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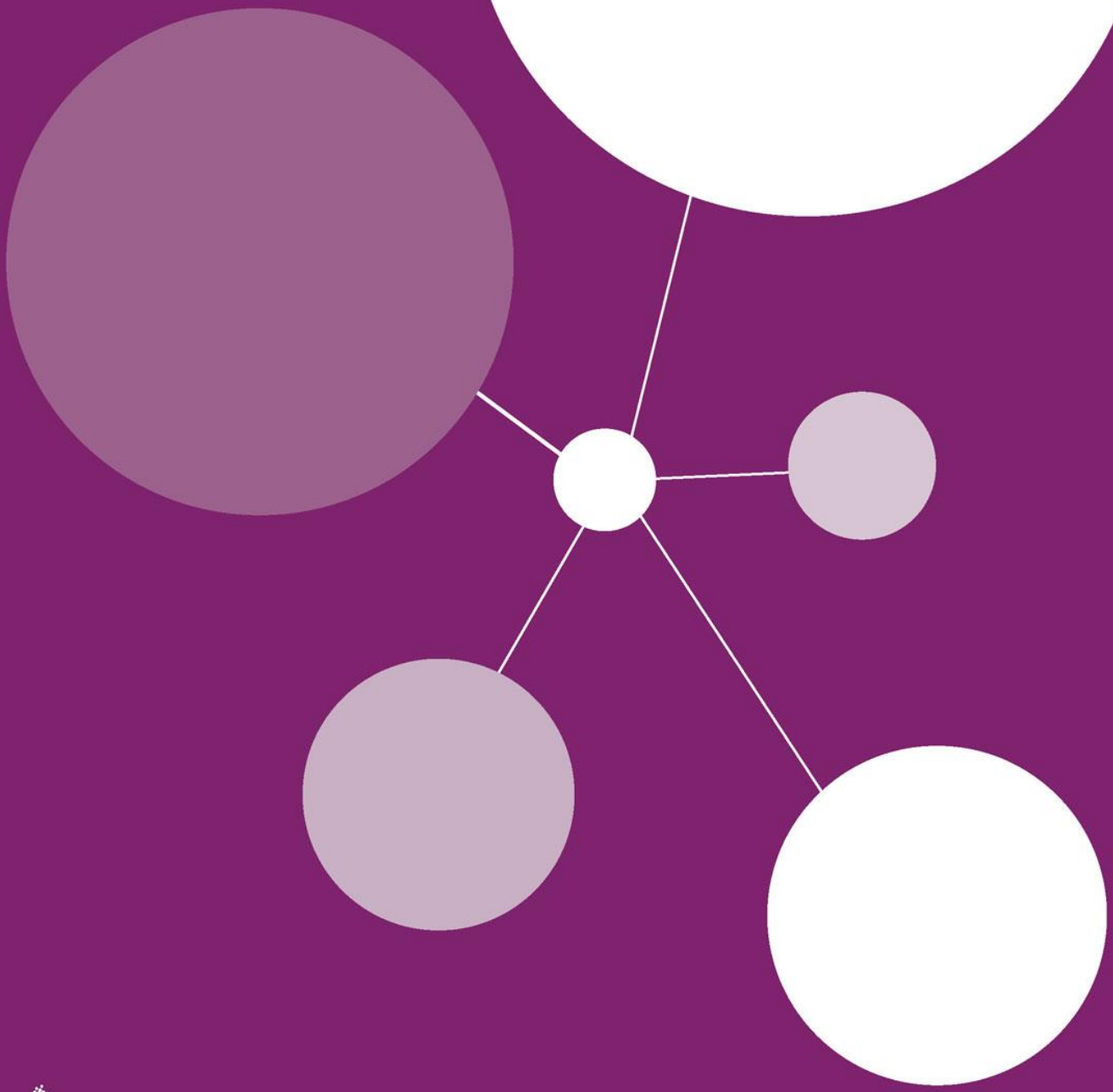
NCRI Lymphoma Clinical Studies Group

Annual Report 2015-16



Partners in cancer research

NCRI Lymphoma CSG Annual Report 2015-16

1. Executive Summary (including top 3 achievements in the year)

The Lymphoma CSG has had a successful year. The top achievements are:

1. Results of the RAPID trial of PET directed therapy in early stage Hodgkin lymphoma published NEJM, April 2015 - This paper was accompanied by an editorial and is practice changing. The results of this trial that show PET negative patients after chemotherapy do not require radiotherapy prompted a keynote debate at the ICML, Lugano in June 2015, an invitation to write a chapter for the 50th anniversary edition of Seminars in Haematology and to review Canadian guidelines.
2. Results of the international RATHL trial of PET directed therapy in advanced Hodgkin lymphoma presented in Plenary Session at ICML Lugano, June 2015 and to be published NEJM June 2016 - This is the first international lymphoma trial led by the UK and will be practice changing; results show that a PET adapted approach produces excellent outcomes in this population of patients and bleomycin can be avoided in PET negative patients. A second abstract describing the benefits of less rather than more bleomycin presented in oral session at ICML Lugano, June 2015.
3. Preliminary results of the IELSG 32 trial in primary CNS lymphoma presented in Plenary Session at ICML Lugano, June 2015 - The results of this trial will be practice changing; they show that the addition of rituximab and thiotepa to methotrexate and cytosine arabinoside improve remission rates three year PFS and OS. Although entering the study late, the UK was the third highest recruiter and has firmly established itself as a major player in CNS lymphoma research.
4. Presentation of the preliminary results of REMoDL-B trial at ASH meeting December 2015 - This trial showed that molecular phenotyping of diffuse large B cell lymphoma is possible in real time supporting personalised medicine approaches for patients diagnosed with these tumours. The results of REMoDL-B have been taken forward in the ARGO trial which will provide a platform for the investigation of new agents based on molecular characteristics.

2. Structure of the Group

The Lymphoma CSG is largely representative of UK clinical practice and comprises haematologists, medical, paediatric and clinical oncologists, consumers, pathologists and imaging experts. It also includes two trainees (Dr Okusan and Dr Ahearne) who we hope will gain

valuable experience from their 18 month attachment, the Research Director of Bloodwise (Dr Alasdair Rankin) and CEO of the Lymphoma Association (Mr Jonathan Pearce).

In selecting new CSG members we seek to both maintain the professional and geographical balance with inclusion wherever possible of colleagues from all parts of the UK. This year we welcomed Professor Richard Cowan and Dr David Cutter (clinical oncology), Dr Victoria Warbey (imaging), Mr Andrew Barton (consumer), Dr Menne and Dr Burton (haematology) and Dr Maria Calaminici (haematopathology) to the CSG.

3. CSG & Subgroup strategies

Main CSG

Our main priorities in the 2014/15 report were to open frontline trials in Hodgkin lymphoma (HL), follicular lymphoma (FL) and diffuse large B cell lymphoma (DLBCL). In HL a trial proposal with substantial international support (RADAR) has been submitted to Takeda for funding and in FL a PET directed trial (PETREA) has recently been funded by CRUK CRC. In DLBCL a radiotherapy question is being posed in ConRad but unfortunately this has not yet been funded. A platform study (ARGO) in relapsed/refractory DLBCL for the evaluation of new agents and featuring molecular phenotyping has however been funded by Roche and is being submitted to CRUK CRC for endorsement.

The strategy day in October 2015 was a very well attended and successful event. The challenges associated with opening large patient number phase III trials accessible to most centres in the UK was discussed at length and it was concluded that for a variety of reasons these will be fewer in number in future years. However it is still possible to undertake trials of importance to lymphoma patients especially in the fields of process and survivorship and two studies in these fields are underway (START and SECURE).

