ForPatients
by Roche

Diffuse Large B-Cell Lymphoma (DLBCL)Lymphoma

A Study Evaluating the Safety, Efficacy and Pharmacokinetics of Venetoclax in Combination With Polatuzumab Vedotin Plus Rituximab (R) and Cyclophosphamide, Doxorubicin, Prednisone (CHP) in Participants With Untreated BCL-2 Immunohistochemistry (IHC)-Positive Diffuse Large B-Cell Lymphoma (DLBCL)

Trial Status	Trial Runs In	Trial Identifier
Terminated	4 Countries	NCT04790903 2023-507497-40-00 BO42203

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 Ib Study Evaluating the Safety, Efficacy, and Pharmacokinetics of Venetoclax in Combination With Polatuzumab Vedotin Plus Rituximab (R) and Cyclophosphamide, Doxorubicin, Prednisone (CHP) in Patients With Untreated BCL-2 Immunohistochemistry (IHC)-Positive Diffuse Large B-Cell Lymphoma

Trial Summary:

This Phase Ib, open-label, multicenter study evaluates the safety, efficacy, and pharmacokinetics of venetoclax in combination with Pola + R-CHP in previously untreated participants with BCL-2 IHC-positive DLBCL. Approximately 50 participants will be enrolled in this study in five consecutive cohorts each consisting of approximately 10 participants.

Hoffmann-La Roche Sponsor	**Phase 1** Phase

NCT04790903 2023-507497-40-00 BO42203
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

Diffuse large B-cell lymphoma (DLBCL) is the most common type of lymphoma. It affects a type of immune cell called B cells. It often starts in lymphoid tissues and can spread to other organs. The cells look bigger than other cancers when seen under a microscope. Standard treatment for DLBCL is a combination of chemotherapy and immunotherapy. Chemotherapy is a medicine that kills cancer cells. Immunotherapy is a type of medicine that helps a person's own immune system (the body's natural defence) attack cancer cells. Pola-R-CHP is a standard first treatment that combines polatuzumab vedotin (pola) plus rituximab (R), cyclophosphamide (C), doxorubicin (H), and prednisone (P). But some cancers have more Bcl-2 than normal. Bcl-2 proteins are involved in normal cell survival. When cancers are ´Bcl-2-positive', the extra Bcl-2 proteins keep cancer cells alive and help them resist treatment. Better treatments are needed for Bcl-2-positive DLBCL.

This study is testing a medicine called venetoclax (Ven) combined with polatuzumab vedotin (Pola), rituximab (R), and cyclophosphamide, doxorubicin and prednisone (CHP). This is called Ven+Pola+R-CHP. They are being developed to treat Bcl-2-positive DLBCL.

Ven has been approved by health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) for treating other certain types of cancer. Ven+Pola+R-CHP is an experimental combination of medicines. This means health authorities have not approved Ven+Pola+R-CHP for treating DLBCL.

This study aims to look at how well Ven+Pola+R-CHP works against Bcl-2-positive DLBCL that has not previously been treated. It will also check how safe the combination is and how the body processes it.

2. Who can take part in the study?

People of 18 years of age or older with DLBCL can take part in the study. But only if their cancer is Bcl-2-positive on tests. They must not have previously had any medicine for their DLBCL except steroids to control symptoms.

People may not be able to take part in this study if they have had other cancers within the last 2 years, certain infections or liver disease. People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

Participants will be screened to check if they are able to participate in the study. The screening period will take place from 1 day to 1 month before the start of treatment.

Everyone who joins this study will be given treatment in 3-week cycles. A treatment cycle is made up of the days treatment is given and the recovery time. Depending on when they join the study, participants will be given Ven as tablets to be swallowed either:

- Once a day for 5 days of each cycle
- OR once a day for 7 days in Cycle 1, then once a day for 10 days of each cycle

Participants will also be given:

- Pola, R and CH (from CHP), given as a drip into a vein on Day 1 of each cycle
- AND P (from CHP), given as tablets to be swallowed once a day for 5 days of each cycle

This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

During this study, the study doctor will see participants up to 3 times during the first cycle, then once every 3 weeks. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have follow-up visits every 3 months after their last dose of study treatment for as long as they agree to it. Or until their cancer gets worse, they start another anti-cancer treatment or the study finishes. The study doctor will check on the participant's wellbeing during follow-up visits. Participants who start another anti-cancer treatment or their cancer gets worse will receive follow-up visits or telephone calls from the study doctor. They will check on their wellbeing every 6 months for as long as they agree to it until the study ends. Total time of participation in the study will be up to 4 years. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main result measured in the study is the number of participants who have specific unwanted effects during the first 6 weeks.

