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

April 2014

Introducing the new ALLG regular trials newsletter

We know you want to be more up to date on what is happening with ALLG trials, so we have introduced this new regular trial orientated newsletter. The newsletter will appear regularly—every 2 months or so to start with. That way you'll know very quickly which new trials are starting, which are closing and all other trial news. Scroll down to see your favourite trials organised by Disease Groups.

ALLG Trial Centre

The ALLG Trial Centre was set up in mid 2013. This new venture for the ALLG means that all future trials will be run in-house, allowing us full control over all aspects of trial management. Starting from the beginning of 2013, all new trials approved by the SDMC will be coordinated from the ALLG Trial Centre. Already open are AMLM17 and NHL26, with CML11 about to open. NHL27 is submitting to ethics and BM06 is undergoing expressions of interest.

The Trial Centre is co-located with the ALLG Operations Unit at 10 St Andrews Place East Melbourne. For more information contact the ALLG Program Manager Megan Sanders.

Megan Sanders
Program Manager
ALLG Trial Centre

ALLG Trial Centre

Program Manager	Megan Sanders
CRA	Sarah Dewberry
CRA	Bala Ravishankar
CRA	Briony Tupper

Acute Leukaemia/MDS Disease Group

AML/MDS
Disease Group
Chair
Andrew Wei

AMLM18 Registry based at the Alfred aims to register and collect data for non-trial patients as well as patients being enrolled in ALLG trials. Initially for AML, work is currently underway to expand the registry to include lymphoma. Subsequently ALL will be integrated with other diagnoses to follow.

The Registry operates in an interlinked fashion with other AML trials. For this reason, it is essential that sites enrolling patients on AMLM15, AMLM16 and AMLM18 refer to the Interim Recruitment Procedure Manual (available from the ALLG website) which provides information on the recruitment and registration process. If you have any questions on this process , please contact Laura Galletta. Queries relating solely to AMLM18 should still be directed towards Thili Chengodu.

AMLM15 pilot study of lenalidomide maintenance therapy in adult AML is accruing at 10 sites. A total of 98 patients have been enrolled in the registration phase which is now functioning as part of the AMLM18 Registry. The maintenance phase is still open with 30 accrued and currently actively recruiting to Cohort 4 which comprises 40mg lenalidomide.

AMLM16 is a phase II randomised trial of Sorafenib in combination with intensive chemotherapy for previously untreated adult FLT3-ITD positive AML. Current accrual is 17 of a target of 99 patients. The SDMC approved an amendment last year for inclusion of AmBisome as anti-fungal prophylaxis/supportive care. Gilead Science will supply the drug free for trial participants.

AMLM21 phase Ib/II clinical evaluation of Ponatinib in combination with 5-azacitidine in patients failing prior therapy for FLT3-ITD positive AML. This new protocol investigates the FLT3-ITD inhibitor Ponatinib in combination with azacitidine. The study has two parts. The phase I component examine two dose schedules of azacitidine with 6 patients in each group. In Phase II of the study, patients will be randomly assigned to one of 3 groups: Ponatinib alone, azacitidine alone or both drugs. The protocol is nearing final SDMC approval. The target accrual is 87-93 patients over 2-3 years and the trial will be coordinated at the ALLG Trial Centre.

AMLM17 High-Dose lenalidomide in combination with epigenetic therapies for relapsed or refractory AML. The phase I component of this trial is open and has almost completed accrual to cohort 1. The phase II component is being set up and is expected to open once the appropriate dose has been determined from the phase I study.

ALL6 uses a modified version of a paediatric protocol in patients between 15 and 40 years with ALL. The trial is is currently running at 8 sites with more due to open, and has accrued 15 of the target 100 patients. Features include regular testing for MRD and a suite of psychosocial questionnaires. ALL6 has had success with acquisition of funds from philanthropic sources, and from the Adolescent and Young Adult group National Program supported by Canteen and COSA, and additionally from AYA Victoria/Tasmania directly.

The latest amendment was approved by the SDMC in March, and sites can expect to receive information very soon.