The Lymphoma CSG has undertaken many practice changing studies over the last five years. However, we have the ambition to create even more impact and play a bigger part on the international stage as part of our overriding goal to improve outcomes for patients with lymphoma. Crucially we wish to increase the number of academic studies in the portfolio and build on our success of working with industry. In addition we want to breakdown the “postcode lottery” of patient access to clinical trials and are collaborating with consumers, Bloodwise and the Lymphoma Association to achieve this.

High Grade Lymphoma Subgroup (Chair, Dr Andrew Davies)

REMoDL-B completed recruitment of 1,132 patients with DLBCL in June 2015, from 95 UK sites and 20 in Switzerland. The results of secondary endpoints were reported at the American Society of Hematology (ASH) Annual Meeting in December 2015 with an expectation that sufficient number of progression events will be met by Q2 2017 to report the primary endpoint at the International Conference on Malignant Lymphoma (ICML) in 2017. This study has demonstrated that real time gene expression profiling can be delivered on a large prospective scale and used to stratify patients. It clearly demonstrates our capabilities in the UK and is widely regarded a world leading study. Translational endpoints were also presented at the ASH meeting in 2015. Built upon the strengths of molecular stratification in DLBCL, the Precision Medicine in Aggressive Lymphoma (PMAL) Consortium has been formed as a partnership between academia, the CSG and industry. Core funded by a specialist programme grant from Bloodwise, it provides the Subgroup with a platform of internationally leading translational capabilities for application in

future trials (build into ACCEPT and ARGO). These include transciptome analysis, mutational analysis panels, cfDNA analysis, IHC and FISH which will be incorporated in to an umbrella study of targeted novel agents in relapsed DLBCL. Engagement from multiple industry partners has been high.

The observational MaPLE study has opened, extending access to molecular stratification for patients outside the structure of an IMP. To date over 1,500 patients have been entered, initially providing EZH2 mutational analysis and now following an amendment an extended mutational panel and analysis of the 'liquid biopsy' by cfDNA. The study has been recruiting over 100 patients per month.

The IELSG32 trial of primary CNS lymphoma fully recruited, of which the UK was the third largest international recruiter, despite joining the study late and the results presented at the International Conference on Malignant Lymphoma in June 2015 and later published in the Lancet Haematology. This has been practice changing, demonstrating a survival advantage for the addition of rituximab and thiotepa to a methotrexate/cytarabine backbone. The Primary CNS Lymphoma Working Group of the High Grade Subgroup has played a major role in ensuring that this has become a standard of care in the NHS. The Subgroup has continued to collaborate extensively with international partners, resulting in a successful Cancer Research UK bid for a study in secondary CNS lymphoma (IELSG42) and in the design of frontline study (Fiorella) which is currently under consideration. The Subgroup has also opened a study for relapsed PCSL (TIER).

The results of R-CODOX-M/R-IVAC in both high-risk DLBCL and Burkitt's, along with Intestinal T-cell lymphoma study were presented at the ICML in June 2015.

The T-cell Working Party has been active, opening a novel combination study for relapsed disease (RomiCar) and support has been obtained for a T-cell lymphoma Biobank that will be hosted by the University of Leicester. Recruitment to Chemo-T, our current front line study, has been slower than expected.

In DLBCL, a phase Ib/II front-line pilot study (ACCEPT) of a second generation BTK inhibitor with R-CHOP has been endorsed by CRUK and will open in Q2 2016. It is hoped that if the combination is proven to be safe, then this will be rolled out into a large phase III as this is an obvious gap in the portfolio now that REMoDL-B has closed to recruitment. The phase II INCA study, for patients with DLBCL is recruiting well with recruitment just behind projected timelines. This study has a considerable translational component. In response to a key clinical question about the role of radiotherapy in DLBCL with bulk, group members designed the CONRAD study, a large phase III, comparing observation to radiotherapy in patients who were PET negative after immunochemotherapy. This was unfortunately rejected for funding by CRUK (June 2016); refinements will be sought and resubmitted later in the year.

In the relapsed setting, LEGEND has been recruiting steadily and a novel agent trial (TORCH) has been recruiting well. The latter arena is crowded with multiple commercial novel agent studies competing for the population. A study of a PD-L1 inhibitor with obinutuzumab (a second generation anti CD20) and chemotherapy has been funded for the older/co-morbid DLBCL patient and has been submitted for endorsement (ARGO). This will be activated at around 30 sites, so this more frail population will not have to travel to major academic centres for novel combinations. A study for patients with post-transplant lymphoma has been funded by Bloodwise and is currently in set-up. In Burkitt's lymphoma a randomised phase II of the infusional dose

adjusted R-EPOCH regimen against the UK standard R-CODOX-M/R-IVAC has been funded and is currently in set-up. This study is in collaboration with the HOVON Group in the Netherlands.

The international ORCHARRD study for which the UK was the largest contributor, reported at ASH 2014 demonstrating that there was no advantage of ofatumumab over rituximab in combination with DHAP chemotherapy in relapsed/refractory DLBCL. It has been submitted for publication in the Journal of Clinical Oncology (May 2016).

In primary mediastinal B-cell lymphoma, the IESLG 37 PET driven risk adapted study of radiotherapy or observation after immunochemotherapy has recruited below expectation. A number of protocol revisions have been made, to make the inclusion more permissive and it is hoped that this will result in greater numbers of patients entering the study.

In order to address the difficult questions surrounding the management of elderly patients with DLBCL, a new working group has been formed in order to design studies for this population which are poorly represented in clinical trial design.

Working with the Teenage and Young Adults (TYA) CSG, we have opened an opened an observational study with biological correlates in the TYA patient population with NHL. This aims to capture data on all the patients in the UK in this population.

The Subgroup has a highly engaged membership with a busy portfolio. At present, however, there is no patient representation which we are working to change. The trainee representatives have been highly engaged and contributed significantly to successful study design and management. We continue to seek ways to work more closely with the Paediatric Lymphoma Subgroup. We have core strengths in translational work, international collaboration and a network of enthusiastic investigators that are able to deliver.

Low Grade Lymphoma Subgroup (Chair, Professor Simon Rule)

The Low Grade Lymphoma Subgroup has focussed on three main disease areas for its clinical studies: Follicular lymphoma, Waldenstroms macroglobulinaemia and mantle cell lymphoma. All of these diseases have seen an unprecedented development of active novel agents and the challenge has been getting access to them and then incorporating these into relevant clinical studies.

- Follicular NHL

The PACIFICO trial has recently closed with 365 patients enrolled. Despite having to close early due to recruitment issues it is the largest front line follicular lymphoma trial ever run in the UK. This study highlighted how changes in clinical practise can have a major impact on recruitment and this has informed the next generation of trials. To date about one third of the required events have been observed in this trial so there are no imminent publications or presentations planned. The study involved a biobanking component and the sample collection associated with the trial has been good.

With the difficulties associated with the PACIFICO trial the next planned study (PETreA) applies a more permissive approach to therapy and applies a PET directed approach which provides a platform on to which new agents can be tested. Patients who are PET positive following initial immuno-chemotherapy are known to have a poor outcome and in this group the many new agents that are showing promise in this disease can be explored in a sequential manner. The PET negative group has an excellent outcome and strategies for de-escalating therapy can be

explored. This trial has just received full funding from CRUK and should be ready to open early 2017.

In relapsed follicular NHL a collaborative study with the HOVON group (ReBel) will shortly be open which is looking at a bendamustine with lenalidomide combination

- Waldenstrom's Macroglobulinemia

The R2W study was a front line study for WM that completed recruitment ahead of schedule. This trial compared fludarabine with velcade based therapies. The trial involved a phase I run in before opening the phase II study which worked well and lead to the rapid recruitment. The results from this study are being evaluated with a presentation of results likely at the end of the year. As with the follicular studies patient's material has been stored for subsequent studies and there has been a major look at MRD assessment through the Leeds HMDS. The successor trial is already planned and will involve a BTK inhibitor. The new study is a Randomised Phase II/III study of Rituximab and Ibrutinib (RI) versus Dexamethasone, Rituximab and Cyclophosphamide (DRC) as Initial Therapy for Waldenstrom's Macroglobulinaemia (RAINBOW). This has been invited for a full application by CRUK.

