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Evaluating alternative treatment regimens for patients who have diffuse large B-cell lymphoma that is unsuitable for standard treatment

Submission date
12/11/2020

Recruitment status
No longer recruiting

Registration date
10/12/2020

Overall study status
Stopped

Last Edited
29/04/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Diffuse large B-cell lymphoma (DLBCL) is a cancer that starts in white blood cells called B lymphocytes. The standard treatment for DLBCL is a combination of chemotherapy and immunotherapy, referred to as chemo-immunotherapy. Currently, the best results in the treatment of DLBCL are with a chemo-immunotherapy combination called R-CHOP. R-CHOP is not suitable for all patients with DLBCL as one of the drugs can damage the heart. If patients have heart disease or other problems, it may be too risky for them to receive R-CHOP. There have also been some research studies showing that R-CHOP may also be unsuitable for people over the age of 80 years. If this is the case, many patients either receive a reduced dose called mini R-CHOP, or receive one of two alternatives, R-GCVP or R-CEOP. However, outcomes for these treatments are poorer compared to R-CHOP. The aim of this study is to find out whether giving a new drug called polatuzumab vedotin (POLA) in combination with either R-GCP or mini R-CHP is safe and effective. These two combinations are called POLA-R-GCP or POLA-R-mini-CHP.

Who can participate?
Adults who have been diagnosed with DLBCL but their doctors do not think that it would be safe to treat them with R-CHOP because of their age, heart problems, or other significant health problems.

What does the study involve?
Participants will be allocated to one of two different treatment arms based on their age and whether they have other health problems. Patients who are allocated to treatment arm A will receive the following drugs: polatuzumab vedotin, rituximab, gemcitabine, cyclophosphamide, prednisolone. Patients who are allocated to treatment arm B will receive the following drugs: polatuzumab vedotin, rituximab, doxorubicin, cyclophosphamide, prednisolone. Both treatments consist of one period (cycle) of treatment every 21 days (3 weeks) for six cycles. Patients will have initial (screening) tests to confirm they meet all entry criteria, some of these tests will be repeated during the course of the study to assess how the DLBCL is responding to treatment

and to check it is safe to continue. Most of the tests are routine. They include a physical examination and blood tests, a biopsy (likely lymph node), a PET-CT scan, tests to assess heart function including an electrocardiogram and either an echocardiogram or MUGA scan.

What are the possible benefits and risks of participating?
It is hoped that the treatments will help patients who take part although that cannot be guaranteed. The information from this study may help to improve the future treatment of patients with DLBCL. Patients are asked to complete questionnaires about their quality of life which may make their hospital appointments longer, but not more frequent. Some of the PET-CT /CT/MUGA scans required for the study are extra. They use ionising radiation which can cause cell damage that may, after many years or decades, turn cancerous. The chance of that happening to participants is extremely small. polatuzumab, vedotin is a new and unlicensed drug, its side effects are not well known. It is unknown if it could reduce the effectiveness of the other drugs, or produce new/worsened side effects.

Where is the study run from?
The Clatterbridge Cancer Centre NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
August 2019 to July 2023

Who is funding the study?
Roche Products Ltd (Switzerland)

Who is the main contact?
APOLLO Trial co-ordinator
apollo@liverpool.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Hannah Short

Contact details
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Additional identifiers

EudraCT/CTIS number

2019-000842-36

IRAS number
261164

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 41290, IRAS 261164

Study information

Scientific Title
A polatuzumab vedotin containing chemo-immunotherapeutic regimen in patients with diffuse large b-cell lymphoma unsuitable for full-dose R-CHOP therapy

Acronym
APOLLO

Study objectives
The researchers propose that polatuzumab vedotin, a novel and attractive option with demonstrable activity in DLBCL, is safe to combine with otherwise sub-optimal chemo-immunotherapeutic backbones (such as R-GCP or R-mini-CHP) and will likely improve outcomes for patients unsuitable for full-dose R-CHOP.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/04/2020, North West - Liverpool Central Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8197, +44 (0) 2071048387; liverpoolcentral.rec@hra.nhs.uk), REC ref: 19/NW/0743

Study design
Non-randomized; Interventional; Design type: Treatment, Drug, Immunotherapy

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 the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Diffuse large B-cell lymphoma

Interventions
This research study is designed to see if adding polatuzumab vedotin to standard anti-cancer drugs (rituximab, gemcitabine, prednisolone or rituximab, doxorubicin, cyclophosphamide and prednisolone) may be effective for treating patients with DLBCL who cannot be treated with standard treatment as they have other conditions. In addition, the study will investigate whether the side effects are manageable.

