

NCRI Haematological Oncology Clinical Studies Group

Introduction

The Group continues to be successful with an active portfolio and very active subgroups. In last year's report there were concerns about the closure of some large trials and difficulty in developing replacement studies. Happily this situation has largely been reversed and new trials are now funded in myeloma and chronic lymphocytic leukaemia. The Group has been productive in developing phase II studies and the LRF Early Phase Trials Team (LRF ETT) is starting to gain momentum with 11 trials in development. Three of these are now funded and are in start-up phase. Two new commercial trials are open in CLL and others are being developed in the MPD subgroup.

There remain frustrations with the onerous bureaucratic nature of NHS clinical trial development. In particular, delays in agreeing trial sponsorship and obtaining local NHS R&D sign-off can be substantial. The new National Institute for Health Research Coordinating System for gaining Health Service Permission (NIHR CSP) was introduced in November 2008. It has not yet been demonstrated that trial delays are reduced and until local NHS R&D Departments are required to respond within fixed timelines, progress will be slow. These anxieties are well understood by the NIHR and there is a determination to improve matters emphasized by the recent letter to Trust and PCT CEO's from Dame Sally Davies and David Florey at the DH .

The Group underwent its three yearly review in February 2009. Professor Tim Maughan chaired the Panel. The progress review was generally very positive with praise for the wide portfolio, strong publication record and growth of phase II trials. A summary of key strengths of the Group and issues they need to address can be found in Appendix 1.

Membership and structure

The group currently has 24 scientific members. These cover the full range of haematological malignancies (AML, ALL, CLL, MDS, Myeloma, MPD) and specialists in stem cell transplantation and three statisticians. In addition there are three consumer members and seven ex-officio members. Membership includes a representative from the equivalent paediatric group. During the reporting period Dr Ann Hunter and Professor Nigel Russell stepped down from the Group and Professor David Marks and Dr John Snowden have joined the Group. Dr Shabin Syed replaced Dr David Grant as the Leukaemia Research Fund representative.

Haematological cancers are very heterogeneous and the Clinical Studies Group is supported by seven subgroups. These are:

- Adult Lymphoblastic Leukaemia (ALL) Chair- Dr A Fielding
- Acute Myeloid Leukaemia (AML) Chair- Professor A Burnett
- Chronic Myeloid Leukaemia (CML) Chair -Professor Richard Clark
- Myelodysplastic Syndromes (MDS) Chair -Professor D Bowen
- Chronic Lymphocytic Leukaemia (CLL) Chair -Professor P Hillmen
- Myeloma, Chair- Dr S Schey
- Myeloproliferative Disorders (MPD) Chair- Professor MF McMullin

Portfolio and accrual

1971 patients were recruited to Haem Onc studies in 2008-09, representing 18.5% of incidence cases, 10% (1065 patients) were to RCTs and 8.5% (906 patients) were to non RCTs. A summary of trials in the portfolio can be found in Table 1 below:

