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 7

April 2015

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.

ALLG Trial Centre

Fax (Trial Registration, SAEs): +61(0)3 9429 8277

Note new address: 35 Elizabeth St Richmond, Vic

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

PLEASE NOTE SAE AND TRIAL REGISTRATION FAX NUMBERS IN THE BOX ON THE RIGHT

Electronic Data Capture

The rollout of electronic data capture (eDC) in the Trial Centre is progressing rapidly. In a survey of associate members conducted in April 2013, 83% of respondents saw no advantages in continuing with paper CRF over an electronic data collection (eDC) system.

One of the advantages of eDC for site staff is a reduction in data query rates as many queries are resolved in real time from programmed validation checks.

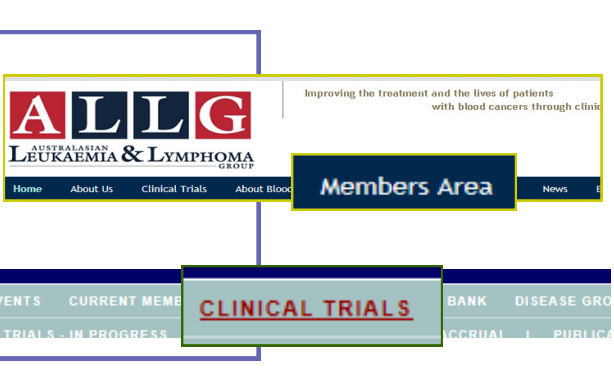
Trial Centre staff have recently undergone training in the system. The first trial to open on eCRF is expected to be CLL07 in April this year, closely followed by transition of the National Blood Cancer Registry onto eCRF. Work has also commenced to transition CML11. For transitioned trials, data entry for CRFs already submitted to the ALLG Trial Centre will be completed by ALLG Trial Centre staff.

Once the first trial opens on eCRF, ALLG Trial Centre Data Manager Sri Joshi will run a helpdesk and a training module will be available to sites participating in trials with eCRF. There will also be a demonstrations of the system at the May 2015 Scientific Meeting in Brisbane. Any questions regarding the eDC implementation should be directed to Megan Sanders, Program Manager.

Trial contacts—visit the website!

WHO IS THE TRIAL CONTACT?

All active trials are on the ALLG Website. Simply click on the **Members Area** then log in. Then select **Clinical Trials**. You will be able to choose trials open to accrual or closed, contact the PI or CRA, download protocols and access other important documents .



Milestones

- **MDS4 RESULTS ORAL PRESENTATION MDS SYMPOSIUM WASHINGTON APR/MAY**
- **AMLM15 CLOSED TO ACCRUAL DUE TO COMPLETION RECRUITMENT FINAL COHORT**
- **NHL21 REACHED FINAL ANALYSIS END-POINT AND FOLLOW-UP COMPLETED**
- **MM16 FIRST PATIENT REGISTERED 2 APRIL 2015**

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
AMLM20 A programme of development for older patients with AML and high risk MDS	Andrew Wei	Ranu Santhosh	EOI closed (places remaining - contact Ranu)
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	Kerina Princi	EOI closed (places remaining - contact Kerina)
AMLM21 A phase Ib/II clinical evaluation of Ponatinib in combination with 5-azacitidine in patients failing prior therapy for FLT3-ITD positive acute myeloid leukaemia	Andrew Wei	TBA	EOI anticipated Q2 2015
NHL29 A Phase II Study of Ibrutinib, Rituximab and mini-CHOP therapy in very elderly patients with newly diagnosed DLBCL	Judith Trotman, Emma Verner	Bala Ravishankar	Call complete (contact Bala with questions)

Announcements and reminders

Trial	Comment	Contact person
ALL5	Tracey Gerber has taken over management from Janey Stone	Tracey Gerber
ALL6	Ranu Santhosh has taken over management from Bereha Kodhr	Ranu Santhosh
CML9	Tracey Gerber has taken over management from Bereha Khodr	Tracey Gerber
MM13	Andrew Budniak has taken over management from Bereha Khodr temporarily	Andrew Budniak

Fax coversheets, CRFs and other documents are being updated to reflect new contact details PLEASE USE THE NEW COVERSHEETS FOR REGISTRATIONS AND SAEs.

ALLG DISCOVERY CENTRE
Formerly known as the National Leukaemia and Lymphoma Tissue Bank, the ALLG biobank has now been renamed the Discover Centre. Address, contact details and procedure for delivering samples remain the same.

New ALLG Trial Centre staff

Tracey Gerber CRA

We are pleased to welcome **Tracey Gerber** into the role of **CRA** commencing March 2015. Tracey has a PhD in Biomedical Science focusing on skeletal muscle metabolism, and her most recent role as Project Manager at the Baker IDI Heart and Diabetes Institute, has required her to implement and manage a trial examining whether a nurse-led intervention is more effective than usual care in metabolic syndrome and diabetes. In addition, Tracey has well-developed analytical skills from her experience in academic research, and her skills are expected to be invaluable in finalising the data for analysis of trials.

Tracey has taken over management of a number of existing trials, including CML9, ALL5 and PT1.

Trials news

Acute Leukaemia/MDS Disease Group

Acute Leukaemia/ MDS Disease Group Chair: ***Andrew Wei***

AMLM15
CI: Andrew Wei
CRA: Amanda Jager ALLG Trial Centre
Currently there are eight patients receiving treatment in cohort M5 which is the final cohort. The Trial Management Committee are currently considering cohort 5 data. As there is a great deal of outstanding data it is now **urgent that all CRFs be submitted as soon as possible**. The follow on study is under development and will be submitted to the July SDMC.

AMLM16
CI: Andrew Wei
CRA: Andrew Budniak, ALLG Trial Centre
A protocol amendment was approved by the SDMC in February. Apart from administrative changes and corrections, the main changes are an amended age range and changes to dosing.

AMLM18 Registry
CI: Andrew Wei
CRA: Amanda Jager: ALLG Trial Centre
An important new development in the Registry is the establishment of a **Registry Management Committee** (RMC) whose main role will be to oversight the registry and manage requests for data. The RMC will meet at regular intervals throughout the year with the first meeting anticipated to be in April. The RMC may include ALLG Trial Centre and Operations staff as well as the SAC and Laboratory Science Committee Chairs and representatives from the Discovery Centre. The involvement of the relevant Disease Group Chair is key along with the participation of a cytogenetics specialist for the AML patients in particular.

Amanda is still contacting sites to provide essential documents. This is an on-going process and all the help provided by sites so far is greatly appreciated.

AMLM20 A programme of development for older patients with acute myeloid leukaemia and high risk myelodysplastic syndrome New!
CI: Andrew Wei
CRA:: Ranu Santhosh ALLG Trial Centre
Documentation for HREC submissions for this study is now in progress. Thank you to Gosford for taking on the lead site role. There are still places available for additional sites to participate—please contact Ranu if interested.

The ALLG is pleased to acknowledge the support for this trial from the Leukaemia Foundation Queensland to the Trial Enabling Program which enables patients to access these novel treatment options.

MDS4
CI: Melita Kennealy
CRA: Ranu Santhosh ALLG Trial Centre
An abstract presenting the main analysis of this study has been accepted for **oral presentation** at the 13th International Symposium for Myelodysplastic Syndromes in Washington in April/May. The authors concluded that despite numerically higher response rates with addition of lenalidomide to Azacitidine, good deliverability of treatment and similar rates of toxicity, there was no benefit of the addition of lenalidomide to azacitidine in this population of higher risk MDS.

Congratulations to Melita Keneally!!!

Aggressive NHL/HL Disease Group

High grade NHL/HL Disease Group Chair: ***Mark Hertzberg***

NHL29 A Phase II Study of Ibrutinib, Rituximab and mini-CHOP therapy in very elderly patients with newly diagnosed DLBCL New!
CI: Judith Trotman, Emma Verner
CRA: Bala Ravishankar, ALLG Trial Centre
Currently R-mini-CHOP chemotherapy is considered a standard treatment for elderly patients. 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 of this trial is to improve the survival of patients over 75 by adding Ibrutinib to R-mini-CHOP. **EOI have now closed**. Concord as lead site has submitted to their HREC, with additional sites from EOI to be added in due course. Thank you to Concord for assistance with lead HREC submission.