- Mantle cell lymphoma

We have two front line studies planned and funded for MCL, one for younger patients and another for older transplant ineligible patients. Both include the front line use of Ibrutinib. The study for older patients (ENRICH) is CRUK funded and compares R-chemo with R-ibrutinib and is the only randomised chemotherapy versus chemotherapy free study in the world for this disease. It is open and recruiting and the NORDIC lymphoma group will join the study later in the year.

The study for younger patients (TRIANGLE) is in collaboration with the European MCL network study and is a randomised trial that compares a standard autografting approach with or without ibrutinib with a third arm that includes ibrutinib but no autograft. This trial has been slow in set up at the sponsor side.

One of the major strengths of the group is its emphasis on the use of bio-banking with a view to subsequent translational research activity. A bio-bank for mantle cell lymphoma has also recently opened with Bloodwise support. This is recruiting very quickly and we anticipate 300 samples by the end 2017. With this timeframe in mind a workshop has been organised in July 2016.

Finally the first UK based MCL trial (FC/FCR) has recently been published and the results of the front line allogeneic transplant study have recently been presented as an oral at both the recent EBMT and BSH meetings.

A trial for front line marginal zone lymphoma (MALIBU) is under discussion with international partners and a number of other studies are being explored that are too premature to include in this report.

Paediatric Non-Hodgkin Lymphoma Subgroup Chair, Dr Amos Burke)

In this reporting year, the structure of the CSG has been reviewed with a view to ensuring it can continue to develop a comprehensive portfolio of research studies that reflects the needs and priorities for children with Non-Hodgkin's Lymphoma. A biologist, Dr Suzanne Turner, has been invited to join the Subgroup and has organised the first national biology meeting for paediatric NHL to inform clinical trials in development. In addition, the Paediatric NHL Subgroup has agreed to work collaboratively with the High Grade Subgroup to focus specifically on the needs of

Teenagers and Young Adult NHL trials and to develop at least two joint trials in areas where there are no trials such as supportive care or follow up within the next two years.

The trial portfolio is strong with a practice changing result from the first interim analysis of InterB-NHL Ritux 2010 showing benefit for Rituximab in paediatric B-NHL. The UKALL 2011 study for acute lymphoblastic leukaemia and lymphoma continues to recruit well. The first commercial study in B-NHL in the UK is in set-up for relapsed B-NHL (Janssen sponsored, Dr Amos Burke Global Lead Investigator and UK CI).

Hodgkin Lymphoma Subgroup (Chair, Dr Graham Collins)

The 2015-16 period has been a year of notable achievements but also serious challenges for the Hodgkin Lymphoma Subgroup.

Achievements:

- The RAPID study (PI: Radford) which assessed a PET-directed radiotherapy question in early stage Hodgkin lymphoma was published in the New England Journal of Medicine in March.
- The RATHL study (PI: Johnson) which was also investigating a PET response-adapted approach was presented in the plenary session at the International Conference of Malignant Lymphoma in Lugano in June 2015. This has since been accepted for publication in the New England Journal of Medicine.
- Following the theme of PET response adaptation, the BREVITY study (PI: Radford) looking at single agent Brentuximab Vedotin (BV) in chemotherapy unfit patients successfully recruited ahead of schedule.
- ECHELON-1 (UK PI: Collins) was a commercial study incorporating BV into the first line treatment of patients with advanced classical Hodgkin lymphoma. The UK was the second largest recruiter and recruited more than the original target.
- In the paediatric and TYA group, the Euronet C2 study (UK PI: Daw) is in set up with a plan to open sites by the end of 2016. This will provide a front line study for children and adults up to their 25th birthday.
- A new front line study for early stage classical Hodgkin, the RADAR study (PI: Radford) has been submitted to the Takeda portal for funding.
- The UK has also been an important country for commercial PD1 inhibitor studies, recruiting well to the Checkmate205 study (PI: Radford, using nivolumab), the Merck087 study (PI: Radford, using pembrolizumab) and now it has open the Javelin Hodgkin trial (PI: Radford, using avelumab).
- Progress is being made to investigate follow up schedules in Hodgkin patients, with the START trial (PI: Radford). This represents an important collaboration with the psycho-social CSG
- The BARD study (Breast screening after radiotherapy) is also making good progress (PI: Radford).

Challenges:

- Currently there is no front line study open for adult patients with classical Hodgkin Lymphoma. Although progress has been made for early stage (see above), progress for advanced stage has been slow. The EuronetC2 study (see above) will cover patients up to the age of their 25th birthday. The RAVEN study (PI: Collins) failed to be supported by Takeda.

Plans are in progress for a study incorporating a PDL1 inhibitor into the front line setting of advanced disease, the RADIAL study (PI: Collins).

- Currently there is no study for adult patients with first relapse of classical Hodgkin Lymphoma. Again a trial was being planned to incorporate the use of brentuximab in this setting, but there was little interest from the pharmaceutical company involved. We are in the early stages of planning a chemotherapy-based question in this group.
- The ANIMATE study is a trial proposal for using a PD1 inhibitor as 2nd line salvage in patients who do not achieve a complete metabolic response after first line salvage. Free drug and a £300,000 grant were agreed from BMS. However, CRUK declined to support the study for the remainder of the cost. This is clearly very disappointing. We are awaiting feedback from CRUK and have approached BMS to determine whether they would be able to fund the whole study.

4. Task groups/Working parties

The BARD (Breast Screening after Radiotherapy) group has been working to devise a nationwide solution to improve screening of women at high risk of breast cancer following radiotherapy for lymphoma (and rarely other cancers) under age 36. BARD membership includes colleagues with expertise in lymphoma, breast cancer, radiotherapy, screening, epidemiology and two consumers. Relevant contracts with NHS England and Public Health England are in place and a comprehensive database comprising approximately 9,000 at-risk women is currently being established in that on an annual basis NHSBSP and GPs can be advised which women need screening that year. Funding of a project manager has been provided by Teenage Cancer Trust for which we are extremely grateful.

The BARD project was signed off by NHSE and PHE in January 2016 and a pilot phase is currently completing in northwest England. Once any learning from this has been incorporated into the processes BARD will be rolled out across the rest of England with completion expected in Q4 2016. Abstracts describing BARD have been submitted to the 2016 NCRI Conference and the 10th ISHL meeting in Cologne (October 2016).

5. Patient recruitment summary for last 5 years

In the Lymphoma CSG portfolio, 19 trials closed to recruitment and 12 opened. I am concerned by the steady fall in recruitment to portfolio studies/trials which reflects a reduction in the overall number of large phase III trials. This trend will be partially addressed by the recent funding of PETREA in the first line treatment of follicular lymphoma and the hoped for funding of RADAR in early stage Hodgkin lymphoma and ARGO in relapsed diffuse large B cell lymphoma. As identified at the Strategy Day however the CSG has to become better at identifying questions that are of importance to patients and are compatible with research activity at smaller centres. These include studies around process and survivorship; studies in both these areas (START and SECURE respectively) are under development.

