ForPatients
by Roche

Diffuse Large B-Cell Lymphoma (DLBCL)

A study to compare glofitamab plus chemotherapy with rituximab plus chemotherapy in people with diffuse large B-cell lymphoma (after previous treatment has not worked)

A Phase III Study Evaluating Glofitamab in Combination With Gemcitabine + Oxaliplatin vs Rituximab in Combination With Gemcitabine + Oxaliplatin in Participants With Relapsed/ Refractory Diffuse Large B-Cell Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	13 Countries	NCT04408638 2020-001021-31 2023-506899-27-00 GO41944

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, open-label, multicenter, randomized study evaluating the efficacy and safety of glofitamab in combination with gemcitabine plus oxaliplatin versus rituximab in combination with gemcitabine and oxaliplatin in patients with relapsed/refractory diffuse large B-cell lymphoma

Trial Summary:

This study will evaluate the efficacy and safety of glofitamab in combination with gemcitabine plus oxaliplatin (Glofit-GemOx) compared with rituximab in combination with gemcitabine plus oxaliplatin (R-GemOx) in patients with R/R DLBCL.

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT04408638 2020-001021-31 2023-506899-27-00 GO41944
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.

Rituximab given with 2 chemotherapy medicines – gemcitabine (Gem) and oxaliplatin (Ox), often called 'GemOx' – is widely used when initial treatments do not work. However it is not approved by health authorities (like the U.S. Food and Drug Administration and European Medicines Agency). New treatments are needed for people with DLBCL that does not respond to or worsens after the first or second treatment.

This study is testing a medicine called glofitamab combined with GemOx. It is being developed to treat DLBCL. Glofitamab plus GemOx is an experimental combination of medicines. This means health authorities have not approved this combination for the treatment of DLBCL after previous treatment has not worked.

This study aims to compare the effects of glofitamab plus GemOx versus rituximab plus GemOx in people with DLBCL that has come back or worsened after previous treatment.

2. Who can take part in the study?

People of 18 years of age or older with DLBCL can take part in the study if they have had at least 1 previous treatment that did not work and cannot be given high-dose chemotherapy followed by a stem-cell transplant.

People may not be able to take part in this study if they have DLBCL that has certain changes (gene mutations) or is fast-growing, or if they have been treated with rituximab plus GemOx, GemOx, glofitamab or similar medicines before. People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

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

Treatment will be given in 'cycles'. A treatment cycle is the period of treatment and recovery time before the next set of treatment is given. In this study, each cycle will last 3 weeks.

Everyone who joins this study will be placed into 1 of 2 groups randomly (like flipping a coin) and given either:

- Glofitamab plus GemOx given as a drip into the vein for up to 8 cycles, then glofitamab alone for 4 cycles
- Rituximab plus GemOx given as a drip into the vein for up to 8 cycles

Participants will have a 2 in 3 chance of being placed in the glofitamab group and a 1 in 3 chance of being placed in the rituximab group. This means that more people will be in the glofitamab group than the rituximab group.

Participants in the glofitamab group will be required to stay in the hospital overnight the first time they are given study treatment. They will be given another medicine called 'obinutuzimab' as a drip into the vein before they are given glofitamab for the first time. This is a safety measure to reduce the chance of an unwanted effect called 'cytokine release syndrome' – when the immune system reacts in an unusual way to an infection or cancer immunotherapy. This can cause a variety of symptoms, such as a fever, nausea, headache, and rash. If this unwanted effect happens, another medicine called 'tocilizumab' will be given as a drip into the vein.

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 every 1 to 3 weeks. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have 1 follow-up visit 6 weeks after their last dose of study treatment during which the study doctor will check on the participant's wellbeing. The study doctor will continue to check the participants' wellbeing through their medical records, follow-up telephone calls or hospital visits every 3 months, for as long as the participant agrees to it. Total time of participation in the study could be up to 5 years depending on how well treatment works. 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 results measured in the study to assess if the medicine has worked is how long participants live.

