

HAEMATOLOGY ONCOLOGY RESEARCH TEAM

JUNE 10 ISSUE 4

WELCOME!

Welcome to the fourth edition of the Haematology Oncology research team newsletter! In this edition we will continue to update you on the latest haematology and lymphoma trial news.

FOCUS ON: MYELOMA AND RELAPSED DLBCL

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AML / MDS

- **AML16:** NCRN study for older AML/high risk MDS.
- **AML17:** NCRN study for adults with AML/high risk MDS.
- **AML Len 5 :** Lenalidomide as monotherapy & in combination with standard chemotherapy for AML/high risk MDS with chromosome 5 abnormalities.
- **Romiplostim:** A study of Romiplostim for thrombocytopenia in low or INT-1 Risk MDS.
- **MDS Registry Study:** European registry for newly diagnosed MDS with low or INT-1 Risk.
- **AZD1152 C14 Mass Balance:** Phase I study assessing metabolism, excretion & PK of AZD1152 and AZD1152 hQPA following IV administration of [¹⁴C]-AZD1152 in AML.
- **MDS 005:** Lenalidomide vs placebo in transfusion-dependent anaemia due to IPSS Low or Int-1 risk MDS without deletion 5q[31].

MYELOMA

- **Myeloma IX:** Myelomatosis therapy trial for patients of all age groups. Relapsed sub protocol.
- **Myeloma X:** Determine the role of a 2nd autologous transplant after high-dose chemotherapy.
- **Myeloma XI:** Thalidomide, Lenalidomide and Bortezomib combinations with maintenance Lenalidomide.
- **Vantage:** Open-label study of Vorinostat with Bortezomib in relapsed/refractory myeloma.
- **KW2478-INT-001:** Phase 2/3 study of KW-2478 with Bortezomib in relapsed/refractory myeloma.

CML

- **Spirit 2:** Randomised comparison of imatinib and dasatinib in newly-diagnosed chronic phase CML.
- **CMML201:** Phase II study of azacitidine in CMML.

TRANSPLANT

- **Ricza:** Adjunctive azacitidine in patients undergoing RIC allogeneic transplantation for AML or MDS.
- **CMV impact:** Immunoprophylactic Adoptive Cellular Therapy Study.

ALL

- **UKALL2003:** UK national randomised trial for children and young adults with ALL.

CLL

- **Admire:** NCRN comparative study of FCR vs FCR plus mitoxantrone in previously untreated CLL.
- **Mable:** A Phase IIIb study of Rituximab with bendamustine or Chlorambucil.
- **CLL009:** Safety and efficacy of Lenalidomide dose regimens in relapsed/refractory B-Cell CLL.
- **Respect:** Use of Lenalidomide in early stage CLL with poor prognostic factors.

STUDIES...OPEN

HODGKIN LYMPHOMA

- **Escalated ABVD:** Phase 1 dose escalation study to find the MTD of doxorubicin in ABVD.
- **RAPID:** Does PET negativity allow the omission of radiotherapy in early stage HL?
- **PAIReD:** Reduced intensity transplantation using the BEAM-Alemtuzumab protocol for primary refractory/relapsed refractory Hodgkin's disease.
- **ReACH:** Reduced intensity sibling allogeneic transplantation for relapsed, chemosensitive, PET positive Hodgkin Lymphoma.
- **RATHL:** PET-adapted dose-escalation of therapy in advanced stage HL.

MANTLE CELL LYMPHOMA

- **MCP3:** Randomised phase 3 comparing FC Vs. FC-Rituximab 1st line.
- **SPRINT:** Randomised phase 3 comparing Lenalidomide to 'dealers choice' chemotherapy.
- **CD19:** As with follicular NHL.

T-CELL LYMPHOMA

- **T-cell project:** Database registration for all T-cell NHL.
- **CHOP-Campath:** Phase 2 dose escalation study to find the MTD of Campath in conjunction with CHOP chemotherapy.

FOLLICULAR LYMPHOMA

- **FORT:** Randomisation of high Vs. low dose radiotherapy for any radiotherapy indication in FL.
- **GAUDI:** Phase 2 study of a 3rd generation anti-CD20 monoclonal in conjunction with chemo, for relapsed FL.
- **SCHRIFT:** Phase 2 study of abbreviated R-Chemo followed by Zevalin in relapsed FL.
- **CD19:** Phase I study of adoptive transfer of autologous T Cells with pre-conditioning chemotherapy and IV IL2 in CD19 positive malignancy.
- **Halozyme:** Randomised s.c versus i.v. rituximab in patients receiving maintenance therapy.