Table 1 Summary of patient recruitment by RCT/Non-RCT

Year	All subjects		Cancer patients only		% of cancer patients relative to incidence	
	Non-RCT	RCT	Non-RCT	RCT	Non-RCT	RCT
2011/2012	2998	617	2931	617	26.4	5.6

Table 2 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
2012/2013	3044	1012	3009	1000	21.7	7.2
2013/2014	1685	879	1685	879	12.1	6.3
2014/2015	804	785	580	785	4.2	5.6
2015/2016	1784	495	680	1784	12.84	3.56

6. Links to other CSGs, international groups and network subspecialty leads

The CSG has extensive links with international groups. These include the IELSG (International Extra-Nodal Lymphoma Study Group) which leads important studies in central nervous lymphoma (lead Cwynarski) and primary mediastinal B cell lymphoma (lead Davies). The RATHL trial (Johnson) in advanced Hodgkin lymphoma involves collaboration with the Nordic, Italian, Australian and New Zealand Lymphoma Groups. In the follow-on study to RAPID (RADAR, Radford) in early stage HL there have been enthusiastic approaches from all of the above plus the EORTC Lymphoma Group and colleagues in Canada, the US, Israel and Switzerland. The BRAVE study evaluating DHAP chemotherapy plus brentuximab vedotin in relapsed/refractory Hodgkin lymphoma is a collaborative venture between centres in the UK, the Netherlands and France.

In addition, the Group is aligned to the Lymphoma Scientific Working Group of European Haematology Association (mainly research focused) and the European Lymphoma Institute (mainly education focused)

7. Funding applications in last year

Table 3 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
July 2015 (CTAAC)			
A randomised Phase III trial to determine the role of consolidation radiotherapy in bulky diffuse large B-cell lymphoma	Outline application	Professor Tim Illidge	Full application invited
December 2015			
PRIZM (now known as RAINBOW): Randomised phase II/III study of Rituximab and Ibrutinib (RI) versus Bortezomib, Cyclophosphamide and Rituximab (BCR) as initial therapy for Waldenstrom macroglobulinaemia	Outline application	Dr Rebecca Auer	Full application invited
ANIMATE: A Phase II study of nivolumab monotherapy in patients with relapsed/refractory Hodgkin lymphoma fit for autologous stem cell transplant who fail to reach complete metabolic remission after first line salvage therapy	Outline application	Dr Graham Collins	Full application invited
PETReA: Phase III evaluation of PET-guided, Response-Adapted therapy in patients with	Outline application	Professor Andrew Pettitt	Full application

previously untreated, high tumour burden follicular lymphoma			invited
May 2016			
ConRad: A randomised Phase III trial to determine the role of consolidation radiotherapy in bulky diffuse large B-cell lymphoma	Full application	Professor Tim Illidge & Dr George Mikhaeel	Not funded
PETReA: Phase 3 evaluation of PET-guided, Response-Adapted therapy in patients with previously untreated, high tumour burden follicular lymphoma	Full application	Professor Andrew Pettitt	Funded
ANIMATE: A Phase II study of nivolumab monotherapy in patients with relapsed/refractory Hodgkin lymphoma fit for autologous stem cell transplant who fail to reach complete metabolic remission after first line salvage therapy	Full application	Dr Graham Collins	Not funded
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
May 2016			
RADAR: An international phase III trial investigating the incorporation of brentuximab vedotin into the treatment of early stage Hodgkin lymphoma using a response adapted approach	Application submitted to Takeda via IIS portal (£6m plus free drug) - UCL Trials Centre	Professor John Radford	Awaited

8. Collaborative partnership studies with industry

The CSG has extensive and effective collaborations with industry and has made a major contribution to pharma's current view that the UK is now an excellent environment in which to undertake clinical research. First line trials in advanced Hodgkin lymphoma (ECHELON-1) and anaplastic large cell lymphoma (ECHELON-2) are sponsored by Takeda and in the case of the international ECHELON-1 trial which has now completed recruitment, the CI for territories outside North America is a CSG member (John Radford).

In the first line treatment of the ABC molecular sub-type of diffuse large B cell lymphoma, the phase III PHOENIX trial sponsored by Pharmacyclics is investigating the value of adding the BTK inhibitor, ibrutinib, to R-CHOP and recruited to target. The CHECKMATE suite of trials sponsored by Bristol-Myers-Squibb involving the PD-1 inhibitor nivolumab in three subtypes of lymphoma has completed at five UK Centres and a portfolio of eight phase Ib/II combination studies (the HARMONY programme) in two subtypes of non-Hodgkin lymphoma sponsored by Roche have been offered to seven UK sites with early phase experience and facilities.

In addition, the CSG is taking part in numerous phase II studies with a wide range of sponsors and recruiting well to these. The investigator led BREVITY study in the first line treatment of Hodgkin lymphoma in the older, frailer and co-morbid population funded by Takeda completed recruitment six months ahead of schedule and an abstract of preliminary results has been submitted to ISHL 2016.

9. Impact of CSG activities

Over the last five years the CSG's research outputs have had a significant impact on clinical practice. In diffuse large B cell lymphoma, the R-CHOP 14 vs 21 trial (Cunningham) showed that in terms of patient outcomes there was no advantage to the 14 day schedule thus confirming R-CHOP 21 as the standard of care in the UK. In Hodgkin lymphoma, the RAPID trial (Radford) showed that a negative PET scan after three cycles ABVD chemotherapy is associated with a very good outcome without further treatment and although the addition of radiotherapy produces a 3.8% improvement in three year PFS this is at the expense of irradiating everyone, most of whom don't need it. These results were published NEJM April 2015.

In advanced Hodgkin lymphoma results of the RATHL trial (Johnson) were presented in Plenary Session at the ICML meeting, Lugano, June 2015 and will be published NEJM June 2016. This international trial led by the UK showed that a negative PET scan after two cycles ABVD was associated with a very good prognosis and that outcome in terms of progression-free survival was the same irrespective of whether ABVD or AVD (bleomycin dropped in AVD) was continued in cycles 3-6.

The development of an NCRI network of quality assured PET imaging facilities by Barrington and O'Doherty has been critical to the success of these studies.

The UK contribution to the IELSG 32 study in primary CNS lymphoma has been very important and although the UK joined the trial two years after activation it was, at close, the third largest recruiter. Preliminary results presented in Plenary Session at ICML, Lugano, June 2015 showed that additional drugs added to the induction regimen improved remission rates, PFS and survival, findings that have changed international practice in this difficult to treat lymphoma. As a result of the interest and commitment of CSG members in this area the UK is now recognised as an increasingly strong player in CNS lymphoma.

10. Consumer involvement

Stephen Wood:

- I have been a patient/consumer member of the Lymphoma CSG since November, 2014. At that time, as noted in the comments to the Annual Report 2015, I was the only consumer on the Group and a second consumer member was appointed in February 2016.
- In October 2015, I took part in the CSG Strategy Day meeting. I played a full part in the meeting with the Chair ensuring that I was involved and listened to at every stage. The Group now has a working five year strategy.
- Apart from contributing to formal CSG meetings, my main involvement with colleagues has been offering a patient's view of leaflets to be used with patients as part of trials/research. I consistently advocate a two slides max. bullet-pointed leaflet covering the main points to go with the full explanatory leaflet which can run to 15-20 pages and is unlikely to be read or understood.
- I am signed up as a patient research ambassador.
- I have been allocated a distinguished mentor (Professor Simon Rule) but I do not think that, as yet, I have worked out how to use him effectively.

11. Open meetings/annual trials days/strategy days

The UK Lymphoma Annual Trials Meeting held annually in November, which features a high profile guest speaker and an update on current, completed and planned studies, has become increasingly well attended over the last five years. In 2015, more than 500 delegates including physicians, nurses, research staff and patient representatives attended the meeting in Senate House, University of London, where Dr Lou Stoudt from NIH, Bethesda was the Mike Bennett Memorial Lecturer. Delegate feedback was excellent.

In addition to this annual fixture, CSG members have been involved in Bloodwise and Lymphoma Association annual and regional meetings and have given lymphoma related talks at updates held by the Royal Colleges of Physicians, Pathologists and Radiologists and British Society for Haematology. Other members have arranged one or two day educational events for physicians and nurses in training (Oxford and Manchester). Feedback from these has also been excellent.