Other key results measured in the study include:

- How long participants live without their cancer getting worse
- The number of participants who do not have cancer on tests or scans after treatment, and how long this response lasts
- How many participants have a reduction of their cancer after treatment, and how long this response lasts
- The time it takes for a participant to have a significant worsening in their lymphoma symptoms, physical health or level of tiredness
- The number and seriousness of unwanted effects

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 glofitamab, rituximab, gemcitabine, oxaliplatin, obinutuzimab and tocilizumab

Participants may have unwanted effects of the drugs 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 and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include:

- Glofitamab – cytokine release syndrome, fever, and a low level of white blood cells
- Rituximab – infections, itching and rash
- Gemcitabine and oxaliplatin – wanting to throw up, a low level of white blood cells and damage to the nerves outside the brain and spinal cord
- Obinutuzimab – a reaction to the drip into a vein, infections, fever
- Tocilizumab – an infection that makes a person have a sore throat, cough, runny nose and sneezing

Known unwanted effects of a drip into the vein include throwing up, wanting to throw up, a feeling of coldness that makes the body shiver, fever, pain or discomfort in the head, shortness of breath, and cough. The study medicines may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT04408638

Trial-identifier: NCT04408638

Inclusion Criteria:

- Histologically confirmed diffuse large B-cell lymphoma (DLBCL), not otherwise specified
- Relapsed/refractory (R/R) disease, defined as follows: Relapsed = disease that has recurred #6 months after completion of the last line of therapy; Refractory = disease that either progressed during the last line of therapy or progressed within 6 months (<6 months) of the last line of prior therapy
- At least one (#1) line of prior systemic therapy
- Participants who have failed only one prior line of therapy must not be a candidate for high-dose chemotherapy followed by autologous stem cell transplant, as defined by the study protocol
- Confirmed availability of tumor tissue, unless unobtainable per investigator assessment. Freshly collected biopsy is preferred. Archival tissue is acceptable
- At least one bi-dimensionally measurable (#1.5 cm) nodal lesion, or one bi-dimensionally measurable (#1 cm) extranodal lesion, as measured on computed tomography (CT) scan
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2
- Adequate hematologic function (unless attributable to the underlying disease, as established by extensive bone marrow involvement or associated with hypersplenism secondary to the involvement of the spleen by DLBCL per the investigator), as defined by the study protocol
- Negative SARS-CoV-2 antigen or PCR test within 7 days prior to enrollment
- Adequate renal function, defined as an estimated creatinine clearance #30 mL/min

Exclusion Criteria:

- Patient has failed only one prior line of therapy and is a candidate for stem cell transplantation
- History of transformation of indolent disease to DLBCL
- High-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements, and high-grade B-cell lymphoma not otherwise specified, as defined by 2016 WHO guidelines
- Primary mediastinal B-cell lymphoma
- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies (or recombinant antibody-related fusion proteins) or known sensitivity or allergy to murine products
- Contraindication to obinutuzumab, rituximab, gemcitabine or oxaliplatin, or tocilizumab
- Prior treatment with glofitamab or other bispecific antibodies targeting both CD20 and CD3
- Peripheral neuropathy assessed to be Grade >1 according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v5.0 at enrollment
- Treatment with radiotherapy, chemotherapy, immunotherapy, immunosuppressive therapy, or any investigational agent for the purposes of treating cancer within 2 weeks prior to first study treatment
- Treatment with monoclonal antibodies for the purposes of treating cancer within 4 weeks prior to first study treatment
- Primary or secondary central nervous system (CNS) lymphoma at the time of recruitment or history of CNS lymphoma
- Current or history of CNS disease, such as stroke, epilepsy, CNS vasculitis, or neurodegenerative disease
- Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection (excluding fungal infections of nail beds) at study enrollment or any major episode of infection (as evaluated by the investigator) within 4 weeks prior to the first study treatment
- Positive SARS-CoV-2 infection within 30 days prior to the first study treatment, including asymptomatic SARS-CoV-2 infection
- Documented SARS-CoV-2 infection within 6 months of first study treatment
- Suspected or latent tuberculosis
- Positive for hepatitis B virus (HBV), hepatitis C virus (HCV), or human immunodeficiency virus (HIV)
- Known or suspected chronic active Epstein-Barr viral infection
- Known or suspected history of hemophagocytic lymphohistiocytosis (HLH)
- Known history of progressive multifocal leukoencephalopathy
- Adverse events from prior anti-cancer therapy not resolved to Grade 1 or better (with the exception of alopecia and anorexia)

- Administration of a live, attenuated vaccine within 4 weeks before first study treatment administration or anticipation that such a live, attenuated vaccine will be required during the study
- Prior solid organ transplantation
- Prior allogeneic stem cell transplant
- Active autoimmune disease requiring treatment
- Prior treatment with systemic immunosuppressive medications (including, but not limited to, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents), within 4 weeks prior to first dose of study treatment
- Corticosteroid therapy within 2 weeks prior to first dose of study treatment (exceptions defined by study protocol)
- Recent major surgery (within 4 weeks before the first study treatment) other than for diagnosis
- Clinically significant history of cirrhotic liver disease