Table 1: Haematology Oncology CSG portfolio

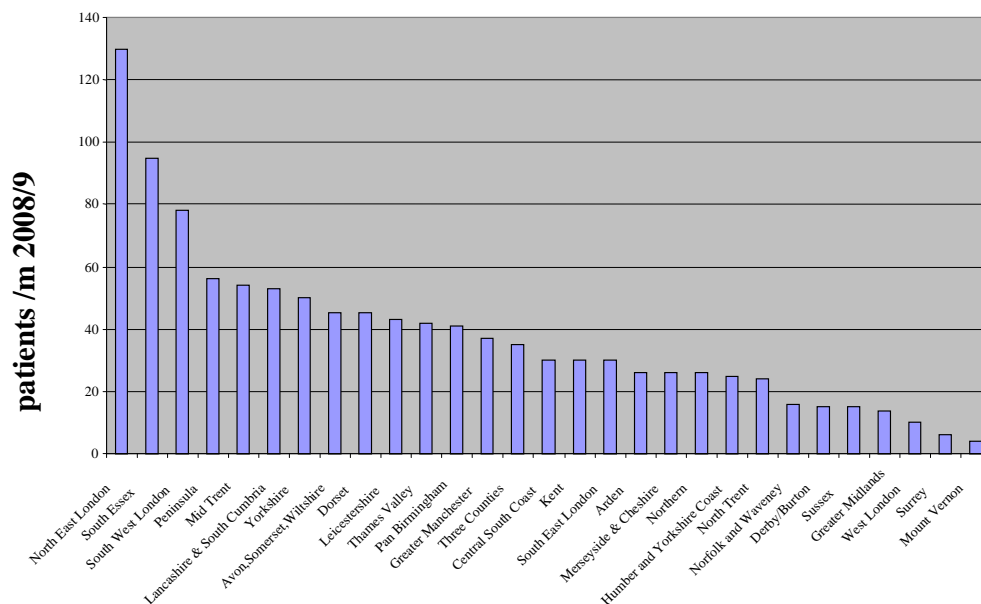
Acronym	Title	PI(s)	Status
ALLR3	An international collaborative trial for relapsed refractory acute lymphoblastic leukaemia (ALL)	Professor Tim Eden, Professor Vaskar Saha, Dr Philip Darbyshire	Open
AML 16	National Cancer Research Institute acute myeloid leukaemia and high risk myelodysplastic syndrome trial 16	Professor Alan Burnett	Open
AML 17	Working parties on leukaemia in adults and children trial in acute myeloid leukaemia or high risk myelodysplastic syndrome 17	Professor Alan Burnett	Open
ARCTIC	Attention dose Rituximib with chemotherapy in CLL, randomised phase II of FCR vs FC Mitoxantrone MiniR	Dr Peter Hillmen	In set up
CLL207	Eradication of minimal residual disease (MRD) in patients with chronic lymphocytic leukaemia (CLL) with alemtuzumab: A phase II study	Dr Peter Hillmen	Open
CMML201	A phase 2 study of azacitidine in chronic myelomonocytic leukaemia (CMML)	Professor David Bowen	In set up
CMV~IMPACT	CMV~IMPACT	Dr Karl Peggs	Open
CMV-ACE	A randomised controlled phase II trial of the adoptive transfer of selected cytomegalovirus-specific cytotoxic T lymphocytes (CMV-CTL) after allogeneic stem cell transplantation (SCT) in patients at risk of CMV disease	Dr Frederick Chen	Open
Early Diagnosis of Invasive Aspergillosis	Early diagnosis of invasive aspergillosis in a high risk group of patients using serum and bronchoalveolar lavage fluid, real time PCR and galactomannan ELISA	Dr Samir Agrawal	Open
EBV associated NK/T cell malignancies	Study of EBV associated NK/T cell diseases and formation of a registry	Dr Christopher Fox	Open
EsPhALL	European intergroup study on post induction treatment of philadelphia positive acute lymphoblastic leukaemia with Imatinib	Professor Vaskar Saha	Open

FCLL	A genetic study of chronic lymphocytic leukaemia and other lymphoproliferative disease	Dr Richard Houlston	Open
MDSBio1	Molecular and functional characterization of bone marrow function in normal subjects, myelodysplastic syndromes (MDS) and secondary disorders of haematopoiesis	Dr Alexander Sternberg, Dr Paresh Vyas	Open
MRC PT1	A randomised trial to compare aspirin versus hydroxyurea/Aspirin in intermediate risk primary thrombocythaemia and hydroxyurea/Aspirin versus anagrelide/Aspirin in high risk primary thrombocythaemia	Professor Tony 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	Professor Ajay Vora	Open
MRD feasibility study	Minimal residual disease monitoring in adult acute lymphoblastic leukaemia: A laboratory feasibility study	Dr Adele Fielding	Open
Myeloma Relapse (Intensive)	Myeloma X relapse (Intensive)-a comparison of high versus low-dose alkylating agent consolidation regimens for relapsed myeloma	Dr Gordon Cook	Open
NCRN042	OMB110913: A phase III, open label, randomized trial of ofatumumab in combination with fludarabine-cyclophosphamide vs. fludarabine-cyclophosphamide combination in subjects with relapsed chronic lymphocytic leukemia	Dr Matthew Cooper	In set up
NCRN043	A phase III, open label, randomized, multicenter trial of ofatumumab-chlorambucil combination vs. chlorambucil monotherapy in previously untreated patients with B-Cell chronic lymphocytic leukemia	Dr Matthew Cooper	Open
NCRN066	NCRN066 – Industry study	Mr Shabir Hasham	In set up
REGiM	REGiM - A randomised controlled trial of prolonged treatment with darbepoetin alpha (EPO), with or without recombinant human granulocyte colony stimulating factor (G-	Dr Samir G Agrawal	In set up