NHL25 REMARC
CI: Judith Trotman
CRA: Bala Ravishankar, ALLG Trial Centre
A protocol amendment was approved in France in late November 2014. The amendment is based on a **change in the statistical assumption** to include 160 confirmed events. The new version of the protocol (V7 of 10/10/2014), and the Lenalidomide investigator brochure V17 will be sent soon to the participating sites for submission to ethics. Due to this amendment the interim analysis has been cancelled and the final analysis will now occur in September 2016.

NHL24
CI: Samar Issa
CRA: Kerina Princi, ALLG Trial Centre
Please remember to fax all registration/randomisation forms to ALLG. Kerina will complete the registration process and randomise the patient using the HOVON web based system. Recruitment unfortunately continues to be slower than expected, with 37 patients recruited to date. **The trial remains open to recruitment—please consider entering your patients into this important study.**

NHL21
CI: Mark Hertzberg
CRA: Briony Tupper, ALLG Trial Centre
The NHL21 trial has now reached the final analysis endpoint and follow-up has ended, so no further trial-specific patient visits are required. Could all sites please submit any outstanding CRFs and DCFs to the ALLG Trial Centre promptly, as we are approaching the final analysis.
Thank you to all who have been involved in this trial now near completion.

Multiple Myeloma Disease Group

Multiple Myeloma Disease Group Chair: ***Peter Mollee***

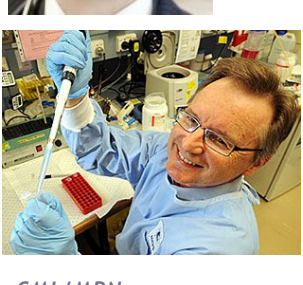
MM14
CIs: Andrew Spencer, Anna Kalf
CRA: Nola Kennedy, Alfred Clinical Research Centre
This trial is currently open to recruitment and the target is for 80 patients to be randomised. So far 43 patients have been randomised.

MM16 Phase II study assessing the effect of carfilzomib treatment on early free light chain kinetics in myeloma patients with renal impairment New!
CI: Joy Ho, Doug Joshua
CRA: Sarah Dewberry, ALLG Trial Centre
This trial for myeloma patients with renal impairment investigating the new drug carfilzomib has just opened the first site, RPA. Other participating sites in this trial are Alfred, Calvary Mater Newcastle, Princess Alexandra and Royal Adelaide, and the ALLG encourages all sites to consider cross referral. **And in breaking news the first patient was registered on 2 April.**

MM18 Single arm, multicentre study of Carfilzomib in combination with Thalidomide and Dexamethasone (CaTD) in patients with relapsed and/or refractory multiple myeloma (RRMM) New!
CI: Hang Quach
This trial focusses on the new drug Carfilzomib in combination with thalidomide and dexamethasone (CaTD) in relapsed /refractory MM patients. It is currently under review by the SDMC and more information will be provided at the May Scientific Meeting.

MM17 A multi-centre single arm study of carfilzomib-thalidomide-dexamethasone(TD-K) for newly diagnosed transplant-eligible multiple myeloma (MM) patients refractory to initial bortezomib-based induction therapy New!
CI: Andrew Spencer
CRA: Nola Kennedy, Alfred Clinical Research Centre
This trial has been approved by the SDMC and is now undergoing financial and contractual arrangements. When ready to open, it will be managed from the Alfred Clinical Research Centre.

CML/Myeloproliferative Disease Group



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

CML11
CIs: David Yeung, Tim Hughes, Andrew Grigg.
CRA: Briony Tupper, ALLG Trial Centre
Briony reminds all sites to inform their trial pharmacists of all newly registered CML11 patients to allow for accurate Peg-Interferon supply forecasting. As part of the rollout of electronic data capture, work has commenced with transitioning CML11 to eCRFs. For transitioned trials, data entry for CRFs already submitted to the ALLG Trial Centre will be completed by ALLG Trial Centre staff. More news on transition of CML11 in the next newsletter.

CML9 TIDELII
CIs: Tim Hughes, Andrew Grigg
CRA: Tracey Gerber, ALLG Trial Centre
This trial has been taken over by the new CRA Tracey Gerber. Tracey will be contacting sites in due course to introduce herself and deal with any outstanding issues. Meanwhile, the discussions are underway to consider plans for long term follow up and analysis of this trial.

