Improving the treatment and the lives of patients with blood cancers through clinical trial research

AUSTRALASIAN LEUKAEMIA AND LYMPHOMA GROUP

Trials Newsletter No 3

August 2014

ALLG trials newsletter

This newsletter is published approximately every two months and provides update information on the ALLG trial program. Other ALLG activities are covered in the general newsletter published three times a year. To see the latest issue click HERE.

Megan Sanders
Program Manager
ALLG Trial Centre

Happy 1st Birthday to the ALLG Trial Centre!!!

The ALLG set up its own Trial Centre last July, with the purpose of allowing the group close day to day management for its trial portfolio. All new ALLG trials are now run in-house. Currently running from the ALLG Trial Centre are AMLM17, BM06, MM16, NHL26, NHL27 and CML11. A number of other trials will commence in the Trial Centre over the next few months including CLL7 and AMLM21. Congratulations to Program Manager Megan Sanders and the team! The Trial Centre is co-located with the ALLG Operations Unit. For more information contact Megan Sanders.

A new development is that there will also be a steady **transition of all trials previously run at BaCT to the ALLG Trial Centre**. Individual plans will be arranged with the trial PIs to ensure a smooth process. Some older trials may transition in September with others to follow in due course. Any questions can be directed to Delaine Smith.

ALLG Trial Centre

Program Manager	Megan Sanders
CRA	Sarah Dewberry
CRA	Bala Ravishankar
CRA	Briony Tupper

For more trial information visit the Members area at the ALLG website

Milestones

- **NHL15 RECRUITMENT SUSPENDED - TMC currently considering action**
- **BM06 first HREC approval in Australia**
- **NHL27 TO CLOSE INTERNATIONALLY LATE OCTOBER 2014**
- **AMLM17 cohort A complete, cohort B open**

Expressions of Interest

The ALLG Trial Centre is currently calling for Expressions of Interest for trial participation. Please reply to the survey registering your interest before the deadline to be considered.

Trial	PI	Contact person	Period for EOI
MM16 Phase II study assessing the effect of carfilzomib treatment on early free light chain kinetics in myeloma patients with renal impairment	Joy Ho	Sarah Dewberry	closed
CML11 PINNACLE Phase II study of nilotinib plus pegylated interferon alfa-2b as first-line therapy in chronic phase CML aiming to maximize CMR and MMR	David Yeung, Tim Hughes, Andrew Grigg	Briony Tupper	places remaining
CLL7 An Australasian, phase II, multicentre, randomised, study investigating efficacy and safety for dose reduced fludarabine, cyclophosphamide and iv obinutuzumab (G-FC3) vs oral chlorambucil and iv obinutuzumab (G-Clb) in previously untreated, comorbid (CIRS score ≥6), elderly (≥65 years old) patients with CLL	Stephen Mulligan, Xavier Badoux, Con Tam	TBA	Expected to open to EOI Q4 2014

Announcements and reminders

Trial	Comment	Contact person
CML10	Note change in contact details for ordering lab kits (see below for details)	Bronwyn Ortlepp
CML11	Sites with HREC approval should commence governance	Briony Tupper
AMLM18	Coordinator Thili Chengodu has resigned, all queries to Nola Kennedy	Nola Kennedy

Acute Leukaemia/MDS Disease Group

AML/MDS Disease Group Chair
Andrew Wei

AMLM21 phase Ib/II clinical evaluation of Ponatinib in combination with 5-azacitidine in patients failing prior therapy for FLT3-ITD positive AML
CI: Andrew Wei
This study of the FLT3-ITD inhibitor Ponatinib has two parts. The phase I component examines two dose schedules of azacitidine with 6 patients in each group. In Phase II of the study, patients will be randomly assigned to one of 3 groups: Ponatinib alone, azacitidine alone or both drugs. The target accrual is 87-93 patients over 2-3 years and the trial will be coordinated at the ALLG Trial Centre. The protocol was approved by the SDMC in June and internal budget and governance arrangements are being set up. It is hoped that EOI will be available in Q4 2014.

AMLM17
CI: Andrew Wei
CRA: Bala Ravishankar
The phase I study continues, with cohort A having enrolled the last patient in July. Cohort B in now open at two sites. EOIs for the phase II study have closed .

AMLM18 Registry is currently coordinated at the Alfred Hospital. The coordinator Thili Chengodu has recently resigned. For the present, please direct any queries to Nola Kennedy until a new coordinator is appointed. The ALLG is currently negotiating transition to eCRFs. At present only AML patients are being registered, but in the coming months the name will change to the National Blood Cancer Registry to reflect the inclusion of other diagnoses.

The Palifermin paper from the AMLM12 study has been **accepted for publication** in the Br J Haematol. Congratulations Ken Bradstock and all participants for the successful conclusion of this component of a flagship ALLG trial!

Aggressive NHL/HL Disease Group

High grade NHL/HL Disease Group Chair
Mark Hertzberg

NHL29 IRIC. A Phase II Study of Ibrutinib, Rituximab and mini-CHOP therapy in very elderly patients with newly diagnosed DLBCL
CIs: Judith Trotman, Emma Verner
The purpose of this new study is to assess the effects of Ibrutinib when it is given together with a reduced dose version of R- CHOP in patients aged >75 years who have been diagnosed with DLBCL. There has been little study of DLBCL therapy in this truly elderly population despite ~40% of cases occurring in patients over 70. With the increase in our aging population, DLBCL in the elderly will become more prevalent. Given the excellent tolerability of Ibrutinib in other lymphoma studies and early data supporting its benefit for the most common subtype of DLBCL, the aim is to improve the survival by combining it with standard treatment (R-mini-CHOP). One feature of the trial is that it will be run in Singapore in addition to Australia and NZ. Total target accrual is 80 over 3 years with 2 years follow up. The protocol underwent an initial review by the SDMC in July.

At the other end of the trial lifecycle, two old studies are currently being finalised. The **ALLG LY04/TROG 01.02 phase 2 study of idarubicin-based combined modality chemotherapy in primary CNS NHL** (PI Peter O'Brien) has reached its formal end. The trial accrued 20 patients between 2001 and 2006. Long term follow up ceased 9/7/2013 and all follow-up and data capture is now complete. Congratulations and thank you to all who participated for your efforts in helping to achieve this goal from both TROG and the ALLG. The study is currently being prepared for publication.

The **ALLG HDNHL4/TROG03.03 Prospective Multicentre Study of Involved-Field Radiotherapy with Transplantation for Patients with Hodgkin's Disease and NHL** (PI AndrewWirth) is also nearing completion. The study data are currently being updated and cleaned with a view to analysis later this year. Watch this space…..

Multiple Myeloma Disease Group

Multiple Myeloma Disease Group Chair
Peter Mollee

MM16 Phase II study assessing the effect of carfilzomib treatment on early free light chain kinetics in myeloma patients with renal impairment
CIs: Joy Ho, Doug Joshua
CRA: Sarah Dewberry ALLG Trial Centre
Newly diagnosed, relapsing or progressive myeloma patients with renal impairment will be given the new drug carfilzomib and serum free light chain (SFLC) measured to determine early effects of the drug on SFLC and SFLC correlation with kidney function after 4 months of treatment. The study will also investigate efficacy of the drug and time until progression. Target accrual is 36 -40. The protocol was approved by the SDMC in March and is expected to commence ethics submissions within the next two months

MM17 A multi-centre single arm study of carfilzomib-thalidomide-dexamethasone (CarTD) for newly diagnosed transplant-eligible multiple myeloma (MM) patients refractory to initial bortezomib-based induction therapy
CI: Andrew Spencer
Newly diagnosed myeloma patients planned to receive a stem cell transplant who respond poorly to their initial treatment have a poor outlook. The commonest initial treatment in Australia incorporates the drug bortezomib. New data has shown that patients who have failed treatment with this may respond to the similar drug carfilzomib. This study will examine the response to switching from bortezomib to carfilzomib early in the initial treatment. Target accrual is 50 over 3 years. The protocol is currently undergoing statistical review and will be submitted to the SDMC in Q4.

