

HAEMATOLOGY ONCOLOGY RESEARCH TEAM

WELCOME!

DECEMBER 10 ISSUE 6

Welcome to the sixth 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: TRANSPLANT AND HODGKIN'S LYMPHOMA

STUDIES...OPEN

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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.
- **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.
- **MDS 005:** Lenalidomide vs placebo in transfusion-dependent anaemia due to IPSS Low or Int-1 risk MDS without deletion 5q[31].
- **Clavella:** Elacytarabine vs investigators choice in late stage AML.

ALL

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

MYELOMA

- **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.
- **Panorama:** HDAc inhibitor with bortezomib and dexamethasone.

CML

- **Spirit 2:** Randomised comparison of imatinib and dasatinib in newly-diagnosed chronic phase CML.

TRANSPLANT

- **Ricaza:** Adjunctive azacitidine in patients undergoing RIC allogeneic transplant for AML / MDS.
- **CMV impact:** Immunoprophylactic Adoptive Cellular Therapy Study.
- **PAIRed:** Reduced intensity transplant for primary refractory/relapsed refractory Hodgkin's.
- **ReACH:** Reduced intensity sibling allogeneic transplant for relapsed, chemosensitive, PET positive Hodgkin lymphoma.
- **MinoAllo:** Low intensity allo transplant in mantle cell lymphoma

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 IN PLANNING

WEBSITE

For more information on any of our trials in setup or currently recruiting please [click here](#) to visit our website

- **YM155:** Phase 1 study of a survivin inhibitor in conjunction with rituximab.
- **CHT25:** Radioimmunotherapy in refractory Hodgkin Lymphoma .
- **BELIEF:** Belinostat, a HDAC inhibitor in relapsed T-cell NHL.
- **PICLLe:** Olaparib in CLL patients with 11q deletion or ATM mutation , or T-Prolymphocytic Leukaemia and Mantle Cell Lymphoma
- **Reveal:** Velcade combination chemotherapy in relapsed or refractory patients with AML amyloidosis
- **Castlemans:** CNTO plus best supportive care in Castleman's disease
- **MUKone:** Bendamustine with Thalidomide and Dexamethasone in relapsed/refractory myeloma

STUDIES...OPEN

HODGKIN LYMPHOMA

- **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.
- **AETHERA:** Randomisation of SGN-35 versus best supportive care post autograft in relapsed Hodgkin Lymphoma

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

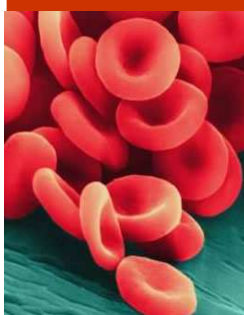
- **GemBex:** Gemcitabine and Bexarotene in cutaneous T-cell lymphoma.
- **T-cell project:** Database registration for all T-cell NHL.
- **CHOP-Campath:** Phase 2 dose escalation study to find the MTD of Campath in conjunction with CHOP.

FOLLICULAR LYMPHOMA

- **FORT:** Randomisation of high Vs. low dose radiotherapy for any radiotherapy indication in FL.
- **CD19:** Phase I study of adoptive transfer of autologous T Cells with pre-conditioning chemotherapy and IV IL2 in CD19 positive malignancy.
- **SparkTHERA:** Randomised s.c versus i.v. rituximab in patients receiving maintenance therapy.
- **PACIFICO:** Randomisation of R-CVP versus R-FC first line in patients over the age of 60.

DLBCL

- **14 Vs 21 PET sub study:** prognostic value of early PET after 2 cycles of R-CHOP.
- **ORRCHARD:** Rituximab-DHAP Vs. Ofatumumab-DHAP in relapsed disease.
- **CD19:** Phase I study of adoptive transfer of autologous T Cells with pre-conditioning chemotherapy and IV IL2 in CD19 positive malignancy.



FOCUS ON... TRANSPLANT

**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 8.



MINO ALLO

Phase II study of low intensity allogeneic transplantation in Mantle Cell Lymphoma.

Patients will enter the study once a suitable donor has been identified and there is an intention to proceed to an allogeneic procedure. All patients will receive RIC allogeneic transplantation and may require DLI therapy depending on response.

Primary Objective: To document the toxicity, feasibility and survival following reduced intensity allogeneic transplantation from HLA-compatible sibling or unrelated donors.

