

NCRI Haematological Oncology Clinical Studies Group

Portfolio and accrual

The Haematological Oncology CSG has had 17 trials open during 2005-06. AML14 closed having reached its target accrual and recognising that the successor trial for older patients with AML and High Risk MDS Haematological Oncology Study Group Report (AML16) was approved in January 2005. It has however taken 18 months from approval of funding to opening of first site. This is largely due to severe delay in arranging agreements between the Trial Sponsor and the 150 potential sites involved. In the past we have had the ability to have rapid transition to a new trial, so this is an example of how new regulations will compromise recruitment.

Twelve trials are of our traditional randomised phase 3 design and accrue most of the patients, of these 5 have formal international collaboration and others have valuable international participation. All haematological cancers are covered (Acute and Chronic Myeloid Leukaemia, Acute and chronic Lymphoid Leukaemia, Myeloma, Thrombocythaemia, high risk Myelodysplasia, Stem Cell Transplantation and where relevant include Adults and Children). Recruitment in England at 2400 represents 27% of available cases which are augmented by recruitment from the rest of the UK, Ireland and Denmark. There are still gaps and therefore opportunities eg such as in relapsed disease or the older frail patients.

A matter of celebration was the closure of the randomised component of the Adult ALL (MRC/ECOG) trial after 18 years of recruitment. AML and Myeloma trials have formed the bulk of the recruitment this year as the CLL4 and PT1 trials closed after active recruitment. The energy being put into translational activity has greatly enhanced the trials, and will increase the associated academic output. The fact that samples have been collected on a regular basis, is a tribute to the Research Nurse support provided by the NCRN.

As always there are major regulatory challenges facing investigators who wish to set up or participate in clinical trials. This will continue to be problematic until such time as centralised initiatives produce model agreements which are accepted by sponsors, funders, Departments of Health and Trusts.

Membership and structure

A new chair was appointed in May 2006. Members were rotated in June 2006. 4 members left the Group and 9 new members were appointed. New working arrangements for the Group will become operational in the autumn.

Future direction

Over the next 3 years the Haematological Oncology Clinical Studies Group will be lead by Dr Don Milligan as the new chair. During this time developmental phase 2 trials in CLL will result in a full phase 3 trial submission. Proposals of a new trial in Adult ALL are under active discussion including a study of liposomal vincristine in the elderly. Myeloma 9 has recruited well and will be amended to incorporate newer agents now available pending plans for a replacement trial.

AML16 will pick up momentum with Translational projects being subject to TRICC applications. The novel application of a pick-a-winner design is meant to generate amendments to incorporate novel agents during the life of the trial. AML15 now enters its last year of its recruitment, having already completed recruitment of the first and largest randomised assessment of the addition of the immunoconjugate Gemtuzumab Ozogamicin. An outline submission for a successor trial (AML17),

which will feature molecular characterisation of each case and assessment of molecular intervention and minimal residual disease monitoring has been developed. A considerable component of this trial will depend on support from the Experimental Cancer Medicine Centre Programme which is being initiated this year.

Haematological Group Portfolio

Acronym	Title	PI(s)	Status
ALL 97	Medical Research Council Trial for Acute Lymphoblastic Leukaemia in Children. To compare steroids and thiopurines	Dr C Mitchell	Closed
AML 12 AD	AML12 MRC working party on leukaemia in adults acute myeloid leukaemia trial 12	Professor Alan Burnett, Professor AH Goldstone, Dr DW Milligan, Dr AG Prentice	Closed
AML 12 CH	AML12 MRC working party on leukaemia in childhood acute myeloid leukaemia trial 12	Dr B Gibson, Dr David Webb	Closed
AML 14	A Randomised Trial for Patients with Acute Myeloid Leukaemia or High Risk Myelodysplastic Syndrome Aged 60 or over	Professor Alan Burnett, Professor AH Goldstone	Open
AML 15	MRC working parties on leukaemia in adults and children. Acute myeloid leukaemia trial 15	Professor Alan Burnett, Professor AH Goldstone, Dr Keith Wheatley	Open
AML 16	National Cancer Research Institute Acute Myeloid Leukaemia and High Risk Myelodysplastic Syndrome Trial 16	Professor Alan Burnett	in Set-up
BSBMT AML Study	A randomised trial of two methods of graft versus host disease (GVHD) prophylaxis for patients with acute myeloid leukaemia undergoing matched sibling allogeneic transplant, aged 15 to 45 years	Dr David Marks	Closed
Campath De-escalation Study	Campath De-escalation Study	Dr Stephen Mackinnon	Open
CEP 701	An open-label Phase II trial of CEP-701 in older patients with Acute Myeloid Leukaemia not considered fit for intensive chemotherapy	Professor Alan Burnett	Closed
EsPhALL	European Intergroup Study on Post Induction Treatment of Philadelphia Positive Acute Lymphoblastic Leukaemia with Imatinib	Professor Vaskar Saha	Open
GIMI	G-CSF and imatinib mesylate intermittently	Dr Tessa Holyoake, Dr Mark Drummond	Open
HOVON-43	Randomised induction and post induction therapy in older patients (=61 yrs of age) with acute myelocytic leukaemia (AML) and refractory anaemia with excess of blasts (RAEB, RAEB-t)	WLJ van Putten, Dr Jonathan Kell	in set-up
LRF CLL4	(MRC Working party on Leukaemia in Adults) Chronic Lymphocytic Leukaemia trial 4: A	Professor D Catovsky	Closed

