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 9

August 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

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For detailed trial information and documents visit the Members area at the ALLG website

Closing old trials

A large number of older ALLG trials are now complete and due for site closure. The ALLG has a formal process to close trials once the analysis is completed and the trial is published. We are aware that there is a backlog in this process for several trials, but it is anticipated that all outstanding trial closure processes will be completed before the end of 2015.

This will apply to the following trials:

ALL3	ALL7	AMLM13	AMLM14
APML4	CMLALL1	HD03	LY03
LY05	NHL11	NHL13	NHL18

Even if you have already closed this trial locally, the formal closure procedures will still need to be completed. Please do not archive trial materials until we contact you. If necessary, please keep your trial active with your ethics committee until the site closure process is complete and you are authorised to notify ethics of closure.

Some international trials require permission from the international body or the procedure will be conducted by them. This includes AMLM14, NHL13 and LY05. We will ensure you are informed about the status of these trials. For two international trials from the EORTC Data Centre patients are being following until death. If you no longer have patients to follow up we can arrange close-out.

For further information about closing old trials contact Janey Stone.

CTN changes

The TGA has recently changed its CTN submission process to an online system, simultaneously abolishing the need for signatures from the PI and HREC. Please communicate this to your HREC and governance departments as required. More information can be found on the TGA Website.

Trial contacts—visit the website!

WHO IS THE TRIAL CONTACT?

Trial responsibilities have changed in the ALLG Trial Centre. Many are noted in specific trials below.

If in doubt simply check on the ALLG Website. Just 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 other important documents.

Milestones

- **NHL21 ANALYSIS COMMENCED AND ABSTRACT SUBMITTED TO ASH**
- **AMLM20 FIRST HREC APPROVAL 24 JULY 2015**
- **CLL6 INTERIM ANALYSIS COMPLETE AND ABSTRACT SUBMITTED TO iwCLL**
- **NHL29 FIRST HREC APPROVAL 1 APRIL 2015**
- **NHL18 PUBLISHED**

Expressions of Interest

The ALLG Trial Centre is currently calling for Expressions of Interest for trial participation. Please reply directly to the relevant contact person.

TRIAL	PI	Contact person	Period for EOI
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	Richa Gaur	EOI anticipated August

ALLG Trial Centre welcomes four new staff!

Senior CRA Sarah Dewberry is currently on Maternity Leave. With four new staff having started recently, many trials have been reallocated. More information under specific trials.

Suzanne Cake Senior CRA

Suzanne Cake (Senior CRA) has 14 years experience in Clinical Research working in both Australia and the UK. She has extensive knowledge in the clinical setting and project management, with previous senior positions in Parexel, Nucleus Network and ICON Plc. Suzanne has an MSc in Clinical Research and is ARCP CCRC accredited. Suzanne commenced as a Senior CRA in the ALLG Trial Centre in May 2015 and will be managing NHL26 and MM16.

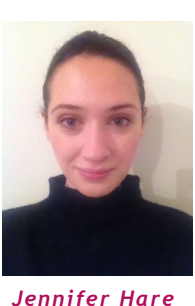
Marlyse Debrincat CRA

Marlyse Debrincat (CRA) has a background in academic and clinical research. She has a PhD in Medical Biology and held a postdoctoral appointment at the Walter and Eliza Hall Institute of Medical Research where her studies focussed on understanding the molecular pathways involved in the regulation of megakaryocytes and platelets and their roles in health and disease. Marlyse has experience in clinical trial management coordinating trials with the Haematology and Oncology Trials team at the Andrew Love Cancer Centre. Marlyse commenced as a CRA in May 2015 at the ALLG Trial Centre and will be managing NHL16, NHL27 and BM06. Marlyse will work part-time (5 days a fortnight).