DLBCL

- **14 Vs 21 PET sub study:** prognostic value of early PET after 2 cycles of R-CHOP.
- **R-CHOP-Z:** Integrating Zevalin radioimmunotherapy into 1st line R-CHOP treatment.
- **R-GCVP:** Substitutes gemcitabine for doxorubicin in those unfit for anthracyclines.
- **ORRCHARD:** Rituximab-DHAP Vs. Ofatumumab-DHAP in relapsed disease.
- **Inotuzumab Ozogamicin:** Phase 2 study of a novel antibody-drug conjugate in relapsed disease. Targets CD22.
- **CD19:** Phase I study of adoptive transfer of autologous T Cells with pre-conditioning chemotherapy and IV IL2 in CD19 positive malignancy.

STUDIES IN PLANNING

- **YM155:** Phase 1 study of a survivin inhibitor in conjunction with rituximab.
- **CHT25:** Radioimmunotherapy in refractory Hodgkin Lymphoma .
- **Agent B:** 1st line Cisplatin/Gemcitabine/Bevacuzimab in T-cell NHL.
- **Belinostat:** HDAC inhibition in relapsed T-cell NHL.
- **Panobinostat:** Phase III trial of a HDAC inhibitor in combination with bortezomib and dexamethasone in relapsed or refractory multiple myeloma.
- **UKALL 14:** Newly diagnosed adults with ALL (≥ 25 years to ≤ 65 years).
- **CP4055-306:** Elacytarabine vs investigators choice in late stage AML.



**WE NEED
YOUR
HELP!**

As a tertiary referral centre we specialise in clinical trials that may not be available anywhere else in your catchment area. We ask you to review all your patients who may be eligible for our studies. We are relying on outside referrals to recruit to these studies, so please get in touch.

If you would like any more information about any of our studies, contact details for the research team are available on page 7.



FOCUS ON... MYELOMA

MYELOMA XI

Randomised comparisons in myeloma patients of all ages of thalidomide, Lenalidomide and bortezomib

We are pleased to announce that the MRC Myeloma XI for all newly diagnosed patients is now open at The Christie.

VANTAGE 095

An international, multicenter, open-label study of Vorinostat (MK-0683) in combination with Bortezomib in patients with relapsed and refractory multiple myeloma.

Treatment of patients with relapsed and refractory multiple myeloma after at least 2 prior treatment regimes who are:

- Refractory to Bortezomib
- Relapsed, refractory, intolerant and/or ineligible to other therapies including IMiD (thalidomide or lenalidomide)

Primary Objective: To define the objective response rate associated with the administration of vorinostat in combination with Bortezomib to patients with relapsed and refractory multiple myeloma.

Inclusion Criteria:

- ≥ 18 years of age
- Refractory to Bortezomib
- Relapsed, refractory, intolerant and/or ineligible to other therapies including IMiD (thalidomide or lenalidomide)
- ECOG ≤ 2
- Measurable disease, defined as quantifiable serum M-protein value and/or, where applicable, urine M-protein of ≥ 200 mg/24 hours
- At least 2 prior (standard or experimental) anti-myeloma regimens

Exclusion Criteria:

- Prior allogeneic bone marrow transplant or planning of any type of transplantation
- Prior treatment with vorinostat or other HDAC inhibitors (patients who have received compounds with HDAC inhibitor-like activity as anti-tumour therapy should not be enrolled, patients which have received such compounds for other indications may enrol after a 30-day washout period.
- Unable to tolerate prior treatment with Bortezomib or hypersensitivity to any compounds of Bortezomib
- Currently receiving corticosteroid therapy
- Pre-existing NCI CTC grade 1 neuropathy with pain or \geq grade 2 neuropathy

FOCUS ON... MYELOMA

KW2478-INT

An open-label, dose escalation, multicenter phase 1/2 study of KW-2478 in combination with Bortezomib in subjects with relapsed and/or refractory multiple myeloma

Primary Objective: Establish safety, tolerability and RP2D of KW-2478 in combination with bortezomib .