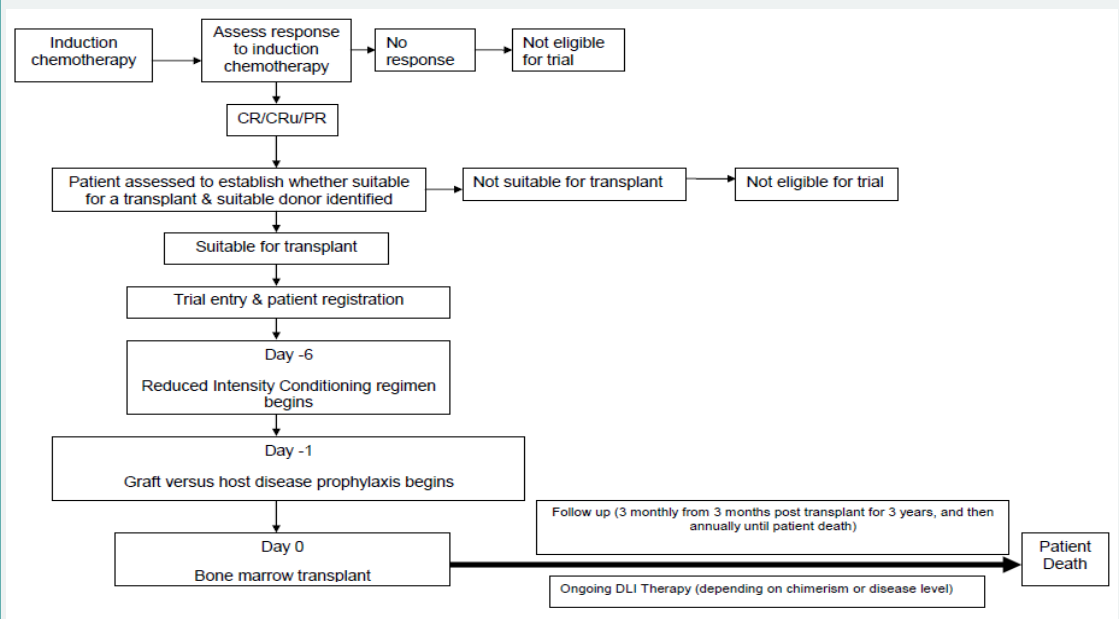
Inclusion Criteria:

- ≥ 18 years of age with a confirmed diagnosis of MCL (as detailed in the protocol)
- No concurrent serious medical condition that would preclude an allograft
- Evidence of PR/CR following prior therapy
- A HLA matched donor

Exclusion Criteria:

- Relapsed or progressive disease
- Previous malignancy in the last 5 years (except non-melanoma skin tumours and stage 0 cervical carcinoma)
- Known serological positivity for HBV, HCV or HIV
- A history of psychological illness or condition that in the opinion of the investigator may adversely affect compliance with planned therapy
- Impaired renal, hepatic or cardiac function, symptomatic respiratory compromise, CNS involvement, Pregnant or lactating women
- ECOG score <2

Study design



FOCUS ON... TRANSPLANT

RICAZA

Phase II study of the tolerability of adjunctive azacitidine in patients undergoing reduced intensity allogeneic stem cell transplantation for acute myeloid leukaemia.

Patients will receive a reduced intensity allogeneic stem cell transplant: fludarabine, melphalan and alemtuzumab as per standard practice or standard FLAMSA RIC regimen followed by azacitidine for 5 days every 28 days commencing on week 6 post transplant for 10 cycles.

Primary Objective: To assess tolerability of post-transplant azacitidine with AML using a RIC regimen, to document the impact on disease relapse, GvHD and chimerism.

Inclusion Criteria:

- ≥ 18 years of age in whom allogeneic transplantation using a myeloablative conditioning regimen is contra-indicated
- Patients with a HLA identical sibling or suitable matched unrelated donor (no greater than a single allele mismatch and considered fit for reduced intensity transplant)

Exclusion Criteria:

- Patients with contraindications to receiving transplant conditioning therapy or azacitidine
- Pregnant or lactating women or adults of reproductive potential not willing to use appropriate medically approved contraception during the trial and for 12 months post azacitidine
- Any co-morbidity that in the investigators opinion will affect the patient participation in this study.

Every issue we will be focusing on a specific study or disease area in order to increase recruitment. Please see our 'focus on pages' this month featuring studies which will be suitable for your transplant and Hodgkins patients.

FOCUS ON... HODGKINS

RATHL (Risk Adapted Therapy Hodgkin Lymphoma)

Phase 3 /NCRI Badged

A study evaluating the role of interim PET scanning post 2 cycles of ABVD in the escalation/de-escalation of chemotherapy in advanced Hodgkin Lymphoma. PET negative subjects are randomised between continuing ABVD or omitting bleomycin with AVD. PET positive subjects escalate to a BEACOPP the 14 regimen, with a second PET scan dictating whether they should receive radiotherapy if still positive.

Inclusion criteria

- Classical Hodgkin lymphoma (HL) Aged 18 or above
- Clinical stage IIB, IIIA, IIIB or IV, or Clinical stage IIA with adverse features:
- No previous chemotherapy, radiotherapy or other investigational drug for HL
- Performance status 0-3
- Adequate marrow/hepatic/renal function
- Patients with a significant history of ischaemic heart disease or hypertension must have an acceptable left ventricular ejection fraction (LVEF) ≥50%
- Lung function tests showing transfer factor within 25% of normal predicted value for the patient



FOCUS ON... HODGKINS

For a bit of festive fun take part in our Christmas puzzle competition on page 7...

RATHL (cont..)

Exclusion criteria

- Poorly controlled Diabetes mellitus
- Other concurrent uncontrolled medical condition
- Cardiac contra-indication to doxorubicin: abnormal contractility on echocardiography or nuclear medicine examination (MUGA)
- Neurological contra-indication to chemotherapy (e.g. pre-existing neuropathy)

BRENTUXIMAB VEDOTIN (SGN-35)

Brentuximab vedotin (SGN-35) is an antibody drug conjugate of a CD30 targeted antibody (cAC10) and an anti-tubulin agent, monomethyl auristatin E (MMAE). The CD30 antigen is present on Hodgkin lymphoma and anaplastic large cell lymphoma cells and activated leukocytes. On binding to the CD30 receptor, the drug is internalised and enzymatically cleaved in lysosomes. Released MMAE binds to tubulin and induces G2/M cell cycle arrest and apoptosis.

Remarkable results for two pivotal phase 2 trials of single agent SGN-35 in relapsed or refractory lymphoma were presented at ASH earlier this month:

In relapsed or refractory HL (n=102):

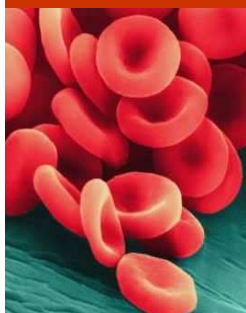
- **75%** of patients achieved an objective response by Cheson 2007 criteria with a median duration of response of 29 weeks by independent central review and 47 weeks by investigator assessment
- **34%** of patients achieved complete remission; the median duration of response for patients in CR had not yet been reached at a median follow-up of approximately one year

In relapsed or refractory ALCL patients (n=58): interim analysis of first 30 treated patients

- **87%** of patients achieved an objective response by Cheson 2007 criteria; duration of objective responses currently range from 4–36 weeks, with responses ongoing in 18 patients
- **57%** of patients achieved complete remission and 33% of patients in CR went on to receive an autologous or allogeneic SCT

Manageable Toxicity:

In both studies, toxicity was manageable and most common adverse events were peripheral sensory neuropathy, fatigue, nausea, upper respiratory tract infection and diarrhoea. The most common Grade 3 or higher adverse events were neutropenia, peripheral sensory neuropathy, thrombocytopenia and anaemia.



FOCUS ON... HODGKINS

AETHERA

A Phase 3 study of SGN-35 following ASCT in relapsed Hodgkin Lymphoma

This randomised, double blind, placebo-controlled Phase 3 study will compare brentuximab vedotin (SGN-35) with best supportive care in patients at high risk of residual Hodgkin Lymphoma (HL) following ASCT. SGN-35 is a novel antibody-drug conjugate which delivers a potent tubular toxin to CD30+ cells. Patients who relapse on placebo will be eligible to receive SGN-35 on the AETHERA extension trial.

Primary Objective: To assess whether SGN-35 can overcome poor prognostic features present at the time of HL relapse. Study endpoints include PFS, overall survival and toxicity.

Study Design: Subjects are randomised 1:1 to receive 16 cycles of SGN-35 or placebo, administered as a 30 minute iv infusion once every 3 weeks. CT scans are performed 3-monthly.

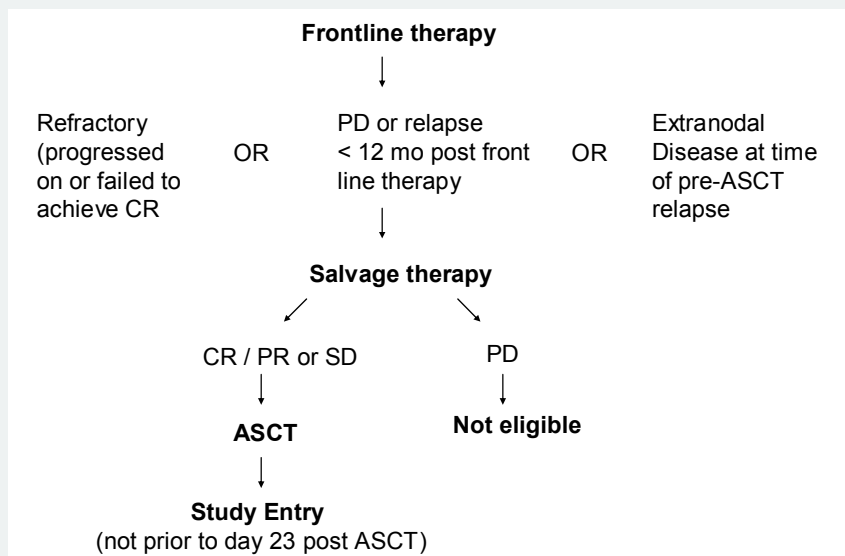
Main Inclusion Criteria:

