NCRI
National
Cancer
Research
Institute

NCRI Haematological Oncology Clinical Studies Group

Annual Report 2017-18

Partners in cancer research

NCRI Haematological Oncology CSG
Annual Report 2017-18

1. Top 3 achievements in the reporting year

Achievement 1

Continued recruitment into and development of Phase III Trials

The Haematological Oncology CSG continues to recruit effectively into a wide portfolio of clinical trials. In the last 12 months we have completed recruitment in 2 Phase III trials – UKALL14 for acute lymphoblastic leukaemia and RIAltO for patients with chronic lymphocytic leukaemia who are unsuitable for fludarabine-based chemotherapy. In addition, the initial FLAIR trial which is a Phase III trial looking at non-chemotherapy approaches in CLL will complete recruitment in June 2018. The overall trial portfolio for the CSG consists of over 100 studies. The CSG has maintained its performance in terms of trial development over the last reporting period. Key achievements include full continued recruitment into the main AML portfolio (AML18/AML19/Li-1) with over 100 randomisations per month, and securing of Cancer Research UK (CRUK) funding for frontline trials in Myeloma (Myeloma XIV and XV) and securing funding from Novartis for MPN (MITHRIDATE). In addition, Aplastic Anaemia WP has successfully recruited into 2 Phase III trials.

Achievement 2

Strengthened participation in translational research

The CSG also provides a framework for coordinating and driving forward research in areas that transcend individual disease areas, such as Supportive Care, Transfusion and Late Effects (SCTLE), Stem-Cell Transplantation, Cellular Therapy and TYA. We continue to pursue a very active translational research programme including the CLL and AML Subgroups leading pilots in Genomics England, the development of the UK Myeloma Research Alliance (UMRA) to bring comprehensive collaborative research under a single umbrella, and the development of an approach for "Personalized Prognostic Predictions for Patients with Myeloproliferative Neoplasms through Integration of Comprehensive Genomic and Clinical Information". This integration with translational research in the UK ensures that our trials portfolio remains at the cutting edge internationally.

Achievement 3

Strengthening links with Phase I/II infrastructure in the UK

The CSG has continued to develop very strong participation in the Phase I/II research infrastructure provided by the Bloodwise Trials Acceleration Programme (TAP), IMPACT, Myeloma UK and CRUK/National Institute for Health Research (NIHR) Experimental Cancer Medicine Centres (ECMC) Networks. We consider it crucial that opportunities to develop and deliver early-phase studies via these networks is fully exploited and integrated into the Phase III trials programme as well as to the translational research activity. It is also important to establish seamless connectivity between early and late phase programmes in all areas and strengthen engagement with the wider scientific community to optimise trial design and align with current funding strategy at CRUK. For example, the rapid development, recruitment and reporting of the Bloodwise TAP CLARITY trial has allowed the modification of the Phase III FLAIR trial to address further important clinical questions extremely efficiently.

2. Structure of the Group

The CSG brings together seven subgroups, each focussing on specific disease areas (AML, ALL, CML, CLL, Myeloma, MPN, MDS), plus the Aplastic Anaemia Working Party (2017-2019). CSG members include 18 clinicians, two statisticians, a senior trial co-ordinator, two consumers, two National Cancer Research Institute (NCRI) trainees and observers from CRUK and Bloodwise. The CSG currently has representation from most regions in the UK including two of the three devolved nations. In the last 12 months the Supportive Care, Transfusion and Late Effects Working Party has completed its term with a representative now on the CSG with the responsibility of working across the CSG.

3. CSG & Subgroup strategies

Main CSG

Maintain a balanced and continuously replenishing portfolio of academic and industry studies in all major disease areas Over the last 12 months the CSG has maintained a balanced portfolio with Phase III trials for all of the main disease entities. In addition, there has been an increase in the utilisation of the Bloodwise TAP programme for Phase II trials.
Biobanking and translation research development The CSG continues to biobank samples from the various Phase III trials and increasingly these biobanked samples are being used for translational research. For example, the UK CLL Biobank based in Liverpool and biobanking samples from all of our Phase II and Phase III trials has now provided samples for over 30 translational projects.
Increase engagement with industry There continues to be close links and support from the pharmaceutical industry particularly in a number of disease areas such as acute myeloid leukaemia, myeloma and chronic lymphocytic leukaemia.
Engage with charity-funded research infrastructure initiatives There has been a close association with the Bloodwise TAP programme which has now delivered over 15 Phase I or II trials most of which are in the Haematological Oncology CSG disease areas including MDS, MPN, AML and CLL.
Engage with Genomic England Ltd (GEL) The haematological Genomics England Clinical Interpretation Partnership (GeCIP) has met and involves many members of the NCRI CSG and Subgroups. The CLL pilot scheme of GEL involves sequencing over 400 patient samples from patients entered into a number of CLL trials.
Increase consumer engagement Consumer representation is present on the CSG and each subgroup. We have also engaged with the patient disease specific groups to assist in the design and oversight of our portfolio of clinical trials.

Acute Lymphoblastic Leukaemia (ALL) Subgroup (Co-Chairs, Dr Adele Fielding and Dr Clare Rowntree)

Maintain a comprehensive programme of clinical research and correlative science accessible to all patients with ALL

Achievements of the Group include the completion of recruitment to UKALL 14. This trial will report initial findings in late 2018-19. The trial for elderly patients with ALL, UKALL60+, has reopened as a CTIMP trial and is now actively recruiting again. The adult ALL Subgroup continues to collaborate closely with the NCRI Children's Cancer & Leukaemia (CCL) CSG Leukaemia Subgroup in design of trials for teenagers and young adults. We actively collaborate with colleagues in Europe through the European Working Group for ALL (EWALL). A joint EWALL trial for elderly patients with Ph+ ALL is due to open later in 2018 and will be sponsored by Cardiff University with Professor Oliver Ottman from the ALL Subgroup leading the study as chief investigator.

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 UKALL14 and UKALL60+ to determine genetic factors that may influence patient outcome related to treatments given.

Provide research training opportunities to generate a pipeline of future Chief Investigators

The main aim for the ALL Subgroup in the coming year is to complete the design of UKALL15 and to submit to CRUK for funding in November 2018. Members of the ALL Subgroup have set up to design and run UKALL15. Professor Adele Fielding will be chief investigator for the entire trial with Dr Clare Rowntree, Dr Tobias Menne, Professor David Marks and Professor Ottman each leading on sections of the trial allowing them to gain experience in running international phase III trials within the UK. In addition, Dr Tobias Menne will be the chief investigator for the next elderly ALL trial that is planned to succeed UKALL60+.

As part of our long-term strategy to maintain a pipeline for new chief investigators for future trials we plan to also recruit a trainee haematologist and a trainee scientist to our Group in 2018.

Acute Myeloid Leukaemia (AML) Subgroup (Chair, Professor Nigel Russell)

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

The AML Subgroup runs three clinical trials for adult patients with AML encompassing AML19 for patients aged 18-60 years; AML18 for patients >60 years fit for intensive therapy and the LI1 trial for elderly AML patients considered not fit for intensive therapy. These trials between them recruit approximately 100 patients per month and AML18 and 19 between then have randomised over 2000 patients.

The AML19 trial also includes a randomisation for relapsed AML. Both trials are currently undergoing amendment, AML19 to lower the age entry to 16 years to include patients with

high risk MDS but low blast cell counts and to incorporate flow cytometric MRD analysis based upon worked carried out in the AML17 trial which demonstrated that high level MRD post course 2 can predict poor overall survival.

AML18 is also undergoing amendment to incorporate a phase 2 study of Vosaroxin and Decitabine for patients with known adverse risk cytogenetics. Also, the upfront randomisation in AML18 is undergoing an amendment to randomise patients between the combination of CPX-351 and DA chemotherapy combined with Mylotarg. This is currently undergoing regulatory approval and both amendments we would hope to open in Q2-Q3 2018.

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

A master data set has been established for the Sanger analysis comprising and combining the genetic data with trial outcome data and patient demographics from over 3000 patients entered into AML trials. A legal agreement has been established between the trials Sponsor, Cardiff University and the Sanger Centre for this purpose. A final lockdown of the data sets is to be made imminently and a prospective statistical analysis plan has been drawn up.
The objectives are firstly to complete an over-arching prognosis analysis combining genomics with cytogenetic information and MRD analysis (predominantly flow but also including molecular). The aim of this being to further address gene – gene interactions over and beyond that previously described and to integrate genomics into our existing risk assessments. Also, our analysis includes older patients which have not have been covered in other studies and also to factor in MRD assessments, an area which we are uniquely placed given the high priority given to this work in AML16 and AML17.

We are also planning studies of the interaction between genomics and individual treatments and trial outcomes to develop predictive biomarkers of response.

Design a follow-up trial for patients not fit for intensive therapy to replace the LI1 trials

LI2 is our successor to LI1 a trial for patients not fit for intensive therapy. The study which is in development plan is to build upon the success of LI1 in evaluating new agents in AML but to have a more personalised approach to include up front genomic analysis with the aim of evaluating targeted therapies for patients whose mutational profile could make them susceptible to a specific therapy, for example a FLT3 inhibitor for patients with an established FLT3 ITD. It was hoped that LI2 would have substantially greater recruitment compared to LI1. Initial therapies would be randomised against a standard for care with either low dose Cytarabine or Azacytidine as a doctor's choice and would include targeted therapies according to molecular findings. Subjects with an adverse molecular profile could be entered into a pilot arm of investigational therapies.