	CSF), versus best supportive care in patients with low-risk myelodysplastic syndromes (MDS)		
RICAZA	Phase II study of the tolerability of adjunctive azacitidine in patients with reduced intensity allogeneic stem cell transplantation for acute myeloid leukaemia and myelodysplasia	Professor Charles Craddock	Open
SPIRIT 2	STI571 Prospective international randomised trial 2: A phase III, prospective randomised comparison of imatinib (STI571, Glivec/Gleevec) 400mg daily versus dasatinib (Sprycel) 100mg daily in patients with newly-diagnosed chronic phase chronic myeloid leukaemia.	Dr Steve OBrien	Open
T-ANK AML	A phase I trial of allogeneic tumour-activated natural killer lymphocytes after low dose TBI and fludarabine for the treatment of selected patients with acute myeloid leukaemia	Dr Panagiotis Kottaridis	Open
TOPPS	A randomised controlled trial of prophylactic vs no-prophylactic platelet transfusions in patients with haematological malignancies (TOPPS: trial of prophylactic platelets)	Dr Simon Stanworth	Open

There are quite large differences in the degree of trial activity between Cancer Networks, see graph over page and work will be undertaken to understand and where possible rectify these differences.

RCT trial entry 2009/9 per million population



Trials in development

The Group has a number of trials in development or set up.

Acute Lymphoblastic Leukaemia

- UKALL 14: Phase III randomised controlled trial in adult ALL.
 Chief Investigator: Dr Adele Fielding
 Population: Adults with ALL
 Questions: Patients identified at high risk will be stratified and receive an allogeneic transplant and RIC technology will be explored in older patients. The use of anti CD20 and 22 antibodies will be evaluated in pre-B ALL. The impact of nelarabine in T ALL will be also evaluated.
 Status: Funded, but additional resource will be needed for MRD studies. Due to open third quarter 2009.
- MARALL: Monoclonal antibodies in ALL. Phase II study combining humanized anti-CD-20 (veltuzumba), anti-CD22 (epratuzumba) or both monoclonal antibodies with intensive chemotherapy in adults with recurrent acute lymphoblastic leukaemia.
 Chief Investigator : A Lister
 Status: Funded by HTA. Opening Quarter three 2009

Chronic Lymphocytic Leukaemia

- ARCTIC:
 (Attention-dose Rituximib with Chemotherapy in CLL). Randomised Phase II of FCR vs FC Mitoxantrone MiniR. 200 patients will be recruited from 20 centres.
 Chief Investigator : Peter Hillmen;
 Status: Funded by HTA. Opening Quarter three 2009
- GSK OMB 111913 (commercial: NCRN042)
 Randomised phase II trial of FC +/- ofatumumab in patients with relapsed CLL.
 Chief Investigator: D Milligan

Status: Due to open 2nd quarter 2009.

- CLL203 (RESPECT)
This is for poor risk early stage CLL. It is phase II study of lenalidomide. The trial has been developed by the LRF ETT and will be run through the Christie Trials Unit.
Chief Investigator: A Bloor
Status: Funded by LRF CTAP. Delayed due to problems with portfolio adoption.
- CLL210: a phase II trial of alemtuzumab, dexamethasone and lenalidomide combination therapy for high-risk CLL
Chief Investigator: A Pettitt
Status: Submitted to FSC now resubmitted to CTAAC. Funding decision awaited.
- CLL8 (CLARET): Phase III randomised trial of alemtuzumab consolidation
Chief Investigator: P Hillmen
Status: Funded by Bayer/Genzyme. Badged by CTAAC. Awaiting results from preceding Phase II CLL207 trial.
- PICCLE: Phase II clinical trial to assess the efficacy and safety of the drug AZD2281, a PARP-inhibitor, in relapsed and refractory Chronic Lymphocytic Leukaemia patients
Chief Investigator: G Pratt
Status: Funded by LRF CTAP. In set-up

Myeloma

- Myeloma XI: Randomised Phase II study of the optimum use of IMiDs and proteasome inhibition to improve outcome of standard treatment for myeloma.
Chief Investigator: G Morgan
Status: Funding agreed by CTAAC subject to PCT agreement to pay for lenalidomide and bortezomib. Due to open quarter 3 2009.
- LenaRIC: Phase II trial. The role of lenalidomide after RIC allogeneic transplant in myeloma.
Chief Investigator: M Cook
Status: Funded by CTAAC. Opening quarter 3 2009.

Myelodysplastic Syndromes

- ReGIM: A phase III, 3 arm study of supportive care study in low risk myelodysplasia comparing best standard of care with erythropoietin and G-CSF support.
Chief Investigator: S Agrawal
Status: Funded.
Status: Delays because of drug supply issues.
- CMML201: A phase II study of 5-azacytidine in chronic myelomonocytic leukaemia (CMML)
To assess the safety, tolerability and efficacy of the demethylating agent 5-azacytidine in the treatment of chronic myelomonocytic leukaemia, a myelodysplastic/myeloproliferative disease with a poor prognosis and no current treatment capable of influencing the natural disease history.
Chief Investigator: D Bowen
Status: Opening quarter 3 2009.