Inclusion Criteria:

- Myeloma confirmed by clonal bone marrow plasma cells > 10%, M-protein in serum or urine (except in non-secretory myeloma) and evidence of end-organ damage attributed to underlying plasma cell proliferative disorder
- Between 1—3 prior regimens for MM which they did not respond or from which they have relapsed
- Life expectancy of ≥ 3 months
- Must not have progressed while receiving any prior Bortezomib alone or in combination (if applicable)

Exclusion Criteria:

- Non-secretory or bi-clonal MM
- Hypersensitivity to boron or mannitol
- Prior treatment with any Hsp90 inhibitors
- Received an allograft transplant

PANOBINOSTAT

A multicenter, randomised, double-blind, placebo controlled phase III study of panobinostat in combination with Bortezomib and dexamethasone in patients with relapsed multiple myeloma

Primary Objective: To compare progression-free and overall survival

Inclusion Criteria:

- Multiple myeloma confirmed by monoclonal immunoglobulin on electrophoresis, bone marrow plasma cells $\geq 10\%$ or biopsy proven plasmacytoma and related organ or tissue impairment
- 1 to 3 prior lines of therapy and requiring treatment for:
 - ◊ relapsed
 - ◊ relapsed to at least on eprior line and refractory to another (by not reaching a MR or progressing under therapy)
- Either serum M-protein $\geq 1\text{g/dl}$ and/or urine M-protein $\geq 200\text{mg/24h}$

Exclusion Criteria:

- Progression under all prior lines of antimyeloma therapy
- Refractory to prior Bortezomib
- Allogeneic SCT recipient presenting with GvHD
- Intolerance to Bortezomib or dexamethasone or components of these
- Prior treatment with DAC inhibitors



FOCUS ON... RELAPSED DLBCL

MYELOMA

Every issue we will be focusing on a specific study or disease area in order to increase recruitment. Please see our 'focus on myeloma pages' this month featuring studies which will be suitable for your myeloma patients. See pages 4 & 5 for more details.

We have several options upcoming for this difficult to treat group of patients, who have relapsed following a rituximab containing chemotherapy, usually R-CHOP. In the **CORAL** study (R-DHAP Vs. R-ICE), refractory patients (relapse <12months) to upfront rituximab-chemo, the results of salvage with R-Chemo then auto-graft remain poor: **response rate: 54% and 2 yr EFS 34%**. So, please consider the following two studies:

ORCHARRD

This Phase 3 randomized trial compares ofatumumab-DHAP to rituximab-DHAP as salvage prior to auto-graft. Rituximab and ofatumumab are 1st and 2nd generation anti-CD20 mAbs respectively.

Primary Objective: Does ofatumumab overcome the poor results with rituximab in this setting?

Inclusion Criteria:

- 2nd line/ 1st relapse only, following R-CHOP. Relapse at any timepoint
- Relapse after CR/PR to R-CHOP :CD 20 +ve required: **repeat biopsy needed**
- Refractory, ie SD/PD: repeat biopsy optional
- PET scan
- 2x LNs $\geq 1.5 \times 1.0$ cm OR 1xLN $\geq 2.0 \times 1.0$ cm, not previously irradiated
- ECOG 0-2
- Eligible for autologous stem cell transplantation

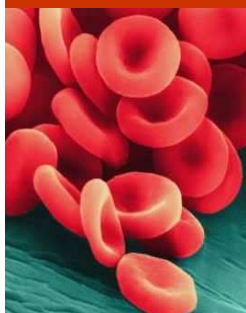
Exclusion Criteria:

- >1 prior lines of therapy, 1st line must contain rituximab+anthracycline/anthracenedione
- XRT >10 Gy
- Steroids >10mg/day prednisolone equivalent
- Uncontrolled medical conditions
- Marrow/hepatic/renal insufficiency
- Active infection

CMC-544

Sponsor: Wyeth
Phase 2 open-label trial

Rituximab+ CMC-544 as salvage prior to autograft. CMC-544 (aka Inotuzumab ozogamicin) is a novel anti-CD22 humanised mAb conjugated to calicheamicin, a very potent cytotoxic. This trial is aimed at those who fail standard salvage (or ORCHARRD), and those who relapse after an autograft. Subject eligibility/selection is complex, so please discuss potential candidates with the research team.



**ARE YOU
GCP
TRAINED?**

If not, please see below for details on how to book....

THE PATERSON INSTITUTE FOR CANCER RESEARCH

Our Honorary Consultant in Haematology, Dr Tim Somervaille, leads the Leukaemia Biology Laboratory in the Paterson Institute for Cancer Research.



The Paterson Institute for Cancer Research

The Paterson Institute for Cancer Research is the leading cancer research institute within The University of Manchester, core funded by Cancer Research UK, the largest independent cancer research organisation in the world. The Manchester Cancer Research Centre (MCRC) has been established in The University of Manchester following the transfer of the Paterson Research Institute to the University.

