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Alternative Ofatumumab containing regimens in less fit patients with chronic lymphoid leukemia (CLL)

Submission date 28/10/2011	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 28/10/2011	**Overall study status** Completed	
Last Edited 02/05/2025	**Condition category** Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/trials-search/a-trial-looking-ofatumumab-people-chronic-lymphocytic-leukaemia-who-cannot-have-more-intensive-treatment-rialto

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2011-000919-22

ClinicalTrials.gov (NCT)
NCT01678430

Protocol serial number
11159

Study information

Scientific Title
A Randomised Investigation of Alternative Ofatumumab containing regimens in less fit patients with chronic lymphoid leukemia (CLL)

Acronym
RIAltO

Study objectives
This is a randomised, controlled, phase III trial comparing ofatumumab and chlorambucil (OChl) with ofatumumab and bendamustine (OB) in patients with chronic lymphocytic leukaemia (CLL) who are considered not fit enough to receive more intensive combination chemotherapy.

The primary purpose of the trial is to establish if OB is more effective at prolonging the worsening of the disease than OChl.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West - Haydock, First MREC approval date 14/09/2011, ref: 11/NW/0548

Study design
Randomised; Interventional; Design type: Treatment

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 (chronic)

Interventions
670 patients are to be enrolled in total (335 per treatment arm) from approximately 100 centres throughout the United Kingdom.

Patients will receive between 3 12 cycles of treatment depending on which treatment arm they are allocated to and how well they respond to the treatment. The schedule of treatment is as follows:
Arm 1: OChl repeated every 28 days for up to 12 cycles depending on clinical response after cycles 3, 6 and 9.
Arm 2: OB repeated every 28 days for up to 6 cycles depending on clinical response after cycle 3.

All patients will be followed up for a minimum of 2 years from trial entry. All laboratory and physical assessments are routine for CLL but additional scientific tests may be performed when specific consent has been given.

Ofatumumab and Bendamustine, Ofatumumab cycle 1: 300mg iv day 1, 1000mg iv day 8
cycle 2 onwards: 1000mg iv day 1
Bendamustine: 70mg/m2 iv days 1 and 2
Cycles to be repeated every 28 days, up to 6 cycles depending on clinical response after cycle 3;
Ofatumumab and Chlorambucil, Ofatumumab cycle 1: 300mg IV day, 100mg iv day 8
cycle 2 onwards: 1000mg iv day 1
Chlorambucil: 10mg/m2 po days 1 to 7
Cycles to be repeated every 28 days, up to 12 cycles depending on clinical response after cycles 3, 6 & 9; Follow Up Length: 24 month(s)

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Ofatumumab, chlorambucil, bendamustine

Primary outcome(s)
Progression-free survival; Timepoint(s): End of trial

Key secondary outcome(s))
1. Comorbidity assessment; Timepoint(s): Baseline; cycles 4, 7 & 10; 2 months post treatment
2. Disease progression; Duration of response; Timepoint(s): Cycles 4, 7 & 10; 2 & 6 months post treatment; end of trial
3. Frailty assessment; Timepoint(s): Baseline
4. Health economic analysis; Timepoint(s): Every 3 months until end of trial
5. Overall survival; Timepoint(s): End of trial
6. Predictive value of biomarkers; Timepoint(s): Baseline; months 6, 12, 18, 24, 36, 42
7. Disease progression
8. Quality of life; Timepoint(s): Every 3 months until end of trial
9. Response including Minimum Residual Disease (MRD) negativity; Timepoint(s): Cycles 4, 7 & 10; 2 & 6 months post treatment
10. Time to treatment failure; Timepoint(s): Cycles 4, 7 & 10; 2 & 6 months post treatment; end of trial
11. Toxicity; Timepoint(s): Every visit until 6 months post treatment
12. Treatment dose administered; Timepoint(s): End of treatment

