compared to the number in later stages of relapse but this was not statistically significant (4.99×10^6/kg in first relapse compared to 4.32×10^6/kg in second relapse, $p = 0.076$). The number of chemotherapy cycles pre-PBSC was not associated with the eventual outcome (ASCT vs. no ASCT) and median CD34 cell dose.
The high utility of PBSC collected (81.6% proceeding to ASCT) underlines the importance of PBSC collection with a view to ASCT in relapsed and refractory lymphomas. Timing of PBSC collection with respect to chemotherapy cycles did not impact on the eventual outcome and median CD34 dose and this is an area for future prospective studies. The current timing of PBSC collection in relapsed and

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refractory lymphomas is better served by using a case by case approach until more prospective randomised studies are available.

BSH24-EP161 | Early CRS predicting ICANS and acute infections predicting progression in DLBCL patients receiving CAR-T therapy

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Background: Chimeric antigen receptor-T cell (CAR-T) therapy products axicabtagene ciloleucel (Axi-cel) and tisagenlecleucel (Tisa-cel) are approved as third line therapy in relapsed/refractory diffuse large B-cell lymphoma (RR-DLBCL) patients. Our analysis of RR-DLBCL patients who underwent CAR-T therapy in our centre identified acute culture positive infections within Day 28 of CAR-T infusion (ACPI28) and C-reactive protein (CRP) before lymphodepletion as key factors influencing the early disease progression. We also identified that the early-onset cytokine release syndrome (CRS) predicts the occurrence and severity of immune-effector cell therapy-associated neurotoxicity (ICANS).
Methods: The clinical details of 50 consecutive patients who underwent CAR-T therapy in third line for RR-DLBCL from 12/2020 to 06/2023 were collected. Survival outcomes were analysed by Kaplan–Meier Method and associations were tested using the log-rank test and Chi-square test.
Results: Median age was 65 years. Axi-cel was infused in 90% of the patients. CRS was seen in 100% (Grades 2/3/4—42%/10%/0%). Grade 3/4 ICANS was seen in 20%. Patients with early onset CRS had a higher incidence of ICANS (75% vs. 38.5%; $p = 0.009$). Early CRS also predicted higher incidence of Grade 3/4 ICANS (29.2% vs. 11.5%; $p = 0.03$).
ACPI28 were seen in five patients (10%). Out of five ACPI28 patients, progressive/relapsed disease (PD) and early death were seen in three and one patients, respectively. At 3 months, 56% had CMR, 4% had PR. Overall non-relapse mortality was 8%.
Median follow-up was 17.7 months. Median progression-free survival (PFS) was 12.4 months (1-year PFS-52.7%); median overall survival (OS) was not reached (1-year OS-68.6%). In univariate analysis, the factors adversely influencing PFS were ACPI28 ($p = 0.007$), elevated CRP at commencement of lymphodepletion ($p = 0.01$), and non-achievement of CMR/PR at 1 month and 3 months ($p < 0.001$). The factors adversely influencing the OS were elevated CRP at commencement of lymphodepletion ($p = 0.005$), ACPI28 ($p = 0.04$) and non-achievement of CMR/PR at 3 months ($p < 0.001$).
Discussion: This study provides evidence for an unexpected association between this ACPI28 and risk of early lymphoma progression. We speculate that this could be due to poor CAR-T expansion due to an adverse cytokine profile precipitated by the immune response to severe infection. We speculate that the observed association between early-onset CRS and occurrence of ICANS could be due to differences in cytokine profile between early and late-onset CRS. Our statistical analysis is limited to univariate analysis due to small sample size. These observations, however, warrant further exploration in a larger cohort suitable for multivariate analysis.

BSH24-EP162 | Integration of palliative care with CAR T services—A first year experience

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Background: Sheffield Teaching Hospitals NHS Foundation Trust became a CAR T centre in November 2022. Recognising that patients may deteriorate rapidly prior to treatment, or if relapsing post CAR T cell therapy, palliative care services are integrated into the patient's pathway from the point of referral. A dedicated palliative care consultant is actively involved in CAR T MDT planning, seeing new patients during their first outpatient assessment and building a relationship with them during admission for CAR T. Dependent on need, some patients are followed up as outpatients post infusion. We describe here our palliative care requirements in the first year, advocating service integration from the outset for future CAR T centres.
Caseload: Sixteen patients were accepted for CAR T, 14 apheresed and 10 patients infused (five for third-line treatment of large B cell lymphoma [LBCL], one second-line LBCL and four mantle cell lymphoma [MCL]). Both acute lymphoblastic leukaemia patients did not reach infusion. Median age was 69 years (range 48–74).
Two patients died pre-apheresis of sepsis-related complications in their referring centre without palliative care input from the CAR T centre. Post-apheresis, another died from an invasive fungal infection. Two patients did not proceed with infusion due to progressive disease associated with deterioration in functional state. Both died in hospital within a week of their planned infusion and received holistic support and symptom management throughout from the palliative care team.
Post CAR T cell therapy, two patients became profoundly deconditioned associated with grade 4 cytopenias and hyperinflammatory features. One died of sepsis-driven multi-organ failure on ICU with palliative care support. Two patients relapsed prior to D+100, one of whom had no further treatment and died in the community. The other declined palliative care input throughout and is receiving further chemo-immunotherapy.
Conclusion: Not all patients have a durable responses to CAR T therapy, and it has serious side effects. In Sheffield,

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weekly collaboration between haematologists, ICU and palliative care consultants facilitates dynamic and personalised care. Holistic assessments elicit physical, psychological, social and spiritual needs of the patients.
Although treatment options for relapsed lymphoproliferative disorders are expanding, uncertainty of outcomes necessitates parallel planning aiming to hope for the best but plan for the worst. Advance care planning discussions should be initiated early including what and who matter most to the patient.
CAR T centres should strive to embed palliative care into their service framework to provide high quality multidisciplinary patient-centred care.

BSH24-EP163 | Positive complement dependent cytotoxicity crossmatch following Covid 19 vaccination in a patient awaiting renal transplantation

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Introduction: Vaccination is known to cause alloimmunization in healthy population and in organ transplant recipients. The effect of Covid-19 vaccination and infection on human leukocyte antigen (HLA) histocompatibility testing in organ transplant recipients and donors is unknown.
Herewith we report a case of a positive Complement Dependent Cytotoxicity (CDC) crossmatch following recent Covid 19 vaccination in a patient awaiting renal transplantation.
Case: A 52 year old male patient with end stage renal disease for 2 years preceding diabetes mellitus for 33 years duration, was planned for live donor renal transplantation. He was on routine medications for chronic kidney disease and on haemodialysis twice a week. He had no history of blood transfusions or previous organ transplantations. He was evaluated for a preemptive renal transplantation from a living donor.
Initial HLA work up and histocompatibility testing performed in March 2021. Three out of six HLA allele group compatibility was noted while panel reactive antibodies (PRA) being negative for both HLA class I and class II.
Both T cell and B cell leucocyte crossmatch by microlymphocytotoxicity test was compatible. Second set of HLA histocompatibility tests were performed after 3 months using a fresh serum sample from the patient and fresh donor cells prior renal transplantation. Surprisingly 2+ IgG antibody reactivity was identified in both B cell and T cell allo-crossmatch and auto crossmatch, indicating pan-panel reactivity with a negative PRA. All possibilities for an incompatible HLA crossmatch with negative PRA were excluded, including recent sensitization, complement activation (dialysis within 24 h, infection), immunoglobulin therapy in past 2–3 weeks. Interestingly the only positive finding was patient receiving two doses of ChAdOx1 nCoV-19 (Covishield) vaccine while receiving the second dose within 1 month of sample collection.
Interval repeating of HLA histocompatibility testing was recommended and repeated positivity was noted in the tests performed in a sample collected after 2 weeks.
Negative results were noted in the compatibility testing performed in a sample collected 1 month after the repeat testing.
Conclusion: This case highlights that recent Covid 19 vaccination may interfere HLA histocompatibility testing. Therefore it is important to assess patients' recent Covid-19 infection and vaccination status prior to concluding the immunological risk for solid organ transplantation.

BSH24-EP164 | Evaluation of apheresis parameters for optimal autologous peripheral blood stem cell harvesting from lymphoma patients

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Background: Autologous haematopoietic stem cell transplantation (HSCT) is a well-established treatment for various haematological malignancies and successful peripheral blood stem cell (PBSC) collection is crucial for its efficacy. Obtaining enough stem cells using as few apheresis procedures as possible is important for the cost-effectiveness and for patient's convenience. This study is aimed at analysing and optimising autologous PBSC collection in lymphoma patients.
Method: A 3-year retrospective analysis was performed using data from January 2019 to December 2021 at a leading UK bone marrow transplant centre.
Results: Total of 306 adult patients were referred for stem cell harvesting with data from 428 apheresis procedures performed on 260 patients. Of those, 171 collections were from 99 (38%) lymphoma patients and 257 apheresis procedures performed on 161 (62%) other patients. Notably, 19.5% of lymphoma patients referred for stem cell collection were not primed due to disease progression, patient choice, or death. Analysis revealed that if the pre-stem harvest peripheral blood $CD34^+$ cell count is less than 20, a significant number of repeat apheresis procedures were required.
Among the 99 lymphoma patients proceeding with stem cell collection, 39.4% had $CD34^+$ counts of <20 on the first day, majority were men (66.7%) with a median age of 56 years (range, 27–75 years) and majority of patients within 51–60 years (66.7%). The main mobilisation regimen was chemotherapy plus G-CSF (69%), with only 5% achieving adequate collection of $>2 \times 10^6$ cells/kg at the first attempt. The majority (74%) required two or more days for adequate stem cell collection, and 49% needed a change in mobilisation protocol. For those using plerixafor, 27% required three or more days for adequate stem cell dose collection. Notably, G-CSF with chemotherapy, excluding cyclophosphamide priming, resulted in a poor mean product $CD34^+$ cell count of $<0.5 \times 10^6$/kg per procedure.

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The harvested $CD34^+$ cell count did not correlate with age or weight of the patients, but a statistically significant positive correlation existed between pre-apheresis circulating $CD34^+$ cell count and harvested $CD34^+$ cells.

Conclusion: Circulating $CD34^+$ count serves as a potential surrogate marker for determining the optimal starting time for PBSC collection. Pre-HPC count of 17 would be required to achieve $CD34^+$ yields $\geq 1.5 \times 10^6$/kg for each apheresis procedure. The optimal cut-off value is 22 for pre-HPC count to achieve $CD34^+$ yields $\geq 2.0 \times 10^6$/kg. Applying appropriate priming protocol and cut-off values for the pre-apheresis peripheral blood $CD34^+$ cells is clinically beneficial for optimising the timing of PBSC collection.

BSH24-EP165 | Characteristics, prognostic indicators and survival among Omani patients diagnosed with chronic lymphoid leukaemia at SQUH

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Background: CLL is a malignant disease of mature B lymphocytes. Clinical presentation and prognosis are variable (with some asymptomatic patients not requiring treatment for years). CLL is not common in the region but there is a noticeable increasing prevalence.[1] There is very limited published data on CLL from the region. This is the first report from Oman aiming to fill the knowledge gap and enhance understanding of the disease's behaviour within this specific population.

Objectives: To study the clinical and laboratory characteristics of Omani patients with CLL. To estimate the overall survival (OS) in all patients, and progression free survival (PFS) and OS in patients who received treatment. To study the effects of prognostic markers on PFS and OS.

Method: This is observational retrospective study included all CLL patients who diagnosed SQUH. Prior to commencing the study, ethical approval was obtained from the research ethical committee. Data retrieval was conducted through the utilisation of personal health records sourced (Trakcare). Statistical analysis was performed employing the SPSS software. Inclusion criteria comprised confirmed CLL patients who aged 18 and above. Exclusion criteria is individuals who did not maintain follow-up at SQUH.

Results: The cohort's median overall survival (OS) was found to be 167 months (95% CI 115–171), whereas the OS among patients requiring treatment was notably lower, at 75 months (95% CI 57–94). PFS in patients who received treatment is 52 months (95% CI: 45–58). Furthermore, patients who achieved a complete response (CR) after first-line treatment demonstrated a significantly longer median OS of 167 months, compared to 75 months among those with partial response (PR) and this difference was found to be statistically significant ($p = 0.042$). In terms of treatment comparison, no statistically significant difference was observed in survival outcomes between patients who received BTK inhibitors and those undergoing chemo-immunotherapy. Moreover, the study conducted a multivariate analysis of various factors including haemoglobin levels, platelet count, number of involved lymph nodes and RAI stage. However, none of these factors showed any statistically significant association with overall survival.