	Randomised Comparison of Chlorambucil, Fludarabine and Fludarabine plus Cyclophosphamide		
MERIT	MyEloma Renal Impairment Trial - A randomised controlled trial of adjunctive plasma exchange in patients with newly diagnosed multiple myeloma and acute renal failure	Dr Diana Samson, Dr Gill Gaskin	Open
MRC AML-HR	Protocol for patients with high risk (resistant, refractory, relapsed or adverse cytogenetic) AML	Professor Alan Burnett	Closed
MRC CLL5	The value of autografting younger patients with high risk chronic lymphocytic leukaemia (CLL). A randomised phase III intergroup trial	Professor D Catovsky, M Michallet, Dr DW Milligan	Open
MRC CML 2000 (IVa)	Medical Research Council/ European Blood and Marrow Transplant Prospective Randomised Trial of Autograft in chronic myeloid leukaemia	Professor JM Goldman	Closed
MRC CML V	A Medical Research Council Prospective Randomised Study to Compare Low-Dose Interferon-Alpha n1 (Welferon) Against High-Dose Interferon-Alpha n1 in Patients with Newly Diagnosed Chronic Phase Myeloid Leukaemia	Dr P Shepherd	Closed
MRC Myeloma IX	Myelomatosis therapy trial for patients of all ages. A randomised trial comparing second generation vs third generation bisphosphonates, induction chemotherapy regimens (CVAD vs CTD, and MP vs CTDa) and thalidomide maintenance vs no maintenance therapy.	Professor Tony Child, Professor Gareth Morgan, Dr G Jackson	Open
MRC MYEL VIII	A Medical Research Council Randomised Trial of Treatment for Inducing First Plateau Phase ABCM versus Three Courses of AMCM Followed by Oral Weekly Cyclophosphamide	Professor Ian McLennan, Dr Donald Milligan	Closed
MRC PT1	A Medical Research Council Randomised Trial to Compare Aspirin versus Hydroxyurea/Aspirin in Intermediate Risk Primary Thrombocythaemia and Hydroxyurea/Aspirin versus Anagrelide/Aspirin in High Risk Primary Thrombocythaemia	Dr John Green, Dr Claire Harrison	Open
MRC UKALL 2003	Medical Research Council Working Party on Leukaemia in Children UK National Acute Lymphoblastic Leukaemia (ALL) Trial UKALL 2003	Dr Ajay Vora	Open
MRC UKALL XII	Medical Research Council Trial for adult patients with acute lymphoblastic leukaemia Under 56 years of Age. To compare related donor transplant versus autologous transplant versus chemotherapy	Professor AH Goldstone	Open
Sodium Valproate	Phase II Study of the Tolerability and Efficacy of the Histone Deacetylase Inhibitor Sodium Valproate given in Conjunction with ATRA (all		Open

	trans retinoic acid) in Patients with Acute Myeloid Leukaemia		
SPIRIT - STI571	Prospective International Randomised Trial. A phase III, prospective randomised comparison of imatinib 400mg versus imatinib 600mg versus imatinib plus pegylated interferon in patients with newly-diagnosed chronic myeloid leukaemia.	Dr S O`Brien	Open
UKALLR3	An International Collaborative Trial for relapsed Refractory Acute Lymphoblastic Leukaemia (ALL)	Professor OB Eden, Dr PJ Darbyshire, Professor Vaskar Saha	Open
UKCLL 01FCM/FCM-R	A randomised phase II trial of fludarabine, cyclophosphamide and mitoxantrone (FCM) with or without rituximab in previously treated chronic lymphocytic leukaemia.	Dr Peter Hillmen	In set-up

Professor Alan K Burnett, Chair

Appendix 1: Key strengths and issues from the Progress Review, June 2005

Strengths:

- A large portfolio and range of trials
- A successful group, which is respected internationally
- Strong and effective leadership
- Strong links with the Paediatric Haem Onc Group with a high accrual into trials, particularly in the area of AML and Myelomas. There is a consistent quality of the trials and a high standard of the publications arising from the trials.
- The banking of 10,000 samples from patients with AML is a considerable strength.
- The group are open and well connected, inclusive and collaborative with the wider community.

The Haematological Oncology Group needs to consider:

- Restructuring the CSG to align its structure more closely with other CSGs
- Whether the Haem Onc and Lymphoma CSGs should remain separate groups
- Where it wished to be in the future and what its medium and long term priorities are
- Succession planning
- How best to “bring on” energetic young members
- Sharing the concept of appointing a translational statistician to mine trial data
- Increasing the number of basic scientists involved with the Subgroups
- The pattern of trial activity and whether or not they should develop trials in each area and whether or not their wish to involve a large number of DGHs had influenced trial design and their portfolio unduly
- Expand the current phase 2 developments