A group comprising of CI Dr Mike Dennis, along with Dr Paresh Vyas, Professor David Bowen and Professor Robert Hills were developing the proposal, contacts had been made with CRUK regarding an application for a Clinical Trial Award however in the interim an application had been made to Bloodwise to continue LI1 recruitment beyond the current award as a no cost extension to allow for completion of randomisation questions that were already ongoing.

Chronic Lymphoblastic Leukaemia (CLL) Subgroup (Chair, Professor Peter Hillmen)

Complete recruitment in the RIAltO trial for patients unfit for fludarabine-based therapy

The RIAltO Trial (**R**andomised **I**nvestigation of **Al**ternative **O**fatumumab- containing regimens in less fit patients with CLL) is a Phase III study that builds on from Complement-1 comparing bendamustine combined with ofatumumab to chlorambucil combined with ofatumumab and commenced recruitment in December 2011. The trial was amended in September 2014 to include an additional factorial randomization to idelalisib versus placebo. Unfortunately, in February 2016 safety signals from both RIAltO and other company-sponsored studies led to the removal of idelalisib from RIAltO. RIAltO re-opened with the original randomization as this remains an important question and closed to recruitment at the end of April 2018. A total of 521 patients were randomized by the end of recruitment.

Consider a replacement for the RIAltO trial for patients unfit for fludarabine-based therapy

Two commercial trials have been adopted into the portfolio and will replace RIAltO for previously untreated patients who are considered unfit for FCR.
The Beigene-sponsored BGB-3111-304 trial compares the next generation Btk inhibitor, zanubrutinib or BGB-3111, with bendamustine plus rituximab. In addition, there is a single cohort study of zanubrutinib for patients with 17p deleted within this trial. BGB-3111-304 will randomize a total of 420 patients with approximately 47 more in the 17p deleted cohort. There are planned to be 15 UK sites.

The GLOW Trial (JNJ-54179060) which is sponsored by Janssen and compares ibrutinib plus venetoclax with chlorambucil plus obinutuzumab. GLOW will recruit a total of 200 patients.

Complete recruitment into the original FLAIR Trial

The FLAIR Trial is a randomized Phase III trial opened to recruitment in August 2014 and is now open in 100 sites in the UK with more in set-up. 850 patients have been randomised into FLAIR (as of 14th May 2018) and the trial is ahead of its target. The randomization of 754 patients to FCR versus IR is expected to fully recruit by June 2018. At this point the IR arm of the trial will be closed, after an analysis by the FLAIR Data Safety Monitoring Board, and the trial will continue with three arms (FCR, Ibrutinib monotherapy and ibrutinib plus venetoclax).

Roll out the amendment of the FLAIR Trial that adds two additional arms to the trial and increases the total number of patients in FLAIR to approximately 1,576 patients

A major amendment to FLAIR to add two new arms (ibrutinib monotherapy and ibrutinib plus venetoclax) was implemented in July 2017. The ibrutinib plus venetoclax is currently being tested in relapsed refractory CLL in the Bloodwise TAP CLARITY Study with to date acceptable toxicity and promising efficacy. The original FLAIR randomization will recruit a total of 754 patients but with the FLAIR amendment this will increase to 1516 patients making FLAIR the largest Phase III CLL Trial ever run. 850 patients have been randomised into FLAIR (as of 14th May 2018) and the trial is ahead of its target.

To date over 30 patients have completed venetoclax escalation. The amended FLAIR will recruit a total of 1516 patients and is anticipated to remain open to recruitment into 2020.

Continue the rapid development of the Bloodwise TAP Trials

Previously treated. The Bloodwise TAP initiative allows for the rapid development of Phase I and II trials to inform the design of the Phase III trials. These include several early Phase Trials testing the biology of response in previously untreated and relapsed/refractory patients to ibrutinib (ICiCLLe), ibrutinib+obinutuzumab (IcICLLe Extension), ibrutinib+venetoclax (CLARITY) and idelalisib (CALiBRe) as well as a ciclosporin (CyCLLe) study designed to optimize assays to assess the dynamics of CLL clones within our trials. The CLARITY Trial completed its initial recruitment of 54 patients in November 2017 and reported the initial very promising efficacy results at ASH in December 2017. An extension to CLARITY which will add obinutuzumab as the third component of treatment for relapsed/refractory patients is in preparation. This will expand on the existing CLARITY cohort and open up more slots for new patients to receive the triple combination.

Richter's transformation. The Bloodwise TAP STELLAR trial for patients with Richter's transformation should open shortly. This trial will test the additional of acalabrutinib to CHOP-R in Richter's syndrome compared in a randomised Phase II design with CHOP-R alone. There will be a cross-over to acalabrutinib in to those failing CHOP-R.

Analyse whole genome sequencing for over 400 paired germ-line tumour samples from the ADMIRE, ARTIC and RIAltO Trials

Whole genome sequencing has been performed on the samples (CLL and paired germ-line) from over 400 patients in our trials. There were some logistic issues to resolve including the confirmation of the appropriate consent and the development of the capacity to analyse the data requiring the building of a new data centre. These issues have now been largely resolved and the data is currently being analysed.

Apply for funding of the UK CLL Biobank

The Biobank is currently supported by a grant from Bloodwise. An outline application to the Medical Research Council (MRC) was unfortunately unsuccessful. Further attempts to secure long-term funding for the Biobank are being pursued.

Chronic Myeloid Leukaemia (CML) Subgroup (Chair, Professor Mhari Copland)

Improve treatment outcomes and patient experience for all CML patients

The NCRI CML Subgroup aims to contribute to the development of best practice in the management of CML. We have identified key new members with expertise that will add value to the group (including in paediatric CML), developed CML management guidelines and delivered high quality clinical trials. A BCSH CML guideline, developed and written by the CML subgroup, is currently being edited, and this will be published later this year. In addition, members of the subgroup have contributed to a consensus document on quantitative PCR testing for BCR-ABL (under review at the British Journal for Haematology).

Subgroup members also contribute to the European LeukemiaNet and the European Investigators for CML (EICML). Detailed analyses of the SPIRIT2, CHOICES and DESTINY clinical trials are ongoing, and final results will be available this year. DESTINY has advanced patient care, demonstrating that it is safe for patients with a sustained deep molecular response (DMR; at least MR4) to half their TKI dose. This strategy is being adopted more widely, particularly for patients experiencing side effects. DESTINY has also demonstrated that stopping therapy in patients with DMR is safe, with any patients losing molecular remission, rapidly regaining a molecular response on restarting TKI.

Develop a clinical trials portfolio

We continue to develop our clinical trials portfolio. SPIRIT2, CHOICES and DESTINY have completed follow-up and end-of-study analyses are underway. The MATCHPOINT trial in blast-phase CML has now reached its recruitment target, and data collection is underway to determine the safety and efficacy of FLAG-IDA chemotherapy in combination with ponatinb. There are currently 3 clinical trials open for patients with TKI failure:

CALLS – a cohort study to evaluate next generation sequencing for identification of BCR-ABL kinase domain mutations in all phases of CML.

OPTIC – a randomised, phase 2 study to evaluate different doses of ponatinib in TKI-resistant chronic-phase CML.

CABL001A2301 – a randomised phase 3 study of asciminib versus bosutinib in chronic-phase CML patients previously failing at least 2 TKIs.

Importantly, we have recently secured funding from CRUK for TASTER (Targeting STEm cell Resistance), which will add a novel small molecule (currently idasanutlin or tazemetostat) into standard TKI therapy for patients with all phases of CML with resistance to multiple TKIs; we are aiming for first patient, first visit q2.2019. With the introduction of generic imatinib, no front-line study in chronic-phase CML is proposed at present. Discussions are underway to develop a follow-up trial to DESTINY.

Deliver high quality, internationally recognised translational research in CML

UK CML Investigators remain at the forefront of translational research in CML. The main translational research strengths in the Subgroup are in leukaemia stem cell biology (Copland/Huntly/Mead), leukaemia immunobiology (Clark, de Lavallade) and developing state-of-the-art PCR and sequencing techniques (Foroni, Khorashad, de Lavallade, Mead, Huntly) The SPIRIT2 Biobank is a rich source of translational research articles and presentations. Samples from both MATCHPOINT and DESTINY have been biobanked and will be an important resource for future translational studies. A detailed programme of immunological and stem cell assays is proposed for the DESTINY samples; funding is being sought for the stem cell assays. Detailed immunological studies (CI: Professor Richard Clark) have been performed on the DESTINY samples and a manuscript is in preparation: [provisional title] 'Changes in T cell subsets on decreasing/stopping tyrosine kinase inhibitor therapy in chronic myeloid leukaemia: Data from the DESTINY trial'. 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.

Increase patient partnership through patient and carer education days

The 2018 patient and carer education day has been organised for Saturday 22nd September (International CML Day), and will take place at the Priory Rooms in Birmingham. The agenda for the day is being developed, and CML Support have been asked to input regarding topics they would like covered. Pharmaceutical companies with an approved product for the treatment of CML will be approached to sponsor the meeting. We also plan to webcast the meeting live to any patients unable to attend Birmingham on the day and make the slide presentations available via the CML Conference website after the meeting.

