

# CALiBRe: Assessment of the Mechanism of Action of idelalisib (CAL101) in B-cell Receptor Pathway Inhibition in CLL

<b>Submission date</b> 05/08/2015	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 06/08/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 07/12/2022	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-how-idelalisib-works-for-people-with-chronic-lymphocytic-leukaemia-calibre>

## Contact information

### Type(s)

Scientific

### Contact name

Dr Francesca Yates

### Contact details

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Institute for Cancer Studies  
Edgbaston  
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United Kingdom  
B15 2TT

## Additional identifiers

### EudraCT/CTIS number

2012-003631-36

### IRAS number

### ClinicalTrials.gov number

## Secondary identifying numbers

18679

# Study information

## Scientific Title

Assessment of the Mechanism of Action of idelalisib (CAL101) in B-cell Receptor Pathway Inhibition in CLL: a non-randomised interventional trial

## Acronym

CALiBRe

## Study objectives

The aims of this mechanistic study are to confirm:

1. The mechanism of action of idelalisib
2. The biological response to idelalisib in two cohorts of patients:
  - 2.1. Treatment naïve
  - 2.2. Relapsed/refractory CLL

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

NRES Committee Yorkshire & The Humber - Leeds West, 11/02/2015, ref: 15/YH/0020

## Study design

Non-randomised; Interventional; Design type: Treatment

## Primary study design

Interventional

## Secondary study design

Non randomised study

## 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

Topic: Cancer; Subtopic: Haematological Oncology; Disease: Leukaemia(Chronic Lymphocytic Leukaemia)

## Interventions

All patients will receive the same treatment (idelalisib) which is taken orally twice daily.  
Study Entry : Registration only

## **Intervention Type**

Drug

## **Phase**

Not Applicable

## **Drug/device/biological/vaccine name(s)**

Idelalisib

## **Primary outcome measure**

Proportion of patients achieving MRD-negative remission by IWCLL criteria; Timepoint(s):  
Ongoing

## **Secondary outcome measures**

1. CLL cell levels as a percentage of total leucocytes in the bone marrow (BM) and absolute counts in the peripheral blood (PB)
2. The proportion of patients with >5%, 0.5-5%, <0.5% CLL cells in cell cycle (expressing Ki67) in the peripheral blood and bone marrow after 6-9 months of idelalisib
3. Change in the expression levels of CD10, CD103, CD11c, CD195, CD196, CD20, CD200, CD22, CD23, CD25, CD27, CD305, CD31, CD38, CD39, CD43, CD49d, CD5, CD79b, CD81, CD95, IgD, IgG, or IgM on CLL cells relative to baseline by more than 50% and at least 500 arbitrary units in median fluorescence intensity
4. Best disease response: Complete Remission (CR); Complete Remission with incomplete marrow recovery (Cri) or Partial Remission (PR), to treatment within the first 6 months of treatment assessed according to the IWCLL Response Criteria
5. Biological response at 1, 6 and 12 months, assessed according to the Modified IWCLL Response Criteria
6. 1 and 2 year progression free survival for relapsed/refractory and treatment naïve patients defined as time from date of registration to date of progression (per the 2008 IWCLL criteria) or death from any cause
7. 1 and 5 year overall survival for relapsed/refractory and treatment naïve patients, defined as the time from date of registration to the date of death from any cause
8. Toxicity of idelalisib within 6 months

## **Overall study start date**

27/03/2012

## **Completion date**

30/05/2017

## **Eligibility**

### **Key inclusion criteria**

Cohort A (treatment naïve)

1. Progressive stage A, stage B or stage C CLL
2. CLL requiring therapy by the IWCLL Response criteria

3. ECOG performance status (PS) of 0,1 or 2
4. Life expectancy of at least 6 months
5. Age  $\geq 18$
6. Prepared to undergo the stipulated investigations within the trial (including bone marrow examinations)
7. Able to give informed consent