There will be 56 patients recruited in total to the study, split evenly across two arms:
Arm A: POLA-R-GCP
Arm B: POLA-R-mini-CHP
Those patients with cardiac/cardiac co-morbid risk factors will be allocated to arm A. Those without cardiac risk factors will be allocated to arm B.

Participants who may be eligible to participate in the study will be identified by the team responsible for their care. The study will be explained by the study doctor and research staff at one of the research sites. Participants will be given time to consider whether to take part in the study before providing informed consent. Participants will attend the clinic for screening, treatment and for regular assessments until 12 months after the last participant has been registered on the study.

Screening
The screening phase of the study will involve the following investigations:
- Written informed consent
- Confirmation of histology and diagnosis
- Complete medical history
- Concomitant medication
- Physical examination
- WHO performance status
- Estimated Glomerular Filtration Rate (eGFR) using MDRD formula
- Full Blood Count (Hb, WBC, platelet count, neutrophil count and lymphocyte count)
- Serum Urea and Electrolytes (Sodium, Potassium, Urea, Creatinine, Calcium and Phosphate)
- Liver Function Tests (albumin, globulins, bilirubin, alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALP))
- Serum LDH and Urate
- Serology for HIV, HBV and HCV
- Whole-body PET scan and CT scan (neck, chest, abdomen and pelvis)
- Bone marrow trephine biopsy*
- Pregnancy test (in women of childbearing age only)
- IPI score
- Cumulative Illness Rating Score-Geriatric (CIRS-G), excluding haematological co-morbidities
- ECG
- Echocardiogram/MUGA scan
*The need for a BM trephine biopsy will be assessed by the local investigator and should be considered to verify if neutropenia or thrombocytopenia are thought to be due to marrow involvement.

Treatment
Participants will receive 6 cycles of treatment, every 21 days. An interim response assessment will be carried out after 3 cycles and will involve a CT scan. If the patient has a partial or complete response, they will receive a further 3 cycles of treatment. An end of treatment FDG-PET/CT scan will determine the final response. Patients will be followed up every 3 months until primary endpoint data collection is complete.

Timeline
Recruitment is predicted to take 12 months and patients will be followed up for a minimum of 12 months. The final analysis will be ~6 months following the last patient last visit.

Sample size
Sample size calculations have been made by the trial statistician for each cohort based on single-stage phase 2 design methodology.

Interim monitoring and analysis
Reviews of study data will be carried out at regular intervals by an Independent Safety and Data Monitoring Committee (ISDMC). The ISDMC will meet after the recruitment of 8 patients to each arm to formally assess adverse events.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Polatuzumab vedotin, rituximab, gemcitabine, prednisolone, rituximab, doxorubicin, cyclophosphamide, prednisolone

Primary outcome measure
Progression-free survival defined as disease progression or recurrence, or death from any cause, (defined as days from the date of cohort assignment to event) occurring within 12 months as assessed by the investigator using the revised Lugano response criteria for malignant lymphoma

Secondary outcome measures
1. The frequency of Grade 3-4 adverse events (AEs) will be assessed according to standard National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 following each cycle of treatment and at each subsequent follow-up visit until 12 months after the last dose of treatment
2. The number of patients completing the 6 planned courses of therapy in each cohort, recorded on treatment forms for each of the 6 planned courses of therapy
3. Investigator-assessed end-of-treatment FDG-PET-CT scan assessed using the revised Lugano response criteria for malignant lymphoma (2016) at the end of treatment
4. Overall survival measured as the time from recruitment until death by any cause
5. Time to next treatment recorded on an additional treatment form throughout study participation
6. Quality of life measured using the EQ-5D patient completed questionnaire pre- and post-treatment and at every 3 monthly follow-up visit
7. Co-morbidity/frailty assessed using echocardiography or nuclear medicine examination [MUGA] pre- and post-treatment (excluding haematological comorbidities)