Myelodysplastic Syndromes (MDS) Subgroup (Chair, Dr Sally Killick)

Develop a portfolio of Phase I, II and III studies which cover low and high risk MDS

1. REDDS – Red blood cell transfusion thresholds and QOL in MDS: a pilot and feasibility study. Collaboration with NHS Blood and Transplant. Dr Simon Stanworth, Dr Bowen & Dr Sally Killick. Recruited planned 38 patients on time. End of recruitment 11/7/17. Currently in data cleaning process, data lock expected April 2018 when data analysis will start.
2. ELASTIC – Azacitidine and eltrombopag. CI Dr Alexander Sternberg. Continued recruitment of high risk MDS patients to the 5th and final cohort, with no dose limiting toxicities. The expansion cohort is now open and recruiting well.
3. MONOCLE - Phase II study in CMML. CI Dr Steve Knapper. Safety and clinical effectiveness of the monocyte targeted HDAC inhibitor, Terfinostat. Recruited to the first phase rapidly. DMC have passed its safety assessment. Futility assessment is ongoing and the study is therefore closed to recruitment until a decision has been made.
4. CATAPULT 001 WT-1 gene modified T cell therapy for AML/MDS. CI Professor Emma Morris. Currently closed due to a change in sponsor with a plan to re-open soon with a target of 5 patients before a futility assessment.
5. MDS Bio-1 – closed to recruitment whilst the new Haem-Bio is worked up. This has been a very successful venture with over 7,000 samples with linked clinical data, this biomedical resource has already contributed to major breakthroughs in understanding the molecular basis of MDS and the basis of response to some treatments, such as lenalidomide. A significant number of publications in the very top impact factor journals have resulted and the Subgroup is looking to link future trial development with this platform. The first successful application of this linked approach is ELASTIC.
6. FIGARO – collaboration with AML Subgroup. CI Professor Charles Craddock. FLAMSA-BU conditioning regimen in patients with AML and MDS undergoing allogeneic stem cell transplantation. Recruited. A follow-on study (COSI) will be informed by the results of FIGARO and is funded.
7. There are seven commercial trials currently listed in the MDS Subgroup portfolio using a number of IMPs.

Priority areas for Clinical Research

1. Randomised Phase II/III trial of Danazol Vs VBaP Vs best supportive care. Dr's Drayson, Culligan, Raghaven, Killick, Mufti. This is a trial investigating danazol and the novel combination of valproate, bezafibrate and medoxyprogesterone for which there is scientific data supporting its use (Dr Drayson's group). It is a trial aimed at low risk MDS, which fulfils the strategic aims of the group. The plan is for the trial to be phase II, then move to phase III with the best arm. CRCTU are reviewing the trial currently and are likely to adopt it. This is an exciting trial which will have important clinical questions, tight diagnostic review and strong translational research over a number of scientific groups. The trial will be open to all UK centres and the plan is to apply to CRUK for funding.

2. TEAMM 2 – collaboration. Dr Drayson & Dr Culligan. Following on from the disappointment of not having RAPRIMA funded, the group have approached Dr Drayson regarding including MDS patients into TEAMM 2 in a similar fashion to RAPRIMA, allowing resurrection of all the hard work by our subgroup over 2 years. This is a supportive care trial investigating antibiotic prophylaxis. Discussion is ongoing and seems very favourable.
3. REDDS2 – the aim is to work collaboratively with Dr Stanworth at NHS Blood and Transplant to design an international, multicentre phase III trial using data from REDDS to inform trial design on transfusion support in patients with lower risk MDS.
4. QOL during supportive care study, based in Sheffield. Final draft protocol completed, for ethics submission. Novel use of a telephone app to record data.
5. LI-2 – collaborative input to trial design for patients with high risk MDS with the AML subgroup.

Collaboration with research groups

The MDS Subgroup continue to collaborate with the MPN & AML Subgroups, 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.

Finally, the MDS Subgroup are working to raise the awareness of MDS trials in the UK. We will be working with the UK MDS Patient Support group to have an up to date list of all recruiting clinical trials for MDS patients on the Patient Support website. There is also discussion around a newsletter from the group going out to UK haematologists and research nurses to promote open trials.

Myeloma Subgroup (Chair, Professor Gordon Cook)

Creation of a new brand for the clinical research cooperative which signifies the collaborative and unified approach within the UK

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. 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.

Foster engagement between practicing Haematologists in the UK, support their endeavours to participate in clinical research and involve them in the public advertisement of our results

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 "umbrella" 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 the National Institute for Health and Care Excellence (NICE), Medicines and Healthcare products Regulatory Agency (MHRA), NHS England (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

Ensure the long-term strategy and continuity of clinical research activity

To ensure the long-term strategy and continuity of clinical research activity, we aim to establish 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 thus there is a need to establish cellar and open biosampling governance. Taken together, we aim to publish our clinically impactful studies in high-ranking journals to change clinical practice.

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

Ensure that basic science research in the UK remains cutting edge

The Subgroup is committed to supporting basic science in MPNs in the UK which continues to be world-leading. Highlights from 2017 include the development of an approach for "Personalized Prognostic Predictions for Patients with Myeloproliferative Neoplasms through Integration of Comprehensive Genomic and Clinical Information" from the research group of Professor Tony Green at the University of Cambridge that was selected for an oral presentation at the American Society of Hematology meeting in December 2017. This work shows how clinical and genomic information can be integrated to support personalised medicine.

Another study presented at the same meeting showed how single cell genomics might be applied to study "Abnormal Megakaryocyte Differentiation and Function in Myelofibrosis" and was presented by Dr Beth Psaila, a clinician scientist from The University of Oxford. The MPN Subgroup supports many highly successful sample banking studies (which provided samples for the above two studies), with over 8000 patients enrolled in studies investigating Ph- MPN, including atypical and familial cases as well as large epidemiological studies. The subgroup also has representation from many academic clinician scientists in training, ensuring that we meet our key strategic aim of supporting the training and career development of the next generation of MPN clinician scientists in the UK.

Ensure that MPN patients have the opportunity to participate in as diverse a portfolio of clinical trials as possible

The current MPN portfolio encompasses over 35 studies with a range of interventional and observational studies form both commercial and academic sponsors with an excellent track record of recruiting patients and with several members taking lead roles in these trials as global CIs. The subgroup also prioritises studies investigating very rare subtypes of MPN such as systemic mastocytosis or 8p11 myeloproliferative neoplasms. For example, results of the Blu-285 study in systemic mastocytosis, including a number of UK investigators on the MPN subgroup, were presented at the American Society of Hematology (ASH) meeting in December during the plenary session. Results of the intermediate arm of PT1 were also presented at ASH: "Hydroxycarbamide Plus Aspirin Vs Aspirin Alone in Intermediate Risk Essential Thrombocythemia: Results of the PT-1 International, Prospective, Randomized Clinical Trial". The final patient on the PV arm of the MAJIC study reached the primary endpoint in 2017 and results will be presented and published in 2018.

A key strategic priority for the Subgroup is to deliver MITHRIDATE: 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) - this academic study is now fully funded and will open to recruitment in Q3 2018. This is the first study of ruxolitinib as a first line treatment for PV and will recruit approximately 600 patients over five years.

Participate in and provide educational activities for clinicians and patients

The Subgroup supports regional and national meetings for MPN professionals and patients. In November 2017 we held the Myeloproliferative Neoplasms Advances Day for professionals with over 200 delegates and a range of international speakers. Overall feedback was excellent 8.8/10. The following day we held the MPN patient and carers' day, attended by approximately 250 patients from the UK.

Ensure there are up to date comprehensive national guidelines for MPN via the BSH process

The MPN Subgroup supports guidelines for essential thrombocythemia, polycythaemia vera (PV), myelofibrosis and eosinophilia. Through 2017 we have updated PV guidelines (the new guideline is in submission) and systemic mastocytosis guidelines are in development.

Support NICE appraisal of novel therapeutics in MPN

Members of the Subgroup have supported NICE technology appraisals for ruxolitinib in myelofibrosis and polycythaemia vera.

4. Task groups/Working parties

Remit of Aplastic Anaemia Working Party

For the rest of the duration of this WP, we are planning to finalise one or possibly two new clinical trial proposals, listed below. At the end of the 2-year period, the plan is for the Aplastic Anaemia (AA) WP to join the MDS Subgroup.

Progress to date

The first data analysis for the national randomised trial of HLA epitope matched platelet transfusions for alloimmunised patients with AA, MDS and AML has been completed. The study confirmed primary end-point of non-inferiority of HLA epitope-matched platelets compared to standard HLA matched platelets on platelet count increments. A major benefit is their use in situations where highly sensitised patients for whom no HLA matched platelets are available on standard matching. The abstract has been accepted as an oral presentation for BSH 2018 annual meeting. Current plans are to submit an abstract to a major international blood transfusion meeting, possibly ISBT in Toronto.

Additional funding has now been secured from Novartis Global for the RACE study: Prospective randomized multicentre study comparing horse ATG, ciclosporin with or without eltrombopag as front-line therapy for SAA. This aims to look at the immune signature by CyTOF for response to treatment and to explain the impact of the immune response on the significance of these abnormal clones.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)				
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**
May 2017				
Myeloma XV: RADAR: Risk Adapted therapy Directed According to Response comparing treatment escalation and de-escalation strategies in newly diagnosed patients with multiple myeloma (NDMM) suitable for stem cell translation (TE)	Full application	Professor Kwee Yong	Supported	
TASTER : Defining leukaemic cell clonal architecture to inform and monitor drug responses in the TASTER CML Phase II Clinical Trial	Outline application	Professor Tessa Holyoake	Invited to full	
November 2017				
TASTER: Defining leukaemic cell clonal architecture to inform and monitor drug responses in the TASTER CML Phase II Clinical Trial	Experimental Medicine Award (outline to full application)	Professor Tessa Holyoake		
CRUK/09/006: UKALL14: An international randomised trial for adults with newly diagnosed acute lymphoblastic leukaemia	Late Phase Study Amendment (Full Application)	Professor Adele Fielding	Supported	
Prospective collection of acute myeloid leukaemia samples within the NCRI AML trials	Sample Collection	Professor Oliver Ottmann	Supported	

	(Full Application)			
Other committees				
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**

6. Consumer involvement

This year Lesley Roberts (CSG and Myeloma Subgroup) and John Reeve (ALL Subgroup) completed their terms as consumer members, and we thank them for their contribution, commitment and mentorship.

Dr Gillian Murphy has continued in her role as CSG consumer and we welcomed experienced patient representative and NCRI Trustee, Alan Chant, as the new consumer member in September. Alan has received support from Gillian and from scientific mentor, Professor Gordon Cook, and has completed the NCRI Consumer induction training.

The consumers have continued to play an active role in supporting the CSG, the Subgroups and Working Parties: Alan joined the Myeloma Subgroup and was appointed consumer member for the Aplastic Anaemia Working Party; and Gillian assisted the Supportive Care, Transfusion and Late Effects Working Party (until September).

The CSG's six other subgroups have continued to receive excellent support from experienced patient representatives who each have strong links with blood cancer-specific charities (e.g. as Chief Executive, Founder, Trustees, key staff members, patient ambassadors). All the haematological oncology consumers regularly provide the patient's perspective during meetings and teleconferences.

Highlights this year include:

- CSG Consumers providing comments on several grants for CRUK funding panels (using the NCRI Consumer Tool-kit for guidance).
- Increasing evidence for consumer involvement in trial development within the Subgroups, notably with consumers as collaborators/co-applicants on proposals.
- Presenting at the Annual Trials Meeting on ways in which consumers are involved in supporting research within the CSGs.
- Developing a haemato-oncology focussed report from latest NCPES survey results (subsequent request to present these data at the Annual Trials Meeting).
- Highlighting patient-driven initiatives at CSG meetings to positive effect e.g. the UseMyData Patient Data Citation.
- Creating links between CSG and Subgroup consumers to develop a virtual network.
- Working with strategic committees and trial management groups (e.g. Alan Chant: UK Clinical Research Collaboration Board Member; NIHR NETSCC HTA Board Member; Member of Trial Steering Group for Myeloma XIV, *inter alia*).

7. Priorities and challenges for the forthcoming year

Priority 1

Development of a CSG strategy

The Haematological Oncology CSG is one of the most complex CSGs with 7 Subgroups and 1 Working Party which each have varied portfolios and over 100 trials currently recruiting. A priority for the CSG is to develop a comprehensive strategy which will build on the strengths of our activity whilst supporting the logical and effective development in haematological malignancy.

Priority 2

Replacement of key Phase III trials

The continued development of the AML18 and AML19 trials with the opening of new randomisations in Q2/Q3 2018 as well as the development of the LI2 trial which is the planned successor to LI1 a trial for patients with AML not fit for intensive therapy. The continued development of the replacement for UKALL14 for adult patients with acute lymphoblastic leukaemia.

Priority 3

Continued integration of genomics into clinical trials

Haemato-oncology is an important part of the main GEL programme, eligibility being linked to several trials in AML, CLL and Myeloma. Following closure of the programme in December 2018, there will be a switch to national commissioning of routine molecular diagnostics to centrally performed whole-genome sequencing (WGS), starting with AML/MDS. This will provide a great opportunity to utilise this information to facilitate Phase III trials across the portfolio. To help facilitate this development, the Clinical Lead for the Haemato-Oncology GeCIP has been co-opted onto to the CSG.

Challenge 1

To develop a leadership structure within the Subgroups which reflects the wider leadership structure of the NCRI but also recognizes the diverse activity of the CSG and the limited number of clinicians, scientists and trialists in the haematology community.

Challenge 2

Research funding: It is vitally important that the CSG continues to have Phase III trials open in all of our principle disease areas as the trials are usually considered the standard of care for most UK haematology centres in diseases such as acute myeloid leukaemia and acute lymphoblastic leukaemia.

Challenge 3

Maintaining the Phase I/II capacity for haematological oncology that is provided by the Bloodwise TAP Programme, IMPACT for stem cell transplant and cellular therapies, Myeloma UK Clinical trials network and the CRUK/NIHR ECMC Network.

8. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

A – Main CSG Strategy
B – Acute Lymphoblastic Leukaemia (ALL) Subgroup Strategy
C – Acute Myeloid Leukaemia (AML) Subgroup Strategy
D – Chronic Lymphoblastic Leukaemia (CLL) Subgroup Strategy
E – Chronic Myeloid Leukaemia (CML) Subgroup Strategy
F – Myelodysplastic Syndromes (MDS) Subgroup Strategy
G – Myeloma Subgroup Strategy
H – Myeloproliferative Neoplasms (MPN) Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

Appendix 5 – Recruitment to the NIHR portfolio in the reporting year

Professor Peter Hillmen (Haematological Oncology CSG Chair)

Appendix 1

Membership of the Haematological Oncology CSG

Name	Specialism	Location
Dr Satyen Gohil*	Clinical Research Fellow	London
Dr Charlotte Pawlyn*	Clincial Research Fellow	Surrey
Mr Alan Chant	Consumer	High Wycombe
Dr Gillian Murphy	Consumer	Surrey
Professor Gordon Cook	Haematologist	Leeds
Professor Mhari Copland	Haematologist	Glasgow
Dr Francesco Forconi	Haematologist	Southampton
Professor Peter Hillmen (Chair)	Haematologist	Leeds
Dr Richard Kaczmarski	Haematologist	London
Dr Sally Killick	Haematologist	Bournemouth
Professor Judith Marsh	Haematologist	London
Professor Adam Mead	Haematologist	Oxford
Professor Stephen O'Brien	Haematologist	Newcastle
Dr Andrew Peniket	Haematologist	Oxford
Professor Ciro Rinaldi	Haematologist	Boston
Dr Clare Rowntree	Haematologist	Cardiff
Professor Nigel Russell	Haematologist	Nottingham
Dr Anna Schuh	Haematologist	Oxford
Dr Simon Stanworth	Haematologist	Oxford
Professor Kwee Yong	Haematologist	London
Ms Lavinia Davey	Nurse	Canterbury
Dr Alasdair Rankin	Research Director, Bloodwise	London
Ms Shamyla Siddique	Senior Trails Coordinator	Birmingham
Professor Walter Gregory	Statistician	Leeds
Ms Amy Kirwood	Statistician	London

* denotes trainee member

Membership of the Subgroups

Acute Lymphoblastic Leukaemia (ALL) Subgroup		
Name	**Specialism**	**Location**
Dr Rachael Hough	Clinical Oncologist	London
Professor Oliver Ottman**	Clinical Professor	Cardiff
Mr John Reeve	Consumer	Hampshire
Professor Anthony Moorman**	Epidemiologist	Newcastle
Dr Adele Fielding (Co-Chair)**	Haematologist	London
Professor David Marks**	Haematologist	Bristol
Dr Andrew McMillan	Haematologist	Nottingham
Dr Tobias Menne**	Haematologist	Newcastle
Dr Nick Morley**	Haematologist	Sheffield
Dr Clare Rowntree (Co-Chair) **	Haematologist	Cardiff
Dr Sridhar Chaganti**	Haematologist	Birmingham
Dr Anna Castleton**	Haematologist	Manchester
Dr Bella Wrench	Scientist	London
Dr Caroline Furness	Haematologist	Bristol
Dr Debbie Yallop	Haematologist	London
Ms Amy Kirkwood	Statistician	London
Ms Pip Patrick	Trials Coordinator	London
Ms Laura Clifton-Hadley	Trials Coordinator	London

Acute Myeloid Leukaemia 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	Haematologist	Birmingham
Dr Mike Dennis	Haematologist	Manchester
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
Professor Nigel Russell (Chair)	Haematologist	Nottingham
Dr Paresh Vyas**	Haematologist	Oxford
Dr Robert Lown	Haemato-Oncologist	Southampton
Dr Priyanka Mehta**	Haemato-Oncologist	Bristol
Ms Shamyla Siddique**	Senior Trials Coordinator	Birmingham
Dr Robert Hills**	Statistician	Cardiff
Professor Keith Wheatley	Statistician	Birmingham