MPN01 Myeloplastic Neoplasms Registry
CIs: Cecily Forsyth, Andrew Grigg, David Ross, Wendy Erber
CRA: Penny Owens , Gosford Hospital
A new development for this Registry is a proposal to conduct genetic studies, led by Albert Catalano. The PICF has been submitted to lead HREC and currently HREC comments are being reviewed. More news in the next newsletter.

CML10 CML Registry
CIs: Tim Hughes, Michael Osborne
CRA: Bronwen Ortlepp , Royal Adelaide Hospital
The CML10 CML registry has accrued a total of 645 patients in the main TKI registry (as of mid March). The Registry has a number of subsidiary components. Patients whose treatment changes for any reason are followed through the STOP Registry, currently with 137 patients. The correlative studies (CS) component associated with the registry currently has 78 patients participating.

In addition there is a Trial of Cessation (TOC) program. Currently there are 43 patients in this category with a target of 50. **Once seven more TOC patients enrol in the correlative studies, recruitment to the Registry will close to new patients.** However the Registry will continue to follow existing patients through their treatment journey including crossing over to the STOP registry when treatment changes for any reason. This will continue to study closure.

If you have TOC patients eligible for CS, please contact Bronwen Ortlepp on 08 8222 3619, prior to offering consent to ensure a position is available.

Thank you to all sites who have supported the CML registry over the last five years.

Low grade NHL/CLL Disease Group

NHL/CLL Disease Group ***Chairs Stephen Mulligan, Campbell Tiley***

CLL7 New!
CIs: Stephen Mulligan, Xavier Badoux, Con Tam
CRA: Kerina Princi, ALLG Trial Centre
Expressions of interest have been coming in for this trial for elderly CLL patient with comorbidities with approximately 15 sites so far planning to participate. Although EOI have closed if your site is interested please contact Kerina.

Work on developing the electronic CRFs is very advanced. **CLL7 will be the first trial to open on eCRF.** ALLG Trial Centre Data Manager Sri Joshi will run a helpdesk and a training module will be available to sites. **There will also be a demonstrations of the system at the May 2015 Scientific Meeting in Brisbane**. Any questions regarding the eDC implementation should be directed to Megan Sanders, Program Manager.

The HREC application has been submitted at the lead site and approval is expected in the near future. Thank you to St George for undertaking lead site responsibilities.

CLL6
CI: David Gottlieb, Con Tam, Stephen Mulligan
CRA: Andrew Budniak, ALLG Trial Centre.
The recent andomisation of the 50th patient has signalled commencement of the interim statistical analysis. The purpose of this will be to compare rate of unacceptable mortality reported in the lenalidomide arm to that in the observation arm. The trial started in in July 2014 in France where there are currently 38 sites activated and recruitment is going well. With this support hopefully recruitment timelines overall will be achieved.

NHL14
CI: Ken Bradstock
CRA: Kerina Princi, ALLG Trial Centre.
The original follow-up period for this study was 49 months. However, in order to address the secondary endpoint of overall survival and evaluate rituximab in this patient group, a recent protocol addendum extends the **follow up period until December 2016** with two additional secondary endpoints:

- Response to further therapies, in particular rituximab containing regimens
- Effect of prior rituximab on the duration of subsequent remissions

After reconsenting, patients will be assessed annually or more frequently if clinically indicated and may choose to have their follow up via their GP. Documents for the addendum have been sent to all 30 participating sites. Please respond to Kerina as soon as possible regarding submission to ethics at your site.

BMT Disease Group

BMT Disease Group ***Chair Ian Lewis***

BM06
CI: David Ritchie
CRA: Sarah Dewberry, ALLG Trial Centre
ALLG participation in this international trial coordinated from Sweden is now well and truly off the ground. The international target accrual is 320 and it is hoped that the ALLG will contribute 30-40. All five Australian sites have been activated and four patients already accrued. **This is a fantastic achievement and congratulations to everyone involved.**

This newsletter was edited by Janey Stone and approved by Delaine Smith and Megan Sanders.
Questions or comments? E-mail us at info@allg.org.au