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A trial of CHOP-R therapy, with or without acalabrutinib, in patients with newly diagnosed Richter's Syndrome

Submission date 18/02/2019	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 04/03/2019	**Overall study status** Ongoing	
Last Edited 14/05/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-r-chop-and-acalabrutinib-for-people-with-richters-syndrome-stellar

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT03899337

Clinical Trials Information System (CTIS)

2017-004401-40

Protocol serial number
38923

Study information

Scientific Title
STELLAR: A phase II, randomiSed study of CHOP-R in combination with acalabruTinib comparEd to CHOP-R in patients with newLy diagnosed Richter's Syndrome (RS) and a pLAtfoRm for initial investigations into activity of novel treatments in relapsed/refractory and newly diagnosed RS

Acronym
STELLAR

Study objectives
Adding acalabrutinib to CHOP-R treatment will improve progression-free survival rates for patients with newly diagnosed Richter's Syndrome.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 31/01/2019, South Central – Oxford B REC (Whitefriars, Level 3, Block B, Lewin's Mead, Bristol, BS1 2NT, United Kingdom; +44 (0)207 1048058; nrescommittee.southcentral-oxfordb@nhs.net), ref: 18/SC/0634

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Richter syndrome

Interventions
Participants who have Richter's Syndrome and are suitable for CHOP-R will be recruited by specialised hospitals across the UK. People with another cancer, heart problems, or recent stroke cannot take part. Participants will have a lymph node biopsy, 3-4 bone marrow biopsies, blood samples, and PET-CT and CT scans.

Randomised Trial Component:

Patients will be randomised 1:1 to either treatment with CHOP-R (Standard of Care [SoC]) or CHOP-R + acalabrutinib (Experimental). The induction treatment (CHOP-R) will continue for up to 6 cycles (each cycle is 21 days), and will be given according to the following schedule:

Rituximab, 375 mg/m2, IV infusion, OD, 6 cycles, days of cycle: 1
Cyclophosphamide, 750 mg/m2, IV bolus, OD, 6 cycles, days of cycle: 1
Doxorubicin, 50 mg/m2, IV bolus, OD, 6 cycles, days of cycle: 1
Vincristine, 1.4 mg/m2, IV infusion, OD, 6 cycles, days of cycle: 1
Prednisolone, 40 mg/m2, PO, OD, 6 cycles, days of cycle: 1-5
Acalabrutinib, 100 mg, PO, BD, 6 cycles, continuous thereafter until disease progression toxicity, patient choice or death, days of cycle: 6-21

Patients will be followed up for 2 year survival data.

Single-Arm Platform Studies:

Cohort 1:
Patients registered to Cohort 1 will receive 100 mg acalabrutinib monotherapy, twice daily, continuously from day 1 until disease progression, toxicity, patient choice or death. Patients will be followed up for 2 year survival data.

Cohort 2:
Patients registered to Cohort 2 will receive CHOP-R + acalabrutinib. The induction treatment (CHOP-R) will continue for up to 6 cycles (each cycle is 21 days), and will be given according to the following schedule:

Rituximab, 375 mg/m2, IV infusion, OD, 6 cycles, days of cycle: 1
Cyclophosphamide, 750 mg/m2, IV bolus, OD, 6 cycles, days of cycle: 1
Doxorubicin, 50 mg/m2, IV bolus, OD, 6 cycles, days of cycle: 1
Vincristine, 1.4 mg/m2, IV infusion, OD, 6 cycles, days of cycle: 1
Prednisolone, 40 mg/m2, PO, OD, 6 cycles, days of cycle: 1-5
Acalabrutinib, 100 mg, PO, BD, 6 cycles, continuous thereafter until disease progression toxicity, patient choice or death, days of cycle: 6-21

Patients will be followed up for 2 year survival data.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Acalabrutinib, doxorubicin, vincristine, cyclophosphamide, rituximab, prednisolone

Primary outcome(s)
Progression free survival (PFS); Timepoint(s): Time from randomisation to the date of progression or death from any cause.

Key secondary outcome(s))
1. Overall survival (OS) defined as time from date of randomisation (for randomised trial) or registration (to the relevant cohort for single-arm cohorts) to date of death from any cause
2. Overall response (randomised component only) after cycle 6, defined by the modified Cheson criteria
3. Overall response (cohorts 1 only) after 12 weeks, defined by the modified Cheson criteria

4. PFS (single-arm cohorts only) defined as the time from date of registration to date of progression or death from any cause
5. Quality of life assessed using ECOG performance status and the CLL17 and NHLHG29 questionnaires at the end of cycles 4 and 6 for participants receiving CHOP-R as part of their treatment (randomised cohorts and Cohort 2), and at 12 and 24 weeks for participants receiving acalabrutinib monotherapy (Cohort 1)
6. Toxicity defined as the number of participants who experience one or more adverse event grade 3 or higher or serious adverse event of any grade, recorded from start of treatment until 28 days after the last administration of study drug.
7. Proportion of participants proceeding to allogeneic or autologous stem cell transplantation, measured as number of patients proceeding to transplant on each treatment arm, at confirmation of partial or complete remission

