Australasian Leukaemia & Lymphoma Group (ALLG)

Vision, Mission and Values

Our 2021 vision is

Global leaders...

Achieving our vision will ensure that:

• ALLG is seen as an invaluable partner enabling the efforts of blood cancer specialists.
• ALLG delivers sustainable services and innovative outcomes... the first choice for high quality clinical trial management.
• The innovations of Australasia’s blood cancer specialists improve the lives of more and more blood cancer patients all over the world.

Vision
Global leader, having a global impact by delivering robust services and innovative outcomes to improve the treatments and lives of blood cancer patients.

Mission
To improve the treatment and the lives of patients with leukaemia, lymphoma and other haematological malignancies by advancing ‘leading edge’ clinical trials in Australasia, and to be regarded by the local and international community as the peak research body for these diseases within our geographical areas of operation and influence.

Values

Integrity: we are trustworthy, open, ethical, and fair.

Quality: we maintain rigorous standards for all of our work.

Collaboration: we work as a team to solve problems and achieve goals.

Innovation: we continually improve our standard of excellence.

Strategic Goals

Goal 1: Deliver significant scientific outcomes
Goal 2: Enhance brand and reputations
Goal 3: Foster passionate membership base
Goal 4: Long term sustainability

Summary of the 2016–2021 Strategic Plan

This Research Report provides key stakeholders with an insight into the Australasian Leukaemia & Lymphoma Groups strategic areas of focus, deliverables, and clinical trial operation during 2018.
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Trials in Progress

Acute Leukaemia & Myelodysplasia

18 Disease Group Report

20 ALL06
A Phase II trial of an intensive paediatric protocol incorporating post-induction stratification based on minimum residual disease (MRD) levels for the treatment of adolescents aged 15 years and above, and young adults aged up to 40 years, with newly diagnosed Acute Lymphoblastic Leukaemia (ALL).

21 ALL08
BLAM – A phase IIb study of Blinatumomab + Cytarabine (AraC) and Methotrexate in adult B-precursor Acute Lymphoblastic Leukaemia.

22 ALL09
Phase II Study of Blinatumomab as Induction Therapy in Adolescent and Young Adult Acute Lymphoblastic Leukaemia.

23 AMLM16
Sorafenib in combination with intensive chemotherapy for previously untreated adult FLT3-ITD positive AML: a phase 2 randomised double-blind placebo controlled multi-centre study.

24 AMLM21
A phase I pharmacokinetic evaluation of Ponatinib in combination with 5-azacytidine in patients with FLT3-ITD positive acute myeloid leukaemia (PonAZA).

25 APM105
A phase I pharmacokinetic evaluation of oral arsenic trioxide in previously untreated patients with acute promyelocytic leukaemia.

Bone Marrow Transplant (BMT)

26 Disease Group Report

27 BM12
Prospective, non-blinded, 2 arm, 1:1 randomised study using Cyclophosphamide After Sibling-donor allogeneic stem-cell Transplantation (CAST) in patients with acute leukaemia and myelodysplasia.

Chronic Myeloid Leukaemia & Myeloproliferative Neoplasms (CML & MPN)

28 Disease Group Report

30 CML12
A single arm phase II study to individualize dasatinib dosing based on trough levels and molecular response to maintain efficacy whilst minimising toxicity.

31 MPN01
Myeloproliferative neoplasms registry.

High Grade Non-Hodgkin Lymphoma & Hodgkins Lymphoma (HG NHL HL)

32 Disease Group Report

34 HD10
Treatment optimization trial in the first-line treatment of advanced stage Hodgkin lymphoma; comparison of 4-6 cycles of escalated BEACOPP with 4-6 cycles of BiECADD.

35 NHL29
A Phase II Study of Ibrutinib, Rituximab and mini-CHOP therapy in very elderly patients with newly diagnosed DLBCL (IRIC).

Low Grade Non-Hodgkin Lymphoma & Chronic Lymphocytic Leukaemia (LG NHL & CLL)

36 Disease Group Report

38 CLL06
An Australasian, Phase III, Multicentre, Randomised trial comparing lenalidomide consolidation vs no consolidation in patients with Chronic Lymphocytic Leukemia and residual disease following induction chemotherapy (RESIDUUM).

39 NHL26
A Phase 2 Study of patients treated for relapsed Follicular Lymphoma: with RevinlimiR consolidation added to Rituximab maintenance therapy in those remaining PET positive.

Myeloma

40 Disease Group Report

42 MM16
Phase II study assessing the effect of carfilzomib treatment on early free light chain kinetics in myeloma patients with renal impairment.

Supportive Care

47 Disease Group Report

Laboratory Science

50 Disease Group Report

52 LS17
Studies to delineate the molecular and genomic basis of high-risk ALL in adults – Registry of Acute Lymphoblastic Leukaemia in Australasia Associated Correlative Studies (REGALLIA).

53 LS18
NBCR Prospective project – Mapping the fate of IDH mutant AML.

NBCR & Biobank

54 Coordinator Report

43 MM17
A multicentre single arm study of carfilzomib-thalidomide-dexamethasone (CarTD) for newly diagnosed transplant-eligible multiple myeloma (MM) patient’s refractory to initial bortezomib-based induction therapy.

44 MM18
Single arm, multicentre study of Carfilzomib in combination with Thalidomide and Dexamethasone (CaTD) in patients with relapsed and/or refractory multiple myeloma (RRMM).

45 MM19
A Phase 3 trial of thalidomide-dexamethasone consolidation versus thalidomide-dexamethasone-Ixazomib consolidation for transplant eligible multiple myeloma patients undergoing a single ASCT as part of front-line therapy.

46 MM20
A Multicentre Phase 3 Trial Comparing Elotuzumab-Cyclophosphamide-Thalidomide-Dexamethasone (E-CTD) with Cyclophosphamide-Thalidomide-Dexamethasone (CTD) for the Treatment of Relapsed and/or Refractory Multiple Myeloma (RRMM).
Trials Closed to Accrual

Acute Leukaemia & Myelodysplasia

58 ALL05
A Phase II study of Dasatinib combined with induction chemotherapy in previously untreated de novo Philadelphia Chromosome-Positive Acute Lymphoblastic Leukaemia.

58 AMLM15
A pilot study exploring high-dose lenalidomide maintenance therapy in adult AML.

59 AMLM17
A Strategy of High-Dose Lenalidomide in Combination with Epigenetic Therapies for Relapsed or Refractory Acute Myeloid Leukaemia.

59 AMLM20
A programme of development for older patients with acute myeloid leukaemia and high risk myelodysplastic syndrome.

60 MDS4
A Randomised Phase II study comparing the efficacy of Szacitidine alone versus combination therapy with lenalidomide and Szacitidine in patients with higher risk myelodysplastic syndromes (MDS) and low marrow blast count acute myeloid leukaemia (AML).

Bone Marrow Transplant (BMT)

61 BM06
Phase III Clinical Study of Allogeneic Stem Cell Transplantation with Reduced Conditioning (RIC1) versus Best Standard of Care in Acute Myeloid Leukemia (AML) in First Complete Remission.

61 BM07
A treatment algorithm evaluating the effect of zoledronic acid on bone mineral density loss after allogeneic stem cell transplantation.

Chronic Myeloid Leukaemia & Myeloproliferative Neoplasms (CML & MPN)

62 CML10

62 CML11
Phase II study of nilotinib plus pegylated interferon-alpha-2b as first-line therapy in chronic phase CML aiming to maximize CMR and MR.

63 PT01
A randomised trial to compare aspin vs hydroxyurea/aspirin in ‘intermediate risk’ primary thrombocythaemia and aspin only with observation in ‘low risk’ primary thrombocythaemia.

High Grade Non-Hodgkin Lymphoma & Hodgkins Lymphoma (HG NHL HL)

64 HD08
A randomised Phase III trial to assess response adapted therapy using FDG-PET imaging in patients with newly diagnosed, advanced Hodgkin Lymphoma.

64 NHL21
Early treatment intensification with R-ICE chemotherapy followed by autologous stem cell transplantation using Z-BEAM for patients with poor prognosis diffuse large B-Cell lymphoma as identified by interim PET/CT scan performed after four cycles of R-CHOP-14 chemotherapy.

65 NHL24
Rituximab in Primary Central Nervous System Lymphoma (A randomized HOVON/ALLG intergroup study).

65 NHL25
Double Blind Randomized Phase III study of lenalidomide (REVLIMIDR) maintenance versus placebo in response to elderly patients with DLBCL and treated with first line R-CHOP.

Low Grade Non-Hodgkin Lymphoma & Chronic Lymphocytic Leukaemia (LG NHL & CLL)

66 CLL05
An Australasian, Phase II, multicentre, randomised, dose intensification study investigating oral fludarabine, oral cyclophosphamide and i.v. rituximab (poFCivR) tolerance in previously untreated elderly (≥ 65 years old) patients with chronic lymphocytic leukaemia (CLL).

66 CLL07
An Australasian, phase II, multicentre, randomised, study investigating safety and efficacy for dose reduced fludarabine, cyclophosphamide and i.v. obinutuzumab (G-FC3) versus oral chlorambucil and i.v. obinutuzumab (G-Clb) in previously untreated (≥65 years old) patients with chronic lymphocytic leukemia (CLL).

67 NHL14
An intergroup randomised trial of rituximab versus a watch and wait strategy in patients with advanced stage, asymptomatic, non-bulky follicular lymphoma (Grades 1, 2 and 3a).

67 NHL16
A multicentre, phase II, openlabel, randomized study in patients with advanced follicular lymphoma evaluating the benefit of maintenance therapy with Rituximab (MabTheraR) after induction of response with chemotherapy plus Rituximab in comparison with no maintenance therapy (PRIMA).

68 NHL27
A phase 3 open label randomised study to compare the efficacy and safety of rituximab plus lenalidomide (CC-5013) versus rituximab plus chemotherapy followed by rituximab in subjects with previously untreated follicular lymphoma.

Myeloma

69 MM13
A randomized open-label multicentre phase III trial of Melphalan and Dexamethasone (M Dex) vs Rituxomab, Melphalan and Dexamethasone (BM Dex) for untreated patients with systemic light-chain (AL) amyloidosis.

69 MM14
A prospective randomised Phase II study of single agent pomalidomide maintenance versus combination pomalidomide and low dose dexamethasone maintenance following induction with the combination of pomalidomide and low dose dexamethasone in patients with relapsed and refractory myeloma previously treated with lenalidomide.

70 MM15
A randomized phase III study to compare Bortezomib, Melphalan, Prednisone (VMP) with High Dose Melphalan followed by Bortezomib, Lenalidomide, Dexamethasone (VRD) consolidation and Lenalidomide maintenance in patients with newly diagnosed multiple myeloma.

Supportive Care

71 SC04
Phase II of a novel telehealth-mediated nurse-led intervention to increase oral cancer therapy adherence amongst people with Chronic Myeloid Leukaemia (CML).

Laboratory Science

72 LS12
A phase II trial in patients with previously untreated acute promyelocytic leukaemia to evaluate the effects of: (i) adding arsenic trioxide to all-trans retinoic acid and idarubicin for remission induction, and (ii) adding arsenic trioxide to all-trans retinoic acid as consolidation.

72 LS13
WT-1 expression levels as a marker of Minimal Residual Disease (MRD) in AML.

73 LS14
Biomarkers to assist clinical outcomes in patients with lymphoma.
The Scientific Advisory Committee (SAC) of the ALLG has the prime responsibility of overseeing the scientific direction of the organisation.

The SAC’s roles include: to enable the design, conduct and publication of clinical trial research in haematological malignancies and to facilitate the translation of such research into clinical practice; to ensure scientific rigour is applied to the ALLG’s research activities; to encourage and promote the membership and reputation of the ALLG; to co-ordinate the activities of the various Disease Group Committees; and to advise the Board on matters pertaining to the scientific interest and strategic direction of the ALLG.

2018 was a busy year for the committee. Our focus continued to be the development and conduct of clinical trials with several new trials approved by the SAC in 2018. We received MRFF grant funding for two trials led by Prof David Curtis and Prof Maher Gandhi. We will also see the opening of several new studies across ALLG’s disease groups in 2019. During the year we were able to monitor our progress in clinical trial development against specific milestones set by the SAC. Performance in this regard was pleasing although there are further improvements to be made. Increased engagement with the membership has also been a priority. The ALLG membership remains healthy and each month the ALLG welcomes several new members.

The SAC has begun a program of site visits to better understand the issues that confront sites and hopefully develop solutions to enable greater conduct of clinical trials in patients with blood cancers. The SAC has also commenced some strategic planning for the future. One activity to come out of this is a plan to increase the activity of the various Disease Group Committees in 2019 with the development of several half- or full-day workshops to improve member involvement and trial development.

In my first year as SAC Chair I am, of course, indebted to my fellow colleagues on the SAC. They represent some of New Zealand and Australia’s finest experts in blood cancers, have been a pleasure to work with and have been a great support to me. I would like to acknowledge the contributions of Dr Robert Weinkove and A/Prof Will Stevenson who stepped down from the SAC in November. Both have worked hard in their respective areas of Support Care and Acute Leukaemia leading important initiatives, taking on extra responsibilities when asked and providing valuable advice. Rob’s drive to improve the Scientific Meeting for members and revitalising the Supportive Care Disease Group, and Will’s leadership in the AML Molecular Harmonisation Project have been tremendous. I wish them all the best in their future endeavours and look forward to their ongoing involvement with the ALLG.
I am also indebted to my predecessor, Professor Mark Hertzberg, who toiled so hard over many years to leave the organisation in great shape as one of Australasia’s premier clinical trial groups.

Also, I would like welcome to our new members elected in November: A/Prof Zoe McQuilten and Dr Eliza Hawkes, who will lead the Supportive Care and High Grade Lymphoma and Hodgkin Disease Groups, respectively.

Both have already made enormous scientific contributions to their fields and we look forward to their leadership and expertise in the coming years.

The ALLG is also very fortunate to be overseen by a Board comprised of dedicated directors invested in the success of the ALLG and to have a CEO as talented as Delaine Smith to put our vision for the ALLG into practice. They have taught me much in the last year.

Ultimately, however, the ALLG is our organisation and the future success of the ALLG hinges on the enthusiasm and engagement of the entire membership.

I look forward to continuing to work together with all of you.

A/Prof Peter Mollee
Chairman, ALLG SAC

In 2018 the ALLG membership were proudly represented by the following SAC Committee:

<table>
<thead>
<tr>
<th>Chair</th>
<th>Vice Chair</th>
<th>Committee Members</th>
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<tbody>
<tr>
<td>A/Prof Peter Mollee</td>
<td>Prof David Ritchie</td>
<td>Dr Eliza Hawkes (Elected 2018) Royal and Eastern Health, VIC</td>
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<tr>
<td>Princess Alexandra Hospital, QLD</td>
<td>Royal Melbourne Hospital, VIC</td>
<td>Dr Eliza Hawkes (Elected 2018) Royal and Eastern Health, VIC</td>
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<td></td>
<td>Prof Stephen Mulligan</td>
<td>A/Prof Jake Shortt Monash Health, VIC</td>
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<td></td>
<td>Royal North Shore Hospital, NSW</td>
<td>A/Prof William Stevenson (Jan-Nov 2018) Royal North Shore Hospital, NSW</td>
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<td></td>
<td>Dr David Ross</td>
<td>A/Prof Andrew Wei Alfred Hospital, VIC</td>
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<tr>
<td></td>
<td>Monash University, VIC</td>
<td>Dr Robert Weinkove Wellington Hospital, NZ</td>
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<tr>
<td></td>
<td></td>
<td>Dr Zoe McQuilten (Newly elected in November 2018) Monash University, VIC</td>
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<td>Dr David Yeung South Australia Health, SA</td>
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<td></td>
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<td>Prof Judith Trolman Concord Repatriation General Hospital, NSW</td>
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</table>
The development and conduct of clinical trials continues to be the focus of the SAC and several new trials were approved by the SAC in 2018.

Safety and Data Monitoring Committee (SDMC) Report

The ALLG Safety and Data Monitoring Committee (SDMC) has been established for over 15 years, and serves as an independent body to ensure the safe and effective conduct of ALLG trials. This includes a 6 or 12 monthly review of all active studies, including accrual, adverse events and interim analyses where undertaken, as well as reviewing all new trial protocols.

The workload of the committee continues to increase, which is a reflection of the increased activity of ALLG. The committee has two annual face to face meetings as well as teleconference in the lead up to the scientific meetings of ALLG, with a move to consider out of meeting decisions when required. In 2018, the SDMC reviewed and approved 8 new protocols, including 3 international collaborative studies, and 11 protocol amendments or requests for unplanned analyses.