Myeloproliferative disease:

- COSMYD: Pegylated Interferon trial.
Chief Investigator: MF McMullin and Claire Harrison

Status: Funded by CTAAC. Undergoing design changes.

- VORINOSTAT: Phase II study with the Nordic Group, in patients with ‘advanced’ PV and high risk ET
Chief Investigator: MF McMullin
Status: IN set-up. Awaiting approval by Northern Ireland Clinical Research Network

Acute Myeloid Leukaemia

- RICAZA: Phase II: The role of azacitidine after RIC transplant for AML.
Chief Investigator: C Craddock
Status: Funded
- Len5: A pilot safety / tolerability study of Lenalidomide administered as monotherapy and in combination with standard chemotherapy for Acute Myeloid Leukaemia / high risk Myelodysplastic Syndrome with structural abnormalities of chromosome 5.
Chief Investigator: D Bowen
Status: Funded by CRUK. Opening quarter 2/3 2009.

Translational Science

Table 2 summarises the translational work of each of each of the Group’s subgroups.

Table 2 :Translational studies

Subgroup	Translational Studies
MPD	<ul style="list-style-type: none"> • Analysis of bone marrow pathology in essential thrombocythaemia trials. • Correlation of <i>JAK2</i> V617F status and disease phenotypes in essential thrombocythaemia and idiopathic myelofibrosis • Elucidation of the relationships between <i>JAK2</i> V617F clonality and leukaemic transformation in myeloproliferative disorders • Identification and investigation of new molecular changes in myeloproliferative disorders (<i>JAK2</i> exon 12 mutations and MPL mutations) • Role of SOCS 3 as a biomarker in myeloproliferative disorders • Molecular markers in <i>BCR-ABL</i> negative myeloproliferative disorders • Investigation of genetic defects in idiopathic erythrocytosis
MDS	<ul style="list-style-type: none"> • MDSBio1: characterisation of new diagnostic markers for low-risk Myelodysplastic Syndromes by multiparameter flow cytometry (ASH abstract: Blood 2008 112: Abstract 2670) • REGiM: identification of novel parameters to predict response to haematopoietic growth factor therapy for low-risk MDS. Assays to include genome-wide arrays (SNP), and serum proteomic biomarkers. • Len5: exploratory analysis of minimal residual

	<p>disease by multiparameter flow cytometry. Serum proteomic biomarker analysis for response prediction.</p> <ul style="list-style-type: none"> • CMML201: characterisation of chromatin modification by azacitidine therapy using chromatin immunoprecipitation and clonal sequencing. Exploratory analysis of response by multiparameter flow cytometry.
AML	<ul style="list-style-type: none"> • A large AML tissue bank established at University College Hospital and Cardiff which has more than 10,000 diagnostic samples • Correlation between molecular detection of NPM1 and WT1 and treatment outcome in patients treated with chemotherapy or allogeneic stem cell transplantation • MRD detection in CBF leukaemias and their potential use to guide therapies. • The use of sensitive flow techniques to identify MRD by immunophenotypic signature. • Pharmacokinetics of flt3 inhibitor CEP701 • Correlation between in vitro inhibition of flt3 activity and clinical outcome in patients with flt3ITD+ AML • Impact of maintenance azacitidine on DNA methylation status • Impact of everolimus therapy on mTOR signalling in AML blasts • Correlation of immunophenotypic detection of minimal residual disease and relapse risk in patients treated with chemotherapy or allogeneic stem cell transplantation • Impact of adjunctive azacitidine on immune response to immunodominant antigens such as WT1 and cancer testis antigen after reduced intensity allogeneic stem cell transplantation
Myeloma	<ul style="list-style-type: none"> • RNA expression array studies in newly diagnosed patients with myeloma and correlation with response to chemotherapy and overall survival • Correlation of FISH based cytogenetics with outcome in newly diagnosed myeloma • Impact of salvage chemotherapy using chemotherapy with or without stem cell transplantation on quality of life