Conclusion: The Overall Survival of CLL patients who were managed in SQUH is 167 months which almost similar to regional and international reported survival rate. Age at diagnoses and response to first line treatment were two factors identified to influence the overall survival in our cohort. A regional cytogenetic database is being established to advance our knowledge of CLL our patient cohort.

BSH24-EP166 | Rituximab prior to venetoclax is safe and effective in relapsed/refractory chronic lymphocytic leukaemia

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In 2018 venetoclax/rituximab (VR) was shown to be an effective treatment in refractory/relapsed (r/r) chronic lymphocytic leukaemia (CLL). A key concern with venetoclax is tumour lysis syndrome (TLS). Therefore, the licensed approach is to give venetoclax in a ramp up schedule and once established on full dose, to add in rituximab.

However, there is no clear reason why rituximab should be given after venetoclax. The CLL14 trial of venetoclax/obinutuzumab, a comparable regimen, demonstrated efficacy with an obinutuzumab lead in followed by venetoclax ramp up. The GIVE trial also demonstrated that giving obinutuzumab first appears to abrogate the TLS risk, with TLS risk classification reduced in all patients by the time of venetoclax administration. Therefore, it would seem possible, and potentially even desirable, to give rituximab prior to venetoclax in patients with r/r CLL.

We present here a retrospective study of all patients at a single centre who received venetoclax/rituximab combination therapy since 2019, with an average time to follow-up of 3.2 years. This comprised 10 patients, of whom 6 were treated with standard venetoclax ramp up then rituximab (VR), while four patients were treated with an off-licence protocol wherein rituximab was given first followed by initiation of venetoclax at D22 (RV). In both groups venetoclax was given as per the usual ramp up schedule. TLS risk assessment was made at the time of initiation of venetoclax and managed accordingly.

Rates of TLS were extremely low in both groups with no cases recorded in the RV group and one case in the VR group. In this case it was grade 1 TLS, with a transient rise in creatinine to $>1.5 \times$ ULN, which resolved with no further sequelae. All four patients who received RV had TLS risk scores reduced from intermediate risk at time of rituximab initiation to low risk by the time of venetoclax initiation.

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Outcomes were similar across both groups. In those treated with RV, two patients completed therapy and continued on expectant management, with two still on venetoclax monotherapy at time of follow up. In those treated with VR, four completed therapy and continued expectant management and two had progressed, one of whom had undergone Richter's transformation.
In conclusion, giving rituximab induction therapy prior to venetoclax is safe and does not demonstrate any adverse impact on disease outcomes, with a suggestion it may reduce TLS risk, as previously demonstrated in the venetoclax/obinutuzumab setting.

BSH24-EP167 | A retrospective review of SPEP testing practices and MGUS diagnosis in a community hospital

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Background: Workup for plasma cell disorders starts with SPEP testing which can detect the presence of M-protein. Immunofixation and serum free light chains are usually carried out with SPEP testing to increase test sensitivities up to 97%. Sometimes, testing would not reveal a plasma cell disorder, but rather an incidental entity called MGUS. MGUS is a premalignant condition that carries transformation risk of approximately 1% per year into a malignant plasma cell disorder. Because there are no clear guidelines on appropriate SPEP testing, testing may be performed for symptoms unrelated to plasma cell disorders.
Methods: A retrospective study was conducted in a community hospital setting to look at SPEP testing indications and subsequent MGUS diagnosis. Patients with newly diagnosed MGUS were identified during a 1-year study period from August 2020 to July 2021.
Results: Among the 3888 patients with SPEP testing during this study period, 2973 patients had no prior SPEP and comprised the study population. The most common indications associated with SPEP orders were rheumatologic Diseases ($N=1076$), osteoporosis/osteopenia ($N=641$), and neuropathy ($N=556$). Of the 2973 patients with first-time SPEP orders, only 64 patients (2.1%) were diagnosed with MGUS. Median age at MGUS diagnosis was 72 (range, 37–94) with 47% male and 53% female. All 64 patients had immunofixation testing as indicated by our institution's haematopathologists. In contrast, only 61% ($N=39$) of patients had serum free light chains (FLC) co-testing at the time of initial SPEP. The remaining 39% ($N=25$) of patients had FLC testing after SPEP had resulted and usually after haematology input. Among the MGUS patients, the most common indications associated with SPEP orders were osteoporosis/osteopenia ($N=11$), anaemia ($N=9$), leukaemia/lymphoma ($N=9$), other CBC abnormalities ($N=7$), neuropathy ($N=7$) and constitutional symptoms ($N=6$). Most patients with new MGUS diagnosis were followed by haematologist ($N=50$, 77%). About one-third of those patients (38%, $N=24$) have low-risk MGUS but follow-up frequency varies regardless of MGUS risk.
Conclusion: SPEP tests were ordered for different signs and symptoms, but some of which were unrelated to plasma cell disorders. Until results from the population-based screening study iSTOPMM are finalised, there remains a need for clear guidelines on appropriate SPEP testing. MGUS diagnosis comes with the cost of psychological distress and decrease quality of life. This study also highlights that a portion of the initial workup did not include FLC co-testing, which is essential in screening for monoclonal gammopathy.

BSH24-EP168 | Diagnostics and treatment in AL amyloidosis with cardiac involvement—A dual centre retrospective cohort study

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Background: AL Amyloidosis is characterised by the systemic deposition of agglutinated free light chains within tissues, predominantly the kidneys, brain, liver and myocardium. Amyloid infiltration inevitably progresses to organ dysfunction, causing consistently poor prognosis. Cardiac involvement is seen in 50% of patients and causes Restrictive Cardiomyopathy which culminates in Left Heart Failure. The extent of myocardial involvement is a key predictor of morbidity and mortality, with a median survival time of <6 months when not treated, making it a significant target in enhancing Amyloidosis patient outcomes.
Methods: The primary aim of this study was to review local practice and outcomes, in patients with known AL Amyloidosis and suspected cardiac involvement, across two NHS Trusts. We compiled a list of local patients with histological evidence of Amyloidosis between 2010 and 2023 using MDT (Somerset) coding. Patients with AA or ATTR-type Amyloid were excluded, as were patients without cardiac disease. Using electronic clinical records, we collected information on: Patient demographics; histology findings from bone marrow biopsy; diagnostic modalities (including cardiac biomarkers); the treatments used; and finally duration of survival.
Results: Nineteen patients were identified who met the inclusion criteria, 13 men and 6 women, with a mean age at diagnosis of 66 years. Also, 32% of patients had Kappa-restricted disease and all patients had an underlying lymphoid cell dyscrasia—67% Multiple Myeloma; 20% MGUS; 4% CLL; 9% Waldenstrom's macroglobulinaemia.
While all patients underwent an Echocardiogram at diagnosis, only 53% had an additional Cardiac MRI; furthermore, no patients underwent the current diagnostic Gold Standard,

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Cardiac Biopsy. 89.5% of the cohort had an NTproBNP of >1800 at baseline.

73.7% of patients received bortezomib-based treatment first line, with the remainder receiving lenalidomide and R-Benda. Only 9 (26.3%) patients had more than 1 line of treatment.

At the time of reporting, the cohort mortality rate was 47.4% (9 patients), with the mean age at of death of 67.3 years (50–82). The mean duration from diagnosis to death, or to reporting, was highly variable (range 1.1–101.5 months).

Conclusion: Despite limitation by the small cohort size and retrospective design, this study identifies disparities in the diagnostic workup of our cohort, highlighting the need for a standardised approach to diagnosis. We have recently implemented a local haemato-Cardiology MDT so new presentations of cardiac amyloidosis now receive a joint approach at diagnosis. The surprising proportion of patients with Kappa-restricted disease poses an exciting area for potential further investigation.

BSH24-EP169 | Investigating infection in multiple myeloma patients on anti-CD38 monoclonal antibody treatment

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Background and Purpose: The use of anti-CD38 monoclonal antibodies (MoAbs) has risen in the treatment of multiple myeloma (MM) due to its efficacy and favourable side effect profile, which allows for minimal patient monitoring. However, there is evidence to suggest that anti-CD38 MoAbs increase both the risk of viral and bacterial infections in MM patients, who are already susceptible to infection due to the immunosuppressive nature of their disease. This local practice review investigated infection rates and severity in Cardiff and Vale MM patients on anti-CD38 MoAbs between January 2019 and March 2023.

Methods: A list of Cardiff and Vale patients with MM undergoing anti-CD38 MoAb treatment was produced using Welsh Clinical Portal (the national electronic data portal in Wales). The following key words were used: MM, stage, genetics, autologous stem cell transplant, infection, Covid, antibiotic, prophylaxis, IVIg, discharge and death. The data were collated into a proforma on Excel and graphs were generated to help visualise the results. Common Terminology Criteria for Adverse Events (CTCAE) were also used to grade the individual infections, and the severity of both lymphopenia and neutropenia.

Key Results: Infection rates were 52%, 54% and 50% for the daratumumab monotherapy, daratumumab–bortezomib–dexamethasone, and isatuximab–pomalidomide–dexamethasone treatment groups respectively. Across the three treatment groups, infection grades ranged from 1 to 5 (most severe) in line with CTCAE criteria. Hypogammaglobulinaemia ranged from 93% to 100% across all infected patients and lymphopenia ranged from 50% to 60%. Additionally, in all treatment groups, the use of prophylactic antibiotics was higher in the patients who developed infection.

Conclusions and Implications: Compared to UK-wide data the infection rates and death rates of this local practice review were higher. The immunoglobulin results suggest that immunoparesis was present in most infected patients which likely contributed to high infection rates. Additionally, the use of prophylaxis did not seem to be effective. Further investigation is required to understand why infection rates are higher on average in Cardiff and Vale, than across the UK. This study additionally highlights the vulnerability to infection that exists among MM patients receiving MoAb treatment and makes a case for greater use of prophylactic IVIg. This will have resource implications for UK patients not least due to the recent approval of daratumumab-lenalidomide-dexamethasone for newly diagnosed older patients.

BSH24-EP170 | Triple class refractory patient and carer experience of living with multiple myeloma

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Introduction: Multiple myeloma (MM) is a rare, relapsing, progressive and malignant type of blood cancer. While no cure is available, anti-myeloma treatments aim to control the disease and place patients into prolonged periods of remission.

This research aims to explore the psychological impact and healthcare experiences of people affected by triple class refractory (TCR) MM—defined as those that have not responded to or have relapsed after all three of the major classes of myeloma treatments. More specifically, the research aims to establish the psychosocial impact of the patients journey from the initial diagnosis of MM through to TCR MM, the accrual of personalised medical knowledge over time and how that impacts patients and carers adjustment to a TCR diagnosis.

Methods: Qualitative, semi-structured interviews were conducted with ten TCR participants (seven patients, three caregivers) to explore their journeys from diagnosis, through receiving treatment, navigating care pathways, defining success outcomes, and maintaining quality of life. Interpretative Phenomenological Analysis (IPA) and Dedoose qualitative data analysis (QDA) software were used to develop themes that captured the key aspects of their experiences.

Results: Four themes captured key challenges and areas of unmet need for people with TCR MM: (1) 'diagnostic improvement' defines the need for greater awareness and recognition of MM to reduce diagnostic delays, and the use of appropriate language to reassure patients and carers rather than induce fear, (2) 'identifying my role' highlights the need for clarity in

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the patient's role, involvement in their own care and the need for customised treatment regimens, (3) 'maintaining certainty during uncertainty' focuses on the drivers for the management of health-related quality of life in TCR MM (i.e. pain management, dealing with side effects, maintaining psychological wellbeing and stability, mobility aids and uncertainty in remission), and (4) 'learning to navigate the NHS' identifies the need for clear, transparent, and effective communication within healthcare, alongside clarity on access to clinical trials. **Conclusion:** There are key opportunities to improve the TCR MM journey using more easily accessible language in consultations, transparency in the meaning of biomarkers and psychological support to assist patients to adjust to their new diagnoses. Future work should focus on development and implementation of practical tools throughout the patient journey to support psychological adjustment and pain management, through to the process of identifying, reviewing and decision-making surrounding clinical trials.