#### Cohort B (relapsed/refractory)

1. CLL patients requiring therapy
2. Refractory CLL defined as any of the following:
  - 2.1. Failure to achieve a response (CR or PR by IWCLL criteria) to a purine analogue alone or in combination with chemotherapy, or:
  - 2.2. Relapse within 6 months of responding to a purine analogue alone or in combination with chemotherapy, or:
  - 2.3. Relapse at any time after fludarabine, cyclophosphamide and rituximab (FCR) or bendamustine plus rituximab or:
  - 2.4. Patients with CLL with deletion of chromosome 17p who have failed at least one previous therapy.
3. ECOG performance status (PS) of 0, 1 or 2
4. Life expectancy of at least 6 months
5. Prepared to undergo the stipulated investigations within the trial (including bone marrow examinations)
6. Age  $\geq 18$
7. Able to give informed consent

#### **Participant type(s)**

Patient

#### **Age group**

Adult

#### **Lower age limit**

18 Years

#### **Sex**

Both

#### **Target number of participants**

Planned Sample Size: 40; UK Sample Size: 40; Description: 2 cohorts of 20 patients each: cohort A) treatment naive; cohort B) relapsed/refractory

#### **Total final enrolment**

23

#### **Key exclusion criteria**

Both cohorts A and B

1. Unwilling to undergo the protocol assessments including the bone marrow examinations
2. Active infection
3. Other severe, concurrent (particularly cardiac or pulmonary) diseases or mental disorders that could interfere with their ability to participate in the study
4. Use of prior investigational agents within 6 weeks

5. Pregnancy or lactation
6. Unwilling to use appropriate contraception during and for 30 days following treatment
7. CNS involvement with CLL
8. Mantle cell lymphoma
9. Known HIV positive
10. Active or prior hepatitis B or C
11. Active secondary malignancy excluding basal cell carcinoma
12. Persisting severe pancytopenia (neutrophils  $<0.5 \times 10^9/L$ ) or transfusion dependent anaemia unless due to direct marrow infiltration by CLL (to be confirmed via bone marrow biopsy)
13. Active haemolysis (not controlled with prednisolone at 20 mg or less)
14. Hypersensitivity to the active substance or to any of the excipients listed in the SmPC

Cohort A (treatment naive)

Previous treatment for CLL. This does not include steroids

Cohort B (relapsed/refractory)

Previous treatment with idelalisib or an alternative inhibitor of Bcell receptor pathway

**Date of first enrolment**

13/07/2015

**Date of final enrolment**

31/12/2016

## **Locations**

**Countries of recruitment**

England

Northern Ireland

United Kingdom

**Study participating centre**

**St James's University Hospital**

Leeds

United Kingdom

LS9 7TF

**Study participating centre**

**The Christie NHS Foundation Trust**

Manchester

United Kingdom

M20 4BX

**Study participating centre**  
**Nottingham City Hospital**  
Nottingham  
United Kingdom  
NG5 1PB

**Study participating centre**  
**Queen Elizabeth Hospital**  
Birmingham  
United Kingdom  
B15 2TH

**Study participating centre**  
**Belfast City Hospital**  
Belfast  
United Kingdom  
BT9 7AB

**Study participating centre**  
**The Royal Liverpool University Hospital**  
Liverpool  
United Kingdom  
L7 8XP

**Study participating centre**  
**Kings College Hospital**  
London  
United Kingdom  
SE5 9RS

**Study participating centre**  
**Southampton General Hospital**  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**  
**Churchill Hospital**  
Oxford

United Kingdom  
OX3 7LJ

## Sponsor information

### Organisation

University of Birmingham

### Sponsor details

Edgbaston  
Birmingham, West Midlands  
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United Kingdom  
B15 2TT

### Sponsor type

University/education

### Website

<http://www.birmingham.ac.uk/research/activity/mds/trials/crctu/index.aspx>

### ROR

<https://ror.org/03angcq70>

## Funder(s)

### Funder type

Charity

### Funder Name

Leukaemia and Lymphoma Research

### Alternative Name(s)

### Funding Body Type

Private sector organisation

### Funding Body Subtype

Other non-profit organizations

### Location

United Kingdom

**Funder Name**

Gilead Sciences Ltd

## Results and Publications

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date**

30/09/2023

**Individual participant data (IPD) sharing plan**

The data-sharing plans for the current study are unknown and will be made available at a later date

**IPD sharing plan summary**

Data sharing statement to be made available at a later date

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Basic results</a>		20/09/2022	30/09/2022	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No