

# Safety and tolerability of the combination of veltuzumab and epratuzumab with intensive chemotherapy in patients with relapsed B-cell acute lymphoblastic leukaemia (ALL)

<b>Submission date</b> 12/05/2010	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 12/05/2010	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 24/03/2022	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://cancerhelp.cancerresearchuk.org/trials/a-study-adding-biological-therapy-chemotherapy-acute-lymphoblastic-leukaemia-come-back-after-treatment-marall>

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### EudraCT/CTIS number

2008-002286-32

### IRAS number

**ClinicalTrials.gov number**

NCT01279707

**Secondary identifying numbers**

7566

## **Study information**

**Scientific Title**

Phase I/II study combining humanised anti-CD20 (veltuzumab), anti-CD22 (epratuzumab) or both monoclonal antibodies with intensive chemotherapy in adults with recurrent B-precursor acute lymphoblastic leukaemia (ALL)

**Acronym**

MARALL

**Study objectives**

This is a phase I/II study to determine the safety and tolerability of the combination of veltuzumab and epratuzumab with intensive chemotherapy in patients with relapsed B-cell acute lymphoblastic leukaemia (ALL). A maximum of 55 patients will be treated with a combination of UKALL XII induction chemotherapy and the monoclonal antibodies veltuzumab and epratuzumab. Veltuzumab and epratuzumab are humanised monoclonal antibodies that target CD20 and CD22 surface proteins, respectively. Both of these proteins are expressed on ALL tumour B cells.

One group of patients will receive UKALL XII + veltuzumab; a second, UKALL XII + epratuzumab and if limited toxicity is found in these first two groups, a third group will receive, UKALL XII + both veltuzumab and epratuzumab. Patients will be assessed for safety, tolerability and disease response. Safety and tolerability will be measured by the number of dose limiting toxicities (DLTs) in each group. Disease response will be measured by the microscopic appearance of patient bone marrow samples at day 29, and by molecular tests for tumour cells in bone marrow.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

North London REC 3 approved on the 10th August 2009 (ref: 09/H0709/42)

**Study design**

Multicentre non-randomised interventional screening and treatment trial

**Primary study design**

Interventional

**Secondary study design**

Non randomised controlled trial

**Study setting(s)**

GP practice

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please contact marall@qmc.qmul.ac.uk to request a patient information sheet

## Health condition(s) or problem(s) studied

Topic: National Cancer Research Network; Subtopic: Haematological Oncology; Disease: Leukaemia (acute lymphoblastic)

## Interventions

Cohort A patients:

1. UKALL 12 chemotherapy
2. Veltuzumab at 200 mg/m<sup>2</sup> intravenously on days 8 (as a 2-hour infusion), 15, 22 and 29 (as a 1-hour infusion)

Cohort B patients:

1. UKALL 12 chemotherapy
2. Epratuzumab at 360 mg/m<sup>2</sup> intravenously on days 8, 15, 22, 29 (as a 1-hour infusion)

Cohort C patients:

1. UKALL 12 chemotherapy
2. Epratuzumab and veltuzumab at 360 mg/m<sup>2</sup> and 200 mg/m<sup>2</sup> respectively, intravenously on days 8, 15, 22, 29.

All patients will receive UKALL 12 chemotherapy as shown below:

1. Daunorubicin given at 60 mg/m<sup>2</sup> intravenously on days 1, 8, 15 and 22
2. Dexamethasone given at 10 mg/m<sup>2</sup> orally on days 1 - 5 and days 11 - 14
3. L-asparaginase given at 5,000 iU/m<sup>2</sup> intravenously or intramuscularly on days 17, 19, 21, 23, 25, 27 and 29
4. Methotrexate 12.5 mg given intrathecally on day 24 only (unless central nervous system [CNS] leukaemia detected at relapse)
5. Vincristine given at 1.4 mg/m<sup>2</sup> intravenously on days 1, 8, 15 and 22

Follow-up length: 1 months

Study entry: registration only

## Intervention Type

Drug

## Phase

Phase I/II

## Drug/device/biological/vaccine name(s)

Veltuzumab, epratuzumab

## Primary outcome measure

Assess the safety and tolerability of the combination of veltuzumab and/or epratuzumab with intensive chemotherapy for recurrent adult B-precursor ALL by scoring dose limiting toxicity events in patients.

## Secondary outcome measures

Achievement of morphological and molecular complete remission on Day 29 bone marrow

## Overall study start date

06/01/2010

## Completion date

09/10/2011

# Eligibility

## Key inclusion criteria

1. Aged between 16 and 65 years, either sex
2. Confirmed diagnosis of first recurrence of B-precursor ALL (according to the World Health Organization [WHO] classification)
3. First complete remission (CR1) greater than 6 months
4. WHO/Eastern Cooperative Oncology Group (ECOG) performance status of 0 - 2 and well enough to receive intensive combination chemotherapy
5. Negative pregnancy test in women of childbearing potential. Women will not be considered of child bearing potential if they have undergone surgical removal of the uterus or are post menopausal and have been amenorrhoeic for at least 24 months.
6. Patients must have a cardiac ejection fraction of greater than 50%
7. Patients must have adequate organ function:
  - 7.1. Renal function serum creatinine less than 2.5 x upper limit of normal (ULN) or estimated glomerular filtration rate (eGFR) greater than 50 ml/min (measured EDTA or estimated creatinine clearance, e.g., Cockcroft & Gault)
  - 7.2. Liver function - bilirubin/alanine aminotransferase (ALT) less than 2.5 x ULN
8. Patients must be able to comply with the study schedule

## Participant type(s)

Patient

## Age group

Adult

## Sex

Both

## Target number of participants

Planned sample size: 55; UK sample size: 55

## Total final enrolment

27

## Key exclusion criteria

1. Patients with Philadelphia positive (Ph +ve) ALL
2. Patients at 2nd or greater relapse of their ALL
3. Patients should not have received chemotherapy for relapsed ALL (except corticosteroids for a maximum of 5 days, before joining the study)
4. Patients who have already received greater than 340 mg/m<sup>2</sup> daunorubicin (or equivalent

total anthracycline dose) therapy

5. Patients who have received prior mediastinal radiotherapy

6. Patients with co-morbidities: e.g. uncontrolled hypertension and or poorly controlled diabetes which in the PI's opinion makes them unsuitable for the study

7. Patients with severe psychiatric disorders which in the PI's opinion makes them unsuitable for trial participation

8. Females of childbearing potential and all males must be willing to use an effective method of contraception (hormonal or barrier method of birth control; abstinence) for the duration of the study and for up to 3 months after the last dose of study medication. Note: Subjects are not considered of child bearing potential if they are surgically sterile (they have undergone a hysterectomy, bilateral tubal ligation, or bilateral oophorectomy) or they are post-menopausal (that is amenorrheic for 24 months).

9. Females of childbearing potential must have a negative pregnancy test within 7 days prior to starting the study

10. Females must not be breastfeeding

11. Patients may not receive any other investigational agent during the study

12. Patients should not have received any antibody therapy within 9 months of joining this study

**Date of first enrolment**

06/01/2010

**Date of final enrolment**

09/10/2011

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Centre for Experimental Cancer Medicine**

London

United Kingdom

EC1M 6BQ

## **Sponsor information**

**Organisation**

Queen Mary University of London

**Sponsor details**

Mile End Road

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United Kingdom  
E1 4NS

**Sponsor type**  
University/education

**Website**  
<http://www.qmul.ac.uk/>

**ROR**  
<https://ror.org/026zzn846>

## **Funder(s)**

**Funder type**  
Charity

**Funder Name**  
Cancer Research UK (CRUK) (UK) (ref: C1574/A9768)

**Alternative Name(s)**  
CR\_UK, Cancer Research UK - London, CRUK

**Funding Body Type**  
Private sector organisation

**Funding Body Subtype**  
Other non-profit organizations

**Location**  
United Kingdom

**Funder Name**  
Immunomedics Inc (USA)

## **Results and Publications**

**Publication and dissemination plan**  
Not provided at time of registration

**Intention to publish date**

**Individual participant data (IPD) sharing plan**

Not provided at time of registration

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Basic results</a>				No	No
<a href="#">Plain English results</a>			24/03/2022	No	Yes
<a href="#">HRA research summary</a>			28/06/2023	No	No