ALLG AUSTRALASIAN LEUKAEMIA & LYMPHOMA GROUP

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

AUSTRALASIAN LEUKAEMIA AND LYMPHOMA GROUP

Trials Newsletter No 2

May 2014

ALLG trials newsletter

Here is the second issue of the new trials newsletter. Scroll down to see your favourite trials organised by Disease Groups. We plan to publish newsletters about every two months, so you can expect to see one in your inbox in July, September and November this year.

Megan Sanders
Program Manager
ALLG Trial Centre

ALLG Trial Centre

All ALLG new trials are now run in-house, allowing us full control over all aspects of trial management. Already open are AMLM17, NHL26 and CML11. NHL27 close to opening and BM06 is undergoing expressions of interest. The Trial Centre is co-located with the ALLG Operations Unit at 10 St Andrews Place East Melbourne. For more information contact the ALLG Program Manager Megan Sanders.

Achievements so far include trimmer paper CRFs and the preparation of critical SOPs to ensure trial documentation is uniform. We plan to roll out electronic data capture over the next year. In a survey in May 2013, 83% of associate members who responded were in favour of eCRFs. Automatic validation checks will decrease manual checking and query resolution time and result in better quality data.

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

- MM15 CLOSED TO ACCRUAL 15 April 2014, trial reached international target of 1500
- CML11 ACTIVATED 3 April 2014, Royal Adelaide currently open, two patients recruited
- MPN01 ACTIVATED 22 April 2014 Gosford Hospital. Currently open to accrual at Gosford and Austin, 4 patients recruited
- NHL25 CLOSED TO ACCRUAL 11March 2014, trial reached international target of 621 patients randomised

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	June - July
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	Briony Tupper	places remaining
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	David Ritchie	Sarah Dewberry	closed
AMLM17 Phase II	Andrew Wei	Bala Ravishankar	closed
NHL27	Pauline Warburton	Bala Ravishankar	closed

Announcements and reminders

Trial	Comment	Contact person
MM15	Sites without registered patients complete study drug disposal, return pharmacy logs and completed delegation logs.	Nola Kennedy
NHL24	Send data needed for interim analysis	Stella Vlachos
NHL25	Fax progression/death CRFs in real time	Ruth Columbus
NHL27	Trial expected to open to accrual in July	Bala Ravishankar

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. This new protocol with PI Andrew Wei investigates the FLT3-ITD inhibitor Ponatinib in combination with azacitidine. The study 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 protocol is nearing final SDMC approval. The target accrual is 87-93 patients over 2-3 years and the trial will be coordinated at the ALLG Trial Centre. It is expected to open in Q4 2014.

AMLM17 The phase I study is underway, with an urgent safety measure having recently being implemented. The TMC is currently assessing cohort A. The next cohort is expected to open in June. EOIs for the phase II study have closed and site selection should be completed in Q3 with the study planned to start in Q4.

ALL6 uses a modified version of a paediatric protocol in patients 15 - 40 years with ALL and has accrued 20 of the target 100 patients. Currently running at 10 sites it is due to open at Townsville, RPA and Princess Alexandra in May - July. Features include regular testing for MRD and a suite of psychosocial questionnaires. An **amendment was reviewed by the SDMC** in April. The changes include a new eligibility criterion of bone marrow blast count ≥20% and new appendices on dose modifications and sample collection.

AMLM18 Registry aims to register and collect data for non-trial as well as ALLG trial patients. Coordinated by Thili Chengodu at the Alfred, current accrual is 239 from 17 sites.

Initially set up for AML, work is currently underway to enlarge the registry to include uncommon lymphoma with ALL to follow. The long term plans are to incorporate existing ALLG Registries in MPN and CML and eventually **expand the project into a national haematology registry for all diagnoses.**

Such a system will have many advantages including standardised baseline testing, facilitation of sample collection for the Tissue Bank and sites will have digital access to their own site data.