Chronic Lymphoblastic Leukaemia (CLL) Subgroup		
Name	**Specialism**	**Location**
Dr Satyen Gohil*	Clincial Research Associate	London
Mr Garry Bisshopp	Consumer	Sussex
Mr Nick York**	Consumer	
Dr David Allsup	Haematologist	Hull
Dr Adrian Bloor	Haematologist	Manchester
Professor Stephen Devereux	Haematologist	London
Dr Chris Fegan	Haematologist	Cardiff
Dr Francesco Forconi	Haematologist	Southampton
Dr Chris Fox	Haematologist	Nottingham
Professor Peter Hillmen (Chair)	Haematologist	Leeds
Dr Scott Marshall	Haematologist	Sunderland
Dr Chris Pepper	Haematologist	Cardiff
Professor Andre Pettitt	Haematologist	Liverpool
Dr Christopher Pocock**	Haematologist	Canterbury
Dr Guy Pratt**	Haematologist	Birmingham
Dr Anna Schuh	Haematologist	Oxford
Dr Ben Kennedy	Haemato-Oncologist	Leicester
Professor Martin Dyer	Haemato-Oncologist	London
Ms Dena Cohen	Statistician	Leeds

Chronic Myeloid Leukaemia (CML) Subgroup		
Name	**Specialism**	**Location**
Ms Sandy Crane	Consumer	
Dr Nauman Butt**	Haematologist	Liverpool
Dr Jenny Bryne	Haematologist	Nottingham
Professor Richard Clark	Haematologist	Liverpool
Professor Mhairi Copland (Chair)	Haematologist	Glasgow
Dr Paolo Gallipoli	Haematologist	Cambridge
Dr Andrew Goringe	Haematologist	Cardiff
Dr Brian Huntly	Haematologist	Cambridge
Dr Adam Mead	Haematologist	Oxford
Professor Stephen O'Brien	Haematologist	Newcastle
Dr Graeme Smith	Pathologist	Leeds

Myelodysplastic Syndromes (MDS) Subgroup		
Name	**Specialism**	**Location**
Ms Sophie Wintrich**	Consumer	
Mr Dan Wiseman	CRUK Representative	Manchester
Professor David Bowen	Haematologist	Leeds
Dr Catherine Cargo**	Haematologist	Leeds
Professor Jamie Cavenagh	Haematologist	London
Dr Tim Chevassut**	Haematologist	Brighton
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 (Chair)	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 Lynn Quek	Haematologist	Oxford
Dr Manoj Raghavan	Haematologist	Birmingham
Dr Kavita Raj**	Haematologist	London
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
Mr Alan Chant	Consumer	Maidenhead
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
Professor Gordon Cook (Chair)	Haematologist	Leeds
Dr Mark Cook	Haematologist	Bristol
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**	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 Charlotte Pawlyn*	Haematology Registrar	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	
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
Dr Peter Campbell**	Haematologist	Cambridge
Dr Frederick Chen**	Haematologist	Birmingham
Dr Eibjilin Conneally**	Haematologist	London
Professor Nick Cross**	Scientist	Southampton
Dr Mark Drummond	Haematologist	Glasgow
Dr Andrew Duncombe	Haematologist	Southampton
Dr Hesham Eldaly	Pathologist	Cambridge
Dr Joanne Ewing	Haematologist	Birmingham
Ms Sonia Fox**	Senior Trials Coordinator	Birmingham
Dr Sebastian Francis**	Haematologist	Sheffield
Dr Mamta Garg	Haematologist	Leicester
Dr Anna Godfrey**	Haematologist	Cambridge
Professor Tony Green	Haematologist	Cambridge
Professor Claire Harrison	Haematologist	London
Dr Clodagh Keohane**	Haematologist	Cork
Dr Stephen Knapper	Haematologist	Cardiff
Dr Jashmid Khorashad	Scientist	Imperial
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 Beth Psaila**	Haematologist	Oxford
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
Mrs Sonia Fox**	TAP Trials Team Leader	Birmingham

* denotes trainee member

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

The Haematological Oncology CSG 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 CSG 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 CSG'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.

Priority areas for clinical research

The CSG aims to maintain a balanced and continuously replenishing portfolio of academic and industry studies in all major disease areas, using data from the CSG's early-phase trial programmes to inform on the next generation of phase III studies. In addition to the 7 disease specific sub-groups the CSG 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 CSGs 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 CSG'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 CSG 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 CSG in order to plan the portfolio and minimise competition for niche study populations.

Engagement with charity-funded research infrastructure initiatives
The CSG 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 CSG 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 will be a switch 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 CSG.

Trial delivery
Delivering trials to time and target remains one of the key priorities of the CSG. It is therefore important that the CSG engages effectively with the delivery networks. This will be achieved by involving Subspecialty Leads (SSLs) in CSG meetings and by continuing to showcase the CSG 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 CSG 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 CSG has broad geographical representation.

CSG membership
In order for the CSG to fulfil its function, it is crucial that CSG 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 CSG also places much emphasis on statistician representation. The appointment of a senior trial coordinator to the Group provides expertise in trial delivery. The CSG 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 CSG has implemented the rotation of sub-group 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 CSG is committed to contributing to this process by taking part in the CSG Trainee Scheme.

B – Acute Lymphoblastic Leukaemia (ALL) Subgroup Strategy

Strategic aims

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 aim is to have a front-line trial for all patients with newly diagnosed ALL in the UK with the priority for 2018-19 being to complete the design of UKALL 15 and to submit to CRUK for funding in November 2018.

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.

Challenge 1

Maintaining high quality upfront studies for all newly diagnosed patients with ALL in the UK.

Challenge 2

The year-long closure of UKALL 60+ by the MHRA to transfer the study to an IMP study has led to recruitment being behind target. The challenge now is to complete recruitment to this trial which requires further funding to the additional funding already obtained.

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
To analyse treatment response in relationship to mutational profile in a collaboration with the Sanger Institute based upon an analysis of samples from over 2,400 patients entered into our trials. This will help inform the design of the next generation of NCRI AML trials.

Challenge
To design and fund the LI2 trial a follow-up trial for patients not fit for intensive therapy to replace the LI1 trials.

D – Chronic Lymphoblastic Leukaemia (CLL) Subgroup Strategy

The aim of the CLL Subgroup is to improve the outcome of treatment for patients with CLL including those who are fit for intensive fludarabine-based therapy, the elderly, unfit and those with poor risk CLL such as those with Richter's transformation. The strategy is to develop a streamlined approach with a series of rapidly recruiting phase II trials under the auspices of the Bloodwise Trials Acceleration Programme recruiting patients with relapsed refractory CLL. The results of these phase II trials feed directly into the phase III programme in which previously untreated patients are treated with the novel combinations from the TAP programme.
In addition, the Biobanking of samples from the CLL trials over the last 10 years is supporting a comprehensive portfolio of translation research in numerous centres across the UK which add further value to the portfolio. We are the only collaborative group internationally that is using the assessment of minimal residual disease to define duration of therapy with the novel targeted treatments, such as ibrutinib and venetoclax, with the ultimate aim of curing CLL. There is a comprehensive pharmaco-economics programme associated with the trial portfolio in ensure that the advances made can be translated rapidly into the NHS and other healthcare systems worldwide.

Key aims

1. Now that the RIAltO trial (CI: Professor Andrew Pettitt) for patients unfit for fludarabine-based therapy has completed recruitment we will be concentrating on follow-up and moving towards analyse of the trial outcome. RIAltO eventually recruited 521 patients and will be the only study worldwide to test the front-line application of bendamustine plus a CD20 antibody (ofatumumab) compared to chlorambucil plus ofatumumab approach, which is the standard of care.
2. Recruitment of 754 patients into the original FLAIR Trial (CI: Professor Peter Hillmen) that compares a non-chemotherapy approach (ibrutinib plus rituximab) against the standard of care for patients considered fit for fludarabine-based therapy (FCR) will be completed in June 2018. FLAIR is the largest trial addressing this question and should report it's initially in results in approximately 2020 depending on the outcome of the Interim Analysis.
3. The amendment of the FLAIR Trial that adds two additional arms to the trial (ibrutinib monotherapy and ibrutinib plus venetoclax) and increases the total number of patients in FLAIR to approximately 1,516 patients has now been implemented. The initial 31 patients randomised to ibrutinib plus venetoclax have been commenced on venetoclax successfully. When the original FLAIR completes recruitment (expected in the first half of 2018) the ibrutinib plus rituximab will be dropped (after a decision by the DSMB) and three arms (FCR, ibrutinib monotherapy and I+V) will continue to recruit. The trial is expected to continue recruiting until 2020.
4. We are hoping to amend the FLAIR trial further by including patients with chromosome 17p deleted (or TP53 mutated) into only the I compared to I+V arms of the trial. At present these patients are excluded from the trial.
5. To continue the rapid development of the Bloodwise TAP Trials including reporting the initial responses in the CLARITY trial (CI: Professor Peter Hillmen) of ibrutinib plus venetoclax. We aim to expand cohorts of patients in CLARITY further testing novel combinations such as I+V+obinutuzumab.
6. We will continue the development of trials for rare variants of CLL which have poor outcomes with standard therapies, such as Richter's transformation. The STELLAR TAP

Trial (CI: Professor Anna Schuh) for Richter's transformation testing a novel combination of chemoimmunotherapy plus acalabrutinib, a second generation Btk inhibitor, should open in 2018.

7. The analysis of the whole genome sequencing for over 400 paired germ-line and tumour samples from the ADMIRE, ARCTIC and RIAltO Trials recruited from the UKCLL Biobank via the Genomics England (CI: Professor Anna Schuh) will be performed in the next 12 months. This is a unique opportunity that is expected to revolutionize our understanding of CLL and, as the samples are from our trials, will maximize their impact.
8. Application for funding of the UKCLL Biobank (CI: Professor Andrew Pettitt) to ensure the continued support of this essential component of the Subgroup's activity. Unfortunately, the MRC Outline Application was rejected and at the moment the Biobank is funded by Bloodwise. Other sources of funding are being considered for this essential part of our activity.
9. Finally, with the appointment of Professor Hillmen as the CSG chair we will be replacing him as the Chair of the CLL subgroup in 2018.

