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

Submission date
12/05/2010

Registration date
12/05/2010

Last Edited
24/03/2022

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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

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Additional identifiers

Clinical Trials Information System (CTIS)
2008-002286-32

ClinicalTrials.gov (NCT)

NCT01279707

Protocol serial number
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 epratzumab 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

Study type(s)
Treatment

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^2 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^2 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^2 and 200 mg/m^2 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^2 intravenously on days 1, 8, 15 and 22
2. Dexamethasone given at 10 mg/m^2 orally on days 1 - 5 and days 11 - 14
3. L-asparaginase given at 5,000 iU/m^2 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^2 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, epratzumab

Primary outcome(s)
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.

Key secondary outcome(s))
Achievement of morphological and molecular complete remission on Day 29 bone marrow

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 amenorrhoic 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

Healthy volunteers allowed
No

Age group
Adult

Sex
All

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^2 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
United Kingdom

England

Study participating centre
Centre for Experimental Cancer Medicine
London
United Kingdom
EC1M 6BQ

Sponsor information

Organisation
Queen Mary University of London

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, Cancer Research UK (CRUK), 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

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			24/03/2022	No	Yes