Richa Gaur CRA

Richa Gaur (CRA)

Richa commenced her role as a CRA in ALLG in July 2015. Prior to that, she held senior positions in CROs most recent being inVentiv Health Clinical in the Neuroscience division working primarily in the area of clinical assessment (phase II-III). Richa brings in over 9 years of clinical trial project management experience including data management and business development. She will manage CML11 and AMLM21.



Jennifer Hare Clinical Trial Assistant

Jennifer Hare (Clinical Trial Assistant) most recently worked as a CRA with the London Regional Cancer Program in Canada, coordinating a prospective cohort study that is evaluating the risk of recurrence in women with luminal A breast cancer. Prior to this, she completed an MSc in Epidemiology, with a specialisation in biostatistics at the University of Melbourne. Jennifer will be assisting with entry of the National Blood Cancer Registry data into the new eDC platform and data entry on several paper-based trials.

Trials news

Acute Leukaemia/MDS Disease Group

Acute Leukaemia/ MDS Disease Group Chair: Andrew Wei

AMLM20 New!

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

CI: Andrew Wei

CRA: Ranu Santhosh ALLG Trial Centre

AMLM20 will be the first trial to open under the Trials Enabling Program in collaboration with the Leukaemia Foundation Queensland. The lead sponsor of the trial is Cardiff University (UK) and the ALLG targeted accrual is 60 patients over 6 months from 10 sites across Australia.

AMLM21 New!

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

CI: Andrew Wei

CRA: Richa Gaur ALLG Trial Centre

FLT3-ITD is a common mutation found in approximately 25% of patients with AML. This mutation is linked to a high chance of relapse after chemotherapy and poor outcome. This study aims to look at combining the FLT3-ITD inhibitor Ponatinib with Azacitidine. The study has two parts. To start Phase Ib will investigate safety and tolerability in two dose schedules. The subsequent Phase II will randomise patients to 2 arms: Ponatinib with and without Azacitidine.

This trial is currently in set-up. **Look out for the EOI which will be sent out in the coming weeks.**

AMLM15

CI: Andrew Wei

CRA: Amanda Jager ALLG Trial Centre

Following the trial's closure to recruitment on 14/5/2015 work is underway to complete outstanding activities. The TMC will meet in August to review the final cohort. For those hospitals participating in the final cohort please submit your CRFs in real time. As we are quickly approaching the main analysis, it is essential that we receive all outstanding CRFs as soon as possible.

AMLM16

CI: Andrew Wei

CRA: Andrew Budniak ALLG Trial Centre

The 3-year interim analysis will occur in December 2015, so CRFs relating to events are critical. **Please ensure you send in Relapse and Death Forms if relevant as soon as the event occurs.** Following a SUSAR for cardiac arrest in April, the SDMC emphasized importance of electrolyte monitoring and ECG assessment of patients prior to each treatment.

AMLM17

CI: Andrew Wei

CRA: Bala Ravishankar ALLG Trial Centre

An urgent safety measure was implemented in early 2014 which excluded patients who are platelet transfusion refractory or who do not fulfil normalised coagulation parameters. Registered patients must also demonstrate return of haematological parameters to screening levels before commencing the next cycle. The recent protocol amendment incorporating these measures was approved by the SDMC in July (protocol v 3.6)

AMLM18 Registry

CI: Andrew Wei

CRA: Amanda Jager ALLG Trial Centre

Participating sites are currently submitting paper CRFs for the AMLM18 Registry. Once the eCRF is activated, all paper CRFs that have been received will be entered by ALLG Trial Centre staff. However in a couple of months there will be a deadline beyond which paper CRFs will no longer be accepted. **If you have any outstanding data to be provided, please send it to us to enter as soon as possible!**

ALL6

CI: Matt Greenwood (replacing Ken Bradstock)

CRA: Ranu Santhosh ALLG Trial Centre

Ken Bradstock was the initiator and CI for this trial until his recent retirement. Matt Greenwood from RNS has now taken over this responsibility. Ranu Santhosh has taken over trial management from Bereha Khodr. A confidential events analysis is planned for the near future.