BSH24-EP172 | Switching from covalent BTKi to BCL2i improves outcomes versus using a sequential BTKi in CLL/SLL

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Introduction: Despite improved efficacy and safety of targeted agents for CLL/SLL, including covalent BTKi- (cBTKi) and BCL2i-based regimens, some patients discontinue for reasons other than disease progression (PD), switching to regimens with same or different mechanisms of action. This study assessed real-world treatment outcomes of patients with CLL/SLL switching to a cBTKi- or BCL2i-based regimen following discontinuation of a cBTKi-based regimen.
Methods: Data were from the CLL Collaborative Study of Real-World Evidence (CORE), an international, retrospective observational study (23 centres). Adult BCL2i-naïve patients with CLL/SLL who discontinued their cBTKi-based regimen for reasons other than PD or therapy completion were included. Patients subsequently switched to a cBTKi- (cBTKi cohort) or BCL2i-based (BCL2i cohort) regimen. Treatment outcomes included overall response (OR), progression-free survival (PFS) and time to next treatment or death (TTNT-D). Logistic regression and Cox proportional hazards models, controlling for multiple covariates including patient characteristics, assessed OR, PFS and TTNT-D, respectively.
Results: The study included 121 BCL2i-naïve patients who discontinued their first cBTKi-based regimen and switched to subsequent treatment with a cBTKi- (44 [36.4%]) or BCL2i-based regimen (77 [63.6%]). Most common subsequent regimen was second-generation cBTKis (34/44 [77.3%]) or BCL2i (venetoclax monotherapy: 43/77 [55.8%] and venetoclax + anti-CD20: 33/77 [42.9%]). Most common reason (>80%) for prior cBTKi discontinuation was intolerance. Most patient characteristics were similar between cohorts; but significant differences included: median time from diagnosis to cBTKi or BCL2i initiation (91.0 vs. 62.6 months), median duration of discontinued-cBTKi (19.6 vs. 10.8 months), ECOG = 0 (50.0% vs. 27.3%), and elevated LDH (29.5% vs. 46.8%). Median follow-up duration was 11.6 and 16.4 months for cBTKi and BCL2i, respectively. Among 79 patients with recorded response, the OR was higher for BCL2i than cBTKi (83.6% vs. 62.5%). The adjusted odds of achieving OR were significantly higher for BCL2i than cBTKi (4.6 times [CI: 1.2–18.0]). The PFS KM estimates were higher for BCL2i versus cBTKi at 12 (87.3% vs. 79.1%) and 24 months (78.0% vs. 73.0%). Treatment with BCL2i reduced the hazard of progression/death by 70% (adjusted HR: 0.3 [CI: 0.1–0.8], $p = 0.023$) versus cBTKi. Results were similar for TTNT-D.
Conclusions: Patients switching to BCL2i-based regimens post-cBTKi compared to sequencing through consecutive cBTKis were more likely to respond to therapy and had lower hazard of progression/death, further highlighting the

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effectiveness of BCL2i in real-world settings. The impact of switching to agent(s) in a different class or retreating with agent(s) in the same class is a key consideration in optimising care.

BSH24-EP173 | Venetoclax; implementation of out-patient monitoring

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Background: Venetoclax (Venclexta) is a targeted treatment that is designed to kill cancerous B-lymphocytes that cause the disease known as chronic lymphocytic leukaemia. Patients on venetoclax (Venclexta) require close monitoring due to risk of tumour lysis syndrome (TLS). Within the trust there were no formal documentation and monitoring service for patients undergoing treatment consisting of venetoclax (Venclexta).
Aims and Objectives: Look at current challenges of the monitoring service and implement specific guidelines as well as a standard operating procedure to support safe monitoring. Good opportunity for service development.
Method: An audit of all early patients identified six key themes: (1) TLS risk stratification, (2) prevention and treatment of TLS, (3) blood monitoring, (4) appointment schedule, (5) patient information/contact and (6) patient information with regards to medication.
Results: Poor documentation of risk stratification was observed; risk was not always reviewed post initial ramp. All patients being treated as high risk resulted in un-necessary hospital stay. With regard to prevention and treatment of TLS, data suggested that there was no clear pathway of when, where and who received prophylaxis medication. There was also no pathway in place for the management and treatment of TLS. Blood monitoring and blood tests were not always requested, were not on time, and the documentation of results was poor with no designated person to inform the patient.
With regard to the appointment schedule, patients were often admitted to the ward although that could be ramped in out-patient setting. The booking team struggled with the complicated regime. Ramping took 5 weeks that equalled 15 visits for blood tests alone.
Regarding patient information/contact, patients reported difficulty in understanding the ramping process. They also were unsure of the timing of medication and the safety of increasing dosage. Patients were not always informed of blood results; therefore, the CNS team would often received lots of calls about appointments, schedule and blood tests.
Medication was often delivered to the wrong clinical area, resulting in patients not receiving the medication in a timely manner.
Conclusion: The audit has enabled us to review the current process, create a patient pathway/SOP, and devise a new clinical note, "Venetoclax Monitoring" to standardise patient information. This has led to the implementation of an ACP led Venetoclax clinic. This also has led to improved safety and monitoring of patients receiving Venetoclax therapy and has resulted in positive patient feedback.

BSH24-EP174 | Beyond hospital doors—Bringing cancer treatment to the patients' own home; the Rotherham experience

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We describe here the establishment of a bespoke home chemotherapy service for treating haematological malignancies in a district hospital setting, with an initial funding grant from Janssen. The aim of the Home Systemic Anti-Cancer Treatment (SACT) Service pilot was to assess whether we could improve quality of life for cancer patients by: (1) reducing the inconveniences around coming to hospital such as stresses of parking, requiring a family member to bring the patient in, travel expenses and so forth, (2) improving efficiency by increasing chair capacity on the chemotherapy day unit to accommodate more patients requiring intravenous chemotherapy.
This pilot was initially commenced predominantly for elderly patients with multiple myeloma requiring subcutaneous treatments but was later extended to conditions such as acute myeloid leukaemia and lymphoma. It was delivered by two specialist chemotherapy trained nurses recruited to deliver the SACT outreach service. The nurses conducted pre-SACT assessments, requested relevant blood tests, performed observations prior to treatment administration and administered subcutaneous SACT. They were responsible for triaging patients and escalating to the responsible consultant if there were any concerns with the patients' health. Additionally, a part-time pharmacy technician was also recruited to support the clinical and technical pharmacy team. Practical considerations and concerns around safety were addressed including safe administration and transport of SACT, storage, waste disposal of cytotoxic medications, spillage and extravasation, access to patient records in the community and accurate documentation.
Our pilot delivered significant benefits to both patients and the hospital. Over 8 months, treating 33 patients freed up 109 h per week of chair capacity on our day unit, allowing us to treat more patients requiring intravenous chemotherapy for other malignancies. A patient feedback survey revealed very positive experiences, with all patients highly commending the service and recommending it for other patients. Patients especially commented on reduced hospital attendances, waiting times and savings on travel costs. Additionally, they were able to carry out regular daily tasks without disruption on treatment days.
Recognising its success, the trust has committed to fund the service beyond the pilot phase, making them the first in Yorkshire to offer this transformative service. This decision

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demonstrates a commitment to patient-centred care and paves the way for wider adoption of this new service model in a district hospital setting. Our project has demonstrably delivered a safe, efficient and accessible service model for haematology patients, their families and medical teams.

BSH24-EP175 | A snapshot of UK clinical trial activity in myeloma

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The pace of myeloma research has increased dramatically in recent years. Clinical trials provide data to shape future treatment strategies and enable patients to access innovative treatments that would otherwise be unavailable. The Clinical Service Excellence Programme (CSEP) is a Myeloma UK best practice initiative for hospitals that deliver myeloma care. As part of CSEP assessment, hospitals are asked about their research and clinical trial activity. Patients complete an anonymous survey on their experience of care, which includes questions on clinical trial participation. These data provide a snapshot on clinical trial activity in myeloma.

Hospital self-assessment data were collected from 53 hospitals who have completed, or were completing, CSEP accreditation between September 2020 and December 2023. In addition, 1163 patient experience surveys were reviewed to determine clinical trial activity in three areas: recruitment, informing patients of results and patient experience.

The results showed that 100% of hospitals discuss suitable clinical trial options for patients at multidisciplinary team meetings. Eighty-five percent of hospitals refer patients to trials at their own trust or health board, and 75% refer patients to other hospitals. The data also showed that 92% of hospitals routinely gave all newly diagnosed and relapsing patients details of any relevant clinical trials and 98% of hospitals could refer patients to a research nurse. Within the patient survey data, 443 patients (38%) said they had been invited to take part in a trial. This is less than the 43% of respondents of the 2022 National Cancer Patient Experience Survey who had cancer research opportunities discussed with them. From the CSEP data, 312 patients (27%) took part in trials. Seventy-one percent of patients who took part in trials were informed of the results and asked about their experience. It is disappointing that over a quarter of patients were not informed of the outcome or asked to provide feedback.

The results show that although hospitals appear proactive in discussing clinical trials with patients, just under a third of patients surveyed actually participated in a trial. The majority of patients are informed of the results of their trials which helps them to understand how their participation has contributed to wider myeloma research. Patients were also asked about their trial experience and it is hoped this feedback will inform patient-centred trial development in the future. Understanding more about factors influencing trial access and patient choice is important in identifying strategies to increase trial participation.

BSH24-EP176 | Management of monoclonal gammopathy of undetermined significance patient group, by haematology advanced nurse practitioners

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Two haematology advanced nurse practitioners were employed by NHS Forth Valley in July 2021. The consultant who led on the initiative for the ANP role in haematology had identified the condition MGUS as a suitable disease and patient group for management by ANPs.

About 6000 people per year, in the UK, are diagnosed with MGUS–monoclonal gammopathy of undetermined significant. It is a condition that affects plasma cells. MGUS is not a type of blood cancer, but there is a small risk of it developing into a blood cancer.

The MGUS clinic commenced November 2021 and accommodates 10 patients per week. The ANP holds a 20 min consultation, which includes reviewing blood tests, assessing for any new health concerns or symptoms. The consultation is usually performed via telephone but there is also scope for face to face consultation when needed/felt appropriate.

Since commencing, this clinic has captured, and overseen the management of, more than 200 patients with MGUS or asymptomatic myeloma in NHS Forth Valley.

We have recently looked at a snapshot of the previous 3 months of MGUS activity (52 patients) aiming to capture the following:

- Patient age.
- Risk stratification.
- Follow-up schedule.
- If referral to consultant required.
- Change in serum electrophoresis.
- Change in serum free light chain ratio.
- Change in haemoglobin.
- Change in renal function.
- Embroilment (in other health conditions/factors).

This snapshot audit highlighted that there was one patient with a change in Hb (IDA) and only one change in renal function (known CKD and highlighted to primary care). Two patients were referred back to the Consultant due to rising serum electrophoresis and/or SFLC. Patient age ranged from 42 to 95 years old. Risk stratification involved a combination of low/low-intermediate/high intermediate risk. Of the 52 patients 14 were previous treated myelomas/asymptomatic myeloma or plasmacytoma.

The findings of the audit would suggest that ANPs can safely manage patients with MGUS. Abnormalities in blood checks

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were detected and investigated and managed appropriately. Rising tumour markers were detected and referred back to medical team. In more recent months, ANPs confidence has grown in this group of patients, and their monitoring requirements, and now also manage previously treated myelomas/asymptomatic myeloma and plasmacytoma.

BSH24-EP177 | Real world characteristics and outcomes for triple class exposed myeloma patients on pomalidomide and dexamethasone

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Multiple myeloma (MM) is an incurable haematological malignancy with limited treatment options, especially in heavily pre-treated patients with relapsed/refractory MM (RRMM). These patients may receive at least one proteasome inhibitor (PI), immunomodulatory agent (IMiD) and anti-CD38 monoclonal antibody (anti-CD38 mAb) and thus become triple class exposed (TCE). Studies using historical data indicate that pomalidomide and dexamethasone (PomDex) is a commonly used regimen for patients after TCE but there is limited evidence on the characteristics and clinical outcomes of these patients in current real world UK practice.

This retrospective observational study used collated, de-identified secondary care electronic health records from patients diagnosed with MM from four UK NHS partners. The dataset included demographics, diagnoses, medications, imaging and pathology reports, laboratory and microbiology results and systemic anti-cancer therapy data. Study eligibility was based on presence of MM diagnosis (ICD code C90.0), TCE status (received ≥1 PI, iMiD and anti-CD38 mAb), and receipt of ≥1 line of therapy (LOT) after becoming TCE between 2015 and 2023 (start date of next LOT after TCE was study index). Descriptive demographic and clinical characteristics were reported. Overall survival (OS) and progression-free survival (PFS) were characterised using Kaplan–Meier curves.

