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

AUSTRALASIAN LEUKAEMIA AND LYMPHOMA GROUP

Trials Newsletter No 9

October 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
35 Elizabeth St
Richmond, Vic 3121

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

Launch of eCRF!!!

CLL7 has opened to accrual and gone live with eCRF. This very exciting new development is a first for the ALLG. The study opened at St George Hospital in mid-September. The electronic data capture system will usher in a whole new era for the ALLG, one of no more paper! The switch from paper CRFs to electronic will improve data accuracy, making it a far more efficient and less burdensome effort for our member sites. Electronic data entry greatly simplifies and accelerates the whole clinical trial process bringing us results quicker.

The ALLG especially thanks Con Tam and ALLG staff Sri Joshi and Kerina Princi for their contributions to setting up this new system for the CLL07 trial.

The only site currently operating in the new system is St George, who have viewed the demo CD and have the passwords and access information. As the system is rolled out, their will be further training provided. Most importantly, Sri will run a help desk, to help sites settle into the new program.

The eCRF system is MARVIN supplied by XClinical Software and Services. The system will allow full entry of all data elements required and includes an audit trail, data checks, saving of site information, generation of reports and trial news. Come and meet Sri for a demonstration of the system at the Data Managers/Research Nurse Day on 11 Nov at the Scientific Meeting.

What will this mean for current trials?

CLL07 has started directly into the digital system. The next trial to go electronic will be **CML11**. Currently ALLG Trial Centre staff are entering all the data from the existing paper CRFs. Once this is complete, CML11 will also go live with the eCRF, anticipated to occur before the end of November. The next cab off the rank will be the **National Blood Cancer Registry (formerly AMLM18)**, which is aiming for December. **NHL29**, for which paper CRFs also have to be entered, will follow later.

Milestones

- **CLL7 OPEN TO ACCRUAL 22 SEPTEMBER 2015**
- **NHL29 OPEN TO ACCRUAL 11 SEPTEMBER 2015**
- **MM16 ACCRUAL SUSPENDED 10 AUGUST 2015**
- **BM06 OPEN TO ACCRUAL IN NZ (CHRISTCHURCH 26/8/2015 AND WELLINGTON 31/8/2015)**
- **CML10 CLOSED TO ACCRUAL 14 SEPTEMBER 2015**
- **MM14 CLOSED TO ACCRUAL 8 OCTOBER 2015**

Expressions of Interest

The ALLG Trial Centre is currently calling for Expressions of Interest for trial participation. Please contact us as follows:

TRIAL	PI	Contact person	Period for EOI
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	Andrew Spencer	Nola Kennedy	EOI expected to open October/ November
CLL07 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	Amanda Lane	EOI closed
MM18 Single arm, multicentre study of Carfilzomib in combination with Thalidomide and Dexamethasone (CaTD) in patients with relapsed and/or refractory multiple myeloma (RRMM)	Hang Quach	Andrew Budniak	EOI expected to open January 2016

ALLG Trial Centre welcomes new staff

We thank Bala Ravishankar, Richa Gaur and Ranu Santhosh for their contributions to ALLG trials and wish Sarah well on Maternity Leave. We welcome new staff who commenced in September.

Amanda Lane
CRA

Amanda Lane (CRA) has a background in academic and clinical research. She completed a Bachelor of Medical Science with Honours at the University of Wollongong and a PhD with the Heart Research Institute at The University of Sydney. Prior clinical positions held include Study Coordinator at the University of Wollongong, Clinical Trials Assistant with inVentiv Health Clinical and CRA with Quintiles. Amanda commenced as a CRA in the ALLG Trial Centre in September 2015 and will be managing CML11 and AMLM21.

Christine Vergara
CRA

Christine Vergara (CRA) has over four years of experience in clinical research and clinical trials/data coordination and administration both in Australia (CMAX Adelaide) and Singapore (National University Cancer Institute, Singapore). She was also the key administrator of Cancer Therapeutics Research Group, an Asia-Pacific collaborative group on cancer clinical research. Christine has extensive experience in ethics submission, preparation of clinical trial study documents, site start-up activities, grants application and submission of grant reports. Aside from her double degrees in the health sciences (Biology and Nursing), she also has strong communication and organizational skills. Her work ethics are demonstrated through successful internal and external collaborations in multi-cultural, multi-disciplinary and multi-geography environments. Christine commenced as a CRA in September 2015 at the ALLG Trial Centre and will be managing NHL29, NHL21, NHL25 and AMLM17.

