ForPatients
by Roche

Diffuse Large B-Cell Lymphoma (DLBCL)

A Study to Evaluate the Efficacy and Safety of Polatuzumab Vedotin in Combination with Rituximab and CHP (R-CHP) Versus Rituximab and CHOP (R-CHOP) in Previously Untreated Patients with Diffuse Large B-Cell Lymphoma

A Study Comparing the Efficacy and Safety of Polatuzumab Vedotin With Rituximab-Cyclophosphamide, Doxorubicin, and Prednisone (R-CHP) Versus Rituximab-Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP) in Participants With Diffuse Large B-Cell Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	23 Countries	NCT03274492 2017-002023-21 2024-516904-40-00 GO39942

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial Comparing the Efficacy and Safety of Polatuzumab Vedotin in Combination With Rituximab and CHP (R-CHP) Versus Rituximab and CHOP (R-CHOP) in Previously Untreated Patients With Diffuse Large B-Cell Lymphoma

Trial Summary:

This Phase III, randomized, double-blind, placebo-controlled study will compare the efficacy, safety, and pharmacokinetics of polatuzumab vedotin plus R-CHP versus R-CHOP in participants with previously untreated diffuse large B-cell lymphoma (DLBCL).

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT03274492 2017-002023-21 2024-516904-40-00 GO39942
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	# 18 Years & # 80 Years	No

1. Why is this study needed?

Diffuse large B-cell lymphoma (known as ‘DLBCL’) is a type of blood cancer. B-cells (also called lymphocytes) are a type of white blood cell that help fight infections. DLBCL develops when B-cells grow abnormally. When this study started in 2017, the standard first treatment for DLBCL was a group of medicines that kill cancer cells, called ‘R-CHOP’. Some people’s DLBCL may continue to get worse after being given R-CHOP, meaning that the medicine has not worked. In those cases where R-CHOP does not work, doctors may give people various types of different treatments. Researchers are interested in looking at new medicines that might help improve outcomes in people with previously untreated DLBCL.

Polatuzumab vedotin is an ‘antibody-drug conjugate’ that is made up of a combination of a ‘monoclonal antibody’ that recognises cancer cells and a ‘chemotherapy’ that kills the cancer cells when it reaches them and stops them from multiplying.

This study is being done to find out how well polatuzumab vedotin works for people with CD20-positive DLBCL. CD20 is a marker or signal on the surface of B-cells. This study also aims to find how safe it is when given together with rituximab, chemotherapy (cyclophosphamide and doxorubicin), and a steroid (prednisone). This combination of medicines is known as ‘Pola-R-CHP’.

Study participants will be given either R-CHOP or Pola-R-CHP.

2. Who can take part in the study?

People who are at least 18 years old but not more than 80 years of age with DLBCL can take part in the study if they have CD20-positive DLBCL, have not already received treatment for DLBCL, were at least capable of all self-care, but may have been unable to carry out any work activities. People may not be able to take part in this study if they had a history of indolent (very slow-growing) lymphoma, had a history of severe allergic or anaphylactic reactions to any of the medicines within the R-CHOP combination, had cancer that had spread to the brain or spinal cord. People who are pregnant or currently breastfeeding cannot take part in the study.

3. How does this study work?

In this study, a larger number of people with DLBCL were either given Pola-R-CHP or R-CHOP (the standard treatment for DLBCL). This was to find out about the unwanted effects of polatuzumab vedotin and to see how effective polatuzumab vedotin was at preventing the worsening (growth or spread) of DLBCL. During the study, people were selected by chance to get one of two treatments. The treatments were selected at random by a computer and were given once every 3 weeks (a ‘treatment cycle’). The treatments are described below.

‘R-CHOP’ is an existing treatment given to people with DLBCL.

- R-CHOP is a combination of:
    - **R – rituximab** (an immunotherapy)
    - **C – cyclophosphamide** (a chemotherapy)
    - **H – doxorubicin** (a chemotherapy)
    - **O – vincristine** (a chemotherapy)
    - **P – prednisone** (a steroid that reduces inflammation or swelling)

‘Pola-R-CHP’ is the combination that was studied here, it works in a different way to R-CHOP. The ‘O’ (vincristine chemotherapy) was replaced by ‘P’ (polatuzumab vedotin).

- Pola-R-CHP is a combination of:
    - **Pola - polatuzumab vedotin** (a medicine that targets cancerous B-cells, then releases chemotherapy inside the cells, making them die)
    - **R – rituximab**
    - **C – cyclophosphamide**
    - **H – doxorubicin**
    - **P – prednisone**

Polatuzumab vedotin is being evaluated as a replacement for vincristine in the R-CHOP regimen.

Polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, and vincristine were given by intravenous infusion (involves inserting a needle into the vein and delivering medications directly into a person’s bloodstream). Prednisone (or other steroid equivalents) was given as a tablet.