Aggressive NHL/HL Disease Group

High grade
NHL/HL Disease
Group Chair
Mark Hertzberg

After 20 years in the making, **NHL7 has just been published in Am J Hematol: Hertzberg, Matthews and Stone et al. A Phase III randomised trial of high-dose CEOP + filgrastim versus standard dose CEOP in patients with non-Hodgkin lymphoma: 10 year follow-up data. Australasian Leukaemia and Lymphoma Group (ALLG) NHL07 trial.** Congratulations to the authors, who worked hard to bring publication of this phase III randomised trial to fruition. To access the publication control/click here.

NHL24 Rituximab in primary CNS lymphoma is open with an accrual of 27 in Aust/NZ. This trial is being run in collaboration with the Dutch group HOVON. With an international target of 200, there is still quite a way to go. We encourage you to refer suitable patients to a participating site. For further information contact the Trial Manager Stella Vlachos.

NHL25 REMARC, being conducted in collaboration with the French group LYSARC, has accrued a 48 of a local target of 80 with 12 sites actively accruing. It is anticipated that the trial will reach the international target of 603 and close around October this year.

NHL11 Hyper CVAD trial has just completed final analysis. The PI John Seymour is currently working on the manuscript. Results will be available soon.

The DG is considering a number of **HL studies** including studies from the UK and from the German group. Come along to the May Scientific Meeting to hear more!

Multiple Myeloma Disease Group

Multiple Myeloma Disease Group Chair Peter Mollee

MM15 is about to close to accrual having almost reached the international target. This phase III trial was run by the International Myeloma Network, with Andrew Spencer as the ALLG PI. We contributed 17 patients to the trial from four sites—Alfred, Princess Alexandra, Nepean and Canberra.

MM16 Phase II study assessing the effect of carfilzomib treatment on early free light chain kinetics in myeloma patients with renal impairment . This new protocol with PI Joy Ho is in advanced development and was approved by the SDMC in March. EOIs will go out in April/May. For further information contact Megan Sanders.

Renal impairment or kidney failure occurs in up to 50% of MM patients and has been shown to greatly reduce patient survival. Studies have shown that improving kidney function results in better survival. In this study, patients with renal impairment with newly diagnosed, relapsing or progressive myeloma will be given a new drug, carfilzomib. Light chain measurements will be taken soon after carfilzomib is given to determine correlation with kidney function after 4 months of treatment. The study will also investigate efficacy of the drug and time until progression.

MM6 has been an ALLG success story. The trial closed to accrual March 2005 and the last patient finished 12 months in June 2006. 34 centres had ethics approval and 269 patients were registered from 29 centres and 243 participants randomised. Patients continue on trial until disease progression. The trial PI is Andrew Spencer. It was coordinated from the Alfred Trial Centre by Nola Kennedy.

The trial has generated 5 publications and 11 presentations, including at ASH, ASCO, EHA and International Myeloma Workshop .

CML/Myeloproliferative Disease Group

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

CML11 PINNACLE Phase II study of nilotinib plus pegylated interferon alfa-2b as first-line therapy in chronic phase CML aiming to maximize CMR and MMR .

The treatment of CML and the expected survival has been revolutionised since the introduction of tyrosine kinase inhibitors (TKIs) such as nilotinib. Despite their effectiveness, these drugs will never totally remove CML affected cells from the body. In order to do so, other features of the patient's immune system may need to be harnessed. One possibility is using externally administered interferon (IFN) to augment the response induced by the TKI.

BCR-ABL levels, duration of survival and time until disease worsens are some of the methods that will test the response to the drug combination in newly diagnosed chronic phase CML. Patients will commence taking nilotinib for 3 months, and once tolerated, will simultaneously be treated with injected pegIFN for up to 2 years of total study treatment. Patients can continue taking nilotinib beyond this time provided they are receiving benefit. Options are available for patients to decrease or increase their dose or to switch to another TKI, imatinib, to ensure a balance between drug effectiveness and minimal side effects.

The trial is about to open, and will be run by the ALLG Trial Centre coordinated by Briony Tupper. PIs are David Yeung, Tim Hughes and Andrew Grigg. The accrual target is 100 over two years. The lead site for ethics (Eastern seaboard only) is the Austin and most sites will be activated over the period March to May. So far 13 centres spanning all states in Australia have been confirmed with a total of 15 participating sites planned.

Low grade NHL/CLL Disease Group

NHL/CLL Chairs Stephen Mulligan, Campbell Tiley

The ALLG **submitted a grant application for CLL7 to the PdCCR scheme (Cancer Australia and funding partners)** via the NHMRC application system. The application is for 3 years funding commencing 2015.Chief Investigators for the grant application are Stephen Mulligan and Con Tam. Associate Investigators included Bryony Kuss, Xavier Badoux and Giles Best. The outcome will be known at the end of 2014.

CLL is the most common leukaemia in Australia accounting for 30% of adult leukaemia. Quality remissions prolonging lifespan are possible in younger patients who are able to tolerate intensive chemotherapy, but not so for older patients with comorbidities. To date, research has focussed on those <61 years of age. Yet, the median age of CLL diagnosis is 72 years with a perception that many are too old or frail to undergo active, disease eradicating treatment. There is an urgent need to develop effective therapies specifically for the older population. CLL7 will redefine the treatment paradigm for those disadvantaged by age and disease. Patients are randomised to one of two treatment arms: (1) Fludarabine, cyclophosphamide and novel agent GA101 or (2) chlorambucil (Cbl) and GA101. The aim is to determine whether G-FC is tolerable and more effective than G-Cbl in this elderly comorbid patient group. The trial incorporates substantial laboratory correlative studies and a suite of QOL and frailty measures.

The protocol was approved by the SDMC in February 2014. The ALLG is negotiating funding support from Roche Australia.

NHL27 Phase III randomized study rituximab plus lenalidomide vs rituximab plus chemotherapy followed by rituximab in patients with previously untreated follicular lymphoma. This trial with PI Pauline Warburton is currently submitting to ethics committees. The international collaboration with LYSARC in France will be run from the ALLG Trial Centre and managed by CRA Bala Ravishankar.

NHL26 RePLy, the ALLG's first in-house study and a world-first study of PET-directed therapy in relapsed follicular lymphoma, opened last November. It is designed to improve on the very poor prognosis of patients who remain PET+ after initial re-induction therapy and consists of lenalidomide added to rituximab maintenance therapy. The PI Judith Trotman says: "The efficacy of lenalidomide in follicular lymphoma offers the potential to obtain remission for patients who have responded only partially to conventional immunochemotherapy."

Prior to commencement of maintenance therapy, all patients undergo a study-funded PET scan. Royal Prince Alfred PET department will ensure rigorous high quality PET QC across the accredited PET centres. Patients who are PET+ receive lenalidomide plus rituximab, those who are PET neg receive standard of care which is rituximab alone.

With only 15 sites activated, cross-referral will be critical. This has already happened with the first patient enrolled at Concord being referred from Liverpool hospital. Judith urges all members to support this study and refer patients to a participating site.

BMT Disease Group

BMT DG Chairs David Ritchie, Ian Lewis

BM06 Phase III Clinical Study of Allogeneic Stem Cell Transplantation with Reduced Conditioning (RICT) versus Best Standard of Care in Acute Myeloid Leukemia (AML) in First Complete Remission.

The ALLG will participate in this international study run by the Transatlantic Leukaemia Study Group (based in Sweden and Canada). The international PI is Mats Brune from Sahlgrenska University Hospital in Göteborg , Sweden, and ALLG PI is David Ritchie.

Study population encompasses AML patients, 51-70 years, in CR1 with an indication for allo-SCT but for whom a full myeloablative conditioning is not advisable due to age and/or medical impairment. This study assesses if patients who are suitable for a transplant (and have a suitable donor) have better results if they are treated with a transplant compared to those patients who would have had a transplant but no suitable bone marrow donor was available so instead received standard chemotherapy.

The ALLG BMT subgroup decided on participation in this important study as the optimal post remission consolidation therapy in this older group is far from determined. The trial results will show whether future treatment of AML in patients over 50 should always include BMT whenever possible.

The trial has been approved by the SDMC and is currently undergoing EOI. It is expected to be run in the 5 transplant centres in Australia and NZ. International target is 330 of which 206 have already been accrued. The target for the ALLG is 40 patients.

This newsletter was designed and edited by Janey Stone and approved by Delaine Smith and Megan Sanders.

Questions or comments? E-mail us at Dilupa.Uduwela@petermac.org