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 12

August 2016

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 THE CORRECT FAX NUMBER AND ADDRESS OF THE ALLG TRIAL CENTRE

ALLG Trial Centre

Fax: +61(0)3 9429 8277

Ground floor
35 Elizabeth St
Richmond, Vic 3121

Boost the CML11 PInNACLe trial

This trial for younger, fitter CML patients has been underway for two years and current accrual is 49 (target 100). The treatment involves the addition of Peg-IFN to standard nilotinib. The interferon is at a lower dose than previously, with fewer side effects. Even though both drugs are currently available in Australia, this combination is still considered experimental for the treatment of CML.

Now is a critical time for this trial and we need your help to ensure all eligible patients are offered participation.

HELP WITH CROSS REFERRAL IF YOU CAN

If you see a newly diagnosed CML patient who will be treated with Nilotinib, please consider referring them to a site that has this study open.

NSW – Concord, Calvary Mater Newcastle
Qld - Princess Alexandra
South Australia - Flinders Medical Centre, Royal Adelaide
Tas - Royal Hobart
Victoria – Alfred, Austin, Box Hill, Monash Medical Centre

Contact Kerina for further information.

CIs: Tim Hughes, David Yeung, Andrew Grigg
CRA: Kerina Princi

Milestones

- AMLM21 FIRST HREC APPROVAL (ALFRED), OPENED TO ACCRUAL 7 JUNE 2016
- NHL24 CLOSED TO ACCRUAL 30 MAY 2016 (INTERNATIONAL TARGET ACHIEVED)
- MM17 FIRST HREC APPROVAL 16 MAY 2016 (Alfred, Royal North Shore, Royal Adelaide)
- BM06 CLOSED TO ACCRUAL 1 JULY 2016
- AMLM20 FIRST SITE ACTIVATED (ROYAL DARWIN), OPEN TO ACCRUAL 16 AUG 2016
- AMLM17 COHORT C OPENED 19 AUGUST 2016

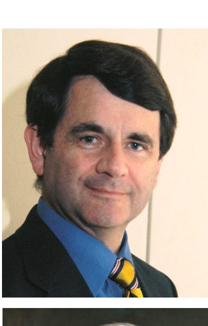
Expressions of Interest

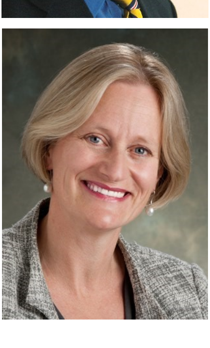
The ALLG Trial Centre is currently calling for the following new trial Expressions of Interests

TRIAL	PI	Contact person	Period for EOI
CML12 A single arm phase II study to individualize dasatinib dosing based on trough levels and molecular response to maintain efficacy whilst minimising toxicity	David Yeung, Tim Hughes, Andrew Grigg	Drazenka Macic	EOI closed (two places remaining - contact Drazenka)
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	Flora Yuen	EOI open (places remaining - contact Nola)
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 (places remaining - for information control/click HERE

Trials news

Low grade NHL/CLL Disease Group





NHL/CLL Disease Group Chairs: Stephen Mulligan, Judith Trotman

CLL5
CIs: Stephen Mulligan
CRA: Kerina Princi

The original intent of the CLL5 study was to follow all patients for disease and survival status indefinitely, but due to protocol inconsistencies, data was actually collected for only 12 months. **In order to analyse the impact of treatment on the overall survival and progression free survival, protocol changes have been necessary to provide for extended follow up.** The amendment will be simply for retrospective collection of patient data from existing medical records, with no mandated patient visits or interventions, and with a close out (censor) date of 1/1/2016. The amendment will be reviewed at the October SDMC and the documents for submission to HRECs will be sent out to sites soon afterwards.

NHL26
CIs: Judith Trotman
CRA: Suzanne Cake

NHL26 RePLY is a world-first study of PET-adapted therapy in relapsed FL, using R2 (rituximab plus lenalidomide) as consolidation therapy. Current accrual is 16 patients from 8 sites, and a total of 14 sites have been activated to participate in the trial.

Despite the compelling scientific and clinical merit of NHL26 : the efficacy data and safety profile of R2; access to PET scans in a non-reimbursed environment; reassurance of post-induction PET-scans; and potential benefit to PET+ patients with a poor prognosis, recruitment to the NHL26 study remains slow.

In order to improve recruitment, a protocol amendment is being considered by the July SDMC. By removing Inclusion criterion 3 and to allow registration of patients who have received chemotherapy, if the clinician thinks it appropriate, rather than the strict adherence to GELF criteria. Suzy will distribute information to sites once the amendment is approved.

We also strongly encourage cross-referral from non-participating sites - this also receives a separate cross-referral payment.