During this study, the study doctor will see participants every 21 days during the treatment period for 8 cycles (6 treatment cycles with all the medicines and then 2 treatment cycles of only rituximab, regardless of the combination of medicines that they received in the first 6 cycles). They will see how well the treatment is working and any unwanted effects participants may have. Participants will have follow-up visits 20 times every 3 months starting after completing the study treatment, during which the study doctor will check on the participant’s well being OR will receive a follow-up telephone call from the study doctor to check on their well being every 6 months after completing the study treatment. Participants have the right to stop study treatment and leave the study at any time if they wish to do so.

What are the main results measured in this study?

The main results measured in the study to assess if the medicine has worked was by seeing how many people had no worsening (growth or spread) of their DLBCL, known as progression-free survival, after 2 years. Other key results measured in the study include

how long the participants lived without any significant problems or events that indicate the disease is getting worse, the percentage of participants whose cancer shows no signs of being active after finishing treatment, and length of time that patients are still alive after starting treatment.

4. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. However, the information collected in the study can help other people with similar health conditions in the future. It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. However, these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options for treatment.

Risks associated with the study drug

Participants may have unwanted effects from polatuzumab vedotin and chemotherapy used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

Participants will be told about the known unwanted effects of polatuzumab vedotin and chemotherapy, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include nerve damage causing pain and weakness (peripheral neuropathy), nausea, low levels of a type of white blood cell called neutrophils (neutropenia), diarrhoea, anaemia, constipation, fatigue, alopecia (hair loss), decreased appetite, and fever.

The study medicine(s) may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.

Inclusion Criteria:

- Previously untreated participants with cluster of differentiation 20 (CD20)-positive DLBCL, including one of the following diagnoses by 2016 World Health Organization (WHO) classification of lymphoid neoplasms: DLBCL, not otherwise specified (NOS) including germinal center B-cell type, activated B-cell type; T-cell/histiocyte-rich large B-cell lymphoma; Epstein-Barr virus-positive DLBCL, NOS; anaplastic lymphoma kinase (ALK)-positive large B-cell lymphoma; human herpesvirus-8 (HHV8)-positive DLBCL, NOS; High-grade B-cell lymphoma with MYC and B-cell lymphoma 2 (BCL2) and/or B-cell lymphoma 6 (BCL6) rearrangements (double-hit or triple-hit lymphoma); High-grade B-cell lymphoma, NOS
- Availability of archival or freshly collected tumor tissue before study enrolment
- International Prognostic Index (IPI) score of 2-5

- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2
- Life expectancy greater than or equal to (>/=)12 months
- Left ventricular ejection fraction (LVEF) >/= 50 percent (%) on cardiac multiple-gated acquisition (MUGA) scan or cardiac echocardiogram (ECHO)
- Adequate hematologic function
- Female participants: Agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods and refrain from donating eggs.
- Male participants: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom and agreement to refrain from donating sperm.

Exclusion Criteria:

- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies or known sensitivity or allergy to murine products
- Contraindication to any of the individual components of CHOP, including prior receipt of anthracyclines
- Prior organ transplantation
- Current Grade greater than (>) 1 peripheral neuropathy by clinical examination
- Demyelinating form of Charcot-Marie-Tooth disease
- History of indolent lymphoma
- History of follicular lymphoma grade 3B
- B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma (grey-zone lymphoma)
- Primary mediastinal (thymic) large B-cell lymphoma
- Burkitt lymphoma
- Prior treatment with cytotoxic drugs within 5 years of screening for any condition (example [e.g.], cancer, rheumatoid arthritis) or prior use of any anti-CD20 antibody
- Prior use of any monoclonal antibody within 3 months of the start of Cycle 1
- Prior therapy for DLBCL, with the exception of nodal biopsy
- Corticosteroid use >30 mg/day of prednisone or equivalent, for purposes other than lymphoma symptom control
- Participants with central nervous system (CNS) lymphoma (primary or secondary involvement), primary effusion DLBCL, and primary cutaneous DLBCL
- Vaccination with live vaccines within 28 days prior to the start of Cycle 1
- Any investigational therapy within 28 days prior to the start of Cycle 1
- History of other malignancy that could affect compliance with the protocol or interpretation of results
- Evidence of significant, uncontrolled, concomitant diseases that could affect compliance with the protocol or interpretation of results, including significant cardiovascular disease or pulmonary disease
- Recent major surgery (within 4 weeks prior to the start of Cycle 1), other than for diagnosis
- History or presence of an abnormal electrocardiogram (ECG) that is clinically significant in the investigator's opinion, including complete left bundle branch block, second- or third-degree heart block, or evidence of prior myocardial infarction
- Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection (excluding fungal infections of nail beds) at study enrollment or significant infections within 2 weeks before the start of Cycle 1
- Clinically significant liver disease, including active viral or other hepatitis, current alcohol abuse, or cirrhosis
- Prior radiotherapy to the mediastinal/pericardial region
- Participants with suspected active or latent tuberculosis
- Positive test results for chronic hepatitis B and hepatitis C infection
- Known history of human immunodeficiency virus (HIV) seropositive status
- Positive results for the human T-lymphotrophic 1 virus (HTLV-1)
- Participants with a history of progressive multifocal leukoencephalopathy

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