Of 201 TCE patients who received ≥1 subsequent LOT between 2015 and 2023, 77 (38.3%) received PomDex. The next most frequently received regimen was ixazomib, lenalidomide and dexamethasone (29, 14.4%) and all other regimens were received by fewer than 10% of TCE patients. In the PomDex group, 40 (51.9%) were male, 50 (64.9%) were of white ethnicity, mean age 68.9 years (standard deviation, SD 10.4), median Charlson comorbidity score of 1 (interquartile range, IQR 0–2), median Eastern Cooperative Oncology Group (ECOG) performance score within 90 days prior to index was 0 (IQR 0–1) with 57.1% missing data, and 21 (27.3%) patients received a prior stem cell transplant. Mean MM duration at index was 5.4 years (SD 3.3). Patients typically received three or four prior LOTs (maximum 9). Median OS was 9.7 months (95% confidence interval, CI 7.7–14.9) and median PFS was 3.9 months (95% CI 3.3–4.8). This study found that PomDex was the most common subsequent therapy received by patients in the UK after they become TCE, but clinical outcomes are poor for this group. The findings demonstrate the value of routinely collected real world data for longitudinal assessments of treatment patterns and outcomes in UK myeloma patients.

BSH24-EP178 | Characteristics of newly diagnosed myeloma patients with and without transplant: Real-world 'big data' from England

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Objectives: Despite being a rare disease, multiple myeloma (MM) is the second most common haematological malignancy in the UK. However, there is paucity of evidence on the rapidly evolving treatment landscape and outcomes in the real-world clinical setting. The purpose of this study was to understand the characteristics and routine treatment patterns of patients with MM in England.

Methods: This was a retrospective cohort study of adult patients newly diagnosed with MM in England between 1 January 2014 to 31 August 2021, identified using the cancer analysis system (CAS, an individual level, population-wide database). Treatment progression and line of therapy (LoT) were derived algorithmically using systemic anti-cancer therapy (SACT) data recorded between 1 January 2014 to 31 May 2021. Stem cell transplant (SCT) status (recorded vs. not recorded during follow-up) was determined from linked hospital episode statistics (HES) data until 31 March 2021.

Results: In total, 24 329 newly diagnosed patients were identified based on ICD-10:C90.0. Further to technical exclusion criteria being applied, 19 847 patients were included in the time to treatment initiation analysis. Approximately 26% of these patients began first line treatment within 1 month of diagnosis, while 51% had a record of taking longer than 6 months to begin treatment (median time to treatment initiation: 6.4 months [95% CI: 5.9–6.9]). 12 095 patients had valid SACT records for analysis of transplant rates. Of these, 3419 (28.3%) received an SCT during follow-up. Compared to those who did not receive an SCT, these patients were generally younger (median age at 1 LoT of 61.0 vs. 76.0 years) and had longer follow-up (median follow-up from start of 1 LoT of 40.0 vs. 22.2 months).

Conclusions: Findings from this study broadly align with published UK literature but also provide an updated snapshot of RWE pertaining to patients with MM in England.

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BSH24-EP179 | A matching-adjusted indirect comparison of ELEVATE-TN versus SEQUOIA: In treatment-naïve chronic lymphocytic leukaemia

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Introduction: An unanchored matching-adjusted indirect comparison (MAIC) was used to compare the efficacy and safety of acalabrutinib with/without obinutuzumab versus zanubrutinib in patients with treatment-naïve CLL/SLL using individual patient data (IPD) from ELEVATE-TN and published aggregate data from SEQUOIA.

Methods: Patients were matched based on variables considered prognostic/predictive of investigator-assessed progression-free survival (INV-PFS) in an exploratory multivariate Cox-regression analysis. The efficacy analysis INV-PFS in randomised patients with baseline data (acalabrutinib + obinutuzumab, $n = 162$; acalabrutinib monotherapy, $n = 163$; zanubrutinib, $n = 241$) using October 2021 data cut-off (DCO) for ELEVATE-TN and October 2022 DCO for SEQUOIA. The safety analysis assessed odds ratios (ORs) of adverse events (AEs). For safety, the ELEVATE-TN September 2020 DCO was matched with the median treatment exposure from the SEQUOIA October 2022 DCO. Confidence intervals (CI) of 95% were used.

Results: In the efficacy analysis, acalabrutinib + obinutuzumab and acalabrutinib monotherapy effective sample sizes (ESSs) post-matching were 124 (76%) and 105 (64%) respectively. Post-matching, 36-month INV-PFS was 95% (95% CI: 90–97) with acalabrutinib + obinutuzumab which was higher than zanubrutinib (84%; 95% CI: 79–88). The MAIC-weighted Cox hazard ratio (HR) showed INV-PFS was longer with acalabrutinib + obinutuzumab versus zanubrutinib (HR: 0.41; 95% 0.23–0.74). Acalabrutinib monotherapy 36-month INV-PFS (86%; 95% CI: 78–91) was similar to zanubrutinib (84%; 95% CI: 79–88). The MAIC-weighted Cox HR showed no evidence of a difference versus zanubrutinib (0.91; 95% CI: 0.53–1.56).

No significant differences in the odds for most AE categories were seen for acalabrutinib + obinutuzumab compared with zanubrutinib, except for higher odds of having any grade neutropenia (OR: 2.19, 95% CI: 1.33–3.60) and arthralgia (OR: 2.33, 95% CI: 1.37–3.96) with acalabrutinib + obinutuzumab. The odds of hypertension (any grade) were significantly lower with acalabrutinib monotherapy (OR: 0.44, 95% CI: 0.20–0.99) than zanubrutinib, whereas there were no significant differences in the odds of other AEs. No significant differences in the odds of atrial fibrillation/flutter between acalabrutinib + obinutuzumab (OR: 0.66, 95% CI: 0.25–1.73) or acalabrutinib monotherapy (OR: 1.69, 95% CI: 0.66–4.36) and zanubrutinib were observed.

Conclusions: Acalabrutinib + obinutuzumab had improved efficacy by INV-PFS versus zanubrutinib, while acalabrutinib monotherapy and zanubrutinib showed similar efficacy. The safety profiles of acalabrutinib with/without obinutuzumab and zanubrutinib were largely similar, with a few exceptions:acalabrutinib + obinutuzumab was associated with higher odds of any grade neutropenia and arthralgia than zanubrutinib. The odds of hypertension (any grade) were lower with acalabrutinib monotherapy than with zanubrutinib. Limitations of MAIC analyses mean the results should be viewed as hypothesis-generating.

BSH24-EP180 | Real-world outcomes of triple-class exposed patients with relapsed multiple myeloma in England: Follow-up analysis

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Introduction: Relapsed/refractory multiple myeloma (RRMM) is an incurable disease, with patients often progressing through the standard treatments including proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs) and monoclonal antibodies (e.g. anti-CD38). For patients exposed to these main classes of therapies ('triple-class exposed'; TCE), limited effective treatment options are available through England's National Health Service (NHS) despite recently licensed innovative agents (e.g. bispecific antibodies, CAR-T). Elsada et al. (2021) previously characterised the clinical picture of TCE RRMM patients in England based on routine administrative clinical data. We aimed to provide updated insights into the treatment patterns in this TCE RRMM cohort and report the real-world clinical outcomes with the most commonly used regimen in this population.

Methods: A non-interventional study previously established a fixed cohort of TCE RRMM patients in England, and retrospectively analysed treatment patterns using data from the National Cancer Registration and Analysis Service with healthcare and mortality data pooled from linked datasets. Recorded data included anonymised patient/disease information, as well as overall survival (OS), time to next treatment (TTNT) and distribution of subsequent treatments after index line of therapy (LOT) (≥3 prior lines). A 2023 protocol amendment extended the study period

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from December 2019 to March 2023 (i.e. patients diagnosed between 2013 and 2021), resulting in a median follow-up of 23.0 months compared to 6.4 months in the original study. Data from Cancer Drugs Fund treatments were not accessible.

Results: TCE RRMM patients ($n = 1422$; including ≥3 prior LOTs) received a wide range of treatments (>20 regimens), thereby highlighting the absence of an established standard of care. The most common index regimen was pomalidomide + dexamethasone (Pom + Dex, $N = 896$; 63.0%). Within the Pom + Dex subgroup, Pom + Dex was predominantly used at the index line following TCE ($n = 764/896$, 85%). Other index line regimens included bortezomib + panobinostat (Bor + Pano), ixazomib + lenolidomide, and daratumumab monotherapy. TCE RRMM patients treated with Pom + Dex had median TTNT of 6.57 months (95% CI: 5.95, 7.06) and median OS of 8.64 months (95% CI: 7.72, 9.69). Among Pom + Dex patients, 27.1% ($n = 243$) received a subsequent LOT with over half receiving Bor + Pano ($n = 137$; 56.4%). Other subsequent therapies included belantamab mafodotin and melphalan + thalidomide.

Conclusion: The Pom + Dex regimen continues to be widely used for treating TCE RRMM in England, with Bor + Pano frequently used as subsequent therapy. Overall survival with Pom + Dex remains poor at <1 year, highlighting the urgent need to improve access to novel therapies at this stage.

BSH24-EP181 | Multiple myeloma with central nervous system disease: Three cases from Nottingham City Hospital

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Central nervous system (CNS) involvement is rare in myeloma, affecting <1% of patients. Prognosis is poor, with median overall survival (OS) of ≤7 months following diagnosis. The evidence base for therapy is limited. Case reports recommend systemic therapy combining an immunomodulatory agent with an anti-CD38 monoclonal antibody, alongside intrathecal triplet therapy (methotrexate, cytarabine, hydrocortisone). We report a single centre's experience managing three CNS myeloma cases between 2017 and 2023.

1. The patient was 44 years old and was diagnosed with myeloma in 2015, which was treated with CVD (cyclophosphamide, bortezomib and dexamethasone) and autologous stem cell transplant (ASCT). Thirteen months post-transplant, he developed back pain, blurred vision and thigh swelling. Blood analysis showed relapsed myeloma. Thigh biopsy confirmed plasmacytoma. CT of head, MRI of spine and cerebral spinal fluid (CSF) analyses showed CNS disease. ESHAP (etoposide, methylprednisolone, cytarabine and cisplatin) was commenced with fortnightly intrathecal cytarabine. There was biochemical progression after 4 weeks. Therapy was changed to RCD (lenalidomide, cyclophosphamide and dexamethasone) with ixazomib replacing cyclophosphamide from cycle three. Very good partial response (VGPR) was attained.
   Intrathecals were continued for 10 months. MRI of brain at 4 months showed improvement, with complete resolution at 13 months, sustained at 27 months. Despite further systemic relapses, CNS disease remained in remission. Shortly after commencing eighth line therapy, the patient died from infectious complications.
2. The patient was 83 years old and was diagnosed with myeloma in 2017, which was treated with bortezomib/dexamethasone, cyclophosphamide/dexamethasone and most recently ixazomib/lenalidomide/dexamethasone (IRD). The patient responded well, but IRD was discontinued after eight cycles due to intolerance. Four weeks later, the patient developed a scalp mass. Blood analysis showed disease progression. MRI head and CSF confirmed CNS disease.
   Pomalidomide/dexamethasone was commenced alongside intrathecals. The patient had one cycle of methotrexate, cytarabine and hydrocortisone, and then three cycles of cytarabine and hydrocortisone. The disease progressed biochemically with persistent CSF plasma cells. The patient could not tolerate further treatment and palliative care was commenced. She passed away 2 months later from progressive disease.
3. The patient was 54 years old and was diagnosed with myeloma in 2022, which was treated with VTD-PACE (bortezomib, thalidomide, dexamethasone, cisplatin, doxorubicin, cyclophosphamide and etoposide) and tandem ASCT. Three months post-transplant, he developed headaches and reduced mobility. MRI head and CSF confirmed CNS disease. Blood analysis showed non-secretory myeloma.

KRD (carfilzomib, lenalidomide and dexamethasone) was commenced with triple intrathecals (methotrexate, cytarabine and hydrocortisone). Daratumumab replaced carfilzomib after one cycle following NICE approval of DRd (daratumumab, lenalidomide and dexamethasone).
Repeat MRI of head at 2 months showed improvement and plasma cells were absent in CSF. Treatment is ongoing with DRd and weekly intrathecal cytarabine. Response will be monitored with serial MRI and CSF flow/cytospin.

BSH24-EP182 | Paraneoplastic granulocyte colony-stimulating factor secretion in a patient with multiple myeloma—A case report

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Introduction: Multiple myeloma is a haematological malignancy of plasma cells and patients can present with

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simultaneous neutrophilia, although this is an uncommon finding. One theory of the pathophysiology accounting for this relates to granulocyte colony-stimulating factor (G-CSF) secretion by clonal plasma cells. Comprehensive investigations need to be performed in a patient presenting with both a plasma cell dyscrasia and neutrophilia as it is necessary to exclude a co-existing primary myeloproliferative neoplasm.