Aggressive NHL/HL Disease Group

High grade NHL/HL Disease Group Chair Mark Hertzberg

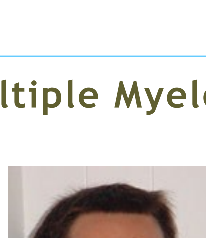
NHL25 REMARC (LYSARC, France) reached the international target of 621 patients randomised and **announced that no new patients were to be consented on 11 March 2014**. Formal closure will be announced once all consented patients are registered. Randomisation should be completed by September this year. The next key event is the interim analysis which will occur when 144 events have occurred, anticipated around September. To follow the number of events Lysarc need information in real time for all patients - please fax the CRFs as soon as progression or death occurs.

The Australian target accrual was 80 patients registered with 55 randomisations. Accrual was slow at first but picked up and we completed the trial with 54 patients with the last registered on 13 May. **Congratulations and thanks to all involved.**

The DSMC will meet in May to review all secondary malignancies which must be reported as SAEs. The **uploading of CT and PET scans for central review** is crucial for the interim analysis. Please upload as soon as possible at your site using the Imagys Webplatform. If your site has not been trained in this system and has not been in contact with Romain Ricci, please contact Ruth Columbus. Also, note that the CT at diagnosis is no longer mandatory, and the CT at randomisation can be uploaded without the CT at diagnosis.

NHL24 Rituximab in primary CNS lymphoma is open with an accrual of 28 in Aust/NZ and 118 internationally (target 200). This trial is being run in collaboration with the Dutch group HOVON. There is an interim analysis planned for September 2014 but the results will not be made public unless the DSMB recommends cessation or amendment. Please remember to send in data needed for this analysis. We also encourage you to refer suitable patients to a participating site. For further information contact the Trial Manager Stella Vlachos.

Multiple Myeloma Disease Group



Multiple Myeloma Disease Group Chair Peter Mollee

MM15 closed to accrual on 15 April having reached the international target of 1500 patients. This phase III trial was run by the International Myeloma Network, with Andrew Spencer as the ALLG PI and was coordinated from the Alfred Hospital by Nola Kennedy.

Twelve Australian sites expressed interest, 7 of which opened. TGA approvals occurred between August and October 2013 and the first patient recruited on 24 October. Four sites (Alfred, Princess Alexandra, Nepean and Canberra) enrolled 17 patients, a good achievement in the short accrual period available to us.

Sites without registered patients (Concord, Prince of Wales and St George) should complete study drug disposal and return Pharmacy logs and signed off delegation logs. Nola Kennedy will restrict general emails now only to the 4 active sites. **Thank you to everyone for your participation.**

MM16 Phase II study assessing the effect of carfilzomib treatment on early free light chain kinetics in myeloma patients with renal impairment
PIs: 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 currently contracts and budgets are being finalised. **EOI will be carried out in June.**

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
PI: Andrew Spencer
New data has shown that patients that have failed treatment with bortezomib may respond to the similar drug carfilzomib. This study with PI Andrew Spencer will examine the response to switching from bortezomib to carfilzomib early in the initial treatment of patients demonstrating a poor early response to bortezomib. The protocol is currently under review by the SDMC. It will be coordinated from the Alfred. Target accrual is 50 over 3 years.

MM13 has been open in Australia since April 2012 but has only accrued 5 patients. PI Peter Mollee discussed **possible reasons for the slow accrual** at the May Scientific Meeting in particular whether the trial hypothesis is still valid. But Peter concluded the trial remains valid and his recommendation is at left!!!

Supportive Care Disease Group

Supportive Care Disease Group Chair Con Tam

SC04 REMIND Phase I/II trial of a novel telehealth-mediated nurse led intervention to increase oral drug therapy adherence amongst people with CML
PI: Penny Schofield
The aim of this study is to help people with CML improve adherence to their oral medication and effectively manage medication side-effects better. The study is being conducted over several phases. with the first phase completed and published Wu et al 2014. The phase II trial is currently open at Peter Mac, Royal Adelaide Princess Alexandra and North Gosford/Wyong Hospitals and has 8 patients enrolled. The 10 week program has two related elements:

- phone based structured nurse counselling sessions
- mobile phone app to remotely prompt medication adherence, monitor side effects and deliver self care advice

Unfortunately recruitment is slower than expected due partly to the eligibility criteria and partly to patients declining participation.

A suitable CML trial to which a phase II or III of REMIND can be attached is under investigation.