Completion date
31/05/2026

Eligibility

Key inclusion criteria
Inclusion criteria for the Randomised Trial:
1. Suitable for anthracycline-containing chemo-immunotherapy
2. Patients with CLL and newly diagnosed biopsy proven DLBCL-type RS
3. ECOG performance status of 0, 1, 2 or 3
4. Age 16 years and over
5. Signed written informed consent prior to performing any study-specific procedures

Inclusion criteria Cohort 1 (progressive RS following chemo-immunotherapy):
1. Patients with relapsed/refractory RS who received anthracycline based chemotherapy with anti-CD20 monoclonal antibody
2. ECOG performance status of 0, 1, 2 or 3
3. Age 16 years and over
4. Signed written informed consent prior to performing any study-specific procedures

Inclusion criteria Cohort 2 (anthracycline-naïve RS patients, diagnosed while on ibrutinib):
1. Ibrutinib-exposed CLL patients who have developed biopsy-proven DLBCL-type RS within four weeks of last dose of ibrutinib
2. No previous anthracycline treatment and suitable for anthracycline-containing chemo-immunotherapy
3. Patients with CLL and newly diagnosed biopsy proven DLBCL-type RS
4. ECOG performance status of 0, 1, 2 or 3
5. Age 16 years and over
6. Signed written informed consent prior to performing any study-specific procedures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Sex
All

Key exclusion criteria
Exclusion criteria ALL:
1. Known central nervous system (CNS) involvement of CLL or DLBCL
2. Any other active malignancy that requires active treatment, with the exception of basal cell carcinoma, in-situ cervical cancer, and non-invasive squamous cell carcinoma of the skin
3. Chronic or ongoing active infectious disease
4. Positive serology for Hepatitis B (HBKnown human immunodeficiency virus (HIV) positive
5. Patients with active bleeding or history of bleeding diathesis (e.g. haemophilia, von Willebrand disease)
6. Patients receiving therapeutic anticoagulation with warfarin or equivalent (e.g. phenoprocoumon)
7. Uncorrected prolonged prothrombin time (PT) or an activated partial thromboplastin time (APTT) > 2 x the upper limit of normal (ULN)
8. Major surgery within 30 days prior to randomisation and/or inadequate recovery from any prior major surgery, toxicity or complications
9. Patients with malabsorption syndrome or medical conditions significantly affecting gastrointestinal function
10. Clinically significant cardiac disease including unstable angina, uncontrolled congestive heart failure, and unstable arrhythmias requiring therapy, with the exception of extra systoles or minor conduction abnormalities
11. Significant concurrent, uncontrolled severe medical condition including, but not limited to, renal, hepatic, haematological, gastrointestinal, endocrine, pulmonary, neurological, cerebral or psychiatric disease
12. History of significant cerebrovascular disease in the 6 months prior to randomisation, including intracranial haemorrhage
13. Known or suspected hypersensitivity to components of the investigational products
14. Patients who have received treatment with any non-marketed drug substance or experimental therapy within 4 weeks prior to proposed start of treatment
15. Current participation in any other interventional clinical study
16. Patients known or suspected of not being able to comply with a study
17. Breastfeeding women or women with a positive pregnancy test at screening
18. Women of childbearing potential and men not willing to use adequate contraception during study and for 3 months after last dose of study therapy

Additional exclusion criteria for the Randomised Trial:
1. Prior therapy with CHOP or any anthracycline containing treatment at any time prior to randomisation
2. Ibrutinib-exposed CLL patients who have been newly diagnosed with RS within four weeks of their last dose of ibrutinib. (Ibrutinib-exposed CLL patients who discontinue ibrutinib due to toxicity or progressive CLL and later (more than four weeks) develop RS are not excluded from the randomised trial component)
3. Previous acalabrutinib exposure

Additional exclusion criteria for Cohort 1 (progressive RS following chemo-immunotherapy):
1. Previous acalabrutinib exposure

Additional exclusion criteria for Cohort 2 (anthracycline-naïve RS patients, diagnosed while on ibrutinib):
1. Prior therapy with CHOP or any anthracycline containing treatment at any time prior to randomisation
2. Previous acalabrutinib exposure

Date of first enrolment
31/03/2019

Date of final enrolment
31/05/2025

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

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

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

Study participating centre
Belfast City Hospital
Lisburn Road

Belfast
United Kingdom
BT9 7AB

Study participating centre
The Clatterbridge Cancer Centre
Clatterbridge Rd
Bebington
Birkenhead
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United Kingdom
CH63 4JY

Study participating centre
Christie Hospital
Wilmslow Road
Manchester
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M20 4BX

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

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

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

Study participating centre
Royal Bournemouth Hospital
Bournemouth
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BH7 7DW

Study participating centre
Royal Hallamshire Hospital
Glossop Road
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S10 2JF

Study participating centre
Southampton General Hospital
Tremona Road
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SO16 6YD

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

Study participating centre
St James' University Hospital
Beckett St
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LS9 7TF

Study participating centre
The Queen Elizabeth Hospital
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B15 2TH

Study participating centre
University College London Hospital
235 Euston Road
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Study participating centre
University Hospital of Wales
Heath Park
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CF14 4XW

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
Acerta Pharma

Funder Name
Bloodwise; Grant Codes: 17003

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

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?
Protocol article	protocol	20/05/2019	22/05/2019	Yes	No
HRA research summary			28/06/2023	No	No