

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

<b>Submission date</b> 12/11/2020	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 10/12/2020	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 29/04/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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

APOLLO Trial Co-ordinator  
Liverpool Clinical Trials Centre  
2nd Floor, Institute in the Park  
Alder Hey Children's NHS Foundation Trust  
Eaton Road  
Liverpool  
United Kingdom  
L12 2AP  
+44 (0)151 794 9768  
apollo@liverpool.ac.uk

## Additional identifiers

Clinical Trials Information System (CTIS)

2019-000842-36

## **Integrated Research Application System (IRAS)**

261164

## **ClinicalTrials.gov (NCT)**

Nil known

## **Protocol serial number**

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

## **Study type(s)**

Treatment

## **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(s)

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

## Key secondary outcome(s)

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)

## Completion date

01/07/2023

## Reason abandoned (if study stopped)

Lack of funding/sponsorship

## Eligibility

### Key inclusion criteria

1. Male and female subjects  $\geq 16$  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  $\leq 50\%$  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  $>100 \times 10^9$  /l; WBC  $>3 \times 10^9$  /l; neutrophils  $>1.0 \times 10^9$  /l at the time of study entry - unless attributed to bone marrow infiltration by lymphoma
  15. Serum bilirubin  $< 50 \mu\text{mol/l}$  and transaminases  $< 2.5 \times$  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  $\leq 20$  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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

16 years

**Sex**

All

**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**

United Kingdom

England

Scotland

**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

United Kingdom

SE1 9RT

**Study participating centre**

**University College London Hospitals NHS Foundation Trust**

University College Hospital

235 Euston Road

London

United Kingdom

NW1 2BU

**Study participating centre**

**University Hospital Southampton NHS Foundation Trust**

Southampton General Hospital

Tremona Road

Southampton

United Kingdom

SO16 6YD

**Study participating centre**

**Nottingham University Hospitals NHS Trust**

Nottingham City Hospital

Hucknall Road

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

### 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

### 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

<b>Output type</b>	<b>Details</b>	<b>Date created</b>	<b>Date added</b>	<b>Peer reviewed?</b>	<b>Patient-facing?</b>
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes