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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	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 06/08/2015	**Overall study status** Completed	
Last Edited 07/12/2022	**Condition category** Cancer	

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

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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 ≥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 ≥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 x 109/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

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OX3 7LJ

Sponsor information

Organisation
University of Birmingham

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