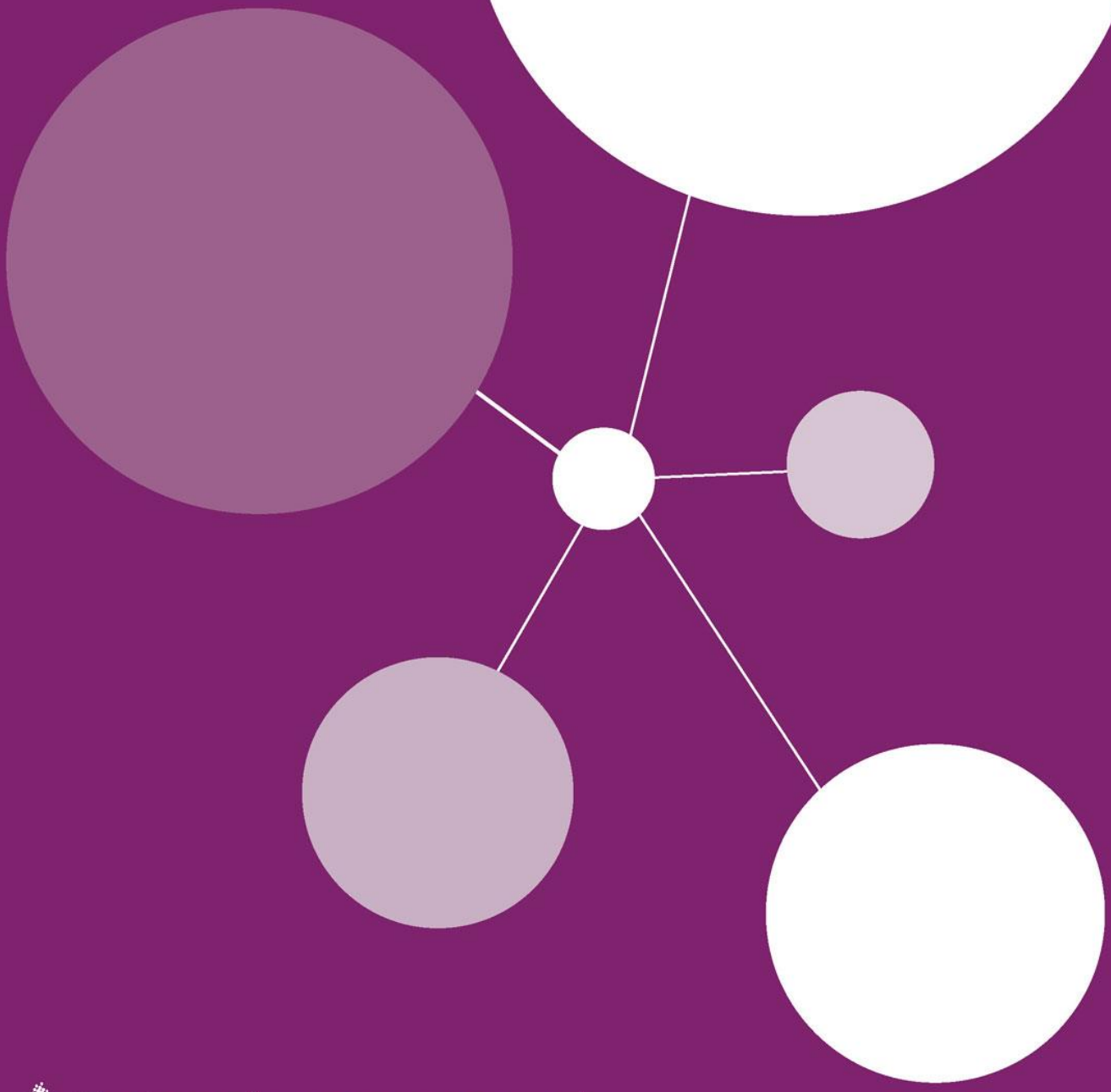
NCRI
National
Cancer
Research
Institute

NCRI Lymphoma Clinical Studies Group

Annual Report 2016-17



Partners in cancer research

NCRI Lymphoma CSG Annual Report 2016-17

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

The Lymphoma CSG has had a successful year with oral presentations at major international meetings and publications in very high impact journals. Funding has been agreed for the international RADAR trial, led by the UK, and the national PETREA trial which will both be opening shortly. We have been challenged to open studies in the survivor space and two of these are in development. One of these, a lung cancer screening study, has been endorsed by the SPED Advisory Group.

Our three top achievements are:

1. Results of the international RATHL trial of PET directed therapy in advanced Hodgkin lymphoma published NEJM June 2016: This is the first international lymphoma trial led by the UK and is 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. Spinoff studies of RATHL have been selected for oral presentation at ICML, Lugano, June 2017.
2. Results of first randomisation of the IELSG 32 trial in primary CNS lymphoma published Lancet June 2016 and results of 2nd randomisation published in Plenary Session at ASH meeting December 2016: The results of this trial are practice changing; they show that the addition of rituximab and thiotepa to methotrexate and cytosine arabinoside improve remission rates, three year PFS and OS. The results of a second randomisation (whole brain RT vs auto-transplantation) currently show equivalence of outcome although additional follow-up is important. Although entering the study late, the UK was the third highest recruiter and has firmly established itself as a major global player in CNS lymphoma research.
3. Results of international GALLIUM trial oral presentation at ASH meeting December 2016: This trial showed that obinotuzumab plus chemotherapy is superior to rituximab plus chemotherapy in the first line treatment of follicular lymphoma.

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, statisticians, imaging experts and representatives of clinical trials units. It also includes three trainees, Drs Okusan, Ahearne and Burns, 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 Martin Dyer (Leicester) and Dr Kim Linton (Manchester) to the CSG.

3. CSG & Subgroup strategies

Main CSG

Our main priorities in the 2015/16 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 supported by Takeda and a budget of £6.2m plus free drug agreed; a protocol has been written and is under review. In FL, a PET directed trial (PETREA) has been funded by Cancer Research UK CRC and set-up is underway. In DLBCL, a radiotherapy question was posed in ConRad but unfortunately this has not been funded in its present form and modifications are underway. A platform study (ARGO) in relapsed/refractory DLBCL for the evaluation of new agents and featuring molecular phenotyping has, however, been funded by Roche. In addition, a first-line study to follow-on from ReMODEL-B has been approved and is in set-up.

The challenges associated with opening large patient number phase III trials accessible to most centres in the UK continues to be an issue and it is generally agreed that for a variety of reasons these will be fewer in number in future years. However, it is still possible to undertake large trials of importance to lymphoma patients and we are pleased with our success with RADAR and PETREA both in the first line setting. In addition, we are keen to grasp opportunities in the field of survivorship and two studies are in development; TRANSFORM (previously known as START) compares traditional hospital based follow-up with patient led e-follow up and a study evaluating screening for lung cancer in lymphoma patients at high risk as a result of treatment. The latter, led by Dr Kim Linton, has been endorsed by the SPED Advisory Group with Professor David Baldwin (SPED Chair) a co-investigator.

The Group has undertaken several 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 and the primary endpoint will be reported 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. This clearly demonstrates our capabilities in the UK and is widely regarded a world leading study. 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.

In DLBCL, a phase Ib/II front-line pilot study (ACCEPT) of a second generation BTK inhibitor with R-CHOP endorsed by CRUK has now opened. 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, Subgroup 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 will be resubmitted.

The observational MaPLE study has now recruited 1,900 patients with DLCBL extending access to molecular stratification for patients outside the structure of an IMP, initially providing EZH2 mutational analysis and is now following an amendment an extended mutational panel and analysis of the 'liquid biopsy' by cfDNA. The study has been recruiting over 40 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, have 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 results of the second randomisation comparing consolidative whole brain radiotherapy to high-dose chemotherapy with peripheral blood progenitor cell rescue was report at American Society of Hematology meeting in December 2016. The Primary CNS Lymphoma Task Group (TG) of the High Grade Subgroup has played a major role in ensuring that this has become a standard of care in the NHS. The TG has continued to collaborate extensively with international partners, resulting in a successful Cancer Research UK bid for a study in secondary CNS lymphoma (IELSG42) which is now open for recruitment. The TG has also opened a study for relapsed PCSL (TIER) which is recruiting well.

The T-cell Task Group has been active, however, our front line study in T-cell lymphoma, (CHEMO-T) closed prematurely at the advice of the DMEC. We are currently seeking new opportunities in front-line cell lymphoma. The RomiCar study in relapsed/refractory T-cell is recruiting well. AVAIL-T, investigating the use of a check-point inhibitor in T-cell lymphoma, is about to open.

In the relapsed DLBCL setting, LEGEND closed following the advice of the Date Monitoring Committee. A novel agent trial (TORCH) has now fully recruited. The latter arena is crowded with multiple commercial novel agent studies competing for the population. A randomised phase II study of a PD-L1 inhibitor with R-GemOX and has been funded and CRUK endorsed for the older/co-morbid DLBCL patients (ARGO). This will be activated at around 30 sites so this 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 is now open. 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 published in the Journal of Clinical Oncology (December 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. As a result it lost CRUK support; funding has been picked up for IELSG and will continue to recruit. 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 Adult (TYA) & Germ Cell Tumour (GCT) CSG, we have 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 Subgroup continues to meet on a regular basis with enthusiastic support from its key members, many of whom dial in to the meetings. The recent plenary presentation by Robert Marcus of the GALLIUM data at the annual ASH meeting was a highlight for the Subgroup last year and this data will soon be published in a major journal. For the major low grade lymphoma subtypes, there has been a marked increase in activity in the last year.

Follicular NHL

- The PETrea study will be opening later this year. The results of the GALLIUM study, particularly with respect to toxicity, confirm the need for such a study. This will be the first large biomarker driven trial in this condition specifically utilizing the strengths of the PET network within the UK. The design will also facilitate the incorporation of novel drugs into the algorithm as required hence future proofing this and allowing us to have a trial for all patients with this condition. In addition, the bio banking approach that was used in the previous follicular lymphoma trial will also be adopted allowing important translational questions to be answered.
- REBEL: This is a relapsed follicular lymphoma trial that is part of international collaboration. It has been hampered due to drug supply problems which have now been resolved and the trial will be opening across a number of sites soon.

- PACIFICO: This frontline study closed during the last year. This is the largest randomized trial yet performed in the UK in this condition. The clinical question being asked was partly superseded by advances in practice but the associated biobank is providing a large reservoir for ongoing research. Results from this study are likely to come next year.

Mantle Cell NHL

- ENRICH: This trial is open and recruiting. It is the only trial worldwide that is comparing novel therapy against chemotherapy as the front line treatment in this condition. International collaboration will begin this year, initially involving the Nordic Group and centres in Ireland. The study includes analysis of MRD as well as bio banking.
- MCL Biobank: This study is open in the majority of hospitals in the country and has recruited over 200 patients to date. This is a unique repository and will provide material to help understand the biology of this condition. There have been a couple of meetings already to discuss potential studies with the samples.
- TRIANGLE: This is a European MCL network trial for younger patients which has just opened in Germany and hopefully will be open in the UK later in the year. It is looking at the incorporation of ibrutinib into front line practice.

Waldenstroms Macroglobulinaemia

- RAINBOW: Following on from the very successful R2W study, this trial looks at the incorporation of ibrutinib into frontline therapy for this disease. This was unfortunately turned down by CRUK but is likely to be funded by a pharmaceutical partner and hopefully will be open early next year.

Trials in evolution

- There are a number of studies that are in the early phases undergoing discussion through the Subgroup. One is in being run across two lymphoma study groups involving transformed follicular lymphoma which is the first time we have had a specific trial for this entity. A TAP proposal will consider the management of patients post ibrutinib. This will be a sequential trial looking at novel agents in the context of MCL but could extend to other histologies. There are also trials that are exploring other novel agents, particularly venetoclax, PD1 antibodies and daratumumab across a variety of malignancies. With all of these studies, the Subgroup strongly encourages associated bio banking and translational research.

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

In this reporting year, the Paediatric NHL Subgroup has begun to work collaboratively with the High Grade Subgroup. There is currently an international trial in development for relapsed ALCL involving Nivolumab which will include paediatric and TYA patients. There are currently no supportive care or survivorship studies and which is an area for development and there is an initiative to pursue a TYA survivorship study.

Notable successes include the presentation of the results of the Inter B-NHL Ritux 2010 Study at ASCO and SIOP 2016.

B-cell studies

The InterB-NHL Ritux 2010 showing benefit for Rituximab in high risk paediatric B-NHL (Burkitt

and DLBCL) will close in 2017 and final publication of the phase II study is expected in early 2018.

SPARKLE, the first international study of Ibrutinib combined with conventional chemotherapy in relapsed/refractory B-NHL sponsored by Janssen, has opened and completed recruitment of part one of the study and it is expected that the randomised part two will open soon, with 10 sites in the UK participating in the study.

Lymphoblastic Lymphoma
The UKALL 2011 study for acute lymphoblastic leukaemia and lymphoma continues to recruit well and will close soon. Based on the outcomes in this study, the Subgroup will lead (Dr Mary Taj) on an LBL sub-study to be included in the next International Study in Acute Lymphoblastic Leukaemia (ALLTogether 2018).

Anaplastic Large Cell Lymphoma
International study proposals have been finalised for frontline and relapsed disease. These are dependent on Pharma engagement in order to access new drugs and this has been the major challenge in the last year.

The Subgroup has seen two senior clinicians retire after many years of contribution to the field of paediatric NHL (Dr Denise Williams and Dr Ayad Atra). New members are being recruited to the Subgroup as a result.

Hodgkin Lymphoma Subgroup (Chair, Dr Graham Collins)

Front line classical Hodgkin lymphoma studies
There are currently no front line studies open in adults or children.

- For the children and TYA age group, the euronet-PHL-C2 study is in set-up with the aim to open to recruitment this year.
- Takeda have agreed to fund RADAR, incorporating brentuximab vedotin into front line early stage classical Hodgkin lymphoma.
- Pfizer have agreed to fully fund a window study of a PDL1 inhibitor (avelumab) in advanced Hodgkin lymphoma and the protocol is nearly finalised.
- MOPED is a study attempting to optimize chemotherapy in advanced Hodgkin lymphoma; the proposal is with the Trials Acceleration programme.

Relapsed classical Hodgkin lymphoma studies

- ANIMATE is a fully funded trial of single agent nivolumab as 2nd line salvage; the protocol is finalized and contracting is ongoing.
- BEECH is a first line salvage study. CRUK did not invite this for a full submission so other funding sources are being investigated.
- The UK has recruited well to commercial studies of PD1 inhibitors for relapsed/refractory Hodgkin lymphoma.

Nodular Lymphocyte Predominant Hodgkin
The paediatric and adult members of the Subgroup have been working closely to develop a protocol for all ages and all stages for this rare disease. Unfortunately, CRUK do not feel this fits with their priorities so other avenues of funding are being sought.

Important developments

- We have appointed a patient representative to the Subgroup.
- We are having a joint BSH/BLPG meeting for Hodgkin lymphoma to highlight scientific and translational awareness for clinical trials in this area.
- We have a trial in set-up looking at follow-up and psychological issues in survivors of Hodgkin lymphoma.

4. Task groups/Working parties

Task groups have been set up for T-cell lymphoma, CNS lymphoma and management of elderly patients all within the High Grade Subgroup.

T-cell lymphoma Task Group

The frontline CHEMO-T trial has closed on the recommendation of the IDMC and ECHELON-2, evaluating anaplastic large cell lymphoma, has completed recruitment and is expected to read out in the next 18 months. The TG is therefore attempting to develop a new, relevant and fundable study; a previous concept (DEFLECT) has been abandoned and a CHOP vs CHOEP proposal was not supported because of low expectation of benefit. The TG has decided that inclusion of novel agents and inclusion of early interim PET to assess response are important requirements and are working on a CHOP + lenalidomide +/-durvalumab design. An updated proposal will be circulated shortly. The phase I/II RomiCar study evaluating efficacy and safety of romidepsin and carfilzomib in PTCL is recruiting and the Avail-T protocol is nearing completion.

CNS Lymphoma Task Group

The IELSG32 manuscript (1y CNS lymphoma) has been submitted for publication. IELSG42 (2y CNS lymphoma) is recruiting to target and an amendment is being submitted to allow more sites to open to recruitment. No DLTs were detected in the phase I part of TIER (recurrent 1y CNS lymphoma) and 25 patients are to be recruited to the study. There is a desire for the study to have an international component (Italy) but this is being hampered by logistical issues.

FIORELLA (1y CNS lymphoma in the elderly) was not funded by CRUK CRC and this is a significant setback to the CNS lymphoma strategy (see challenges listed under item 12). The wider CSG is considering how best to respond to this. There is interest in ACP196, a phase II agent in CNS lymphoma, but more pre-clinical data is required. The welcome CAR-T cell study will open at UCLH in the near future. Potential funding streams for a UK PCNSL registry/database and tissue bank have been discussed.

