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Assessment of venetoclax in combination with Ibrutinib in patients with Chronic Lymphocytic Leukaemia

Submission date 09/03/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 09/03/2016	**Overall study status** Completed	
Last Edited 05/01/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-of-venetoclax-and-ibrutinib-for-chronic-lymphocytic-leukaemia-clarity

Contact information

Type(s)
Public

Contact name
Ms Rebecca Bishop

Contact details
University of Birmingham
Institute for Cancer studies
Edgbaston
Birmingham
United Kingdom
B15 2TT

Additional identifiers

EudraCT/CTIS number
2015-003422-14

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

20572

Study information

Scientific Title
CLARITY: Assessment of VenetoCLAx (ABT-199) in combination with IbRutInib in relapsed /refracTory Chronic LymphocYtic Leukaemia

Acronym
CLARITY

Study objectives
The aim of this study is to increase the effectiveness of ibrutinib by using it in combination with Venetoclax to assess if this is the ideal combination of drug to use and hope that patients can be treated with lower toxicity than standard treatments.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Yorkshire & The Humber – Leeds East Research Ethics Committee, 21/12/2015, ref: 15/YH/0530

Study design
Multi-centre non-randomised study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Cancer; Subtopic: Cancer (Haematological Oncology); Disease: Leukaemia (Chronic Lymphocytic Leukaemia)

Interventions
Ibrutinib: Continuous Ibrutinib treatment of 420mg once daily
Venetoclax: Venetoclax treatment for a maximum of 24 months

Intervention Type

Other

Primary outcome measure
Proportion of patients with <0.01% MRD in the blood and bone marrow at 12 months.

Secondary outcome measures
1. Biological response is monitored throughout the duration of the trial
2. Overall Survival is determined from the date of registration to date of death
3. Progression-free survival (PFS) is monitored throughout the duration of the trial
4. Proportion of patients with <0.01% MRD in the blood and bone marrow is measured after 6 and 24 months of combination therapy
5. Response rate is determined using the International Workshop on Chronic Lymphocytic Leukaemia (IWCLL) criteria after 12 and 24 months of combination therapy
6. Toxicity of combination therapy is measured throughout the duration of trial

Overall study start date
01/03/2016

Completion date
29/10/2022

Eligibility

Key inclusion criteria
1. Aged 18 and over
2. Able to give informed consent
3. Diagnosis of CLL, requiring therapy according to IWCLL criteria (appendix 1)
4. CLL should be assessable for MRD by flow cytometry (CD19, CD5 and CD23 and CD43 co-expression with weak CD20, CD79b/sIg & CD81 expression; to be confirmed by HMDS)
5. Refractory/relapsed CLL defined as any of the following:
5.1. Failure to achieve a response (CR or PR by IWCLL Criteria) to a purine analogue alone or in combination with chemotherapy
5.2. Relapse within 6 months of responding to a purine analogue alone or in combination with chemotherapy
5.3. Relapse at any time after the combination of fludarabine, cyclophosphamide and rituximab (FCR) or bendamustine plus rituximab (or other equivalent monoclonal anti-CD20 antibodies)
5.4. Patients with CLL with deletion of chromosome 17p who have progressed after at least one previous therapy
6. ECOG performance status (PS) of 0, 1, or 2
7. Prepared to undergo the stipulated investigations within the trial (including bone marrow examinations)
8. Adequate bone marrow function (defined below) independent of growth factor or transfusion support, within 2 weeks of screening unless cytopenia is clearly due to marrow involvement of CLL:
8.1. Platelet count ≥ 75 x 109/L; in cases of thrombocytopenia clearly due to marrow involvement of CLL (per the discretion of the investigator), platelet count should be ≥ 30 109/L independent of transfusion
8.2. Absolute neutrophil count (ANC) ≥ 1.0 x 109/L unless neutropenia is clearly due to marrow involvement of CLL (per the discretion of the investigator)
8.3. Total haemoglobin ≥ 90 g/L unless anaemia is due to marrow involvement of CLL (per the discretion of the investigator)

9. Adequate renal and hepatic function at screening:
9.1. Calculated creatinine clearance ≥ 50 mL/min using 24-hour creatinine clearance or modified Cockcroft-Gault equation (using ideal body mass [IBM] instead of mass): eCCR=((140-Age)>IBM (kg).[0.85 if female])/(72.Serum creatinine (mg/dL)) Or, if serum creatinine is in µmol/L: eCCR= ((140-Age)>IBM (kg).[1.23 if male,1.04 if female])/(Serum creatinine (µmol/L)) IBM (kg) = ([height in cm−154] × 0.9)] + (50 if male, 45.5 if female)
10. AST or ALT≤ 3.0 times the upper limit of normal (ULN) of the institution's normal range
11. Bilirubin ≤ 1.5 × ULN. Patients with known Gilbert's syndrome may have a bilirubin level > 1.5 × ULN
12. Prothrombin time (or international normalised ratio) and partial thromboplastin time not to exceed 1.2 times the institution’s normal range

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 50; UK Sample Size: 50

Total final enrolment
53

Key exclusion criteria
1. Transformation of CLL to aggressive NHL (e.g. Richter’s transformation, prolymphocytic leukaemia, or diffuse large B-cell lymphoma or CNS involvement by CLL)
2. A history of any severe, concurrent renal, neurological, psychiatric, endocrine, metabolic, immunologic, cardiac, pulmonary or hepatic diseases that could interfere with the patient’s ability to participate in the study
3. Use of prior investigational agents within 28 days of planned treatment
4. Females who are pregnant or lactating
5. Females of childbearing potential (or males whose partners are of childbearing potential) who are unwilling to use appropriate contraception during and for 3 months following treatment
6. Mantle cell lymphoma
7. Known to be HIV positive
8. Positive test results for chronic hepatitis B infection (defined as positive HBsAg serology)
9. Positive test results for hepatitis C (HCV antibody serology testing). Patients positive for HCV antibody are eligible only if PCR is negative for HCV RNA.
10. Active secondary malignancy excluding basal cell carcinoma
11. Patients requiring or who have received anticoagulation treatment with warfarin or vitamin K antagonists within 1 week of registration
12. Patients requiring concomitant use of strong CYP3A4/5 inhibitors/inducers within 7 days prior to registration
13. Previous treatment with Ibrutinib, venetoclax or an alternative Btk or Bcl-2 inhibitor

14. Inability to tolerate uric acid reducing medications • Undergone an allogeneic stem cell transplant unless beyond 6 months post-transplant and off immune suppressive therapy with no evidence of Graft-versus-Host disease
15. Known hypersensitivity to either of the compounds or to its excipients
16. Patients who have received an anti-CLL monoclonal antibody within 8 weeks prior to registration
17. A cardiovascular disability status of New York Heart Association Class ≥ 3 (Class 3 is defined as cardiac disease in which patients are comfortable at rest but have marked limitation of physical activity due to fatigue, palpitations, dyspnoea or angina pain)
18. Major surgery within 30 days prior to registration
19. Vaccination with a live vaccine within 28 days prior to registration
20. Steroid therapy for anti-neoplastic intent will not be allowed either during or within 7 days prior to registration with the exception of inhalational steroids for the treatment of asthma or COPD, topical steroids, replacement corticosteroid therapy for an inherited or acquired deficiency

Date of first enrolment
01/04/2016

Date of final enrolment
01/12/2017

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Belfast City Hospital
Lisburn Road
Belfast
United Kingdom
BT9 7AB

Study participating centre
University Hospital of Wales
Heath Park

Cardiff
United Kingdom
CF14 4XW

Study participating centre
Christie Hospital
550 Wilmslow Road
Manchester
United Kingdom
M20 4BX

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
United Kingdom
G12 0YN

Study participating centre
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

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

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
St Bartholomew's Hospital
W Smithfield
London
United Kingdom
EC1A 7BE

Study participating centre
St James' Hospital
Beckett Street

Leeds
United Kingdom
LS9 7TF

Sponsor information

Organisation
University of Birmingham

Sponsor details
Edgbaston
Birmingham
England
United Kingdom
B15 2TT

Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

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

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
29/10/2023

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?
Results article	results	20/10/2019	11/06/2020	Yes	No
Plain English results			23/02/2021	No	Yes
HRA research summary			28/06/2023	No	No
Basic results	version 1.0	03/01/2024	05/01/2024	No	No