ISRCTN63375144 https://doi.org/10.1186/ISRCTN63375144

CLL8: a randomised, phase III study to assess alemtuzumab consolidation therapy in patients with Chronic Lymphocytic Leukaemia (CLL) who have responded to previous therapy

Submission date
12/03/2008

Recruitment status
Stopped

Registration date
09/05/2008

Overall study status
Stopped

Last Edited
27/06/2017

Condition category
Cancer

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

2008-003012-35

Protocol serial number
HM07/8281

Study information

Scientific Title
CLL8: a randomised, phase III study to assess alemtuzumab consolidation therapy in patients with Chronic Lymphocytic Leukaemia (CLL) who have responded to previous therapy

Acronym
CLL8

Study objectives
The trial is intended to assess the effect on progression free survival (PFS) of subcutaneous alemtuzumab in B-cell chronic lymphocytic leukaemia (B-CLL) patients who have responded to previous chemotherapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Sunderland Research Ethics Committee, 29/09/2010, ref: 10/H0904/24

Primary study design
Interventional

Study design
Phase III multi-centre randomised controlled open parallel-group trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic lymphocytic leukaemia (CLL)

Interventions
The recruitment target requires that approximately 96 patients are recruited into the trial per year over a three year period (total = 288).

Prior to randomisation a blood and bone marrow sample will be taken from the patient to measure the level of disease. Patients will then be randomised to receive consolidation therapy with alemtuzumab for 6 - 12 weeks or no consolidation therapy. Both minimal residual disease (MRD) negative and MRD positive patients are eligible for the trial.

Patients randomised to no consolidation therapy will not receive any treatment.

Patients randomised to consolidation therapy with alemtuzumab will receive 30 mg subcutaneous infusion three times a week for six weeks. After six weeks of treatment patients

will undergo an assessment of response which will include a further blood sample being taken and a bone marrow sample for those patients who were MRD positive at randomisation. Patients who are assessed as having no detectable CLL (MRD negative) after six weeks of treatment will receive no further treatment with alemtuzumab. Patients who are assessed as having detectable CLL (MRD positive) but showing no improvement will also stop treatment. Patients who are assessed as having detectable CLL (MRD positive) with a reduction in levels after six weeks of treatment will receive a further six weeks of treatment with alemtuzumab. Again such patients will receive 30 mg subcutaneous infusion three times a week for six weeks. Patients will then be assessed for response at the end of treatment which will include a blood and bone marrow sample being taken.

All patients, including those randomised to no consolidation therapy, will then be assessed for a response six months post-randomisation (this assessment can be omitted if within four weeks of the end of treatment assessment in patients who received 12 weeks of treatment with alemtuzumab). All patients will be assessed clinically and with peripheral blood for MRD every three months for three years, although follow up data will only be collected annually. Patients will continue to be followed up annually for survival.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Progression free survival (PFS).

Key secondary outcome(s)
1. Proportion of patients with undetectable minimal residual disease (MRD), measured at the six month post-randomisation follow-up visit
2. Response as measured by National Cancer Institute (NCI)/International Workshop on CLL (IWCLL) criteria:
2.1. For patients receiving treatment with alemtuzumab: after six weeks of treatment (and 12 weeks if applicable)
2.2. For patients not receiving treatment with alemtuzumab: three months post-randomisation
2.3. For all patients: six months after randomisation (omitted if within four weeks of prior assessment) and 12 months after randomisation
3. Overall survival (OS)
4. Time to MRD relapse for patients who are or who become MRD negative
5. Safety and toxicity: measured from consent until 30 days after the last day of the last treatment with alemtuzumab for patients receiving treatment, and until six months after randomisation for patients not receiving treatment with alemtuzumab
6. Quality of life: measured at baseline and 3, 6, 12, 24 and 36 months after randomisation
7. Quality adjusted life years (QALYs)

Please note that the timepoints above only refer to the proportion of patients with undetectable MRD at the six-month post-randomisation follow-up visit, response, safety and quality of life as the other outcomes are not measured at specific time points.

Completion date
01/12/2014

Reason abandoned (if study stopped)
Objectives no longer viable

Eligibility

Key inclusion criteria
1. At least 18 years old, either sex
2. Previous confirmation of B-CLL with a characteristic immunophenotype on peripheral blood flow cytometry
3. Maximum of three prior therapies received for CLL treatment
4. Between 6 and 12 months since completing most recent therapy for CLL
5. Response to most recent chemotherapy treatment for CLL with partial response (PR), near complete response (nCR) or complete response (CR)
6. No prior alemtuzumab therapy
7. Absence of clinically evident lymphadenopathy (largest lymph node less than 2 cm in minimum diameter)
8. Creatinine and bilirubin less than two times upper limit of normal
9. Peripheral B-cell count less than 5 x 10^9 l
10. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Disease progression after response to latest therapy
2. Active infection
3. Past history of anaphylaxis following exposure to rat or mouse derived complementarity determining region (CDR)-grafted humanised monoclonal antibodies
4. Pregnancy, lactation or women of child-bearing potential unwilling to use medically approved contraception whilst receiving treatment
5. Men whose partners are capable of having children but who are not willing to use appropriate medically approved contraception during the study, unless they are surgically sterile
6. Central nervous system (CNS) involvement with CLL
7. Mantle cell lymphoma
8. Other severe, concurrent diseases or mental disorders

9. Known human immunodeficiency virus (HIV) positive
10. Active secondary malignancy
11. Persisting severe pancytopenia (neutrophils less than 0.5 x 10^9/l or platelets less than 50 x 10^9/l)
12. Patients previously treated with allogeneic stem cell transplantation (SCT)

Date of first enrolment
01/06/2008

Date of final enrolment
01/12/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St James's University Hospital
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Sponsor information

Organisation
Leeds Teaching Hospitals NHS Trust (UK)

ROR
https://ror.org/00v4dac24

Funder(s)

Funder type
Industry

Funder Name
Bayer Schering

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No