



Lymphoma Medical and Clinical Oncology Service





Operational Structure

The lymphoma service at The Christie is led by two medical oncologists (John Radford, Kim Linton) and four clinical oncologists (Tim Illidge, Richard Cowan, Maggie Harris and Ed Smith). A fifth clinical oncologist (Clara Chan) has recently been appointed and commences in March 2015. Drs Adrian Bloor and Eileen Parry are integral members of the team for the provision of haematopoietic stem cell transplant services and cutaneous lymphoma dermatology expertise respectively. The Group works closely with Young Oncology Unit for management of TYA patients.

Referrals for specialist treatment and/or second opinions come from the Greater Manchester area (70%) and elsewhere in the UK (30%). Cases are reviewed through three multi-disciplinary team meetings, a weekly Southern Sector MDT serving The Christie, UHSM, Stepping Hill, Macclesfield and Tameside), a weekly Central Sector MDT serving CMFT, Trafford and Tameside) and a fortnightly North West Sector MDT serving Salford, Bolton and Wigan. MDTs provide radiotherapy services, transplant opinions and specialist expertise in systemic therapy including the opportunity for patients to participate in clinical trials. MH and TI also participate in the fortnightly Pennine Acute MDT.

There are ten lymphoma outpatient clinics per week at The Christie, providing patients with

world leading lymphoma treatments and access to one of the largest clinical trial portfolios in the UK. Peripheral clinics are held at Wigan and Tameside, working alongside local haematologists and specialist nurses to deliver systemic therapy locally (The Royal Albert Edward Infirmary for Wigan patients), or in preparation for treatment at The Christie/CMFT (Tameside patients). The supra-regional cutaneous lymphoma service is delivered by The Christie in collaboration with Salford NHS Trust and includes twice monthly clinics and MDT meetings with input from specialised dermatology and haematopathology services. The Manchester Cutaneous Lymphoma service is the second largest in the UK providing specialist therapy including Total Skin Electron Beam Therapy (TSEBT) and Extracorporeal photophoresis (ECP).

Personnel

<p>Consultants Lymphoma DG</p>	<p>Prof John Radford (JR) (Chair Lymphoma DG)</p> <p>Prof Tim Illidge (TI)</p> <p>Prof Richard Cowan (RC) (Cutaneous Lymphoma Lead)</p> <p>Dr Kim Linton (KL)</p> <p>Dr Maggie Harris (MH)</p>
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	Dr Ed Smith (ES) (TYA Clinical Lead) Dr Clara Chan (CC)
Affiliated Consultants	Dr Adrian Bloor (AB) (Haematology Transplant Service) Dr Eileen Parry (EP) (Cutaneous Lymphoma Service)
Clinical Research Fellow	Dr Adam Gibb (AG)
Radiology	Dr Ben Taylor (BT) Dr Rhidian Bramley (RB) Dr Soo Mak (SM) Dr Fenella Wong (FW)
Pathology	Dr Lia Menasce (LM) Dr Patrick Shenjere (PS)
Pharmacy	Sue Stent (SS)
Nurse Clinician	Valerie Good (VG)
Clinical Nurse Specialist	Jane Gibson (JG)
Research Nurses	Susan Neeson (SN) (Team Leader)

	Susanne Allibone (SA) Caroline Hamer (CH) Andrea Whitmore (AW) Joanna Dash (JD) Susanna Smith (SS)
Clinical Trial Administrators	Clare Day (Team Leader) Juliet Harris (JH) Bethany Hiron (BH) Tanya Massey (TM) Catherine Stone (CS)

Activity

The lymphoma team accepts approximately 220 new referrals per year at The Christie site. In 2014, 414 cases were discussed at the Christie-led South Sector MDT, including 282 patients with newly diagnosed, untreated lymphoma. A further 40 patients with cutaneous T cell lymphoma were discussed at a dedicated cutaneous lymphoma MDT. A breakdown of all cases (635) discussed at the South Sector MDT in the two year period from Mar 2013 to Feb 2015 is shown below:



Diagnosis	Treatment status		Treatment Intent			Total (%)
	No previous Rx	Post Rx	Curative	Palliative	Uncertain	
DLBCL	115	94	115	29	65	209 (32.9)
FL	57	45	11	34	26	102 (16.1)
Classical HL	49	47	67	0	3	96 (15.1)
Other low grade B-NHL	35	14	9	17	12	49 (7.7)
PTCL	13	12	14	3	3	25 (3.9)
Mantle cell	8	13	1	5	6	21 (3.3)
Other high grade B-NHL	13	8	10	3	0	21 (3.3)
Cut T cell	13	6	1	4	3	19 (3.0)
Nodular LP HL	12	7	14	0	0	19 (3.0)
CLL	5	9	2	4	3	14 (2.2)
Benign lymphoproliferative	7	0	4	0	0	7 (1.1)
Other	5	11	3	1	5	16 (2.5)
Diagnosis awaited	16	20	8	4	5	36 (5.7)
N/A	1	0	0	0	0	1 (0.2)
Total	349	286	259	170	206	635 (100)

DLBCL – diffuse large B-cell lymphoma; FL – follicular lymphoma; HL – Hodgkin lymphoma; N-NHL – B-cell non-Hodgkin lymphoma; PTCL – peripheral T-cell lymphoma; Cut – cutaneous; LP – lymphocyte predominant; CLL – chronic lymphatic leukaemia; N/A – not applicable

Service Development 2013/14

Key achievements in 2013/14 included;

- New PCNSL referral pathway;** links and a specialist referral pathway from SFRT to The Christie were established with neuro-oncology specialist nursing and allied health professional teams to improve communication and care delivered to patients diagnosed with primary central nervous system lymphoma (PCNSL); this new referral pathway helped implement a new standard of care for patients with PCNSL and resulted in unprecedented recruitment to a phase 3 international clinical trial in previously untreated PCNSL (co-authorship on abstract submitted to 2015 International Conference in Malignant Lymphoma).
- Improved patient access to novel treatments;** the lymphoma team plays a leading role in the clinical investigation of novel therapies within clinical trials, and in making new treatment available to patients through applications to the National Cancer Drugs Fund and compassionate access programmes. In 2014, 79 lymphoma patients received approval for treatment funded by the National Cancer Drugs Fund.
- Managed local follow-up for long term survivors of cancer (ADAPT);** this CQUIN project was developed for patients with HL and DLBCL likely to be cured 5 years after treatment and for whom follow-up with their GPs is appropriate. GPs and



patients receive treatment summaries and individualised advice on management of potential late effects. Following a successful pilot in 25 lymphoma survivors, roll-out to 500 patients is underway. This initiative will free up 500 clinic appointments per year and save an estimated 2000 patient hours with associated savings in transport costs and impact on employment and family life. The involvement of our nurse clinician (VG) was a pivotal factor in the success of this project.

- **Breast screening after radiotherapy database (BARD);** in this project a national database comprising all women (n=9200) at increased risk of breast cancer as a result of radiotherapy under the age of 36 is being established and hosted in Manchester. The lymphoma team is working closely with experts in breast cancer, epidemiology, screening, colleagues at the NHS breast screening programme and patient representatives, and funding has been provided by Teenage Cancer Trust. BARD will transform breast screening for this group of women and make sure appointments are provided in a timely way to avoid the current frustrations associated with non-arrival of appointments and improve the efficiency/effectiveness of the programme.
- **Website development;** the lymphoma team is developing a bespoke lymphoma website to provide information for patients and professionals about the services they offer, available clinical trials, recent

research findings and the national/international work undertaken by Lymphoma Group members. This work is funded by an educational grant of £3k awarded by Takeda and lymphoma group charitable and commercial funds.

- **Update of the Lymphoma Group MDT Charter;** the objectives and organisational aspects of the Lymphoma MDT meeting was revised and updated in June 2014.
- **Updated Radiotherapy Service;** in 2014, a new document updating the entire lymphoma radiotherapy practice was produced, in line with recent published evidence.
- **Total Skin Electron Beam therapy (TSEBT);** Manchester is one of only a handful of centres in the UK offering TSEBT for patients with cutaneous lymphoma. In 2014, the team modified their protocols as a UK initiative in line with recently published data.
- **Cutaneous Lymphoma;** the care provided to patients with advanced cutaneous lymphoma has been enhanced by the inclusion of the newly appointed tissue viability nurse within the Manchester Cutaneous Lymphoma Service.
- **The lymphoma service at Wigan** will be enhanced by the appointment of a new Consultant in Clinical Oncology (CC) starting on 1st March 2015. A purpose built oncology department will be opened on the Wigan Infirmary site within a few months offering comprehensive outpatient



and chemotherapy services for lymphoma patients in collaboration with The Christie.

- **Survivorship Programme in TYA population and Treatment Summary and Care Plan (TSCP) for TYA patients;** two programmes developed by the Lymphoma team were adopted by the Teenage Cancer Trust in 2014 for national roll-out. The Christie hosted the first 'TCT' badged course in Autumn 2014; the majority of attendees were lymphoma patients.
- **The Proton Therapy Programme;** the lymphoma team has been instrumental in developing proton therapy. The programme is awaiting a final decision from the Treasury and will likely form the basis of the national radiotherapy dataset, including standard radiotherapy.

Patient satisfaction

Results of patient satisfaction surveys conducted in the outpatient department by our clinical nurse specialist (JG) in 2010 and 2013 indicate consistently high levels of patient confidence in the team and satisfaction across a range of services. A summary of results is shown in the following table:

Question	2010 (%)	2013 (%)
General		
Introduction made	100	100
Purpose of consultation discussed	100	100
Treated with respect/dignity	96	98
Enough privacy during examination	94	98
Enough privacy during discussion	96	98
Appointment frequency adequate	89	96
Consultation length adequate	95	70
Patient confidence and trust in the team	96	87
Consistent team approach	96	98
Communication, information and involvement in care		
Patient understanding of condition/treatment	98	100
Patient understanding of answers to questions	91	93
Patient involvement in treatment decisions	96	95
Patient views taken into account	91	92
Family/friends involvement in	85	83



treatment plans		
Patients received info pack	96	96
Info pack was helpful	100	96
Information on treatment side effects adequate	100	98
Patient understanding post treatment	91	98
Right amount of information given post treatment	80	89
Clinical trial discussed	54	63
Comms with GP Satisfactory	68	64
- Unable to comment	-	3
% patients who would like copies of letters	-	66
Support needs and provision		
Patients ever needing emotional support	38	32
Patients needing emotional support from CH	-	27
Adequate emotional support provided	-	69
Patients had contact with lymphoma CNS	-	77
CNS was helpful	-	100

Financial support offered	35	29
- not offered but would have been helpful	21	17
Social support offered	21	19
- not offered but would have been helpful	4	9
Community support offered	31	28
- not offered but would have been helpful	5	16

Outcomes

At this time, outcome data collected on the clinical web portal is only available for two years, which is too short for assessing survival in the majority of lymphoma subtypes. A proposal to appoint a data manager for retrospective (pre-CWP) collection of outcome data for common lymphoma subtypes has been raised and will be considered by the lymphoma group at a forthcoming meeting.





Peer Reviewed Publications 2013/14

2014

1. Swerdlow AJ, Cooke R, Bates A, Cunningham D, Falk SJ, Gilson D, Hancock BW, Harris SJ, Horwich A, Hoskin PJ, Linch DC, Lister A, Lucraft HH, Radford J, Stevens AM, Syndikus I, Williams MV; England and Wales Hodgkin Lymphoma Follow-up Group. Risk of premature menopause after treatment for Hodgkin's lymphoma. *J Natl Cancer Inst.* 2014 Aug 19;106(9).
2. Illidge TM, Mayes S, Pettengell R, Bates AT, Bayne M, Radford JA, Ryder WD, Le Gouill S, Jardin F, Tipping J, Zivanovic M, Kraeber-Bodere F, Bardies M, Bodet-Milin C, Malek E, Huglo D, Morschhauser F. Fractionated ⁹⁰Y-ibritumomab tiuxetan radioimmunotherapy as an initial therapy of follicular lymphoma: an international phase II study in patients requiring treatment according to GELF/BNLI criteria. *J Clin Oncol.* 2014 Jan 20;32(3):212-8.
3. Cove-Smith L, Woodhouse N, Hargreaves A, Kirk J, Smith S, Price SA, Galvin M, Betts CJ, Brocklehurst S, Backen A, Radford J, Linton K, Roberts RA, Schmitt M, Dive C, Tugwood JD, Hockings PD, Mellor HR. An integrated characterization of serological, pathological, and functional events in doxorubicin-induced cardiotoxicity. *Toxicol Sci.* 2014 Jul;140(1):3-15.
4. Govi S, Christie D, Mappa S, Marturano E, Bruno-Ventre M, Messina C, Medina EA, Porter D, Radford J, Heo DS, Park Y, Pro B, Jayamohan J, Pavlakis N, Zucca E, Gospodarowicz M, Ferreri AJ; International Extranodal Lymphoma Study Group. The clinical features, management and prognosis of primary and secondary indolent lymphoma of the bone: a retrospective study of the International Extranodal Lymphoma Study Group (IELSG #14 study). *Leuk Lymphoma.* 2014 Aug;55(8):1796-9.
5. Messina C, Ferreri AJ, Govi S, Bruno-Ventre M, Gracia Medina EA, Porter D, Radford J, Heo DS, Park HY, Pro B, Jayamohan J, Visco C, Scarfò L, Zucca E, Gospodarowicz M, Christie D; International Extranodal Lymphoma Study Group (I.E.L.S.G.). Clinical features, management and prognosis of multifocal primary bone lymphoma: a



- retrospective study of the international extranodal lymphoma study group (the IELSG 14 study). *Br J Haematol.* 2014 Mar;164(6):834-40.
6. Bruno Ventre M, Ferreri AJ, Gospodarowicz M, Govi S, Messina C, Porter D, Radford J, Heo DS, Park Y, Martinelli G, Taylor E, Lucraft H, Hong A, Scarfò L, Zucca E, Christie D; International Extranodal Lymphoma Study Group. Clinical features, management, and prognosis of an international series of 161 patients with limited-stage diffuse large B-cell lymphoma of the bone (the IELSG-14 study). *Oncologist.* 2014 Mar;19(3):291-8.
 7. Govi S, Christie D, Messina C, Bruno Ventre M, Gracia Medina EA, Porter D, Radford J, Seog Heo D, Park Y, Martinelli G, Taylor E, Lucraft H, Ballova V, Zucca E, Gospodarowicz M, Ferreri AJ; International Extranodal Lymphoma Study Group (I.E.L.S.G.). The clinical features, management and prognostic effects of pathological fractures in a multicenter series of 373 patients with diffuse large B-cell lymphoma of the bone. *Ann Oncol.* 2014 Jan;25(1):176-81.
 8. Swerdlow AJ, Cooke R, Bates A, Cunningham D, Falk SJ, Gilson D, Hancock BW, Harris SJ, Horwich A, Hoskin PJ, Linch DC, Lister A, Lucraft HH, Radford J, Stevens AM, Syndikus I, Williams MV; England and Wales Hodgkin Lymphoma Follow-up Group. Risk of premature menopause after treatment for Hodgkin's lymphoma. *J Natl Cancer Inst.* 2014 Aug 19;106(9). pii: dju207.
 9. Hoppe R, Illidge T, Specht L, Vogelius I, Yahalom J. Comment on: "clinical features, management, and prognosis of an international series of 161 patients with limited-stage diffuse large B-cell lymphoma of the bone (the IELSG-14 Study)". *Oncologist.* 2014 Dec;19(12):1289.
 10. Dovedi SJ, Adlard AL, Lipowska-Bhalla G, McKenna C, Jones S, Cheadle EJ, Stratford IJ, Poon E, Morrow M, Stewart R, Jones H, Wilkinson RW, Honeychurch J,



- Illidge TM. Acquired resistance to fractionated radiotherapy can be overcome by concurrent PD-L1 blockade. *Cancer Res.* 2014 Oct 1;74(19):5458-68.
11. Illidge T, Cheadle EJ, Donaghy C, Honeychurch J. Update on obinutuzumab in the treatment of B-cell malignancies. *Expert Opin Biol Ther.* 2014 Oct;14(10):1507-17.
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 13. Eichenauer DA, Engert A, André M, Federico M, Illidge T, Hutchings M, Ladetto M; ESMO Guidelines Working Group. Hodgkin's lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2014 Sep;25 Suppl 3:iii70-5.
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 15. Gisselbrecht C, Borchmann P, D'Amore F, Illidge TM, Zinzani PL. Challenging CD30-positive lymphomas--current challenges, new insights and future directions: joining a conversation on CD30+ lymphomas. *Leuk Res.* 2014 Sep;38(9):1003.
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 17. Searle EJ, Illidge TM, Stratford IJ. Emerging opportunities for the combination of molecularly targeted drugs with radiotherapy. *Clin Oncol (R Coll Radiol).* 2014 May;26(5):266-76.
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Oncology Group. Modern radiation therapy for nodal non-Hodgkin lymphoma target definition and dose guidelines from the International Lymphoma Radiation Oncology Group. *Int J Radiat Oncol Biol Phys.* 2014 May 1;89(1):49-58.

19. Hoskin PJ, Kirkwood AA, Popova B, Smith P, Robinson M, Gallop-Evans E, Coltart S, Illidge T, Madhavan K, Brammer C, Diez P, Jack A, Syndikus I. 4 Gy versus 24 Gy radiotherapy for patients with indolent lymphoma (FORT): a randomised phase 3 non-inferiority trial. *Lancet Oncol.* 2014 Apr;15(4):457-63.
20. Illidge T, Cheadle EJ, Donaghy C, Honeychurch J. Update on obinutuzumab in the treatment of B-cell malignancies. *Expert Opin Biol Ther.* 2014 Oct;14(10):1507-17.

2013

1. Gibb A, Greystoke A, Ranson M, Linton K, Neeson S, Hampson G, Illidge T, Smith E, Dive C, Pettitt A, Lister A, Johnson P, Radford J. A study to investigate dose escalation of doxorubicin in ABVD chemotherapy for Hodgkin lymphoma incorporating biomarkers of response and toxicity. *Br J Cancer.* 2013 Nov 12;109(10):2560-5.
2. Gibb A, Jones C, Bloor A, Kulkarni S, Illidge T, Linton K, Radford J. Brentuximab vedotin in refractory CD30+ lymphomas: a bridge to allogeneic transplantation in approximately one quarter of patients treated on a Named Patient Programme at a single UK center. *Haematologica.* 2013 Apr;98(4):611-4.
3. Cooke R, Jones ME, Cunningham D, Falk SJ, Gilson D, Hancock BW, Harris SJ, Horwich A, Hoskin PJ, Illidge T, Linch DC, Lister TA, Lucraft HH, Radford JA, Stevens AM, Syndikus I, Williams MV; England and Wales Hodgkin Lymphoma Follow-up Group, Swerdlow AJ. Breast cancer risk following Hodgkin lymphoma radiotherapy in relation to menstrual and reproductive factors. *Br J Cancer.* 2013 Jun 11;108(11):2399-406. doi: 10.1038/bjc.2013.219. Epub 2013 May 7.
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5. Rose CJ, Naidoo K, Clay V, Linton K, Radford JA, Byers RJ. A statistical framework for analyzing hypothesized interactions between cells imaged using multispectral microscopy and multiple immunohistochemical markers. *J Pathol Inform.* 2013 Mar 30;4(Suppl):S4.
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10. Radford J, Davies A, Cartron G, Morschhauser F, Salles G, Marcus R, Wenger M, Lei G, Wassner-Fritsch E, Vitolo U. Obinutuzumab (GA101) plus CHOP or FC in relapsed/refractory follicular lymphoma: results of the GAUDI study (BO21000). *Blood.* 2013 Aug 15;122(7):1137-43.
11. Wang ML, Rule S, Martin P, Goy A, Auer R, Kahl BS, Jurczak W, Advani RH, Romaguera JE, Williams ME, Barrientos JC, Chmielowska E, Radford J, Stilgenbauer S, Dreyling M, Jedrzejczak WW, Johnson P, Spurgeon SE, Li L, Zhang L, Newberry K, Ou Z, Cheng N, Fang B, McGreivy J, Clow F, Buggy JJ, Chang BY, Beaupre DM, Kunkel LA, Blum KA. Targeting BTK with ibrutinib in relapsed or refractory mantle-cell lymphoma. *N Engl J Med.* 2013 Aug 8;369(6):507-16.
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19. Honeychurch J, Melis MH, Dovedi SJ, Mu L, Illidge TM. Immunogenic potential of irradiated lymphoma cells is enhanced by adjuvant immunotherapy and modulation of local macrophage populations. *Leuk Lymphoma*. 2013 Sep;54(9):2008-15.
20. Illidge T. XVII. Radiotherapy in early stage Hodgkin lymphoma. *Hematol Oncol*. 2013 Jun;31 Suppl 1:92-5.
21. Honeychurch J, Dive C, Illidge TM. Synchronous apoptosis in established tumors leads to the induction of adaptive immunity. *Oncoimmunology*. 2013 Jun 1;2(6):e24501. Epub 2013 Apr 16.



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23. Dovedi SJ, Melis MH, Wilkinson RW, Adlard AL, Stratford IJ, Honeychurch J, Illidge TM. Systemic delivery of a TLR7 agonist in combination with radiation primes durable antitumor immune responses in mouse models of lymphoma. *Blood.* 2013 Jan 10;121(2):251-9.

Research

Clinical research

The lymphoma group has an extensive clinical trial portfolio with most trials included in the NCRN portfolio. They offer commercial and non-commercial studies ranging from first in man phase 1 to phase 4 studies. In 2012/13, 30% of all new referrals were considered for participation in a clinical trial, and 20% of patients were enrolled. This is 2% higher than the national average.

Clinical research is supported by 5 clinical research nurses (WTE 4.3) and 5 clinical trial administrators (WTE 4.2). Staffing is supported by commercial income and funding from CRN, CRUK and LLR.

There are currently 26 studies open to recruitment, 12 studies in active follow up, and 6 in set up and predicted to open in the first quarter of 2015. Of the studies that have opened to recruitment in the past 12 months, the team is over 80% compliant with the 70-day target. An audit of trials at closure to recruitment showed that the Lymphoma Group recruited to target in 90% of cases.

To date in the 2014 financial year, 64 lymphoma patients have been enrolled into a clinical trial. This number is lower than previous years because of the small number of national phase 3 non-commercial studies at present. General plans to boost clinical trial recruitment in the future include an annual clinical trial review day and the development of a lymphoma group web page featuring all available lymphoma trials. Following a very recent increase in lymphoma group research nurse numbers, the group also plans to arrange personal visits to colleagues at regional referring hospitals to provide support and detailed information about trials. Finally, they plan to run a pilot project with 'Tomorrow's Medicines' to highlight the existence of certain areas within the UK where it is more difficult to recruit patients into trials.



List of current recruiting trials:

- BREVITY; phase 2 study investigating brentuximab vedotin monotherapy in older/frailer patients with untreated Hodgkin lymphoma who are unsuitable for ABVD. EudraCT 2012-000214-11
- ECHELON-1; randomised open label phase 3 study of brentuximab vedotin + AVD vs ABVD in patients with untreated advanced stage classical Hodgkin lymphoma. ClinicalTrials.gov Identifier: NCT01324596
- ARROVEN; phase 4 post authorisation safety study investigating brentuximab vedotin in approved indications (Hodgkin Lymphoma, CD30+ systemic anaplastic large cell lymphoma). UKCRN ID 14014
- CHECKMATE-205; phase 2 study investigating nivolumab monotherapy in patients with classical Hodgkin lymphoma relapsed or refractory following autotransplant. ClinicalTrials.gov Identifier: NCT02181738
- PACIFICO; randomised phase 3 study comparing R-FC and RCVP in patients over the age of 60 with untreated follicular lymphoma requiring therapy. ClinicalTrials.gov Identifier: NCT01303887
- BAYER 16349; phase 2 study investigating the intravenous PI3K inhibitor copanalisib in patients with relapsed/refractory follicular lymphoma. ClinicalTrials.gov Identifier: NCT01660451
- C16017; phase 2 study of the oral second generation proteasome inhibitor MLN9708 in patients with relapsed or refractory follicular lymphoma. ClinicalTrials.gov Identifier: NCT01939899
- CHECKMATE 140; phase 2 study of Nivolumab in patients with relapsed or refractory follicular lymphoma. ClinicalTrials.gov Identifier: NCT02038946
- DI-B4; phase 1 dose escalation study investigating the anti CD19 monoclonal antibody DI-B4 in patients with advanced CD19 positive indolent B-cell malignancies. EudraCT 2012-002133-11
- Gilead 0125; phase 3 randomised double blind, placebo controlled trial comparing idelalisib in combination with bendamustine and rituximab in patients with previously treated indolent B-cell lymphoma. ClinicalTrials.gov Identifier: NCT01732926



- CONTRALTO; non-randomised phase 2 open label study of GDC-0199 plus rituximab vs GDC-0199 plus rituximab and bendamustine in patients with relapsed or refractory indolent B cell Non-Hodgkin Lymphoma. ClinicalTrials.gov Identifier: NCT02187861
- IELSG37; randomised open label phase 3 trial comparing radiotherapy consolidation vs no further treatment in patients with primary mediastinal large cell lymphoma who have responded to RCHOP induction therapy. ClinicalTrials.gov Identifier: NCT01599559
- INCA; phase 3 study comparing R-GCVP and R-inotuzumab ozogamicin for untreated DLBCL in patients who are unfit for RCHOP because of existing cardiac disease or significant cardiac risk factors. ClinicalTrials.gov Identifier: NCT01679119
- Phoenix; phase 3 trial evaluating the addition of ibrutinib to RCHOP in untreated DLBCL with a non-GCB phenotype. ClinicalTrials.gov Identifier: NCT01855750
- REMoDL-B; randomised phase 3 trial evaluating the addition of bortezomib to RCHOP in untreated DLBCL stratified by ABC/GCB. ClinicalTrials.gov Identifier: NCT01324596
- Checkmate 139; phase 2 study evaluating nivolumab monotherapy in patients with relapsed or refractory DLBCL who have either failed or are not eligible for autologous stem cell transplant. ClinicalTrials.gov Identifier: NCT02038933
- CHEMO-T; randomised phase 3 trial comparing CHOP and GEM-P in patients with untreated peripheral T cell lymphoma. ClinicalTrials.gov Identifier: NCT01719835
- ECHELON-2; phase 3 trial comparing brentuximab vedotin-CHP and CHOP and CHP- in untreated CD30-positive Mature T-cell Lymphomas. ClinicalTrials.gov Identifier: NCT01777152
- Millenium C25006; single-arm, open-label, phase 4 clinical trial to evaluate the efficacy and safety of brentuximab vedotin monotherapy in patients with relapsed or refractory Systemic Anaplastic Large Cell Lymphoma. ClinicalTrials.gov Identifier: NCT01909934
- ALCANZA; phase 3 trial comparing brentuximab vedotin and investigator choice chemotherapy (methotrexate or bexarotene) in patients with CD30-positive cutaneous T-cell lymphoma. ClinicalTrials.gov Identifier: NCT01578499
- Kyowa 0761-010; randomised open-label phase 3 trial of anti-CCR4 monoclonal antibody KW-0761 (mogamulizumab) vs vorinostat in patients with relapsed cutaneous T-cell lymphoma. ClinicalTrials.gov Identifier: NCT01728805



Clinical trial highlights in 2014 included top recruiter nationally to the ORCHARRD study, the first UK site to enrol a patient on both Checkmate 140 and 205 studies, global top recruiter to the ARROVEN trial, and roles in pivotal clinical trials including the RAPID trial and a phase 2 study of ibrutinib. The national RAPID trial (CI, Radford) showed that PET scanning can be used to identify patients with early stage Hodgkin lymphoma who do not require radiotherapy after chemotherapy. This will reduce the duration and cost of treatment and, most importantly, the incidence of radiation induced second cancers and cardiovascular disease with a positive effect on overall survival. Guidelines are being amended worldwide. Results of the phase 2 study of ibrutinib in mantle cell lymphoma (published in *NEJM* 2013) were outstanding and are changing the management of this aggressive disease worldwide. As a result of this work, ibrutinib was awarded an FDA licence end 2014 and in the UK was added to the Cancer Drugs Fund list in January 2015.

The Manchester Cutaneous Lymphoma service is one of only three within the UK to be invited to join an international research collaborative in cutaneous lymphoma with participants limited to prestigious centres in the USA, Europe, Japan and Australia (The CLIC collaboration). The Manchester service is one of only three centres participating in two international phase III trials in cutaneous lymphoma.

Basic science and translational research

The lymphoma consultants have an extensive programme of basic science and translational research facilitated through academic positions within The University of Manchester. Further details of can be found at the University of Manchester webpages: <http://www.cancer.manchester.ac.uk/>.

Grant Income for clinical, translational and basic laboratory research since 2011:

Teenage Cancer Trust (JR, TCT professor)	£617k
Cancer Research UK (JR, co-I various projects)	£4M
AstraZeneca (JR & KL, co-Is)	£204k
Leukaemia & Lymphoma (JR, PI)	£69k
Kanka Gajendra Foundation (JR, PI)	£71k



MAHSC (JR (PI), KL (co-I))	£10k
Millenium (JR (PI), KL (co-I))	£82k
Christie Hospital (KL (PI), JR (co-I))	£158k
Medical Research Council (KL (PI), JR (co-I))	£59k
UMIP (KL, PI)	£9k
CRUK project grant (KL, PI)	£75k
Pfizer (KL, PI)	£2k
CRUK programme immunotherapy & radiotherapy (TI, PI)	£2.4M
LLR project grant (TI, PI)	£400k
Kay Kendall Research Foundation (TI, PI)	£350k
PCUK (TI, Co-I)	£5M
CRUK lung cancer centre of excellence (TI, Co-I)	£2M
CRUK major centre (radiotherapy research) (TI, Co-I)	£3M

Clinical Audit activity

The lymphoma group conducted 16 clinical audits in 2013/14 including the following topics (audit leads):

1. Re-audit of bone marrow procedures performed by the lymphoma clinical nurse specialist (JR))
2. Haemato-oncology NSSG audit of trial recruitment (MH)
3. Audit of rasburicase use relative to hospital policy (JR)
4. Audit of the use of FDG-PET in the management of new cases of Hodgkin lymphoma and DLBCL presenting to The Christie 2010-11 (BT)



5. A DTC commissioned audit of clinical outcomes following gemcitabine therapy in relapsed / refractory lymphoma (KL)
6. Efficacy of anti-emetic therapy in patients receiving ABVD chemotherapy for Hodgkin lymphoma (KL)
7. Outcome of lymphocyte predominant Hodgkin lymphoma at The Christie (MH)
8. Retrospective review of the demographics, management and outcomes of patients with primary cutaneous B-cell lymphoma, leg type (RC)
9. Lymphoma patient satisfaction survey (KL)
10. Cardiac toxicity in lymphoma survivors (RC)
11. Re-audit of HIV screening in lymphoma (KL)
12. Re-audit of rasburicase use relative to hospital policy (JR)
13. Audit of referral patterns for newly diagnosed and relapsed cases of lymphoma (KL)
14. The response of total skin electron beam therapy for cutaneous T-cell lymphoma using the M-SWAT score (RC)
15. Cutaneous lymphoma patient satisfaction survey (JG)
16. Treatment and clinical outcomes of treatment for peripheral T-cell lymphoma at The Christie and Royal Marsden hospitals (KL)

Ongoing audits

- Clinical outcomes of TSEBT
- Impact of abdominal radiotherapy on renal function
- 10 year clinical outcome of a cohort of patients diagnosed with lymphoma across Manchester in 2004
- Dose distribution to breast tissue for women under 36yrs of age receiving supra- diaphragmatic radiotherapy



- Incidence of lymphopaenia and associated viral complications in patients treated for lymphoma

Educational, Teaching and Training activity at the Christie

The lymphoma team has a close collaborative relationship with the Christie School of Oncology delivering undergraduate and post graduate education to medical students, trainees (clinical oncology, medical oncology, ENT surgeons, haematologists, ophthalmologists, GPs), consultant colleagues, hospital based nurses and allied health professionals and colleagues in primary care. They participate in one of the largest clinical oncology and medical oncology training schemes in the UK, and have a regular attachment of three specialist registrars (1 clinical oncology, 1 medical oncology, 1 haematology) and 1 clinical research fellow on our team. They regularly teach on specialist registrar training days. In 2013, 46 medical students attended lymphoma clinics on the SSB and MRI Oncology Taster Programme (years 3 and 5) and the HLB programme (year 3).

Group members are active participants in the organisation and running of the MRes course in Oncology (RC, KL), and deliver lectures on the BSC pathology course (TI, KL), MRes Oncology course (RC, TI, KL), 5th year prescribing course (MH) and the 3rd year Heart/Lungs and Blood module (MH). In 2015, the lymphoma nurse clinician (VG) set up a dedicated "teaching clinic" for 3rd year medical students.

In 2013/14, the lymphoma consultants supervised 1 PhD student, 3 BSc and 2 MRes students, as well as 3rd to 5th year students doing lymphoma associated projects (PEPs), placements and electives; in 2013, 3 year 4 project option students, 1 year 3 SSC student and 2 year 2 student assistantships. 4 further PhD students are planned for 2015. MH is involved in organising and examining medical students including OSCEs, 4th year Mind and Movement and 3rd year Summative Assessments. RC has previously been an examiner for the Royal College of Radiologists. VG is a medical student OSCE examiner at both The Christie and the Manchester Medical School.

The lymphoma team is represented on the Christie Undergraduate Board (RC, MH, KL, VG) and participates in the annual medical school taster day for 120 6th form students, as well as hosting students for work experience placements in July.

In April 2014 they ran an international conference for Egyptian haemato-oncologists and have subsequently been invited to participate in the Annual Oncology conference in Cairo.

Lymphoma consultants hold esteemed leadership roles within education and are regularly invited to deliver educational lectures at national and international meetings – most recently, ICML, ECCO, Oxford Lymphoma Course, Oxford University (JR), ASH, ICML, ASTRO, NCRI (TI), ESMO, Leicester



Regional Haematology Meeting (KL), and The Christie International Student Oncologist Conference (MH). RC is Director of the Christie School of Oncology and Undergraduate Lead for the Institute of Cancer Sciences. KL and RC are members of the MRes Oncology Board. JAR is UK lead for both the European Lymphoma Institute and the ESMO Scientific Working Group for lymphoma. In 2015, he was elected to Faculty of ESMO as lead for haemato-oncology. He is a member of the ISHL Scientific Committee and will be representing UK Lymphoma at Lunenburg Conference March 2015.

Leadership and Esteem

Since 2010, JR has been the Teenage Cancer Trust Professor of Teenage and Young Adult Cancer Medicine and advises the charity on national/international policy in this area. He is in his second term as chair of the UK NCRI Lymphoma Clinical Studies Group that organises clinical research in lymphoma across the UK. JR also holds advisory positions for government, charities and other bodies including the Lymphoma Association. He is a member of the Scientific Committee of the International Symposium on Hodgkin lymphoma, the editorial board of the Journal of Clinical Oncology and UK lead for the Lymphoma Scientific Working Group of the European Haematology Association.

TI is group leader for the CRUK Targeted Therapy Group, deputy Chair of the ICS and chairman of the Radiation Related Research Group of the Manchester Cancer Research Centre. From 2010-2014 he was chairman of the NCRI Clinical and Translational Radiotherapy Group (CTRad). At The Christie, TI is chairman of the Radiotherapy Related Research Group. He has been programme lead for NIHR Academic Clinical Fellows / Lecturers in Oncology, NW Deanery / Manchester University since 2005, and is a Group leader at the CRUK Paterson Institute. TI also holds leadership positions within the Royal College of Radiologists and has played an extensive role in developing international guidelines for ILROG (radiotherapy in Non Hodgkin Lymphoma) and the British Committee for Standards in Haematology (BCSH) (follicular lymphoma, chronic lymphocytic leukaemia, relapsed Hodgkin lymphoma, diffuse large B-cell lymphoma). He was an organiser for the NCRI annual meeting radiotherapy sessions from 2010-2012.

RC has previously chaired the UK Cutaneous Lymphoma Group and is a current member of the EORTC Cutaneous Lymphoma Task force and the MRC Trial Steering Group.

ES is clinical lead for the Proton Therapy project and has been involved in developing the indications list. He also chairs a national group collecting outcomes data that will form the basis of the national radiotherapy dataset.

KL is a member of the NCRI indolent lymphoma subgroup, the national primary CNS lymphoma subgroup and has recently been invited to join the Gilead medical faculty. She is on the NCC-N/NICE



guideline development group for the management of non-Hodgkin lymphoma and the BCSH writing group developing international guidelines for the management of diffuse large B-cell lymphoma.

JG is a member of the Lymphoma Association nurse advisory panel and also regularly contributes to the writing and reviewing of Lymphoma Association, Leukaemia and Lymphoma Research (LLR) and Macmillan patient literature.