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

AUSTRALASIAN LEUKAEMIA AND LYMPHOMA GROUP

Trials Newsletter No 8

June 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.

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

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

ALLG Discovery Centre

The ALLG was the first cancer collaborative group to embark on biobanking, with the establishment of the National Leukaemia and Lymphoma Tissue Bank over 12 years ago. **Recently renamed the Discovery Centre,** the facility is an essential and irreplaceable resource that underpins translational research into blood cancers in Australia. The course of the development of the Discovery Centre has not been an easy one. It has been necessary to overcome major logistic issues surrounding a network of more than 70 hospitals, diverse ethics committees, hundreds of clinical and laboratory investigators and myriad complex trials each with specific requirements. Logistical issues have also been multi-faceted. Sample collection, local processing and transport require detailed procedures to ensure sample viability upon arrival at the Brisbane facility.

The need to document patient consent to bio-banking in addition to trial sample collection is critical. The current strategy is the creation of a **generic consent form for tissue banking** which it is hoped will preclude the need for repeated ethics approval for every trial. This has been done through a NEAF submission and **Calvary Mater Newcastle as lead site have just received approval**. In 2015 we have also seen the commencement of a three-year partnership between the ALLG, the LFA and the LFQ which will support the future sustainability of the Discovery Centre.

The change of name will necessitate changes in a number of documents which will be dealt with over the next period. Please continue to send samples using defined procedures in the meantime.

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

- **MM16 FIRST PATIENT ACCRUED 2 APRIL 2015**
- **CLL7 FIRST HREC APPROVAL AT ST GEORGE HOSPITAL**
- **AMLM15 CLOSED TO ACCRUAL 14 MAY 2015**

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
AMLM20 A programme of development for older patients with AML and high risk MDS	Andrew Wei	Ranu Santhosh	EOI closed (one place 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 June
CML11 Phase II study of nilotinib plus pegylated interferon as first-line therapy in chronic phase CML aiming to maximize CMR and MM		Tracey Gerber	EOI—places still remaining

Announcements and reminders

Trial	Comment	Contact person
PT1	Tracey Gerber has taken over management from Janey Stone	Tracey Gerber
Trial documents continue to be updated to reflect new contact details PLEASE USE THE NEW COVERSHEETS FOR REGISTRATIONS AND SAEs.		
Ken Bradstock is retiring. New PIs will be appointed for ALL6 and NHL14, and Ken will no longer be a co-investigator for AMLM15. Other changes will be managed as needed. More on Ken Bradstock and his contribution to the ALLG in the July General Newsletter		

Current and upcoming amendments

Trial	Summary of changes
CML9	Limit exposure to 400mg nilotinib
CLL6	Changed response criteria; update the Pregnancy Prevention Plan
AMLM17	Complete urgent safety measure
NHL26	Changed access to maintenance Rituximab on PBS resulting in changed treatment schedule
NHL25	Change to analysis timepoints
AMLM16	Changes in recommended treatment for CBF AML
CLL7	Changes in the schedule of assessments
ALL6, MDS4, CML11	Change of contact details amendments in due course
MM16	Clearer instructions on SFLC testing, changed sample collection, safety reporting

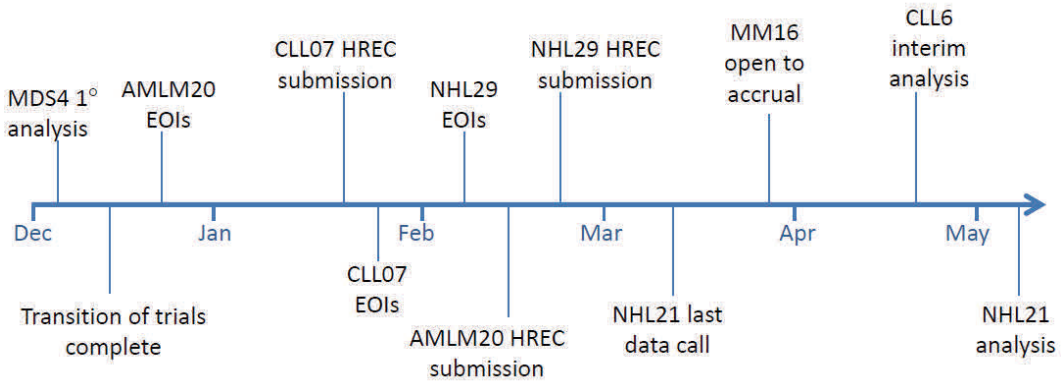
ALLG Trial Centre

Staff changes

We are sorry to announce that Briony Tupper has left the ALLG Trial Centre. Briony started in the Trial Centre in December 2013. During her time, Briony made valuable contributions to NHL26, CML11, NHL21 and in the establishment of trial centre processes. We wish Briony all the best in her future career.