The role of the SDMC has also evolved, such that under the revised 2016 NHMRC guidelines, the ALLG (trial sponsor) through its safety committee (the SDMC) is now responsible for the submission of annual safety reports to HREC’s. The annual reports from Chief Investigators is now critical to achieve this goal, as well as careful review by the SDMC before submission of the annual safety report to the ethics committees.

The committee has also faced new challenges including an increasing number of requests for unplanned or interim analyses of actively recruiting trials. In assessing these, the SDMC needs to consider the potential for bias and loss of clinical equipoise from the preliminary results, as well as balancing the risks of recommending closing a trial prematurely versus the futility of potentially continuing the study.

I would like to acknowledge the excellent work of the Protocol Development Coordinator and the ALLG Trial Centre staff in coordinating the data and papers for the SDMC, and to thank the members of the committee, especially our independent and lay members, for all their hard work.

Prof Peter Browett
Chairman, SDMC
## Responsibilities of the SDMC

**Review**

Reviewing all protocols proposed for ALLG participation, whether ALLG initiated or international.

Reviewing all proposed amendments to protocols prior to HREC submission.

Reviewing urgent alerts involving safety issues and notifications that a stopping rule has been reached, if that stopping rule involves a safety issue.

Reviewing reports on accrual and safety, safety stopping rules, and interim toxicity data for trials.

Reviewing reports on accrual and recruitment rates with specific attention to the likelihood of the study answering its proposed question.

**Assess**

Assessing the impact of independent scientific investigations, especially other trials, on the trial being monitored and recommending changes based on those external results.

**Ratify**

Ratifying any decisions made by other trial management committees.

## 2018 SDMC Membership

### Chair

Prof Peter Browett  
Professor of Pathology  
Haematologist,  
The University of Auckland, NZ

### ALLG Members

Dr Dennis Carney  
Haematologist, Peter MacCallum Cancer Centre, VIC

Dr Robin Filshie  
Consultant Haematologist, St Vincent’s Hospital, VIC

Dr Anthony Mills  
Clinical Haematologist, Princess Alexandra Hospital, QLD

### External Advisors

Dr Lorraine Chantrill  
Senior Staff Specialist Medical Oncology, St Vincent’s Hospital, NSW

Dr Patrick Kelly  
Senior Lecturer in Biostatistics, The University of Sydney, NSW

Mr John Stubbs  
Chief Executive Officer, CanSpeak, NSW

### ALLG SAC Liaisons

A/Prof Jake Shortt  
Monash Health, VIC

A/Prof Peter Mollee  
Princess Alexandra Hospital, QLD

Dr David Ross  
Royal Adelaide Hospital, SA

Dr Eliza Hawkes  
Austin and Eastern Health, VIC
The purpose of the trial centre is to provide members with the support and resources needed to develop, conduct and publish clinical trials. The staff of the trial centre provide a range of expert services to the membership ranging from protocol writing, biostatistical advice, data management, pharmacovigilance, safety and data monitoring support, and data evaluation.

During 2018 the trial centre team supported 10 members with early concept proposals, 11 members with protocol development services, and 4 members develop and finalise clinical trial protocols for activation at sites.

The trial centre staff continued work with the 61 trials in conduct phase; this included 13 trials open to recruitment with another 48 trials in active treatment or follow-up activity. This now takes the ALLG members forward to having conducted 152 clinical trial research projects, with a third of the activity in acute leukaemia, and a third in lymphoma.

Clinical trials are complex and as a mechanism for assurance and safety the sector is heavily regulated. In Australia the ALLG trial centre operates in accordance with the NHMRC, TGA and all applicable state and commonwealth laws. The ALLG trial centre continued to foster professional development activities for staff which saw 100% compliance to Standard Operating Procedure training and implementation, as well 100% competency in Good Clinical Practice (GCP). Maintenance of a highly skilled and responsive workforce is key to the success of the trial centre and underpins our member relations.

The trial centre staff facilitated two clinical trial training days for the ALLG members. Both days were well attended with over 40 members at each of the events. A highlight of the training day on 16 May 2018 was a presentation by Michele Gambrill on the electronic filing of site clinical trial documents, and the 14 November 2018 training day was enhanced with a presentation on the Practicalities and Rationale of 3rd Party EBV-specific T cells by Colm Keane from PAH, and an Introduction to Biosimilars by Jordan Roser from Sandoz.

The trial centre and membership are grateful for the support of Roche to enable the specialist haematology education day to continue; this saw AML/MDS disease covered in a full day program lead by A/Prof Andrew Wai and Prof David Ritchie on the 15 May 2018, and the Multiple Myeloma disease covered in a full day program lead by A/Prof Peter Mollee on the 13 November 2018.
A big thank you to the sCRA team of Amanda Jager, Suzanne Cake and Tracey Gerber who have continued to ensure progression of the operational activities of the ALLG Trial Centre, ably supported by Sarah Baxter filling the Quality Assurance role. We thank past CRAs of the ALLG Trial Centre and thank the 2018 team of Ashlee Burt, Julia Carlson, Rachel Cushion, Jennifer Grigo, Giulia Quattrocchi, Chrissie Risteski, Robyn Hemmes, and Uyen Nguyen on the RMIT Student placement program for their continued outstanding central coordination of ALLG trials.

The ALLG Trial Centre also extends its thanks to the ALLG SDMC who tirelessly provide the oversight of ALLG trials that forms an integral part of the GCP Sponsor responsibilities that the ALLG must uphold in all clinical trials.

Marina Mullins
ALLG Operations Manager

2018 ALLG Trial Centre Staff

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<tr>
<th>Operations Manager</th>
<th>Senior CRA's</th>
<th>CRA's</th>
<th>Trial Support</th>
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<tr>
<td>Marina Mullins</td>
<td>Suzanne Cake</td>
<td>Ashlee Burt</td>
<td>Sarah Baxter</td>
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<td>Tracey Gerber</td>
<td>Julia Carlson</td>
<td>Brock Patton</td>
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<td></td>
<td>Amanda Jager</td>
<td>Rachel Cushion</td>
<td>Adele Lee-Wriede</td>
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<td>Jennifer Grigo</td>
<td>Eva Pesce</td>
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<td>Giulia Quattrocchi</td>
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<td>Chrissie Risteski</td>
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<td>Robyn Hemmes</td>
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<td>Uyen Nguyen</td>
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ALLG Membership and Participating Sites

**LIFE**
This person has made a significant contribution to the objectives of the organisation, and who has accepted the Board’s invitation to become a member on that basis.

A life member shall remain a Member until they are removed or ceases to be a Member in line with the Constitution, rule 6.

**FULL**
This person must have the qualifications to be the Principal Investigators of a clinical trial study.

Full Members may choose a membership of either one, two or three years in duration. A Full Member shall remain a member until they are removed or ceases to be a Member in line with the Constitution, rule 6.

**ASSOCIATE**
This person must participate in a study under the supervision of a Principal Investigator.

Associate Members shall remain members for three years. Membership must be renewed every three years unless the Associate Member is removed or ceases to be a Member in line with the Constitution, rule 6.

**COMMUNITY**
This person must support the organisation and not be a Full Member, Associate Member, or Life Member.

Community Members shall remain a member for five years. Membership must be renewed every five years unless the Community Member is removed or ceases to be a Member in line with the Constitution, rule 6.
### List of sites approved for participation in ALLG trials

**Australia**

<table>
<thead>
<tr>
<th>Name</th>
<th>Other current or recent names</th>
<th>Code</th>
<th>State</th>
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## Participating Sites

### List of sites approved for participation in ALLG trials

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# List of sites approved for participation in ALLG trials

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Trials in Progress
## Contents

### Acute Leukaemia & Myelodysplasia

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Acute Leukaemia & Myelodysplasia

The MDS, ALL and AML disease group is continuing a process of renewal as several trials have been completed and new trials are in the final stages of development.

In 2018, the results from the MDS4 study (PI Kenealy and Seymour) examining the role of lenalidomide (Celgene) in combination with azacitidine were published in Haematologica. This study randomised 160 patients with MDS and oligoblastic AML to azacitidine with or without lenalidomide. The study showed no additional clinical benefit from the addition of lenalidomide, confirming that azacitidine remains the standard of care for these conditions.

The joint NHMRC and LFA-funded AMLM16 trial, which randomized 99 patients with FLT3-ITD AML completed its target accrual and is currently in follow-up phase. This potentially practice-changing trial also included the addition of low-dose ambisome during the induction phase that will permit the safety and efficacy of ambisome (Gilead) as a prophylactic antifungal strategy to be examined. Several correlative studies are underway in preparation for the clinical results of the study that should emerge within the next 24 months.

In ALL, the Adult Young Adolescent ALL06 study (PI Greenwood) also completed recruitment. This study examined the tolerability of an intensified pediatric backbone in the setting of young adult patients with ALL. The study also included important analyses of measureable residual disease (MRD) during therapy, which will have important impacts on current practice and future clinical trial strategies. The follow-on study (ALL09, PI Greenwood) is to incorporate blinatumomab (Amgen) into frontline program care for younger patients, as a means to optimize MRD outcomes in the early phases of therapy.

The National Blood Cancer Registry (NBCR) has recruited over 1,000 patients with AML and represents the umbrella mechanism to streamline the integration of data and tissue samples to active ALLG clinical trials. The NBCR also provides a unique national snapshot of patient care in Australia and provides an important repository of information that will have increasing value to clinicians, industry, government and patients.

A national NGS harmonization project (PI Stevenson) will standardize NGS testing among ALLG treatment centres and undertake a prospective validation of molecular risk stratification in AML using the NBCR as a vehicle for applied research. Another registry-linked project is characterizing the treatment landscape for patients with IDH1 and IDH2 mutations (Celgene), as well as supporting the identification of patients suitable for enrolment to novel IDH inhibitor trials in Australia.

The APML5 study (PI Iland) introduces a novel oral formulation of arsenic (Phebra) into the clinical armamentarium for this disease, with the goal of improving the feasibility of...
health care delivery to this almost-cured AML sub-population. The phase 1 pharmcokinetic study closed to recruitment in July 2018. Phase 2 opened in December 2018 and is actively recruiting among a wide number of ALLG sites.

The ALL08 study (PI Fleming), is pioneering the use of blinatumomab (Amgen) as remission induction therapy for older patients with AML in an attempt to reduce the toxicity associated with intensive chemotherapy. This study opened in 2018 and is actively recruiting. This study is one of the first to use blinatumomab upfront in B-ALL and represents the first step toward the goal of a chemotherapy-free future for patients with B-cell acute leukaemia.

The AMLM21 study (PI Wei), is exploring the safety and tolerability of ponatinib (Takeda) in patients with FLT3-ITD AML in combination with azacitidine. The study has a dose escalation component and recruitment is ongoing.

The AMLM17 study (PI Wei), explored the safety and tolerability of depsipeptide (Celgene) in combination with lenalidomide in patients with advanced AML. This study was completed by the end of 2018 with the final report submitted to Celgene.

A new AML trial is under development, and is looking to introduce a new standard backbone of care incorporating the BCL-2 inhibitor venetoclax (AbbVie) in combination with low-dose ara-C (LDAC). This trial (PI Wei) will stratify patients into adverse and non-adverse cytogenetic risk and explore the tolerability and efficacy of two novel triplet options (midostaurin-Novartis, and pracinostat-Helsinn), to target FLT3 and histone deacetylases, respectively. The goal of this study will be to tackle emergent drug resistance mechanisms and further improve clinical outcomes in older patients.

A new maintenance platform has been developed to study the impact of novel therapies on MRD and the impact on clinical outcomes. The AMLM22 study is currently seeking HREC approval and will incorporate novel drugs targeting BET (GSK) and BCL-2 (AbbVie) to suppress leukemic stem cells and prolong relapse-free survival.

A new collaborative initiative will see the ALLG partner with HOVON (Netherlands) and the AMLSG (Germany), to bring novel FLT3 (Gilteritinib- Astellas), IDH1 (Ivosidenib- Agios) and IDH2 (Enasidenib-Celgene) inhibitors into the frontline setting for adult patients with AML. These important trials (PI’s Wei and Marlton) will see targeted therapies used in a personalized manner and will also explore the role of these novel agents as maintenance therapies in the post-chemotherapy and post-transplant setting.

A/Prof Andrew Wei  
Chair, Acute Leukaemia & Myelodysplasia

A/Prof William Stevenson  
Chair, Acute Leukaemia & Myelodysplasia

Prof David Ritchie  
Chair, Acute Leukaemia & Myelodysplasia
A Phase II trial of an intensive paediatric protocol incorporating post-induction stratification based on MRD levels for the treatment of adolescents aged 15 years and above, and young adults aged up to 40 years, with newly diagnosed Acute Lymphoblastic Leukaemia (ALL).

**Trial chief investigator**
Dr Matthew Greenwood
Dr Luciano Dalla Pozza

**Main trial objectives**
The primary objective is to determine whether a modified form of the BFM-2000 protocol can be administered to patients with newly diagnosed and untreated ALL aged between 15 and 40 years in a comparable timeframe to patients under 15 years of age to be measured by the proportion of patients starting Protocol M by day 94 after commencing therapy.

**CI note**
This is a national clinical trial to find a better way to treat adolescents 15 years and over, and adults up to 40 years, with a bone marrow cancer called acute lymphoblastic leukaemia (ALL). This disease is the most common form of childhood cancer, with over 80% of children cured with chemotherapy. Adults with ALL do much worse, and this trial will examine whether exactly the same treatment given to children can also be given to adults, and if so, are the results as good. The trial closed to recruitment on 29 July 2018 with 86 patients enrolled in the study.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12611000814976

**Trial status:** Manuscript in preparation; publication expected 2019

**Date study opened:** 03/07/2012

**Accrual target (ALLG):** 100

**Final accrual (ALLG):** 86

**Participating sites:** 16

**Number of sites with patients entered:** 14

**Date study closed to accrual:** 29/06/2018

**Support:** The ALL06 study has received funding from collaborating partner organisations including Youth Cancer Network Vic/Tas, Youth Cancer Fund, Canteen and COSA. The study has received funding from the Barr Family Foundation.

**Comments:** Current Protocol Version 5.0, 9 June 2017

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**Study Recruitment**

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ALL08

A phase IIb study of Blinatumomab + Cytarabine (AraC) and Methotrexate in adult B-precursor Acute Lymphoblastic Leukaemia.

**Trial chief investigator**
Dr Shaun Fleming  
A/Prof Andrew Wei  
Dr Ashish Bajel  
Dr Matthew Greenwood

**Main trial objectives**
- To assess the preliminary efficacy of Blinatumomab when administered in combination with chemotherapy (AraC + MTX) for newly diagnosed B-ALL patients aged 40 to 65 as determined by event-free status at 2 years.

**Secondary Objectives**
- To estimate the event-free survival (EFS) distribution for patients treated with this therapy.
- To estimate the clinical response rate (CRR) as determined by CR and CRi at the end of the cycle 2A of Blinatumomab.
- To investigate the depth of response by assessing minimal residual disease by qPCR at the end of the first, second and fourth treatment blocks.
- To estimate the overall survival (OS) distribution for patients treated with this therapy.
- To investigate the tolerability of the combination therapy as determined by dose intensity and the number of patients.

**CI note**
The trial opened to recruitment on 19 April 2018, 7 of the 10 sites were activated with 7 patients recruited.

**Website where trial registered**: Australian New Zealand Clinical Trials Registry: ACTRN12617000084381

**Trial status**: Open to accrual

**Date study opened**: 19/04/2018

**Accrual target (ALLG)**: 30

**Current total accrual (ALLG)**: 7

**Participating sites**: 10

**Number of sites with patients entered**: 4

**Expected accrual date**: 30 April 2020

**Support**: Amgen

**Comments**: Current Protocol Version 1.0, 11 October 2017

**Study Recruitment**

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Phase II Study of Blinatumomab as Induction Therapy in Adolescent and Young Adult Acute Lymphoblastic Leukaemia.

**Main trial objectives**
To determine whether the substitution of blinatumomab for conventional multi-agent chemotherapy in phase 2 induction of the ALL06 protocol leads to improved minimal residual disease negativity rates at day 79 when compared to a historical control cohort treated using standard ALL06 induction.

**Secondary objectives:**
- Evaluation of complete remission (CR) rates, disease free (DFS) and overall survival (OS) using this protocol when compared to the previous ALL06 cohort.
- Evaluation toxicity, both haematologic and non-haematologic in comparison to previous ALL06 cohort.
- Assessment of proportion of patients able to commence protocol M at day 94 when compared to the previous ALL06 cohort.
- Assessment of impact of treatment on physical, functional, and social wellbeing via HRQOL assessments at beginning and end of each phase of treatment and compare with the previous ALL06 cohort.
- To provide an indication of fertility status after treatment and compare fertility outcomes to the ALL06 cohort.

**CI note**
This is a national clinical trial to find a better way to treat adolescents 15 years and over, and adults up to 40 years, with a bone marrow cancer called acute lymphoblastic leukaemia (ALL). This disease is the most common form of childhood cancer, with over 80% of children cured with chemotherapy. Adults with ALL do much worse, and this trial will examine whether the introduction of the new drug, blinatumomab can improve outcomes.

Development for this clinical trial was finalised in 2018 and was submitted to HREC at lead site in November 2018. The trial is expected to open early 2019.
Sorafenib in combination with intensive chemotherapy for previously untreated adult FLT3-ITD positive AML: a phase 2 randomised double-blind placebo controlled multi-centre study.

**Trial chief investigator**  
A/Prof Andrew Wei  
Prof John Seymour  
Prof Andrew Roberts

**Main trial objectives**  
The primary objective is to determine 2-year event-free survival (EFS) in untreated adult AML (age 15–65) with FLT3 ITD mutation administered the FLT3 inhibitor Sorafenib compared to a placebo control group not receiving Sorafenib.

**CI note**  
The ALLG AMLM16 study is an important trial to determine the role of FLT3 inhibitors in patients with FLT3-ITD AML. Relapse after chemotherapy is high in FLT3-ITD AML and the AMLM16 study will randomise 99 patients receiving chemotherapy to sorafenib or placebo. The study will also answer important questions regarding the metabolism of sorafenib and factors, which may affect the efficacy of the targeted therapy. This study has received funding support from the LFA and the NHMRC. Trial closed in May 2018 with 102 patients recruited. Results expected in 2020.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12611001112954

**Trial status:** Closed to accrual

**Date study opened:** 05/12/2012  
**Date 1st patient enrolled:** 25/01/2013  
**Accrual target (ALLG):** 99  
**Final accrual (ALLG):** 102  
**Participating sites:** 20  
**Number of sites with patients entered:** 18  
**Date study closed to accrual:** 28/05/2018  
**Support:** Bayer Australia Ltd, Gilead Sciences, NHMRC, Leukaemia Foundation  
**Comments:** Current Protocol Version 5.0, 5 February 2016

### Study Recruitment

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A phase Ib/II clinical evaluation of Ponatinib in combination with 5-azacitidine in patients with FLT3-ITD positive acute myeloid leukaemia (PonAZA).

**Main trial objectives**

**Phase I b:**
Ponatinib and Azacitidine
To assess the tolerability and recommend a Phase II dose of azacitidine in combination with ponatinib in patients with FLT3-ITD AML who have failed prior therapy or who are unfit for intensive chemotherapy.

**Phase II:**
To assess the preliminary efficacy of ponatinib alone or in combination with azacitidine in patients with FLT3-ITD AML.

**CI note**
A common mutation called FLT3-ITD is found in approximately 25% of patients with acute myeloid leukaemia (AML), and this mutation is linked to a high chance of relapse after chemotherapy and a poor outcome for these patients. This study aims to look at combining a drug which inhibits FLT3-ITD called Ponatinib and combining it with another drug called Azacitidine, which has already been used with other FLT3 inhibitors. The trial recruited 16 cohort 1 patients, 5 of which are evaluable for dose determination of next cohort.

**Study Recruitment**

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<td>2018</td>
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A phase I pharmacokinetic evaluation of oral arsenic trioxide in previously untreated patients with acute promyelocytic leukaemia.

**Trial chief investigator**
Prof Harry Iland
A/Prof Andrew Wei

**Main trial objectives**
- To document the pharmacokinetic characteristics and bioavailability of an oral capsule formulation of ATO;
- To determine the recommended phase 2 dose (RP2D) of oral ATO for use in a subsequent phase 2 study to examine efficacy.

**Secondary objectives:**
- To assess the safety of oral ATO relative to IV ATO – no hypothesis tests are planned;
- To evaluate the efficacy of consolidation with ATO and ATRA.

**CI note**
HREC approval to begin Phase 2 received in December 2018. Recruitment is underway.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12616001022459

**Trial status:** Opened to accrual

**Date study opened:** 07/06/2017

**Date 1st patient enrolled:** 23/06/2017

**Accrual target (ALLG):** 28

**Current accrual (ALLG):** 9

**Participating sites:** 15

**Number of sites with patients entered:** 4

**Date Phase 1 closed to accrual:** July 2018 (Phase 1)

**Support:** Phebra

**Comments:** Current Protocol Version 5.0, 27 March 2018

**Study Recruitment**

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Trials in Progress

Bone Marrow Transplant (BMT)

The BMT group has had a very active year in 2018. Data from BM06 (The use of reduced intensity allogeneic transplantation in older patients with AML) is undergoing full analysis and has been the subject of poster presentations at EBMT and the Canadian Transplant Meeting and the data in the sibling transplant recipients was presented as an oral presentation at ASH 2018. We anticipate the publications of the major findings and multiple sub-studies in 2019.

The BM12 (CAST-Cyclophosphamide After Sibling Transplant) study has been actively developed throughout 2018 and successfully received MRFF funding. This exciting study, the first BMT randomised study undertaken by ALLG, will examine the impact of T-cell depleting post-transplant cyclophosphamide compared to conventional GVHD prophylaxis on the development of debilitating chronic GVHD. There are many integrated correlative scientific studies attached to this study including analyses of immune reconstitution and rates of opportunistic infection in transplant recipients.

As a group, we have also been actively involved in the development of AML risk stratification guidelines in which recommendations for consideration of allogeneic transplantation are incorporated.

The BMT group are excited that our studies are directly contributing to a better understanding of transplantation biology and improved clinical care.

In terms of key achievements for 2018, we presented an Oral Presentation at ASH 2018.

Our key finding included an analysis of donor/no-donor sibling allogeneic transplant recipients, we found that there were reduced relapse rates, but no improvement in overall survival was seen at 3 years. Data from the matched unrelated donor recipients is currently being analysed.

This year we would also like to congratulate A/Prof David Curtis and Dr Sushrut Patil for receipt of the MRFF funding that has made BM12 possible.

Prof David Ritchie
Chair, Bone Marrow Transplant (BMT)

Chair
Prof David Ritchie

Committee
Sharon Avery
Ashish Bajel
Leanne Berkahn
Ken Bradstock (Life Member)
Andrew Butler
Lynette Chee
Julian Cooney
David Curtis
Nada Hamad
Devendra Hiwase
Olen Kennedy
Amil Khot
John Kwan
Stephen Larsen
Ian Lewis
Andrew Lim
John Moore
Nalini Patil
Sushrut Patil
Duncan Purtil
Anthony Schwarer
Jeff Szer
Patricia Walker
Agnes Yong
John Seymour

References:
Publication Number: 205
Submission ID: 110260
TITLE: Reduced Intensity Conditioned Sibling Transplantation Versus No Transplant in Intermediate or High Risk Acute Myeloid Leukemia: A Prospective Multi-Center Study in Patients 50-70 Years in First Complete Remission and with at Least One Potential Sibling Donor (ClinTrialGov 00342316)
BM12

Prospective, non-blinded, 2 arm, 1:1 randomised study using Cyclophosphamide After Sibling-donor allogeneic stem-cell Transplantation (CAST) in patients with acute leukaemia and myelodysplasia.

**Trial chief investigator**
Dr David Curtis
Dr Sushrut Patil

**Main trial objectives**

**Primary objectives:**
To compare rates of composite graft-versus-host disease free and relapse-free survival (GRFS) in patients receiving post-transplant cyclophosphamide in combination with cyclosporin compared to the standard cyclosporin and methotrexate GVHD prophylaxis in sibling donor peripheral blood stem cell recipients.

**Secondary objectives:**
- To assess rates of engraftment.
- To assess rates of non-relapse mortality (NRM) at 12 and 24 months.
- To assess overall survival at 12 and 24 months.
- To assess the risk of disease relapse at 12 and 24 months.
- To assess rates of acute GVHD.
- To assess rates of chronic GVHD at 12 and 24 months.
- To assess incidence of hepatic veno-occlusive disease.
- To assess quality of life at prior to transplant and then at days +30, +60, +90, +180, +365, +730.
- To assess health economic impact of the two regimens.

**CI note**
The first site was activated on 5 December 2018. We are currently working towards activating the remaining 7 sites.

---

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12618000505202

**Trial status:** Open to accrual

**Date study opened:** 05/12/2018

**Date 1st patient enrolled:** Early 2019

**Accrual target (ALLG):** 134

**Current total accrual (ALLG):** 0

**Participating sites:** 1

**Number of sites with patients entered:** 0

**Expected accrual date:** December 2020

**Support:** MRFF

**Comments:** Current Protocol Version 1.0, 16 July 2018
The CML/MPN group continues to design and conduct innovative and impactful research with the aim of improving the lives of our patients globally. Despite significant improvements in the life span of CML patients brought about by the introduction of tyrosine kinase inhibitors (TKIs) such as imatinib, nilotinib and dasatinib, a number of important research questions remain. These include the selection of optimal frontline therapy to maximise efficacy and minimise long term toxicity, finding new therapies for advanced phase CML and enhancing success of treatment free remission strategies.

During 2018, the group continued to explore ways to improve access for patients with myelofibrosis, polycythaemia and essential thrombocytosis. With each clinical study is an innovative suite of correlative studies aimed to enhance our understand of the underlying mechanisms of therapeutics.

The CML11 (Pinnacle) study will have all 60 patients reaching their primary end point in Feb 2019. This study enrolled treatment naïve CML patients and started them on nilotinib (Tasigna, Novartis) treatment, adding pegylated interferon (PegIntron, MSD) after 3 months of TKI monotherapy. Combination therapy continues until month 24, when the primary end point of MR4.5 is measured. Results from the interim analysis were presented as an oral abstract at the American Society of Hematology (ASH) meeting in Dec 2018 (Yeung et al 2018). Key results included a 12-month MMR rate of 78.3% and 12 month MR4.5 rate of 33.8%. There are comparable or superior to results reported in the literature with nilotinib monotherapy. Results from the primary end point analysis is expected to submitted as an ASH abstract in 2019.

The CML 12 (Direct) study enrolment improved dramatically in Q3&4 in 2018 after getting off to a slow start and is now expected to enrol all 80 patients by the end of 2019. In this study, patients have their dasatinib doses adjusted according to their trough levels, with the aim of minimising toxicity, pleural effusion. An interim analysis looking at efficacy of the strategy, based on the achievement of early molecular response (BCR-ABL1 at 3 months) and MMR at 12 months of the first 25 patients will be performed in June this year, forming the basis of an ASH abstract submission.

The CML08 (TWISTER) long term results were published in the prestigious journal Leukemia. (Ross, et al 2018). This study was one of the first to study the outcomes of imatinib discontinuation after a stable deep molecular response. Eighteen out of 40 patients remain alive and in TFR with a median follow-up of 8.6 years. Highly sensitive BCR-ABL1 DNA PCR was used to show that the level of residual disease slowly declines during TFR. The nature of these cells and why they appear to be declining is an area of active investigation.

Meanwhile, a sub study of CML09 compared BCR-ABL1 response kinetics by mRNA with genomic DNA during first-line treatment was published in Haematologica (Pagani, et al 2018) with an accompanying commentary from Professor Jerry Radich (Seattle). During the first few months the level of BCR-ABL1 DNA was higher by DNA than by mRNA, but at later time points there was very good agreement between the two methods. Interestingly, the expression ratio (mRNA:gDNA) was lower for patients with e13a2 (b2a2) transcripts, adding to the literature suggesting that there might be biological differences related to transcript type.
In MPN, the contribution of the ALLG to the landmark PT1 study from the UK Medical Research Council was recognised with the inclusion of Dr Cecily Forsyth as a co-author in a recent publication in the Journal of Clinical Oncology (Godfrey, et al 2018). This paper reported the outcome of patients with intermediate risk essential thrombocythaemia. In patients aged 40-59 without specific high-risk features and on treatment with aspirin there was no reduction in vascular events with the addition of hydroxurea.

The past year saw the listing of pegylated interferon (Pegasys) on the PBS for the treatment of MPN. A number of members of the Disease Group, led by Dr Cecily Forsyth, put together a review paper on the place of pegylated interferon, which was published in the Internal Medicine Journal (Forsyth, et al 2018). Whilst this was not an official ALLG activity it highlights the potential for interactions between ALLG members to lead to useful output in addition to interventional clinical trials.

Looking forward, our trials under development include the proposal of an ANZ treatment free remission registry, and an upfront study called Aspect (Asciminib prospective study to eliminate CML in combination with TKIs). Asciminib is a novel BCR-ABL inhibitor, docking at the auto-inhibitory myristoyl site rather than the ATP binding pocket where the other TKIs bind. In the phase I study, it appeared safe and tolerable across a wide range of oral dosing regimens, and in combination with ATP-binding TKIs, with a promising early efficacy signal. A clinical trial proposal has been developed to use this novel agent in the frontline setting, with the expectation that such an agent will have similar efficacy as a second generation TKI, but without the associated toxicity. The proposal is currently under consideration.

The CML/MPN chairs would like to thank all contributors to our clinical studies, including staff and members at centres that cross refer.

Dr David Yeung
Chair, Chronic Myeloid Leukaemia & Myeloproliferative Neoplasm (CML & MPN)

Dr David Ross
Chair, Chronic Myeloid Leukaemia & Myeloproliferative Neoplasm (CML & MPN)

References:


CML12

A single arm phase II study to individualize dasatinib dosing based on trough levels and molecular response to maintain efficacy whilst minimising toxicity.

**Trial chief investigator**
Prof Timothy Hughes,
Prof Andrew Grigg,
Dr David Yeung

**Main trial objectives**
The aim is to minimise the cumulative incidence of adverse events, especially pulmonary toxicities, of dasatinib therapy by using therapeutic drug monitoring (TDM) to adjust the dasatinib dose without compromising efficacy in CML-CP patients.

**Secondary objectives:**
To study the incidence of treatment related pleural effusion in CML-CP patients aged ≥60 years, treated with TDM dose optimised dasatinib.

**CI note**
Protocol Amendment sent to sites to expand eligibility to patients >18 years in an attempt to boost recruitment.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12616000738426p

**Trial status:** Opened to accrual

**Date study opened:** 04/11/2016

**Date 1st patient enrolled:** 13/12/2016

**Accrual target (ALLG):** 80

**Final accrual (ALLG):** 41

**Participating sites:** 30

**Number of sites with patients entered:** 11

**Date study closed to accrual:** December 2020

**Support:** Bristol-Myers Squibb

**Comments:** Current Protocol Version 4.0, 21 August 2018

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**Study Recruitment**

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Myeloproliferative neoplasms registry.

**Trial chief investigator**
Dr Cecily Forsyth  
Prof Andrew Grigg  
Dr David Ross  
Prof Wendy Erber

**Main objectives**
- Provide epidemiological and descriptive data on current patterns of diagnosis and treatment of MPNs; estimate rates of key clinical events (thrombosis, haemorrhage, progression to MF/AML, death) and treatment response/intolerance;  
- Establish collaborations with basic and translational research groups to provide access to a well-characterised MPN patient cohort;  
- Analyse outcome according to clinical/diagnostic parameters AND according to novel parameters arising from correlative science projects run by registry partners;  
- Provide investigators with data for planning and feasibility assessment of future clinical trials.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: AACTRN12613000138785

**Trial status:** Currently in analysis

**Date study opened:** 22/04/2014

**Date 1st patient enrolled:** 22/04/2014

**Accrual target (ALLG):** 250

**Current total accrual (ALLG):** 251

**Participating sites:** 14

**Number of sites with patients entered:** 14

**Recruitment target reached:** March 2017

**Support:** Novartis

**Comments:** Current Protocol Version 2.0, June 2013

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**Study Recruitment**

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| 2018 |                | on hold
High Grade Non-Hodgkin Lymphoma & Hodgkin Lymphoma (HG NHL & HL)

I am honoured to be appointed the new chair of the High-grade Lymphoma Disease group of the ALLG and thank Mark Hertzberg for his leadership, mentorship and ongoing contribution to the group.

In November, Peter Mollee stepped down from his role as co-chair of the high-grade group and we look forward to Tara Cochrane from the Gold Coast University Hospital taking up the position in 2019.

We have exciting times ahead with three new ALLG-led studies in the pipeline, and growth of clinical trial partnerships with new collaborators, such as the German Hodgkin Lymphoma Study group and Global T-cell Lymphoma Consortium. We also plan an expansion of the group activity to include a formalised initiative to increase Australasian-led efforts in non-interventional research, development of National Guidelines for management of lymphoma and improved access for remote and rural sites to lymphoma research. In order to achieve these goals, we will be working more closely with the ALLG Low-grade Lymphoma Disease Group, Lymphoma and Related Diseases Registry, the Australasian T-cell Lymphoma Network and the Snowdome foundation.