Case: We describe a patient case of a 48 year old male who was assessed in 2012 due to an IgGL paraprotein of 5 g/L and persistent neutrophilia in range of $19–24 \times 10^9$/L. Past medical history included fatty liver disease and type 2 diabetes mellitus. Bone marrow biopsy showed a small population of clonal plasma cells <10% and significant myeloid hyperplasia. BCR-ABL, JAK2 V617F, CALR and MPL mutation tests were negative ruling against a primary myeloproliferative neoplasm. Molecular analysis showed no mutation in the CSF3R gene and in a patient with a plasma cell disorder, this allowed exclusion of chronic neutrophilic leukaemia. A diagnosis of monoclonal gammopathy of undetermined significance (MGUS) with secondary neutrophilia was made.

The patient was followed up with a rise in the IgGL paraprotein level over time to a peak of 26 g/L in 2022. He developed progressive anaemia and thrombocytopenia with persistent neutrophilia in range of $12–18 \times 10^9$/L. Repeat bone marrow biopsy showed myeloid hyperplasia and 10% clonal plasma cells. A diagnosis of plasma cell myeloma was made. Serum G-CSF level was measured to be 2117.42 pg/mL which is markedly raised. In 2023, he was commenced on six cycles of targeted therapy for multiple myeloma, with bortezomib and dexamethasone for cycles 1 and 2 and addition of daratumumab from cycle 3 onwards. Following treatment, IgGL paraprotein has reduced to 2 g/L indicating partial response. The repeat serum G-CSF level after treatment for multiple myeloma had decreased to 166 pg/mL, but was still above normal range. As a result, he has a persistent neutrophilia. The detected high G-CSF level in association with multiple myeloma and the subsequent reduction in G-CSF level and paraprotein level following treatment confirms a diagnosis of paraneoplastic neutrophilia secondary to plasma cell dyscrasia.

Conclusion: G-CSF secreting multiple myeloma is a rare disease that should be considered by haematologists when patients present with features of a plasma cell dyscrasia and persistent neutrophilia.

BSH24-EP183 | Thromboprophylaxis in multiple myeloma patients receiving immunomodulatory-drugs and the rate of thrombotic and bleeding complications

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Background: Immunomodulatory-drugs (IMiDs) are important agents in the treatment of multiple myeloma (MM), but are associated with an increased risk of arterial and venous thrombotic events. This risk is exacerbated when given in combination with corticosteroids and is particularly high during the early phase of treatment when monoclonal protein levels are higher. All patients should have a VTE risk assessment when treatment is initiated and be given appropriate thromboprophylaxis. Studies including Myeloma XI conclude that thrombosis is still frequent when IMWG VTE thrombosis prevention guidelines are followed. Historically, thromboprophylaxis was with antiplatelet agents, low-molecular weight heparin (LMWH) and less commonly warfarin. Modern practice has tended to shift towards direct oral anticoagulant (DOAC) use.

Methods: We conducted an audit to evaluate VTE prescribing practice in IMiD-treated MM patients at University Hospitals Birmingham NHS Foundation Trust. Stratified sampling was conducted of every fourth patient from a list of all MM patients who had been initiated on lenalidomide or pomalidomide between 01/01/2017 and 30/03/2023. Twenty-seven patients were excluded as they had not completed a whole cycle or had less than 6 months follow-up, giving a final sample size of 58. The IMPEDE risk scores were calculated, the type of VTE thromboprophylaxis recorded, and the nature of all bleeding and thrombotic events evaluated.

Results: Overall, 49 lenalidomide and 9 pomalidomide patients were audited. 55/58 (95%) patients were prescribed thromboprophylaxis: 25 were given a DOAC; 21 LMWH; 8 aspirin; and 1 warfarin. Median follow-up time was 15 months. IMPEDE risk score calculations showed that seven patients were low-risk, 45 patients were intermediate-risk, and 6 patients were high-risk.

Four adverse thrombotic events were recorded; three arterial events and one venous event. These patients all had intermediate-risk IMPEDE scores. Two patients were taking prophylactic LMWH at the time of event. One patient experienced two adverse events; taking a DOAC prior to the first event (stroke) and clopidogrel prior to the second (NSTEMI). One patient experienced an adverse bleeding event, a subdural haematoma, while taking aspirin. This patient had intermediate risk based on the IMPEDE score, but their platelet count was low (33×10^9/L) when IMiD therapy was initiated, suggesting that this patient should not have received thromboprophylaxis.

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Conclusion: The bleeding rate was low (1.7%) in this audit, but the thrombotic rate was still significant at 5.2%. This highlights the importance of VTE risk assessments and prescribing appropriate thromboprophylaxis in this population.

BSH24-EP184 | Incidentalomas in patients with multiple myeloma, MGUS and plasmacytomas—Results of 150 PET-CTs

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Background: Incidentalomas are new, incidental, asymptomatic, suspected tumours found radiologically. Patients with long term relapsing–remitting malignancies such as multiple myeloma often have multiple full body scans at an older age potentially increasing the chance of such findings.
Positron emission tomography CT (PET-CT) scans, used to stage myeloma, can identify incidental malignant changes early, however they can also unearth benign lesions. Further investigation into such findings can be an emotional burden to the patient and an economic burden to the healthcare system.
The aim of this study was to evaluate incidentaloma rate from PET-CT scanning in patients with multiple myeloma, monoclonal gammopathy of undetermined significance (MGUS), and plasmacytomas.
Methodology: PET-CT scan reports of patients with multiple myeloma, MGUS and plasmacytomas from January to August 2023 scanned at Norfolk and Norwich University Hospital were evaluated. Findings were compared to previous scans and records to ensure the lesions were new. Patients were excluded if their scan was performed at our hospital on behalf of smaller district general hospitals, due to limited access to those medical records.
Results: One hundred and fifty PET-CT scans were evaluated. Median patient age was 73 years (range 38–91). Forty-six scans (31%) identified incidentalomas. Thirty-three patients were referred for further investigation. Overall, 9 (6%) of patients had an incidental malignancy or pre-malignancy confirmed.
Four renal incidentalomas were identified, of which 2 (50%) were found to be malignant, requiring nephrectomy. In contrast, all of the eight hepatic and eight ENT-related incidentalomas identified were determined to be non-malignant on further evaluation. The most common incidentaloma category was colorectal (15 patients), of which the majority were polyps or focal bowel wall uptake of FDG. Following colonoscopy, three patients were diagnosed with pre-malignant adenomas, and one patient with suspected rectal malignancy. Non-malignant findings requiring follow-up were also identified, such as one patient with newly identified liver cirrhosis requiring further ultrasound surveillance.
Conclusion: Incidentalomas can lead to an early diagnosis of malignancy or pre-malignancy which could be considered a benefit. However, the vast majority of findings ultimately turn out to be benign and can be a burden to the patient and healthcare system.
Our study identified an incidentaloma rate of 31% of scans, with 22% of scanned patients referred for further investigation, but only 6% concluding a new incidental malignant or pre-malignant disease.

BSH24-EP185 | Teclistamab monotherapy first experience in patient with refractory multiple myeloma in Russia

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Background: On 25 October 2022, the US FDA granted accelerated approval to Tecvayli™, the first bispecific B-cell maturation antigen-directed CD3 T-cell engager, for adult patients with relapsed or refractory multiple myeloma who received at least four prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and demonstrated the disease progression on the last therapy. The Russian governments have not approved Tecvayli™ yet.
Aims: To present the first Teclistamab monotherapy experience in patient with triple-class-exposed refractory multiple myeloma in Russia.
Description: A 39-year-old Caucasian female has been treated in Russian Cancer Research Centre named after N.N. Blokhin since December 2022, with IgG-kappa multiple myeloma, R2-ISS = 3 (high risk, 1q21 amplification). The progression of the disease was extremely aggressive with extramedullary spreading involving liver, CNS and breasts. Within 8 months of treatment, including the proteasome inhibitor, two immunomodulatory agents, the anti-CD38 antibody, cytostatic agents and radiation therapy, the refractory type of disease progression was stated. Haematopoietic stem cell transplant and CAR T-cell therapy were not considered due to the inefficiency of the previous treatment and massive tumour growth along with severe vital status. The silver lining was bispecific monoclonal antibody monotherapy. Starting in August 2023, teclistamab therapy was initiated after the health government approval had been granted. According to the step-up dosing schedule we had been escalating as prescribed and by November 2023, eight injections had been administered.
Results: Teclistamab resulted in the patient's vital status clinical improvement, time to treatment response was 1.5 month. Partial metabolic response (PET/CT-DS 4; IMPeTUs) and MRD-negativity rate were achieved after 2.5 months of treatment. Adverse events were following: cytokine release syndrome (CRS), grade I (ACTCT)—while escalating up to

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0.3 mg/kg; neurological toxicity, including immune effector cell-associated neurotoxicity syndrome, grade III—while escalating up to 1.5 mg/kg; hypogammaglobulinemia (IgG 1.39 g/L).

Conclusion: Nowadays the number of patients with triple-class-exposed multiple myeloma is dramatically increasing. The complexity of applying CAR T-cell therapy in Russia, along with the scanty variety of treatment methods, make that increasing cohort hopelessly palliative, and get in the way of preventing refractoriness. We presented the first experience of Teclistamab monotherapy in Russia, demonstrating antitumor efficacy, along with clinically significant improvement in patient's somatic status, and giving hope to those who have ran out of other options. Life-threatening reactions can occur in patients receiving Tecvayli; nevertheless, it shows favourable toxicity profile and antitumor efficiency.

BSH24-EP186 | Newly diagnosed multiple myeloma VRD protocol treatment precursory results

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Background: Over decades multiple myeloma has a tendency towards improvement in treatment outcomes, however remaining on incurable cancer diseases list. Risk-adapted strategy, optimal induction and consolidation regimens, supportive care—all of those make further outcomes improve.

Aims: To estimate precursory single-centre trial results of VRD regimen treatment outcomes among newly diagnosed multiple myeloma patients—candidates for a stem cell transplant (SCT).

Methods: All patients have been administered with VRD regimen induction therapy, followed by MRD-adapted strategy. Cancer treatment efficiency has been estimated according to IMWG-criteria (2011). Risk stratification has been carried out according to mSMART 3.0. The Kaplan–Meier survival curves have been used, differences between groups have been detected by the log-rank test.

Results: In Russian Cancer Research Centre named after N.N. Blokhin among 50 patients with newly diagnosed multiple myeloma, who received VRD regimen 80% got ≥4 induction cycles (median—5), common response rate was 90% (complete response [CR]—34%, a very good partial response [VGPR]—45%, partial response [PR]—11%). Four patients got progression, three patients died. Seven patients achieved MRD-negative rate after induction cycles (16%). High cytogenetic risk patients ($n = 9$) had worse results (CR—2, VGPR—4), and only one patient achieved MRD-negative status. By November 2023, 44 patients had completed induction cycles, 21 had administered SCT, 5 were receiving consolidation therapy and 13—supportive therapy. The median age was 55 years (34–65), 27 were males (54%). Disease stages were following: R-ISS: I—27 (54%), II—9 (18%), III—14 (28%). Nine patients (18%) had high cytogenetic risk (del17p, t(4;14), t(14;16), 1q21). PET/CT scans were administered on admission to the hospital, before and after SCT: on the disease onset 80% of patients had unfavourable prognosis (>3 extramedullary lesions, SUVmax >4.2). During induction therapy 70% of patients had vertebroplasty. With a median follow-up of 14.5 months, 12-month progression-free survival (PFS) was 86%, 12-month overall survival (OS) was 93%. More importantly, PFS and OS were tended to be higher in patients who had been administered SCT.

Conclusion: Triple-component VRD regimen being administered as induction therapy among newly diagnosed multiple myeloma patients associates with thorough antitumor effect, high cytogenetic risk patients included. On the other hand, the frequency of achieving MRD-negative rate remains low, which does not contradict to previous research data. Currently, the end point is personalization of chosen therapy according to the post-transplantation MRD-rate.

BSH24-EP187 | Venetoclax + obinutuzumab for chronic lymphocytic leukaemia: Is stringent TLS monitoring proportional to risk?

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Background: Venetoclax + obinutuzumab (VenO) has been available as a first line treatment option for CLL in England since 2021. Although well tolerated, stringent tumour lysis syndrome (TLS) monitoring during venetoclax dose escalation, and risk of obinutuzumab-associated infusion related reactions (IRRs) can make treatment initiation onerous. We aimed to review adverse events and TLS monitoring frequency during the first two cycles of VenO for patients treated at a single NHS site.

Methods: In this retrospective study we collected data on consecutive patients treated with VenO at Gloucestershire Hospitals between May 2021 and October 2023. The primary outcome was the rate of venetoclax induced biochemical and clinical TLS. Secondary outcomes included the rate of obinutuzumab IRRS requiring unplanned hospital admission and/or treatment delay.

Results: In total, 28 patients initiated VenO. At baseline, median age was 69 years (range 35–80), Eastern Cooperative Oncology Group (ECOG) performance status was ≥2 in 4 patients (14%), median lymphocyte count was 145×10^9/L (range 6–675), 10 patients (36%) had maximum lymph node diameter >5 cm and 21 patients (75%) had estimated glomerular filtration rates (eGFR) <80 mL/min. Post obinutuzumab

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pre-phase and pre-first dose venetoclax, median lymphocyte count dropped to 1.7×10^9/L (range 0.34–12.2). Seven patients (25%) commenced venetoclax as an inpatient for additional monitoring. All patients received allopurinol or rasburicase prophylaxis and had TLS monitoring bloods, as minimum, at 6 and 24 h post venetoclax 50 and 100 mg dose initiation. Twelve patients (43%) continued TLS monitoring for 200 mg, and 6 patients (21%) for 400 mg dose initiation. In total, there was one case of biochemical TLS following 50 mg dose initiation in a high-risk patient which resolved by 24 h following IV hydration. There were no episodes of clinical TLS.

In 21 patients receiving first obinutuzumab as an outpatient, 4 (19%) required unplanned admission due to IRRs. Of seven electively admitted for their first dose, three experienced adverse effects that delayed subsequent therapy (IRR = 2; TLS = 1).

Conclusion: The low frequency of venetoclax related TLS observed in this study illustrates the success of obinutuzumab loading and venetoclax dose escalation in mitigating against TLS. It suggests that current TLS monitoring recommendations are excessive relative to actual risk. Results suggest that first dose obinutuzumab poses a significantly higher risk to patients and encourages judicious elective admissions. A large scale, multi-site retrospective study is recommended to consolidate the findings of this study.

BSH24-EP188 | EPIC: A non-interventional cohort study of patients with chronic lymphocytic leukaemia treated with first-line acalabrutinib

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Background: Acalabrutinib, a second-generation Bruton tyrosine kinase inhibitor (BTKi), has shown an acceptable safety profile and high response rates in clinical trials of treatment naïve patients with chronic lymphocytic leukaemia (CLL). Here we present a second interim analysis (IA) of patients with CLL who were initiated on first-line acalabrutinib within the UK Early Access Programme (EAP).

Methods: This is an ongoing observational multi-centre cohort study involving retrospective data collection from medical records (ClinicalTrials.gov: NCT05557695). Treatment-naïve patients with CLL from nine 9 UK clinical centres who initiated acalabrutinib (index) as part of the UK EAP between 1 April 2020 and 1 April 2021 were eligible to participate. For this IA, data cut-off was 31 May 2023.

Results: One hundred and one patients were included in this IA. Median (interquartile range (IQR)) age at index was 73.8 (66.1–78.4) years; 56% ($n = 57/101$) of patients were male; 89% ($n = 83/93$) of patients were White British, 6% ($n = 6/93$) were White other, 3% ($n = 3/93$) were Asian, 1% ($n = 1/93$) were Mixed ethnicity (missing data $n = 8$). Median (IQR) duration of follow-up was 32.4 (29.2–35.4) months; 89% ($n = 90/101$) of patients had follow-up ≥1 year and 84% ($n = 85/101$) ≥2 years. 88% ($n = 52/59$) of patients had an Eastern Cooperative Oncology Group performance status (PS) 0–1, 10% ($n = 6/59$) had PS of 2, 2% ($n = 1/59$) had PS of 3 (missing $n = 42$). 50% ($n = 40/80$) of patients had a creatinine clearance <60 mL/min at index. The continuation rate ($n = 100$) at 12 and 24 months was 81.0% (95% confidence interval [CI], 73.7%–89.1%) and 74.0% (95% CI, 65.9%–83.1%), respectively (1 patient not recorded). 68% ($n = 69/101$) of patients remained on treatment at the time of data cut. Of those patients reporting reasons for treatment discontinuation, 48% ($n = 15/31$) were due to adverse events (AEs; of the 14/15 patients reporting type of AEs resulting in discontinuation, 14% (2/14) was reported for each of the following AEs; cardiovascular, haematoma, headache and urinary tract infection), 6% ($n = 2/31$) due to disease progression, 3% ($n = 1/31$) due to patients' decision and 42% ($n = 13/31$) other reasons (1 unknown).

Conclusion: This IA reports 12 and 24-month real-world acalabrutinib continuation rates of 81.0% (95% CI, 73.7%–89.1%, $n = 100$) and 74.0% (95% CI, 65.9%–83.1%, $n = 100$), respectively, in treatment naïve patients with CLL in UK. These findings provide clinical decision makers with valuable insights into acalabrutinib use in the real-world as well as highlighting the importance of BTKi AE management in a real-world clinical setting. Further IAs are planned.

BSH24-EP189 | Experience of the use of belantamab mafodotin in a UK teaching hospital

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Introduction: Belantamab mafodotin (Blenrep) is an antibody-drug conjugate; a monoclonal antibody against the B-cell maturation antigen conjugated with a cytotoxic agent (microtubule inhibitor) used on a compassionate basis in the treatment of relapsed refractory multiple myeloma (RRMM) in the UK.

Methods: We present our experience of using Blenrep. As per the DREAMM2 study eligibility criteria, patients were selected to receive Blenrep based on confirmed RRMM after having received at least four previous treatments including a proteasome inhibitor (PI), immunomodulatory agent (IMID) and anti-CD38 monoclonal antibody (CD38a). In our centre, 11 patients received Blenrep between July 2022 and September 2023.

A patient pathway was devised to facilitate fewer patient visits in conjunction with ophthalmology for repeat monitoring of ocular toxicities. Ophthalmology appointments were scheduled prior to initiation and the next three doses of Blenrep and then continued as required.

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Data were gathered retrospectively from online patient clinical records, and analysed using Excel. Categorical variables are expressed as percentages and numeric variables as median with interquartile range.

Results: Our cohort of patients (45% male; median age diagnosed 70 years) received Blenrep after a median of 5 (range 4–6) former therapies, including: PI (90% bortezomib, 9% carfilzomib, 45% ixazomib), IMID (72% thalidomide, 81% lenalidomide, 72% pomalidomide) and CD38a (81% daratumumab, 18% isatuximab). Additionally, 81% had undergone an autologous stem cell transplant (SCT), 27% second autologous SCT and 27% an allogeneic SCT.

Fifty-four percent of patients achieved a partial remission (PR) within 1–3 months of commencing Blenrep with 18% then achieving a very good partial response (VGPR) in 4–6 months. Nine percent ($n = 1$) patient achieved VGPR and remains on Blenrep without any toxicity. Unfortunately, 36% ($n = 4$) were refractory, 9% ($n = 1$) progressed after initial response after 1 month.

With a median follow up of 6.7 months (range 3.5–10.6) the dose was reduced in 45% ($n = 5$), with cytopenias (60%) and ocular toxicity (40%) being the main culprit. This necessitated treatment cessation in 36% ($n = 4$) of them despite PR. The median time receiving Blenrep was 2.1 months (1.5–6.3).

Conclusion: Blenrep monotherapy can induce a fast remission and could potentially be brought forwards in the treatment algorithm for RRMM, especially with monitoring of side effects and appropriate dose reductions. Having a largely manageable side effect profile, this offers feasibility for use of Blenrep in district general hospitals, useful in patients with limited mobility. Further analysis is required to investigate the impact of Blenrep in a larger cohort of patients.

BSH24-EP190 | Venetoclax effectiveness after Bruton tyrosine kinase inhibitors in chronic lymphocytic leukaemia: An international real-world study

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Introduction: Venetoclax has demonstrated efficacy in previously untreated and relapsed/refractory chronic lymphocytic leukaemia/small lymphocytic leukaemia (CLL/SLL). However, evidence on venetoclax effectiveness following covalent Bruton tyrosine kinase inhibitors (cBTKi) is limited.

Methods: The CLL Collaborative Study of Real-World Evidence (CORE), a retrospective, international, multicenter, observational study provided data for adult CLL/SLL patients who received a venetoclax-based regimen after discontinuing a cBTKi-based regimen. Baseline characteristics at venetoclax initiation were summarised using descriptive statistics. Clinical response (physician-assessed medical charts reported overall response rate [ORR], complete or partial response [CR, PR]), time-to-next treatment/death (TTNT-D) and progression-free survival (PFS) were stratified by line of therapy (LOT; 1L → 2L and 2L → 3L) and by prior exposure to CT/CIT (2L → 3L).

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Results: Of 2020 patients, 1287 (63.7%) received a cBTKi in ≥1 LOT; 184 patients (14.3%) discontinued cBTKi (intolerance: 83 [45.1%], progression: 78 [42.4%]) and initiated venetoclax (115 monotherapy; 69 combined with rituximab/obinutuzumab). Mean age at venetoclax initiation was 68.6 (median: 68.2) and 69.0% male. Among tested patients, 41/61 (67.2%) had unmutated IGHV and 28/109 (25.7%) had del(17p)/TP53. Average follow-up time from venetoclax initiation was 19.6 months (median: 16.6).

Overall, the ORR was 78.0% (CR: 43.3%, PR: 34.6%) in patients with a documented response ($n = 127$). Median TTNT-D was 39.5 months (95% CI: 30.4, not reached [NR]) with 12- and 18-month rates of 82.3% and 72.4%. Median PFS was 43.2 months (95% CI: 31.9, NR), with 12- and 18-month rates of 82.8% and 75.1%.

Among patients who started venetoclax-based therapy post-cBTKi as 1L → 2L ($n = 65$), the ORR was 84.1% (CR: 54.5%, PR: 29.5%, [$n = 44$]). Median TTNT-D was NR (95% CI: 31.9, NR) but the 12- and 18-month rates were 85.0% and 73.9%. Median PFS was 43.2 months (95% CI: 39.5, NR) with 12- and 18-month rates of 86.4% and 81.8%.

Among patients who started venetoclax-based therapy post-cBTKi as 2L → 3L ($n = 67$), the ORR was 78.3% (CR: 41.3%, PR: 37.0%, [$n = 46$]). Median TTNT-D was 44.2 months (95% CI: 37.0, NR) with 12- and 18-month rates of 83.1% and 76.5%. Median PFS was 44.1 months (95% CI: 31.8, NR) with 12- and 18-months rates of 85.2% and 80.4%. ORR, TTNT-D, and PFS were similar for patients with/without CT/CIT exposure prior to cBTKi.

Conclusions: These results demonstrate that venetoclax is effective overall, and when used in 2L or 3L following cBTKi therapy, with/without CT/CIT exposure. As the CLL treatment paradigm continues to evolve, these results provide valuable evidence to inform modern clinical practice.

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BSH24-EP191 | Myeloma masquerading as myeloproliferative neoplasm (MPN)—A case report

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Neutrophilia is a common full blood finding, often reactive or due to myeloproliferative neoplasm (MPN). A rare cause is plasma cell disorders, which can present with neutrophilia via various mechanisms. Treatment of such presentations may require combined cytoreductive and plasma cell-directed therapies.

A 70-year-old female presented with fatigue and a profound neutrophilia (51.4×10^9/L). A blood film showed neutrophilia, left shift and toxic granulation. The lack of reactive trigger and persistence of the neutrophilia triggered urgent leukaemia clinic review and investigations.

Bone marrow was hypercellular with increased granulopoiesis with no dysplasia or excess blasts. Plasma cells were increased at 8% of nucleated cell count (NCC). Karyotype (46, XX) and molecular testing showed no evidence of BCR-ABL. NGS (next generation sequence) testing identified only a TET2 variant of unknown clinical significance. Peripheral blood was negative for JAK2 V617F, CALR and MPL mutations. Computed tomography (CT) showed borderline splenomegaly (14 cm), no lymphadenopathy or lytic lesions. ALP was 362 iu/L and LDH 279 iu/L. An IgA kappa paraprotein (13.0 g/L) was noted without background immune suppression and a kappa lambda ratio of 2.01.

Pegylated interferon (PEG-IFN) 45 µg fortnightly was given initially for an undifferentiated MPN (MPN-U) with an associated monoclonal gammopathy of undetermined significance. Due to poor tolerance, falling Hb and failure to respond, PEG-IFN had to be discontinued—Hb 89 g/L, neutrophils 59.1×10^9/L, LDH 498 iu/L ALP 533 iu/L.

A repeat bone marrow biopsy showed marked granulopoiesis and increasing number of plasma cells to 10%–15% of NCC. Paraprotein had also risen to 22.6 g/L. Positron Emission Tomography (PET)-CT showed diffuse intense FDG uptake (SUV 13.8) in the bone marrow but no lytic lesions. A multi-disciplinary decision was made to treat as myeloma with Lenalidomide and Dexamethasone, with the goal of exploiting the immunomodulatory effects to control the plasma cell load and reduce neutrophilia. After four cycles of treatment, the patient's fatigue, clinical and laboratory parameters have improved, neutrophils 9.3×10^9/L, Hb 10^9 g/L, ALP 262 iu/L, LDH 136 iu/L, paraprotein 6.6 g/L.