- ≥ 18 years of age and a histologically confirmed diagnosis of HL
- ECOG PS 0 or 1
- ASCT in the previous 30-45 days and recovery of marrow function by day +45 (ANC ≥ 1 , and unsupported platelets ≥ 50)
- High risk of residual HL post ASCT indicated by at least one of the following:
 - Refractory HL i.e. progressing on or failing to achieve CR after standard first-line treatment
 - Progression or relapse occurring < 12 months from the end of first-line treatment
 - Extranodal disease at the time of pre-ASCT relapse

Main Exclusion Criteria:

- Previous treatment with SGN-35
- Previous allogeneic transplant
- Progressive disease following ASCT

Eligibility and stratification:



NEWS

ARE YOU
GCP
TRAINED?

If not, please see below for details on how to book on to a course at The Christie

WORLDS LARGEST EARLY PHASE CLINICAL TRIALS UNIT OPENS AT THE CHRISTIE

The newly completed £35 million three storey building opened its doors to patients on Monday 22nd November and includes the biggest chemotherapy facility in the UK.

It is hoped the new unit will help develop new treatments for a whole range of cancers and save lives across the globe.

2,400 patients a year will be able to access the latest treatments through the clinical trials, with around 200 drug trials going on at any one time. Up to 700 chemotherapy and clinical trial patients a week will be treated in the new centre which has 70 beds and 65 treatment chairs. Along with 19 consulting rooms, special pharmacy and research laboratory, processing around 11,000 blood and tissue samples every year.

For the full press release and video please [click here](#).



GCP TRAINING

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.

For dates and to book on please contact Rachael Baxter in R&D on 0161 446 8153 or email Rachael.Baxter@christie.nhs.uk.

MERRY CHRISTMAS



The research team would like to wish everyone a very merry Christmas and a happy new year!



Get into the festive spirit and complete our Christmas puzzle! The answers to each clue can be found in the word search and the first letter of each clue spells a famous Christmas song. We will be giving a PRIZE (tbc) to the first person to email us with the name of the song (Antonia.Veale@christie.nhs.uk).

M	D	Y	A	V	T	R	E	E	S	A	M	P	F
I	O	R	A	N	G	E	U	T	A	N	N	T	R
N	M	S	S	C	L	I	J	H	W	O	T	H	O
C	W	R	A	P	P	I	N	G	R	R	I	G	S
E	A	T	N	I	O	D	G	T	M	T	N	I	T
S	G	M	D	R	T	C	R	B	E	H	S	L	B
P	X	A	Y	S	W	E	K	G	L	P	E	E	I
I	M	T	C	E	S	K	I	M	O	O	L	D	T
E	L	N	L	N	W	O	F	G	O	L	L	L	E
S	E	O	A	E	Y	U	L	E	G	L	I	E	D
T	O	D	W	C	N	I	B	O	R	C	T	G	L
P	N	F	S	N	O	W	B	A	L	L	I	N	W
O	R	G	T	V	R	D	N	S	R	P	S	A	S
C	M	C	S	T	N	E	M	A	N	R	O	H	O

CLUES

- What do you get if you cross a snowman with a vampire? (9)
- Which winter bird steals christmas presents (5)
- What monkey would you turn into if you ate too many satsumas? (10)
- What do you call a cat on a beach at christmas? (10)
- Whats a female christmas tree called? (6)
- What do liverpool sing at christmas? ____ never walk alone (4)
- What do you get if you eat too many christmas decorations (11)
- What do reindeer hang on their antlers? (10)
- What do you call an eskimo cow? (7)
- Where do snowmen go to dance? (8)
- Which gallagher brother likes christmas? (4)
- Which reindeer stops nausea? (12)
- What does eminem do at christmas? (8)
- Who hides in the bakery at christmas? (10)
- What dessert would you put on the top of the christmas tree? (12)
- Where do polar bears go to vote? (9)



CONTACT DETAILS

**NEXT
ISSUE**
March 10

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

Myeloma & Mantle Cell Lymphoma

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