Congratulations to chief investigators of the NHL29 (IRIC) study, Judith Trotman and Emma Verner, along with their collaborating sites, for completing recruitment. It is a real challenge to recruit elderly patients to trials in aggressive lymphoma, and we eagerly await the results.

HD10 (GHSG) opened at 10 sites, and has so far recruited 26 patients. Our first collaboration with the German HL study group is proving to be a success to date.

NHL31 (TREBL) is an exciting trial lead by CI Maher Gandhi of Princess Alexandra Hospital in Brisbane. It was awarded a MRFF grant and will use scientific rationale based on work from Maher’s laboratory at University of Queensland. Patients with immunosuppression-associated lymphoproliferative disorders will be treated with rituximab and ibrutinib, followed by EBV-CTLs generated in David Gottlieb’s laboratory. This is a real collaborative effort involving laboratory sciences, clinical haematology, infectious diseases and transplant medicine. The study will open at selected sites in each state in mid 2019.

The NHL32 (BLOCK CNSL) study is being developed by two new investigators to ALLG: Dr Gareth Gregory of Monash Health, and Eliza Hawkes, of the Olivia Newton John Cancer and Research Centre. This new multicentre study incorporates chemotherapy, rituximab followed by pembrolizumab in previously untreated primary CNS lymphoma.

NHL33 (WAMM) is in the early phases of development. PI Hawkes has developed the study in collaboration with ALLG investigators Tam, Cheah, Trotman and Mollee to recruit transplant-eligible MCL patients to a “window” study of rituximab plus acalabrutinib followed by R-DHAOx, transplant and maintenance R+A.
It will open in late 2019 and aims to use newer techniques in MCL such as MRD assessment, and PET to evaluate response.

Leading the Australian contribution to the Global T-Cell Lymphoma Consortium is Dejan Radeski, from Sir Charles Gardiner. Via the ALLG, the TCL consortium will bring a suite of investigator-initiated phase I-II studies evaluating novel therapies in TCL. We all look forward to participating in these. The Consortium also allows collaboration in Australian-designed investigator-initiated studies so we welcome ideas for these.

The recently formed ArtNET (Australian Radionucleotide Trials Network), is working with the ALLG to formally accredit PET centres around Australia allowing central PET review within our lymphoma trials. The quality of PET assessments is essential to reporting of clinical trial outcomes in lymphoma, and we urge members to liaise with their local Nuclear Medicine Departments to facilitate this.

MyHodgkinMyHealth, is a non-interventional study using digital health to record patient late effects from treatment. This international initiative is being led by Trotman. We look forward to joining the digital health as an organisation.

Congratulations to the forty-five lymphoma researchers who have worked together on a large-scale analysis of real-world data sets. The group have currently completed six projects in a very short period of time.

Moving into 2019, we have four projects underway, and all 10 thus far have included contributions from international collaborators. We look forward to continuing the momentum and partnerships developed with the Lymphoma and Related Diseases Registry, the Snowdome Foundation and the Australasian T-cell Lymphoma Network.

Dr Eliza Hawkes
Chair High Grade Non-Hodgkin Lymphoma & Hodgkin Lymphoma (HG NHL & HL)

Acknowledgements
-The Medical Research Future Fund for support of Maher Gandhi’s NHL32 study.
-Owen O’Connor from Columbia University and the Global TCL Consortium for our ongoing collaborations.
-The German Hodgkin Study Group for our collaboration on the HD10 study.
-Snowdome Foundation for support of our non-interventional research program
HD10

Treatment optimization trial in the first-line treatment of advanced stage Hodgkin lymphoma; comparison of 4-6 cycles of escalated BEACOPP with 4-6 cycles of BrECADD.

**Trial chief investigator**
Prof Mark Hertzberg
Dr Georgina Hodges

**Main trial objectives**
The aim of the trial is to prove that the new chemotherapy regimen, BrECADD, is non-inferior to BEACOPP as first-line treatment in advanced stage classical Hodgkin lymphoma patients up to aged 60.

**CI note**
Open-label, prospective, multicenter trial with two parallel groups and central stratified randomization (minimization method). Patients are randomized to receive chemotherapy with escalated BEACOPP (standard group) or with BrECADD (experimental group). After the first two cycles, a restaging is performed by contrast-enhanced computed tomography (ceCT) and positron-emission tomography (FDG PET/CT) in all patients in order to guide response-adapted continuation of therapy consisting of 4 or only 2 additional cycles of randomized chemotherapy in case of a PET positive or negative staging result, respectively. A second restaging will be performed after completion of chemotherapy; Patients with PET-positive residual disease will receive local irradiation, while patients in complete remission do not receive radiotherapy.

Registered 28 patients in Australia with 16 sites being activated during 2018.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12617000087358p

**Trial status:** Opened to accrual

**Date study opened:** 07/02/2018

**Date 1st patient enrolled:** 20/04/2018

**Accrual target (International):** 1500

**Accrual target (ALLG):** 90

**Final accrual (International):** 220

**Final accrual (ALLG):** 26

**Participating sites:** 16

**Number of sites with patients entered:** 10

**Date study closed to accrual:** June 2020

**Support:** Millennium Pharmaceuticals, Takeda Oncology, University of Cologne (Germany), Leukaemia Foundation

**Comments:** Current Protocol Version 5, 24 November 2017
A Phase II Study of Ibrutinib, Rituximab and mini-CHOP therapy in very elderly patients with newly diagnosed DLBCL (IRIC).

**Main trial objectives**
The primary objective of this study is to assess the safety and efficacy of ibrutinib-R-mini-CHOP in subjects with DLBCL as measured by deliverability and overall survival, respectively.

**Secondary objectives:**
The NHL29 (IRIC) study is a Phase II Study of Ibrutinib, Rituximab and mini-CHOP therapy in patients aged ≥75 years with newly diagnosed Diffuse Large B Cell Lymphoma (DLBCL). We face a rapidly aging population who represent a substantial proportion of patients with this common lymphoma. Elderly patients often have a different disease biology and tolerance of and willingness to undergo full dose chemotherapy. The potential to substitute full dose CHOP chemotherapy with less toxic mini-CHOP and this B cell enzyme inhibitor (BTKi) has appeal to both investigators and patients alike. This study of 80 patients will determine if the addition of Ibrutinib to both antibody and reduced doses chemotherapy will be well tolerated in the elderly and improve their survival by an additional 15%. We have all 20 sites across Australia open and we are ahead of our enrolment target with 60 patients currently registered on study. We are optimistic for full recruitment ahead of schedule.

Study closed to recruitment in December after reaching the target of 80 patients.

**Study Recruitment**

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**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12616000738426p

**Trial status:** Opened to accrual

**Date study opened:** 04/11/2016

**Date 1st patient enrolled:** 13/12/2016

**Accrual target (ALLG):** 80

**Final accrual (ALLG):** 80

**Participating sites:** 30

**Number of sites with patients entered:** 11

**Date study closed to accrual:** December 2018

**Support:** Janssen

**Comments:** Current Protocol Version 4.0, 21 August 2018
The focus of the Low Grade Lymphoma group continues to be on identifying potential clinical trial options of a number of promising new agents. Both signaling pathways and the micro-environment are emerging as important targets for therapy in the low grade lymphomas with multiple ongoing studies internationally.

The NHL27 RELEVANCE trial comparing Rituximab and Lenalidomide with Rituximab and CHOP in first line treatment of follicular lymphoma (FL) failed to meet its primary endpoint with a comparable 3yr PFS of 77% in the rituximab-lenalidomide group and 78% in the R-CHOP group. This study was published in NEJM concurrently with its presentation at EHA in June 2018.

The ongoing NHL26 (RePLy) study seeks to improve the poor prognosis of patients with relapsed FL who remain PET+ after re-induction rituximab-chemotherapy, by adding lenalidomide to rituximab maintenance. Given the data supports the efficacy of the combination of lenalidomide and rituximab in the RELEVANCE study we encourage all ALLG members to screen patients with relapsed FL who have had CT confirmed ≥ stable disease 4-6 weeks after rituximab-chemo (any number of cycles permitted) to refer to their local recruiting NHL26 site.

The NHLLOW5/TROG 99.03 study conducted by MacManus and Seymour was an important collaboration with the Trans-Tasman Radiation Oncology Group (TROG).

The study with almost 10 years median follow-up demonstrated systemic therapy with (R)-CVP after IFRT for early stage FL reduced relapse outside radiation fields and significantly improved PFS (59% vs. 41% at 10 years), but no OS difference was identified. The subset of patients treated with IFRT and rituximab-containing systemic therapy had exceptional PFS, >80% at 5 years, with no relapses so far identified beyond 3.5 years. Patients who received systemic therapy had fewer transformations to aggressive lymphoma than those treated with RT alone and PET-staged patients had superior PFS.

These important findings were published in the Journal of Clinical Oncology (JCO 36,2918-25, 2018) and the paper was accompanied by an editorial. This trial provides the only useful high-level evidence currently available in the literature to help select management strategy in early stage FL. Trial biomarker specimens will be analysed in the coming three years as part of an NHMRC funded study that commenced in 2018. Principal investigator of the translational study is Gandhi.

In Jan 2019, Johnston and Trotman will open the ALLG’s (NHL30) participation in the UK-led PETReA Study of PET-guided Response-Adapted therapy in high tumour burden FL. Having demonstrated in several studies the powerful predictive value of
post-induction PET on both PFS and OS it is now timely to utilise PET as a platform for response adapted therapy in FL.

It is also important to add another large frontline international collaboration in FL to the ALLG’s portfolio and the opening of six sites nationally has been enabled by funding support from Snowdome and the Leukaemia Foundation Australia. This 820 patient study is aimed to improve the poor outcome of patients who remain PET+ after first-line therapy by randomising these patients to standard rituximab maintenance vs. rituximab plus lenalidomide, and to compare rituximab maintenance with observation alone in patients who become PET negative after first-line treatment. A significant previous hurdle to the ALLG’s participation in the PETReA study is now overcome by the inclusion of indolent lymphoma as an indication for PET scanning in Medicare Benefits Schedule. The strongly predictive PET data from the NHL16 PRIMA study was a major component of the data submitted to Medical Services Advisory Committee in the application for this MBS listing.

Similarly, the PET in GALLIUM data presented demonstrating the 5-fold risk of progression and 5-fold risk of death in patients failing to obtain complete metabolic response further validated PET-response adapted platform of PETReA. Plans are underway to collaborate with Roche in a protocol amendment to include patients treated in induction with Obinutuzumab-chemotherapy.

ALLG members Gareth Gregory is leading a correlative research project (LS21) in conjunction with Beigene’s Magnolia trial. LS21 is expected to drive recruitment to the uncommon lymphoma registry in 2019.

Prof Stephen Mulligan  
Chair, Chronic Lymphocytic Leukaemia (CLL)

Prof Judith Trotman  
Chair, Low Grade Non-Hodgkin Lymphoma (LG NHL)
An Australasian, Phase III, Multicentre, Randomised trial comparing Lenalidomide consolidation vs no consolidation in patients with Chronic Lymphocytic Leukemia and residual disease following induction chemotherapy (RESIDUUM).

**Trial chief investigator**
Prof David Gottlieb  
Dr Constantine Tam  
Prof Stephen Mulligan

**Main trial objectives**
To investigate if lenalidomide is capable of extending progression free survival (PFS) from the start of lenalidomide treatment in CLL patients.

**CI note**
This trial is open to patients over the age of 18 that meet eligibility criteria and who have not had previous treatment for CLL. Patients are randomised to either Lenalidomide treatment or no Lenalidomide treatment after having completed initial CLL treatment with standard chemotherapy FCR. Patients will undergo 3 treatment cycles of FCR and then undergo blood tests which determine if they can continue with further FCR chemotherapy. Further blood tests are collected prior to the patients commencing randomisation treatment.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12610000060044

**Trial status:** Closed to accrual

**Date study opened:** 09/05/2011

**Date 1st patient enrolled:** 27/05/2011

**Accrual target (Inter):** 320 (Registered); 192 (Randomised)

**Accrual target (ALLG):** 160 (Registered); 91 (Randomised)

**Final accrual (Inter):** 607 (Registered); 143 (Randomised)

**Final accrual (ALLG):** 207 (Registered); 70 (Randomised)

**Participating sites:** 22

**Number of sites with patients entered:** 19

**Date study closed to accrual:** 22/02/2018

**Support:** Celgene Pty Ltd

**Reason for closure:** Closed due to safety concerns with Lenalidomide

**Comments:** Current Protocol Version 8.0, 20 July 2015
A Phase 2 Study of patients treated for relapsed Follicular Lymphoma: with Revlimid® consolidation added to Rituximab maintenance therapy in those remaining PET positive (RePLY).

**Trial chief investigator**
Prof Judith Trotman

**Main trial objectives**
The primary objective is to determine the percentage of patients converting from PET+ after reinduction immunochemotherapy to PET- after 6 months of commencing Lenalidomide consolidation.

**CI note**
NHL26 RePLY, is a world-first study of PET-directed therapy for relapsed follicular lymphoma. It is a Phase 2 Study enrolling patients after they have completed treatment for relapsed disease, with Revlimid® consolidation added to Rituximab maintenance therapy in those remaining PET positive. The demonstrated efficacy of Lenalidomide in treatment of follicular lymphoma offers the potential to obtain remission for these patients who have responded poorly to conventional immunochemotherapy. Lenalidomide at an initial dose of 10mg/d for 21 days every four weeks is added for patients who remain PET+. While overall recruitment has been slow the study is well on track to answer its primary endpoint: the rate of conversion to PET negative status in sixteen evaluable patients after six months of Rituximab + Lenalidomide. Please refer patients as they approach the end of their re-induction therapy to your local participating site for screening.

Recruitment remains ongoing with 33 patients recruited by December 2018.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12613000106730

**Trial status:** Open to accrual

**Date study opened:** 01/11/2013

**Date 1st patient enrolled:** 04/11/2013

**Accrual target (ALLG):** Approx. 80 (16 PET+)

**Current total accrual (ALLG):** 33

**Participating sites:** 13

**Number of sites with patients entered:** 9

**Expected accrual date:** December 2018

**Support:** Celgene Pty Ltd

**Comments:** Current Protocol Version 5.0, 16 June 2016
Myeloma

The ALLG Myeloma Disease Group aims to support its members to produce high quality clinical research which will improve the outcomes of patients with myeloma. The group is focussed on investigating new therapies with the aim of improving clinically meaningful outcomes and to incorporate novel translational studies into every protocol with the aim of improving understanding of myeloma biology, new therapy development and improved disease monitoring. It is hoped to build a portfolio of studies that encompasses the breadth of disease presentations in myeloma.

Our key trial achievements for 2018 include MM17, a study of carfilzomib, thalidomide and dexamethasone for transplant-eligible myeloma patients with a suboptimal response to initial bortezomib-based induction therapy, completed accrual ahead of schedule. While the MM18 study offered our first collaboration with the Asian Myeloma Network, completed rapid accrual of the Australian cohort and is successfully accruing in Asian sites.

Interim results of the MM16, MM17 and MM18 studies were presented as posters at the 2018 American Society of Haematology meeting.

In the MM16 trial of myeloma patients with renal impairment, carfilzomib and dexamethasone showed disease response rates comparable to patients with normal renal function in the ENDEAVOR study.

There was no increased acute kidney injury due to carfilzomib; instead, creatinine and eGFR improved with time, with a greater improvement in the 20/56 dose group and in treatment naive patients. The results also demonstrated the value of early serum FLC kinetics measured at C1D3 and C1D10 in predicting renal response. A suboptimal early serum free light chain may be an appropriate indicator to use a higher dose density to achieve a better renal outcome.

The preliminary analysis of the ALLG MM17 trial demonstrated that early response adaptive escalation to carfilzomib, thalidomide and dexamethasone results in high response rates (overall response rate 72%), including MRD negativity in 43%, in patients failing bortezomib-based induction therapy.

The preliminary analysis of the ALLG MM18/ AMN003 study demonstrated that the carfilzomib, thalidomide and dexamethasone combination is a tolerable regimen for patients with relapsed and refractory myeloma with a safety profile in line with previous reports for each of carfilzomib and thalidomide. Initial response rates appear very promising and durable with responses up to 13.7 months thus far in some patients.