We are pleased to announce that two new staff members commenced in May: Suzanne Cake as a full-time senior CRA and Marlyse Debrincat as a part-time CRA (5 days a fortnight). More about the new staff in the next newsletter.

Trial Centre activity Dec 2014 - May 2015



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

Recruitment to this trial closed on 14/5/2015 with the registration of the 10th patient to cohort M5. Overall 115 patients were accrued to the study with 45 of these receiving maintenance treatment. Thank you to everyone for your involvement in the study and a very special thankyou and congratulations to the 5 hospitals who accrued the 10 patients in the final cohort (M5): Alfred (3), Queen Elizabeth (2), Austin (2), Barwon Health (1), Royal Adelaide (2).

As we are quickly approaching the main analysis, it is essential that all sites submit all outstanding CRFs as soon as possible. For those hospitals participating in the final cohort please submit your CRFs in real time, as a second TMC meeting will be held shortly to review all data.

AMLM16

CI: Andrew Wei

CRA: Andrew Budniak ALLG Trial Centre

This trial of untreated adult AML with FLT3-ITD has accrued 40 of a target 99. Twelve of 18 activated sites have contributed patients. If your site has been activated but hasn't yet recruited any patients, **remember you receive a bumper payment of $1000 for your first participant!** Also in order to make sending the correlative study samples to the Discovery Centre easy, there are pre-printed labelling stickers provided. Please contact Andrew Budniak if you need a supply.

AMLM18 Registry

CI: Andrew Wei

CRA: Amanda Jager ALLG Trial Centre

The development of the eCRF is progressing well. A Registry working group consisting of Andrew Wei, Teresa Morgan, Sri Joshi and Amanda Jager have been meeting regularly to finalise the eCRF requirements for the Registry. The AML data fields have undergone review and been finalised. Once the eCRF has been built and user acceptance testing completed patient data from existing paper CRFs will be entered and it is **anticipated the on-line system will go live to sites, around October 2015**. The AML pages will be released first followed by Uncommon Lymphoma and ALL.

Meanwhile training of site staff has started with a presentation by Sri Joshi on the Data Managers Day at the May SM. Clinicians were also shown a short presentation.

ALL5

CI: Andrew Grigg

CRA: Tracey Gerber ALLG Trial Centre

Since taking over the trial Tracey has focused on procedures to bring it to a conclusion. Thank you to the sites who have completed the data clarification requests. Please remember to complete Follow Up Form P for all live patients and Molecular Response Form O in the event that a patient dies or completes the 5 year follow up.

ALL6

CI: Matt Greenwood (replacing Ken Bradstock)

CRA: Ranu Santhosh ALLG Trial Centre

Thank you to everyone for assisting with the recent process to ensure that all sites are on most recent Protocol version 2.

Coordinating Investigator Ken Bradstock retired at the end of May. Ken has had a long interest in ALL and in the AYA population. Believing there was a need for effective treatment of the AYA age group, Ken proposed the concept for the trial which commenced in 2012. The new CI will be Matt Greenwood, and documentation regarding the change will be sent out in June/July.

Best wishes to Ken for his retirement from the whole team at the ALLG Trial Centre! Watch out for more about his contribution to the ALLG in the July General Newsletter.

Aggressive NHL/HL Disease Group

High grade NHL/HL Disease Group Chair: Mark Hertzberg

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 truly 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.

Thanks to all sites who sent in an **EOI—there has been an outstanding response**. Selected sites are assembling their approval documents. Other sites will be advised of vacancies as they arise. The plan is to accrue 80 patients from 20 Australian sites over 2-3 years. **In an exciting development, the National Cancer Centre in Singapore will also participate.** As well as the usual per patient payment for sites, there will also be a **payment for cross referral**.

NHL24

CI: Samar Issa

CRA: Kerina Princi, ALLG Trial Centre

A total of 162 (158 eligible) patients were registered in the trial between 3/8/2010 and 9/4/2015. Currently 26 institutions (ALLG - 10, HOVON - 16) are active of which 22 have at least one patient. The interim safety analysis in February based on 132 patients was satisfactory and the trial was approved to continue. With a target of 200 , it is anticipated the trial may close to accrual toward the end of 2015 or early 2016.

NHL25

CI: Judith Trotman

CRA: Bala Ravishankar, ALLG Trial Centre

The new protocol amendment is designed to manage tolerability and reduce withdrawals and involves an amended dosing scheme in response to toxicities experienced. The amendment documents will be distributed soon. Bala will also contact sites regarding outstanding diagnostic samples. Thank you to everyone who has sent the CT/PET scan CDs to LYSA-Imaging.

The interim analysis planned for August 2013 was deferred due to insufficient number of events. It will now take place this year, with the final analysis at 296 events expected in June 2019.

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

CI: Joy Ho, Doug Joshua

CRA: Sarah Dewberry, ALLG Trial Centre

MM16 trial is now open to recruitment. Currently 3 sites are active, Royal Prince Alfred Hospital, the Alfred and Calvary Mater Newcastle, each of which has recruited one patient. Two more sites will be activated in the near future - Royal Adelaide and Princess Alexandra. Once 10 patients are registered, accrual will be temporarily suspended with a TMC and SDMC review.

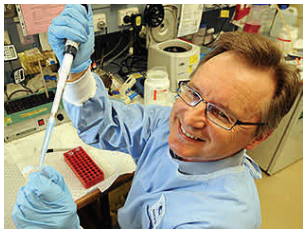
MM17 A multi-centre single arm study of carfilzomib -thalidomide-dexamethasone(TD-K) for newly diagnosed transplant-eligible multiple myeloma (MM) patients refractory to initial bortezomib-based induction therapy New!

CI: Andrew Spencer

CRA: Nola Kennedy, Alfred Clinical Research Centre

This trial aimed at patients refractory to initial bortezomib has been approved by the SDMC and is now undergoing contractual arrangements. As soon as this is complete, it will be managed from the Alfred Clinical Research Centre. The plan is 50 patients from 15 sites. Contact Nola with any queries.

CML/Myeloproliferative Disease Group



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

CML11

CIs: David Yeung, Tim Hughes, Andrew Grigg.

CRA: Tracey Gerber, ALLG Trial Centre

There have been excellent outcomes with TKIs for CML. However, increasing numbers of patients are now on long term medication. Treatment emphasis is now shifting to the intermediate goal of deep molecular response, ultimately leading to treatment free remission, especially in younger patients.

Seven sites are now active in this trial with 6 more to come. Accrual is 16. As there is capacity for 20 sites please contact Tracey if your site would like to join the trial. The eCRFs are expected to be released over the next 1-2 months . Data entry for paper CRFs already received will be completed by ALLG Trial Centre staff.

CML9

CIs: Tim Hughes, Andrew Grigg

CRA: Tracey Gerber, ALLG Trial Centre

A big thank you to the sites who have responded to the data clarification requests. Changes to the Nilotinib IB edition 10 regarding cardiovascular events warranted an amendment to the protocol and PICF which is expected in Q3 2015. Also a reminder that all patients who are off protocol for any reason are still followed up at 6 monthly. The only exception are patients who have officially withdrawn and submitted the Revocation of Consent form.

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. **This will be the first trial to use eCRF.** ALLG Trial Centre Data Manager Sri Joshi will run a helpdesk and a training module will be available to sites. Thank you to St George for undertaking lead site responsibilities.

NHL27

CI: Pauline Warburton

CRA: Marlyse Debrincat, ALLG Trial Centre.

Responsibility for this trial has been taken over by the new member of the ALLG Trial Centre Marlyse Debrincat.

LYSA recently provided a detailed newsletter updating trial progress since accrual closed last year. The **second interim analysis will occur in Q2 2016 with the goal of analysing the first 500 randomised patients.** CRFs must be received by LYSA by 30/11/2015 and data cleaning and queries will follow. Contact Marlyse with any queries.

NHL26

CI: Judith Trotman

CRA: Suzanne Cake, ALLG Trial Centre.

The original target was 80 patients at 15 sites. Accrual has been slow, with only 10 patients accrued to date. However more than anticipated have been PET+, so there may only need to be approximately 15 more patients before ceasing accrual. **Please consider cross-referring eligible patients on completing therapy to this study to enable an answer to an early primary endpoint.** The aim is to complete recruitment in 2016.

The recent amendment was necessitated due to changes in the PBS criteria for the use of rituximab maintenance from 2 monthly to 3 monthly. This amendment also allows for the use of (now PBS approved) subcutaneous rituximab treatment, once available. The visit schedule for PET negative patients has been amended to correlate with the 3 monthly rituximab visits.

NHL16

CI: John Seymour

CRA: Marlyse Debrincat, ALLG Trial Centre.

The extended follow up has now been approved at >90% of participating sites. Thank you to all for this strong response. Please complete the CRFs from the patients' medical records and retain at the site. A process of monitoring is being set up, and once this is finalised **the monitors will collect the CRFs and despatch them directly to LYSARC.** Please do NOT send any CRFs to the ALLG Trial Centre.

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. The three participating Australian sites have been activated and four patients already accrued. Two NZ sites are expected to be activated very soon.

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