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.

Moving forward, 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 – recently funded by CR-UK-EMERP and (2) to develop a de-escalation/discontinuation follow-up study to DESTINY. We also have a cohort study 'CALLS' (CI: Dr Hugues de Lavallade) opening in sites across the UK, a commercial study in collaboration with Incyte to assess Next Generation Sequencing for the diagnosis of BCR-ABL mutations. We currently have two commercial studies open – both for patients with chronic-phase CML with TKI resistance: (1) OPTIC, which is a phase 2 dose finding study of different doses of ponatinib; and (2) CABL001A2301, a phase 3 study (2:1 randomisation) comparing asciminib with bosutinib. We will continue to engage with industrial partners, where appropriate to open additional commercial studies in the UK. In terms of a front-line study for patients with newly diagnosed chronic phase CML, following the withdrawal of funding for SPIRIT3 and the introduction of generic imatinib, we acknowledge that this is a challenging area for clinical trial development at present, but we plan to re-visit in the future.
2. Presentations/Publications: DESTINY and CHOICES will be presented at EHA in June 2018. Final manuscripts are currently in preparation. The de-escalation phase of the DESTINY clinical trial has been published in Lancet Haematology (Clark et al, Lancet Haematology 2017;4:e310-316). SPIRIT2 is currently undergoing data cleaning and statistical analyses, with a view to abstract submission to ASH (August deadline for December meeting) and a manuscript later this year. In addition, the Subgroup is preparing a BCSH guideline to advise on practical management of CML, and has contributed to a consensus document about BCR-ABL PCR testing (currently under review at the British Journal of Haematology).
3. Correlative science: The clinical trial biobanks continue to be a rich source for research projects and publications. Over the next 12 months, the Subgroup aims to secure finding to further evaluate samples from the DESTINY clinical trial. The correlative science work packages for TASTER are currently in development. Discussions surrounding GeCIP and sample collection for CML continue, but it is acknowledged that this is challenging as only extreme responders will be evaluated; the mechanism for doing this has yet to be defined.
4. 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 education day later in the year – Birmingham on 22nd September 2018.

5. Subgroup membership: Over the next 12 months, I need to consider succession planning for CML subgroup chair as I will step down in July 2019. In addition, I would be keen to enrol a trainee member and a clinical nurse specialist to the group.

F – Myelodysplastic Syndromes (MDS) Subgroup Strategy

The strategy of the MDS Subgroup is to develop a portfolio of Phase I, II and III studies which cover, as much as possible, low risk and high risk MDS and supportive care questions across all groups.

April 2018 has seen the end of the tenure of Dr Dominic Culligan as Chair and this role has been taken over by Dr Sally Killick. The MDS subgroup has expressed their gratitude to Dr Culligan for his hard work, supportive approach, clear mind, drive and passion leading and guiding the group over the last 6 years.

MDS continues to be a difficult disease with regards designing and delivering clinical trials. The patients are mainly elderly (median age 73 years), managed in district hospitals around the UK and many receive supportive care alone with no active drug therapy. Patients often have multiple co-morbidities and find it difficult to travel distances to take part in trials. Although there are now some proven agents which are licensed in MDS, namely azacitidine in high risk MDS and lenalidomide in del(5q), there is still a paucity and this needs to be built upon but remains challenging.

The strategic 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. The 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 (AML18/19/LI-1) 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. As part of our NCRI AML subgroup collaboration, we have put forward a major amendment to NCRI AML 19 trial to enable a wider range of high risk MDS patients to take part.

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. There has been success from the group in this area over the last year.

Investigator led clinical trials open to recruitment/closed in the last 12 months:

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 planned 38 patients on time. End of recruitment 11/7/17. Currently in data cleaning process, data lock expected April 2018 when data analysis will start.
2. ELASTIC – Azacitidine and eltrombopag. CI Dr A Sternberg. Continued recruitment of high risk MDS patients to the 5th and final cohort, with no dose limiting toxicities. The expansion cohort is now open and recruiting well.
3. MONOCLE - Phase II study in CMML. CI Dr Steve Knapper. Safety and clinical effectiveness of the monocyte targeted HDAC inhibitor, Terfinostat. Recruited to the first phase rapidly. DMC

have passed its safety assessment. Futility assessment is ongoing and the study is therefore closed to recruitment until a decision has been made.

4. CATAPULT 001 WT-1 gene modified T cell therapy for AML/MDS. CI Prof Emma Morris. Currently closed due to a change in sponsor with a plan to re-open soon with a target of 5 patients before a futility assessment.
5. MDS Bio-1 – closed to recruitment whilst the new Haem-Bio is worked up. This has been a very successful venture with over 8,000 samples with linked clinical data, this biomedical resource has already contributed to major breakthroughs in understanding the molecular basis of MDS and the basis of response to some treatments, such as lenalidomide. A significant number of publications in the very top impact factor journals have resulted and the Subgroup is looking to link future trial development with this platform. The first successful application of this linked approach is ELASTIC.
6. FIGARO – collaboration with AML subgroup. CI Prof C Craddock. FLAMSA-BU conditioning regimen in patients with AML and MDS undergoing allogeneic stem cell transplantation. Recruited. A follow-on study (COSI) will be informed by the results of FIGARO and is funded.
7. There are seven commercial trials currently listed in the MDS subgroup portfolio using a number of IMPs.

Priority areas for Clinical Research

1. Randomised Phase II/III trial of Danazol Vs VBaP Vs best supportive care. Dr's Drayson, Culligan, Raghaven, Killick, Mufti. This is a trial investigating danazol and the novel combination of valproate, bezafibrate and medoxyprogesterone for which there is scientific data supporting its use (Dr M Drayson's group). It is a trial aimed at low risk MDS, which fulfils the strategic aims of the group. The plan is for the trial to be phase II, then move to phase III with the best arm. CRCTU are reviewing the trial currently and are likely to adopt it. This is an exciting trial which will have important clinical questions, tight diagnostic review and strong translational research over a number of scientific groups. The trial will be open to all UK centres and the plan is to apply to CRUK for funding.
2. TEAMM 2 – collaboration. Dr's Drayson & Culligan. Following on from the disappointment of not having RAPRIMA funded, the group have approached Dr Drayson regarding including MDS patients into TEAMM 2 in a similar fashion to RAPRIMA, allowing resurrection of all the hard work by our subgroup over 2 years. This is a supportive care trial investigating antibiotic prophylaxis. Discussion is ongoing and seems very favourable.
3. REDDS2 – the aim is to work collaboratively with Dr Stanworth at NHS Blood and Transplant to design an international, multicentre phase III trial using data from REDDS to inform trial design on transfusion support in patients with lower risk MDS.
4. QOL during supportive care study, based in Sheffield. Final draft protocol completed, for ethics submission. Novel use of a telephone app to record data.
5. LI-2 – collaborative input to trial design for patients with high risk MDS with the AML subgroup.

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.

Finally, the MDS subgroup are working to raise the awareness of MDS trials in the UK. We will be working with the UK MDS Patient Support group to have an up to date list of all recruiting clinical

trials for MDS patients on the Patient Support website. There is also discussion around a newsletter from the group going out to UK haematologists and research nurses to promote open trials.

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 "umbrella" 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 aim to establish a robust plan centered 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 thus there is a need to establish cellar and open biosampling governance. Taken together, we aim to publish our clinically impactful studies in high-ranking journals to change clinical practice.

Links to other CSGs, international groups and network subspecialty leads

The myeloma sub-group doesn't have any formal links with other CSG, though some peripheral involvement in our study discussion have been had with CTRad.

Until recently, the European Myeloma Network (EMN) has not included the UK trialists. Following a very constructive meeting in Paris in April 2018, there is now a move to become more collaborative as European myeloma clinical trialists, under the auspices of the EMN. This is to be ratified at the EMN board meeting in September 2018.

Funding applications in last year

Mostly CRUK. We confirmed the CRUK funding for two frontline phase III studies, Myeloma XIV and XV, due to open in the second half of 2018.However, some Bloodwise TAP funding has been successful, with NIHR funding a recently closed phase III (TEAMM study). We are in the process of devising a supportive care platform, ENCOMPASS which we intend to submit for funding consideration to NIHR

The funding for the early phase trials network, MUK CTN, has undergone a review, and a call for submissions to deliver a different funding model has been made in Q1 2018. The UKMRA has submitted a proposal for a core grant (Concept and Access Research Programme; CARP - CI G Cook) and is currently under consideration.

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 and UKMRA Myeloma XV is supported by CRUK and Amgen, Celgene and Sanofi.

In the early phase trials setting, we have industry partnership with Takeda (MUK8), Karyopharm (MUK12) and Takeda with some contribution from Celgene and Janssen and Amgen (MUK9).

Impact of CSG activities

The recently closed phase III studies have established the role of salvage ASCT (NCRI Myeloma X) and maintenance therapy in first line along with sequential biological agent-based induction (NCRI Myeloma XI/XI+). Myeloma X has informed both national and international guideline developments and an impact on real world clinical care has been demonstrated (BSBMT and EBMT registry activity highlighting the increase in the number of sASCT performed since the study reported.