	<ul style="list-style-type: none"> • Evaluation of impact of bortezomib salvage therapy on the ability to mobilise haematopoietic stem and progenitor cells in patients with relapsed myeloma • Role of serum free light chains in assessing response to treatment in newly diagnosed patients with myeloma • Impact of free light chain removal by extended haemodialysis on renal function in newly diagnosed patients with acute renal failure
CML	<ul style="list-style-type: none"> • Correlative studies of plasma inhibit levels and clinical response in newly diagnosed patients with CML • Clinical relevance of expression of Oct1 and other candidate TKI transporters • Impact of first and second generation TKIs on residual leukaemic stem cell population and correlation with clinical response • Role of abl kinase mutation detection on prediction of response to 2nd generation tyrosine kinase inhibitors • Role of immunotherapy using vaccination to BCR;ABL, WT1 and other candidate immunodominant antigens in suboptimal responders to imatinib • Tolerability and activity of adjunctive imatinib in patients undergoing reduced intensity allogeneic stem cell transplantation for imatinib resistant CML
CLL	<ul style="list-style-type: none"> • A tissue bank (compliant with Good Laboratory Practice), funded by CRUKhas now been established at the University of Liverpool, for the NCRI CLL Trials in order to encourage an even more active translational research programme. • Minimal residual disease (MRD) is a key end-point in almost all of the CLL trials including a primary end-point in one (the NCRI CLL207 Trial). • The analysis of the p53 pathway by both molecular and functional assays is a key component of our trials identifying a poor risk group of patients with CLL who are being treated with specific therapies. • The thorough analysis of prognostic markers from the LRF CLL4 trial has allowed the use of these stratify patients in order to test early therapy in poor risk Stage A patients. • Single nucleotide polymorphism (SNP) analysis is being applied to samples from the LRF CLL4 trials in order to identify areas of the genome which may be of interest in CLL.
ALL	<ul style="list-style-type: none"> • Development of a network of laboratories to standardise MRD measurements in adults to guide therapy in UKALL 14

Meetings

A very successful Annual Trials Meeting was held at the Royal College of Physicians in London on June 15th 2009. The meeting was divided into adult and paediatric trials and over 400 delegates attended. The date for 2010 is Tuesday May 25th.

As an experiment the British Society of Haematology invited the NCRI to showcase new trials at the Annual Scientific Meeting in Brighton in April 2009. Despite an early start the session was well attended. It is probable that this arrangement will continue in 2010.

Collaborations

The Group collaborate with a number of international groups on various trials. These are shown in Table 3.

Table: 3 International collaborations

Acute Lymphoblastic leukaemia trials:	
• UKALL 12	In partnership with ECOG
• UKALL 14	In partnership with ECOG (ECOG funding awaited)
Acute Myeloid Leukaemia trials:	Collaboration with the Dutch group in HOVON-43
• AML 17	Denmark, New Zealand and Norway
• AML 16	Denmark, New Zealand and Australia
Chronic Lymphocytic Leukaemia:	
• LRF CLL 4 trial	Argentina
• MRC CLL	Patient entry from Christchurch, New Zealand
• MRC CLL5	In partnership with the EBMT. Part of an EBMT Intergroup trial. Data support from Leiden Lead Group for the international GSK study on chlorambucil+/ofatumumab Participant in ERIC and development of European collaboration in long term follow up
MPD:	
• PT 1 Trial	France and Australia and New Zealand

3-year strategy

The Group's 3 year strategy is to:

- Establish common policies for bio-banking trial material for all tumour types
- Sustain high level of output of publications in both clinical trial outcomes and translational science in high impact journals.
- Establish at least one study in partnership with the Primary Care or Palliative CSGs
- Maintain the international reputation of the Group in haematological research

Priorities for next year

The priorities for next year are to:

- Get UKALL 14, Myeloma XI, ARCTIC, and the GSK CLL trials opened and recruiting quickly. To ensure that trials recruit on schedule.
- Overcome local R&D delays

Professor Donald W Milligan, Chair

Appendix 1

Haem Onc CSG Key strengths and issues from the Progress Review, February 2009

The Group was commended for their excellent work and the key strengths of the Group identified at the February 2009 review were:

- High and well deserved international reputation
- Impressive levels of accrual particularly to AML and CLL
- Impressive number of publications
- Broad extensive portfolio which addresses all disease subtypes
- Internationally outstanding PTI trial
- Innovative, efficient designs for the AML 16 and AML 17 trials
- Strong leadership at both Chair and Subgroup Chair level
- Smooth transition from old to new structures with the new subgroup structure well bedded in
- Good strategies for involving young researchers and researchers from DGHs in the Subgroups
- Tissue banking

The Panel identified the following issues which the Haem Onc CSG needs to consider:

- CLL work is becoming less competitive
- Strengthening CML, MPD and Myeloma work
- Integrating consumers more effectively into the main meetings
- Systematic collection of tissues to be expanded to all disease subtypes
- Formal processes for accessing tissues to be put in place
- The impact of recent ODAC guidance on the acceptance and use of biomarkers in clinical trials needs to be discussed, possibly with TCSG
- Consideration should be given to studies relating to living with the disease (eg psychosocial aspects, fatigue, infection) and working with the cross cutting CS(D)Gs on such studies
- Broadening the membership to include allied health professionals and health economists if the above approach is followed
- Identifying ways in which low recruiting networks can be encouraged and supported to improve their accrual
- Collaborating on international trials