High grade lymphoma in the elderly Task Group

An increasing number of older/frailer patients are presenting with aggressive lymphomas and the main question is how best to treat this population, many of whom have significant co-morbidities. A prospective data collection form is being developed with the University of Liverpool to determine factors which lead to dose reductions and outcomes associated with these. This work will facilitate the development of new trial protocols.

5. Patient recruitment summary for last 5 years

In the Lymphoma CSG portfolio, nine trials closed to recruitment and 22 opened.

The numbers of patients enrolled into interventional studies has increased slightly in the 2016/17 year but remains half of that seen in 2012/13. This is due to the closure of large phase III trials in Hodgkin lymphoma (RATHL) and diffuse large B cell lymphoma (ReMODeL-B). The soon to open RADAR (in Hodgkin lymphoma) and PETReA (in follicular lymphoma) trials will help to reverse the trend but it is clear that additional large number studies are required. Currently in development are the ConRad (the lung cancer screening trial) and TRANSFORM (a trial investigating different forms of follow-up) which will require large numbers and it is hoped that funding can be secured for all three. Members of the CSG are aware of the need to develop studies addressing pragmatic questions of importance to patients and the NHS.

It is important to be aware that the big phase III interventional trials of therapy are less commonly deployed than they were 5-10 years ago and phase I and II studies are far more prominent. This is reflected in the large number of trials opened in year (22). This also confirms that the UK has become a go-to destination for international pharma with several current and previous CSG members identified as key opinion leaders in their fields (Radford, Davies, Rule, Collins, Johnson, Illidge) and are frequently sought out for advisory boards and other advisory roles.

Table 1 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	785	804	785	580	5.6	4.2
2015/2016	1784	495	1784	495	12.84	3.56
2016/2017	1321	521	1321	521	9.50	3.75

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

The CSG has extensive links with international groups. These include IELSG (International Extra-Nodal Lymphoma Study Group) which leads important studies in central nervous lymphoma (CIs: Cwynarski and Fox) and primary mediastinal B cell lymphoma (CI: Davies). The RATHL trial (CI: 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, CI: 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.

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). Closer co-operation with the French and German groups is planned with Gilles Salles (Lyon, France) an expert in indolent lymphoma invited to be the Mike Bennett memorial lecturer at the UK Lymphoma Annual Trials Meeting in November 2017.

7. Funding applications in last year

The Group have submitted 10 study/trial applications for funding this year which results from a concerted effort to up our game in this area. However, it is disappointing that FIORELLA and

RAINBOW failed to secure funding as both were highly competitive follow-on studies in CNS lymphoma and Waldenstroms Macroglobulinaemia by Dr Chris Fox and Dr Rebecca Auer, respectively. It is unclear whether alternative funding sources will be identified.

ConRad is an important, potentially practice changing, study that was not supported by CRUK CRC in its present form and modifications are underway. ANIMATE was also not supported by CRC but Bristol Myers Squib subsequently agreed to fund this study.

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
May 2016			
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
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
November 2016			
A phase II study of obinutuzumab plus gemcitabine, oxaliplatin and atezolizumab in patients with refractory/relapsed diffuse large B-Cell lymphoma who are not candidates for high-dose therapy	Full (Endorsement)	Dr Andrew Davies	Supported
FIORELLA: randomized phase ii trial on comorbidity- and fitness-tailored treatment in elderly patients with newly diagnosed primary CNS lymphoma	Full application	Dr Christopher Fox	Not Funded
RAINBOW: Randomised phase II/III study of Rituximab and Ibrutinib (RI) versus Dexamethasone, Rituximab and Cyclophosphamide (DRC) as initial therapy for Waldenstrom macroglobulinaemia	Full application	Dr Rebecca Auer	Not Funded
PETReA Sample Collection	Sample Collection	Professor Andrew Pettitt	Not Funded
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
RADAR (international; early stage HL)	IIS, Takeda	Professor John Radford	Funded
WATCH (UK and Australia; advanced HL)	IIS, Pfizer	Dr Graham Collins	Funded
BioPET (translational spinoff from RAPID)	Bloodwise	Dr Kim Linton	Awaiting decision

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, the CI for territories outside North America is a CSG member (Radford). Data for ECHELON-1 are currently being analysed and will be submitted to the ASH meeting December 2017.

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 results has been selected for oral presentation at ICML Lugano June 2017.

9. Impact of CSG activities

Over the last five years, the CSG's research outputs have had a major 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 do not need it. These results were published in NEJM, April 2015.

In advanced Hodgkin lymphoma, results of the RATHL trial (Johnson) were presented in a plenary session at the ICML Lugano meeting in June 2015 and published by the NEJM in 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 three to six. The development of a 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 were presented in a plenary session at ICML, Lugano, June 2015, and published in The Lancet in June 2016. These showed that additional drugs added to the induction regimen (known as MATRix) 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.

Members of the CSG have been very active in NICE appraisals and in particular considerable effort was put into the numerous rounds of evaluation (2016/17) in connection with brentuximab vedotin in classical Hodgkin lymphoma. It was very gratifying to hear in May 2017 that BV has been approved by NICE for use in patients relapsing after autologous stem cell transplantation and additional data with respect to its use in refractory patients who have never achieved remission is being collected from CSG members and the wider community.

10. Consumer involvement

Andy Barton is currently the sole consumer member of the Lymphoma CSG following the sad death of Stephen Wood in July 2016 and the CSG therefore needs to recruit an additional consumer representative. Committee members have been asked to explain the function and importance of the role to patients within their own clinical practices and encourage them to apply. We are confident this approach will result in another consumer joining Andy before the next CSG meeting.

This past year, Andy has completed his two days of consumer training, attended both consumer forum meetings in July and February and CSG meetings in October and April. He is intending to attend the NCRI Conference in November 2017 having missed the opportunity in 2016 and at the last meeting it was agreed that he would join the Low Grade Subgroup, for which the next meeting is in September. It is clear that the membership of a Subgroup is key to being able to contribute fully to the CSG and he welcomes this opportunity.

Andy continues to be very active outside of the CSG with his involvement with both the Lymphoma Association and Bloodwise.

11. Open meetings/annual trials days/strategy days

The UK Lymphoma Annual Trials meeting in November features a high profile guest speaker and an update on current, completed and planned studies is a fixture for the CSG and has become increasingly well attended over the last five years. In 2016, more than 500 delegates including physicians, nurses, research staff and patient representatives attended the meeting in Senate House, University of London where Dr Craig Moskowitz from Memorial Sloan Kettering Cancer Center, New York 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 sessions held by the Royal College 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.

12. Priorities and challenges for the forthcoming year

These priorities and challenges reflect the current Chair's view of the current situation for the CSG but may change with the appointment of a new Chair following completion of his six year term in July 2017. It is acknowledged that the incoming Chair may wish to review these priorities and challenges following appointment.

Top 3 priorities

1. Open the funded PETReA, WATCH and RADAR trials and meet early recruitment targets. Initial recruitment can be slow with new studies and the Group must make effort to overcome this using newsletters, recruitment tables and by featuring at the UK Lymphoma Annual Trials meeting.
2. Design and obtain funding for a first line study in diffuse large B cell lymphoma suitable for all UK Centres. DLBCL is the commonest sub-type of lymphoma and a replacement for the highly successful REMODeL-B study is required.
3. Obtain funding for survivor studies currently in development (TRANSFORM and lung cancer screening) and go on to develop a significant portfolio of studies in this area which are important to patients and can be associated with large numbers.

Challenges

1. There was extensive discussion at the last CSG meeting concerning the perceived shortage of haematological oncology expertise on CRUK CRC and the possible bearing of this on funding decisions. This was prompted by the recent failure to secure funding for Dr Fox's and Dr Auer's excellent new studies (primary CNS lymphoma in the elderly and Waldenstroms macroglobulinaemia, respectively), both of which followed on from very successful studies in the same areas undertaken by these investigators. Although it is understood that not every cancer site can be fully represented on CRC, it is the case that all solid cancers have some similarities and are fundamentally different from liquid cancers and lymphoma. Haematological cancers may therefore be at a disadvantage and discussions about how this might be rectified would be welcome.
2. The Group needs to get better at encouraging/supporting all CSG members and the wider lymphoma community to come forward with study/trial ideas and move these forward to grant submissions. Currently there is a relatively small core of individuals who achieve this in the Lymphoma CSG but for the UK to be competitive in the longer term, we need to widen the pool of CIs. This is a big issue and one that depends on Trusts (because many CSG members have primary NHS contracts) understanding the importance and value of research and providing job plans which facilitate this activity.
3. In addition to evaluating new agents, we must develop trials and studies that address dilemmas of routine treatment decision making and/or are of importance to patients. A great example of this type of study is ConRad which unfortunately in its current design did not get funded by CRUK CRC. Modifications to the design are underway and it is hoped that these will lead to CRC support. These studies, in addition to being of great value to guiding routine practice, also tend to require large numbers which in an era of falling recruitment is strategically important.

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
Mr Jonathan Pearce	CEO, Lymphoma Association	Aylesbury
Dr David Burns*	Clinical Lecturer	Birmingham
Professor Richard Cowan	Clinical Oncologist	Manchester
Dr David Cutter	Clinical Oncologist	Oxford
Dr Amit Sud*	Clinical Research Fellow	London
Dr Maria Marzolini*	Clinical Research Fellow	London
Mr Andrew Barton	Consumer	Northwich
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
Professor Simon Rule	Haematologist	Plymouth
Professor Martin Dyer	Haemato-Oncology	Leicester
Dr Andrew Davies	Medical Oncologist	Southampton
Dr Kim Linton	Medical Oncologist	Manchester
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
Ms Amy Kirkwood	Statistician	London
Mrs Louise Stanton	Statistician	Southampton

* denotes trainee member

Membership of the Subgroups

Low Grade Lymphoma Subgroup		
Name	**Specialism**	**Location**
Professor Peter Hoskin	Clinical Oncologist	Middlesex
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

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 Andrew Wotherspoon	Histopathologist	London
Dr Andrew Davies	Medical Oncologist	Southampton
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**	Trial Coordinator	Birmingham
Dr Emma Seaford*		

High Grade Lymphoma Subgroup		
Name	**Specialism**	**Location**
Dr Matthew Ahearne**	Clinical Lecturer	Leicester
Dr Maria Marzolini*	Clinical Research Fellow	London
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
Dr Wendy Osborne	Medical Oncologist	Newcastle
Dr Amos Burke	Paediatric Oncologist	Cambridge
Professor Andrew Jack	Pathologist	Leeds

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 Amit Sud*	Clinical Research Fellow	London
Arzhang Ardavan	Consumer	
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
Dr Patrick Medd	Haematologist	Plymouth
Dr Fiona Miall	Haematologist	Leicester
Professor Peter Johnson	Medical Oncologist	Southampton
Professor John Radford	Medical Oncologist	Manchester
Dr Stephen Daw	Paediatric Haematologist	London
Ms Amy Kirkwood**	Statistician	London

*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 • Palliative and Supportive Care • Primary Care • Screening, Prevention and Early Diagnosis (SPED) Advisory Group.	TBD at next CSG mtg TBD at next CSG mtg TBD at next CSG mtg TBD at next CSG mtg	March 2016 March 2016 March 2016 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 Subgroup 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

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.

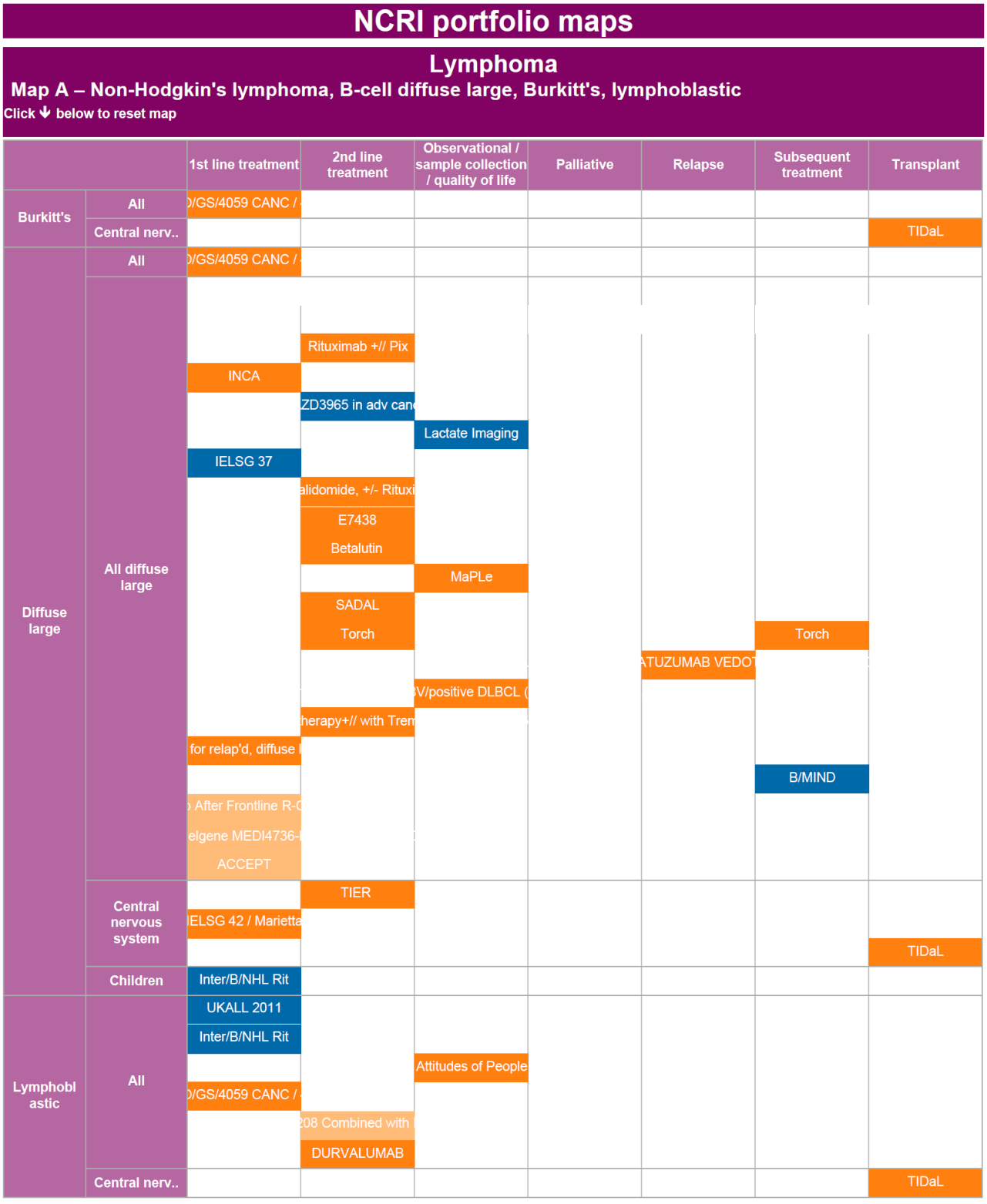
E – Hodgkin Lymphoma Subgroup Strategy

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 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	nib in children and TYA with 64052781NHL1001 PROCLAIM-001	CHRONOS/4 CC/90011/ST/001 tion Rituximab for Patients CD20 in CD32b positive B/	Biomarker ident HORIZONS	ituximab and bendamustine Nivolumab combi	UK Haplo v1.0 to in Relapsed/Refractory D TIDaL
Any low grade B-cell	All	ENRICH	IPI/145 & Ofatumumab	NFkB in CLL Pathogenesis Of Lymphom		ProT4 (Prophyla
Follicular	All	IPI/145 CANC / 4784 T/P10/ Follicular Lymphom Rituximab in patients with ase Inhibitor, Treatment for	Oral MLN9708 PF/05280586 VS RITUX ReBeL study: a OLATUZUMAB VEDOTIN /	MaPLe		ProT4 (Prophyla
Mantle cell	All		PCI/32765 (Ibrutinib) An Open/label, MERCK / MS200662_0001	MCL Biobank		
Marginal ..	All	d safety study of PQR309 i				

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

Open Multi CSG | Null | In Setup, Waiting .. | In Setup, Waiting ..
Open Single CSG | In Setup, Waiting .. | In Setup, Waiting .. | 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	Supportive care	Transplant
All NHL T-cell	All	COBALT Study PROCLAIM-001	AZD3965 in adv canc. Masit. Dexa. + Gem BAY 1862864/17845 ADCT-402-101		Lactate Imaging Biomarker ident Stem Expan.+diff		UK Haplo v1.0 TIDaL
Angio-immune	All		Patients with Patients with CHECKpoint in participants with				
Cutaneous	All		Brentuximab Vedo.	Brentuximab Vedo.		PROCLIPI	
Enteropathy	All						
Lymphoblastic	All	UKALL 2011 Kinase (BTK) Ibrutinib in					
Natural killer	All	EBV/specific T/cells			EBV assoc NK/T		
Perpheral	All		Brentuximab Brentuximab Vedo. RomiCar	Brentuximab Brentuximab Vedo. RomiCar			

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

Open Multi CSG
Open Single CSG
Null
In Setup, HRA Ap..
In Setup, Waiting ..
In Setup, Waiting ..
In Setup, Waiting ..

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		Oral PQR309 in Patients with Replased or Refractory Lymphomas	Arroven		TIDaL
All	All	AVELUMAB PROCLAIM-001	Brentuximab Vedo. with Relapsed or Refractory Hodgkin CHECKpoint pathway and nivoluMab clinical participants with Advanced Tumours and	Brentuximab Vedo.	Lactate Imaging Whole body PET/ human B cell lymphoma/associated South Coast Observational Study Biomarkers and classical Hodgkin lymphoma National cohort study of late effects of Hodgkin lymphoma treatment	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
In Setup, HRA Ap..
In Setup, Waiting ..
In Setup, Waiting ..

Appendix 4

Publications in the reporting year

Study	Reference
AITL	Townsend W, Johnson RJ, Pottinger BT, Counsell N, Smith P, Chadwick H, et al. A phase II clinical trial of fludarabine and cyclophosphamide followed by thalidomide for angioimmunoblastic T-cell lymphoma. An NCRI clinical trial. CRUK number C17050/A5320. Leuk Lymphoma. 2016;57(9):2232-4
RATHL	Johnson P, Federico M, Kirkwood A, Fossa A, Berkahn L, Carella A, et al. Adapted Treatment Guided by Interim PET-CT Scan in Advanced Hodgkin's Lymphoma. N Engl J Med. 2016;374(25):2419-29
RCHOP-14 vs 21	Gleeson M, Hawkes EA, Cunningham D, Chadwick N, Counsell N, Lawrie A, et al. Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) in the management of primary mediastinal B-cell lymphoma: a subgroup analysis of the UK NCRI R-CHOP 14 versus 21 trial. Br J Haematol. 2016;175(4):668-72
	Kühnl A, Cunningham D, Counsell N, Hawkes EA, Qian W, Smith P, Chadwick N, Lawrie A, Mouncey P, Jack A, Pocock C, Ardeshna KM, Radford J, McMillan A, Davies J, Turner D, Kruger A, Johnson P, Gambell J, Rosenwald A, Ott G, Horn H, Ziepert M, Pfreundschuh M, Linch D. Outcome of Elderly Patients with Diffuse Large B-cell Lymphoma Treated with R-CHOP: Results from the UK NCRI R-CHOP14v21 trial with combined analysis of molecular characteristics with the DSHNHL RICOVER-60 trial. Ann Oncol. 2017 Apr 7. doi: 10.1093/annonc/mdx128. [Epub ahead of print]
Improving Survival of Patients With Hodgkin Lymphoma Over 4 Decades: Experience of the British National Lymphoma Investigation (BNLI) With 6834 Patients	Kwan A Chadwick N, Hancock B. Clinical Lymphoma Myeloma and Leukemia. 2016
Radiation dose-response for heart failure after Hodgkin lymphoma	Frederika A. van Nimwegen & Georgios Ntentas, Sarah C. Darby, Michael Schaapveld, Michael Hauptmann, Pieternella J. Lugtenburg, Cecile P.M.Janus, Laurien Daniels, Flora E. van Leeuwen, David J. Cutter& Berthe M.P. Aleman. RISK OF HEART FAILURE IN SURVIVORS OF HODGKIN LYMPHOMA: EFFECTS OF CARDIAC EXPOSURE TO RADIATION AND ANTHRACYCLINES. Blood First Edition Paper, prepublished online January 31, 2017; DOI 10.1182/blood-2016-09-740332
Long-term hospitalisation	Kathrine Rugbjerg, Maja Maraldo, Marianne C. Aznar, David J.

rates among 5-year survivors of Hodgkin lymphoma in adolescence or young adulthood: A nationwide cohort study	Cutter, Sarah C. Darby, Lena Specht and Jørgen H. Olsen. Int. J. Cancer: 00, 000–000 (2017) DOI: 10.1002/ijc.30655
REMoDL-B trial	C Burton et al. Gene expression profiling and mutation analysis can aid treatment decision making in aggressive B cell lymphoma patients
Nivolumab for classical Hodgkin's lymphoma after failure of both autologous stem-cell transplantation and brentuximab vedotin: a multicentre, multicohort, single-arm phase 2 trial	Younes A et al. Lancet Oncol. <https://www.ncbi.nlm.nih.gov/pubmed/27451390#> 2016 Sep;17(9):1283-94. doi: 10.1016/S1470-2045(16)30167-X. Epub 2016 Jul 20.
Safety and efficacy of abexinostat, a pan-histone deacetylase inhibitor, in non-Hodgkin lymphoma and chronic lymphocytic leukemia: results of a phase II study	Ribrag V, Kim W, Bouabdallah R, Lim ST, Coiffier B, Illes A, Lemieux B, Dyer MJS, Offner F, Felloussi Z, Kloos I, Luan Y, Vezan R, Graef T, Morschhauser F. Haematologica. 2017 May;102(5):903-909. doi: 10.3324/haematol.2016.154377. Epub 2017 Jan 25
Long-term follow-up of patients with CLL treated with the selective Bruton's tyrosine kinase inhibitor ONO/GS-4059	Walter HS, Jayne S, Rule SA, Cartron G, Morschhauser F, Macip S, Karlin L, Jones C, Herbaux C, Quittet P, Shah N, Hutchinson CV, Fegan C, Yang Y, Mitra S, Salles G, Dyer MJ. Blood. 2017 Apr 4. pii: blood-2017-02-765115. doi: 10.1182/blood-2017-02-765115 [Epub ahead of print]
Safety and efficacy of obinutuzumab with CHOP or bendamustine in previously untreated follicular lymphoma	Grigg A, Dyer MJ, Díaz MG, Dreyling M, Rule S, Lei G, Knapp A, Wassner-Fritsch E, Marlton P. Haematologica. 2017 Apr;102(4):765-772. doi: 10.3324/haematol.2016.152272. Epub 2016 Dec 23
New Agents to Treat Chronic Lymphocytic Leukemia	Walter HS, Salles GA, Dyer MJ. N Engl J Med. 2016 Jun 2;374(22):2185-6. doi: 10.1056/NEJMc1602674#SA2
Inter-B-NHL Ritux 2010	Veronique Minard-Colin, Anne Auperin, Marta Pillon, Amos Burke, James Robert Anderson, Donald A. Barkauskas, Keith Wheatley, Rafael Delgado, Sarah Alexander, Anne Uyttebroeck, Catherine Bollard, Jozsef Zsiros, Monika Csoka, Gisele Goma, Anne Tulard, Catherine Patte, Thomas G. Gross; Results of the randomized Intergroup trial Inter-B-NHL Ritux 2010 for children and adolescents with high-risk B-cell non-Hodgkin lymphoma (B-NHL) and mature acute leukemia (B-AL): Evaluation of rituximab (R) efficacy in addition to standard LMB chemotherapy (CT) regimen. J Clin Oncol 34, 2016 (suppl; abstr 10507)

Appendix 5

Major international presentations in the reporting year

Study	Conference details
Mini Allo trial	Reduced Intensity Conditioning transplantation (RIC) as part of first line therapy for Mantle cell lymphoma: results from the Phase II Mini Allo trial results presentation; EHA (European Haematology Association) – June 2016, Copenhagen
	European Society for Blood and Bone Marrow Transplantation (EBMT) - 3-6 April, Valencia
	Main trial results, British Society of Haematology (BSH) – April 2016, Glasgow
Whole body functional and anatomical MRI	10th ISHL (International symposium on Hodgkin Lymphoma) – October 2016, Cologne
	Radiological Society of North America (RSNA) – December 2016, Chicago
GALLIUM study	Oral presentation, ASH (American Society of Haematology) – December 2016, San Diego
R2W	Oral presentation, ASH (American Society of Haematology) – December 2016, San Diego
	Oral presentation, International Workshop on Waldenstrom's Macroglobulinaemia (IWWM) - October 2016, Amsterdam
	Rebecca Auer, Roger Owen, Shirley D'Sa, Guy Pratt, Bilyana Popova, Laura Clifton-Hadley, Oliver Schofield, Nicholas Counsell, Paul Smith.R2W: Subcutaneous Bortezomib, Cyclophosphamide and Rituximab (BCR) versus Fludarabine, Cyclophosphamide and Rituximab (FCR) for initial therapy of Waldenstrőm's macroglobulinaemia: a randomised phase II study - Primary endpoint results presented at ASH, December 2016, San Diego
	Rebecca Auer, Roger Owen, Shirley D'Sa, Guy Pratt, Bilyana Popova, Laura Clifton-Hadley, Oliver Schofield, Nick Counsel, Paul Smith.Randomised Phase 2 trial in Waldenstrőm's macroglobulinaemia Subcutaneous Bortezomib, Cyclophosphamide and Rituximab (BCR) versus Fludarabine, Cyclophosphamide and Rituximab (FCR) for initial therapy of Waldenstrőm's macroglobulinaemia: a randomised phase II study - 9th IWWM workshop in Amsterdam, October 2016, awarded an Abstract prize as a top 5 Abstract
R-CHOP-14 vs 21 trial	Oral presentation, EHA (European Haematology Association) – June 2016, Copenhagen
	Oral presentation, ASH (American Society of Haematology) – December 2016, San Diego
	Initial analysis, ASH (American Society of Haematology) – December 2016, San Diego
Low Rates of CNS relapse in	Oral presentation, ASH (American Society of Haematology) –

High Risk DLBCL Patients Treated with R-CODOX-M and R-IVAC Chemotherapy	December 2016, San Diego
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	Main trial results, British Society of Haematology (BSH) – April 2016, Glasgow
The addition of Rituximab to CODOX-M & IVAC in first Line therapy of poor risk Burkitt Lymphoma (IPI 3-5) yields an excellent outcome	Main trial results, British Society of Haematology (BSH) – April 2016, Glasgow
Inter-B-NHL Ritux 2010	Veronique Minard-Colin, Anne Auperin, Marta Pillon, Amos Burke, James Robert Anderson, Donald A. Barkauskas, Keith Wheatley, Rafael Delgado, Sarah Alexander, Anne Uyttebroeck, Catherine Bollard, Jozsef Zsiros, Monika Csoka, Gisele Goma, Anne Tulard, Catherine Patte, Thomas G. Gross; Results of the randomized Intergroup trial Inter-B-NHL Ritux 2010 for children and adolescents with high-risk B-cell non-Hodgkin lymphoma (B-NHL) and mature acute leukemia (B-AL): Evaluation of rituximab (R) efficacy in addition to standard LMB chemotherapy (CT) regimen. J Clin Oncol 34, 2016 (suppl; abstr 10507) – ASCO, May 2016
RAPID trial	John Radford gave a seminar on early stage Hodgkin Lymphoma and the impact of the RAPID trial on international practice - visiting Professor, Memorial Sloan Kettering Cancer Centre, New York, May 2016
	John Radford. Early stage Hodgkin lymphoma including impact of RAPID trial on management of early stage Hodgkin lymphoma Educational Programme – ASCO, May 2016
RATHL study	Oral presentation, ISHL (International symposium on Hodgkin Lymphoma) - Cologne
RAPID & RATHL trials	John Radford talk on late toxicity of treatment in Hodgkin lymphoma and role of PET adapted approaches (RAPID and RATHL trials) - International Symposium Hodgkin Lymphoma, Cologne, Germany, October 2016
	John Radford chaired session on late treatment toxicity including talk on impact of response adapted approaches (RAPID and RATHL) - NCRI Conference, Liverpool, November 2016