The strategy day in October 2015 was a very well attended and successful event. The challenges associated with opening large patient number phase III trials accessible to most centres in the UK was discussed at length and it was concluded that for a variety of reasons these will be fewer in number in future years. However, it is still possible to undertake trials of importance to lymphoma patients especially in the fields of process and survivorship and two studies in these fields are underway (START and SECURE).

12. Priorities and challenges for the forthcoming year

Priorities:

1. Open a new front-line trial in Hodgkin lymphoma
   This was a priority in 2014/15 report and remains so in 2015/16. A trial design (RADAR) that builds on the experience obtained with RAPID and incorporates a PET response adapted design, the targeted agent brentuximab vedotin and translational components has been agreed by the group. A proposal and request for funding (£6m plus free drug) has been submitted to Takeda via their IIS portal and their response is awaited. Support for international collaboration has been received from the EORTC Lymphoma Group and colleagues in Scandinavia, Israel, Australia, New Zealand, Canada, the US and most recently the Swiss SAKK group.
2. Develop a platform for evaluating new agents in aggressive non-Hodgkin lymphoma
   This builds on the excellent work undertaken by Davies and Johnson in the REMoDL-B trial where real time molecular phenotyping was shown to be feasible in patients with diffuse large B cell lymphoma. The ARGO trial (Davies) currently in development will provide patients with relapsed/refractory DLBCL with a pragmatic chemotherapy to which relevant new molecules can be added as required. A panel of translational studies will also be performed. It is hoped that pharma will find this “new agent test bed” highly attractive and conducive to undertaking early phase research in the UK.
3. Open a non-IMP study
   The importance of undertaking these was highlighted at the CSG Strategy Day in October 2015 and two are in development:
   - START is being developed in collaboration with Armes and Foster (Psychosocial CSG) to compare “long” and “short” hospital based follow-up after treatment for Hodgkin lymphoma in terms of PFS, OS, quality of life, and use of other medical

services. It will also facilitate the evaluation of serum TARC as a marker of relapse and if there is a strong correlation a subsequent biomarker led follow-up trial will be designed.

- SECURE is being developed in collaboration with Wald (Wolfson Institute of Preventive Medicine, London), Sharples (Leeds CTU), Ray (cardiologist, Manchester), Swerdlow (epidemiologist, London), and Gale (cardiovascular science, Leeds) to address the issue of increased risk of death from cardiovascular disease in patients cured of lymphoma.

Challenges:

1. The power of pharma in influencing trial design
   In view of the CSG's ambition to evaluate new agents with improved efficacy and reduced toxicity, all of the priorities listed above are dependent on the co-operation and support of pharma. This is usually challenging as they often have their own views on trial design and even if they are prepared to support an investigator led phase III protocol they may wish to make it a registration study with a view to obtaining a licence for a new indication. This factor combined with the expense of undertaking large randomised phase III trials undermines the ability of academic groups to lead research of this type. The financial challenges recently experienced by Bloodwise exacerbate this issue.
2. Increasing demands of NHS Trusts
   In financially challenging times, NHS Trusts are increasingly reluctant to allow their clinicians to attend meetings and undertake research that they may see as unproductive and not contributing to solving today's problems. We have to resist this pressure by pointing out that research is the means to improving outcomes for patients and making our interventions more effective and efficient. One way of highlighting this is by entering pieces of practice changing research into the Health Service Journal awards; this has already been done (ADAPT project) and will continue to be encouraged by the CSG.
3. Increasing overall trial recruitment
   Opening trials in lymphoma types where large numbers of patients are affected and non-IMP trials are very important but in addition providing relevant and timely information is crucial. This is challenging because NHS Trusts differ widely in terms of clinical trial activity and so there are many patients who are simply not made aware of the opportunities available. Our work with Bloodwise, the Lymphoma Association and Tomorrow's Medicines to directly inform patients using social media techniques is addressing this issue.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

A – Main CSG Strategy
B – High Grade Lymphoma Subgroup Strategy
C – Low Grade Lymphoma Subgroup Strategy
D – Paediatric Non-Hodgkin Lymphoma Subgroup Strategy
E – Hodgkin Lymphoma Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Professor John Radford (Lymphoma CSG Chair)

Appendix 1

Membership of the Lymphoma CSG

Name	Specialism	Location
Dr Matthew Ahearne*	Clinical Lecturer	Leicester
Professor Richard Cowan	Clinical Oncologist	Manchester
Dr David Cutter	Clinical Oncologist	Oxford
Dr Jessica Okosun*	Clinical Research Fellow	London
Mr Andrew Barton	Consumer	Northwich
Mr Stephen Wood	Consumer	Derbyshire
Dr Maria Calaminici	Haemapathologist	London
Dr Cathy Burton	Haematologist	Leeds
Dr Rebecca Auer	Haematologist	London
Dr Graham Collins	Haematologist	Oxford
Dr Kate Cwynarski	Haematologist	London
Dr Christopher Fox	Haematologist	Nottingham
Dr Pam McKay	Haematologist	Glasgow
Dr Andrew McMillan	Haematologist	Nottingham
Dr Tobias Menne	Haematologist	Newcastle
Dr Alison Milne	Haematologist	Basingstoke
Professor Simon Rule	Haematologist	Plymouth
Dr Andrew Davies	Medical Oncologist	Southampton
Professor John Radford (Chair)	Medical Oncologist	Manchester
Dr Stephen Daw	Paediatric Haematologist	London
Dr Amos Burke	Paediatric Oncologist	Cambridge
Dr Victoria Warbey	Physician in Nuclear Medicine	London
Dr Alasdair Rankin	Research Director, Bloodwise	London
Mr Paul Smith	Senior Research Coordinator	London
Ms Amy Kirkwood	Statistician	London
Mrs Louise Stanton	Statistician	Southampton
Mr Jonathan Pearce	CEO, Lymphoma Association	Aylesbury

* denotes trainee member

Membership of the Subgroups

High Grade Lymphoma Subgroup		
Name	**Specialism**	**Location**
Dr Matthew Ahearne*	Clinical Lecturer	Leicester
Dr Catherine Burton	Haematologist	Leeds
Dr Sridhar Chaganti	Haematologist	Birmingham
Dr Graham Collins	Haematologist	Oxford
Dr Nagesh Kalakonda	Haematologist	Liverpool
Dr Andrew McMillan	Haematologist	Nottingham
Dr Russell Patmore	Haematologist	Hull
Dr Saad Rassam	Haematologist	London
Dr Simon Rule	Haematologist	Plymouth
Dr Andrew Davies (Chair)	Medical Oncologist	Southampton
Professor Andrew Jack	Pathologist	Leeds

Low Grade Lymphoma Subgroup		
Name	**Specialism**	**Location**
Professor Peter Hoskin	Clinical Oncologist	Middlesex
Miss Alison Learwood	Consumer	York
Dr Kirit Ardeshna	Haematologist	London
Dr Nicola Bienz	Haematologist	Wexham
Dr Chris Hatton	Haematologist	Oxford
Dr Andy Haynes	Haematologist	Nottingham
Dr Pam McKay	Haematologist	Glasgow
Professor Andrew Pettitt	Haematologist	Liverpool
Dr Saad Rassam	Haematologist	London
Professor Simon Rule (Chair)	Haematologist	Plymouth
Professor Peter Johnson	Medical Oncologist	Southampton
Professor John Radford	Medical Oncologist	Manchester