Completion date
30/04/2018

Eligibility

Key inclusion criteria
1. CLL requiring treatment by National Cancer Institute/International Workshop on Chronic Lymphocytic Leukemia (NCI/IWCLL) 2008 criteria. At least one of the following criteria:

1.1. Progressive marrow failure as manifested by the development of, or worsening of, anaemia and/or thrombocytopenia
1.2. Massive (i.e. 6 cm below the left costal margin) or progressive or symptomatic splenomegaly
1.3. Massive (i.e. 10 cm in longest diameter) or progressive or symptomatic lymphadenopathy
1.4. Progressive lymphocytosis with an increase of more than 50% over a 2-month period or lymphocyte doubling time (LDT) of less than 6 months
2. No prior therapy for CLL
3. Full-dose rituximab-fludarabine, cyclophosphamide (R-FC) considered inappropriate for at least one of the following reasons
3.1. Age 75 or greater
3.2. WHO performance status 2 or 3
3.3. Cardiac impairment (New York Heart Association (NYHA) class II)
3.4. Respiratory impairment (bronchiectasis or moderate Chronic obstructive pulmonary disease (COPD))
3.5. Renal impairment (estimated Glomerular Filtration Rate (eGFR) 10-30 ml/min)
3.6. Any other significant co-morbidity or factor that makes R-FC inappropriate
4. Considered able to tolerate chlorambucil (Chl) at the dose used in the LRF CLL4 trial (10mg /m2 d1-7)
5. Written informed consent ; Lower Age Limit 16 no age limit or unit specified

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Neutrophil count less than 1.0 x 109/l or platelet count less than 50 x 109/l unless due to CLL*
2. Uncontrolled auto-immune haemolytic anaemia or thrombocytopenia
3. Active infection
4. Seropositivity for HIV, HCV or HBV (surface antigen or core antibody)
5. Severe renal impairment (eGFR less than 10ml/min)
6. Severe hepatic impairment (serum bilirubin more than twice the upper limit of normal) unless due to CLL or Gilberts syndrome.
7. Concurrent treatment with glucocorticoids equivalent to more than prednisolone 20mg od
8. Prior treatment with monoclonal antibody therapy within the last 3 months.
9. Yellow fever vaccination within 4 weeks prior to treatment start
10. Known hypersensitivity to ofatumumab, bendamustine or chlorambucil or any of their excipients
11. CNS involvement with CLL
12. History of Richter transformation
13. Concomitant malignancies within the last 3 years except successfully treated non-melanoma skin cancer or carcinoma in situ.
14. Major surgery within 28 days prior to randomisation
15. WHO performance status 4

16. Severe cardiac disease including unstable angina, acute myocardial infarction within six months prior to randomization, congestive heart failure (NYHA III-IV), and arrhythmia (excluding extra systoles or minor conduction abnormalities) unless controlled by therapy.
17. Any serious underlying medical or psychological conditions, which could impair the ability of the patient to participate in the trial or compromise ability to give informed consent
18. Treatment within a clinical trial within 30 days prior to trial entry.
19. Adult patient under tutelage (not competent to sign informed consent).
20. Pregnant or lactating women.
21. Women of childbearing potential, including women whose last menstrual period was less than one year prior to screening, unable or unwilling to use adequate contraception from study start to one year after the last dose of protocol therapy. Adequate contraception is defined as hormonal birth control, intrauterine device, double barrier method or total abstinence.
22. Male subjects unable or unwilling to use adequate contraception methods from study start to one year after the last dose of protocol therapy.

Date of first enrolment
01/12/2011

Date of final enrolment
30/04/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Liverpool CRUK Centre
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Sponsor information

Organisation
Royal Brompton & Harefield NHS Foundation Trust

ROR
https://ror.org/02218z997

Organisation

Royal Liverpool and Broadgreen University Hospitals NHS Trust

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
Napp Pharmaceuticals (UK)

Funder Name
Chugai Pharma UK Ltd (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2017		Yes	No
Results article		17/04/2025	02/05/2025	Yes	No
HRA research summary			28/06/2023	No	No

Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes