NCRI Advancing Cancer Research Together

NCRI Haematological Oncology Group

Annual Report 2020 - 2021

NCRI Partners

NCRI is a UK-wide partnership between research funders working together to maximise the value and benefits of cancer research for the benefit of patients and the public. A key strength of the NCRI is our broad membership with representation across both charity and government funders as well as across all four nations in the United Kingdom.

List of Appendices

NCRI Haematological Oncology Group

Annual Report 2020-21

1. Top achievements in the reporting year (up to three)

Achievement 1
Achievement 2
Achievement 3

2. Structure of the Group

3. Haematological Oncology Group & Subgroup strategies

Haematological Oncology Group.

Acute Lymphoblastic Leukaemia (ALL) Subgroup (Chair, Dr Clare Rowntree)

Achievements

Dr Tom Fox, Trainee representative for both the Haem Onc Group and the ALL Subgroup, collated the outcomes of haematology oncology patients with COVID-19 infection and this was published in the BJHaem in 2020. He is now collaborating with colleagues in Toronto to collate a larger series of patients (3500). The outcomes of these patients are due to be published in Blood 2021. Whilst this work was not outlined in our strategy for 2020-21 for obvious reasons, this data have been very valuable to UK haemato-oncologists when discussing the risks of COVID-19 infection with their patients.

After a prolonged process due to the COVID-19 pandemic, CRUK turned down the application by the ALL Subgroup for funding UKALL 15. Professor Fielding and Dr Clare Rowntree are now working with colleagues from ALL working groups across Europe as part of the European Working Group for Adult

ALL (EWALL), in partnership with industry colleagues from AMGEN, to design a multinational phase III randomised trial for patents with Ph- B-cell ALL. The aim of the group will then be to incorporate this trial proposal within a wider trial design for all adult patients with B-cell and T-cell ALL.

Professor Anthony Moorman has recently submitted a manuscript to the Journal of Clinical Oncology describing the novel risk scoring system developed from data generated by the UKALL 14 trial. Investigators from Professor Moorman's research group utilised clinical outcome data, minimal residual disease data and cytogenetic data from the UKALL 14 data set to devise a risk score - UKALL -PI – that can better define clinically meaningful risk groups to determine therapy. The aim of the Subgroup is to use this risk stratification score within UKALL 15.

ALLTogether is a multinational paediatric ALL trial that has just opened in the first site within the UK. The adult ALL group have worked with the paediatric ALL group to open this trial to adult patients up to the age of 30 years within the UK.

Dr Tobias Menne has worked with NHSE on behalf of the ALL Subgroup to enable adult patients with B-cell ALL access to Rituximab immunotherapy alongside chemotherapy as standard of care in England. This was approved by NHSE in January 2021 and is expected to significantly reduce relapse rates and improve overall survival for patients with B-cell ALL within the UK.

Dr Nick Morley has completed work with CRUK, on behalf of the ALL Subgroup, to design regimen specific SACT consent forms for patients receiving immuno-chemotherapy for de novo and relapsed / refractory ALL. This will enable patients across the UK to have equal access to information relating to toxicity of therapy at the time of consent for treatment. This work was identified by our Consumer representative on the ALL Subgroup as being a priority for patients.

The UK led EWALL ALL trial for elderly patients with Philadelphia positive ALL was adopted as a portfolio study by the NIHR CRN April 2021, and has opened in France (CI - Professor Oliver Ottman). Several UK sites are in set up and are due to open later in 2021.

We significantly increased the regular membership of the ALL Subgroup in 2021 due to the ability to hold virtual meetings since the start of the pandemic. This will be very positive for the future sustainability and succession planning of the Subgroup.

Acute Myeloid Leukaemia (AML) Subgroup (Chair, Professor Charles Craddock)

Achievements

Publication of the FIGARO trial in the Journal of Clinical Oncology (Craddock C et al J Clin Oncol 2021: 39:768-778). FIGARO is one of the largest randomised trial of reduced intensity conditioning regimens in adults allografted for AML and the only prospective analysis of the prognostic impact of pre-transplant immunophenotypically determined MRD on transplant outcome. The demonstration that the intensified FLAMSA-Bu conditioning regimen is not associated with improved transplant outcome has had an impact on global transplant practice and had substantial benefits to the NHS in terms of saved drug costs and bed days.

Opening on time of the VICTOR trial through the UK trials Acceleration Programme (TAP) network. VICTOR is the first randomised trial of venetoclax based therapy compared with intensive chemotherapy in newly diagnosed fit adults with AML and has the potential to change international practice. Despite the COVID-19 pandemic it opened in less than 12 months and the effectiveness of the TAP research network will facilitate rapid recruitment.

Effective collaboration, for the first time with the key European AML trial cooperatives, HOVON and AMLSG, to develop EVOLVE-1 a randomised trial of the impact of adding gilteritinib to venetoclax

based therapy in older adults with newly diagnosed AML. In addition to the effective development of the globally significant EVOLVE-1 trial this effective collaboration between the NCRI AML Subgroup, HOVON and AMLSG has strategic implications for the development of additional collaborative trials which are currently under discussion.

Successful delivery of the 2nd UK NCRI AML Academy in September 2020. This highly effective 36-hour format attracted more than 300 delegates who attended either virtually or in person and is in the process of being developed into a more regular interactive forum for the UK AML community

Establishment of a function AML WP Scientific Community co-chaired by Prof P Vyas and B Huntly. This inclusive meeting serves as an important forum for interaction between the UK scientific community and clinical triallists and is already serving to accelerate delivery of translational initiatives including embedded genomics and MRD studies.

Priorities and Progress

Priority 1: Run large multicentre clinical trials across the UK and with international collaborators.
The AML 18 and 19 trials continue to recruit well. AML19 has been extended with a midotarg pilot study question, funded by Pfizer, and recruitment will close at the end of October 2021. The follow on trial, AML 20, is currently under development but has been hampered by the adverse impact of the COVID-19 pandemic on the generation of Phase I/II trials.

The IMPACT trials network represents one of only two transplant trials networks in the world and recruitment to the highly original AMADEUS and COSI transplant studies addressing strategies to improve outcome in patients allografted for AML quickly re-opened to recruitment following a short COVID-19 suspension and are recruiting well. Italian sites will soon be opening to COSI and the option of opening Australian and US sites for AMADEUS is being worked up.

In response to COVID-19, the IMPACT network has been involved in opening the COVID-19 BMT trial looking at patients who have received a bone marrow transplant and develop COVID-19. An ASH abstract is planned for August 2021. The PACE study, rolled out via the TAP network, has collected a large volume of outcome data for AML patients during COVID-19.

Priority 2: Analyse treatment response in relationship to mutational profile in collaboration with the Sanger Institute.

Data from the AML 18 trial is currently being analysed to study the impact of the diagnostic mutational profile on response to distinct intensive chemotherapy modalities. In separate studies the FIGARO trial, the second largest randomised trial of reduced intensity conditioning regimens in adults allografted for AML, has permitted the first ever prospective analysis of the prognostic impact of pre-transplant immunophenotypically determined MRD on transplant outcome. These data are being built on in the currently recruiting COSI and AMADEUS trials and will represent a valuable integrated assessment of the impact of diagnostic genomics and pre-transplant MRD status on survival and relapse post-transplant.

Priority 3: Design a follow-up trial for patients not fit for intensive therapy to replace the LI-1 trials.

The LI-1 study is now closed and has recruited a total of 1070 patients, making it the largest trial of its kind globally. Two treatment arms remain open, but it is expected that all patients are likely to complete treatment by the end of 2021. The Lenalidomide and BCT 100 arms are expected to be submitted to ASH 2021. The tosedostat paper is under review with BJHaem. The Quizartinib (AC220) paper that was presented last year is under review with Blood. In addition, letters will be submitted to describe the Ganetespib. A wider paper in relation to Quality of Life (QoL) is also planned for 2021.

Following on from LI1, the EVOLVE trials are being developed in collaboration with HOVON and AMLSG. The aim is to develop a rational method of looking at venetoclax combination therapies and molecularly stratifying patients, as the Li-1 data highlighted that some patients did better than

others. The ambition is to deliver these trials on a European platform, and discussions have also been had with New Zealand and Australia. Negotiations with the relevant pharmaceutical companies are well advanced to secure drug support for EVOLVE-1 which will be a randomised trial of Ven-Aza-Gilteritinib vs Ven-Aza-Placebo for FLT-3 mutant patients, both ITD/TKD. The trial aims to be open by the end of the year 2021.

Priority 4: Develop a Subgroup structure that facilitates involvement of all who are interested in AML research including clinicians, trainees, trialists, allied professionals (including nurses and pharmacists), scientists and consumers.

Over the reporting year, the new structure of the AML Subgroup has continued to develop. Key to these changes has been the development of an underpinning Steering Committee which focuses on new trial development consistent with the policy mapped out by Professor Peter Hillmen. At the same time several empowered subcommittees designed to develop strategy in the following areas have been develop: Scientific Committee (see above), Supportive Care (led by Prof S Stanworth), Disease Relapse (led by Dr V Potter and Prof M Copland). These are already informing future trial design and have also served as important vehicles permitting a broader inclusion of younger investigators. The group continues to be well supported by patient representatives and there is an ambition to develop a Patients Day.

A key initiative has been the successful establishment of the NCRI AML Academy which in October 2020 hosted many delegates - including regional haematologists and research nurses. Attracting a range of international speakers this 24-hour meeting received excellent feedback and will be repeated annually with the next meeting scheduled to take place in Birmingham in September 2021.

Chronic Lymphocytic Leukaemia (CLL) Subgroup (Chair, Dr Anna Schuh)

The aim of the CLL Subgroup is to run a portfolio of clinical trials across the UK, ideally with international collaborators. We will continue to generate Phase II data via the TAP infrastructure and will inform our Phase III flagship study ERASE focussing on MRD 10-6 eradication after doublet therapy.

Furthermore, we aim to identify molecular signatures of (1) treatment resistance in MRD and (2) progression from high-count MBL to CLL in our experimental medicine programmes.

Achievements

The FLAIR study has successfully achieved its recruitment target despite the challenges due to the pandemic. Recruitment into the main arms is now closed, but the arm for patients with TP53 mutations remains open. The CLARITY, CLL210 and RIALTO study results have been published. Results of the CHOP-OR genomics and transcriptomics study are published in Blood. The umbrella manuscript of the CLL Genomics England Pilot has been submitted to Nature Genetics. Further analyses are planned.

Despite the COVID-19 pandemic, STELLAR and Oxplored recruited new patients, although recruitment slowed down during the lockdown.

We have a final protocol design for the new Phase 3 Study ERASE and have identified Beigene as our pharma partner.

We have also started to develop an early phase portfolio exploiting UK-based intellectual property: Maveric (Ingo Ringhausen, Cambridge), CAR-T and ROR-1 bi-specific antibodies (UCL).

We have attracted funding from Innovate UK to sequence 400 individuals (800 genomes) with pre-malignancy recruited into Oxplored to identify potential drivers of progression.

The Subgroup hosted the most successful iwCLL Workshop Edinburgh 2019 under Chairmanship of Peter Hillmen. Pete has just been appointed as the new Chair of the iwCLL following Michael Hallek. Anna Schuh was elected as one of seven females to the board of the iwCLL (n=20) in 2019.

Publications:

1. Hillmen, P., Rawstron, A. C., Brock, K., Muñoz-Vicente, S., Yates, F. J., Bishop, R., . . . Munir, T. (2019). Ibrutinib Plus Venetoclax in Relapsed/Refractory Chronic Lymphocytic Leukemia: The CLARITY Study.. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, *37*(30), 2722-2729. doi:10.1200/jco.19.00894
2. Pettitt, A. R., Jackson, R., Cicconi, S., Polydoros, F., Yap, C., Dodd, J., . . . Hillmen, P. (2020). Lenalidomide, dexamethasone and alemtuzumab or ofatumumab in high-risk chronic lymphocytic leukaemia: final results of the NCRI CLL210 trial.. *Haematologica*, *105*(12), 2868-2871. doi:10.3324/haematol.2019.230805
3. Offner, F., Robak, T., Janssens, A., Govind Babu, K., Kloczko, J., Grosicki, S., . . . Hillmen, P. (2020). A five-year follow-up of untreated patients with chronic lymphocytic leukaemia treated with ofatumumab and chlorambucil: final analysis of the Complement 1 phase 3 trial.. *British journal of haematology*, *190*(5), 736-740. doi:10.1111/bjh.16625
4. COSMIC is about to be published as a letter in BJH BJH-2021-00449.R1
5. Pettitt, a. et al (2019). brief co-administration of idelalisib may improve the long-term efficacy of frontline chemoimmunotherapy in chronic lymphocytic leukaemia: 3-year follow-up from the rialto trial. hematol oncol, 37: 217-218. https://doi.org/10.1002/hon.32_2630
6. Appleby, N., Eyre, T. A., Cabes, M., Jackson, A., Boucher, R., Yates, F., . . . Schuh, A. (2019). The STELLAR trial protocol: a prospective multicentre trial for Richter's syndrome consisting of a randomised trial investigation CHOP-R with or without acalabrutinib for newly diagnosed RS and a single-arm platform study for evaluation of novel agents in relapsed disease.. *BMC cancer*, *19*(1), 471. doi:10.1186/s12885-019-5717-y

Experimental Medicine and Correlative Science

1. Klintman, J., Appleby, N., Stamatopoulos, B., Ridout, K., Eyre, T. A., Robbe, P., . . . Schuh, A. (2020). Genomic and transcriptomic correlates of Richter's transformation in Chronic Lymphocytic Leukemia. *Blood*. doi:10.1182/blood.2020005650
2. Wojdacz, T. K., Amarasinghe, H. E., Kadalayil, L., Beattie, A., Forster, J., Blakemore, S. J., . . . Strefford, J. C. (2019). Clinical significance of DNA methylation in chronic lymphocytic leukemia patients: results from 3 UK clinical trials.. *Blood advances*, *3*(16), 2474-2481. doi:10.1182/bloodadvances.2019000237
3. Davenne, T., Klintman, J., Sharma, S., Rigby, R. E., Blest, H. T. W., Cursi, C., . . . Rehwinkel, J. (2020). SAMHD1 Limits the Efficacy of Forodesine in Leukemia by Protecting Cells against the Cytotoxicity of dGTP.. *Cell reports*, *31*(6), 107640. doi:10.1016/j.celrep.2020.107640
4. Blakemore, S. J., Clifford, R., Parker, H., Antoniou, P., Stec-Dziedzic, E., Larrayoz, M., . . . Strefford, J. C. (2020). Clinical significance of TP53, BIRC3, ATM and MAPK-ERK genes in chronic lymphocytic leukaemia: data from the randomised UK LRF CLL4 trial.. *Leukemia*, *34*(7), 1760-1774. doi:10.1038/s41375-020-0723-2
5. Catovsky D, Else M. Early clinical trials in chronic lymphocytic leukaemia in the UK. *Br J Haematol*. 2020
   https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.17159?af=R
6. Else M, Blakemore SJ, Strefford JC, Catovsky D. The association between deaths from infection and mutations of the BRAF, FBXW7, NRAS and XPO1 genes: a report from the LRF CLL4 trial. *Leukemia*. 2021
   https://www.nature.com/articles/s41375-021-01165-w
7. Abstract to EHA evaluating established prognostic factors in the ARCTIC/ADMIRE cohort, a manuscript is also being drafted.

Also, here is the complete list of 32 publications arising from the LRF CLL4 trial:

https://www.icr.ac.uk/our-research/research-divisions/division-of-molecular-pathology/lrf-cll4-trial

Challenges

The main challenge for the Subgroup has been the COVID-19 pandemic combined with a lack of funding opportunities. The CLL Subgroup met twice via ZOOM in the past year with monthly meetings by the ERASE trial management group.

COVID-19 lockdown had a disastrous impact on patients with cancer with an estimated 350,000 patients not (yet) diagnosed in 2020 alone. From a trial group perspective, the entire process from protocol design to study approval, recruitment and scientifically meaningful documentation of follow-up has been severely impacted upon with consequences that will reach far beyond the end of the pandemic.

In addition, there were many changes to the protocol designs of ERASE and STELLAR primarily because of potential pharma partners wanting to engage, but then pulling out due to acquisitions and changes in strategy that no longer included CLL as a priority disease.

Chronic Myeloid Leukaemia (CML) Subgroup (Chair, Dr Dragana Milojkovic)

Achievements

MATCHPOINT study - MAnagement of Transformed CHronic myeloid leukaemia with POnatinib and INTensive chemotherapy (MATCHPOINT) trial, to investigate PON in combination with the intensive chemotherapy regimen fludarabine, cytarabine, idarubicin and granulocyte-colony stimulating factor (FLAG-IDA) in BP-CML. Oral presentation ASH 2019; winner of the John Goldman Abstract Prize competition BSBMTCT Scientific Day 2021; manuscript submitted.

Predictive Score for Successful Treatment Free Remission in Chronic Myeloid Leukemia - centres from the NCRI Subgroup provided the validation set for the study analysis, oral presentation at ASH, submitted for review, 2021.

Launch of BSH guidelines at the annual meeting, Update - 26 July 2020. https://b-s-h.org.uk/guidelines/guidelines/guideline-on-the-diagnosis-and-management-of-chronic-myeloid-leukaemia

Progress

1. **Improve treatment outcomes and patient experience for all CML patients**

The BCSH CML guideline was published (BJHaem. 2020;191(2):171-193) and presented at the BSH 2020. Subgroup members contributed to the ELN 2020 recommendations [(Leukemia, 34, 966–984 (2020)] and participated in the European Investigators for CML (EICML). The CHOICES study was also published (Leukemia. 2020;34(7):1775-1786). The DESTINY study has advanced treatment free remission (TFR) approaches, improving TFR after TKI de-escalation. Further follow- up after EOT has been sought from all Subgroup members Nov 2020, with analysis in progress.

2. **Clinical trials (CT) portfolio in development**

The MATCHPOINT trial in CML- blast phase (BP) evaluated FLAG-IDA chemotherapy with ponatinib (PON) and has been submitted for publication. A follow-up to MATCHPOINT using asciminib (ASC) is under review (ABLATE). Recruiting CT: CALLS: NGS for BCR-ABL kinase domain mutations in CML; TASTER: (Targeting STEm cell Resistance) , adds a novel small molecule (currently tazemetostat) into standard TKI therapy for CML CP or AP with TKI resistance; study redesign requested by CRUK has been submitted. IIT in development; BOS-STOP- TFR study for bosutinib discontinuation; second line (2L) ASC after failure of 1L 2G-TKI (RASLAUST). Commercial studies (Novartis) 1L and 3L+ (failure of at least 2 TKIs). Completed studies: OPTIC: PON in TKI-resistant CML; AScemble: ASC vs bosutinib in CML post 2 TKIs; Ask4more: ASC added to imatinib (IM) vs continued IM vs switch to nilotinib in CML-CP previously treated with IM; Sun-Pharma (Vodobatinib)/K0706; a Novel TKI, for CML/ Ph+ ALL. The SPIRIT-2 study remains unpublished, due to obstacles minuted by the NCRI before, however a SPIRIT-2 sub-analysis has been published.' Additional chromosomal abnormalities at chronic myeloid leukemia diagnosis predict an increased risk of progression. Clark RE, et al. 2021 Feb 23;5(4):1102-1109).

3. **<u>MAJOR CHALLENGE;</u> Specific request for NCRI for support for resolution: SPIRIT-2, and SPIRIT-1. A serious initiative for the Subgroup to resolve on behalf of the patients and investigators.**

Despite numerous meetings with Newcastle over 18 months, the Subgroup is no further, has no access to the Spirit -2 database, and despite revisions of the manuscript, no changes have been answered or addressed. Spirit-1 remains unpublished in addition.

4. **Deliver high quality, internationally recognised translational research in CML**

UK CML Investigators remain at the forefront of translational research in CML, addressing leukaemia stem cell biology, leukaemia immunobiology and developing state-of-the-art PCR and sequencing techniques. The SPIRIT2 Biobank is a rich source of translational research articles and future presentations. Samples from both MATCHPOINT and DESTINY have been biobanked and will be essential for future translational studies. The TASTER clinical trial will deliver 3 translational work packages in addition to the clinical trial to better understand the biology of leukaemia stem cells and identifying and validate novel CML stem cell targets.

5. **Increase patient partnership through patient and carer education days**

The last meeting took place 09/2019 with around 100 CML patients and carers in attendance, was webcast live and presentations are available via the CML Support website. The 2020 patient and carer education day has been deferred until 2021.

A major advantage would be to obtain access to the Spirit-2 database with engagement of the CI, to explore data from around 800 recruited patients. **The lack of access to the SPIRIT-2 database and lack of response for manuscript queries for publication continues to be a major disadvantage to the CML Subgroup and hinders its international reputation.**

With regard to COVID-19 activities, the CML Subgroup has obtained ethics to survey the outcome of CML patients after COVID-19 infection (n= 60 patients, currently analysed) which is then reported to International Chronic Myeloid Leukemia Foundation (iCMLf) and was reported at ASH 2020: (CANDID study, 649 ww patients, 65 submitted from the UK, one of the highest European recruiters). Subgroup members combined patient data to produce a Predictive Score/on-line calculator for Successful Treatment Free Remission in CML, presented at ASH and now submitted. BOS-STOP study has obtained £300k funding from Pfizer, and CML investigators would like to participate in the study (Dr Tim Brummendhorf). Ethics has been obtained for a UK national review of named patient asciminib outcomes from the Subgroup members, who have the highest number of treated patients of study

in Europe. The UK CML registry now has ethics approval, includes paediatric CML patients- 3 centres have now engaged to enter patients; 900 patients have been recruited to date.

Priority for the forthcoming year

Publication of the Spirit-2 study and transfer of the Spirit-2 database for analysis, in addition to the Spirit-1 study. A similar study to Spirit-2 (German CML study 4) has produced in excess of 25 publications, for comparison.

Challenge

Unfortunately, lack of CI engagement requiring third party input has still not resulted in any outcome. Further request for NCRI formal investigation and support on behalf of all UK CML investigators and patients.

Myelodysplastic Syndromes (MDS) Subgroup (Chair, Dr Beth Payne)

Changes developed over the last 12 months

The Aplastic Anaemia Working Party is now led by Dr Austin Kulasekararaj following Professor Judith Marsh's retirement. The group took the opportunity to thank Judith for her huge contribution to the field of bone marrow failure over many years, furthering knowledge in the science and improving treatment outcomes. Her presence in the field will be missed but we wish her a happy and healthy retirement.

Terms of Reference document for the Senior Leadership Roles embedded into the group. This allows natural succession planning.

Election of an Executive Board with rotational lead roles – vice-chair, biobank/governance, translational science, early phase/industry trials, communications. This approach is now successfully in place and has increased focus and productivity of the Subgroup.

Appointment of an Early Career Researcher ECR) representative to the Subgroup through the NCRI ECR scheme – an ECR has been in place now for 2-3 years (extended due to the pandemic). We have developed a key competency template for future appointments. The ECR was involved in developing this. Mentoring is provided by the Chair of the MDS Subgroup and also by the investigators of a chosen trial in early development. The ECR was part of the REPAIR MDS trial development group, where they have had a very productive experience having direct input in to the trial design and helped write the patient information. The trainee was also part of a COVID-19 data collection: Impact of SARS-CoV-2 (COVID-19 infection) on UK patients. Accepted as an abstract with the BSH.

Production of a Strategy Document that engages the whole group emphasising our strengths and direction of travel with emerging themes. A thematic approach would allow us to concentrate on common areas across the disease as a whole (and allied conditions) rather than the current focus on disease subtypes. This work is ongoing.

Improvement in communication to haematologists and patients of available trials around the UK that are open and recruiting. The communications lead is responsible for uploading all relevant current trials to the UK MDS Patient Support website. A twitter account is being explored.

Stronger links with Consumers (see below; Priority areas - new workflow & Consumer activities).

Successes from the group over the last year:

Publications

1. REDDS – Red blood cell transfusion thresholds and QoL in MDS: a pilot and feasibility study. Collaboration with NHS Blood and Transplant. Dr's Stanworth, Bowen & Killick. Recruited on time. Published: Red cell transfusion in outpatients with myelodysplastic syndromes: a feasibility and exploratory randomised trial. Stanworth SJ, Killick S, et al. Br J Haematol 2020 Apr; 189(2):279-290.

2. De-Iron; A phase 2 trial of the activity and safety of Deferasirox administered at early iron loading in patients with transfusion-dependent Myelodysplastic Syndromes. Killick SB, et al. Br J Haematol 2020 Jun; 189(6):e237-e240.

3. Impact of SARS-CoV-2 (COVID-19 infection) on UK patients. Joint collaboration of NCRI MDS Subgroup and UK MDS Patient Support. Presented at the BSH annual education 2021 meeting as a poster. P Krishnamurthy, J Chawick (trainee rep), S Wintrich (UK MD Patient Support), J Hayden, M Kenyon, A Kulasekararaj, D Culligan, D Bowen & S Killick.

4. A phase 1b Study of Eltrombopag and Azacitidine in patients with high risk Myelodyspalstic syndromes. A Sternberg, R Boucher, H Coulthard, M Raghavan, D Culligan, A Jackson, C Cargo, M Dennis, M Metzner, R Moore, D Bowen, P Vyas. ASH abstract poster presentation 2020. Blood (2020) 136 (Supplement 1): 10. Manuscript close to submission.

Grants

1. REPAIR MDS – Repurposed Drugs to Improve Haematological Responses in MDS. M Raghavan (co CI), S Jenkins (co CI), C Bunce, S Killick, D Culligan, M Drayson. JP Moulton Foundation £1.1 million application successful. Blood Cancer UK. Warwick Clinical Trials Unit. This will be the first UK investigator led randomised trial run through the NCRI MDS Subgroup. Particular strengths of this application were robust feasibility input from both CIs and Consumer input in the form of face to face regional patient support groups, Survey Monkey and Face Book. The Consumer feedback helped trial design.

2. AMMO study; ASTX727 monotherapy in CMML and MDS/MPN overlap. CI Dr Dan Wiseman. Blood Cancer UK funded £300,000. TAP adopted.

Consumer activities

1. Impact of SARS-CoV-2 (COVID-19 infection) on UK patients. Joint collaboration of NCRI MDS Subgroup and UK MDS Patient Support.

2. REPAIR MDS – Repurposed Drugs to Improve Haematological Responses in MDS. Particular strengths of this application were robust feasibility Consumer input in the form of face to face regional patient support groups, Survey Monkey and Face Book. The Consumer feedback helped trial design and patient information.

3. Encouraging group members to participate as an 'expert panel' in upcoming online patient meetings, to discuss clinical trial options, research in a 30-minute slot. Overall, the Zoom meetings are well attended, and may have encouraged participation from patients from all corners of the UK.

Myeloma Subgroup (Chair, Dr Rakesh Popat)

The Myeloma Subgroup has remained active during 2020-21 and made significant progress to its aims.

Portfolio development: 2 major 1st line trials (Myeloma XIV and XV) have been designed, funded and opened to enrolment. The Myeloma XII salvage ASCT trial has been enrolling ahead of target (up to the pandemic). A multi-arm relapsed study (ProMMise) has been designed and funding agreed.

Innovation: The Myeloma XV trial has multiple "cassettes" for post ASCT consolidation built in which are adaptable. The high-risk arm has been designed to be amended as the results of the MUK9b high risk trial reports. The ProMMise trial is a "platform" trial with 3 arms for relapsed myeloma and may be amended to incorporate further arms

Efficiency and Performance: The Myeloma XII trial has enrolled 440 patients to date, ahead of target up to the pandemic, the MUK 12 phase 2 trial completed enrolment at 60 patients. The Myeloma XI trial has generated 11 high impact publications (clinical and translational) in the past year. Other trials that have also published: PADIMAC (BJH), MUK-5 (Haematologica), CARDAMON (toxicity – BJH), MUK-12 trial design (BMJ open).

Communication: The leadership team for the Subgroup have continued to interact on Teams and the Subgroup held 1 virtual meeting through the pandemic. This provided clear discussions and input to ongoing trials and developments.

Commercial Opportunities: Industry engagements continued virtually with the development of the ProMMise platform trial (GSK), the Bitten trial concept (Amgen), IMPACTal concept (Janssen). The UKMRA Myeloma XV is supported by BMS £310,270 and Sanofi £4,036,526 over a 5 year period. GSK have awarded £2.3 million for the Phase 1 ProMMise trial platform for relapsed myeloma Autolus has awarded UCL £3,223,611 over 3 years for the Phase 1 Mcarty CAR-T cell trial.

Successful Grants: Myeloma XV £191,008 (CRUK) for this reporting period (total of £1.5 million), Bloodwise £191,008 grant activated in January 2021 for associated translational work. Additional funding from Industry was secured). Successful funding from the MRC (DPFS award) was secured of £3.4 million for "Treating Multiple Myeloma and Diffuse Large B Cell Lymphoma by Targeting the NF-κB Pathway with the First-in-Class GADD45β/MKK7 Inhibitor, DTP3".

Health Technology Appraisals: The Myeloma XI trial results were used in the successful NICE appraisal of lenalidomide maintenance post ASCT.

Future Growth and Development: Each trial TMG has a new investigator, the Subgroup has continued to grow as new investigators are encouraged to join in a collaborative environment. A clear line of succession is established with the appointment of vice-chair who works closely with the Subgroup Chair. The senior leadership team has met to identify areas of trial development and investigators to take this forward.

Translational Activity: The senior leadership team has commenced the dialogue to a national co-ordinated biobank. Trial samples have been used effectively to generate key outputs. The Myeloma XI trial samples have been highly influential in understanding the prognosis of myeloma genetics.

Myeloproliferative Neoplasms (MPN) Subgroup (Chair, Dr Adam Mead)

In response to the enormous potential impact of COVID-19 for MPN patients, members of the Subgroup have led a number of different activities to inform and support the care of MPN patients through the pandemic:

- We carried out a UK-based survey of COVID-19 infection in patents with MPN. This study included 77 MPN patients with documented SARS-CoV2 infection and described that older MPN patients and those receiving ruxolitinib, might be at increased risk of adverse outcomes following COVID-19 infection. The study provided useful data to inform evidence-

based risk stratification of MPN patients with regards to risk of COVID-19 infection (Salisbury et al, Leukemia, 2021).

- We reported antibody responses following COVID-19 vaccination in MPN patients, including identification of potentially impaired immune response to vaccination in some patients Harrington et al, Leukemia, 2021 & Choudhury et al, BJH, 2021).
- We have provided treatment, shielding and vaccination guidance for patients with MPN throughout the pandemic via the MPN Voice website and carried out a number of patient webinars to make sure our patient population was kept fully up to date. For example, the MPN Voice Webinar held on 1st August 2020 was attended by 300 patients with very positive feedback.
- Clinical trial activity was necessarily delayed during the peaks of the pandemic, but nevertheless we have made important progress in our academic-led clinical trial portfolio over the past year. This phase 1 PROMise study (CI: Professor Adam Mead) opened to recruitment and as of June 2021 has recruited the first patient. This study is funded through the CRUK Combinations Alliance and is testing the safety and efficacy of combining a BET inhibitor with ruxolitinib treatment in patients with myelofibrosis. The phase 3 MITHRIDATE study: a Multicenter International sTudy comparing ruxolitinib with either HydRoxycarbamIDe or interferon Alpha as first line ThErapy for high risk polycythemia vera (CI: Professor Claire Harrison) is open to recruitment, with over 20 patients randomised as of June 2021. This is the first study of ruxolitinib as a first line treatment for PV and will recruit approximately 600 patients over five years.
- We have received funding from Celgene/BMS for the FEDORA study: A phase II study to evaluate the tolerability, safety and activity of fedratinib combined with ropeginterferon alfa-2b in patients with myelofibrosis. This is an innovative first line academic led (CI: Professor Mary-Frances McMullin) study with extensive associated biobanking.
- The results of the MOSAICC Study were published: an exploratory case-control study of polycythemia vera (PV), essential thrombocythemia (ET), and Myelofibrosis (MF). This is the largest case control study in MPNs to date and confirms the previously reported associations with obesity and cigarette smoking from cohort studies in addition to novel associations (Duncombe et al, Hemasphere, 2020)
- We have submitted a BSH Good Practice Paper on “The use genetic tests to diagnose and manage patients with myeloproliferative and myeloproliferative/myelodysplastic neoplasms, and related disorders” to help provide guidance on the appropriate use of genetic tests in MPN patients

4. Cross-cutting research

5. Funding applications in last year

Table 1 Funding submissions in the reporting year

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
Cancer Research UK*					
March 2021					
Evaluation of key Biomarkers for the prediction of successful treatment-free remission (TFR) in chronic myeloid leukaemia	Biomarker Project Award	Professor Mhairi Copland	Conditionally Supported		
December 2020					
AML Follow Up	Clinical Trial Award - Extension (May2020)	Professor Nigel Russell	Supported		
EWALL-PH-03: An open label, 3-arm, Randomised phase II study to Compare the Safety and Efficacy of Ponatinib in combination with either Chemotherapy or Blinatumomab with Imatinib plus Chemotherapy as front-line therapy for patients aged 55 years and over with Philadelphia chromosome positive ALL	Endorsement (May2020)	Professor Oliver Ottmann	Preliminary		
Other committees**					
Study	**Committee & application type**	**CI**	**Outcome**	**Level of Group input**	**Funding amount**

**CRUK CRC applications for table 1 completed by NCRI Executive.*
***Other applications in the table to be completed by Group Chair*

6. Consumer involvement

Gillian Murphy

Prior to this reporting period, Consumer Member Alan Chant stepped down from the Research Group, the Myeloma Subgroup, and as an NCRI Trustee. We thank Alan for his long-standing involvement with the NCRI and Consumer Forum and commend his outstanding impact as a patient representative. He continues as a Trustee for Myeloma UK and lay representative for the Oxford Biomedical Research Centre amongst other roles.

Consumer Member Gillian Murphy has continued her active involvement with the Research Group and ALL Subgroup. Gillian participated in Group meetings, with an emphasis this year on highlighting blood cancer patients' concerns regarding COVID-19 (including shielding, access to treatment, impact of pausing clinical trials and vaccination efficacy). Gillian has consistently raised awareness of these issues via Blood Cancer UK's Policy Panel, the All Party Parliamentary Group on Blood Cancers and the NHS Cancer Programme Patient and Public Voice Forum. She was invited to join the Blood Cancer UK Vaccination Task Force and the British Society for Bone Marrow Transplantation and Cellular Therapies Subcommittee on Vaccinations (BSBMTCT). In addition, Gillian's input ensured that the recovery of cancer clinical trials was included in NHS England's coronavirus Cancer Services Recovery Plan after noting that clinical research was not featured in the draft plan.

Gillian has strengthened her close links with NCRI Partner Blood Cancer UK, contributing to a new Research Strategy (in preparation); producing a blog in response to a high level of interest in patient involvement which was generated by the charity's research priority setting survey (https://bloodcancer.org.uk/news/how-can-i-get-involved-in-blood-cancer-research/), and inputting into the development of the Clinical Trials Support Service. Her involvement with Anthony Nolan includes participation in the newly formed Policy Insights Panel and providing patient insight to the Late Effects Practice Guidelines group. To increase awareness of patient and public involvement in laboratory-based research, Gillian co-developed an online training workshop for early-career researchers at UCL. Gillian is currently a member of two TMGs (ToTEM, CAROUSEL).

The Research Group benefits from experienced Consumer Members on its seven Subgroups, all having close links with patient organisations. Sandy Craine (CML Subgroup) is co-founder and Director of CML Support and Alisia O'Sullivan (MPN Subgroup) has links with MPN Voice. Nick York (Advocacy Officer, Leukaemia Care), David Innes and Garry Bisshopp (both CLL Support Association) are Consumer Members for the CLL Subgroup. Nick is a TMG member for the OXPLORED study. Sophie Wintrich (MDS Subgroup and Chief Executive of MDS UK Patient Support Group) is involved with the REPAIR MDS trial.

Gillian (ALL Subgroup) was a co-applicant on the recent UKALL15 trial application and her Subgroup involvement has been noted by British Society of Haematology President, Professor Adele Fielding (https://onlinelibrary.wiley.com/doi/10.1111/bjh.17166). Gillian also contributed to Subgroup member Dr Tobias Menne's successful appeal for NHS England approval of rituximab for adult ALL patients. Jane Leahy and Richard Castle (AML Subgroup) are Blood Cancer UK Ambassadors. Jane has been contributing to lay summary of results for the AML17 trial and to the development of a study looking at deprivation geography in relation to AML outcomes. Richard has reviewed trial consent forms, requesting that fertility preservation considerations be included. Jane and recently recruited NCRI Consumer Forum member, Anna Mamwell, are members of the VICTOR TMG.

Richard, Jane, Anna, Gillian (co-opted from the ALL Subgroup) and other patient representatives are members of a PPI group working with the LWBC-aligned NCRI AML Supportive Care/Transfusion Working Party (https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.16708), contributing views to research projects on infections (faecal transplantation to restore the microbiome post-treatment) and fatigue. To address issues of fatigue, Anna and Gillian (plus two PPI group members) worked alongside researchers to develop a proposal for a randomised pre-

habilitation study (PROPEL, submitted March 2021), changing the intervention timings and guiding the level of support for patients in the control arm. Anna is a co-applicant and Gillian a collaborator for PROPEL.

Following a highly competitive recruitment round, we welcome Marie Sams and Franko Kowalczuk as new Consumer Members for the Research Group (to be mentored by Gillian). We also welcome Sally Jeans to the Myeloma Subgroup, with Anna Mamwell, Elizabeth Dean and Andy Deutsch joining the Consumer Forum. Consumer involvement within the Research Group is extensive and we look forward to opportunities to expand upon existing networking activities, including virtual meetings with all Haematological Oncology Consumers.

Consumer representatives Marie Sams and Franko Kowalczuk were newly appointed to the Haematological Oncology Group this year and therefore were not asked to provide a report.

Nick York and Garry Bisshopp (CLL Subgroup Consumers)

The past year has been very difficult for patient groups due to a total absence of face-to-face meetings in order to comply with COVID-19 restrictions. As a patient I have been further hampered by having to 'shield'.

However, the enhanced digital connection between the CLL Subgroup, patient groups and patients are what has helped to facilitate the extraordinary amount of focussed support delivered to patients at a time of absolute uncertainty at times.

For example, one of the upsides of these restrictions has been the uptake of **Webinars by the CLL Support Association (CLLSA) and Leukaemia Care (LC).** These have enabled a larger audience both in numbers and geographically. Most CLLSA and LC webinars have been supported by speakers from this Subgroup. These were:

- **April 2020, Webinar:** 'Coronavirus and chronic lymphocytic leukaemia (CLL)' Shielding guidance and support, how COVID-19 is affecting the lives of chronic lymphocytic leukaemia (CLL) patients - Professor Chris Fegan, University Hospital of Wales,
- **May 2020, Webinar:** 'CLL and COVID-19 shielding update' - Dr Piers Patten, Consultant Haematologist and Honorary Senior Lecturer, King's College Hospital NHS Foundation Trust
- **Jun 2020, Webinar:** 'CLL treatments and trials available pre-COVID; how COVID-19 has affected hospitals; shielding, risks and immunity' - Prof. Peter Hillmen, Consultant in Clinical Haematology at Leeds Teaching Hospitals NHS Trust
- **Jun 2020, Webinar:** 'Shielding in England an update and Q&A for blood cancer patients' – for CLL - Dr. Renata Walewska, Consultant Haematologist, Royal Bournemouth Hospital, Chair UK CLL Forum.
- **Jun 2020, Webinar:** 'Shielding in Wales an update and Q&A for blood cancer patients' – for CLL - Dr Nilima Parry – Jones consultant haematologist and MDT Chair Aneurin Bevan University Health Board.
- **Jun 2020, Webinar:** 'CLL treatment – a changing landscape' - Professor Anna Schuh, consultant haematologist, Chair of the NCRI CLL clinical research group and Director of Molecular Diagnostics at Oxford University; Dr David Allsup, Senior Lecturer in Haematology and CLL lead at Queens Centre for Oncology and Haematology at Castle Hill Hospital, Hull
- **Jul 2020, Webinar:** 'CLL in the time of COVID' - Dr Ben Kennedy, Consultant Haematologist, Leicester Royal Infirmary
- **Aug 2020, Webinar:** 'Navigating changes as shielding pauses' – For CLL - Professor Chris Fegan, University Hospital of Wales,

- **Sep 2020 Webinar:** 'Management of CLL Patients in a District General Hospital Setting' - Dr Satarupa Chaudhuri, Consultant Haematologist BSH Regional Education Lead Cancer Lead Haematology (PAT) Teen age and Young adult Cancer Lead (PAT), Royal Oldham Hospital
- **Oct 2020, Webinar: '**CLL in a time of Pandemic' - Dr Samir Agrawal, Senior Lecturer in Haematology at the Queen Mary University of London and a Consultant Haemato-Oncologist at St Bartholomew's Hospitals and The Barts Health NHS Trust, London
- **Nov 2020, Webinar:** 'Trials in CLL. A Treating Doctor's Perspective' - Prof. Adrian Bloor, Clinical Director of Haematology at Manchester University.
- **Nov 2020, Webinar:** 'Immunisations and living with the challenges of a compromised immune system' – Professor Guy Pratt, Consultant Haematologist, University Hospitals Birmingham NHS Foundation Trust & Dr Helen Parry, Clinical lecturer in Haematology Institute of Immunology and Immunotherapy, NIHR Clinical Lecturer. University of Birmingham and Queen Elizabeth Hospital, Birmingham
- **Dec 2020, Webinar:** 'COVID-19 Vaccine Update' - Dr. Renata Walewska, Consultant Haematologist, Royal Bournemouth Hospital - Prof. Saul Faust, Professor of paediatric immunology and infectious diseases, Director, NIHR Southampton Clinical Research Facility, Clinical Director, Wessex NIHR Clinical Research Network
- **Jan 2021, Webinar:** 'Looking Forward with CLL/SLL: Time to think about Early Stage Disease' - Dr Niamh Appleby, haematologist and researcher at the Oxford University Molecular Diagnostics
- **Feb 2021, Webinar:** 'Living well with CLL' - Professor Chris Fegan, University Hospital Wales
- **Mar 2021, Webinar:** 'Living well on active monitoring' – For CLL- Dr Chris Fox, Consultant Haematologist at Nottingham University Hospitals NHS Trust.
- **Mar 2021, Webinar:** ''Where next for treatment in CLL/SLL?' - Prof. Peter Hillmen, Consultant in Clinical Haematology at Leeds Teaching Hospitals NHS Trust
- **Mar 2021, Webinar:** 'Next steps with shielding and vaccination for COVID-19' - Professor Paul Moss, Institute of Immunology and Immunotherapy, Deputy Head of College of Medical and Dental Sciences, Professor of Haematology at Birmingham University & Professor Chris Fegan, University Hospital Wales

Also Confirmed:

- **Apr 22 2021, Webinar:** 'How genetics may have influenced your CLL/SLL' - Dr David Allsup, senior lecturer in haematology in the Hull York Medical School and honorary NHS consultant in haematology at the Hull University Teaching Hospital Trust - Prof. James Allan, Professor of Cancer Genetics, Newcastle University Reporting on this paper:
- **Apr 26 2021, Webinar:** 'CLL first-line treatments update'- Professor George Follows, Consultant Haematologist at Cambridge University Hospitals Trust
- **Apr 28 2021, Webinar: '**Autoimmune complications of CLL' with Dr. Helen Marr, Consultant Haematologist, Freeman Hospital, Newcastle on Tyne.
- **May 5 2021, Webinar: '** CLL second-line and subsequent treatments update' - Dr Tahla Munir, Consultant in Clinical Haematology at Leeds Teaching Hospitals NHS Trust.
- **Jun 9 2021, Webinar:** with Dr. Renata Walewska, Consultant Haematologist, Royal Bournemouth Hospital, Chair UK CLL Forum.
- Leukaemia Care have also provided webinars supported by speakers from this Subgroup. *(Nick will be able to comment on these.)*

NCRI Trial Information for Patients: We have continued to update the NCRI trials Portfolio and post to both the CLLSA and LC websites. I acknowledge the help from Dr S Iyengar in checking these updates.

NCRI PPI trial patient representatives are now invited to join the Subgroup meetings to report about trials: Marc Auckland, Jackie Martin, Nick York

Collaborative Consumer Survey between the UKCLL Forum, CLL Support and Leukaemia (Prof Chris Fegan, Dr Renata Walenska, Marc Aukland, Nick York): Its aim was to gain understanding of the impact on patients of COVID-19 infection, pandemic restrictions, and their needs in the community during 2020/21. This has helped shape services and priorities to respond quickly to support information needs of patients appropriately. Part of the webinar series has also been to keep patients informed as more is known and service provision and guidelines changed during 2020/21. The scale and level of patient engagement was astounding; nearly 5000 CLL patient responses were received across 5 surveys across 2020/21.

The pandemic outcome of increased digital connection between Consumers, PPI trial reps, and the clinical research community has resulted in some very positive development and collaboration. An example has been working through trial transitions and developments during 2020. Particularly the FLAIR end for patients as they reach 6 years and delays in STATIC commencing. Regular updates to the patient community and clinical community have reduced the negative impact of delays in patients transitioning. Also, the increased individual trial PPI involvement in the meetings is aiding to extend resources of PPI representation and improve communication lines. I have myself been able to become more involved in providing PPI support to engage patients with several developing NCRI studies with Study group members.
It is very reassuring to see the hard work of the group to bring a new trials portfolio together has taken shape and PPI involvement is growing.

7. Collaborative partnership studies with industry

8. Priorities and challenges for the forthcoming year

Priority
Challenge

Professor Peter Hillmen (Haematological Oncology Group Chair)

Appendix 1

Membership of the Haematological Oncology Group

Name	Specialism	Location
Dr Lesley Anderson	Chair in Health Data Science	Aberdeen
Dr Gillian Murphy	Consumer	Surrey
Mr Franko Kowalczuk	Consumer	London
Mrs Marie Sams	Consumer	Coventry
Professor Charles Craddock	Haematologist	Birmingham
Dr Rakesh Popat	Haematologist	London
Dr Thomas Fox*	Haematologist	London
Professor Peter Hillmen (Chair)	Haematologist	Leeds
Dr James Cavet	Haematologist	London
Professor Oliver Ottmann	Haematologist	Cardiff
Dr Gillian Horne*	Haematologist	Glasgow
Dr Beth Payne	Haematologist	London
Dr Ram Malladi	Haematologist	Cambridge
Professor Adam Mead	Haematologist	Oxford
Dr Dragana Milojkovic	Haematologist	London
Professor Stephen O'Brien	Haematologist	Newcastle
Dr Clare Rowntree	Haematologist	Cardiff
Dr Anna Schuh	Haematologist	Oxford
Dr Simon Stanworth	Haematologist	Oxford
Dr Simon Watt	Haematologist	Manchester
Professor Kwee Yong	Haematologist	London
Ms Lavinia Davey	Nurse	Canterbury
Ms Amy Kirwood	Statistician	London

Consumer Representation

Name	Location
Dr Gillian Murphy	Surrey
Mr Franko Kowalczuk	London
Mrs Marie Sams	Coventry

Trainee Members

Name	Specialism	Location
Dr Thomas Fox	Haematologist	London
Dr Gillian Horne	Haematologist	Glasgow

Membership of the Subgroups

Acute Lymphoblastic Leukaemia (ALL) Subgroup		
Name	**Specialism**	**Location**
Dr Rachael Hough**	Clinical Oncologist	London
Dr Gillian Murphy	Consumer	Surrey
Professor Anthony Moorman	Epidemiologist	
Dr Thomas Fox*	Haematologist	London
Dr Clare Rowntree (Chair)	Haematologist	Cardiff
Dr Andrew McMillan	Haematologist	Nottingham
Professor David Marks	Haematologist	Bristol
Dr Nicholas Morley	Haematologist	Sheffield
Dr Tobias Menne	Haematologist	Newcastle
Professor Oliver Ottmann	Haematologist	Cardiff
Dr Bela Wrench	Haematologist	London
Ms Amy Kirkwood	Statistician	London
Ram Malladi	Haematologist	Manchester
Lindsay George	Haematologist	Birmingham
David Burns	Haematologist	Birmingham
Annie Latif	Haematologist	Glasgow
Richard Kelly	Haematologist	Leeds
Laura Clifton-Hadley	Senior Trials Manager	London
Tom Creasey	Haematologist	Newcastle
Michelle Lannon	Haematologist	Newcastle
Amit Patel	Haematologist	Cambridge
Anna Castleton	Haematologist	Manchester
Debbie Yallop	Haematologist	London
Sridhar Chaganti	Haematologist	Birmingham

Acute Myeloid Leukaemia (AML) Subgroup		
Name	**Specialism**	**Location**
Dr Harpreet Kaur**	Consultant Haematologist	Sheffield
Dr Panos Kottaridis**	Consultant Haematologist	London
Mr Richard Castle**	Consumer	
Dr Sahra Ali**	Haematologist	Hull
Professor David Bowen	Haematologist	Leeds
Dr Jamie Cavenagh**	Haematologist	London
Professor Richard Clark**	Haematologist	Liverpool
Professor Mhari Copland**	Haematologist	Glasgow
Dr Dominic Culligan	Haematologist	Aberdeen
Professor Charles Craddock (Chair)	Haematologist	Birmingham
Dr Mike Dennis	Haematologist	Manchester
Dr Panos Kottaridis	Haematologist	London
Dr Sylvie Freeman	Haematologist	Birmingham
Dr Ann Hunter**	Haematologist	Leicester

Dr Brian Huntly**	Haematologist	Cambridge
Dr Gail Jones	Haematologist	Newcastle
Professor Asim Khwaja**	Haematologist	London
Dr Steven Knapper	Haematologist	Cardiff
Professor Mary McMullin	Haematologist	Belfast
Dr Frank Mussai**	Haematologist	Birmingham
Dr Paresh Vyas**	Haematologist	Oxford
Dr Robert Lown	Haemato-Oncologist	Southampton
Dr Priyanka Mehta**	Haemato-Oncologist	Bristol
Ms Shamyla Siddique**	Senior Trials Coordinator	Birmingham

Chronic Lymphocytic Leukaemia (CLL) Subgroup		
Name	**Specialism**	**Location**
Mr Garry Bisshopp	Consumer	Sussex
Mr Nick York**	Consumer	
Dr Ingo Ringshausen	Clinical Research Fellow	Cambridge
Dr David Allsup	Haematologist	Hull
Dr Adrian Bloor	Haematologist	Manchester
Dr Chris Fegan	Haematologist	Cardiff
Dr Shankara Paneesha	Haematologist	Birmingham
Dr Francesco Forconi	Haematologist	Southampton
Dr Toby Eyre	Haematology	Oxford
Dr Parag Jasani**	Haematologist	London
Dr Renata Walewska	Haematologist	Bournemouth
Dr Helen McCarthy	Haematologist	Bournemouth
Dr Chris Fox	Haematologist	Nottingham
Dr Satyen Gohil	Haematologist	London
Dr Piers Patten	Haematologist	London
Dr Alison McCaig	Haematologist	Glasgow
Dr Dima El-Sharkawi**	Haematologist	London
Dr Nicolas Martinez**	Haematologist	Nottingham
Dr Claire Hutchinson	Haematologist	Plymouth
Professor Peter Hillmen**	Haematologist	Leeds
Dr Rosalynd Johnston	Haematologist	Sussex
Dr Helen Marr	Haematologist	Newcastle
Dr Kate Cwynarski	Haematologist	London
Dr Claire Roddie	Haematologist	London
Dr Scott Marshall	Haematologist	Sunderland
Dr Murali Kesavan	Haematologist	Oxford
Dr Talha Munir	Haematologist	Leeds
Professor Daniel Catovsky	Haematologist	London
Dr Sunil Lyengar	Haematologist	London
Dr George Follows	Haematologist	Cambridge

Professor Andrew Pettitt	Haematologist	Liverpool
Dr Christopher Pocock**	Haematologist	Canterbury
Professor Stephen Devereux	Haematologist	London
Dr Guy Pratt**	Haematologist	Birmingham
Dr Anna Schuh (Chair)	Haematologist	Oxford
Dr Ben Kennedy	Haemato-Oncologist	Leicester
Professor Martin Dyer	Haemato-Oncologist	London
Mr Marc Auckland	Patient Representative	London
Ms Jackie Martin	Patient Representative	Midlands
Mr David Innes	Patient Representative	
Ms Lelia Duley	Patient Representative	Nottinghamshire
Dr Chris Pepper	Scientist	Cardiff
Professor Tatjana Stankovic	Scientist	Birmingham
Professor Richard Houlston	Scientist	London
Professor Jonathan Strefford	Scientist	Southampton
Dr Melanie Oats	Senior Biobank Manager	Liverpool

Chronic Myeloid Leukaemia (CML) Subgroup		
Name	**Specialism**	**Location**
Ms Sandy Crane	Consumer	London
Dr Jenny Bryne	Haematologist	Nottingham
Dr Joanne Ewing	Haematologist	Birmingham
Dr Andrew Virchis**	Haematologist	London
Dr Kate Rothwell**	Haematologist	Huddersfield
Professor Oliver Ottmann**	Haematologist	Cardiff
Professor Richard Clark	Haematologist	Liverpool
Professor Mhairi Copland**	Haematologist	Glasgow
Dr Dragana Milojkovic (Chair)	Haematologist	London
Professor Jane Apperley**	Haematologist	London
Dr Seonaid Pye**	Haematologist	Southampton
Dr Paolo Gallipoli	Haematologist	Cambridge
Dr Andrew Goringe	Haematologist	Cardiff
Dr Brian Huntly	Haematologist	Cambridge
Professor Stephen O'Brien	Haematologist	Newcastle
Dr Anupama Rao**	Paediatric Haematologist	London

Myelodysplastic Syndromes (MDS) Subgroup		
Name	**Specialism**	**Location**
Ms Sophie Wintrich**	Consumer	London
Professor David Bowen	Haematologist	Leeds
Dr Catherine Cargo	Haematologist	Leeds
Dr Beth Payne (Chair)	Haematologist	London
Dr John Chadwick	Haematologist	Manchester
Professor Jamie Cavenagh**	Haematologist	London
Dr Tim Chevassut**	Haematologist	Brighton
Dr Daniel Wiseman	Haematologist	Manchester

Dr Dominic Culligan	Haematologist	Aberdeen
Professor Ghulam Mufti**	Haematologist	London
Dr Simone Green**	Haematologist	Hull
Dr Wendy Ingram	Haematologist	Cardiff
Dr Harpreet Kaur**	Haematologist	Sheffield
Dr Sally Killick	Haematologist	Bournemouth
Dr Austin Kulasekararaj**	Haematologist	London
Professor Judith Marsh**	Haematologist	London
Dr Juliet Mills	Haematologist	Worcester
Professor Ken Mills**	Haematologist	Belfast
Dr Jane Parker	Haematologist	Northampton
Dr Manoj Raghavan	Haematologist	Birmingham
Dr Kavita Raj**	Haematologist	London
Dr Mark Drummond**	Haematologist	Glasgow
Dr Paresh Vyas**	Haematologist	Oxford
Dr Alexander Sternberg	Haematologist	Swindon
Dr Christopher Dalley**	Haemato-Oncologist	Brighton
Dr Priyanka Mehta**	Haemato-Oncologist	Bristol
Ms Rebecca Bishop**	Senior Trial Coordinator	Birmingham
Dr Rachel Blundred**	Senior Trial Coordinator	Birmingham
Ms Aimie Houlton	Statistician	Birmingham

Myeloma Subgroup		
Name	**Specialism**	**Location**
Ms Clare Shaw**	Clinical Trials Network Manager	London
Mrs Sally Jeans	Consumer	Birkshire
Dr John Ashcroft**	Haematologist	Yorkshire
Dr Holger Auner**	Haematologist	London
Dr Supratik Basu**	Haematologist	Wolverhampton
Dr Reuben Benjamin**	Haematologist	London
Dr Jenny Bird	Haematologist	Bristol
Dr Stella Bowcock**	Haematologist	London
Professor Jamie Cavenagh**	Haematologist	London
Dr Andy Chantry	Haematologist	Sheffield
Dr Mike Chapman**	Haematologist	Cambridge
Dr Shirley D'sa**	Haematologist	London
Dr Hannah Hunter**	Haematologist	Plymouth
Dr Matthew Jenner	Haematologist	Southampton
Dr Martin Kaiser**	Haematologist	London
Dr Kamaraj Karunanithi**	Haematologist	Stafford
Dr Bhuvan Kishore**	Haematologist	Birmingham
Dr Ceri Marrin**	Haematologist	Cardiff
Professor Atul Mehta**	Haematologist	London
Dr Kim Orchard**	Haematologist	Southampton
Dr Roger Owen **	Haematologist	Leeds

Dr Rakesh Popat (Chair)	Haematologist	London
Dr Guy Pratt	Haematologist	Birmingham
Dr Neil Rabin**	Haematologist	London
Dr Karthik Ramasamy	Haematologist	Oxford
Professor Steve Schey**	Haematologist	London
Professor John Snowden**	Haematologist	Sheffield
Dr Richard Soutar**	Haematologist	Glasgow
Dr Matthew Streetly**	Haematologist	London
Dr Jane Tighe**	Haematologist	Aberdeen
Dr Cathy Williams**	Haematologist	Nottingham
Professor Kwee Yong**	Haematologist	London
Dr Charles Crawley**	Haemato-Oncologist	Cambridge
Professor Mark Drayson	Immunologist	Birmingham
Ms Monica Morris**	Myeloma UK Representative	London
Mr Eric Low**	Myeloma UK Representative	London
Dr Sarah Brown	Statistician	Leeds
Professor Walter Gregory**	Statistician	Leeds
Ms Wendy Notowicz**	UK Myeloma Forum Representative	

Myeloproliferative Neoplasms (MPN) Subgroup		
Name	**Specialism**	**Location**
Ms Alisia O'Sullivan**	Consumer	London
Mr Tim Somervaille**	CRUK Representative	Manchester
Dr Sahra Ali	Haematologist	Hull
Dr Joanna Baxter**	Scientist	Cambridge
Dr Nauman Butt	Haematologist	Liverpool
Dr Catherine Cargo**	Haematologist	Leeds
Professor Ciro Rinaldi**	Haematologist	Lincolnshire
Dr Eibjilin Conneally**	Haematologist	London
Professor Nick Cross**	Scientist	Southampton
Dr Mark Drummond	Haematologist	Glasgow
Dr Andrew Duncombe	Haematologist	Southampton
Dr Joanne Ewing	Haematologist	Birmingham
Ms Sonia Fox**	Senior Trials Coordinator	Birmingham
Dr Sebastian Francis**	Haematologist	Sheffield
Dr Anna Godfrey**	Haematologist	Cambridge
Dr Jennifer O'Sullivan*	Haematologist	Oxford
Professor Claire Harrison	Haematologist	London
Dr Clodagh Keohane**	Haematologist	Cork
Dr Stephen Knapper	Haematologist	Cardiff
Dr Jonathan Lambert**	Haematologist	London
Dr Donal McLornan**	Haematologist	London

Professor Mary McMullin	Haematologist	Belfast
Dr Adam Mead (Chair)	Haematologist	Oxford
Dr Dragana Milojkovic**	Haematologist	London
Dr Jyoti Nangalia	Haematologist	Cambridge
Dr Rebecca Frewin**	Haematologist	Gloucestershire
Dr Deepti Radia **	Haematologist	London
Dr Shekouhi Satareh**	Haematologist	London
Dr Mallika Sekhar**	Haematologist	London
Dr Frances Wadelin	Haematologist	Nottingham
Dr Jonathan Wallis**	Haematologist	Newcastle
Ms Louise Wallis**	Research Nurse	Bournemouth
Ms Claire Woodley**	Research Nurse	London
Ms Shamyla Siddique**	Senior Trials Coordinator	Birmingham
Mrs Sonia Fox**	TAP Trials Team Leader	Birmingham

* denotes trainee member
**denotes non-core member

Appendix 2

Haematological Oncology Group & Subgroup Strategies - 2018

A – Haematological Oncology Group Strategy

The Haematological Oncology Group was originally established through the merging of several independent MRC Working Groups which became Subgroups under the new NCRI structure. Although the WGs were individually successful, the establishment of a parent Group created an opportunity to consider research priorities in a more holistic way, identify common objectives and share best practice. This resulted in the development and delivery of a new generation of cutting-edge studies. Owing to the accessibility of fresh tumour material, haematological oncology has always led the way in molecular stratification, and the advent of new technologies, coupled with the development of highly targeted therapies, now presents an opportunity for haematological oncology be at the vanguard of the development of precision medicine in cancer.

Scientific strategy
The Groups's overall scientific strategy is to improve the objective and patient-reported outcome of haematological cancers through the development and evaluation of stratified and/or response-adapted approaches to therapy based on predictive biomarkers and sensitive quantification of residual tumour burden, coupled with the optimisation of supportive care and of recognition and management of late effects. At the core of this strategy is the need for innovative trial design, coupled with high-quality biobanking as a platform for biomarker discovery/development and the identification of new drug targets. It is crucial to ensure optimal connectivity between clinical research and basic/ translational science in order to produce the strongest possible funding applications. It is also important to ensure seamless connectivity between the Group's early-phase clinical research and late-phase trials to ensure that the early-phase trials have an explicit purpose within the portfolio and that preliminary observations of interest are subjected to definitive testing in the most efficient way possible.

<u>Priority areas for clinical research</u>
The Group aims to maintain a balanced and continuously replenishing portfolio of academic and industry studies in all major disease areas, using data from the Group's early-phase trial programmes to inform on the next generation of phase III studies. In addition to the 7 disease specific Subgroups the Group has established a Working Party to develop research proposals in Aplastic Anaemia. The Group aims to apply a more co-ordinated approach to transplant studies by working more closely with the BSBMT and establish closer collaborative links with the CCL and TYA Group's to ensure an optimally co-ordinated approach for all TYA patients with leukaemia.

Biobanking and translational research
Precision medicine requires the identification of molecularly defined patient subgroups who are likely to benefit from specific, targeted therapies. This, in turn, requires the identification of new drug targets and the development of predictive biomarkers. Samples obtained from patients recruited into clinical trials provide an ideal – and in many cases unique - resource for such translational research, and one of the Group's priorities is to ensure that all of its major studies are supported by high-quality biobanking coupled with a comprehensive and co-ordinated programme of correlative science employing cutting-edge technologies. It is equally important that information generated from laboratory research programmes is used to inform on the design of new clinical trials.

Engagement with industry

Industry engagement is of fundamental importance to the Group owing to the need to investigate new drugs that are not available through the NHS. Pharma companies may also provide a potential source of funding for trial coordination, biobanking and correlative science. The Group's relationship with industry has evolved in an organic fashion through the endeavours of individuals to develop clinical trials and is, for the most part, excellent. It is, however, crucial that all proposals for new industry-sponsored studies are discussed with the Group in order to plan the portfolio and minimise competition for niche study populations.
Engagement with charity-funded research infrastructure initiatives
The Group is fortunate to have access to additional clinical research capacity via the TAP, IMPACT and Myeloma UK Clinical Trials Networks. To fully exploit the opportunities provided by these initiatives, it is crucial that there is full strategic alignment between all parties through cross-membership of the respective groups. The Group also needs to links in with the CRUK/NIHR ECMC Network, especially given the proposal to form a Haemato-Oncology Group within the ECMC Network.

Engagement with Genomic England Ltd (GEL)
Haemato-oncology has been at the vanguard of the GEL 100,000 Genomes Project owing to the relative ease in obtaining fresh tumour material. Following closure of the programme in December 2018, there has been a switch to national commissioning of routine molecular diagnostics to centrally performed whole-genome sequencing (WGS), starting with AML/MDS. In order to facilitate close links with the NHSE WGS the Clinical Lead for the Haemato-Oncology GEL Clinical Interpretation Partnership (GeCIP) has been co-opted onto to the Group.

Trial delivery
Delivering trials to time and target remains one of the key priorities of the Group. It is therefore important that the Group engages effectively with the delivery networks. This will be achieved by involving Subspecialty Leads (SSLs) in Group meetings and by continuing to showcase the Group portfolio at the annual trials review meeting. Consideration is being given to holding a national joint meeting with SSLs.

Consumer engagement
Consumer representation on the Group is crucial, not only for writing and commenting on patient information sheets, but also for formulating new research questions, gauging patient acceptance of new studies, optimising trial design and publicising new studies within the patient community. It is also important that the Group has broad geographical representation.

Research Group membership
In order for the Gorup to fulfil its function, it is crucial that members cover a broad range of expertise including the seven main disease areas (AML, ALL, CML, CLL, MPN, MDS, myeloma). Given the importance of optimising trial design, the Group also places much emphasis on statistician representation. The appointment of a senior trial coordinator to the Group provides expertise in trial delivery. The Group feels that the balance in membership is about right but that it could benefit from the inclusion of a senior research nurse at the next rotation. The Group has implemented the rotation of Subgroup Chairs according to the NCRI guidance with a rotation of the chairs of the ALL, AML and MDS in the last 12 months.

Training opportunities
The long-term sustainability of clinical research depends on there being a pipeline of future clinical researchers, and it is crucial that the clinical research community provides training opportunities for such individuals. The Group is committed to contributing to this process by taking part in the Group Trainee Scheme. In addition, the Group is encouraging the membership and participation of trainee representatives on each disease Subgroup.

B – Acute Lymphoblastic Leukaemia (ALL) Subgroup Strategy

Priorities and challenges for the forthcoming year

Priority 1

The main priority of the ALL Subgroup is to improve the outcomes of treatment for patients with ALL. This includes working in collaboration with paediatric colleagues to determine the optimal treatment for young adults resulting in improved survival whilst limiting long term toxicity effects such as infertility and secondary malignancies. It also includes determining a standard of care for patients unfit for intensive treatments including elderly patients and those with comorbidities.

The group developed a proposal for a national phase III trial, UKALL 15, for all adult patients with de novo ALL. This trial design was developed in partnership with AMGEN and was submitted to CRUK spring 2020. The proposal was not funded by CRUK largely due to the lack of a randomised treatment intervention question for the main part of the trial design.
Consequently, the ALL Subgroup are now collaborating with other ALL working groups within the European Working Group for Adult acute lymphoblastic leukaemia (EWALL) to design a randomised phase III trial in partnership with AMGEN that will be run across multiple European countries and will form the basis of a newly designed proposal for UKALL 15 within the UK.

Priority 2

Patients of all ages with relapsed / refractory ALL continue to have extremely poor outcomes and designing phase II trials for these patients in collaboration with partners from industry is an important part of our strategy within the ALL Subgroup.
The aim is to offer a program of phase II studies offering novel therapies including CAR-T cell approaches to patients with high risk disease as well as those with relapsed / refractory disease

Priority 3

In addition to providing good clinical trials for patients with ALL in the UK, the group is also focusing on developing a large and productive programme of correlative science. A CRUK program grant was awarded to enable work on samples from our upfront studies UKALL 14 and UKALL 60+ to determine genetic factors that may influence patient outcome related to treatments given.
A priority for the ALL Subgroup for 2021-22 is to publish both the outcomes of patients with T-cell ALL treated within UKALL 14 and the correlative scientific data relating to the same cohort of patients that has been generated from this CRUK funded work.