The Leukaemia Biology Laboratory

The Leukaemia Biology Laboratory is one of a number of research groups based at the Paterson Institute. The aim of the group is to further the understanding of the biology of human leukaemia stem cells, in order to identify genes and cellular pathways that are critical for their function and which could be targeted by novel therapies.

DATES TO KEEP IN MIND!

ADVANCES IN HAEMATOLOGY RESEARCH 2010 STUDY DAY

Monday 28th June 2010

- Haematology Trials from a Local and National Perspective
- New and Emerging Treatments in AML, CLL, and Myeloma
- Prognostic and Molecular Monitoring in AML and CLL
- Reduced Intensity Transplant Trials in Hodgkins Lymphoma
- Recruitment of Teenagers and Young Adults in Clinical Trials

Fee is £100 (includes lunch), to book please contact education.events@christie.nhs.uk.

There are only a few places left so book now to avoid disappointment!

IS YOUR GCP TRAINING UP TO DATE?

If you are working in clinical trials, it is essential that you complete GCP training every 2 years.

The following dates for Christie GCP training are available:

Thursday 3rd June 2010

Friday 3rd September 2010

Update sessions are being held on:

Wednesday 2nd June 2010 (am or pm session)

Thursday 2nd September 2010 (am or pm session)

To book on please contact Rachael Baxter in R&D (Rachael.Baxter@christie.nhs.uk).



CONTACT DETAILS

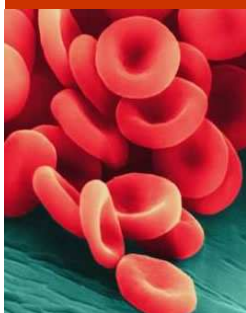
**NEXT
ISSUE**
Sept 10

In our next issue we will be focusing on...

AML & Follicular non-Hodgkin lymphoma

ADDRESS

Haematology and Transplant Unit,
The Christie NHS Foundation Trust,
Wilmslow Road,
Manchester,
M20 4BX.



LYMPHOMA TEAM

Name	Job Title	Telephone	Email
Professor John Radford	Consultant	0161 446 3612	John.Radford@christie.nhs.uk
Dr Kim Linton	Consultant	0161 918 7227	Kim.Linton@christie.nhs.uk
Dr Adam Gibb	Clinical Research Fellow	Bleep via Switch	Adam.Gibb@christie.nhs.uk
Professor Tim Illidge	Consultant	0161 918 7225	Timothy.Illidge@christie.nhs.uk
Dr Richard Cowan	Consultant	0161 466 3409	Richard.Cowan@christie.nhs.uk
Dr Maggie Harris	Consultant	0161 446 3302	Margaret.Harris@christie.nhs.uk
Dr Ed Smith	Consultant	0161 446 3952	Ed.Smith@christie.nhs.uk
Susan Neeson	Lead Research Nurse	0161 446 3019	Susan.Neeson@christie.nhs.uk
Caroline Hamer	Research Nurse	0161 918 7226	Caroline.Hamer@christie.nhs.uk
Suzanne Allibone	Research Nurse	0161 918 7220	Suzanne.Allibone@christie.nhs.uk
Tanya Massey	Data Manager	0161 446 3874	Tanya.Massey@christie.nhs.uk
Hannah Johnson	Senior Clinical Trial Assistant	0161 446 3711	Hannah.Johnson@christie.nhs.uk

HAEMATOLOGY TEAM

Name	Job Title	Telephone	Email
Dr Adrian Bloor	Consultant / Research Lead	0161 446 3657	Adrian.Bloor@christie.nhs.uk
Dr Mike Dennis	Consultant	0161 446 3271	Mike.Dennis@christie.nhs.uk
Dr Jim Cavet	Consultant	0161 446 3278	Jim.Cavet@christie.nhs.uk
Dr Tim Somervaille	Consultant	0161 446 8420	Tsomervaille@picr.man.ac.uk
Michelle Davies	Lead Research Nurse	0161 918 7248 (12679)	Michelle.Davies@christie.nhs.uk
Simeon Mitton	Research Nurse	0161 446 8093	Simeon.Mitton@christie.nhs.uk
Nita Smeeton	Research Nurse	0161 446 8298	Nita.Smeeton@christie.nhs.uk
Joanne Allen	Research nurse (Young Oncology Unit)	0161 918 7098 (12343)	Joanne.Allen@christie.nhs.uk
Benjamin Kisaka	Senior Clinical Trial Assistant	0161 918 7224	Benjamin.Kisaka@christie.nhs.uk
Antonia Veale	Clinical Trials Coordinator	0161 918 7222	Antonia.Veale@christie.nhs.uk