Appendix 2

2008/09 Publications and abstracts

AML Subgroup

Walsby E, Walsh V, Pepper C, Burnett A, Mills K. Effects of the aurora kinase inhibitors AZD1152-HQPA and ZM447439 on growth arrest and polyploidy in acute myeloid leukemia cell lines and primary blasts. *Haematologica*. 93(5):662-9, 2008

Mead AJ, Gale RE, Hills RK, Gupta M, Young BD, Burnett AK, Linch DC. Conflicting data on the prognostic significance of FLT3/TKD mutations in acute myeloid leukemia might be related to the incidence of biallelic disease.. [Comment. Letter] *Blood*. 112(2):444-5;

Wang L, Giannoudis A, Lane S, Williamson P, Pirmohamed M, Clark RE. Expression of the uptake transporter hOCT1 is an important determinant of the response to imatinib in chronic myeloid leukaemia. *Clinical Pharmacology and Therapeutics* 2008; 83: 258-264. ****translational work on imatinib transport****

Clark RE, Davies A, Pirmohamed M, Giannoudis A. Pharmacologic markers and predictors of responses to imatinib therapy in patients with chronic myeloid leukaemia. *Leukemia and Lymphoma* 2008; 49: 639-642. ****invited review article****

Giannoudis A, Davies A, Lucas CM, Harris RJ, Pirmohamed M, Clark RE. Effective dasatinib uptake may occur without human Organic Cation Transporter 1 (hOCT1): implications for the treatment of imatinib resistant chronic myeloid leukaemia. *Blood* 2008, 112: 3348-3354. ****translational work on imatinib transport****

Drummond MW, Heaney N, Kaeda J, Nicolini F, Clark RE, Wilson G, Shepherd P, Tighe J, McLintock L, Hughes T, Holyoake TL. A pilot study of continuous imatinib vs. pulsed imatinib with or without G-CSF in CML patients who have achieved a complete cytogenetic response. *Revised version submitted to Leukemia December 2008.* ****This is the definitive report of the Glasgow based GIMI study****.

Rojas JM, Owen S, Knight K, Wang LH, Clark RE. Naturally occurring CD4⁺ CD25⁺ FOXP3⁺ T regulatory cells are increased in chronic myeloid leukaemia patients with high BCR-ABL transcripts and can suppress anti-BCR-ABL responses. *Submitted to Blood December 2008.* ****translational work that arose from our EPIC vaccination trial****

ALL Subgroup

Jacob M. Rowe, Georgina Buck, Anthony V Moorman, Martin S Tallman, Susan M Richards, Adele K Fielding, Alan K. Burnett, Ian M Franklin, Peter H. Wiernik, Hillard M Lazarus, Elisabeth Paietta, Mark R. Litzow, David I Marks, Selina Luger, Gordon W. Dewald, and Anthony H. Goldstone Standard Consolidation/Maintenance Chemotherapy Is Consistently Superior to a Single Autologous Transplant for Adult Patients with Acute Lymphoblastic Leukemia: Results of the International ALL Trial (MRC UKALL XII/ECOG E2993) *Blood (ASH Annual Meeting Abstracts)*, Nov 2008; 112: 3314

Marc R Mansour, Maria Luisa Sulis, Veronique Duke, Letizia Foroni, Sarah Jenkinson, Christopher G Allen, Rosemary E Gale, Georgina Buck, Sue Richards, Elisabeth Paietta, Martin Tallman, Anthony H Goldstone, Jacob M. Rowe, Adolfo A. Ferrando, and David C

Linch Unlike Paediatric T-ALL, Notch-1 and FBXW7 Mutations Do Not Seem to Predict a Better Outcome in Adult Patients: Data from the UKALLXII/ECOG2993 Protocol Blood (*ASH Annual Meeting Abstracts*), Nov 2008; 112: 2548.

B. R. Patel, Keiren Kirkland, R. Pearce, Richard E Clark, Charles F. Craddock, Effie Liakopolou, Adele K Fielding, Stephen Mackinnon, Eduardo Olavarria, Michael N Potter, Nigel H. Russell, Bronwen E. Shaw, Anthony H. Goldstone, and David I Marks T-Cell Depleted Unrelated Donor Stem Cell Transplants Appear to Be of Value for Adult Philadelphia Chromosome Negative ALL Patients and Should Be Evaluated Prospectively in New Large Group Studies Blood (*ASH Annual Meeting Abstracts*), Nov 2008; 112: 4413.

