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Combination fludarabine and cyclophosphamide (FC) plus Ofatumumab at Standard or Mega dose In Chronic lymphoid leukemia (CLL)

Submission date
29/07/2011

Recruitment status
No longer recruiting

Registration date
21/09/2011

Overall study status
Completed

Last Edited
15/12/2021

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-comparing-different-doses-ofatumumab-chronic-lymphocytic-leukaemia-cosmic

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2011-000796-14

Protocol serial number
HM10/9652

Study information

Scientific Title
Combination fludarabine and cyclophosphamide (FC) plus Ofatumumab at Standard or Mega dose In Chronic lymphoid leukemia (CLL): a phase II, multi-centre, randomised, open, parallel group trial

Acronym
COSMIC

Study objectives
This trial will assess the efficacy of standard dose and high (mega) dose of ofatumumab in combination with chemotherapy (fludarabine and cyclophosphamide) in relapsed B-CLL patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Research Ethics Committee: Yorkshire & The Humber – Leeds East, 24/10/2011, ref: 11/YH/0260

Study design
Phase II multi-centre randomised open parallel group trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic Lymphocytic Leukaemia (CLL)

Interventions
1. Fludarabine, cyclophosphamide and standard dose ffatumumab (Standard Of-FC):
1.1. Fludarabine (oral*) - 24mg/m2/day - Day 1 to 5 (Cycle 1 to 6)
1.2. Cyclophosphamide (oral*) - 150mg/m2/day - Day 1 to 5 (Cycle 1 to 6)
1.3. Ofatumumab [intravenous (IV)] - 300mg - Day 1 and 1000mg Day 8 (Cycle 1 only)
1.4. Ofatumumab (IV) - 1000mg - Day 1 (Cycle 2 to 6)

2. Fludarabine, cyclophosphamide and high dose ofatumumab (Mega-Of-FC):
2.1. Fludarabine (oral*) - 24mg/m2/day - Day 1 to 5 (Cycle 1 to 6)
2.2. Cyclophosphamide (oral*) - 150mg/m2/day - Day 1 to 5 (Cycle 1 to 6)
2.3. Ofatumumab (IV) - 300mg - Day 1 (Cycle 1) followed by 2000mg weekly for 8 doses, followed by 2000mg monthly for 3 doses

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Fludarabine, cyclophosphamide, ofatumumab

Primary outcome(s)
Proportion of patients achieving a Complete Response (CR or CR(i)), as defined by International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria. Measured 3 months after the therapy.

Key secondary outcome(s))
1. Proportion of patients with undetectable minimal residual disease (MRD)
2. Overall response rate defined as complete or partial remission by International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria
3. Progression-free survival at 2 years
4. Overall survival at 2 years
5. Time to MRD relapse in MRD negative patients
6. Safety and toxicity

Completion date
01/07/2013

Eligibility

Key inclusion criteria
1. At least 18 years old
2. Chronic lymphocytic leukaemia requiring therapy
3. Previous treatment with at least one chemotherapeutic regime
4. Be capable of giving written informed consent
5. World Health Organisation (WHO) performance status (PS) of 0, 1, or 2
6. Life expectancy of at least 12 weeks
7. Considered fit enough to receive fludarabine-based combinations

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment

Key exclusion criteria

1. Fludarabine refractory: defined as no response to or relapse within 6 months of fludarabine alone or in combination with cyclophosphamide (FC)
2. Relapse within 12 months of FC with rituximab (FCR)
3. Deletion of chromosome 17p on fluorescent in-situ hybridisation (FISH) [will be performed in Haematological Malignancy Diagnostic Service (HMDS) at screening]
4. Previous treatment with ofatumumab either alone or in combination with chemotherapy
5. Toxicity attributable to purine analogues such as autoimmune haemolytic anaemia, neurological toxicity or allergy
6. Active infection
7. Other severe, concurrent (particularly cardiac or pulmonary) diseases or mental disorders that could interfere with their ability to participate in the study
8. Patients with a creatinine clearance of less than 30ml/min (either measured or derived by the Cockcroft-Gault formula)
9. Pregnant, lactating or women of child bearing potential unwilling to use medically approved contraception whilst receiving treatment and for 12 months after treatment has finished
10. Men whose partners are capable of having children but who are not willing to use appropriate medically approved contraception whilst receiving treatment and for 12 months after treatment has finished, unless they are surgically sterile
11. Subjects who have current active hepatic or biliary disease (with exception of patients with Gilbert's syndrome, asymptomatic gallstones, liver metastases or stable chronic liver disease per Investigator assessment)
12. Treatment with any known non-marketed drug substance or experimental therapy within 5 terminal half lives or 4 weeks prior to enrolment, whichever is longer, or currently participating in any other interventional clinical study
13. Other past or current malignancy. Subjects who have been free of malignancy for at least 2 years, or have a history of completely resected non-melanoma skin cancer, or successfully treated in situ carcinoma are eligible.
14. Prior treatment with anti-CD20 monoclonal antibody or alemtuzumab within 3 months prior to start of therapy
15. Chronic or current infectious disease requiring systemic antibiotics, antifungal, or antiviral treatment such as, but not limited to, chronic renal infection, chronic chest infection with bronchiectasis, tuberculosis and active Hepatitis C
16. History of significant cerebrovascular disease in the past 6 months or ongoing event with active symptoms or sequelae
17. Known human immunodeficiency (HIV) positive
18. Clinically significant cardiac disease including unstable angina, acute myocardial infarction within six months prior to randomisation, congestive heart failure New York Heart Association (NYHA III-IV), and arrhythmia unless controlled by therapy, with the exception of extra systoles or minor conduction abnormalities.
19. Significant concurrent, uncontrolled medical condition including, but not limited to, renal, hepatic, gastrointestinal, endocrine, pulmonary, neurological, cerebral or psychiatric disease which in the opinion of the Investigator may represent a risk for the patient.
20. Positive serology for Hepatitis B (HB) defined as a positive test for HBsAg. In addition, if negative for HBsAg but HBcAb positive (regardless of HBsAb status), a HB DNA test will be performed and if positive the subject will be excluded
21. Positive serology for hepatitis C (HC) defined as a positive test for HCAb, in which case reflexively perform a HC RIBA immunoblot assay on the same sample to confirm the result screening laboratory values:

21.1. Platelets <50 x 109/L (unless due to involvement by CLL)
21.2. Neutrophils <1.0 x 109/L (unless due to involvement by CLL)
21.3. Creatinine clearance below 30ml/min (between 30 and 60ml/min the fludarabine dose will be reduced)
21.4. Total bilirubin >1.5 times upper normal limit (unless due to CLL involvement of liver or a known history of Gilberts disease)
21.5. Alanine aminotransferase (ALT) >2.5 times upper normal limit (unless due to CLL involvement of liver)
21.6. Alkaline phosphatase >2.5 times upper normal limit (unless due to disease involvement of the liver or bone marrow by CLL)

Date of first enrolment
01/01/2012

Date of final enrolment
01/07/2013

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
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

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?
Results article		01/08/2021	04/06/2021	Yes	No
Protocol article	protocol	20/09/2016		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes