

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

<b>Submission date</b> 29/07/2011	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 21/09/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 15/12/2021	<b>Condition category</b> Cancer	<input type="checkbox"/> 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

### Contact name

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## Additional identifiers

### EudraCT/CTIS number

2011-000796-14

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

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

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

Not available in web format, please use contact details to request a participant information sheet

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

Chronic Lymphocytic Leukaemia (CLL)

### **Interventions**

1. Fludarabine, cyclophosphamide and standard dose ofatumumab (Standard Of-FC):
  - 1.1. Fludarabine (oral\*) - 24mg/m<sup>2</sup>/day - Day 1 to 5 (Cycle 1 to 6)
  - 1.2. Cyclophosphamide (oral\*) - 150mg/m<sup>2</sup>/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/m<sup>2</sup>/day - Day 1 to 5 (Cycle 1 to 6)
  - 2.2. Cyclophosphamide (oral\*) - 150mg/m<sup>2</sup>/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 measure**

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.

## **Secondary outcome measures**

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

## **Overall study start date**

01/01/2012

## **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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

82

**Total final enrolment**

62

**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  $<50 \times 10^9/L$  (unless due to involvement by CLL)

21.2. Neutrophils  $<1.0 \times 10^9/L$  (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**

England

United Kingdom

**Study participating centre**

**St James's University Hospital**

Leeds

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# Sponsor information

## Organisation

Leeds Teaching Hospitals NHS Trust (UK)

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## Sponsor type

Hospital/treatment centre

## ROR

<https://ror.org/00v4dac24>

# Funder(s)

## Funder type

Industry

## Funder Name

GlaxoSmithKline

## Alternative Name(s)

GlaxoSmithKline plc., GSK plc., GSK

## Funding Body Type

Government organisation

## Funding Body Subtype

For-profit companies (industry)

## Location

United Kingdom

# Results and Publications

## Publication and dissemination plan

The results will be published in July 2018.

## Intention to publish date

01/07/2018

## 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="#">Protocol article</a>	protocol	20/09/2016		Yes	No
<a href="#">Results article</a>		01/08/2021	04/06/2021	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No