GUIDELINES FOR USE OF ANTI-FUNGAL AGENTS
The guidelines published in 2004 are to be updated. Mature drafts will be circulated in early June with a view to submission in July and publication in October.
For further information contact Monica Slavin.

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 .
PIs: David Yeung, Tim Hughes, Andrew Grigg.
CRA: Briony Tupper, ALLG Trial Centre
This trial was activated on 3 April and Royal Adelaide is currently open to accrual with two patients enrolled. NMA HREC approval has been received. Unfortunately the trial will not be available in NZ. Accrual target is 100 over two years.

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. Interested sites should contact Briony Tupper.

MPN01 Myeloproliferative Neoplasms Registry
PIs: Cecily Forsyth, Andrew Grigg, David Ross, Wendy Erber
There has been minimal data collection on Ph-neg MPNs in Australia, but more recently interest has been generated by availability of new treatment modalities.

The main aim of the registry is to obtain data on current patterns of diagnosis and therapy of MPNs and determine rates of key clinical events. Collaboration with basic and translational research groups is also planned and it is hoped the registry will assist with planning and feasibility assessment of future trials.

Ccentral coordination is at Gosford which is also the Australian lead site. Currently Gosford and Austin are open to accrual and up to 15 sites covering all Australian states and 3 in NZ are likely to participate. Interested sites should contact Penny Owens at Gosford.

PT1. This NCRI study (Australian PI Cecily Forsyth) had the longest accrual period of any ALLG trial. The high risk arm closed in 2004 and was published in 2005. The intermediate risk arm (Aspirin vs Hydrea) closed in July 2013; no results are available yet. The low risk arm (observational only) closed in April 2013 and also has no results yet available. The follow up period has been extended to April 2024. All Australian sites will close at the end of 2014 except for Gosford which will continue to provide follow up data. For further information contact Chris Russell.

Low grade NHL/CLL Disease Group

NHL/CLL Disease Group Chairs Stephen Mulligan, Campbell Tiley

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
PIs: Stephen Mulligan, Xavier Badoux, Con Tam
The 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 undergoing contract negotiation and EOIs are expected mid year.

NHL27 Phase III randomized study rituximab plus lenalidomide vs rituximab plus chemotherapy followed by rituximab in patients with previously untreated follicular lymphoma.
PI: Pauline Warburton
CRA: Bala Ravishankar, ALLG Trial Centre
This international trial (LYSARC France) will run at 10 sites in Australia with an accrual target of 30. The lead site for NMA is Concord and ethical approval is complete. Providing site activation procedures have been completed it is anticipated accrual will open in late July. INC Research will be study monitors. Given accrual rates internationally, it is likely that accrual will end approximately April 2015.

NHL26 RePLy, the ALLG's first in-house study and a world-first study of PET-directed therapy in relapsed follicular lymphoma is designed to improve on the very poor prognosis of patients who remain PET+ after initial re-induction therapy.

Prior to commencement of maintenance therapy, all patients undergo a study-funded PET scan. Patients who are PET+ receive lenalidomide plus rituximab, those who are PET- receive standard of care which is rituximab alone.

Seven of 15 sites have been activated - with more to follow. **Cross-referral will be critical.** Currently 3 patients of a target of 80 have been accrued, one of these a cross referral to Concord from Liverpool. The aim is to complete accrual by early 2016.

BMT and cellular therapies Disease Group

BMT Disease Group 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
PI: David Ritchie
CRA: Sarah Dewberry, ALLG Trial Centre
This study assesses if patients who are suitable for a transplant with a donor have better results if they are treated with a transplant compared to those patients who would have had a transplant but no suitable bone marrow donor was available so instead received standard chemotherapy.

The international target is 330 of which 226 have already been accrued. The target for the ALLG is 40 patients over 2 years. Participating sites are RMH, Royal Adelaide, RPA, Royal North Shore and Wellington, with RMH lead site in Australia. Christchurch Hospital joined the trial independently but will join the ALLG effort in the future. It is important that patients be referred to a participating site prior to HLA typing of a sibling donor or initiating MUD search.

International PI Mats Brune from Sahlgrenska University Hospital (Göteborg Sweden) at the May Scientific Meeting.

EOIs have closed. Please contact Sarah Dewberry immediately if you still wish to join in.

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

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