UKALL14

‘REGISTRATION ONLY’ SUB-STUDY

TRAINING AND Q&A SESSION

‘Registration only’ sub-study - overview

From implementation of protocol v.11.0 onwards, newly-diagnosed B-cell patients can now enter a UKALL14 ‘registration only’ sub-study.

- Main aim is to collect basic data and samples to address laboratory aims
- Standard ALL treatment as per local clinician’s choice
- No IMPs or NIMPs
- New CRFs to collect limited data
- No safety reporting

‘Registration only’ sub-study - aims

Please refer to Protocol Appendix 1, section 2

Data and samples collected on ‘registration only’ sub-study patients will be used to address the following laboratory aims:

- To characterise the genomic landscape of adult ALL
- To investigate the clonal origins of relapsed ALL
- To define a T-cell signature which predicts response to allo-HCT
- To develop global risk models in adult ALL that integrate demographic, genetic and response information

‘Registration only’ sub-study - informed consent

Please refer to Protocol Appendix 1, Section 3

- Informed consent must be obtained from the patient by a delegated person prior to any trial-specific intervention

- There are 2 patient information sheets/consent forms to give to patients:
  - ‘Registration only’ sub-study PIS/consent
  - Optional **Additional Genetic Testing – Buccal Swab** PIS/consent
    - Consent can be obtained for buccal swab at any time. We ask that as many patients as possible give samples to further our understanding of leukaemia.

- Document details of the consent process in the patient’s notes:
  - when the PIS was given
  - discussion(s) about the trial with the patient
  - when consent was taken
  - who took consent

‘Registration only’ sub-study - informed consent

Please refer to Protocol Appendix 1, Section 3

- 24 hours should be allowed for patients to consider participation in the trial
  - If this is not possible, patients may consent on the same day provided the member of staff taking consent is satisfied that the patient understands the trial and its implications and follows up with the patient to confirm ongoing willingness to participate and documents this in patient notes
- Remember to complete the patient number on the top of the consent form following trial registration
- The original consent form plus one copy must be stored at site (one in the ISF & one in the patient’s medical notes).
- The patient must also be given a copy – document in the notes that this has been done.
- Do not send consent forms to UCL CTC.

Results required before sub-study entry

Patients cannot enter the sub-study until the results below confirming eligibility are known:

Results required before registration
Percentage of bone marrow blasts to confirm diagnosis of ALL (if not yet available, copy of diagnostic report)
Patient's disease lineage
Medical history (specifically history of hepatitis B & C and HIV)
Negative pregnancy test (women of childbearing potential)

Please refer to Protocol Appendix 1 for a full list of screening investigations and eligibility criteria.

‘Registration only’ sub-study - eligibility

Please refer to Protocol Appendix 1, section 5

Inclusion criteria	Exclusion criteria
a) Patients aged ≥25 and ≤65 old with ALL or aged ≥19 and ≤65 old with Philadelphia chromosome positive ALL	a) Mature B-cell leukaemia (eg. Burkitt’s lymphoma)
b) Newly diagnosed, previously untreated ALL (a steroid pre-phase is permitted but not required)	b) Known HIV infection
c) Written informed consent	c) Known history of hepatitis B infection*
	d) Known history of hepatitis C infection*
	e) Pregnant or lactating women
	f) Blast transformation of CML

**As per national MHRA guidance, hepatitis testing must be done prior to administering rituximab*

‘Registration only’ sub-study - registration

Please refer to Protocol Appendix 1 Section 6

- Pre-registration evaluations should be carried out as per local policy.
- Complete ‘Registration only’ sub-study Registration form in full (including contact details on front page) and fax/email to UCL CTC
- If sending by email, patient identifiable information (NHS no, DOB) must be redacted before sending and then provided to CTC by telephone
- Please allow a minimum of 2 hours for registrations to be processed (cut off time for same day processing is 4pm)
- CTC will fax/email confirmation of the patient’s registration, with trial number, back to the site
- Provide patient with a copy of their signed consent form.

'Registration only' sub-study - samples at study entry

Please refer to Protocol Appendix 1 Section 8.3

Samples taken prior to consent can be used, but cannot be sent until patient has given their consent.

Test	Sample required	Send to
MRD baseline testing	3-5ml bone marrow in EDTA or 30-50ml blood in EDTA	UCL Cancer Institute MRD lab
Constitutional DNA (optional)	Buccal swab	UCL Cancer Institute MRD lab
Cytogenetics	Report from local cytogenetics tests	Leukaemia Research Cytogenetics Group, Newcastle

‘Registration only’ sub-study - treatment

Please refer to Protocol Appendix 1 Section 7

- Treatment for ‘registration only’ patients is decided by the local clinician
- May follow the UKALL14 backbone regimen but it is not mandated
- Any drugs used to treat ‘registration only’ patients will not be regarded as IMPs
- Drugs must be sourced from hospital stock and will not be reimbursed
- Follow local practice with regards to recovery/continuation at each phase
- Accountability logs are not required - follow standard local practice regarding drug traceability.

'Registration only' sub-study
- samples during treatment/follow up

Test	Sample required	When	Send to
End of phase 1 MRD	3-5ml bone marrow aspirate in EDTA	Count recovery at end of phase 1	UCL Cancer Institute MRD lab *Report can be sent on special request*
End of phase 2 MRD	3-5ml bone marrow aspirate in EDTA	Count recovery at end of phase 2	UCL Cancer Institute MRD lab *Report will be sent within 10 days of receipt*
Post-transplant MRD	3-5ml bone marrow aspirate in EDTA	Every 3 months post non-myeloablative transplant	UCL Cancer Institute MRD lab
MRD at relapse	3-5ml bone marrow aspirate in EDTA *or* 30-50ml peripheral blood in EDTA (if WBC >$30x10^9$/l)	When relapse suspected/ confirmed	UCL Cancer Institute MRD lab

'Registration only' sub-study - data management

NEW CRFs

- **'Registration only' Registration form** – study entry, before starting induction treatment
- **'Registration only' Induction form** – after induction phase 1 and phase 2
- **'Registration only' Treatment form** – after each phase of treatment/every 3 months during maintenance
- **'Registration only' Annual Follow Up form** – from anniversary of completion of treatment/transplant

And if transplant is given:

- **'Registration only' Transplant Day 100 form**
- **'Registration only' GvHD form**

EXISTING CRFs

- **Relapse form** *(send ASAP)*
- **Death form** *(send ASAP)*
- **Lost to Follow Up form** *(send ASAP)*
- **Centre Transfer form** *(send ASAP)*

CRFs should be sent within 30 days of timepoint unless stated otherwise

N.B. CRFs are still in development and subject to change

'Registration only' sub-study - safety reporting

- **AEs, SAEs or pregnancies do not need to be reported to the CTC for 'registration only' sub-study patients**

- Clinicians should report adverse reactions and serious adverse reactions to the MHRA via the Yellow Card scheme, as per routine post-marketing surveillance.

UKALL14 Trial Team Contact Details

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