Challenge 1

The ALL Subgroup were not successful in securing funding from CRUK for UKALL 15 in 2020-21. Accessing funding for large complex national trials from charitable bodies such as CRUK in the future is likely to be a challenge, partly due to a reduction in funds for many research funding groups as a consequence of the COVID-19 pandemic. The Subgroup will continue to focus efforts on collaborating both with international colleagues and with pharma partners such as AMGEN in order to develop a trial design for UKALL 15 that may be able to attract funding from a combination of non charitable and charitable sources

Challenge 2

Recruitment to key trials for the ALL Subgroup, such as ALLRIC ALLO and the Seludex trial for patients with relapsed / refractory ALL, are behind targets as a consequence of all clinical trials being temporarily suspended in 2020 due to the global COVID-19 pandemic.

The TMG for the ALLRIC ALLO trial are in discussions with international partners such as Australia with the aim of recruiting patients from outside of the UK. The ALL Subgroup are actively advertising the Seludex trial but there are concerns that it may have to close due to funding coming to an end before it has reached its' accrual target.

C – Acute Myeloid Leukaemia (AML) Subgroup Strategy

The aim of the AML Subgroup is to run large multicentre clinical trials across the UK and with international collaborators. Our objectives to improve outcome by introducing selective, novel and molecularly targeted therapies into the existing backbone of chemotherapy combinations developed in previous trials. Furthermore, we aim to identify molecular signatures of treatment response that will allow appropriate stratification of therapy.

Priority 1: Run large multicentre clinical trials across the UK and with international collaborators

Priority 2: Analyse treatment response in relationship to mutational profile in collaboration with the Sanger Institute

Priority 3: Design a follow-up trial for patients not fit for intensive therapy to replace the LI-1 trials

Priority 4: Develop a Subgroup structure that facilitates involvement of all who are interested in AML research including clinicians, trainees, trialists, allied professionals (including nurses and pharmacists), scientists and consumers.

Challenges for the forthcoming year

- Accessing novel therapies for inclusion in AML 20 and at the same time ensuring access to funding for this large national trial
- Ensuring incorporation of high quality translational science within the AML 20 study, by collaborating with the newly formed Science sub-committee
- Ensuring full recruitment to the COSI and AMADEUS transplant trials which currently respectively represent the only randomised trial of the TBF conditioning regimen and the only randomised post-transplant maintenance studies in the world
- Pioneering the development t of sustainable funding streams for AML trials through the establishment of a novel trial delivery vehicle capable of delivering a mixed portfolio of academically prioritised academic investigator initiated and commercial trials

D – Chronic Lymphoblastic Leukaemia (CLL) Subgroup Strategy

Our overarching strategy has not changed and consists of underpinning our excellent clinical research portfolio with an innovative and comprehensive experimental medicine programme.

The following outstanding research questions are key:

1. CLL remains largely incurable. Development of resistance to targeted therapies given as monotherapy invariably occurs at least in the relapsed setting. Combination therapy given to treatment-naïve patients might change this pattern. However, the molecular mechanisms underlying therapy resistance are only incompletely understood.

FLAIR and ERASE and their biological sub-studies directly address this question.

2. Data on long-term side-effects of the new agents and their impact on QoL in the real world remains largely unknown and is currently not systematically captured.

A long-term registry is being set-up via the Leeds CTRU (P Hillmen)

In parallel, we will try to evaluate live-feeds from NHS databases into the GEL data centre as a complementary way to accessing clinical outcome data (A Schuh)

3. As patients live longer, high-grade transformation is seen more frequently. It remains to be seen whether the incidence of this life-threatening complication will reduce as targeted agents move into frontline. In the meantime, there is a high unmet clinical need for this patient group.

STELLAR (CI: A Schuh), the new platform trial for patients with high-grade transformation recruited 17 patients during the COVID-19 pandemic and is opening new sites.

4. Patients struggle with the concept of "watch and wait". A more precise definition of the disease risk at all its stages including the early diagnosis stage is required.

Oxplored is a prospective sample collection study that recruits 1650 probands with a pre-malignant B-cell phenotype.

5. Important infrastructure to deliver our strategy been set up (broad range of clinical and scientific expertise; central biobanking; access to GEL data centre), but a more coordinated translational research programme spanning across biological mechanisms, diagnostics, novel drug target discovery is required to build a truly "experimental medicine" programme. Our working groups address this.

1. (Epi)Genomics (Jon Strefford)
2. Molecular diagnostics (A Rawstron; A Schuh)
3. Biobanking (A Pettitt; M Oates)
4. Early & late Phase clinical trials (T Munir, P Hillmen)
5. Rare LPDs (S Iyengar)
6. Early interception (A Schuh)
7. Micro-environment/basic science (P Patten)
8. Novel immunotherapy (A Bloor)
9. High-grade transformation (A Schuh)
10. Real-life data collections (C Fox, A Hockaday)
11. Patient communication (B Kennedy)
12. Training (TBD)

In addition to working together to deliver on the strategic aims described above, the working group will develop:

- Sustainable solutions for delivery of a joint genotype-phenotype database that would be accessible to all Subgroup members with data feeds from NHS digital; Genomics England, interactions with Horizon and other similar data sharing initiatives
- Opportunities for joint and/or coordinated grant applications
- Effective and co-ordinated interactions with pharma and biotech
- Opportunities for joint working and sharing of resources with other Subgroups in the Research Group and the Lymphoma Research Group.
- Expansion of international collaborations: Joint trials in rare molecular subtypes and Global Haematology.

E – Chronic Myeloid Leukaemia (CML) Subgroup Strategy

The aim of the CML Subgroup is to improve treatment outcomes and patient experience for all CML patients. In order to achieve this, our strategy is to develop a clinical trials portfolio, including

both academic and commercial studies, which will enable us to offer a clinical trial to the majority of CML patients at all stages of their treatment journey. Over the next 12 months, a key deliverable will be opening the TASTER clinical trial (CI: Professor Mhairi Copland). A second aim is to deliver high quality, internationally recognised translational research in CML through the continued support and management of the SPIRIT2, DESTINY and MATCHPOINT clinical trial CML Biobanks.

Our strategy over the next 12 months is to develop in the following areas:

1. Clinical trials: our key strategic aims are to (1) open the TKI-resistance study TASTER –funded by CR-UK-EMERP by q2. 2021; (2) to develop a de-escalation/discontinuation follow-up study to DESTINY; (3) to complete recruitment to the cohort study 'CALLS' (CI: Dr Hugues de Lavallade) open in sites across the UK, a commercial study in collaboration with Incyte to assess Next Generation Sequencing for the diagnosis of BCR-ABL kinase domain mutations; (4) continue to recruit to the commercial studies: IIT in development; BOS-STOP- TFR study for bosutinib discontinuation; second line (2L) ASC after failure of 1L 2G-TKI (RASLAUST). Commercial studies (Novartis) 1L and 3L+ (failure of at least 2 TKIs). Having previously been excluded from ASC studies in Europe, we have been active in FPFV, and now secured 1L and >3L ASC studies. Observational studies: CML registry, UK ASC studies, COVID-19 outcome studies, all in progress with existing ethics approval. TFR calculator score submitted for publication.
2. Presentations/Publications: DESTINY and CHOICES clinical trials published, MATCHPOINT is submitted to JCO, BCSH CML published in the British Journal of Haematology. We plan to identify further sub-studies from SPIRIT2 for presentation/publication, but this has not happened- **SPIRIT-2 represents a serious failure of trial delivery and I officially request a formal investigation by the NCRI.**
3. Correlative science: The clinical trial biobanks continue to be a rich source for research projects and publications. The correlative science work packages for TASTER are in progress (Copland, Vetrie; results from GeCIP are in progress, and we will consider how we progress with this and identify further potential subsets of patient samples for analysis.
4. CML Registry: The CML Subgroup is committed to developing a Registry to collect data on CML patients, in particular in relation to treatment-free remission and paediatric CML. Funding to develop the Registry has been obtained from Incyte and Pfizer; sites that are open are Liverpool and Hammersmith, Kings is currently submitting ethics. 900+ patients have been recruited.
5. Patient partnership: We have a consumer representative on our Subgroup who is a very active contributor to meetings and study design. We will be holding a patient and carer September 2021. The meeting will also be webcast live and available for download thereafter to reach as many patients as possible.
6. Subgroup membership: Professor Copland has stepped down as Subgroup chair, and Prof Dragana Milojkovic has been appointed. The Subgroup will discuss appointing a clinical nurse specialist to the CML Subgroup.

F – Myelodysplastic Syndromes (MDS) Subgroup Strategy

The main priority for the MDS Subgroup is to improve the outcome of treatment and quality of life for patients with MDS and allied conditions. The strategy of the MDS Subgroup is to develop a portfolio of Phase I, II and III studies which covers MDS and the allied conditions. The aplastic anaemia working party is part of this Subgroup.

MDS remains a difficult disease with regards designing and delivering clinical trials. The group have worked to build on the changes to the Subgroup introduced over the last two years, which is now gathering momentum, evident by our success during this time.

Changes developed over the last 12 months:

- The aplastic anaemia working party is now led by Dr Austin Kulasekararaj following Professor Judith Marsh's retirement. The group took the opportunity to thank Judith for her huge contribution to the field of bone marrow failure over many years, furthering knowledge in the science and improving treatment outcomes. Her presence in the field will be missed but we wish her a happy and healthy retirement.

- Terms of Reference document for the Senior Leadership Roles embedded into the group. This allows natural succession planning.

- Election of an Executive Board with rotational lead roles – vice-chair, biobank/governance, translational science, early phase/industry trials, communications. This approach is now successfully in place and has increased focus and productivity of the Subgroup.

- Appointment of a trainee representative to the Subgroup through the NCRI trainee scheme – a trainee has been in place now for 2-3 years (extended due to pandemic). We have developed a key competency template for future appointments. The trainee was involved in developing this. Mentoring is provided by the chair of the MDS Subgroup and also by the investigators of a chosen trial in early development. The trainee was part of the REPAIR MDS trial development group, where they have had a very productive experience having direct input in to the trial design and helped write the patient information. The trainee was also part of a COVID-19 data collection: Impact of SARS-CoV-2 (COVID-19 infection) on UK patients. Accepted as an abstract with the BSH.

- Production of a Strategy Document that engages the whole group emphasising our strengths and direction of travel with emerging themes. A thematic approach would allow us to concentrate on common areas across the disease as a whole (and allied conditions) rather than the current focus on disease subtypes. This work is ongoing.

- Improvement in communication to haematologists and patients of available trials around the UK that are open and recruiting. The communications lead is responsible for uploading all relevant current trials to the UK MDS Patient Support website. A twitter account is being explored.

- Stronger links with consumers (see below; Priority areas - new workflow & consumer activities).

The aim of the group is to design and develop clinical trials by bringing together pertinent and timely clinical questions with high quality scientific research. We continue to engage the wider non-clinical MDS scientific community to fully utilise the expertise available in the UK. We have expanded our work with the consumer group, an area we wish to develop further. Our portfolio includes investigator led studies, links to the NCRI AML Subgroup to facilitate MDS trial entry and a strong commercial portfolio.

High risk MDS is well represented in both the NCRI AML trials (as there is considerable overlap in treatment approaches), and the commercial portfolio where many trials seek to improve survival over single agent azacitidine in high risk MDS with novel agents.

The challenge to the MDS Subgroup has been to deliver clinical trials in patients with low risk disease where there is an unmet need. These patients account for approximately two thirds of MDS patients where the aims of treatment are to improve bone marrow failure, improve QOL & the consequences of supportive care and delay the progression to high risk MDS. In addition, the group have a strong track record of recruiting to trials for CMML (MONOCLE), another unmet need and a focus of the group.

Priority areas for Clinical Research

1. Development of a MDS Platform Trial – Austin Kulasekararaj, David Bowen, Simon Stanworth & John Norrie. Main goal is to design a platform for sequential randomised trials of therapy for Low Risk MDS including monitoring strategy. Aim to delay need for transfusion, maintain TI state and improve QoL. Hope to offer early intervention and early access to novel drugs.

2. REPAIR MDS; Randomised Phase II trial of Danazol Vs VBaP. This trial will investigate danazol and the novel combination of valproate, bezafibrate and medoxyprogesterone for which there is scientific data supporting its use. It is a trial aimed at low risk MDS, which fulfils the strategic aims of the group. This trial will have important clinical questions, tight diagnostic inclusion and strong translational research over a number of scientific groups. The trial will be open to all UK centres wishing to take part. Trial management group meeting weekly. Protocol written. REC/MHRA approved. Site selection & feasibility ongoing. Plan to open first site Q3-4 2021 (delayed due to the pandemic).

3. REDDS2 – Dr Stanworth (NHS Blood and Transplant). Following the success of REDDS (see above recent publication), this is another pilot feasibility study. This will compare standard red cell transfusion regimens with a novel weekly transfusion programme whereby the blood is genotyped matched but not cross matched within the individual patient. Will pilot feasibility of functional assessments (using a Fitbit-type device and questionnaire: mobility, exercise level, frailty measures). Study is open in Melbourne (via Monash University). Trial has been held back due to the pandemic. Likely that the UK will be a separate arm of the study. Small number of UK sites identified. First UK sites about to open.

4. AMMO study; ASTX727 monotherapy in CMML and MDS/MPN overlap. CI Dr Dan Wiseman. Unmet need for a UK trial for CMML following the closure of MONOCLE. Randomised 2:1 phase II trial ASTX727 against best supportive care. Drug provided by company. Discussed with the IWG and NCRI MPN groups. TAP approved. Target recruitment 75 patients. This study has been funded through Blood Cancer UK. Target to open the trial Q3-4 2021.

5. Trial of transplantation in poorer prognosis 'low risk' MDS. TDG in place. CI Dr Victoria Potter.

6. EVOLVE – collaborative input to trial design for patients with high risk MDS with the AML Subgroup.

7. New workflow planned on QoL and patient experience.

    a. Engaging with and understanding the research priorities of MDS patients.
    b. NCRI AML 18 & LI-1 HR-MDS QoL data Subgroup analysis – collaboration with the AML trial group

8. Aplastic Anaemia working group:
   Regeneron antibody (anti-IL2Rgamma chain) first in human trial: trial will be starting in the next few weeks. Aim to screen first patient in KCH in 4 weeks. In vitro T-reg expansion study: aim to start in July/ August 2021.

The MDS Subgroup continue to collaborate with the MPN & AML groups, NHS Blood and Transplant and the Aplastic Anaemia Working Party. The group feeds into the UK MDS Forum and presents at the Annual UK MDS Forum Education Day and Executive Board every autumn.

G – Myeloma Subgroup Strategy

Strategic outline:

The UK Myeloma Research Alliance (UKMRA) was generated conceptually in 2014, as an initiative to bring comprehensive collaborative research under a single working group to delivery patient-impactful research into a collegiate work stream, with common goals and aligned strategy. The aim of the UKMRA is to be an internationally recognized cooperative with truly impacting clinical research that facilitates change in clinical practice within the UK and beyond whilst strategically providing the evidence-base for commissioning and regulatory authority decision-making. In order to drive this aim, we set up a senior leadership team to focus developing and delivering strategic goals in 4 aligned areas: Research Governance, Trial Design, Translational Research and Industry Liaison. This document sets out our aims in each of these areas, and how we aim to deliver these.

UKMRA Aims

Fundamental to the UKMRA strategy, our aims are:

- Portfolio Development - incorporating efficient trial design methodologies to ensure maximum impact with minimum time to delivery impact.
- Innovation – utilizing “platform” style trial designs to ensure a constant and seamless integration of new drugs into the portfolio.
- Efficiency and Performance – through the UKMRA governance structure we aim to make available all trials to all feasible sites.
- Internal and External Communication – through the leadership roles within the UKMRA, the relevance to both the myeloma community and pharmaceutical industry will be current and maintained via a comprehensive communications strategy.
- Commercial Opportunities – increase the scope of commercial partnerships and trial design to complement existing commercial clinical development programmes.
- Health Technology Appraisals – liaising with NICE, MHRA, NHSEngland (and devolved governments) where appropriate to support appropriate market access trials of key relevance to the NHS and UK patients
- Future Growth and Development –a continual monitoring of progress and especially external-facing partnerships will allow adaptability with regular review

To ensure the long-term strategy and continuity of clinical research activity, we have established a robust plan centred on the development of succession planning through engagement of new personnel to work alongside established researchers. We aim to have correlative science at the centre of our studies and are working to establish clear and open biosampling governance. This approach has led to the completion and publishing of clinically impactful studies in high-ranking journals that have the potential to change clinical practice.

Links to other Research Groups, international groups and network subspecialty leads

The myeloma Subgroup doesn't have any formal links with other Research Groups, though some peripheral involvement in our study discussion have been had with CTRad.

The UK has now formally joined the EMN with representation on both the senior and junior board. The UK is leading an EMN retrospective COVID-19 data collection study and is considering participating in further studies. We have been planning a trial in collaboration with the Australasian Leukaemia & Lymphoma Group (ALLG) within the UK Myeloma Research Alliance/ Myeloma UK Concept and Access Research Programme and will be submitting for funding this year.

A number of sub-speciality leads are part of the Subgroup. We will be looking at the portfolio map with them in more detail to understand where gaps and high competition areas are.

Funding applications in last year

We confirmed the CRUK funding for two frontline phase III studies, Myeloma XIV (CI: G Cook) and XV (CI: K Yong), both of which are now open. Myeloma XV was awarded £191,008 for this reporting period (total of £1.5 million), Bloodwise £191,008 grant activated in January 2021 for associated translational work. Additional funding from Industry was secured (see below). Successful funding from the MRC (DPFS award) was secured of £3.4 million for "Treating Multiple Myeloma and Diffuse Large B Cell Lymphoma by Targeting the NF-κB Pathway with the First-in-Class GADD45β/MKK7 Inhibitor, DTP3" (CI: H Auner).

Both Myeloma XIV and XV were fully developed within the Myeloma Subgroup. The DTP3 study is led by Imperial College and was developed with input from the Myeloma Subgroup

Collaboration partnership studies with industry

We have industry funding partnerships with our late phase trial programme. Myeloma XII ACCoRD study is supported by CRUK and Takeda, UKMRA Myeloma XIV is supported by CRUK and Takeda with some contribution from Celgene. The UKMRA Myeloma XV is supported by BMS £310,270 and Sanofi £4,036,526 over a 5 year period.

In the early phase trials setting, we have industry partnership with Takeda (MUK8) (CI: G Cook), Karyopharm (MUK12, CI: M Kaiser) and Takeda with some contribution from Celgene and Janssen and Amgen (MUK9 CI: M Kaiser & M Jenner). GSK have awarded £2.3 million for the ProMMise trial platform (CI R Popat) for relapsed myeloma which will be run through the UKMRA-Myeloma UK Concept and Access Research Programme. Autolus has awarded UCL £3,223,611 over 3 years for the Mcarty CAR-T cell trial.

Impact of Research Group activities

The Myeloma XI trial has had major impact to myeloma practice with multiple high impact publications. It has demonstrated the activity of a front-line carfilzomib quadruplet regimen for newly diagnosed myeloma, the impact of pre-ASCT consolidation for those achieving < VGPR and significantly has contributed to the NICE approval of lenalidomide as maintenance post ASCT. The translational outputs have been instrumental to the understanding of myeloma genetics. Importantly this study was one of the first major studies to show the poor prognostic impact of chromosomal 1q amplification. The PADIMAC trial was published demonstrated the effect of stratifying patients to a non-ASCT pathway according to depth of response. The MUK-5 trial was published and the first to show the benefit of carfilzomib maintenance over observation.

Open meetings, trials days, strategy days

Due to the impact of the COVID-19 pandemic we held 1 group meeting and 1 senior leadership meeting. The trials day was cancelled in 2020, but will be going ahead in 2021.

Priorities and challenges for the forthcoming year

The priorities for the next 12 months are to formalise the processes for the innovation and development of myeloma clinical trials with the aim to increase the number of successful grant applications. In order to do this the newly formed Senior Leadership Team (SLT) will meet 4 times per year in addition to the myeloma Subgroup meetings to review ongoing trial concepts and advise on progress. The SLT will identify gaps in research and commission working groups to develop study concepts and introduce innovate efficient trial designs to maximise value and impact. The success of previous trials such as Myeloma XI, MUK9b will be taken forward to formulate new concepts.

The following trials are prioritised for enrolment:

1. Myeloma XIV: Fitness
2. Myeloma XV: Radar
3. Myeloma XII: Accord

The following trials in development are prioritised for opening:

1. ProMMise
2. DTP3
3. Mcarty

The following areas have been prioritised for concept development:

1. Novel immunotherapy post ASCT consolidation strategy
2. Patients relapsing early post ASCT

Overall, the aims are to continue to promote inclusivity and continuity planning with early co-ordinated working to secure core funding for our early phase portfolio and to engage with industry partners to secure new agents for phase I/II delivery in the face of strong international competition.

The impact of the pandemic and Brexit has left us with the challenge of continuing to develop an academic portfolio in the face of strong competition from innovative Industry trial designs and other co-operative groups. This year's strategy is therefore to increase our engagement with Industry with multiple showcase events to ensure that opportunities are formed.

Significantly, the EMN has continued to grow and attracts significant Industry investment to develop academic trials. As a result, the aim is to integrate further with the EMN; however, this need to be undertaken cautiously to maintain recruitment into UK developed trials that are supported by UK funders.

Myeloma Subgroup Publications

Myeloma XI Trial Clinical Publications

Bygrave C, Pawlyn C, Davies F, Craig Z, Cairns D, Hockaday A, Jenner M, Cook G, Drayson M, Owen R, Gregory W, Morgan G, Jackson G, Kaiser M. Early relapse after high-dose melphalan autologous stem cell transplant predicts inferior survival and is associated with high disease burden and genetically high-risk disease in multiple myeloma. Br J Haematol. 2021 May;193(3):551-555. doi: 10.1111/bjh.16793. Epub 2020 Jun 10. PMID: 32524584.

S Bird, D Cairns, F Davies, K Boyd, T Menzies, G Cook, M Drayson, W Gregory, M Jenner, J Jones, M Kaiser, R Owen, G Jackson, G Morgan & C Pawlyn. (2021) Sex Differences in Multiple Myeloma Biology but not Clinical Outcomes: Results from 3894 Patients in the Myeloma XI Trial. Clinical Lymphoma, Myeloma Leukaemia (in press).

RM de Tute, G Cook, DA Cairns, JM Brown, J Cavenagh, AJ Ashcroft, JA Snowden, C Williams, K Yong, E Tholouli, M Jenner, A Hockaday, MT Drayson, TCM Morris, AC Rawstron & RG Owen, on behalf of the National Cancer Research Institute Haemato-oncology Clinical Studies Group. (2021) Impact of minimal residual disease (MRD) in relapsed myeloma: results from the NCRI Myeloma X (intensive) trial. British Journal of Haematology (in press)

GH Jackson, C Pawlyn, DA Cairns, A Striha, C Collett, A Waterhouse, JR Jones, J Wilson, C Taylor, B Kishore, M Garg, C Williams, K Karunanithi, J Lindsay, MW Jenner, G Cook, N Russel, MT Drayson, MF Kaiser, RG Owen, WM Gregory, FE Davies & GJ Morgan for the UK NCRI Haemato-oncology Clinical Studies Group. (2020) Optimising the value of IMiD drugs during induction and maintenance in transplant non-eligible patients with newly diagnosed multiple myeloma: results from Myeloma XI, a multicenter, open-label, randomized, phase 3 trial. British Journal of Haematology doi: 10.1111/bjh.16945.

C Pawlyn, DA Cairns, T Menzies, J Jones, M Jenner, G Cook, K Boyd, M Drayson, M Kaiser, RG Owen, W Gregory, G Morgan, G Jackson & FE Davies. (2020) Autologous stem cell transplant is safe and effective for fit older myeloma patients. Haematologica doi.org/10.3324/haematol.2020.262360

GH Jackson, C Pawlyn, DA Cairns, R de Tute, A Hockaday, J Jones, B Kishore, M Garg, C Williams, K Karunanithi, J Lindsay, A Rocci, J Snowden, M Jenner, G Cook, N Russell, M Drayson, W Gregory, M Kaiser, R Owen, FE Davies & G Morgan. (2020) A Quadruplet Regimen Carfilzomib, Lenalidomide, Cyclophosphamide and Dexamethasone as Induction Therapy for Multiple Myeloma Prior to Autologous Stem Cell Transplantation. PLOS Med (in press).

GH Jackson, FE Davies, C Pawlyn, DA Cairns, A Striha, C Collett, A Waterhouse, JR Jones, B Kishore, MGarg, CD Williams, K Karunanithi, J Lindsay, D Allotey, S Shafeek, MW Jenner, G Cook, NH Russell, MF Kaiser, MT Drayson, RG Owen, WM Gregory & GJ Morgan. (2020) Lenalidomide Before And After ASCT For Transplant-Eligible Patients Of All Ages In The Randomized, Phase III, Myeloma XI Trial. Haematologica. haematol.2020.247130; Doi:10.3324/haematol.2020.247130

CA Bradbury, Zoe Craig, G Cook, C Pawlyn, DA Cairns, A Hockaday, A Paterson, MW Jenner, JR Jones, MT Drayson, RG Owen, MF Kaiser, WM Gregory, FE Davies, JA Child, GJ Morgan & GH Jackson, On behalf of the UK NCRI Haemato-oncology Clinical Studies Group. (2020) Thrombosis

in Patients with Myeloma Treated in the Myeloma IX and Myeloma XI Phase III Randomized Controlled Trials. Blood doi: 10.1182/blood.2020005125.

Translational outputs from Myeloma XI Trial:

Croft J, Ellis S, Sherborne AL, Sharp K, Price A, Jenner MW, Drayson MT, Owen RG, Chown S, Lindsay J, Karunanithi K, Hunter H, Gregory WM, Davies FE, Morgan GJ, Cook G, Atanesyan L, Savola S, Cairns DA, Jackson G, Houlston RS, Kaiser MF. Copy number evolution and its relationship with patient outcome-an analysis of 178 matched presentation-relapse tumor pairs from the Myeloma XI trial. Leukemia. 2020 Dec 1. doi: 10.1038/s41375-020-01096-y. Epub ahead of print. PMID: 33262523.

Hoang PH, Cornish AJ, Sherborne AL, Chubb D, Kimber S, Jackson G, Morgan GJ, Cook G, Kinnersley B, Kaiser M, Houlston RS. An enhanced genetic model of relapsed IGH-translocated multiple myeloma evolutionary dynamics. Blood Cancer J. 2020 Oct 14;10(10):101. doi: 10.1038/s41408-020-00367-2. PMID: 33057009; PMCID: PMC7560599.

Shah V, Sherborne AL, Johnson DC, Ellis S, Price A, Chowdhury F, Kendall J, Jenner MW, Drayson MT, Owen RG, Gregory WM, Morgan GJ, Davies FE, Cook G, Cairns DA, Houlston RS, Jackson G, Kaiser MF; on behalf of NCRI Haematology Clinical Studies Group. Predicting ultrahigh risk multiple myeloma by molecular profiling: an analysis of newly diagnosed transplant eligible myeloma XI trial patients. Leukemia. 2020 Nov;34(11):3091-3096. doi: 10.1038/s41375-020-0750-z. Epub 2020 Mar 11. PMID: 32157174; PMCID: PMC7584474.

PADIMAC Trial

R Popat, N Counsell, R de Tute, D De-Silva, EH Phillips, JD Cavenagh, T Adedayo, N Braganca, C Roddie, M Streetly, S Schey, MBC Koh, J Crowe, TC Morris, G Cook, P Smith, L Clifton-Hadley, N Rabin, R Owen & K Yong. (2021) Using depth of response to stratify patients to front line Autologous Stem Cell Transplant or not: Results of the phase II PADIMAC study. British Journal of Haematology (in press).

Cardamon Trial

M Camilleri, Maria Cuadrado, E Phillips, W Wilson, R Jenner, G Pang, S Kamora, M Streetly, R Popat, C Bygrave, R Owen, J Cavenagh, M Chapman, J Sive, L Eccersley, M Sheaff, R Benjamin, K Ramasamy, G Cook, A Virchis, SJ Chavda, L Clifton-Hadley, MA Scully & K Yong. (2021) Thrombotic microangiopathy in untreated myeloma patients receiving carfilzomib, cyclophosphamide and dexamethasone on the CARDAMON study. Submitted to British Journal of Haematology (in press)

MUK-5 Trial

Carfilzomib or bortezomib in combination with cyclophosphamide and dexamethasone followed by carfilzomib maintenance for patients with multiple myeloma after one prior therapy: results from a multi-centre, phase II, randomized, controlled trial (MUKfive). Yong KL, Hinsley S, Auner HW, Bygrave C, Kaiser MF, Ramasamy K, De Tute RM, Sherratt D, Flanagan L, Garg M, Hawkins S, Williams C, Cavenagh J, Rabin NK, Croft J, Morgan G, Davies F, Owen RG, Brown SR. Haematologica. 2021 Apr 29. doi: 10.3324/haematol.2021.278399

MUK9 Clinical trial:

Brown S, Sherratt D, Hinsley S, Flanagan L, Roberts S, Walker K, Hall A, Pratt G, Messiou C, Jenner M, Kaiser M; Myeloma UK Early Phase Clinical Trial Network. MUKnine OPTIMUM protocol: a screening study to identify high- risk patients with multiple myeloma suitable for novel treatment approaches combined with a phase II study evaluating optimised combination of biological therapy in newly diagnosed high-risk multiple myeloma and plasma cell leukaemia. BMJ Open. 2021 Mar 24;11(3):e046225. doi: 10.1136/bmjopen-2020-046225. PMID: 33762245; PMCID: PMC7993167.

H – Myeloproliferative Neoplasms (MPN) Subgroup Strategy

The overarching strategy of the MPN Subgroup is to build a strong diverse network of clinicians, nurses, scientists in partnership with patients. Our aims are to:

- Ensure that basic science research in the UK remains cutting edge.
- Develop new scientists and clinician scientists to carry forward today's legacy.
- Ensure that MPN patients (encompassing a broad range of different disease entities) have the opportunity to participate in as diverse a portfolio of clinical trials as possible.
- Support sample banks in MPN and deliver results from them.
- Participate in and provide educational activities for clinicians and patients this includes guidelines as well as face to face educational meetings.
- Ensure there are up to date comprehensive national guidelines for MPN via the BSH process.
- Support NICE appraisal of novel therapeutics in MPN.

Biobanking and translational research

The Subgroup supports cutting-edge translational research through large sample banks of MPN samples and promoting strong links between clinical and scientific research programmes. Over the last few years, members of the Subgroup, utilizing MPN sample banks, have made a number of major international contributions to the understanding of the genetics and biology of MPNs including the description of somatic mutations of *JAK2*, *CALR* and *EZH2*. Going forward, the Subgroup will continue to support patient biobanks, including sample collections linked to clinical trials.

There are extensive biobanking protocols built into academic studies run through the Subgroup, including PT1, MAJIC, PHAZAR, TAMARIN, MITHRIDATE, PROMise and forthcoming FEDORA studies and translational research studies utilizing these samples are underway. Through strong links with industry, members are also working with sample banks collected in industry studies, e.g. we have carried out genetic analysis of the RESUME cohort of myelofibrosis patients (genetic analysis over 200 samples available; Choudhury et al, Leukemia 2020), PAC203 study (120 myelofibrosis patients) and PRM151 (genetic analysis 150 myelofibrosis patients). We have established a new study focused on familial MPNs (INForMeD study) that is recruiting well in Oxford and will be rolled out to a number of other sites over the next 12 months.

Priority areas for clinical research

The Subgroup oversees clinical trials (phase I, II and III) across a broad range of different disease entities. Our overarching strategy is to ensure that clinical trial options are available for patients with each disease type (including rare diseases) both at first line and following failure of standard therapy. The key disease areas are:

- MPN epidemiology; we plan to open a large and innovative epidemiological study over the next 12 months (MOSAICC) aiming to better understand factors which predispose to MPN development.
- Polycythaemia vera; here we have opened a large randomised trial of ruxolitinib versus best available therapy later this year (MITHRIDATE; CI: Claire Harrison).
- Essential thrombocythaemia; here a first line trial is currently lacking and is a priority for the Subgroup.
- Myelofibrosis; these patients with more advanced MPN have a major unmet need and we have a number of commercial trials in the portfolio as first and subsequent lines of therapy.

A number of studies are testing the safety and efficacy of ruxolitinib in combination with IMP e.g. bromodomain inhibition in myelofibrosis (CRUK funded PROMise study is currently recruiting) and an innovative first line study combining the JAK inhibitor fedratinib with pegylated interferon received funding from Celgene/BMS and will begin recruitment in 2021/2022.

Engagement with Industry

The Subgroup works in close partnership with industry as exemplified by a number of studies with Subgroup members as global CI and a large number of industry studies, complementing academic studies, in the portfolio. Collaborations with industry have also been instrumental in supporting translational research in MPNs through funding of sample collections (MAJIC study). Collaboration with industry has also been essential to help underpin funding of major academic trial initiatives, e.g. MITHRIDATE is funded in part through Novartis, FEDORA is funded by Celgene/BMS and PROMise is funded through the CRUK combinations alliance in partnership with Plexxikon.

Engagement with charity-funded research infrastructure initiatives

The Subgroup is closely linked with charity funded clinical research through the Bloodwise TAP network which has been instrumental in the delivery of a number of studies including MAJIC (first TAP study), PHAZAR, TAMARIN and MOMBAT.

Engagement with Genomic England Ltd (GEL)

MPNs are an excellent and tractable disease model to apply next generation sequencing technology and MPN Subgroup members are fully engaged with the GEL initiative. Up to now, recruitment has been hampered by GEL requirements for germline control DNA which is not practical in most GMCs. In order to address this, we are working closely with GEL to establish new sample collection pipelines that will allow patients with unclassifiable MPNs to be recruited. Over 250 MPN patient samples have been sequenced through GEL, including samples from MAJIC and PHAZAR clinical trials and data analysis is currently underway.

Trial delivery

The Subgroup has an excellent track record of successful delivery of trials and high recruitment into industry studies internationally.

Consumer engagement

The Subgroup has longstanding and ongoing Consumer representation. The Subgroup works closely with a national MPN charity (MPN voice) and oversees a number of patient/carer meeting nationally each year.

Appendix 3

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	Group involvement in the trial
1. *SPIRIT-2; DOI: 10.1182/bloodadvances.2020003570	Additional chromosomal abnormalities at chronic myeloid leukemia diagnosis predict an increased risk of progression; improved stratification of CML- CP at presentation	SPIRIT-2 study
2. *CHOICES; doi: 10.1038/s41375-019-0700-9.	Targeting quiescent stem cells in CML impervious to TKI therapy	CHOICES study
3.		
4.		
5.		

* These publications have been provided by the CML Subgroup Chair and have not been updated by Peter Hillmen.

Appendix 4

Recruitment to the NIHR portfolio

Summary of patient recruitment by Interventional/Non-interventional and number of studies opened/closed.

Year	All participants		Cancer patients only*		Number of studies	
	Non-interventional	Interventional	Non-interventional	Interventional	Opened	Closed
2016/17	5636	2603	5336	2603	47	28
2017/18	5463	2433	5463	2433	47	42
2018/19	3698	2414	3656	2414	43	44
2019/20	1990	1475	1982	1475	39	51
2020/21	566	872	566	871	27	14

*This data is based on a proxy from CPMS (the NIHR database used to collect patient recruitment data) and includes diagnostics, screening and prevention patients.

Appendix 5

Annual report feedback 2019-20

02 November 2020

Dear Peter

Re: NCRI Haematological Oncology Group Annual Report 2019-20

I am writing to you with regards to the Haematological Oncology Group Annual Report 2019-20.

Due to the challenging time for all in the healthcare sector resulting from COVID-19 and the unprecedented impact on the activity of both the Groups itself and wider research activities, ranging from the time available for research work versus clinical commitments to the funding of new trials and the recruitment of existing trials, the NCRI allowed the Groups to submit reduced report this year if they were able to do so.

We received 12 out of 15 Group reports which was reviewed at a two day meeting on the 12th and 13th October 2020 by a panel consisting of some former NCRI Group Chairs, NCRI CMPath Chair, former NCRI CTRad Chair and the current Strategic Advisory Group Chair, NCRI Head of Research Groups and representatives from the NIHR Cancer Coordinator Centre, NCRI Consumer Forum, NHS Cancer Alliances, epidemiology, CTU/basic science, allied health profession and the Canadian Cancer Clinical Trials Network.

Due to no report being received for the Haematological Oncology Group, the Panel was unable to review the Group's progress this year. However, they would like to share a summary of the generic points raised at the review. Please share the contents of this letter with your members for discussion at the next Group meeting.

Generic feedback for all the Groups

Strategic objectives and the impact of COVID 19

- Due to the research funding challenges and restrictions on NHS resources resulting from COVID 19, the Panel recommended the Groups evaluate their strategic objectives and focus on the most important priorities or questions that need to be answered as it would not be feasible for the Groups to be doing everything they planned or continue to "plug in the gaps." Additionally, the Panel suggested looking for more cost-efficient methods of working where they can.
- The Panel felt that the strategic objectives for most Groups were too broad especially in the current climate. The Groups were asked to provide specific, measurable aims for their strategic objective and attach timelines/metrics to them.

National Cancer Research Institute, 2 Redman Place, London, E20 1JQ
T: +44 (0)20 3469 8798 **W:** www.ncri.org.uk

Multidisciplinary approach to research and membership

- The Panel noted the importance of collaborative and multidisciplinary working, especially in the current climate, and would encourage all Groups to continue to reach out to other relevant NCRI Groups and consider the NCRI strategic priorities where appropriate.

Linking with the wider research community

- The Groups were asked to link with the wider research community and engage with relevant networks, in particular, with researchers who are developing or are running large national platform studies when there is one available in the disease site e.g. PrecisionPanc (Upper GI Group) and TRACERx (Lung Group). The NCRI recognised that there is a role for them to play in promoting collaboration and will be working with the partners to encourage greater interaction between the Groups and the networks in future.

Funding opportunities

- Given the potential decrease in funding opportunities, the Groups are encouraged to explore alternative funding sources and collaborations e.g. with industry, government funders, NHS Cancer Alliances etc.

Consumers involvement:

- The Panel encouraged Groups to integrate public and patient involvement (PPI) in all aspects of the Group's activities e.g. study design, proposal development, prioritisation of strategic areas etc.
- The Panel wanted to ensure that the consumer activity was captured throughout the report and not just in the consumer section, especially where the consumer reports are missing.

If you have any comments on this year's process, please send them to Nanita Dalal (Nanita.Dalal@ncri.org.uk) for collation.

Best wishes,

Professor Meriel Jenney
Annual Reports Review Committee Chair, NCRI
Consultant Paediatric Oncologist,
University Hospital of Wales

Dr Gillian Rosenberg
Head of Research Groups,
NCRI

National Cancer Research Institute, 2 Redman Place, London, E20 1JQ
T: +44 (0)20 3469 8798 **W:** www.ncri.org.uk

Appendix 6

Quinquennial review feedback - 2015

1. Comments and recommendations

The Panel thanked the CSG team for the documentation provided and the openness with which they had engaged in discussions. The Panel identified a number of strengths of the Group and issues which the Group need to consider:

Strengths

- The review panel considered the Group to be outstandingly high achievers
- A successful and well organised Group, with strong leadership
- Extended membership within subgroups is working well
- A balanced portfolio containing an impressive number of studies, embracing novel trial designs, plus large scale phase III trials that scale the populations
- Continue to develop studies that only the UK is able to undertake, e.g. de-escalation studies
- Accrual exceeding that of the rest of Europe
- A high success rates with funders
- Strong consumer involvement
- Consideration being given to quality of life studies
- Collaborations with other groups
- An open approach welcoming others to bring ideas to the Group and to join the Group
- Strong biobank resources to allow translation of knowledge into future trial design
- Translational studies are well organised - the next step would be to design specific studies on which the UK can take the lead

Issues for the CSG to consider

- The review panel challenged the Group to become international leaders as well as national leaders
- Further exploration of international collaborations for rare tumour types
- The review panel await the outcome of the Supportive Care, Transfusion and Late Effects Working Party with interest
- How to help other CSGs and to share their routes to success
- The main CSG comprises mainly of Consultant Haematologists and it was suggested that this should be reviewed and revised
- It was noted that succession planning has commenced and the review panel encouraged further thought to be given to this important topic
- The CSG should lead on a workshop to explore cellular pathology

In concluding the review Professor Seymour thanked everybody for participating in the review and the NCRI CRG Team for preparing the paperwork and organising the review.

The business of the meeting took 4 hours. ***The Group will be reviewed in 5 year's time.***

NCRI Advancing Cancer Research Together

National Cancer Research Institute
2 Redman Place,
London, E20 1JQ
org.uk