Neutrophilia may be the presenting abnormality in myeloma. Pathogenetic mechanisms include G-CSF secreting plasma cell clone, reaction to known myeloma-associated cytokine profile and co-existent MPN. The failure to respond to cytoreductive therapy and the prompt symptomatic, blood count and biochemical response to Lenalidomide in our case confirms the link of neutrophilia to the plasma cell clone. It would be interesting to see if future relapses, if any, will have the same findings.

BSH24-EP192 | Single-centre outcomes for high and ultra-high risk myeloma patients since the introduction of lenalidomide maintenance

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Background: Myeloma patients with high-risk (HR) and ultra-high-risk (UHR) cytogenetics remain a population of unmet need. The OPTIMUM/MUKnine trial demonstrated improved outcomes with 5-drug induction and extended consolidation for UHR patients. Myeloma XI showed

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greatest benefit from lenalidomide maintenance in patients with a single genetic abnormality and limited benefit in those with multiple genetic abnormalities or 1q gain. mSMART guidelines recommend combined proteasome inhibitor/lenalidomide maintenance in HR and UHR disease. There is therefore no consensus for optimum therapy in this subgroup and the benefit of lenalidomide maintenance in this cohort is not fully clear.

We undertook a single-centre retrospective analysis of HR and UHR MM patients treated intensively since lenalidomide maintenance received NICE approval in March 2021.

Methods: Data were collected from transplant eligible MM patients diagnosed at Nottingham City Hospital between March 2021 and September 2023 with HR or UHR cytogenetics. HR was defined by one of t(4;14), t(14;16), del(17p), gain(1q) or del(1p) with UHR carrying ≥2 markers. Time to next treatment (TTNT) was defined as time from starting initial treatment to commencing second line therapy or death.

Results: Twenty-six patients were identified with a median age of 61. Nineteen HR [2t(4;14), 1t(14;16), 5 del(17p), 10 gain(1q), 1 del(1p)] versus 7 UHR. First line regimens were 13 × DVTD, 8 × VTD, 3 × VCD, 2 × Myeloma XV. Median follow up was 19.8 months. Median TTNT was 22.6 months for the entire cohort, 22.6 months for HR versus 11 months for UHR ($p = 0.17$). Median OS was not reached for the entire cohort. Median OS in HR was not reached versus 13.4 months in UHR ($p = 0.0036$ (HR 0.08 [95% CI 0.01–0.62])). Seven of 19 HR patients progressed to next treatment, one pre ASCT, one who declined ASCT and five post ASCT. Four of seven UHR patients progressed to next treatment, all prior to ten patients thus far had commenced lenalidomide maintenance with median TTNT from starting maintenance 21.2 months.

Conclusion: This analysis confirms the poor outcomes for UHR patients in a single centre real-world setting, significantly inferior to HR patients. Progression prior to autograft and maintenance highlights that the introduction of lenalidomide maintenance alone may have minimal impact on this cohort and supports the rationale for more increased intensity induction regimens, such as that utilised in OPTIMUM/MUKnine, to be available as standard of care.

Data interpretation is limited by small sample size and does not account for cases where cytogenetic testing failed.

BSH24-EP193 | Pirtobrutinib in post-cBTKi CLL/SLL with/without prior BCL2i: Phase 1/2 BRUIN study ~30 months follow-up analysis

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Background: Covalent (c) Bruton tyrosine kinase inhibitor (BTKi) treatment of chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) is efficacious, yet relapse occurs. Sequential treatment with B-cell lymphoma 2 protein inhibitor (BCL2i) is primarily administered when progression occurs on cBTKi. Pirtobrutinib is a highly selective, non-covalent (reversible) BTKi. Here, we report updated pirtobrutinib efficacy in CLL/SLL.

Methods: Patients with pre-treated CLL/SLL received pirtobrutinib monotherapy from the multicenter Phase 1/2 BRUIN study (NCT03740529).

Results: As of 05-May-2023, among 282 post-cBTKi patients with CLL/SLL, 154 (55%) had no prior-BCL2i therapy (BCL2i-N) and 128 (45%) had (BCL2i-E); median age: 69 years (range, 36–88). Median lines of prior therapy were 4 (range, 1–11) for post-cBTKi (BCL2i-N: 3; BCL2i-E: 5). ORR for post-cBTKi patients was 72% (95% CI, 66.4–77.1); ORR including partial response with lymphocytosis (PR-L) was 82% (95% CI, 76.5–85.9) for post-cBTKi (BCL2i-N: 83.1% [95% CI, 76.2–88.7]; BCL2i-E: 79.7% [95% CI, 71.7–86.3]). Post-cBTKi patients included a 19-patient subgroup with one prior line of cBTKi therapy and second line therapy of pirtobrutinib, with ORR including PR-L (89.5% [CI 95%, 66.9–98.7]). Median DoR was 18.4 months (95% CI, 15.3–20.4) for post-cBTKi (BCL2i-N: 24.9 months [95% CI, 18.4–32.0]; BCL2i-E: 14.8 months [95% CI, 12.0–17.4]). At median follow up of 27.5 months, median PFS was 19.4 months (95% CI, 16.6–22.1) for post-cBTKi (BCL2i-N: 23.0 months [95% CI, 19.6–28.4]; BCL2i-E: 15.9 months [95% CI, 13.6–17.5]). At median follow up of 29.3 months, median OS was not estimable; the 24-month rate was 73.2% (95% CI, 67.4–78.2) for post-cBTKi (BCL2i-N: 83.1% [95% CI,75.9–88.2], BCL2i-E: 60.6% [95% CI,50.9–68.9]). In the CLL/SLL cohort ($n = 282$), predominating TEAEs were fatigue (36.9%), diarrhoea (28.4%), cough (27.3%) and contusion (26.2%). Among Grade ≥3 TEAEs, neutropenia/neutrophil count decreased (28.4%) was most frequent, hypertension (4.3%) and atrial fibrillation/flutter (1.8%) were infrequent. BCL2i-N and BCL2i-E patients exhibited similar AE profiles. Grade ≥3 neutropenia/neutrophil count decreased was higher in BCL2i-E patients (36.7% vs. 21.4%), with also higher baseline neutropenia (27.3% vs. 11.0%). TRAEs resulted in 7 (2.5%; 4 BCL2i-N, 3 BCL2i-E) patient discontinuations.

Conclusions: Pirtobrutinib maintains promising and durable efficacy in patients with post-cBTKi heavily pre-treated CLL/SLL. ORR was high with good pirtobrutinib tolerance and low discontinuation rates due to drug-related toxicity, regardless of prior BCL2i status. Overall, BCL2i-E population exhibited shorter PFS, likely due to a more heavily pretreated status. These results suggest continual BTK pathway inhibition following a cBTKi may be an important sequencing consideration in the treatment of CLL/SLL.

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BSH24-EP194 | Genomic evolution/resistance during pirtobrutinib therapy in covalent BTK-inhibitor (cBTKi) pre-treated chronic lymphocytic leukaemia patients (update)

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Background: Most patients (pts) discontinue cBTKi for progression or intolerance. BTK Cysteine 481 (C481) substitution is known to contribute to acquired resistance to cBTKi. Pirtobrutinib, a highly selective, non-covalent (reversible) BTKi has favourable oral pharmacology that enables continuous BTK inhibition throughout the daily dosing interval regardless of intrinsic rate of BTK turnover. Pirtobrutinib has demonstrated broad efficacy in pts with chronic lymphocytic leukaemia (CLL) following prior therapy, including those treated with a prior cBTKi, independent of BTK C481 mutational status (Mato et al., *NEJM*, 2023). Here we report genomic evolution in pts with CLL treated with pirtobrutinib in a larger cohort of pts with longer follow-up than previously reported.
Methods: Relapsed cBTKi pre-treated CLL pts in the phase 1/2 BRUIN trial (NCT03740529) who subsequently developed disease progression (PD) on pirtobrutinib monotherapy were included. Targeted next-generation sequencing (NGS) was centrally performed on peripheral blood mononuclear cells collected at baseline and within 4 months of PD.
Results: As of 5 May 2023, 86 cBTKi pre-treated CLL pts had paired NGS data available at baseline and pirtobrutinib PD. The median number of prior lines of therapy was 4 (range, 1–10), and 74 pts (86%) had discontinued prior cBTKi due to PD. Median time on treatment was 16 months (range, 1.2–39 months). The overall response rate (ORR), including partial response with lymphocytosis, was 83% (95% CI, 73–90). The most common baseline mutations were BTK (53%), TP53 (48%), SF3B1 (35%), ATM (23%), and NOTCH1 (20%). In 46 pts, 64 BTK mutations were detected at baseline including C481S ($n=45$), C481F/R/Y ($n=11$), and T474I/F/S ($n=6$). Among 42 pts with C481, complete clearance was observed at PD in the majority of pts (86%, 36/42, complete clearance = 55%, 23/42). In 38 (44%) pts, 52 acquired BTK mutations were detected including gatekeeper mutations (T474I/F/S/L/Y, $n=25$ in 22 pts), kinase-impaired (L528W, $n=14$ in 14 pts), C481S/R/Y ($n=6$ in 4 pts) and others. A total of 83 non-BTK acquired mutations were observed at PD in 45 pts (52%), including 14 TP53 mutations in 12 pts (14%), and 6 PLCG2 mutations in 6 pts (7%).
Conclusions: Despite this cohort representing the first relapsing CLL pts from BRUIN, and presenting with frequent baseline BTK mutations, response to pirtobrutinib was high (ORR = 83%), with some BTK C481 clearance observed. At progression, the majority of pts (56%) either acquired non-BTK mutations or did not acquire any resistance mutations in this panel, suggesting alternative resistance mechanisms.

BSH24-EP196 | Assigning disease risk in new multiple myeloma: Improving practice to prepare for risk-adaptive treatment strategies

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Background: Upfront treatment for newly diagnosed multiple myeloma (NDMM) is currently guided mainly by age and comorbidities. However, various clinical trials are exploring risk-adaptive treatment strategies, guided either by cytogenetic features at diagnosis or minimal residual disease (MRD) treatment responses. Recommendations on prognostic laboratory investigations were initially made by NICE in 2016. In 2021, BSH/UK Myeloma Forum recommended calculating R-ISS and carrying out cytogenetic analysis using interphase FISH on CD138-selected cells in all NDMM patients. In 2022, R2-ISS was validated to calculate the additive value of each single risk feature, including 1q(gain), resulting in a further refined risk stratification system dividing patients into four more balanced risk groups.
Aim: The multiple myeloma diagnostic work-up at Addenbrooke's Hospital was audited against 2021 national guidelines published by BSH/UK Myeloma Forum.
Methodology: Diagnostic data was retrospectively collected on all NDMM patients between May 2021–August 2023. This included recommended blood tests, bone marrow aspirate and trephine biopsy, immunophenotyping, FISH, and imaging (CT skeletal survey, whole body MRI and/or PET CT scans). The myeloma FISH panel [including t (11;14), t(4;14), t(14;16), del(17p), and 1q(gain)] was performed on patients <76 years with ≥5% plasma cells on immunophenotyping as per laboratory policy.
Results: Ninety NDMM patients were identified, with a median age of 76 years (range 43–96). All 90 patients had FBC,

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U&E, LFT, bone profile and 89/90 patients had serum electrophoresis, SFLC and albumin. LDH and B2M was done in 73/90 and 78/90 respectively. 83/90 patients had bone marrow biopsy done, with FISH carried out in 49/83. FISH results were unavailable in 34/83 patients (age >76 years, $n=17$; plasma cells <5%, $n=6$; both reasons, $n=10$; aspirate not available, $n=1$). In the 49 patients who had FISH cytogenetics, t(11;14) was performed in $n=47$, del(17p) in $n=46$, t(4;14) in $n=47$, t(14;16) in $n=32$, and 1q(gain) in $n=46$. 88/90 patients had at least one imaging modality performed as part of their diagnostic work-up. CT skeletal survey was the commonest imaging modality (71/90), with 11/90 patients having Whole Body MRI and 3/90 having PET-CT scan. We were able to calculate R-ISS score for 27/90 patients and R2-ISS for 39/90.

Conclusion: A gap was identified in performing some prognostic investigations including B2M, LDH and FISH. This is being addressed by modifying MDT practice to assess B2M and LDH in all patients, and changing the age and plasma cell percentage cut-offs for performing FISH.