Hodgkin Lymphoma Subgroup		
Name	**Specialism**	**Location**
Dr Eve Gallop-Evans	Clinical Oncologist	Cardiff
Professor Peter Hoskin	Clinical Oncologist	Middlesex
Dr Jessica Okosun*	Clinical Research Fellow	London
Dr Kirit Ardeshna	Haematologist	London
Dr Catherine Burton	Haematologist	Leeds
Dr Graham Collins (Chair)	Haematologist	Oxford
Dr Pam Mckay	Haematologist	Glasgow
Dr Andrew McMillan	Haematologist	Nottingham
Professor Peter Johnson	Medical Oncologist	Southampton
Professor John Radford	Medical Oncologist	Manchester
Dr Stephen Daw	Paediatric Haematologist	London
Mr Paul Smith**	Research Associate	London
Ms Amy Kirkwood**	Statistician	London

Paediatric Non-Hodgkin Lymphoma Subgroup		
Name	**Specialism**	**Location**
Dr Ayad Atra	Haematologist	London
Dr Andrew McMillan	Haematologist	Nottingham
Professor Owen Smith	Haematologist	Dublin
Dr Robert Wynn	Haematologist	Manchester
Dr Keith McCarthy	Histopathologist	Wye Valley
Dr Stephen Daw	Paediatric Haematologist	London
Dr Amos Burke (Chair)	Paediatric Oncologist	Cambridge
Dr Denise Williams	Paediatric Oncologist	Cambridge
Dr Mary Taj	Paediatric Oncologist	London
Dr Suzanne Turner	Pathologist	Cambridge
Dr Simon Bomken	Specialist Registrar	Newcastle
Professor Keith Wheatley**	Statistician	Birmingham
Mr Andrew Raxworthy-Cooper**		Birmingham

*denotes trainee member **denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Strategic objective	Action	CSG Lead	Date	Outcomes
1a. Portfolio development (general)	Development by each subgroup of prioritisation process for the development and set up of studies that takes account of CTU capacity, available funding opportunities and clinical need	AD/ SR/ GC/ JR	May 2016	
	Make sure that a first line study is always available for each of the main lymphoma sub-types – Hodgkin lymphoma, diffuse large B cell lymphoma and follicular lymphoma ***2 year target: open new first line studies in each of these lymphoma sub-types**	AD/ SR/ GC/ AB	March 2018	
	Embed translational science and tissue banking into all new studies	AD/ SR / GC/ AB	Ongoing commitment	
	Build on internationally leading work in PET adapted approaches and integrate circulating and tissue based biomarkers into these ***2 year target: open 3 new studies involving PET/other biomarker integration**	SB/ AD/ SR/ GC/ AB	March 2018	
	Consider other areas for study such as treatment pathways, follow-up after treatment and late effects of treatment ***2 year target: open 2 new non-IMP studies**	RC	March 2018	
1b. Portfolio development (cross cutting themes)	Identify leads within the Lymphoma CSG to link with the following cross cutting CSGs with the aim of developing joint studies :			
	• Radiotherapy	TBD at next CSG mtg	March 2016	
	• Palliative and Supportive Care	TBD at next CSG mtg	March 2016	
	• Primary Care	TBD at next CSG mtg	March 2016	
	• Screening, Prevention and Early Diagnosis (SPED) Advisory Group.	TBD at next CSG mtg	March 2016	
	***2 year target: open 2 studies in these areas**		March 2018	
1c. Portfolio development (other CSGs)	Establish regular contact with TYA CSG to work together to widen participation in research studies by young people especially in the areas of Hodgkin lymphoma and survivorship	GC/ AM	May 2016	
	Establish regular contact with Haematology CSG	JR	May 2016	
	Establish early contact with Breast, Lung and other CSGs as appropriate in connection with studies involving second cancers.	All	Ongoing commitment	

Strategic objective	Action	CSG Lead	Date	Outcomes
2. Increase early phase clinical trial activity and participation	Increase the availability of early phase studies for patients with relapsed/refractory disease by:			
	• Agreeing a development plan so more centres are able to undertake and deliver early phase studies to time and target. ***3 year target: 10 sites routinely involved in phase I/II research**	AD/ SR/ GC/ AB/ AM	October 2016	
	• Promote and monitor the referral of patients between centres so that more are given the opportunity of participating in early phase studies	AM/ AB	October 2016	
	• With the Lymphoma Association develop a clinical trials information portal suitable for patients and clinicians	GC/ Lymphoma Association	2016	
	• Develop social media approaches to improve penetration of information about clinical trials into the patient population (pilot project with Tomorrow's Medicines). ***2 year target: 3 studies use social media techniques to raise awareness**	AD/ JR/ LA/ Bloodwise	March 2018	
	• Work closely with Bloodwise TAP and pharma	All	Ongoing commitment	
	• Highlight the importance of early phase trials at new consumer feedback and dissemination day (see section 6)	All	Ongoing commitment	
3a. Raising profile	Routine dissemination of results from studies through annual UK Lymphoma Trials meeting and CSG Annual Report	UCL Cancer Trials Centre/ All	Annual commitment	
	Monitor delegate feedback from annual trials meeting and adapt programme in response to this	UCL Cancer Trials Centre/ JR	Annual commitment	
	Monitor submission of abstracts to the following meetings and increase proportion of **same** abstract presented at international and national meetings: • NCRI Cancer Conference • ASH • ASCO • EHA • ISHL, Cologne • ICML, Lugano • BSH	All	First report March 2017	
	Establish annual consumer dissemination event (see section 6)	JR/ LA/ Bloodwise	March 2017	

Strategic objective	Action	CSG Lead	Date	Outcomes
3b. Maximise efficiency of clinical trial set up	Monitor set up times for all CSG academic/commercial studies and review these at CSG meeting Monitor success rate with grant awarding bodies Work closely with pharma to facilitate flow of early phase studies to UK sites	All	Ongoing commitment March 2017 Ongoing commitment	
4. CSG structure and function	Establish paediatric NHL working group to meet on same day as and report into high grade NHL sub-group. *** 2 year target: 2 paediatric NHL studies opened**	AB/AD	March 2018	
	Establish survivorship studies working group. ***2 year target: 2 survivorship studies opened**	TBD at next CSG meet	March 2018	
	CSG chair and sub-group chairs to hold quarterly TC to review progress and maintain momentum	AD/ SR/ GC/ AB/ JR	June 2016	
	Grow future capability/capacity – offer subgroup members new to research role in new studies so they can gain experience and take the future lead	AD/ SR/ GC/ AB	March 2016	
	Maintain/grow collaborative relationship with Bloodwise and Lymphoma Association. Representatives of both organisations invited to attend main CSG meeting.	All/ Bloodwise/ LA	Ongoing commitment	
	Collect feedback of trainee experience of the main CSG and subgroups. Review and if necessary revise: • Role • Selection Process • Tenure Period • Funding	TBD	First report March 2017	
	***2 year target: Each trainee features on author list of a peer reviewed abstract/paper written by the CSG**	All	First report March 2017	

Strategic objective	Action	CSG Lead	Date	Outcomes
5. Strengthen UK wide and international working	Make sure CSG membership is broadly representative of all parts of the UK Designate leads for key international groups: • IELSG • ELI • EHA Lymphoma Working Group ***2 year target: 3 international studies opened** Identify funding opportunities for travel to attend meetings with international partners	JR AD and TBD TBD at next CSG meet JR and TBD AD/ SR/ GC AD/ JR	Ongoing commitment March 2016 March 2016 March 2016 March 2018 September 2016	
6. Patient and Public Involvement and Impact	Increase the number of consumers involved in the sub groups and main CSG. CSG members to identify potentially suitable consumer representatives from their own practices and support/encourage these to apply ***1 year target: At least 1 consumer representative attached to all sub-groups and linked to NCRI Consumer Forum** . With Bloodwise and Lymphoma Association establish annual consumer engagement and dissemination event. Venue to rotate around the UK. Monitor and respond to attendee feedback.	All AD/ SR/ GC/ AB JR with LA and Bloodwise	Ongoing commitment March 2017 Ongoing commitment	