Open meetings, trials days, strategy days

UKMRA Trials day June 2016, 2017 and the 2018 meeting is planned for 6th June 2018. We continue to have 3 additional business meetings per year, and quarterly senior leadership team meetings/telecons.

Priorities and challenges for the forthcoming year

The aim for the coming 12 months is to ensure the strategic integration of young investigators in the research programme of the sub-group continues, under the ethos of inclusivity and continuity planning. We need 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.

A leadership challenge is the impact of any NCRI representation restrictions placed on our collaborative. T currently works well, with the vice-chair elected to succeed the chair, who represents our group on the Haemato-oncology CSG. We have worked hard to form a cohesive and collaborative group, headed up by the senior leadership team. This has under-pinned our success to date and any disruption tom this could jeopardize further success.

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 e.g. two polycythaemia guidelines will be published in 2018.
- 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, and the forthcoming MITHRIDATE study and translational research studies utilizing these samples are underway with high-impact publications anticipated over the coming 12 months. Through strong links with industry, members are also working with sample banks collected in industry studies, e.g. RESUME and PAC203 studies of myelofibrosis (over 200 samples available). We have established a new study focused on familial MPNs (INForMeD study) that has recruited over 60 participants 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 (PV); here we will be opening a large randomised trial of ruxolitinib versus best available therapy later this year (MITHRIDATE; A Multicenter International sTudy comparing ruxolitinib with either HydRoxycarbamIDe or interferon Alpha as first line ThErapy for high risk polycythemia vera. This academic study is now fully funded and will open to recruitment later in 2018. This is the first study of ruxolitinib as a first line treatment for PV and will recruit approximately 600 patients over 5 years. CI: Claire Harrison).

- Essential thrombocythaemia (ET); here a first line trial is currently lacking and is a priority for the Subgroup. We are exploring the possibility of a trial investigating the use of NOACs in high risk ET.
- Second line trial options are available for PV and ET patients including TAMARIN (actively recruiting) and MOMBAT (in set up; planned to open over the next 12 months) studies. These innovative studies have both resulted from translational research in the UK and are focused on repurposing of established treatments (tamoxifen in TAMARIN and methotrexate in MOMBAT) for therapy of MPN patients.
- 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. New studies over the next 12 months will combination studies of ruxolitinib with Navitoclax or bromodomain inhibition in myelofibrosis.
- Accelerated phase and blast crisis MPN – we anticipate that the PHAZAR study (combining azacitidine with ruxolitinib) will complete recruitment over the next 12 months.

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 by Novartis.

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 and TAMARIN.

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. We are also prioritising clinical trial banked samples for inclusion into the GEL programme.

Trial delivery

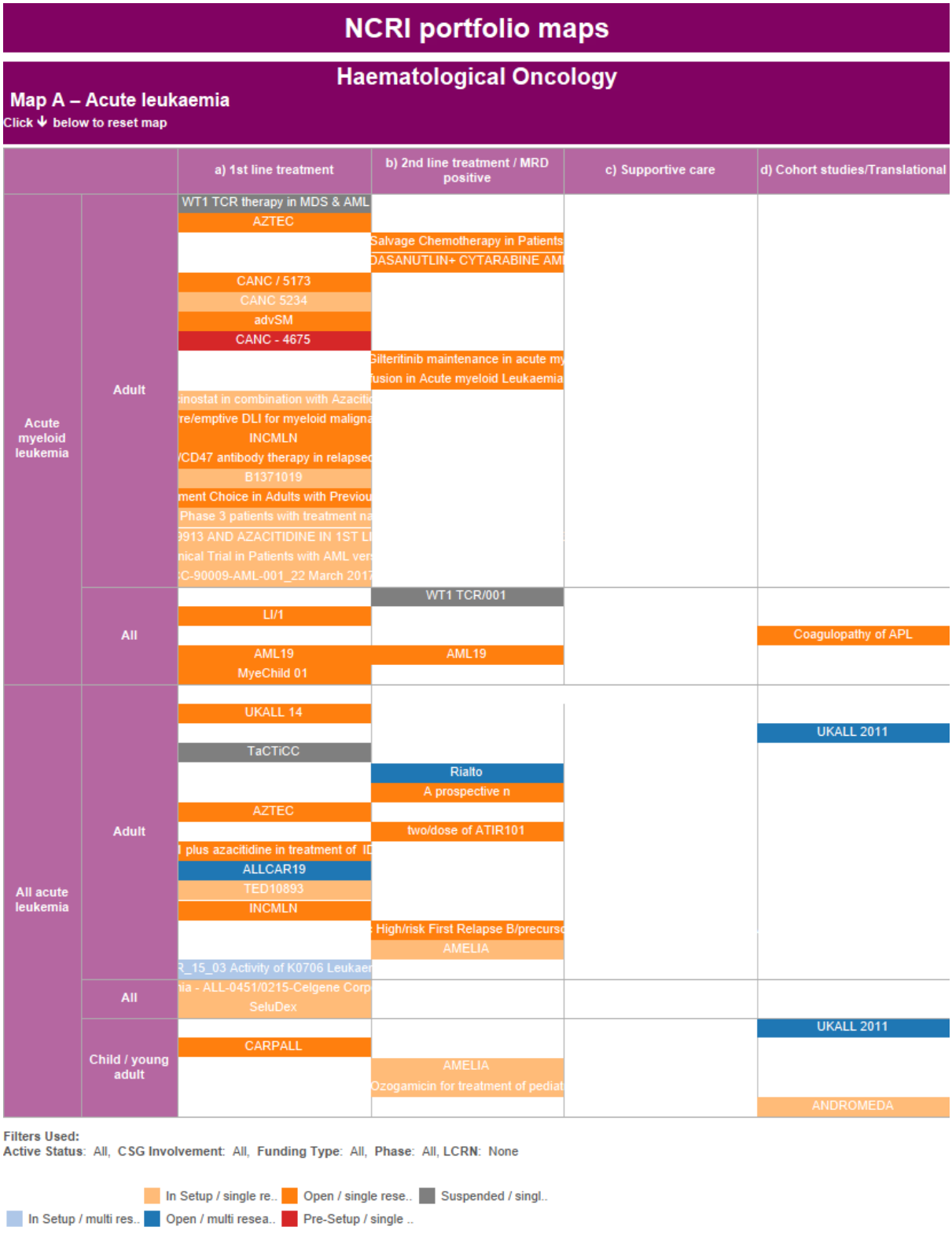
The Subgroup has an excellent track record of successful delivery of trials and high recruitment into industry studies internationally.

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

Portfolio maps



NCRI portfolio maps

Haematological Oncology

Map B – Chronic leukaemia

Click ↓ below to reset map

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

In Setup / single re.. | Pre-Setup / single .. | Suspended / singl..
In Setup / multi res.. | Open / single rese.. | Suspended / multi ..

NCRI portfolio maps

Haematological Oncology

Map C – Myelodysplastic syndrome, myeloproliferative neoplasms, transplant trials

Click ↓ below to reset map

		a) 1st line treatment	b) 2nd line treatment / MRD positive	c) Supportive care	d) Cohort studies/Translational
Myelodysplastic syndrome	All	LI/1 AZACITIDINE + BSC ELASTIC	Risk Myelodysplastic Syndrome CANC / 4888		MDSBio
		advSM TAMARIN AZACITIDIN +// DURVALUMAB Atsral-3 Venetoclax in MDS PF-04449913 AND Anaemia with Lower Risk MDS			
Myeloproliferative neoplasms	All	Givinostat in JAK2V617F positive CMNs		treatment pathways for MF in the	Clonal BC Disorders Molecular patho MPN-associated myelofibrosis &
Transplant trials	All	ProT4 (Prophyla UK Haplo v1.0 ICAT WT1 TCR therapy in MDS & AML REVERSE Brincidofovir for Adenovirus	ProT4 (Prophyla ICAT		CMV TCR Gene Therapy (CMV TCR001) CARD treated with a matched unrelated

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

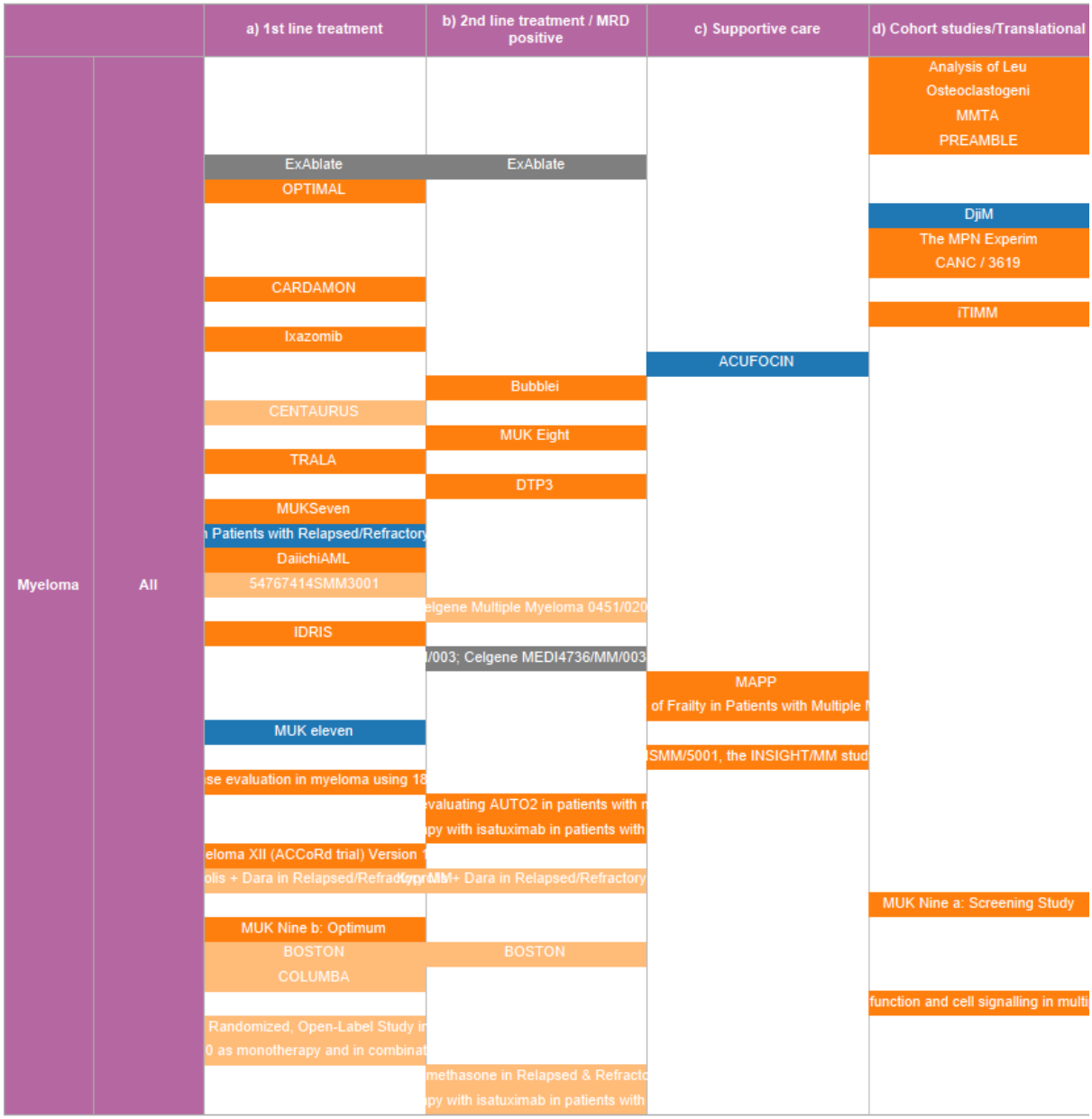
In Setup / single re.. Open / single rese..
Open / multi resea.. Suspended / singl..

NCRI portfolio maps

Haematological Oncology

Map D – Myeloma

Click ↓ below to reset map



Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

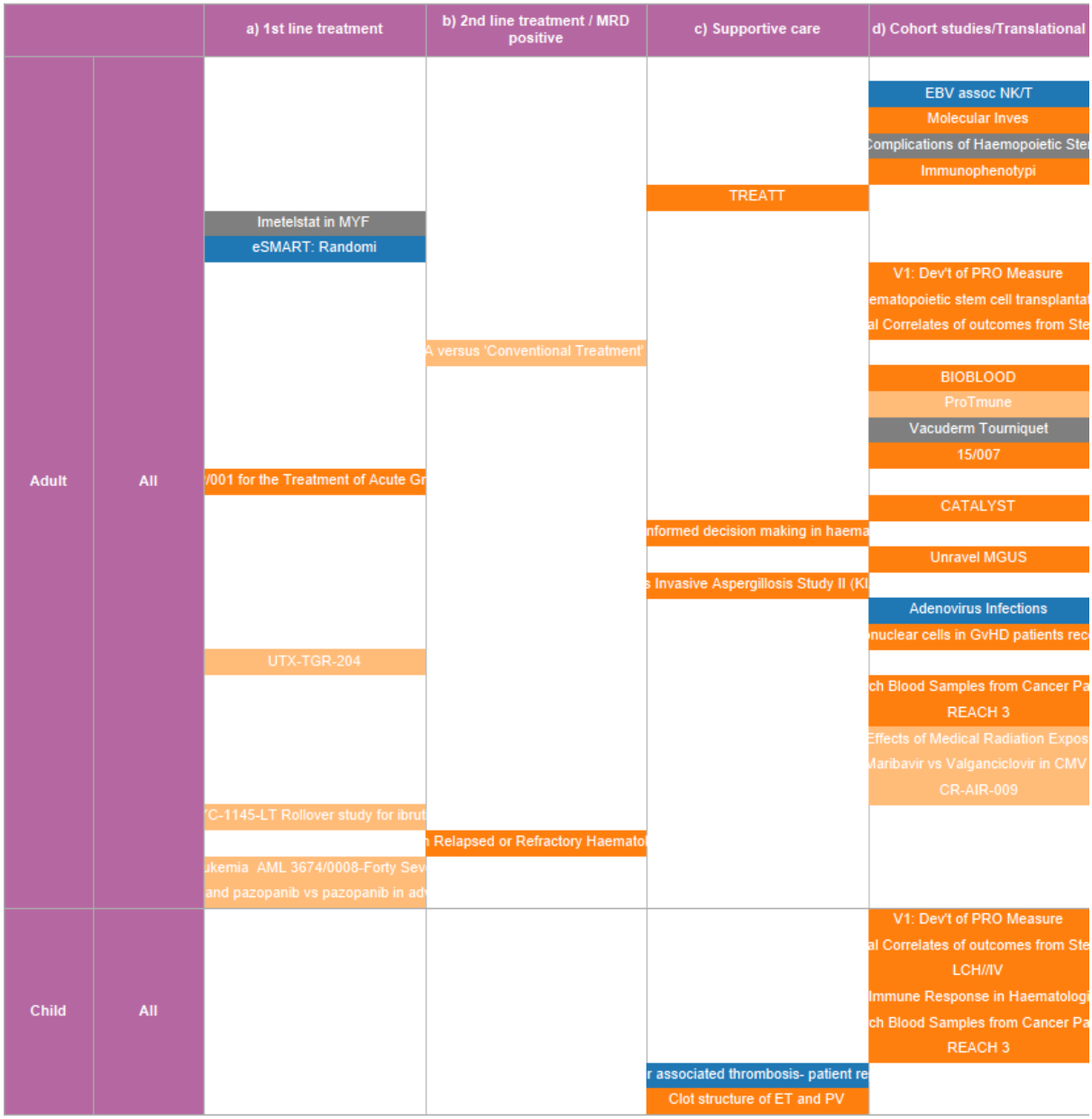
In Setup / single re.. Open / single rese..
Open / multi resea.. Suspended / multi ..

NCRI portfolio maps

Haematological Oncology

Map E – Other studies

Click ↓ below to reset map



Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

Open / multi resea.. Suspended / multi ..
In Setup / single re.. Open / single rese.. Suspended / singl..

Appendix 4

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Ruxolitinib vs best available therapy for ET intolerant or resistant to hydroxycarbamide. Harrison CN et al, Blood. 2017 Oct 26;130(17):1889-1897	This paper was selected by the editors of Blood as one of the top 10 most outstanding manuscripts of 2017. This is the first investigator led study of ruxolitinib worldwide and defines the role of this drug in the management of high-risk ET patients with hydroxycarbamide resistance/intolerance: in contrast to patients with PV, ruxolitinib does not represent the first choice for most ET patients resistant or intolerant to HC, with the possible exception of those severely symptomatic, particularly for pruritus.	MPN Subgroup developed
2. De-escalation of tyrosine kinase inhibitor dose in patients with chronic myeloid leukaemia with stable major molecular response (DESTINY): an interim analysis of a non-randomised, phase 2 trial. Clark RE et al, Lancet Haematol. 2017 Jul;4(7):e310-e316	The study is practice changing as for the first time it is safe to reduce therapy in CML patients that have obtained at least a major molecular remission.	CML Subgroup developed

3. Measurable Residual Disease at Induction Redefines Partial Response in Acute Myeloid Leukemia and Stratifies Outcomes in Patients at Standard Risk Without NPM1 Mutations. Freeman SD et al, J Clin Oncol. 2018 May 20;36(15):1486-1497	The subject of an editorial in the same edition of Journal of Clinical Oncology. The findings have also been integrated into the risk stratification of the AML19 trial by amendment.	AML Subgroup developed
4. Results of the randomized phase IIB ADMIRE trial of FCR with or without mitoxantrone in previously untreated CLL. Munir T et al, Leukemia. 2017 Nov;31(11):2416-2425		
5. Pegylated-asparaginase during induction therapy for adult acute lymphoblastic leukaemia: toxicity data from the UKALL14 trial. Patel B et al, Leukemia 2017 Jan;31(1):58-64	Changed the use of pegylated-asparaginase in UKALL14 and in routine practice.	ALL Subgroup developed

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Haematological Oncology CSG portfolio, 37 trials closed to recruitment and 39 opened.

Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2013/2014	2925	3027	2818	3027	21.4	23.0
2014/2015	3132	3320	2972	3320	22.5	25.2
2015/2016	2370	2747	2370	2743	17.97	20.80
2016/2017	5534	2578	5522	2571	41.87	19.49
2017/2018	5309	2366	5277	2366	40.01	17.94