MDS3

CI: Melita Kenealy

CRA: Ranu Santhosh ALLG Trial Centre

The manuscript of MDS3 is being written with publication anticipated before the end of the year. Meanwhile with the trial nearing completion, participating sites will be closed over the coming months.

Aggressive NHL/HL Disease Group

High grade NHL/HL Disease Group Chair: Mark Hertzberg

Co-Chair: Peter Mollee

NHL29 IRiC study. 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

There is a recognised unmet need for evidence-based treatment paradigms for elderly patients with DLBCL. The aim of this study is to improve the survival of patients over 75 by adding Ibrutinib to R-mini-CHOP. Given the limitations of deliverability of full-dose CHOP, it is anticipated patients will find the option of a less-toxic enzyme inhibitor instead of intensive chemotherapy very attractive.

The governance process is progressing well. The first site to open will be Concord and all other sites will be opened in a phased manner over the next couple of months. It is also hoped that the trial will run at the National Cancer Centre Singapore. The target accrual is 80 from 20 sites across Australia, NZ and Singapore over 3 years.

NHL24

CI: Samar Issa

CRA: Kerina Princi, ALLG Trial Centre

When CNS lymphoma causes poor cognitive function because of high cancer burden and critical location of the cancer in the deep brain region, patients may not be able to make a decision about trial participation. A new relative/friend ICF allows a suitable alternative person to give consent. This is now undergoing ethical review at some sites including Royal Hobart, Princess Alexandra and Middlemore. The relative/friend ICF only applies to the first 28 days of treatment, after which the patient is expected to have recovered sufficiently to make their own decision to continue in the trial.

NHL21

CI: Mark Hertzberg

CRA: Bala Ravishankar, ALLG Trial Centre

This trial has now commenced final analysis and an abstract has been submitted to ASH. **Congratulations Mark**!

NHL25

CI: Judith Trotman

CRA: Bala Ravishankar, ALLG Trial Centre

The trial DSMC met in June 2013 and noted no safety concerns but recommended a protocol amendment based on the lower than expected number of events occurring. The amendment was approved by the SDMC in July and will be with sites during August.

NHL18

CI: David Goldstein

Contact: Janey Stone, ALLG Trial Centre

This trial, which was coordinated internationally by the Austrian group AGMT, has recently been published. The trial closed some years ago, however a mature answer has emerged and the data has generated considerable interest. This result reinforced the outcomes of the ECOG study which examined the same maintenance question in DLCBL. **However in this study, men who received maintenance appeared to do better than women especially in the low IPI group. This apparent sex difference may perhaps be related to pharmacokinetics.** Men over 60 have more rapid clearance of rituximab, which may influence the ability of maintenance to reverse the poorer prognosis of men with DLBCL.(*Jaeger et al Haematologica. 2015; Epub ahead of print April 24, 2015*)

David Goldstein thanks the sites that contributed patients: Concord, Gosford and Murray Valley Private. There is a large data base available to interrogate and **opportunities for further analyses and collaborations will probably be available soon.**

Congratulations David!

Myeloma Disease Group

Multiple Myeloma Disease Group

Co-Chair: Hang Quach

MM16

CI: Joy Ho, Doug Joshua

CRA: Suzanne Cake ALLG Trial Centre

Five sites have now been activated and 7 patients registered. Accrual will be suspended when the 10th patient is registered (approx. Sept/Oct) while the safety analysis is carried out to determine whether recruitment may continue at a higher carfilzomib dose. Sites will be notified in writing of the recruitment suspension and the subsequent SDMC/TMC decision. Please contact Suzy prior to approaching any new patients to check that there is a place available in cohort 1.

MM17 A multicentre single arm study of carfilzomib-thalidomide-dexamethasone (CarTD) 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, which will be run from the Alfred Hospital, plans to recruit 50 patients from 15 sites over 18 months. The trial is currently in set-up and EOI are expected to be sent out in September/October.

CML/Myeloproliferative Neoplasms Disease Group

CML/MPN Disease Group Chair: Con Tam

Co-Chair: Tim Hughes

CML11

CIs: David Yeung, Tim Hughes, Andrew Grigg

CRA: Richa Gaur, ALLG Trial Centre

Richa Gaur has now taken over responsibility for this trial. Currently there are 8 sites activated with 5 more to come and 18 patients have been registered. The trial will transition to eCRF in the coming months. Apart from registrations, data submissions will be suspended while Trial Centre staff enter paper-based data. Submissions will then re-open on eCRF. Sites will be informed of precise timelines. Please submit any completed paper CRFs now.

CML9

CIs: Tim Hughes, Andrew Grigg

CRA: Tracey Gerber, ALLG Trial Centre

The trial is now in follow-up for long term endpoints and all sites should have received information about the trimmer data collection requirements. A letter about the increased cardiovascular risk of 400mg BD nilotinib has been sent to all sites, and a protocol amendment to reduce the dose to 300 mg BD in certain circumstances was approved at the July SDMC. Patients will be reconsented once ethical approval is obtained.

PT1

CIs: Cecily Forsyth

CRA: Tracey Gerber, ALLG Trial Centre

Long term follow-up is continuing. Julie Temple from the international trial centre will be in contact with sites soon regarding the annual collection of CRFs.

Low grade NHL/CLL Disease Group

NHL/CLL Disease Group Chair: Campbell Tiley

Co-Chairs: Stephen Mulligan Judith Trotman

NHL26

CI: Judith Trotman

CRA: Suzanne Cake, ALLG Trial Centre

Eleven patients out of a target of 80 have been registered to date. The financial support for this trial is generous with ppp $2500 for PET-pos patients and $1000 for PET-neg. The good news is there has been a higher proportion of PET+ patients than anticipated, suggesting that it may be possible to close accrual after another 15 patients. The aim now is to complete recruitment in 2016.

At the May Scientific Meeting, Judith Trotman urged clinicians at activated sites that have not entered patients to do so. She also encouraged cross-referral from non-participating sites, noting that this also receives a payment.

Why you should support this local study:

- This is a **world-first study of PET-adapted therapy** in relapsed FL, using rituximab & lenalidomide as consolidation therapy.
- **Access to PET** scans in a non-reimbursed environment
- **Reassurance** of post-induction PET- scans
- **Potential benefit** to PET+ patients with a poor prognosis

As Judith pointed out at the May SM, "If we boost our recruitment rate we can promptly answer our primary endpoint."

CLL7

CIs: Stephen Mulligan, Xavier Badoux, Con Tam

CRA: Kerina Princi, ALLG Trial Centre

Responding to an identified critical need, ASCO recently published a set of guidelines aimed at improving the evidence base for treating older adults with cancer. The existing ALLG CLL7 trial was designed to meet this very need. The trial will open in the near future and has particularly attracted interest from regional sites in Australia such as Darwin.

CLL6

CI: David Gottlieb, Con Tam, Stephen Mulligan

CRA: Andrew Budniak, ALLG Trial Centre.

The July SDMC approved a protocol amendment which included increased study duration from 7 to 9 years and minimum of 3 months for haematological recovery. It also updates PR criteria. The 50th patient interim analysis is now complete. Thank you to sites for sending in the CRFs but we can't let you rest on your laurels. Owing to bumper recruitment by the French, the 100th patient interim analysis is rapidly approaching. Andrew particularly requests the Response and MRD CRFs.

BMT Disease Group

BMT Disease Group Chair: Ian Lewis

BM06

CI: David Ritchie

CRA: Marlyse Debrincat, ALLG Trial Centre

Sarah Dewberry is currently on Maternity Leave and this trial is now being managed by Marlyse Debrincat.

Two New Zealand sites are to be activated in August. Christchurch opened independently but will now recruit under ALLG sponsorship. Wellington will also be activated as an ALLG site.

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