Dr Anna Kalff presented the ALLG MM14 trial at the European Haematology Association Meeting and American Society of Hematology Meeting. This study in relapsed and refractory myeloma treated patients
with four cycles of pomalidomide and dexamethasone induction. After these four cycles, patients with stable disease (SD) or better were randomised to receive POM alone (P) or combined with LoDEX (Pd) as maintenance. After initial disease control with POM-LoDEX, patients continuing with POM-LoDEX had superior PFS compared to maintenance with POM alone. However, this early PFS benefit is lost and reversed by 18 months; and in those randomised patients who went on to receive post-progression therapy, more durable responses and superior survival were seen in those previously treated with POM alone. Correlative studies are underway to investigate the immunological mechanisms behind these observations.

MM21, a study of lenalidomide, daratumumab and dexamethasone for transplant-eligible myeloma patients with a suboptimal response to initial bortezomib-based induction therapy, has been designed and is planned to open early 2019. This study will aim to improve the outcome of patients who respond poorly to bortezomib, a group associated with a poor prognosis. The study has several translational studies to learn more about mechanisms of resistance and disease biology.

FRAIL-M is a stratified, randomised, Bayesian adaptive trial designed to identify which treatment options maximise efficacy whilst controlling toxicity below a certain threshold within each frailty stratum (fit, intermediate-fit and frail). The study will compare the efficacy, safety and cost-effectiveness of bortezomib, lenalidomide and dexamethasone (VRd) with lenalidomide and dexamethasone (Rd) in fit and intermediate-fit non-transplant eligible patients with newly diagnosed myeloma. In the frail group Vd will be compared to Rd. The optimal doses of lenalidomide and bortezomib within each frailty category will be defined as part of this novel trial design.

Congratulations to Professor Andrew Spencer for publishing two meta-analyses, based in part, on the ALLG MM11 trial.

The ALLG Myeloma Disease Group had two face-to-face meetings in 2018 at the ALLG Scientific Meeting. In 2019 we hope to have a larger workshop in association with the November Scientific Meeting to further develop the trial program. The Myeloma Disease group will continue to work in collaboration with AMaRC, the Myeloma and related Diseases Registry, Myeloma Australia and the Leukaemia Foundation to improve outcomes for patients with myeloma. We also look forward to ongoing collaborations with the Asian Myeloma Network given the success of our first trial together.

A/Prof Peter Mollee
Chair, Myeloma

A new trial MM22 (FRAIL-M) is in development after being awarded with an MRFF grant. The trial will examine myeloma therapy in the elderly with treatment delivery altered according to frailty assessment.
Phase II study assessing the effect of carfilzomib treatment on early free light chain kinetics in myeloma patients with renal impairment.

**Trial chief investigator**
Prof Joy Ho
Prof Douglas Joshua

**Main trial objectives**
- To assess the effect of carfilzomib on serum free light chain measurements early in the treatment of myeloma patients with renal impairment (eGFR 15–40 ml/min).
- To determine if there is a relationship between changes in serum free light chain levels in the early phases of treatment and renal function after 4 cycles of treatment.

**CI note**
The MM16 study started recruitment in April 2015 and by August 2015, had completed recruitment of the first cohort of 10 patients. An interim analysis was carried out as per protocol by the SDMC and TMC, which approved the trial for progressing to the next phase utilising a higher dose of the trial drug carfilzomib. Recruitment started for the second cohort in March 2016. Since then 20 further patients have been recruited; the rate of recruitment had decreased from the first cohort due to a number of factors that were outside the control of the trial, including a compassionate access programme and competing trials, including one that was set up within the ALLG with overlapping eGFR. An interim analysis was presented in May 2018. A full analysis is expected in 2020.

**Website where trial registered**: Australian New Zealand Clinical Trials Registry: ACTRN12614000301662

**Trial status**: Open to accrual

**Date study opened**: 24/03/2015

**Date 1st patient enrolled**: 02/04/2015

**Accrual target (ALLG)**: 36–40

**Final accrual (ALLG)**: 32

**Participating sites**: 5

**Number of sites with patients entered**: 5

**Date study closed to accrual**: December 2018

**Support**: Amgen

**Comments**: Current Protocol Version 3.0, 8 February 2018

### Study Recruitment

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A multicentre single arm study of carfilzomib-thalidomide-dexamethasone (Car-TD) for newly diagnosed transplant-eligible multiple myeloma (MM) patients refractory to initial bortezomib-based induction therapy.

**Main trial objectives**
- To determine the overall response rate (ORR) to treatment with Car-TD salvage therapy in NDMM patients who have had a sub-optimal response to a bortezomib-based induction therapy, where a sub-optimal response is defined as the failure to achieve at least a minimal response (MR) with a minimum of 2 cycles of a prior bortezomib-based induction therapy or a partial response (PR) with 4 cycles of a prior bortezomib-based induction therapy.
- To evaluate the tolerability and safety profile of Car-TD salvage therapy when administered to NDMM patients who have had a sub-optimal response to a bortezomib-based induction therapy. This study closed to recruitment in 2018, reaching the target of 50 patients who has sub-optimal responses to initial bortezomib-based induction therapy.

**CI note**
The study has progressed solidly and will be looking at publications in the near future. The success of this study was the inspiration of the upcoming study ALLG MM21, looking at the same patient population with different novel agents.

**Study Recruitment**

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**Website where trial registered**: Australian New Zealand Clinical Trials Registry: ACTRN12615000934549

**Trial status**: Open to accrual

**Date study opened**: 13/09/2016

**Date 1st patient enrolled**: 28/09/2016

**Accrual target (ALLG)**: 50

**Current total accrual (ALLG)**: 38

**Participating sites**: 6

**Number of sites with patients entered**: 3

**Expected accrual date**: June 2018

**Support**: Amgen

**Comments**: Current Protocol Version 1.0, 2 February 2015
Single arm, multicentre study of Carfilzomib in combination with Thalidomide and Dexamethasone (CaTD) in patients with relapsed and/or refractory multiple myeloma (RRMM).

**Trial chief investigator**
Dr Hang Quach

**Main trial objectives**
To assess the progression free survival (PFS) in patients with RRMM who have had 1 to 3 prior lines of therapies, treated with combination carfilzomib, thalidomide and dexamethasone (CaTD).

**CI note**
The MEDSAFE/REC process was completed in NZ (lead site) Middlemore Hospital with the TMC carrying out the first safety cohort analysis in August. The committee concluded that the safety rules for withholding of dose increase were not met and the trial was approved to proceed with the protocol defined Carfilzomib dose increase to 20/56 mg/m2.

In a first for the ALLG, the trial opened in Asia under the auspices of the Asian Myeloma Network with CI Prof Wee Joo Chng in Singapore.

The AMN team continued to activate sites and recruit patients. We are currently leading up to the interim analysis - 1 year after the recruitment of 50 ALLG patients, to be completed in the later half of 2019.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12615000818538

**Trial status:** Open to accrual

**Date study opened:** 27/02/2017

**Date 1st patient enrolled:** 17/03/2017

**Accrual target (Inter):** 100

**Accrual target (ALLG):** 50

**Current accrual (Inter):** 64

**Current accrual (ALLG):** 50

**Participating sites:** 11

**Number of sites with patients entered:** 9

**Date study closed to accrual:** July 2018

**Support:** Amgen

**Comments:** Current Protocol Version 4.0, 30 July 2018

![Study Recruitment](image)

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A Phase 3 trial of thalidomide-dexamethasone consolidation versus thalidomide-dexamethasone-ixazomib consolidation for transplant eligible multiple myeloma patients undergoing a single ASCT as part of front-line therapy.

**Trial chief investigator**
Prof Andrew Spencer

**Main trial objectives**
To determine whether the addition of ixazomib to thalidomide and low dose dexamethasone maintenance therapy post-ASCT for MM patients improves progression free survival (PFS).

**CI note**
This study will determine whether the addition of the oral proteasome inhibitor ixazomib prolongs the duration of myeloma disease control when added to standard post autologous consolidation with thalidomide and corticosteroids. During 2018 the trial continued solid progress with site activations and with registration including randomisation.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry:ACTRN12616000772448

**Trial status:** Open to accrual

**Date study opened:** 15/12/2016

**Date 1st patient enrolled:** 12/01/2017

**Accrual target (ALLG):** 310 (Registered); 280 (Randomised)

**Current total accrual (ALLG):** 31

**Participating sites:** 5

**Number of sites with patients entered:** 3

**Expected accrual date:** December 2020

**Support:** Takeda


### Study Recruitment

![Graph showing study recruitment from 2017 to 2018](image)

- **Actual accrual:** 31 (2017), 75 (2018)
- **Cumulative actual accrual:** 79 (2017), 106 (2018)
- **Cumulative expected accrual:** 100 (2017), 200 (2018)
A Multicentre Phase 3 Trial Comparing Elotuzumab-Cyclophosphamide-Thalidomide-Dexamethasone (E-CTD) with Cyclophosphamide-Thalidomide-Dexamethasone (CTD) for the Treatment of Relapsed and/or Refractory Multiple Myeloma (RRMM).

**Trial chief investigator**
Prof Andrew Spencer
Dr Krystal Bergin

**Main trial objectives**
To determine the progression-free survival (PFS) with E-CTD when compared with CTD for the treatment of RRMM.

**CI note**
Elotuzumab is a manufactured protein directed against a target found on multiple myeloma cells. Elotuzumab was observed to destroy myeloma cells in laboratory studies, and results of earlier clinical studies in patients with myeloma showed encouraging results when used in combination with lenalidomide and dexamethasone. During 2018, this study underwent a protocol amendment to close the standard of care arm, Dexamethasone, Thalidomide and Cyclophosphamide due to slower than expected accrual. In doing so, this trial will now enable up to 100 patients to access Elotuzumab with Dexamethasone, Thalidomide and Cyclophosphamide.

**Website where trial registered:** Australian New Zealand Clinical Trials Registry: ACTRN12616001030460p

**Trial status:** Open to accrual

**Date study opened:** 16/01/2017
**Date 1st patient enrolled:** 14/02/2017

**Accrual target (ALLG):** 300 (Randomised)
**Final accrual (ALLG):** 19

**Participating sites:** 7
**Number of sites with patients entered:** 5
**Date study closed to accrual:** December 2020

**Support:** Bristol-Myers Squibb


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### Study Recruitment

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Supportive Care

The ALLG Supportive Care group aims to alleviate the symptoms and complications of blood cancers and to minimise toxicities of treatment.

The group is currently focussing on studies that investigate strategies to prevent infections that can occur during and after treatment.

As a group we are also looking at red cell transfusion thresholds and are planning comparative research in this space; this is a highly relevant to older patients who have a blood cancer diagnosis. Group members are also involved in developing and publishing Australasian Supportive Care guidelines.

In 2018, the ALLG endorsed RATIONAL Study opened at two new sites (Waikato Hospital in New Zealand and Royal Hobart Hospital in Australia). Recruitment continued and is close to completion. The survey of clinician practices for managing hypogammaglobulinaemia secondary to haematological malignancies was conducted.

In 2018, the ALLG endorsed RATIONAL Study opened at two new sites (Waikato Hospital in New Zealand and Royal Hobart Hospital in Australia). Recruitment continued and is close to completion. The survey of clinician practices for managing hypogammaglobulinaemia secondary to haematological malignancies was conducted.

The survey of clinician practice found variation in practice with regard to use of immunoglobulin replacement, particularly criteria for stopping immunoglobulin therapy. Few clinicians use prophylactic antibiotics before commencing immunoglobulin replacement and most expressed interest in recruiting to a clinical trial comparing prophylactic antibiotics to immunoglobulin replacement.

Completed during 2018, the REDDS Study demonstrated the feasibility of allocating an older, outpatient based MDS population to different red cell transfusion thresholds. The findings of this study support the feasibility of undertaking a phase III study to compare different red cell transfusion thresholds in MDS powered for patient-centred outcome.

The findings of the REDDS Study were presented in December at the American Society of Hematology (ASH) conference in San Diego. This study was conducted in collaboration with the UK NHS Blood and Transplant (NHSBT) Clinical Trials Unit (Chief Investigator Dr Simon Stanworth).

The ALLG Supportive Care Group had its first concept development workshop with the Cancer Supportive Care Clinical Studies Collaborative (CSCCSC) to identify areas for study in haematological supportive care in September 2018.

Dr Zoe McQuilten
Chair, Supportive Care

Key collaborations:
Transfusion Research Unit, Monash University UK
NHSBT Clinical Trials Unit

Funding support:
National Blood Authority
Australian and New Zealand Society of Blood Transfusion (ANZSBT)

References:

Chairs
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Dr Zoe McQuilten

Committee
Asma Ashraf
Sharon Avery
Xavier Badoux
Peter Bardy
Ashanka Beligaswatte
Anoop Enjeti
Shane Gangatharan
Nada Hamad
Anna Johnston
Maya Latimer
Allison Mo
Ruth Spearing
Ferenc Szabo
Constantine Tam
Patricia Walker
Erica Wood
Kyle Mason
Gerdeep Parmar
Mark Polizzato
John Seymour
Dipti Talaulikar
Constantine Tam
Campbell Tiley
Robert Weinkove
Laboratory Science

Rapidly advancing technologies such as gene sequencing will allow us to select the most effective treatments for people with blood cancers, while avoiding unnecessary therapies. The Laboratory Sciences Committee designs and conducts both correlative studies that run alongside ALLG clinical trials, and stand-alone projects using samples donated to the ALLG Biobank.

During trial design, the Committee helps Investigators identify the best laboratory techniques to answer their research questions and advises on sample processing and storage. We review applications from researchers wishing to access samples stored in the ALLG Biobank, which are linked to clinical data in the National Blood Cancer Registry (NBCR). The Committee aims to add clinical and scientific value to the ALLG’s trial portfolio by assessing the response of blood cancers to treatment, and by helping to identify biomarkers that predict treatment response and prognosis.

Our key trial achievements for 2018 include LS17 (REGALLIA) seeks to inform the biology of high-risk ALL, particularly the increasingly recognised entity of Philadelphia chromosome-like disease. This involves an integrated pipeline of mutation detection technologies and drug sensitivity profiling. 2018 has seen REGALLIA open across multiple ALLG sites with current accrual at 47 cases.

LS18 utilises the NBCR to track the disposition of isocitrate dehydrogenase (IDH)-mutant AML cases in the Australian context. This is of particular interest given the rapid clinical development of inhibitors of mutant IDH. LS18 has now collected data from 13 ALLG sites on 219 AML cases bearing IDH mutations.

LS19 will facilitate harmonisation of next generation sequencing (NGS)-based mutation detection in AML across ALLG sites. As the mutational profile of AML is increasingly important for the definition of disease risk, assessment of treatment responses and identification potential drug targets, stringency around the detection and reporting of variant alleles is of paramount importance. In association with the Royal College of Pathologists of Australasia (RCPA) Quality Assurance Program, 73 diagnostic AML samples with high-quality DNA yield have been distributed to nine molecular laboratories at ALLG sites. Return of NGS results from all laboratories is anticipated by Q1 2019 to allow interlaboratory comparisons and subsequent harmonisation.

New trials in development for 2019 include LS20 as a progression of the existing LS19 “molecular harmonisation” protocol into the setting of minimal residual disease (MRD) monitoring. With the delineation of an increasing spectrum of mutations that can be tracked at MRD levels there is an unmet need to standardise such testing and further inform clinical significance.

Moreover, with new trial platforms like the AMLM22 maintenance protocol, trends of MRD will become a valuable end-point in ALLG AML studies. LS20
will facilitate standardisation of MRD monitoring across ALLG sites as an adjunct to clinical trials and to inform the clinical interpretation of emerging MRD markers.

LS21 is a new protocol which has been developed to determine the molecular profile of marginal zone lymphoma and identify genomic lesions which predict sensitivity to Bruton tyrosine kinase (BTK) inhibition. Marginal zone lymphoma is a rare disease with an anticipated 50% response rate to BTK inhibition. Predictors of primary sensitivity to BTK inhibitors such as BGB3111 (or zanubrutinib) have not been defined in prospective studies. Further, the genomic landscape of sub-entities such as extranodal marginal zone lymphoma have not been mapped. L21 will utilise whole exome sequencing to molecularly characterise lymphomas from subjects at ALLG sites participating in the BGB3111 study. The molecular profile will then be correlated to responses in order to inform biomarkers of BTK inhibitor sensitivity.


This analysis utilised biomarker samples from ALLG NHL21. The research was subsequently featured as an invited plenary presentation at the 11th International Symposium in Hodgkin Lymphoma (Cologne).


The Laboratory Sciences Committee convened at the May meeting, receiving presentations from Prof David Curtis and Dr Gareth Gregory. Prof Curtis discussed plans for correlative science embedded in the BM12 trial, evaluating post-transplant cyclophosphamide as graft vs. host disease prophylaxis. Dr Gregory provided background on the marginal zone lymphoma genome and discussed plans for the genomic correlates to be performed in the LS21 protocol. The ensuing open Laboratory Sciences session was chaired by A/Prof Dipti Talaulikar and included presentations by Dr Josh Casan, Prof Maher Gandhi, Dr Dominik Beck and Prof John Pimanda.