Currently under development is Hang Quach's proposal for a single arm study of **CATD (carfilzomib, thalidomide and dexamethasone) in patients with relapsed/refractory MM.** This study might see involvement from countries in Asia via the Asian Myeloma Network with the ALLG retaining overall sponsor responsibilites. There are a number of advantages to this regimen, including the fact that the carfilzomib/thalidomide combination, as opposed to lenalidomide, is a more affordable regimen that will be more applicable to the Asia-Pacific region. Hang Quach has been selected by the ALLG to attend the ACORD protocol development workshop to be held on the NSW Central Coast in September to develop the concept into a protocol.

Supportive Care Disease Group

Supportive Care Disease Group Chair: Con Tam

SC03 Controlling Chemotherapy Induced Nausea and Vomiting for Cancer Patients
CI: Christine Carrington
Nausea and vomiting are common side effects of cancer chemotherapy and both can significantly impact on a patient's wellbeing and quality of life while receiving cancer treatment or even lead to serious medical complications requiring extended hospitalisation. Currently, there is no consensus on the use of prophylactic antiemetics for R-CHOP in NHL. The outcome data from this study will assist in determining the optimal prophylactic antiemetic regimen to minimise the occurrence of CINV. These issues have never been investigated previously in this patient population. The SC03 study was previously approved by the SDMC but budgetary issues have delayed its implementation. Most recently it has **been submitted to the Leukaemia Foundation for a Grant-in-Aid (Supportive Care)** as a project is a proof of concept/pilot study for funding in 2015.

CML/Myeloproliferative Disease Group

CML/MPN Disease Group Chairs: Con Tam, Tim Hughes

CML11 PINNACLE Phase II study of nilotinib plus pegylated interferon alfa-2b as first-line therapy in chronic phase CML aiming to maximize CMR and MMR .
CIs: David Yeung, Tim Hughes, Andrew Grigg.
CRA: Briony Tupper, ALLG Trial Centre
Newly diagnosed CML patients will commence taking nilotinib for 3 months, and once tolerated, will simultaneously be treated with injected pegIFN for up to 2 years of total study treatment. Patients can continue taking nilotinib beyond this time provided they are receiving benefit. Options are available for patients to decrease or increase their dose or to switch to imatinib, to ensure a balance between drug effectiveness and minimal side effects. Sites that have HREC approval should progress with their Governance Approval and Clinical Trial Research Agreement, while any other interested sites should contact Briony Tupper.

CML10 is an observational registry for all patients with CML on TKI. Having commenced in 2010 the registry has passed the 500 patient milestone, and in May had 515 patients registered at 19 sites. Congratulations to the trial centre at Royal Adelaide! Associated with the TKI registry is the STOP registry to follow patients who switch therapy for intolerance or resistance. The July SDMC approved an amendment to accrual to the STOP registry.

A number of **correlative studies** are also associated with the registries. Lab kits usually take 2-3 weeks to be delivered as they go via Australia Post. For any queries re delays please email Stephanie Arbon or phone 08-8128 4304 to confirm that she received the initial lab kit request. For further information contact Bronwyn Ortlepp.

Low grade NHL/CLL Disease Group

NHL/CLL Chairs Stephen Mulligan, Campbell Tiley

CLL7 Australasian, phase II, multicentre, randomised, study investigating efficacy and safety for dose reduced fludarabine, cyclophosphamide and iv obinutuzumab (G-FC3) vs oral chlorambucil and iv obinutuzumab (G-Clb) in previously untreated, comorbid (CIRS score ≥6), elderly (≥65 years old) patients with CLL
CIs: Stephen Mulligan, Xavier Badoux, Con Tam
This protocol for this randomized phase II trial of two treatments in CLL was approved by the SDMC in February 2014. Target accrual is 120 patients and it is expected that 15 - 20 sites will participate. The trial is currently in the budget/contract phase and will be run by the ALLG Trial Centre. Outcome from the NHMRC/PdCRR grant application will be available in December.

NHL27 Phase III randomized study rituximab plus lenalidomide vs rituximab plus chemotherapy followed by rituximab in patients with previously untreated follicular lymphoma.
CI: Pauline Warburton
CRA: Bala Ravishankar, ALLG Trial Centre
This international trial was planned to run at 10 sites in Australia. Unfortunately we have recently received notification from LysARC that the international accrual rate is quicker than expected, and the trial will close to accrual in late October 2014. It is expected that only ALLG sites that have completed governance will have an opportunity to activate this trial. We thank all interested sites for their efforts, and particularly Concord for the work with the NMA HREC submission.

NHL26 RePLy
CIs: Judith Trotman, Michael Fulham, Anna Johnstone
CRA: Briony Tupper, ALLG Trial Centre
This trial currently has 10 active sites and all four PET centres have been accredited. The trial newsletter #2 sent out in July covered a range of points clarifying aspects of the protocol and frequently asked questions. Also for all sites: keep up those screening logs! They are an important tool for us to monitor study recruitment (or screen failures) so please remember to record every patient considered or approached , not just those formally screened and registered.

Exciting news in relation to CLL6! Following slower than expected accrual since opening in May 2011, all arrangements have been finalized for the **trial to open in France** under the auspices of the French CLL group (GOELAMS). The amended protocol approved by the SDMC in March is a unified version for both France and Australia. The French sites will be using different staging criteria to determine eligibility. It is expected that the French will be able to recruit perhaps half the target and help achieve total target accrual within the original timeframe.

The specific logistics of French participation will be managed by **Bereha Khodr** who will liaise between the ALLG and France. Australian sites continue to be managed for the present by Marijana Vanevski in BaCT.

NHL16 PRIMA study main analysis was published in the Lancet in 2011. The follow-up period has now been extended to 31/12/2016 as part of an amendment to the protocol, approved by the ALLG SDMC in March. The justification is the exceptional results at 4 and 6 years in terms of PFS and lack of toxicity. Further follow-up will extend these findings and allow additional data on safety and late toxicity to be collected including second malignancies. The extension to follow-up will be applied in all participating countries. Patients will be asked to re-consent to the additional data collection .

It is great to note that there have been three further publications relating to this study in 2014 plus an oral presentation recently at ASCO. These will be listed in the forthcoming August general ALLG newsletter and on the website.

NHL15/TROG01.02 A prospective single arm trial of involved field radiotherapy alone for stage I-II low grade non-gastric marginal zone lymphoma
CI Michael MacManus
Trial Manager: Juliana di Iulio
Given that the accrual period has been much longer than expected, the TMC decided to temporarily suspend accrual at 71 patients and a statistical review has taken place. The TMC is currently considering if the trial should permanently cease accrual.

BMT Disease Group

BMT DG Chairs David Ritchie, Ian Lewis

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 CR
CI: David Ritchie
CRA: Sarah Dewberry, ALLG Trial Centre
This study assesses if patients treated with a transplant do better than patients who would have had a transplant but no suitable donor was available. The trial is coordinated internationally by the Trans-Atlantic Leukemia Study Group based in Sweden.

Confirmed participating sites are RMH, Royal Adelaide, Royal North Shore and Wellington, with RMH lead site in Australia. There will also be one or two NSW sites. Christchurch Hospital is currently participating independently but is planned t come under ALLG sponsorship in the future. First HREC approval has been obtained in Australia. The July SDMC approved a protocol amendment specifying a number of matters in relation to reporting of SAEs. This amendment will be distributed soon and we will present a summary in the next newsletter.

This newsletter was edited by Janey Stone and approved by Delaine Smith and Megan Sanders.

Questions or comments? E-mail us at Dilupa.Uduwela@petermac.org