B – High Grade Lymphoma Subgroup Strategy

1. To increase recruitment of patients with high grade lymphomas into rationally designed clinical trials by opening high-quality studies across the range of histological variants that are accessible throughout the UK.
2. To capture our enhanced knowledge of the biology of high grade lymphoma and diagnostics in the design of rationally targeted studies that appropriately stratify patients according to their molecular phenotype. This is a unique strength of the UK Subgroup and one which has already demonstrated success.
3. To develop a suite of phase II studies, under an umbrella protocol, for patients with relapsed DLBCL, targeting patient specific oncogenic aberrations in collaboration with industry. In addition the group will focus on T-cell lymphomas, by establishing a Working Group, and seek to expand the portfolio further in this area.
4. To build upon the success of the Primary Central Nervous System Working Group and to further design studies in this area, playing a major role in International collaborative study delivery.
5. To ensure that there is a balanced portfolio between academic and commercial sponsored studies in the portfolio. The group has already benefited from good relationships with Industry and will further promote these by increasing investigator initiated trials.
6. To enhance links with International Groups to deliver trials in rarer histological sub-types.
7. To enhance training opportunities in clinical trial development and management, in order that the next generation of Chief Investigators have the appropriate skill set to take on these leadership roles.

C – Low Grade Lymphoma Subgroup Strategy

The strategic approach of the low grade CSG align with the main CSG portfolio development plans.

1. We aim to have front line studies open in the main histological sub-types within the next 6-9 months. We have chosen to focus on Follicular, Mantle cell NHL as well as Waldenstroms macroglobulinaemia. The ENRICH trial in mantle cell NHL has recently opened, the front line follicular study PETREA has gained funding through CR-UK and is progressing well and finally the RAINBOW study has been invited as a full proposal to the next CR-UK clinical trials committee.
2. Include translational science into our clinical trials as a standard. The previous follicular NHL trial (PACIFICO) incorporated biobanking into the protocol and as a consequence a number of translational studies are in place. This will continue with the subsequent study. With MCL there is an LLR funded biobank that is recruiting extremely well, this will be available for patients entering the ENRICH trial. A scientific steering group for the MCL biobank will meet next month to map out the potential projects for this material. With respect to the WM trials, the recently completed study (WM1) included storage of material at Leeds and this will be the case with the next study. We would anticipate a number of publications through this process in the next year or so.
3. We aim to include appropriate biomarkers into trial design. With the PETREA study, this is a PET directed approach utilising the expertise that exists in this area in the UK. In MCL and WM the role of PET is not so clear but MRD appears to be pivotal as such centralised MRD analysis in Leeds is built into these studies.
4. Including novel agent therapy within trials where appropriate in order for them to be at the cutting edge and be internationally relevant. Both frontline MCL and WM trials include

a randomisation to a BTK inhibitor within a chemotherapy free arm. This is novel and with the MCL trial, international collaboration with the NORDIC group is the first in a number of likely partnerships. The FL study is a template study that allows the sequential integration of novel agents into the PET positive arm making this an attractive study for international collaboration as well as industry partners.

5. Incorporate patient focussed quality measures within trials. The ENRICH trial includes both quality of life and pharmaco-economic elements. We wish to include such factors into all of the major trials. The PETREA study as a large 'all comers' study offers an opportunity to study a number of these and other questions.

D – Paediatric Non-Hodgkin Lymphoma Subgroup Strategy

Strategy document 2015-2018 (*revised 2016)

Theme		Strategic objectives
1	Developing a comprehensive portfolio of research studies that reflects the needs and priorities for children Non-Hodgkin's Lymphoma	a) Interventional studies I. Identify gaps in evidence for treatment and develop studies where there is greatest need. These will be agreed at a meetings of Paediatric NHL subgroup and reviewed on an ongoing basis. II. Ensure that where biologically appropriate studies are developed that cover the appropriate paediatric and young adult age-range. III. Due to the rare nature of children's cancers, focusing on maximising the output of the clinical trials that are designed by: • Considering newer methods for study design, such as Multi Arm, Multi Stage (MAMS) design and probability analysis • Ensuring clinical trials are efficient as possible, including answering as many questions as possible IV. Embedding biology and tissue banking into studies with appropriate funding to allow participation at all sites. b) Imaging I. Review the opportunities for the development of studies investigating the role of new imaging modalities with a focus on PET (CT/MRI) in Paediatric and young adult NHL.
2	Increasing early phase activity and participation	i. Increase early phase activity and opportunities for novel agents being used in paediatric studies. • Work with the Novel Agents subgroup of the CCL CSG to increase the number of studies open to paediatric and young adult patients with NHL
3	Delivery, engagement with sites	i. Ensuring successful delivery of studies through integration with National Institute for Health Research: Cancer to engaging with PTCs and Young Adult Units • Establish good working with newly appointed LCRN subspecialty leads for Lymphoma, Children and Young Adults.
4	Strengthen international working	i. Work with the clinical trials unit(s) to promote UK as site for Sponsorship of international studies in NHL.
5	CSG structure and function	• Ensure the structure of the Group is appropriate and succession planning for Chair and members is in place • *Work collaboratively with High Grade subgroup and revise meeting to coincide with reciprocal representation on each group. • Establish strong collaboration with adult and TYA communities for the development of joint/ shared trials. • Establish strong representation for UK biology
6	Consumer involvement and impact	i. Seek appropriate input into study development from Consumer representation in Lymphoma, CCL and TYA CSGs as needed.

E – Hodgkin Lymphoma Subgroup Strategy

There are several strands to the strategy for the Hodgkin subgroup:

1. To further develop the collaboration between paediatric and adult investigators to produce clinical trials for all ages and all stages of disease
2. To develop world leading and potentially practice changing first line randomised clinical trials to build on the successes of RAPID and RATHL
3. To open a study for patients with nodular lymphocyte predominant Hodgkin lymphoma
4. To develop a risk-adapted trial for relapsed classical Hodgkin Lymphoma incorporating novel agents where possible and investigating situations in which stem cell transplantation can safely be omitted.
5. To investigate all stages of the patient journey: first line treatment, follow up strategies, psychosocial impact of disease, relapse strategies and late effects

Appendix 3

Portfolio maps

NCRI portfolio maps

Lymphoma

Map A – Non-Hodgkin's lymphoma, B-cell, diffuse large, Burkitt's, lymphoblastic

Click ↓ below to reset map

		1st line treatment	2nd line treatment	Observational / sample collection / quality of life	Palliative	Subsequent treatment	Transplant
Burkitt's	All	ONO/GS-4059 CANC - 4644					
Diffuse large	All	ONO/GS-4059 CANC - 4644					
	All diffuse large	PARP inhib in B cell malig INCA IELSG 37 Lenalidomide POLATUZUMAB	Rituximab +/- Pix AZD3965 in adv canc. LEGEND E7438 Betalutin SADAL MOR00208C203 MOR00208C204 Monotherapy+/- with	Lactate Imaging MaPLe			
	Central nervous system	IELSG 42 - Marietta	TIER Polatuzumab Vedotin				
	Children	Inter-B-NHL Rit					
Lymphoblastic	All	UKALL 2011 Inter-B-NHL Rit ONO/GS-4059 CANC - 4644	Combined with DURVALUMAB				

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG Null
Open Multi CSG In Set-Up Pending ..

NCRI portfolio maps

Lymphoma

Map B – Non-Hodgkin's lymphoma, B-cell
Click ↓ below to reset map

		1st line treatment	2nd line treatment	Observational / sample collection / quality of life	Subsequent treatment	Transplant
All B-cell NHL	All	ENRICH	A Phase I trial -DI-B4 Urelumab	Biomarker ident PROCLIPI T caspase activation in lym	BAY 80-6946	UK Haplo v1.0
Any low grade B-cell	All	R2W: Randomised	COMPLEMENT GS-1101 (CAL-101) NCRN580 IPI-145 & Ofatumumab Ibrutinib + Lenali. CANC - 3721	NFkB in CLL		ProT4 (Prophyla
Follicular	All	PACIFICO IPI-145 CANC - 4784 OLATUZUMAB VEDOTIN T-P10- Follicular Lymphom	Oral MLN9708 Nivolumab rFL PF-05280586 VS RITUX GDC-0199 IPI-145 + Rituximab Polatuzumab Vedotin ReBeL study: a A phase II stud	MaPLe		ProT4 (Prophyla
Mantle cell	All		PCI-32765 (Ibrutinib) An Open-label,	MCL Biobank		
Marginal zo..	All			Lym1		

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. | Open Single CSG | In Set-Up Pending ..
Open Multi CSG | Null | Suspended Single ..

NCRI portfolio maps

Lymphoma

Map C – Non-Hodgkin's lymphoma, T-cell
Click ↓ below to reset map

		1st line treatment	2nd line treatment	3rd line treatment	Observational / sample collection / quality of life	Transplant
All NHL T-cell	All	COBALT Study	AZD3965 in adv canc. Masit. Dexa. + Gem		Lactate Imaging Biomarker ident PROCLIPI Stem Expan.+diff ChemoT caspase activation in lymphoma	UK Haplo v1.0
Angio-immune	All					
Cutaneous	All		Brentuximab Vedo.	Brentuximab Vedo.		
Enteropathy	All					
Lymphoblastic	All	UKALL 2011				
Natural killer	All	EBV-specific T-cells			EBV assoc NK/T	
Perpheral	All	CHEMO-T ECHELON-2	Brentuximab Brentuximab Vedo. RomiCar	Brentuximab Brentuximab Vedo. RomiCar		

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG
Open Multi CSG

NCRI portfolio maps

Lymphoma

Map D – Hodgkin's lymphoma
Click ↓ below to reset map

		1st line treatment	2nd line treatment	3rd line treatment	Observational / sample collection / quality of life	Transplant
Adults	All	ECHELON		Arroven		
All	All		Brentuximab Vedo. MK3475	Brentuximab Vedo.	Lactate Imaging Whole body PET- CD4+ T cell targeting of human B cell lymphoma-associated antigens ChemoT caspase activation in lymphoma	UK Haplo v1.0
Children	All	EuroNet PHL-LP1				

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

Open Multi CSG
Open Single CSG
Null

Appendix 4

Publications in the reporting year

Mantle cell trial

Rule S, Smith P, Johnson PW, Bolam S, Follows G, Gambell J, Hillmen P, Jack A, Johnson S, Kirkwood AA, Kruger A, Pocock C, Seymour JF, Toncheva M, Walewski J, Linch D. The addition of rituximab to fludarabine and cyclophosphamide chemotherapy results in a significant improvement in overall survival in patients with newly diagnosed mantle cell lymphoma: results of a randomized UK National Cancer Research Institute trial. Haematologica. 2016 Feb;101(2):235-40. doi: 10.3324/haematol.2015.128710. Epub 2015 Nov 26. (2016)

Tucker D, Peggs K, Cook G et al. Reduced intensity conditioned allogeneic stem cell transplantation (RIC-allo) as front-line therapy for mantle cell lymphoma (MCL): results from the UK phase II mini allo study (CRUK: C7627/A9080). Br. J. Haematol. 2016;173 supple:19.

RATHL

Barrington SF, Kirkwood AA, Franceschetto A, Fulham MJ, Roberts TH, Almquist H, Brun E, Hjorthaug K, Viney ZN, Pike LC, Federico M, Luminari S, Radford J, Trotman J, Fosså A, Berkahn L, Molin D, D'Amore F, Sinclair DA, Smith P, O'Doherty MJ, Stevens L, Johnson PW. PET-CT for staging & early response: results from 'Response Adapted Therapy in Advanced Hodgkin Lymphoma' (RATHL) (CRUK/07/033). Blood. 2016 Jan 8. pii: blood-2015-11-679407. [Epub ahead of print] (2016)

RAPID

Radford J, Illidge T, Counsell N, Hancock B, Pettengell R, Johnson P, Wimperis J, Culligan D, Popova B, Smith P, McMillan A, Brownell A, Kruger A, Lister A, Hoskin P, O'Doherty M, Barrington S. Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma. N Engl J Med. 2015 Apr 23;372(17):1598-607. doi: 10.1056/NEJMoa1408648.

Appendix 5

Major international presentations in the reporting year

RATHL trial
Peter Johnson. Response-Adapted Therapy based on interim FDG-PET scans in advanced Hodgkin Lymphoma: first analysis of the safety of de-escalation and efficacy of escalation in the international RATHL STUDY (CRUK/07/033) Oral - Major findings, plenary session at ICML Lugano, June 2015.

C. Hague Pulmonary function and grade 3/4 clinical events in PET negative patients taking part in the international RATHL trial: a comparison of 12 vs 4 doses of bleomycin (CRUK/07/033) Oral – secondary analysis, ICML Lugano, June 2015.

RAPID trial
John Radford. PET score following 3 cycles ABVD has greater prognostic value than pre-treatment risk stratification in the RAPID trial in early stage Hodgkin lymphoma (HL) Oral – secondary analysis, ICML Lugano, June 2015.

Front line therapy with R-CODOX-M & R-IVAC in Poor Risk Diffuse Large B Cell Lymphoma (IPI 3-5) yields a good outcome without transplantation: Results of a Phase 2 UK NCRI Trial
Andrew McMillan; Oral - major findings, ICML Lugano, June 2015.

A UK Lymphoma Clinical Study Group Phase II Evaluation of High Dose Chemotherapy and Autologous Stem Cell Transplantation in Intestinal and other aggressive T-cell Lymphomas
M. Lannon. Oral – major findings, ICML Lugano, June 2015.

IELSG32 study
A.J.M. Ferreri, K. Cwynarski, E. Pulczynski, M. Ponzoni, M. Deckert, L.S. Politi, C.P. Fox, P. La Rosée, A. Ambrosetti, A. Roth, C. Hemmaway, F. Ilariucci, K. Linton, R. Soffietti, T. Pukropp, M. Binder, M. Balzarotti, A. Fabbri, P. Johnson, J. Sonderskov Gorlov, F. Cavalli, J. Finke, M. Reni, E. Zucca, G. Illerhaus. THE ADDITION OF THIOTEPA AND RITUXIMAB TO HIGH DOSES OF ANTIMETABOLITES SIGNIFICANTLY IMPROVES OUTCOME IN PRIMARY CNS LYMPHOMA: THE FIRST RANDOMIZATION OF THE IELSG #32 TRIAL. Oral – major findings, plenary session at ICML Lugano, June 2015.

REMoDI-B trial
Sharon L. Barrans, PhD[1], Andrew J Davies, MRCP[2*], Ming Wang[3*], Ming-Qing Du, MB, PhD[4], Christoph Mamot, MD[5*], Keith Pugh, PhD[6*], Josh Caddy[7*], Matthew A Care, PhD[8*], Jan Taylor[1*], Reuben M Tooze, PhD, FRCP[1,8], Tom Maishman[9*], Louise Stanton, PhD[6*], Debbie Hamid[6*], Andrew McMillan, PhD[10], Paul Fields, MD, PhD[11], Andrew Jack, PhD, MB[1] and Peter Johnson, MD[12].* Real-Time Molecular Classification of Diffuse Large B-Cell Lymphoma (DLBCL) By Gene Expression Profiling (GEP): Successful Delivery of a Routine Service for Randomization of Patients Onto the Multicenter Remodl-B Trial (ISRCTN 51837425) Oral – major findings, ASH meeting, December 2015