Overall study start date
23/08/2019

Completion date
01/07/2023

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. Male and female subjects ≥16 years of age at the time of enrolment
2. Ability to understand and sign written informed consent
3. Adequate contraceptive precautions if relevant
4. No active malignant disease other than non-melanotic skin cancer or carcinoma in situ of the uterine cervix in the last 3 years
5. ECOG performance status 0-2, at the time of screening
6. Measurable disease
7. Previously untreated histologically proven CD20 and CD79b +ve Diffuse large B cell non-Hodgkin's lymphoma (DLBCL) according to the current World Health Organisation 2016 classification including all morphological variants:
7.1. DLBCL, not otherwise specified (NOS) including GCB and ABC
7.2. T-cell/histiocyte rich large B lymphoma
7.3. Epstein Barr virus positive DLBCL NOS
7.4. ALK-positive large B cell lymphoma
7.5. HHV8 positive DLBCL, NOS
7.6. High-grade B cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements (double hit or triple hit lymphoma)
7.7. High-grade B cell lymphoma, NOS
8. The B-cell nature of the proliferation must be verified by the positivity with anti-CD20 and anti-CD79b antibodies before entry to the study. A central pathology panel will review all histology
9. At least one bi-dimensionally measurable lesion, defined as >1.5 cm in its longest dimension as measured by CT or MRI
10. Availability of archival or freshly obtained tumour tissue
11. No previous chemotherapy, radiotherapy, or other investigational drug for this indication
12. Patients with a cardiac status that does not allow the administration of 6 courses of R-CHOP as defined by an ejection fraction of < = 50% either assessed by echocardiography or nuclear medicine examination [MUGA] or New York Heart Association classification Grade III or IV. If the ejection fraction is > 50% but there is evidence of other significant co-morbid cardiac risk factors (i.e. Hypertension, Diabetes Mellitus, previous history of Ischaemic heart disease, previous cardiac dysfunction, renal impairment etc.) that may preclude full dose anthracycline use, these patients may be considered for trial entry
13. Adequate bone marrow function as defined by:
14. Platelets >100 x 10e9 /l; WBC >3 x 109 /l; neutrophils >1.0 x 10e9 /l at the time of study entry - unless attributed to bone marrow infiltration by lymphoma
15. Serum bilirubin < 50 µmol/l and transaminases < 2.5 x upper limit of institutional normal range unless elevated levels attributed to lymphoma
16. Glomerular filtration rate >30 ml/min as assessed by urinary creatinine clearance or

Cockcroft-Gault Formula
17. No concurrent uncontrolled medical condition
18. Life expectancy >3 months
19. Bulky stage IA (defined as lymph node or lymph node mass greater than 10 cm in diameter), stage IB, stage II, stage III and stage IV
20. Patients receiving corticosteroid treatment with ≤20 mg/day of prednisolone or equivalent must be documented to be on a stable dose of at least 4 weeks duration prior to the start of Cycle 1
21. If glucocorticoid treatment is urgently required for lymphoma symptom control prior to the start of treatment, prednisolone 1 mg/kg or equivalent is permitted to a maximum of 14 days as a pre-phase treatment

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 56; UK Sample Size: 56

Total final enrolment
0

Key exclusion criteria
1. History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies or known sensitivity or allergy to murine products
2. Patients with central nervous system or meningeal involvement by the lymphoma
3. Contraindication to any of the individual components of mini-CHP or GCP including prior administration of anthracyclines.
4. Prior organ transplantation
5. Demyelinating Charcot-Marie-Tooth disease
6. Burkitt lymphoma
7. Primary mediastinal B-cell lymphoma
8. Prior treatment with cytotoxic drugs within 5 years of screening for any condition (e.g. cancer, rheumatoid arthritis) or prior use of any anti-CD20 antibody.
9. Patients with a previous diagnosis of low-grade lymphoma (NB: a concurrent finding of low-grade NHL in the BM at presentation is allowed) and patients with non-bulky stage IA disease
10. Patients with positive serology for HIV, HTVL-1, HCV, HepBcAb, HepBsAg
11. Patients with suspected active Tuberculosis or latent Tuberculosis
12. Pregnancy or lactation or intending to become pregnant during the study
13. Peripheral neuropathy >Grade 1
14. Known active bacterial, viral, fungal or parasitic infections

15. Illicit drug or alcohol abuse; active viral or other hepatitis or cirrhosis
16. Prolonged corticosteroid use >20 mg/day of prednisolone or equivalent for purposes other than lymphoma symptom control

Date of first enrolment
01/05/2022

Date of final enrolment
30/05/2022

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
Clatterbridge Cancer Centre
Clatterbridge Road
Bebington
United Kingdom
CH63 4JY

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Guy’s Hospital
Great Maze Pond
London
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SE1 9RT

Study participating centre
University College London Hospitals NHS Foundation Trust
University College Hospital
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NW1 2BU

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
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SO16 6YD

Study participating centre
Nottingham University Hospitals NHS Trust
Nottingham City Hospital
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Nottingham
United Kingdom
NG5 1PB

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
The Christie NHS Foundation Trust
The Christie
550 Wilmslow Road
Withington
Manchester
United Kingdom
M20 4BX

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

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Sponsor information

Organisation
Clatterbridge Cancer Centre NHS Foundation Trust

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
http://www.clatterbridgecc.nhs.uk/

ROR
https://ror.org/05gcq4j10

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche; Grant Codes: ML41135

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Publication and dissemination plan
1. Planned publication in a high-impact peer-reviewed journal
2. Additional files aren't currently available

Intention to publish date
31/12/2023

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?
HRA research summary			28/06/2023	No	No