BSH24-EP197 | Impact of obesity on melphalan dosing in myeloma patients undergoing autologous stem cell transplantation

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Background: Autologous stem cell transplantation (ASCT) with melphalan conditioning remains standard of care for suitable myeloma patients. Data is limited on melphalan dosing in obesity, with concerns these patients may be underdosed. Obesity is defined as body mass index (BMI) >30, while overweight adults have a BMI between 25 and 30. We assessed the impact of different dosing strategies on ASCT associated morbidity and mortality.

Methods: We identified 117 myeloma patients who underwent ASCT between 2021 and 2022. One patient with severe obesity (BMI >50) was excluded. We compared 4 groups; non-obese and obese groups with a body surface area (BSA) calculated according to total body weight (Non-obese TBW and Obese TBW); non-obese and obese groups with a BSA calculated according to an adapted body weight (Non-obese aBW and Obese aBW). Adapted body weight calculations were based on actual and ideal body weight (ABW and IBW) and a correction factor based on clinical choice. Outcome measures included time to engraftment, antiemetic escalation, continuous subcutaneous infusion (CSCI) use, length of admission, intensive care unit (ICU) admission and mortality. Relevant comorbidities that may impact melphalan dosing decisions were assessed.

Results: Ninety-three ($n=53/57$) of non-obese patients received melphalan dosing based on their TBW. The remainder were dosed on IBW ($n=1$), ABW ($n=2$), or a fixed BSA of 2 m^2 ($n=1$). Seventy-five percent ($n=44/59$) of obese patients were dosed based on TBW. The remainder received doses calculated by ABW ($n=13$), IBW ($n=1$) or an average of ABW and TBW ($n=1$). There was no difference in the length of admission, engraftment dates, antiemetic escalation, CSCI use and ICU admission. More detailed results will be presented at this meeting.

Discussion: More patients in the obese group received dosing based on aBW than the non-obese group. Obese patients receiving non-adjusted dosing did not experience more toxicity than those who received adjusted dosing or non-obese patients. Surrogate markers of toxicity including intensive care admission were equivalent. Transplant related mortality is low. Comorbidities appear equivalent between the groups. Comorbid patients received a reduced dose of 140 mg/m^2 melphalan, but there were no cases of dose reduction based on obesity alone.

Conclusion: We recommend obese patients (BMI <40) undergoing ASCT for multiple myeloma should receive melphalan based on their actual body weight rather than adapted body weight. Absolute dose reductions (i.e. to 140 mg/m^2) should be reserved for patients with other significant comorbidities. Melphalan dosing in severe obesity (BMI ≥40) should be based on clinical judgement.

BSH24-EP198 | Real-world experience of implementation of quadruplet chemotherapy for myeloma patients in an NHS cancer centre

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Daratumumab combined with bortezomib, thalidomide and dexamethasone (Dara-VTD) is a recently approved regimen for induction and consolidation in untreated multiple myeloma patients eligible for autologous stem cell transplant (ASCT).[1] Compared to the previously employed VTD therapy, Dara-VTD demonstrated significantly improved response and overall survival with comparable safety outcomes.[2]

We report on the experience for all consecutive patients commencing Dara-VTD as the first UK quadruplet induction therapy between February 2022 to May 2023 at Guy's cancer centre, a myeloma treatment centre. Coordinated efforts between the myeloma team and regional transplant team are crucial for timely stem cell harvest and ASCT, executed at the regional transplant centre.

Unless contraindicated, patients are advised to undergo a dental assessment and initiate zoledronic acid, at Dara-VTD initiation, in order to prevent skeletal-related events and enhance overall survival.[3]

Results: Twenty-four patients were deemed transplant eligible at the time of diagnosis, or which 22 patients were transplanted. Of these, 10 patients received additional planned chemotherapy pre-harvest (3 patients received an additional

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cycle of VTD, 7 patients received two additional cycles of VTD, pre-harvest). Three patients needed salvage chemotherapy due to disease progression pre-transplant, with DT-PACE ($n=2$) and ESHAP ($n=1$).

Following transplant, median time to bone marrow engraftment (assessed as first occurrence of peripheral blood neutrophil count greater than 1×10^9/L following stem cell return) was 14 days (IQR 1 day).

Two patients did not proceed to transplant, one due to patient choice and one due to multidisciplinary team concern re co-morbid disease.

Twelve patients did not have the dose of thalidomide escalated from 50 mg od to full dose (100 mg) after cycle 1, and seven patients had dose reductions of dexamethasone due to toxicity.

Fourteen patients (58%) commenced zoledronic acid within the first four cycles of Dara-VTD.

Conclusion: Implementing a new quadruplet regimen as standard of care for transplant eligible myeloma patients has demanded careful assessment for toxicity, as well as coordination of treatment to allow timely commencement of bisphosphonate therapy following dental review, as well as timely transition to transplantation.

BSH24-EP199 | Initial findings from a first-in-human phase 1a/b trial of NX-5948, a selective BTK degrader

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Background: Although BTK inhibitors (BTKi) are effective in B-cell malignancies, emerging BTK resistance mutations as well as potential growth-promoting kinase-independent scaffolding function of BTK, present an unmet need. NX-5948 is a novel, orally administered small molecule that induces specific BTK protein degradation by the cereblon E3 ligase.

Materials and Methods NX-5948-301 (NCT05131022) is a Phase 1, first-in-human, dose-escalation and cohort-expansion trial evaluating NX-5948 in relapsed/refractory CLL and NHL/WM. Key eligibility criteria: ≥2 prior lines; measurable disease per indication-specific response criteria; ECOG PS 0–1. Phase 1a (3 + 3 dose escalation) evaluates safety of NX-5948. Approximately 110 patients (30 in Phase 1a, 80 in Phase 1b) may be enrolled and treated until confirmed PD or unacceptable toxicity.

Results: As of 17 October 2023, 26 patients were enrolled in Phase 1a and received NX-5948 at 50 ($n=7$), 100 ($n=6$), 200 ($n=6$), 300 ($n=4$) or 450 mg ($n=3$) orally once daily. Median age was 63.5 (range 42–79) years; female/male ratio 30.8%/69.2%; ECOG PS 0/1 23.1%/76.9%; primary diagnoses were CLL ($n=7$), DLBCL ($n=7$), MCL ($n=5$), MZL ($n=3$), WM ($n=2$), FL ($n=1$), and PCNSL ($n=1$). Median no. of prior therapies was 4.0 (range 2–10). NX-5948 was well tolerated with no DLTs and no TEAEs resulting in drug discontinuation. The most common all-grade TEAEs were purpura/contusion (46.2%, all grades 1–2), thrombocytopenia (38.5%), and neutropenia (30.8%). The most common grade ≥3 TEAEs were neutropenia (19.2%), thrombocytopenia (7.7%), COVID-19 (7.7%), and pneumonia (7.7%). No atrial fibrillation/flutter or hypertension was reported. There were four related grade ≥3 TEAEs (three neutropenia, one thrombocytopenia) but no related SAEs. Median treatment duration was 2.0 (range 0.5–12.6) months. NX-5948 exhibited dose-dependent PK and a half-life of ~24 h. Rapid, robust and sustained BTK degradation was observed, regardless of absolute BTK starting level, tumour type, or dose. In the six out of seven patients with CLL, NX-5948 showed clinical benefit (three PR and three SD). In the 19 patients with NHL/WM, there were 2 PMR, 1 PR, and 3 SD; 8 patients are still on treatment.

Conclusion: Current findings in this heavily pre-treated population are encouraging and indicate that NX-5948 is safe and well tolerated and has promising clinical activity, supporting continuation of its development in CLL and NHL. NX-5948 also exhibits dose-dependent PK, resulting in rapid, robust and sustained BTK degradation.

BSH24-EP200 | Targeted use of RNA fusion panels in the diagnostic work-up of selected haematological malignancies

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Background: Chromosomal rearrangements including translocations, inversions and deletions are recurrent oncogenic drivers of haematological neoplasms. Their detection provides crucial diagnostic and prognostic information and in some cases can inform targeted therapy. Routine diagnostic work-up of haematological neoplasms traditionally

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employs FISH and G-banded karyotype as techniques to identify rearrangements, but some remain undetected using standard techniques, and subsequent analysis for fusion gene partners can be time-consuming. RNA fusion panels provide an opportunity to screen for a large number of chromosomal rearrangements in a single assay, and detect some translocations that may not be detectable using standard methods.

Aims: To assess the utility of current practice in a Specialist Integrated Haematological Malignancy Diagnostic Service (SIHMDS) of performing RNA fusion panel in the work-up of haematological neoplasms where FISH and karyotype has not detected a clear diagnostic or risk stratifying finding, or where FISH was suggestive of a possible fusion gene.

Methods: A retrospective service evaluation of 49 consecutive cases referred for RNA fusion panel testing (Illumina TruSight RNA Fusion Panel) by a regional SIHMDS between December 2021 and October 2023.

Results: The commonest indication for RNA fusion panel was acute leukaemia (AML, B-ALL, MPAL, T-ALL) or myeloid sarcoma in the absence of a clear diagnostic or risk-stratifying finding (80%).

Clinically relevant fusion genes were detected in 17/49 samples (34%). The additional information resulted in a change to diagnostic sub-classification in 8/49 (16%) of cases. Information which gave rise to a targeted therapy or alteration in management plan was detected in four cases (8%). There was detection of a new clinically actionable MRD marker in 7/49 cases (14%).

Where the underlying diagnosis was B-ALL ($n = 12$) a clinically relevant fusion gene was detected in 58% of cases. For AML or myeloid sarcoma ($n = 17$), the rate of detection was 41%. Of four cases with hyper-eosinophilia, no fusion genes were detected, and of four chronic myeloid neoplasms, a fusion was detected in one case.

The median time from request to report was 20.5 days with a range of 9–28 days.

Conclusions: Addition of an RNA fusion panel to the work-up of appropriately selected haematological neoplasms results in a high rate of detection of actionable findings in a clinically useful time-frame. It is most likely to be beneficial in work-up of acute leukaemia where standard of care testing has not detected a clear diagnostic or risk stratifying finding, or where FISH was suggestive of a possible translocation.

BSH24-EP201 | Is It A Major Or Minor Problem? Transfusion Errors In Haemopoietic Stem Cell Transplants 2011–2022

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Introduction: Serious Hazards of Transfusion (SHOT) is the UK independent haemovigilance scheme, which accepts reports on transfusion serious adverse events (SAE) and reactions (SAR). In allogeneic haemopoietic stem cell transplants (HSCT) ABO/D-mismatches may occur, thus blood components must be compatible with donor and recipient ABO/D type. Additional transfusion specific requirements apply to HSCT patients such as irradiation for prevention of graft vs host disease. Patients may require shared care and/or involvement of multidisciplinary teams for effective clinical management of the HSCT. These factors contribute to SAE, including incorrect blood component transfused (IBCT), in HSCT patients.

Methodology: IBCT errors accepted by SHOT from 2011 to 2022 involving HSCT patients were reviewed to identify trends and preventative measures.

Results: Overall, 351 errors and 154 near miss reports were reviewed, of which 70/505 (13.9%) involved paediatric patients, with no deaths or major morbidity related to the transfusion. Most errors occurred with non-urgent transfusions 248/351 (70.7%) and originated in the ward setting 235/351 (67.0%).

IBCT-wrong component transfused (WCT) errors (178/351, 50.7%) mostly occurred in the laboratory 129/178 (72.5%). Most were failure to provide the correct ABO 103/178 (57.9%) or D type 43/178 (24.2%) component. Information technology was implicated in 124/178 (69.7%) including failure to update laboratory information management systems (LIMS) and failure to heed flags/alerts in LIMS. The pre-administration checklist was used in 64/178 (36.0%) cases but failed to prevent the error.

IBCT-specific requirement not met (SRNM) errors (173/351, 49.3%) mostly originated in the clinical area 125/173 (72.3%). A lack of clear communication resulted in a failure to provide irradiated components in 115/173 (66.5%). Inappropriate use of electronic issue resulted in 8/173 (4.6%) errors.

Discussion: HSCT-related errors may under-reported, as it is difficult to identify where patients have received components of their original blood group in error. As the number of HSCT patients increase with advances in treatment options, robust systems for safe transfusion must be embedded. These include LIMS flags that are not easily overridden and clear information, communicated from the clinical area to the laboratory in a timely manner. There should be mechanisms for continuity of shared care, for example discharge communications should contain essential transfusion information and accessible across teams. All staff involved in the care of HSCT patients should be aware of the specific requirements for transfusion, and patients empowered with this information. This is of particular importance in paediatric patients, who may have other transfusion needs throughout their lifetime.

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