At the November meeting, Dr Clare Gould presented a new methodology for probing T-cell receptor specificity as a tool for immunotherapy. Following updates on LS17 and LS21, Prof Maher Gandhi described planned correlative studies associated with NHLOW5.

Throughout the year, the committee has received updates on Biobank and NBCR activities. On behalf of the committee, I would like to particularly thank Naomi Sprigg for her service to the ALLG Biobank; we wish her all the best for her future endeavours. We are also delighted to welcome Adele Lee-Wriede as the new ALLG Biobank coordinator.

A/Prof Jake Shortt
Chair, Laboratory Science
LS17

Studies to delineate the molecular and genomic basis of high-risk ALL in adults – Registry of Acute Lymphoblastic Leukemia in Australasia Associated Correlative Studies (REGALLIA).

Trial chief investigator
Dr David Yeung

Laboratory Research
Analyses performed at SAHMRI include: phospho-flow, TLDA, PCR, FISH, mRNA Seq, in vitro drug sensitivity screening to kinase inhibitors.

2018 status
The LS17 study is the correlative science component of the Regallia project. Patients with newly diagnosed acute lymphoblastic leukemia who sign up to the NBCR are asked to provide a blood and/or marrow sample for LS17, which is sent to Prof Deb White’s lab at the South Australian Health and Medical Research Institute in Adelaide for phosphor-flow, Taqman Low Density Array (TLDA) and RNA-seq, with the aim of identifying the underlying genetic pathology. The laboratory results are correlated with clinical baseline characteristics held by the ALL registry of the NBCR, the other arm of the Regallia project. The overall aim is to further delineate the underlying pathobiology of high risk ALL cases, such as BCR-ABL1 like ALL, recently admitted into the WHO diagnostic criteria as a provisional entity.

This study is supported by Bristol-Myers Squibb and will recruit 150 participants over a three year period with information collected for up to five years. Molecular biology information gathered will be used to develop sensitive, specific and robust diagnostic assays for ALL diagnostics. In vitro sensitivity of various molecular lesions, as gathered by phosphor-flow, will predict for sensitivity to currently available small molecule inhibitors, allowing for planning of phase I/II clinical studies.

The study opened on 6/02/2017 at the Royal Adelaide Hospital (ADE). Sites participation to LS17 requires supplementary ethics and governance approval and additional sites will be opened to recruitment in 2018.

The study is open at the following sites: Alfred Hospital, Box Hill Hospital, Princess Alexandra Hospital, Royal Adelaide Hospital, Royal Brisbane and Women’s Hospital, Royal Melbourne Hospital, St George Hospital, and Westmead Hospital. Current accrual 42 participants: Target accrual: 150 participants.
Trial chief investigator
A/Prof Andrew Wei

Laboratory Research
This non-interventional Celgene-funded project aims to:
• determine the incidence of mutations in the catalytic domain of IDH (IDH1-R132, IDH2-R172 and IDH2-R140) within the cohort of AML patients registered on the NBCR,
• assess the therapeutic landscape of patients with these mutations at diagnosis,
• document patterns of associated gene mutations,
• expand the treatment regimens administered to IDH1/2 positive patients.

2018 status
Evidence supporting the outcomes for patients harbouring the IDH1/2 mutations is conflicting with reports suggesting a favourable prognosis for intermediate risk patients and other studies indicating an overall decrease of their survival rate.

With the scope to gain a better understanding of the management and outcomes of this patient cohort, data from a total of 425 AML patients who have been tested for the presence of any of the three IDH mutations will be collected and analysed. The project was launched on 30th November 2017. During 2018 the accrual reached 188 participants.
The **NBCR** was established by the ALLG in 2012 to collect information on AML clinical practice and as a pathway for registration to ALLG investigator initiated clinical trials.

Initially, the NBCR collected clinical data of participants diagnosed with Acute Myeloid Leukaemia (AML) and four types of Uncommon Lymphoma (UL). Since the beginning of 2017, those diagnosed with Acute Lymphoblastic Leukaemia (ALL) have been able to volunteer to join the NBCR.

Patients provide informed consent for the collection of clinical and laboratory data and the optional provision of biobanking blood and bone marrow samples. Data regarding base line demographics, AML diagnosis, treatment, response, transplantation and clinical outcomes.

At 31 December 2018, 1219 cases of AML treated at 37 centres have been registered. The median age is 59 years (range 16-92). WHO disease and cytogenetic classification are verified by central medical monitors using de-identified FBE, bone marrow morphology, flow cytometric, cytogenetic and molecular reports scanned into the NBCR.

During 2018, two laboratory science projects have been running under the NBCR: LS17 and LS18. The LS17 is an ALL study, which centres on the identification of new molecular features that have an impact on patients’ survival with the view to aid future discovery of novel drugs. At present, 47 participants have enrolled in LS17.

The LS18 is an AML study focussing on patients presenting a particular set of mutations that have become relevant to the AML therapeutic landscape. Since LS18 commencement in late 2017, 188 AML patients have been recruited to the study.

In 2018, the ALLG received 6 requests for data, which will be included in international scientific publications. Looking forward into 2019, the ALLG will be increasing data acquisition to better promote the availability of the NBCR clinical information and tissue samples to the scientific community. Further to this, the ALLG will continue to seek financial support for the NBCR activities to ensure the ongoing financial viability of this crucial platform.

The **ALLG Biobank**, located at the Hunter Cancer Biobank (HCB) Newcastle, New South Wales, is the central biorepository that receives, processes, stores and distributes a wide array of bio-specimens from human tissue samples including blood, bone marrow, plasma, and DNA.

These bio-specimens are collected from donors with a haematological malignancy who are participating in ALLG investigator initiated clinical trials and the ALLG National Blood Cancer Registry (NBCR).

**Eva-Rachele Pesce, PhD**
**NBCR Coordinator**

**Adele V Lee**
**Biobank Coordinator**
Baseline Characteristics

Age, median years (range) 59 (16 –92)

White cell counts (x 10^9/L), median (IQR) 6.9 (2.3 –32.4)

MRC 2010 cytogenetic classification, %
- Favourable 16
- Intermediate 64
- Adverse 20

Gene mutations, % (proportion with available data)
- FLT3-ITD positive (71%) 23
- NPM1 (56%) 35
- IDH1 or IDH2 (16%) 29

WHO 2008 classification
- Not otherwise specified (Available for 69%) 28.4
- Myelodysplasia-related changes 23.6
- Provisional (mutated NPM1 or CEBPA) 17.4
- Recurrent genetic abnormalities 16.9
- Therapy-related myeloid neoplasms 4.9
- Unknown or other diagnoses 8.8

Biobank Specimens 2018

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>PARTICIPANTS</th>
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<td>NBCR ALL</td>
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Trials Closed to Accrual
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Acute Leukaemia & Myelodysplasia

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<td>AMLM15</td>
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Chronic Myeloid Leukaemia & Myeloproliferative Neoplasms (CML & MPN)

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High Grade Non-Hodgkin Lymphoma & Hodgkins Lymphoma (HG NHL & HL)

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Low Grade Non-Hodgkin Lymphoma & Chronic Lymphocytic Leukaemia (LG NHL & CLL)

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Myeloma

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Supportive Care

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Laboratory Science

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<td>LS13</td>
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<td>LS14</td>
<td>73</td>
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</table>
**ALL05**

A Phase II Study of Dasatinib Combined with Induction Chemotherapy in Previously Untreated de novo Philadelphia Chromosome-Positive Acute Lymphoblastic Leukaemia.

**Trial chief investigator**
Prof Andrew Grigg

**Main trial objectives**
Investigation of the safety and tolerability of dasatinib in combination with induction chemotherapy for Ph+ ALL.

**Trial status:** Manuscript in preparation; publication expected 2019

**Date study opened:** 14/10/2008

**Accrual target (ALLG):** 20

**Final accrual (ALLG):** 20

**Participating sites:** 9

**Number of sites with patients entered:** 6

**Date study closed to accrual:** 27/04/2012

**Reason for closure:** Reached accrual target

**Support:** Bristol-Myers Squibb

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**AMLM15**

A pilot study exploring high-dose lenalidomide maintenance therapy in adult AML.

**Trial chief investigator**
A/Prof Andrew Wei

**Main trial objectives**
**Primary objectives**
1. To assess safety and tolerability of lenalidomide maintenance in AML patients in 1st remission;
2. To determine the MTD of Lenalidomide during the first cycle of maintenance therapy.

**Trial status:** Manuscript in preparation; publication expected 2019

**Date study opened:** 19/08/2011

**Accrual target (ALLG):** Approx 30-50

**Final accrual (ALLG):** Registration Phase: 98 | Maintenance Phase: 45

**Participating sites:** 10

**Number of sites with patients entered:** 10

**Date study closed to accrual:** 14/05/2015

**Reason for closure:** Reached accrual target

**Support:** Celgene Pty Ltd
### AMLM17

**A Strategy of High-Dose Lenalidomide in Combination with Epigenetic Therapies for Relapsed or Refractory Acute Myeloid Leukaemia**

**Trial chief investigator**
A/Prof Andrew Wei  
Dr Peter Tan

**Main trial objectives**

**Phase I**
- To determine the maximum tolerated dose of romidepsin when used in combination with lenalidomide for the treatment of patients with relapsed or refractory AML.

**Phase II**
- To investigate the efficacy of two novel treatments (high dose lenalidomide + azacitidine and high dose lenalidomide + romidepsin) compared with a control treatment (high dose lenalidomide alone) in patients with relapsed or refractory AML as measured by the complete remission (CR or CRi) rate following two cycles of therapy.

**Trial status:** Manuscript in preparation; publication expected 2019  
**Date study opened:** 06/11/2013  
**Accrual target (ALLG):** Phase I: 18 | Phase II: 120  
**Final accrual (ALLG):** Phase I (Cohort A): 2  
**Participating sites:** 3  
**Number of sites with patients entered:** 3  
**Date study closed to accrual:** March 2017  
**Reason for closure:** Issue with treatment efficiency and delivery  
**Support:** Celgene Pty Ltd

### AMLM20

**A programme of development for older patients with acute myeloid leukaemia and high-risk myelodysplastic syndrome.**

**Trial chief investigator**
A/Prof Andrew Wei

**Main trial objectives**
The primary objective is to compare Low Dose Ara-C (LD Ara-C) versus available novel approaches.

**Trial status:** Closed to Recruitment in Australia. Close out to occur in 2019  
**Date study opened:** 23/02/2016  
**Accrual target (INT):** 1000  
**Accrual target (ALLG):** 60  
**Final accrual (INT):** 883  
**Final accrual (ALLG):** 3  
**Participating sites:** 5  
**Number of sites with patients entered:** 2  
**Date study closed to accrual:** 06/04/2017  
**Reason for closure:** Inadequate accrual  
**Support:** The Leukaemia Foundation Australia
A pilot study exploring high-dose lenalidomide maintenance therapy in adult AML.

**Trial chief investigator**
Prof John Seymour

**Main trial objectives**
The primary objective is to demonstrate improved efficacy with the combination of LEN and AZA compared to AZA alone in patients with MDS, nonproliferative CMML and low marrow blast count AML, with acceptable toxicity of the combination.

**Trial status**: Manuscript published 2018

**Date study opened**: 13/12/2010

**Accrual target (ALLG)**: 160

**Final accrual (ALLG)**: 160

**Participating sites**: 30

**Number of sites with patients entered**: 28

**Date study closed to accrual**: 03/12/2013

**Reason for closure**: Reached accrual target

**Support**: Celgene Pty Ltd
**BM06**

Phase III Clinical Study of Allogeneic Stem Cell Transplantation with Reduced Conditioning (RICT) versus Best Standard of Care in Acute Myeloid Leukemia (AML) in First Complete Remission.

**Trial chief investigator**
Prof David Ritchie  
Mats Brune (MD, PhD, Sweden)

**Collaborating Group**
Transatlantic Leukemia Study Group (TRALG)  
Canadian Blood and Marrow Transplantation Group

**Main trial objectives**
The primary objective of this study is to determine in a group of elderly AML CR1 patients with a potential matched sibling donor (MSD) whether a reduced intensity conditioning transplantation (RICT) leads to a superior overall survival compared to standard of care. Primary endpoint is Overall Survival.

**Trial status**: Interim report publish 2018, full publication expected 2019

**Date study opened**: 11/08/2014

**Accrual target (INT)**: 320

**Accrual target (ALLG)**: 30-40

**Final accrual (INT)**: 360

**Final accrual (ALLG)**: 14

**Participating sites**: 5

**Number of sites with patients entered**: 2

**Date study closed to accrual**: 30/06/2016

**Reason for closure**: Reached accrual

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**BM07**

A treatment algorithm evaluating the effect of zoledronic acid on bone mineral density loss after allogeneic stem cell transplantation.

**Trial chief investigator**
Prof Andrew Grigg

**Main trial objectives**
To investigate the prophylactic use of zoledronic acid prior to allogeneic stem cell transplant (alloSCT) to alleviate the bone mineral density loss normally associated with BMT and subsequent steroid therapy as determined at day 100 and day 365 post-transplant compared with baseline, where day 0 is the day of transplant.

**Trial status**: Published

**Date study opened**: 06/08/2008

**Accrual target (ALLG)**: 120

**Final accrual (ALLG)**: 82

**Participating sites**: 8

**Number of sites with patients entered**: 7

**Date study closed to accrual**: 16/08/2013

**Reason for closure**: Interim analysis number achieved

**Support**: Novartis Australia
CML10


Trial chief investigator
Prof Timothy Hughes

Main trial objectives
TKI Registry
To collect the range and frequency of indications for TKI cessation.

STOP Registry
To determine the clinical status of patients changing to a next-line therapy.

Correlative Studies
In patients commencing another TKI therapy, correlate results of other assays with the response to next-line therapy.

Trial status: Publication expected 2019
Date study opened: 08/06/2010
Accrual target (ALLG): TKI Registry: 1,000 | STOP Registry: 200 | Correlative Studies: 60
Final accrual (ALLG): TKI Registry: 679 | STOP Registry: 157 | Correlative Studies: 90
Participating sites: 22
Number of sites with patients entered: 21
Date study closed to accrual: 30/11/2015
Reason for closure: Reached accrual target
Support: Novartis Australia, Bristol-Myers Squibb

CML11

Phase II study of nilotinib plus pegylated interferon alfa-2b as first-line therapy in chronic phase CML aiming to maximize CMR and MMR.

Trial chief investigator
Prof Timothy Hughes
Prof Andrew Grigg
Dr David Yeung

Main trial objectives
To determine the rate of MMR at 12 months and MR4.5 at 24 months, defined as BCR-ABL RQ-PCR ≤0.1% and ≤0.0032% (IS) respectively, in patients treated with nilotinib up front, followed by introduction of pegylated interferon alfa-2b at 3 months in addition to continuing treatment with nilotinib.

Trial status: Presentation and publication for ASH expected 2019
Date study opened: 03/04/2014
Accrual target (ALLG): 60
Final accrual (ALLG): 60
Participating sites: 14
Number of sites with patients entered: 12
Date study closed to accrual: 17/02/2017
Reason for closure: Reached accrual target
Support: Novartis Australia, MDS
A randomised trial to compare aspirin vs hydroxyurea/aspirin in ‘intermediate risk’ primary thrombocythaemia and aspirin only with observation in ‘low risk’ primary thrombocythaemia.

**Trial chief investigator**
Dr Cecily Forsyth

**Main trial objectives**
1. To assess the incidence of thrombosis and major haemorrhage while receiving Aspirin in low risk patients.
2. To assess if use of Hydroxyurea (also known as hydroxycarbamide) in intermediate risk patients reduces the number of thromboses and major haemorrhage events when added to aspirin.
3. What is the effect of the treatment modalities on quality of life?
4. High risk patients were initially randomised and some treated with anagrelide. Collection of data to continue to assess the incidence of thrombosis and major haemorrhage long term.

**Trial status**: Publication expected 2019
**Date study opened**: 01/08/1997
**Accrual target (INT)**: Low Risk Arm: 250 / Intermediate Risk Arm: 560
**Accrual target (ALLG)**: 50
**Final accrual (INT)**: 1,403 [Low Risk Arm: 259 / Intermediate Risk Arm: 377 / High Risk Arm: 809]
**Final accrual (ALLG)**: 47
**Participating sites**: 10
**Number of sites with patients entered**: 7
**Date study closed to accrual**: 30/04/2013
**Reason for closure**: The decision to close recruitment a year early was made per the advice of the Trial Steering Committee to allow the collection of follow-up data prior to complete trial closure
**Support**: Orphan
## HD08

A randomised Phase III trial to assess response adapted therapy using FDG-PET imaging in patients with newly diagnosed, advanced Hodgkin Lymphoma.

** Trial chief investigator  
Dr Leanne Berkahn  
Prof Judith Trotman  

** Main trial objectives  
This study will test the hypotheses:  
1. Can FDG-PET imaging be reproducibly and effectively applied in the early assessment of response to chemotherapy for a risk-adapted treatment strategy in advanced Hodgkin lymphoma?  
2. Can a negative FDG-PET scan after 2 cycles of ABVD chemotherapy be used to predict a group in which it is safe to reduce therapy by the subsequent omission of bleomycin, without detriment to their progression-free survival?  
3. Does treatment intensification in response to positive FDG-PET imaging after 2 cycles of ABVD improve the outcome by comparison with previous series?

<table>
<thead>
<tr>
<th>Trial status</th>
<th>Date study opened</th>
<th>Accrual target (INT)</th>
<th>Accrual target (ALLG)</th>
<th>Final accrual (INT)</th>
<th>Final accrual (ALLG)</th>
<th>Participating sites</th>
<th>Number of sites with patients entered</th>
<th>Date study closed to accrual</th>
<th>Reason for closure</th>
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<td>100</td>
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<td>85</td>
<td>17</td>
<td>16</td>
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<td>Reached accrual target</td>
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## NHL21

Early treatment intensification with R-ICE chemotherapy followed by autologous stem cell transplantation using Z-BEAM for patients with poor prognosis diffuse large B-Cell lymphoma as identified by interim PET/CT scan performed after four cycles of R-CHOP-14 chemotherapy.

** Trial chief investigator  
Prof Mark Hertzberg  
Prof Rodney Hicks  

** Main trial objectives  
The primary objective is to demonstrate an absolute improvement of 25% in two-year progression-free survival (PFS) from 40% to 65% in those patients with advanced stage DLBCL who have been identified with a positive interim treatment PET/CT scan and switched to early treatment intensification using R-ICE chemotherapy followed by HDCT/ ASCT in comparison with historical outcomes.

<table>
<thead>
<tr>
<th>Trial status</th>
<th>Date study opened</th>
<th>Accrual target (ALLG)</th>
<th>Final accrual (ALLG)</th>
<th>Participating sites</th>
<th>Number of sites with patients entered</th>
<th>Date study closed to accrual</th>
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<tr>
<td>Manuscript published 2018</td>
<td>06/05/2009</td>
<td>165</td>
<td>162</td>
<td>23</td>
<td>20</td>
<td>22/01/2013</td>
<td>Reached accrual target of PET positive patients</td>
<td>Bayer, Roche, Amgen</td>
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</table>
**NHL24**

Rituximab in Primary Central Nervous System Lymphoma. A randomized HOVON/ALLG intergroup study.

**Trial chief investigator**
Dr Samar Issa

**Main trial objectives**

**Primary objective:**
To assess the effect of the addition of rituximab in a standard chemotherapy regime on EFS in newly diagnosed PCNSL.

**Secondary objective:**
To evaluate the effect of the addition of rituximab to a standard chemotherapy regimen with respect to toxicity.

**Trial status:** Published 2018

**Date study opened:** 16/11/2010

**Accrual target (INT):** 200 (100 per arm)

**Accrual target (ALLG):** 80

**Final accrual (INT):** 202

**Final accrual (ALLG):** 43

**Participating sites:** 11

**Number of sites with patients entered:** 8

**Date study closed to accrual:** 30/05/2016

**Reason for closure:** Reached accrual target

**Support:** Roche

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**NHL25**

Double Blind Randomized Phase III study of lenalidomide (REVLIMID®) maintenance versus placebo in responding elderly patients with DLBCL and treated with R-CHOP in first line.

**Trial chief investigator**
Prof Judith Trotman

**Main trial objectives**

**Primary objective:**
To determine the benefit estimated by the progression-free survival associated with lenalidomide maintenance compared to placebo in responding patients treated in first line with R-CHOP for diffuse large B-cell lymphoma.

**Secondary objectives:**
1. percentage of patients who convert from PR to CR;
2. efficacy according to the response to R-CHOP;
3. overall survival in both groups of patients (with and without lenalidomide maintenance);
4. safety of lenalidomide in maintenance.

**Trial status:** Publication planned 2019

**Date study opened:** 01/05/2009

**Accrual target (INT):** 621 (Randomized Patients)

**Accrual target (ALLG):** 80

**Final accrual (INT):** 650 (Randomized Patients)

**Final accrual (ALLG):** 54 (Registered); 49 (Randomized)

**Participating sites:** 14

**Number of sites with patients entered:** 12

**Date study closed to accrual:** 08/09/2014

**Reason for closure:** Reached global accrual target

**Support:** Celgene Pty Ltd
CLL05

An Australasian, Phase II, multicentre, randomised, dose intensification study investigating oral fludarabine, oral cyclophosphamide and i.v. rituximab (poFCivR) tolerance in previously untreated elderly (65 years old or over) patients with chronic lymphocytic leukaemia (CLL).

**Trial chief investigator**
Prof Stephen Mulligan

**Main trial objectives**
To investigate the safety and tolerability of oral fludarabine plus i.v. rituximab (FR5), and oral fludarabine plus oral cyclophosphamide in varying dose intensity with i.v. rituximab (FCR3 and FCR5), in patients 65 years old or over with previously untreated CLL.

**Trial status:** Publication expected 2019

**Date study opened:** 28/10/2008

**Accrual target (ALLG):** 120

**Final accrual (ALLG):** 120

**Participating sites:** 29

**Number of sites with patients entered:** 29

**Date study closed to accrual:** 19/07/2012

**Reason for closure:** Reached accrual target

**Support:** Roche, Bayer

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CLL07

An Australasian, phase II, multicentre, randomised, study investigating safety and efficacy for dose reduced fludarabine, cyclophosphamide and i.v. obinutuzumab (G-FC3) versus oral chlorambucil and i.v. obinutuzumab (G-Clb) in previously untreated, comorbid (CIRS score ≥6), elderly (≥65 years old) patients with chronic lymphocytic leukaemia (CLL).

**Trial chief investigator**
Prof Stephen Mulligan
A/Prof Constantine Tam
Dr Xavier Badoux

**Main trial objectives**
The primary objective is to evaluate the safety of G-FC3 and G-Clb as measured by the incidence of grade 3+ non-haematological and grade 4 haematological adverse events.

**Trial status:** Closed to Accrual

**Date study opened:** 22/09/2015

**Accrual target (ALLG):** 32

**Final accrual (ALLG):** 32

**Participating sites:** 11

**Number of sites with patients entered:** 7

**Date study closed to accrual:** 21/11/2017

**Reason for closure:** Reached accrual target

**Support:** Roche
NHL14

An intergroup randomised trial of rituximab versus a watch and wait strategy in patients with advanced stage, asymptomatic, non-bulky follicular lymphoma (Grades 1, 2 and 3a).

**Trial chief investigator**
Prof Ken Bradstock

**Main trial objectives**
A randomised phase III trial to determine whether initial treatment with rituximab in patients with advanced stage asymptomatic follicular lymphoma (grades 1, 2 and 3a) results in a significant delay in the initiation of chemotherapy or radiotherapy and the impact of each strategy on patient-related quality of life.

**Trial status:** In follow up
**Date study opened:** 01/12/2006
**Accrual target (INT):** 360
**Accrual target (ALLG):** 100
**Final accrual (INT):** 360
**Final accrual (ALLG):** 78
**Participating sites:** 28
**Number of sites with patients entered:** 23
**Date study closed to accrual:** 01/05/2009
**Reason for closure:**Reached accrual target
**Support:** Roche

NHL16

A multicentre, phase III, open-label, randomized study in patients with advanced follicular lymphoma evaluating the benefit of maintenance therapy with Rituximab (MabThera®) after induction of response with chemotherapy plus Rituximab in comparison with no maintenance therapy (PRIMA).

**Trial chief investigator**
Prof John Seymour

**Main trial objectives**
To evaluate the benefit of maintenance therapy with rituximab as measured by progression-free survival (PFS) in comparison with no maintenance therapy after induction of response with chemotherapy plus rituximab in patients with high tumour burden follicular lymphoma.

**Trial status:** Publication expected 2019
**Date study opened:** 30/12/2004
**Accrual target (INT):** 1200
**Accrual target (ALLG):** 120
**Final accrual (INT):** 1200
**Final accrual (ALLG):** 158
**Participating sites:** 31
**Number of sites with patients entered:** 30
**Date study closed to accrual:** 01/07/2007
**Reason for closure:** Inadequate accrual
**Support:** Roche Australia, Roche NZ
A phase 3 open label randomized study to compare the efficacy and safety of rituximab plus lenalidomide (CC-5013) versus rituximab plus chemotherapy followed by rituximab in subjects with previously untreated follicular lymphoma.

**Trial chief investigator**
Dr Pauline Warburton

**Main trial objectives**
The primary objective of the study is to compare the efficacy of rituximab plus lenalidomide to rituximab plus chemotherapy followed by rituximab in patients with previously untreated follicular lymphoma. Efficacy determination will be based upon the co-primary endpoints of complete response (CR/CRu) rate at 120 weeks and PFS assessed by the IRC using the IWG (Cheson, 1999) criteria.

<table>
<thead>
<tr>
<th>Trial status:</th>
<th>Published 2018</th>
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<tbody>
<tr>
<td>Date study opened:</td>
<td>14/08/2014</td>
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<tr>
<td>Accrual target (INT):</td>
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<tr>
<td>Accrual target (ALLG):</td>
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<td>Final accrual (ALLG):</td>
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<td>Number of sites with patients entered:</td>
<td>1</td>
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<tr>
<td>Date study closed to accrual:</td>
<td>10/11/2014</td>
</tr>
<tr>
<td>Reason for closure:</td>
<td>Reached global accrual target</td>
</tr>
</tbody>
</table>
A randomized open-label multicentre phase III trial of Melphalan and Dexamethasone (MDex) vs Bortezomib, Melphalan and Dexamethasone (BMDex) for untreated patients with systemic light-chain (AL) amyloidosis.

**Trial chief investigator**
A/Prof Peter Mollee

**Collaborating Group**
European Myeloma Network (EMN)

**Main trial objectives**

**Primary objective:**
To compare in patients treated with MDex or BMDex haematologic response after 3 cycles.

**Secondary objectives:**
To compare in patients treated with MDex or BMDex:
1. complete haematologic response rate after 3 cycles and after completion of therapy;
2. haematologic response rate at completion of therapy;
3. organ response rates at 3, 6, 9 and 12 months;
4. treatment-related mortality;
5. toxicity;
6. overall and progression-free survival;
7. time to haematologic and organ response;
8. quality of life.

A prospective randomised Phase II study of single agent pomalidomide maintenance versus combination pomalidomide and low dose dexamethasone maintenance following induction with the combination of pomalidomide and low dose dexamethasone in patients with relapsed and refractory myeloma previously treated with lenalidomide.

**Trial chief investigator**
Prof Andrew Spencer
Dr Anna Kalff

**Main trial objectives**

1. To evaluate the change in NK cell quantification (an increase in 30% of NK cell numbers in the pom arm compared to pom-dex): assessed by flow cytometry of CD3-CD56+CD16+PBMC that were collected at start of induction and at maintenance cycle 6.

2. The change in NK cell function (an increase of NK-cell lysis by 30% in the pom arm compared to pom-dex): assessed via lysis of 51Cr-labelled K562, and myeloma cell lines (e.g. U266) in vitro at different effector: target ratios using patients’ PBMC that were collected at start of induction and at maintenance cycle 6.
A randomized phase III study to compare Bortezomib, Melphalan, Prednisone (VMP) with High Dose Melphalan followed by Bortezomib, Lenalidomide, Dexamethasone (VRD) consolidation and Lenalidomide maintenance in patients with newly diagnosed multiple myeloma.

**Trial chief investigator**
Prof Andrew Spencer
Dr Hang Quach

**Collaborating Group**
European Myeloma Network (EMN)

**Main trial objectives**

- To assess the efficacy of VMP versus high-dose therapy (HDT) and stem cell transplantation in patients with previously untreated multiple myeloma, as measured by the progression free survival.

- To evaluate the effect of consolidation with VRD followed by Lenalidomide maintenance with no consolidation but Lenalidomide maintenance alone on progression free survival.

**Trial status**: Publication expected 2019

**Date study opened**: 01/08/2013

**Accrual target (INT)**: 1500

**Accrual target (ALLG)**: 150

**Final accrual (INT)**: 1500

**Final accrual (ALLG)**: 17

**Participating sites**: 7

**Number of sites with patients entered**: 4

**Date study closed to accrual**: 15/04/2014

**Reason for closure**: Reached global accrual target
Phase II of a novel telehealth-mediated nurse-led intervention to increase oral cancer therapy adherence amongst people with Chronic Myeloid Leukaemia (CML).

**Trial chief investigator**
A/Prof Penelope Schofield

**Main trial objectives**
To evaluate a nurse-led, telehealth-mediated intervention employing web and mobile based reminder systems (Remind) to help people with CML improve adherence to their oral medication and effectively manage medication side-effects better.

<table>
<thead>
<tr>
<th>Trial status</th>
<th>Published 2018</th>
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<tbody>
<tr>
<td>Date study opened</td>
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<tr>
<td>Accrual target (ALLG)</td>
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<tr>
<td>Final accrual (ALLG)</td>
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<td>Participating sites</td>
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<td>Number of sites with patients entered</td>
<td>4</td>
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<td>Date study closed to accrual</td>
<td>19/03/2015</td>
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<tr>
<td>Reason for closure</td>
<td>Inadequate accrual</td>
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</table>
Trials Closed to Accrual

A phase II trial in patients with previously untreated acute promyelocytic leukaemia to evaluate the effects of: (i) adding arsenic trioxide to all-trans retinoic acid and idarubicin for remission induction, and (ii) adding arsenic trioxide to all-trans retinoic acid as consolidation.

**Trial chief investigator**
Prof Harry Iland

**Chief investigator**
A/Prof Frank Firkin

**Lab Research**
Arsenic levels in relation to toxicity and efficacy in APML. Frank Firkin has been involved in an extensive study on the question of whether toxicities in APML4 were due to arsenic, and how this relates to blood arsenic levels.

2018 Status
Accumulation of arsenic in blood during induction and consolidation resulted in mean levels of 1.5 μM at completion of each cycle. The arsenic concentration in erythrocytes was twice that of serum with a substantially greater proportion as inorganic arsenic, to suggest tissue inorganic arsenic is likely to be substantially greater than measured in serum, where the predominant methylated arsenic catabolic profile more closely resembles that excreted in urine. The kinetic picture was consistent with progressive accumulation of arsenic to a steady state with most arsenic in methylated form of uncertain clinical significance, in contrast to the rapid elimination inferred from single dose studies. The overall range of blood arsenic levels was associated with molecular remission, and while there was a trend for toxicities to be associated with higher levels, statistical significance was not achieved due to the multiplicity of confounding clinical variables.

Laboratory Science

**LS13**

Biomarkers to assist clinical outcomes in patients with lymphoma.

**Trial chief investigator**
Prof Maher Gandhi

2018 Status
Sample acquisition and sample analysis. In 40% of cases of classical Hodgkin lymphoma (cHL), Epstein-Barr virus (EBV) latency-II antigens [EBV nuclear antigen 1 (EBNA1)/latent membrane protein (LMP)1/LMP2A] are present (EBV1cHL) in the malignant cells and antigen presentation is intact. Previous studies have shown consistently that HLA-A*02 is protective in EBV1cHL, yet its role in disease pathogenesis is unknown. To explore the basis for this observation, gene expression was assessed in 33 cHL nodes. Interestingly, CD8 and LMP2A expression were correlated strongly and, for a given LMP2A level, CD8 was elevated markedly in HLA-A*02– versus HLA-A*021 EBV1cHL patients, suggesting that LMP2A-specific CD81 T cell anti-tumoral immunity may be relatively ineffective in HLA-A*02– EBV1cHL. To ascertain the impact of HLA class I on EBV latency antigen-specific immunodominance, we used a stepwise functional T cell approach. In newly diagnosed EBV1cHL, the magnitude of ex-vivo LMP1/2A-specific CD81 T cell responses was elevated in HLA-A*021 patients. Furthermore, in a controlled in-vitro assay, LMP2A-specific CD81 T cells from healthy HLAA*02 heterozygotes expanded to a greater extent with HLAA*02-restricted compared to non-HLA-A*02-restricted cell lines. In an extensive analysis of HLA class I-restricted immunity, immunodominant EBNA3A/3B/3C specific CD81 T cell responses were stimulated by numerous HLA class I molecules, whereas the subdominant LMP1/2Aspecific responses were confined largely to HLA-A*02. Our results demonstrate that HLAA*02 mediates a modest, but none the less strong, EBV-specific CD81 T cell response than non-HLA-A*02 alleles, an effect confined to EBV latency-II antigens. Thus, the protective effect of HLA-A*02 against EBV1cHL is not a surrogate association but reflects the impact of HLA class I on EBV latency-II antigen-specific CD81 T cell hierarchies.

Results were presented as an oral abstract at ASH 2013 and published in Clinical and Experimental Immunology, 2016 Feb;183(2):206-20. ‘The impact of HLA class I and EBV latency-II antigen-specific CD8+ T cells on the pathogenesis of EBV1 Hodgkin lymphoma.’
LS14

Wt-1 expression levels as a marker of Minimal Residual Disease (MRD) in AML.

**Trial chief investigator**
A/Prof Paula Marlton  
Mr Russell Saal

**2018 Status**
Sample acquisition and sample analysis. Sample collection is proceeding as part of the AMLM12 trial and independent of the trial at PAH. Peripheral blood samples have been tested for Wt-1 transcript levels at diagnosis. Over-expression was confirmed in a high proportion of cases. Diagnostic levels have been correlated with overall survival. Increasing levels of Wt-1 correlated with poorer survival within cytogenic risk group. MRD testing has been largely completed. Statistical analysis to correlate with outcome is ongoing. Results published in 2018.
Publications, Presentations & Abbreviations
<table>
<thead>
<tr>
<th>Trial</th>
<th>Title</th>
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<tbody>
<tr>
<td>AMLM_X22</td>
<td>Tiong IS, Reynolds J, Bradstock KF, Seymour JF and Wei AH, on behalf of the Australasian Leukaemia &amp; Lymphoma Group. Dissecting causes for improved survival among patients with acute myeloid leukemia in two different eras receiving identical regimens in sequential randomized studies. Blood Cancer Journal 8:84</td>
</tr>
<tr>
<td>SUPPORTIVE CARE DISEASE GROUP</td>
<td>J Wong, EM Wood, P Crispir, R Weinkove on behalf of the Australasian Leukaemia and Lymphoma Group (ALLG) Supportive Care Group. Managing hypogammaglobulinaemia secondary to haematological malignancies in Australia and New Zealand: a clinician survey. Internal Medicine Journal e pub 21 August 2018</td>
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<td>Trial</td>
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2016

Trial  Title


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<td>Trial</td>
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2018

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<tbody>
<tr>
<td>AMLM20</td>
<td>Hills RK, Thomas I, Burnett AK, Hemmaway CJ, Dignum H, Russell NH and Dennis M. The Achievement of Complete Remission Is Associated with Improved Quality of Life in Non-Intensively Treated Patients with Acute Myeloid Leukemia: Results of the UK NCRI LI-1 Trial. 60th Annual Meeting of the American Society of Hematology, San Diego, 1-4 Dec 2018 (oral presentation)</td>
</tr>
<tr>
<td>CLL5</td>
<td>Mulligan SP, Gill D, Cull G, Berkahn L, Simpson D, Campbell P, Harrup RA, Mackinlay NJ, Tam CS, Badoux X, Best OG and BJ Kuss. Durable Responses in Fit Elderly Patients with Chronic Lymphocytic Leukemia (CLL) in a Randomised, Fludarabine-Based, Immunochemotherapy Dose-De-Escalation Study - Long-Term Follow-up By Treatment Arm and Mutational Status. 60th Annual Meeting of the American Society of Hematology, San Diego, 1-4 Dec 2018</td>
</tr>
<tr>
<td>CLL7</td>
<td>Mulligan SP, Freeman JA, Badoux X, Eek R, Cull G, Mackinlay NJ, Murphy NE, Carradice DP, Solterbeck AC, Best OG, Tam CS and Kuss BJ. Randomized Trial in Unfit, Elderly Chronic Lymphocytic Leukemia (CLL) Patients with Comorbidities of Dose-Reduced Oral Fludarabine and Cyclophosphamide Plus Obinutuzumab (FC+G) Versus Chlorambucil Plus Obinutuzumab (Cbl+G) As Front-Line Therapy. 60th Annual Meeting of the American Society of Hematology, San Diego, 1-4 Dec 2018</td>
</tr>
<tr>
<td>CML9</td>
<td>Kok CH, Paistrikangkrai S, Yeung DT, Liu L, Saunders VA, Dang P, Yong ASM, White DL and Hughes TP. Integration of Multiple Bioassays Using Machine Learning to Identify High-Risk CP-CML Patients Treated with Frontline Imatinib. 60th Annual Meeting of the American Society of Hematology, San Diego, 1-4 Dec 2018</td>
</tr>
<tr>
<td>MM16</td>
<td>Ho PJ, Spencer AS, Mollee PM, Enjeti AK, Horvath N, Bryant CE, Trotman J, Gibbs S and Joshua DE. Early Serum Free Light Chain (SFLC) Kinetics Is Highly Predictive of Renal Response in Carfilzomib/Dexamethasone (Cfz/Dex) in Myeloma (MM) Patients with Renal Impairment (RI) - Interim Analysis of the Australian ALLG MM16 Trial. 60th Annual Meeting of the American Society of Hematology, San Diego, 1-4 Dec 2018</td>
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<th>Trial</th>
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<tbody>
<tr>
<td><strong>APML04</strong></td>
<td>Iland H. The ALLG approach to incorporating arsenic trioxide: APML4 (final analysis) and APML5 (encapsulating therapy). 7th International Symposium on Acute Promyelocytic Leukaemia, September 2017, Rome. (invited oral presentation)</td>
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## 2017

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<th>Trial</th>
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<tbody>
<tr>
<td><strong>APML04</strong></td>
<td>Iland H. The ALLG approach to incorporating arsenic trioxide: APML4 (final analysis) and APML5 (encapsulating therapy). 7th International Symposium on Acute Promyelocytic Leukaemia, September 2017, Rome. (invited oral presentation)</td>
</tr>
<tr>
<td><strong>CML11</strong></td>
<td>Hughes A, Clarson J, White DL, Yeung D, Hughes TP and Yong ASM. Nilotinib in Combination with Pegylated Interferon Alfa-2b for CP-CML Leads to High Molecular Response Rates: Interim Results of the Pinnacle Study. American Society of Hematology Annual Meeting, Atlanta 9-12 December 2017</td>
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2017 (continued)

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<th>Trial</th>
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</table>


CML8, CML10  Hughes A, Clarson J, White DL, Ross DM, Hughes TP, Yong A. Enhanced Natural Killer and Cytotoxic T Lymphocyte Responses, with Decreased Monocytic Myeloid Derived Suppressor Cells May Promote Treatment Free Remission in Chronic Myeloid Leukemia Patients Following Tyrosine Kinase Inhibitor Cessation. American Society of Hematology 59th Annual Meeting; 3-6 December; San Diego. (oral presentation)

CML8, CML10  Shanmuganathan N, Branford S, Braley J, Hiwase D, Yeung DT, Ross DM, Hughes TP. For Patients with Sustained MR4-MR4.5, Less Frequent Molecular Monitoring during the First 12 Months after Tyrosine Kinase Inhibitor Cessation Is Viable for Timely Detection of Loss of MMR. American Society of Hematology 59th Annual Meeting; 3-6 December; San Diego.


CML9  Pagani I, Kok C, Wang J, Saunders V, Van der Hoeck M, Heatley S, Schwarer A, Hughes T, White D, Ross D. Mitochondrial DNA mutations at diagnosis are linked to response in TKI treated chronic myeloid leukaemia patient. HAA Annual Scientific Meeting; 13-16 November; Melbourne. (oral presentation)


### 2016 (continued)

#### Trial | Title
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**NHLLOW5** | MacManus M, Fisher R, Roos D, O’Brien P, Macann A, Tsang R, Christie D, McGuire B, Joseph D, Seymour J. Treatment with six cycles of CVP or R-CVP after involved field radiation therapy (IFRT) significantly improves progression-free survival compared to IFRT alone in stage I-II low grade follicular lymphoma: Results of TROG 99.03 / ALLG NHLLOW5. Royal Australian and New Zealand College of Radiologists Annual Scientific Meeting; 13-16 October; Gold Coast, Australia.

**NHLLOW5** | MacManus M, Fisher R, Roos D, O’Brien P, Macann A, Tsang R, Christie D, McGuire B, Joseph D, Seymour J. Treatment with six cycles of CVP or R-CVP after involved field radiation therapy (IFRT) significantly improves progression-free survival compared to IFRT alone in stage I-II low grade follicular lymphoma: Results of an international multicenter, randomized controlled trial. American Society for Radiation Oncology; 25-28 September; Boston. (oral presentation)

### 2015

#### CLL

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### 2015 (continued)

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<tbody>
<tr>
<td>CLL5</td>
<td>Sandhu S, Mackinlay N, Coyle L, Best G, Mulligan S. Detailed long-term follow-up of treatment-naïve Chronic Lymphocytic Leukaemia (CLL) patients in the Australasian Leukaemia and Lymphoma Group (ALLG) CLL5 Trial; data on 17 (15% of total cohort) patients from a single-institution. International Workshop in Chronic Lymphocytic Leukaemia; Sydney.</td>
</tr>
<tr>
<td>CLL7</td>
<td>Mulligan S, Tam C, Badoux X, Kuss B. A phase II study investigating safety and efficacy of dose reduced fludarabine, cyclophosphamide and obinutuzumab versus chlorambucil and obinutuzumab in untreated, comorbid, elderly patients with chronic lymphocytic leukaemia (CLL). International Workshop in Chronic Lymphocytic Leukaemia; Sydney.</td>
</tr>
<tr>
<td>CML6, CML9</td>
<td>Branford S, Yeung DT, Ross DM, Braley J, Seymour JF, Hughes TP. BCR-ABL1 levels at landmark time-points during imatinib therapy are predictive of time to a deep molecular response and can guide therapy switch decisions where treatment discontinuation is the goal for patients with CML. Annual Scientific Meeting of the HAA; Adelaide.</td>
</tr>
<tr>
<td>CML9</td>
<td>Eadie LN, Hughes TP. White DL. The clinical significance of early Imatinib induced ABCB1 overexpression in chronic phase CML Patients: A TIDEL II Sub-Study. American Society for Hematology Annual Meeting; San Diego.</td>
</tr>
<tr>
<td>CML9</td>
<td>Eadie LN, Hughes TP. White DL. The clinical significance of ABCB1 overexpression in predicting outcome of CML patients undergoing first-line imatinib treatment: A TIDEL II sub-study. Annual Scientific Meeting of the HAA; Adelaide.</td>
</tr>
<tr>
<td>CML9</td>
<td>Pagani I, Kok C, Heatley SL, Hughes TP. White DL, Ross DM. Mitochondrial DNA variants are common in CML patients. Annual Scientific Meeting of the HAA; Adelaide.</td>
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2015 (continued)

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<tr>
<th>Trial</th>
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<tbody>
<tr>
<td>MDS4</td>
<td>Kenealy M, Benson W, Stevenson W, Eek R, Zantomio D, Cunningham I, Hiwase DK, Cowan L, Vlachos S, Zannino D, Seymour JF. The addition of lenalidomide to azacitidine achieves higher responses but no improvement in twelve month clinical benefit or PFS; main analysis of the Australian ALLG MDS4 trial. Annual Scientific Meeting of the HAA; Adelaide.</td>
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<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<tr>
<td>ADR</td>
<td>Adverse drug reaction</td>
</tr>
<tr>
<td>AE</td>
<td>Adverse event</td>
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<tr>
<td>AGITG</td>
<td>Australasian Gastro-Intestinal Trials Group</td>
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<td>ALL</td>
<td>Acute lymphoblastic leukaemia</td>
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<td>ALLG</td>
<td>Australasian Leukaemia and Lymphoma Group</td>
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<td>ALTG</td>
<td>Australasian Lung Cancer Trials Group</td>
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<td>AML</td>
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<td>ANZ BCTG</td>
<td>Australian New Zealand Breast Cancer Trials Group</td>
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<td>ANZCHOG</td>
<td>Australian and New Zealand Children's Haematology Oncology Group</td>
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<td>ANZGOG</td>
<td>Australia New Zealand Gynaecological Oncology Group</td>
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<td>ANZCTR</td>
<td>Australian New Zealand Clinical Trials Registry</td>
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<td>ANZMGTG</td>
<td>Australia and New Zealand Melanoma Trials Group</td>
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<td>ANZUP</td>
<td>Australian and New Zealand Urogenital and Prostate Cancer Trials Group</td>
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<td>APML</td>
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<td>ASSG</td>
<td>Australasian Sarcoma Study Group</td>
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<tr>
<td>BaCT</td>
<td>Centre for Biostatistics and Clinical Trials</td>
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<tr>
<td>BCR-ABL</td>
<td>An oncogene fusion protein consisting of BCR and ABL</td>
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<td>BM</td>
<td>Bone marrow</td>
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<td>BMAT</td>
<td>Bone Marrow Aspirate and trephine</td>
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<tr>
<td>BMS</td>
<td>Bristol Myers Squibb</td>
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<td>CA</td>
<td>Cancer Australia</td>
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<tr>
<td>CBF</td>
<td>Core binding factor</td>
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<td>CML</td>
<td>Chronic myeloid leukaemia</td>
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<td>CMR</td>
<td>Complete Molecular Response</td>
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<tr>
<td>CNS</td>
<td>Central nervous system</td>
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<td>CNSL</td>
<td>Central nervous system lymphoma</td>
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<td>COGNO</td>
<td>Cooperative Trials Group for Neuro-Oncology:</td>
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<td>COSA</td>
<td>Clinical Oncology Society of Australia</td>
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<td>CRF</td>
<td>Case report form</td>
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<td>CSF</td>
<td>Cerebral spinal fluid</td>
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<td>CT</td>
<td>Computed Tomography (=CAT scan)</td>
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<td>CTA</td>
<td>Clinical Trials Australia</td>
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<td>CTN</td>
<td>Clinical trial notification</td>
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<td>CTRA</td>
<td>Clinical trial research agreement</td>
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<td>DGC</td>
<td>Disease Group Committee</td>
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<td>DLT</td>
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<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<td>Ethics Committee</td>
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<td>ECOG</td>
<td>Eastern Co-operative Oncology Group</td>
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<td>eCRF</td>
<td>Electronic case report form</td>
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<td>EORTC</td>
<td>European Organisation for Research and Treatment of Cancer</td>
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<td>FAC</td>
<td>Finance Audit Committee</td>
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<tr>
<td>FCR</td>
<td>Fludarabine, cyclophosphamide, rituximab chemotherapy</td>
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<td>Fli3</td>
<td>Fms-like tyrosine kinase 3</td>
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<td>GCP</td>
<td>Good Clinical Practice</td>
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<td>GELA</td>
<td>Groupe d’Etude des Lymphomes de l’Adulète, Trial Cooperative group France</td>
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<tr>
<td>GSK</td>
<td>GlaxoSmithKline</td>
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<tr>
<td>HCVAD</td>
<td>Hyper-CVAD (Cyclophosphamide, Vincristine, Daunorubicin, Desamethasone)</td>
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<td>HD</td>
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<tr>
<td>HE</td>
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<td>HOMER</td>
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<td>IB</td>
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<tr>
<td>ICE</td>
<td>Chemotherapy regimen- Ifosfamide, carboplatin and etoposide</td>
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<td>ICH GCP</td>
<td>International Conference on Harmonisation, Good Clinical Practice</td>
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<tr>
<td>IIT</td>
<td>Investigator-initiated trial</td>
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<tr>
<td>MBVP</td>
<td>Chemotherapy regimen- Methotrexate, Teniposide, BCNU and Prednisolone</td>
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<tr>
<td>MDS</td>
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<td>MM</td>
<td>Multiple myeloma</td>
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<td>MMR</td>
<td>Major molecular response</td>
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<td>MRD</td>
<td>Minimal residual disease</td>
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<td>memorandum of understanding</td>
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<td>NCI CTC</td>
<td>National Cancer Institute Common Toxicity Criteria</td>
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<td>NHL</td>
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<td>NMRC</td>
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<td>OS</td>
<td>Overall survival</td>
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<td>French trial: Stop Imatinib</td>
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<td>TCDM</td>
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<td>Victorian Cancer Agency</td>
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<td>WHO</td>
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</table>
Acknowledgement of Support and Sponsorship

Thank you for your contribution to the ALLG.

We gratefully acknowledge your support and sponsorship of ALLG Clinical Trials.
The Australasian Leukaemia & Lymphoma Group's 2018 Research Report is a collaboration of input from all involved with the ALLG.

Thank you.

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