Sandra Lowe (NSW Project Coordinator) has been working on promoting awareness of ALLG trials across NSW for 2 years and also provided great assistance to the ALLG trial centre and the tissue bank. We thank CINSW and Sandra for their support for the ALLG.

Trials news

Low grade NHL/CLL Disease Group

NHL/CLL Disease Group Chair: Campbell Tiley

CLL7

CIs: Stephen Mulligan, Xavier Badoux, Con Tam

CRA: Kerina Princi, ALLG Trial Centre

This is the very first ALLG trial to commence its operations fully with the new eCRF. Commencing from 22 September, this trial opened to accrual using the Marvin digital system. See above for further information or contact Kerina with any queries.

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

CI: Judith Trotman, Emma Verner

CRA: Christine Vergara, ALLG Trial Centre

This trial for elderly patients with DLBCL opened to accrual with the activation of Concord on 11 September. Other sites will open 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. Target accrual is 80 from 20 sites across Australia, NZ and Singapore over 3 years. The trial will operate using paper CRFs for a time until it transfers to the new eCRF, anticipated to occur late this year or early next year.

Look out for the trial newsletter to be distributed in late October.

Note that Christine has taken this trial over from Bala Ravishankar who has resigned from the ALLG.

NHL25

CI: Judith Trotman

CRA: Christine Vergara, ALLG Trial Centre

The new CRA for this trial is Christine Vergara. The trial includes monitoring, and visits will be scheduled before the end of 2015. Please start completing CRFs now in order to be prepared for these visits.

NHL21

CI: Mark Hertzberg

CRA: Christine Vergara, ALLG Trial Centre

Congratulations to Mark Hertzberg for being awarded an oral presentation for this trial at ASH in December! In order to support Mark's presentation, Christine has sent out a modified radiotherapy CRF. Please return the completed forms as soon as possible as they are essential for the presentation.

Acute Leukaemia/MDS Disease Group

Acute Leukaemia/ MDS Disease Group Chair: Andrew Wei

NATIONAL BLOOD CANCER REGISTRY (FORMERLY AMLM18)

CI: Andrew Wei

CRA: Amanda Jager, ALLG Trial Centre

eCRF!

The AMLM18 Registry has now been renamed the National Blood Cancer Registry. All participating sites should have received the amendment to carry out this change. Please submit before the end of the year. The eCRF for the AML and uncommon lymphoma fields is nearly finalised. Once that is complete, the Trial Centre staff will enter existing paper data in the eDC system and **the digital system will then be released to sites in December.**

AMLM16

CI: Andrew Wei

CRA: Andrew Budniak, ALLG Trial Centre

There have unfortunately been a number of protocol violations where patients have been given the wrong dose of investigational product. **Please note that the correct dose is 2 x 200mg, twice daily, a total of 800mg/day.** Also please note that the inclusion criterion for FLT3 positivity now requires a fraction not a percentage. There is now a tool on the Registration Form which will help you carry out the calculation.

ALL6

CI: Matthew Greenwood

CRA: Amanda Jager, ALLG Trial Centre

This study is undergoing an interim analysis at present. Please send in all outstanding data and responses to queries to assist the analysis process.

Supportive Care Group

Supportive Care Chair: Rob Weinkove

MDS_X1 Anaemia and red cell transfusion practice in myelodysplastic syndromes

New!

CI: Rob Weinkove

Red cell transfusion dependence is common in patients with MDS. Although transfusion is central to care of MDS patients, there is little prospective data to inform transfusion thresholds. On one hand, large randomised trials have shown that restrictive transfusion policies lead to improved survival. On the other hand, observational and single-arm studies in MDS suggest that raising haemoglobin to higher levels leads to improved quality of life and better function.

ALLG members Zoe McQuilten, Rob Weinkove, Melita Kenealy and Erica Woods plan to analyse data from the ALLG's MDS3 and MDS4 trials, to document red cell transfusion thresholds and to seek associations between haemoglobin levels and quality of life in an Australian context. **They hope this will help inform design of a future multicentre trial of transfusion thresholds in MDS, and eventually inform Australasian practice.**

Myeloma Disease Group

Multiple Myeloma Disease Group Chair: Peter Mollee

Co-Chair: Hang Quach

MM16

CI: Joy Ho, Doug Joshua

CRA: Suzanne Cake, ALLG Trial Centre

Recruitment to Cohort 1 was suspended on 10 August when all spots became filled. The SDMC and TMC need to review the results and make a decision before recruitment starts for Cohort 2, which may be at a higher carfilzomib dose. Sites will be notified in writing of the SDMC/TMC decision.

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

EOI for this trial, which will be run from the Alfred Hospital, will be sent out to sites who have previously participated in MM trials in October. Fifteen sites engaged in transplanting MM are needed. If you have not participated in ALLG MM trials in the past, but are interested in this trial, please contact Nola.

MM14

CI: Andrew Spencer, Anna Kalff

CRA: Nola Kennedy, Alfred Clinical Research Centre

This trial closed to accrual on 8 October. The trial closed because there are enough registered patients to get to the target randomised number of 80. The trial opened in March 2013, and registered a total of 164 patients. **Congratulations to the CIs and all participating sites for bringing this trial to a successful conclusion.**

Nola has noted that sites are doing a fabulous job with completing and sending in the CRFs. In relation to the correlative studies, analysis of the specimens will take place when all possible samples for cycle 6 maintenance have been received – anticipated to be in around 10 months' time.

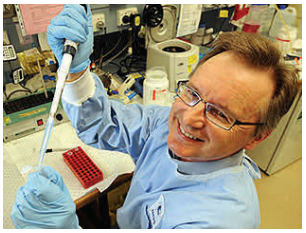
CML/Myeloproliferative Neoplasms Disease Group

CML/MPN Disease Group Chair: Con Tam

CML12 A single arm phase II study to individualize dasatinib dosing based on trough levels and molecular response to maintain efficacy whilst minimising toxicity New!

CIs: David Yeung, Tim Hughes, Andrew Grigg

CML patients treated with tyrosine kinase inhibitors such as dasatinib enjoy excellent leukaemia free survival. However, a number of patients experience treatment related toxicity such as pulmonary effusions and pulmonary arterial hypertension. This may lead to treatment discontinuation. The data from various studies suggest a role for dose adjustment with therapeutic drug monitoring (TDM) to minimise toxicity and preserve efficacy.



Co-Chair:
Tim Hughes

The design of the CML12 DIRECT study is based on the premise that TDM and subsequent dose adapted dasatinib will preserve efficacy and yet minimise toxicity, especially pulmonary effusions. A previous study suggested that the elderly are likely to have higher plasma trough dasatinib drug levels and are particularly at risk of pulmonary effusions. The CML12 study therefore postulates that interventions should be aimed at patients over 60 years of age.

CML10

CIs: Tim Hughes, Michael Osborn

CRA: Bronwen Ortlepp, IMVS

CML10 closed to recruitment on 8/10/2015. The registry achieved its target to recruit 50 patients having a 'trial of cessation' and correlative studies sample collection. Please contact Bronwen urgently if any patients have been offered consent. Also, please notify all responsible people at your sites. The status of the registry as a whole now is:

TKI Registry: Closed to recruitment
Correlative Studies: Closed to recruitment
STOP Registry: Patients already enrolled on the TKI registry will continue to enrol to STOP registry. Data collection will only occur if they change treatment. Patients already on STOP will continue to have data collected on their changes of treatment.

The study opened in May 2010 and accrued a total of more than 650 patients in 5 years and 4 months. A big thank you to all 22 sites who contributed patients.

BMT Disease Group

BMT Disease Group Chair:
Ian Lewis

BM06

CI: David Ritchie

CRA: Marlyse Debrincat, ALLG Trial Centre

Both New Zealand sites have now been activated. Christchurch Hospital, which was already accruing and is the lead site in NZ, came under ALLG sponsorship and was activated on the 26/8/2015. Wellington Hospital, a new site for the trial, was activated on the 31/8/2015.

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