Elisabeth Paietta, Xiaochun Li, Sue Richards, Janis Racevskis, Gordon W. Dewald, Jacob M. Rowe, Martin S Tallman, Hillard M Lazarus, Mark Litzow, Anthony H. Goldstone, and Peter H. Wiernik Implications for the Use of Monoclonal Antibodies in Future Adult ALL Trials: Analysis of Antigen Expression in 505 B-Lineage (B-Lin) ALL Patients (pts) on the MRC UKALLXII/ECOG2993 Intergroup Trial. *Blood (ASH Annual Meeting Abstracts)*, Nov 2008; 112: 1907.

Elisabeth Paietta, Xiaochun Li, Sue Richards, Janis Racevskis, Gordon W. Dewald, Jacob M. Rowe, Martin S Tallman, Hillard M Lazarus, Mark R. Litzow, Anthony H. Goldstone, and Peter Wiernik Outcome in Philadelphia Chromosome Positive (Ph+) Adult ALL Patients (Pts) May Be More Determined by CD25 Expression Than by Ph Status Per Se. *Blood (ASH Annual Meeting Abstracts)*, Nov 2008; 112: 1500.

Adele K. Fielding, Susan M. Richards, Hillard M. Lazarus, Mark R. Litzow, Selina M. Luger, David I. Marks, Andrew K. McMillan, Jacob M. Rowe, Martin S. Tallman, and Anthony H. Goldstone Does Imatinib Change the Outcome in Philadelphia Chromosome Positive Acute Lymphoblastic Leukaemia in Adults? *Data from the UKALLXII/ECOG2993 Study*.

Bella Patel, Anthony H. Goldstone, Philip Ross, Sue Richards, Letizia Foroni, R. Chopra, and Adele Fielding The Impact of Imatinib Therapy on Adult Philadelphia Positive Acute Lymphoblastic Leukaemia (ALL): *Early Results from the UKALL12/ECOG 2993 Study*.

Myeloma Subgroup

Sylvia Feyler, Andy Rawstron, Graham Jackson, John Snowden, Kim Hawkins, and Roderick J. Johnson. Thalidomide Maintenance Following High Dose Therapy in Multiple Myeloma: A UK Myeloma Forum Phase 2 Study.

David C. Johnson, Suzanne Grindle, Faith Davies, David Gonzalez, Christine Ramos, Kim Hawkins, Suzanne Bell, Heather Kesby, S. Vincent Rajkumar, Erik Rasmussen, John Crowley, Emily Blood, J. Anthony Child, Brian G.M. Durie, Brian G. Van Ness, and Gareth J. Morgan Inherited Genetic Variation and the Risk of Developing Venous Thrombosis with Thalidomide treatment in Myeloma Patients

Faith E. Davies, J. Anthony Child, Kim Hawkins, Susan Bell, Julia Brown, Mark T. Drayson, Graham H. Jackson, and Gareth J. Morgan. Newly Diagnosed Myeloma Patients Are at Risk of Venous Thrombotic Events - High Risk Patients Need To Be Identified and Recieve Thromboprophylaxis: The MRC Experience.

Roger G. Owen, J. Anthony Child, Andy C. Rawstron, Sue Bell, Kim Cocks, Faith E. Davies, Graham H. Jackson, Gareth J. Morgan, and Mark T. Drayson. Defining Complete Response in Multiple Myeloma: Role of the Serum Free Light Chain Assay and Multiparameter Flow Cytometry.

Gareth J. Morgan, Faith E. Davies, Roger G. Owen, Andrew C. Rawstron, Sue Bell, Kim Cocks, Walter Gregory, Graham Jackson, Mark T. Drayson, Matthew W. Jenner, and James A. Child. Thalidomide Combinations Improve Response Rates; Results from the MRC IX Study.

Gareth J. Morgan, David C. Johnson, John Crowley, John Shaughnessy, Jr., Pieter Sonneveld, Brian Durie, Christine Ramos, Brian G. Van Ness, Bart Barlogie, Antje Hoering, Jeff Haessler, Dalsu Baris, Michael Katz, Vincent S. Rajkumar, and H. Goldschmidt. The Genetic Contribution to the Aetiology of Thalidomide Associated VTE

ASH Dec 9th-13th 2008

Gareth J Morgan, MD, PhD 1, Graham H Jackson 2, Faith E Davies, MD 3, Mark T Drayson 4, Roger G Owen 5, Walter M Gregory 6, Dena C Cohen 6, Alex J Szubert, Susan E Bell, Fiona Ross and James A Child. Maintenance Thalidomide May Improve Progression Free but Not Overall Survival; Results from the Myeloma IX Maintenance Randomisation. *Oral Presentation* 656.