Other key results measured in the study include:

- The number and seriousness of unwanted effects over the whole study
- The number of people who do not have cancer on scans after treatment
- The number of participants who have a specific level of reduction in the size of their tumour after completing treatment
- The amount of time between participant's cancer first responding to treatment and the cancer getting worse
- How long people live without their cancer getting worse
- How Ven and Pola get to different parts of the body, and how the body changes and gets rid of them

5. 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. But 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. But 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 of treatment.
Risks associated with the study medicines Participants may have unwanted effects of the medicines 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.
Venetoclax, polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin and prednisone Participants will be told about the known unwanted effects of venetoclax, polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin and prednisone and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include fever, feeling or being sick, a feeling of coldness that makes the body shiver, feeling tired, pain or discomfort in the head, rash, hair loss, frequent watery stools, infections and lower amounts of certain types of blood cells.

Known unwanted effects of a drip into a vein include feeling or being sick, a feeling of coldness that makes the body shiver, low or high blood pressure, fever, reddening of the skin, pain or discomfort in the head, rapid heart rate, heart beat out of rhythm, frequent watery stools, shortness of breath and cough.

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 CD20-positive DLBCL.
- BCL-2 protein overexpression by IHC, as assessed by local testing.
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2.
- International Prognostic Index (IPI) 2-5.
- Life expectancy of more than 6 months.
- Left ventricular ejection fraction (LVEF) # 50%, as determined on cardiac multiple-gated acquisition (MUGA) scan or cardiac echocardiogram (ECHO).
- Availability of archival or freshly collected tumor tissue prior to study enrollment.
- At least one bi-dimensionally fluorodeoxyglucose-avid measurable lymphoma lesion on PET/CT scan, defined as > 1.5 cm in its longest dimension on CT scan.
- Adequate hematopoietic function.
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception, and agreement to refrain from donating eggs.
- For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom, and agreement to refrain from donating sperm.

Exclusion Criteria:

- Current diagnosis of unclassifiable B-cell lymphoma.
- Prior treatment for indolent lymphoma.
- Current Grade > 1 peripheral neuropathy.
- Prior organ transplantation.
- Prior use of any monoclonal antibody within 3 months and any investigational therapy within 28 days prior to the start of Cycle 1.
- Vaccination with live vaccines within 28 days prior to the start of Cycle 1.
- Prior therapy for DLBCL and High-Grade B-cell Lymphoma (HGBCL) with the exception of palliative, short-term treatment with corticosteroids.
- Recent major surgery (within 6 weeks prior to the start of Day 1 of Cycle 1), other than for diagnosis.
- History of other cancers within 2 years prior to screening.
- Any active infection that, in the opinion of the investigator, would impact participant safety within 7 days prior to Day 1 of Cycle 1.
- Serious infection requiring oral or IV antibiotics within 4 weeks prior to Day 1 of Cycle 1.
- Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the participant's safe participation in and completion of the study.
- Positive test for Hepatitis B/C Viruses (HBV/HCV) and Human T-cell Leukemia Virus (HTLV)-1.
- Known infection with HIV.
- History of progressive multifocal leukoencephalopathy.
- Suspected active or latent tuberculosis.
- Clinically significant history of liver disease, including viral or other hepatitis or cirrhosis.
- Substance abuse, including non-prescription drug and alcohol dependence, within 12 months prior to screening.
- Pregnant or breastfeeding, or intending to become pregnant during the study within 6 months after the final dose of venetoclax, 9 months after the final dose of polatuzumab vedotin, or 12 months after the final dose of rituximab.
- History or presence of an abnormal ECG that is clinically significant in the investigator's opinion.
- Malabsorption syndrome or other condition that would interfere with enteral absorption.
- Blood transfusion within 14 days prior to screening.