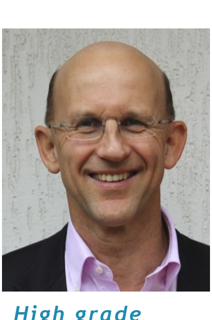
NHL27
CIs: Pauline Warburton
CRA: Amanda Lane

A new protocol amendment is being considered at the July SDMC. The main changes involve new timing of endpoints for analysis and an updated Pregnancy Prevention Plan. There is also a revised ALLG specific appendix. The documents for submission to your HREC will be sent out shortly.

NHL16
CIs: John Seymour
CRA: Christine Vergara

The extension study will close at the end of 2016. All CRFs are expected to be completed, monitored and received by Lysarc by February 2017.

Aggressive NHL/HL Disease Group



High grade NHL/HL Disease Group
Chair: Mark Hertzberg

Co-Chair: Peter Mollee

NHL25
CI: Judith Trotman
CRA: Christine Vergara

The final analysis for the primary endpoint is now underway, following database lock on 30 June. **Thank you to all ALLG participating sites for your contribution in meeting this deadline.** The ALLG sites were one of the first international groups to produce clean data - well done to all participating sites and keep up the good work!

NHL24
CI: Samar Issa
CRA: Kerina Princi

This trial closed to accrual on 30 May when the international target was reached. A total of 202 patients were accrued, with 43 of them from Australia/NZ. **Congratulations to Samar, participating sites and everyone else involved - this is a fantastic contribution to an international trial.**

NHL29 IRIC
CIs: Judith Trotman, Emma Verner
CRA: Christine Vergara

A total of 17 sites have now been activated for this trial. Feedback from study coordinators has been very positive. Christine Lee (Concord Hospital) said, "It is my absolute privilege to be involved in this well-designed trial!" Some coordinators noted the QOL and geriatric assessments were quite demanding. The CIs responded:

"Thank you for these considered comments. While we understand that the QOL and geriatric assessment questions are time consuming, in this very elderly patient population, so underrepresented in clinical trials, it is very important that these assessments are documented. We do appreciate your time and effort in doing this."

Judith Trotman and Emma Verner (Chief Investigators)

NHL21
CI: Mark Hertzberg
CRA: Christine Vergara

The manuscript for publication is well advanced, having been submitted and comments now being addressed. Watch this space for a new publication later this year!

HD8
CI: Judith Trotman, Leanne Berkahn
CRA: Suzanne Cake

Congratulations to Leanne Berkahn and Judith Trotman on the publication of the HD08 study on the use of interim PET-CT scans in advanced Hodgkin Lymphoma. The trial was run under the auspices of Cancer Research UK and accrued over 1200 patients globally. The ALLG contributed 85 patients from 16 sites. The results were published in June in NEJM. (*P Johnson et al Adapted treatment guided by interim PET scan in advanced Hodgkin's Lymphoma New England Journal of Medicine 374: 2419-2429 (2016)).* In the trial, PET scans after two cycles of standard chemotherapy directed either less or more intensive chemotherapy.

Judith Trotman said "The interim PET-scan enabled us to identify those patients with a very high probability of survival. This study showed we can tailor their therapy, sparing them the lung toxicity of continued exposure to Bleomycin as well as the serious side effects and infertility consequences of intensive chemotherapy. This approach, along with a reduction in the need for radiotherapy, should substantially reduce damage to healthy tissues and the risk of second cancers caused by treatments."

Acute Leukaemia/MDS Disease Group

Acute Leukaemia/MDS Disease Group
Chairs: Andrew Wei, Will Stevenson

ALL6
CI: Matthew Greenwood
CRA: Amanda Jager

This important trial in AYA patients with ALL opened in July 2012 and to date has accrued 59 patients. A major amendment to the trial is being considered at the July SDMC. **The trial design has been changed, to allow patients to consent to diagnostic samples & QOL prior to deciding whether to take part in the study.** This is to prevent the need to re-biopsy patients .This will also allow the patient more time to review the PICF and decide on participation. The amendment also includes simplification and correction of errors in the schedule of investigations to make it much easier to manage the trial tests required. There are also a number of other changes and corrections.

NATIONAL BLOOD CANCER REGISTRY (FORMERLY AMLM18)

eCRF!

CI: Andrew Wei
CRA: Amanda Jager
NBCR Coordinator: (TBA)

In order to simplify the process of registering patients in the NBCR, we plan to release a combined PICF shortly. Currently there are separate PICFs for the data and the samples. The sample component will still remain optional. **The functioning of the Registry has been enhanced by the creation of a new role that of NBCR coordinator.** Currently the position is vacant, and until it is filled, please contact Amanda Jager with any queries about the Registry.

AMLM17
CI: Andrew Wei
CRA: Christine Vergara

The last cohort in this trial, which incorporated sequential dosing with lenalidomide and romidepsin, has been permanently closed, as this schedule has been shown to be less less efficacious and has resulted to prolonged cytopenias. A new protocol amendment which was approved by the SDMC in June and is now being submitted to HRECs. The main change is the addition of a new cohort, which provides for concurrent dosing of lenalidomide (25 mg daily D1-21) and romidepsin (12 mg/m^2 D1, 8, 15) rather than sequential. **Recruitment to Cohort C (dose level 2A) opened on 19/8/2016.**

AMLM15
CI: Andrew Wei
CRA: Amanda Jager

Data cleaning activities are currently underway for the main analysis of this trial. Please submit all outstanding CRFs and answer all outstanding data queries as soon as possible for data requested up until the end of April 2016.

AMLM20
CI: Andrew Wei
CRA: Drazenka Macic

We are delighted to announce that this important international trial is open to accrual. Funding by the Trials Enabling Program, a collaboration between the ALLG and the Leukaemia Foundation, allows the ALLG to offer participation in this UK sponsored trial to Australian patients. Royal Darwin Hospital was the first site activated and the trial opened on 16 August 2016. The trial will run at 10 sites in Australia.

AMLM21
CI: Andrew Wei
CRA: Amanda Lane

We are pleased to notify you that the AMLM21 study has opened to recruitment! The lead site Ethics approval was finalised on 19 May 2016 and Ponatinib was also delivered to Melbourne in May. The trial was activated on 7 June and the Alfred was the first site opened. Other sites are going through set up procedures and should come on board soon. You can download the study documents from the ALLG website.

MDS4
CI: Melita Kenealy
CRA: Tracey Gerber

Preparation for the final analysis is now advanced. Endpoint data is being cleaned with data censored on 15/3/2016. Response data is being reviewed by CI Melita Kenealy. Thank you to sites who have submitted CRFs and data query responses. Study coordinators, please ensure that all outstanding CRFs and queries are submitted as soon as possible.

MDS3
CI: Melita Kenealy

Congratulations to Melita Keneally on publication of this trial!

The study accrued 80 patients from 15 sites between 2008 and 2009 (M Kenealy et al. Leukemia & Lymphoma epub 7/6/2016). The authors conclude that the combination of azacitidine and thalidomide in the patient population was tolerable without unexpected toxicity and encouraging responses support further investigation of combination approaches with hypomethylating agents and immunomodulatory drugs.

CML/Myeloproliferative Neoplasms Disease Group

CML/MPN Disease Group Chairs
Con Tam
David Yeung

CML9
CIs: Tim Hughes, Andrew Grigg, David Yeung
CRA: Tracey Gerber

This is one of the most important trials ever undertaken by the ALLG and accrued 210 patients from 27 sites 2007 - 2011. The trial has already generated a number of publications. **This study is currently being analysed so that results can be reported at the 2016 ASH conference.** Thank you very much to the sites who have submitted CRFs and data query responses. For those who are yet to submit outstanding requests, it would be greatly appreciated if all outstanding CRFs and queries could be submitted asap. We are looking forward to seeing the final outcome of this trial!

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
CRA: Drazenka Macic

This trial is currently undergoing ethical review. We hope to receive approval shortly and the trial is expected to open September/October. **There are at present 13 sites and places are still remaining for two more sites to participate.**

BMT Disease Group

BMT Disease Group Chair: Ian Lewis

BM06
CI: David Ritchie
CRA: Tracey Gerber

The trial closed to accrual on 1/7/2016, as sufficient patients had been registered to meet the target of 320 patients achieving CR1 and having a potential eligible donor (inclusion). Inclusions will continue until the end of August. The ALLG registered a total of 14 patients from two sites (Royal Melbourne and Royal Adelaide). Of these, 11 have been included, with one more possible in the next period. An abstract to ASH is planned.

A big thank you to all sites that participated in this trial.

Myeloma Disease Group

Multiple Myeloma Disease Group
Co-Chair: Peter Mollee

Co-Chair: Hang Quach

MM16
CI: Joy Ho
CRA: Suzanne Cake

This trial utilises Carfilzomib/dexamethasone until progression, to answer the important question of the utility of SFLC measurements in renal failure and the prediction of renal recovery, and the efficacy and tolerability of this regimen in patients with renal impairment. Cohort 2 is currently open to recruitment at 5 sites: RPA, Calvary Mater Newcastle, The Alfred, Royal Adelaide and Princess Alexandra. **We encourage clinicians at other sites to refer your patients to these participating centres.**

It is also important to remember that MM patients with newly diagnosed or relapsed/refractory disease must have the following:

1. acute renal injury as the cause of reduced renal function, with creatinine clearance 15-40 ml/min at screening (calculated by the CKD-EPI and MDRD formulae)

2. Difference between involved and uninvolved free light chain ≥ 300 mg/L

Newly diagnosed patients can be transplant eligible or transplant-ineligible.

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: Flora Yuen, Alfred Clinical Research Centre

This trial is managed by the Alfred Clinical Research Centre and Flora Yuen is the CRA responsible. Three sites now have HREC approval and accrual is expected to open shortly. There is room for more sites, as up to 15 can participate. If you have not participated in ALLG MM trials in the past, but are interested in this trial, please contact Flora.

The ALLG Trials Newsletter is edited by Janey Stone and approved by Delaine Smith and Megan Sanders.

Questions or comments? E-mail us at info@allg.org.au