Myeloma Brian A Walker, Paola E Leone, Nicholas J Dickens, Matthew W Jenner, Laura Chiecchio, GianPaolo Dagrada, Fiona M Ross, Faith E Davies and Gareth J Morgan. High Resolution Genomic Profiling Using Single Nucleotide Polymorphism Microarrays Identifies Multiple Novel Genomic Minimally Deleted Regions in Multiple

MPD Subgroup

Wilkins BS, Erber WN, Bareford D, Buck G, Wheatley K, East CL, Paul B, Harrison CN, Green AR*, Campbell PJ*. Bone marrow pathology in essential thrombocythemia: interobserver reliability and utility for identifying disease subtypes. *Blood*, 111: 60-70, 2008. (*joint senior authors)

Percy MJ, Beer PA, Campbell G, Dekker A, Green AR, Oscier D, Rainey MG, van Wijk R, Wood M, Lappin TRJ, McMullin MF and Lee FS. Novel exon 12 mutations in the HIF2A gene associated with erythrocytosis. *Blood*, 111: 5400-5402, 2008.

Beer PA, Campbell PJ, Scott LM, Bench AJ, Erber WN, Bareford D, Wilkins BS, Reilly JT, Hasselbalch HC, Bowman R, Wheatley K, Buck G, Harrison CN, Green AR. MPL mutations in myeloproliferative disorders: analysis of the PT-1 cohort. *Blood*, 112: 141-149, 2008.

Cross NCP, Daley GQ, Green AR, Hughes TP, Jamieson C, Manley P, Mughal T, Perrotti D, Radich J, Skoda R, Soverini S, Vainchenker W, Verstovsek S, Villeval J-L, Goldman JM. BCR-ABL1-positive CML and BCR-ABL1-negative chronic myeloproliferative disorders: some common and contrasting features. *Leukemia* 1-15, 2008.

Bercovich D, Ganmore I, Scott LM, Wainreb G, Birger Y, Elimelech Arava, Shocah C, Cazzaniga G, Biondi A, Basso G, Cario G, Schrappe M, Stanulla M, Strehl S, Haas OA, Mann G, Binder V, Borkhardt A, Kempinski H, Trka J, Bielorei B, Avigad S, Stark B, Smith O, Dastugue N, Bourquin J-P, Tal NB, Green AR, Izraeli S. Mutations of JAK in acute lymphoblastic leukaemias associated with down's syndrome. *Lancet*, 2008

Zhao R, Follows GA, Beer PA, Scott LM, Huntly BJP, Green AR*, Alexander DR*. Inhibition of the Bcl-x_L deamidation pathway in myeloproliferative disorders. (*joint senior authors). *N. Engl J Med*. In press.

Fourouclas N, Li J, Gilby DC, Campbell PJ, Beer PA, Goodeve AC, Reilly JT, Green AR, Bench AJ. Methylation of the Suppressor of Cytokine Signalling 3 (SOCS3) gene in Myeloproliferative Disorders. *Haematologica*. In press.

Elliott J, Suessmuth Y, Scott LM, Nahlik K, McMullin MF, Constantinescu SN, Green AR, Johnston JA. SOCS3 tyrosine phosphorylation as a potential bio-marker for myeloproliferative

neoplasms associated with mutant JAK2 kinases. *Haematologica*. *In press*. *MPL mutations in myeloproliferative disorders: analysis of the PT-1 cohort*.

Abstracts

Susan E. Robinson, Peter J. Campbell, Georgina Buck, Keith Wheatley, Jacqueline A. Cutler, Ruth B. Wheeler, Savita Rangarajan, Beverley J. Hunt, Anthony R. Green, Claire N. Harrison_Impact of Platelet Glycoprotein Polymorphisms upon Clinical Events in Essential Thrombocythaemia Patients Enrolled in the PT1 Trial. Session Type: *Poster Session, Board #733-*

Philip Beer, Peter Campbell, Wendy Erber, Linda Scott, Anthony Bench, David Bareford, Wilkins Bridget, Keith Wheatley, Georgina Buck, Claire Harrison, Anthony Green677] Clinical Significance of MPL Mutations in Essential Thrombocythemia: Analysis of the PT-1 Cohort. Session Type: *Oral Session*

Percy MJ, Beer PA, Campbell G, Dekker AW, Green AR, Oscier D, Rainey MG, van Wijk R, Wood M, Lappin TRJ, McMullin MF, Lee FS. Familial erythrocytosis associated with a mutational hotspot in the HIF2A gene *Haematologica* (2008) 93 (s1) 179.

