

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

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

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Additional identifiers

Clinical Trials Information System (CTIS)

2012-003631-36

Protocol serial number

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

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

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**

United Kingdom

England

Northern Ireland

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

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

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?
Basic results		20/09/2022	30/09/2022	No	No
HRA research summary			28/06/2023	No	No