ForPatients
by Roche

Non Hodgkin Lymphoma (NHL)

An Open-Label Phase lB/II Study of Glofitamab and Atezolizumab or Polatuzumab Vedotin in Adult Patients With Relapsed/Refractory B-Cell Non-Hodgkin's Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	6 Countries	NCT03533283 2023-505222-34-00 NP39488

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:

An Open-Label, Multi-Center, Phase IB/II Study of Glofitamab and Atezolizumab or Polatuzumab Vedotin (Plus a Single Pre-Treatment Dose of Obinutuzumab) in Adult Patients With Relapsed/Refractory B-Cell Non-Hodgkin's Lymphoma

Trial Summary:

This is an open-label, single arm, multicenter, dose finding, Phase Ib study in order to assess the maximum tolerated dose (MTD) and/or recommended Phase II dose (RP2D) for this combination treatment and to evaluate the general safety, tolerability, pharmacokinetic (PK), pharmacodynamic, and preliminary anti-tumor activity of this combination treatment in adult patients. This study includes an additional open-label imaging feasibility sub-study using a tracer in adult participants with relpased/refractory B-cell non-Hodgkin's lymphoma to image CD8+T-cells at baseline and after treatment with glofitamab, including pre-treatment with obinutuzumab.

Hoffmann-La Roche
Sponsor

Phase 1/Phase 2
Phase

NCT03533283 2023-505222-34-00 NP39488
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the NP39488 clinical trial needed?

B-cell non-Hodgkin lymphoma (NHL) is a common type of cancer that affects a type of immune cell called B-cells. Although there has been progress in treating NHL, many people who have NHL may not respond to treatment (their disease is refractory) or their cancer returns (relapses). New treatment combinations, such as glofitamab with atezolizumab or polatuzumab vedotin, could help people with relapsed or refractory (R/R) B-cell NHL to live longer. Glofitamab is approved by health authorities for the treatment of a type of B-cell NHL (known as 'diffuse large B-cell lymphoma'). Glofitamab and atezolizumab are the experimental drugs in this clinical trial, which means health authorities have not approved glofitamab on its own for treating other types of B-cell NHL. Polatuzumab vedotin is only approved by the health authorities in some countries for treating B-cell NHL so polatuzumab vedotin may not be available to all participants who take part in the trial.

This clinical trial aims to test the safety and effectiveness of different dose combinations of glofitamab with atezolizumab or polatuzumab vedotin in people with R/R B-cell NHL and to understand how the body processes these treatment combinations.

2. How does the NP39488 clinical trial work?

This clinical trial is recruiting people with R/R B-cell NHL. People who take part in this clinical trial (participants) will be given the clinical trial treatment glofitamab in combination with atezolizumab for up to 1 year OR glofitamab in combination with polatuzumab vedotin for up to 9 months unless they have very severe side effects, their cancer gets worse or they decide to leave the trial. Treatment will be given in 21-day cycles – a treatment cycle includes receiving the treatment and the recovery time before the next dose is given. Participants receiving glofitamab in combination with atezolizumab who have no cancer on scans after 8 cycles of treatment (about 6 months), will stop receiving the clinical trial treatment and will continue to be monitored in the trial – if a participant’s cancer returns then another 9 cycles of treatment will be provided.

The clinical trial doctor will see them 5 times during the first 2 weeks, and then every 3 weeks. These hospital visits will include checks to see how the participant responds to the treatment and any side effects they may have. Participants will be seen 1 month after the last dose of treatment, then every 3–6 months for as long as they agree to it. Total time of participation in the clinical trial could be more than 3 years. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the NP39488 clinical trial?

The main clinical trial endpoint (the main result measured in the trial to see if the drug has worked) is the maximum dose of glofitamab that can be given with other anti-cancer treatments before very severe side effects occur. The other clinical trial endpoints include:

- The number and seriousness of any side effects

- How the body processes the anti-cancer drugs and how the drugs affect the immune system
- The number of participants whose cancer disappears or gets smaller and the amount of time this lasts if disease then progresses
- The number of participants whose cancer disappears, gets smaller or stays the same
- The amount of time it takes for participants to first have a response to treatment and for the cancer to disappear
- The amount of time between the start of the trial and participants' cancer worsening
- How long participants live

4. Who can take part in this clinical trial?

People can take part in this trial if they are aged 18 years or over and have no other treatment options available for their NHL. People may not be able to take part in this trial if they have certain lymphomas, have/had certain medical conditions such as infections, stroke, heart disease, autoimmune disease or other advanced cancers, or have received certain other treatments including organ or stem-cell transplant. People who are pregnant or breastfeeding or are planning to become pregnant during or soon after the clinical trial also cannot take part.

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be placed into a group depending on the treatments available in their country and the clinical trial doctors' decision, and given either:

- **Glofitamab and atezolizumab**
    - glofitamab as an infusion into the vein on Days 1 and 8 for the first 21-day cycle, and then every 3 weeks from Cycle 2 for up to 17 cycles
    - atezolizumab as an infusion into the vein every 3 weeks from Cycle 2 for up to 17 cycles
- **Glofitamab and polatuzumab vedotin**
    - glofitamab as an infusion into the vein on Days 8 and 15 for the first 21-day cycle, and then every 3 weeks (Cycles 2–12)
    - polatuzumab vedotin as an infusion into the vein on Day 2 of the first 21-day cycle, and then every 3 weeks (Cycles 2–6)

Everyone will also be given a pre-treatment drug called 'obinutuzumab' as an infusion into the vein 1 week before they are given glofitamab. This is to reduce the risk of a side effect called 'cytokine release syndrome'. Participants may also receive tocilizumab as an infusion into the vein if they experience cytokine release syndrome during the clinical trial.

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

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly.

Participants will be told about the known side effects of glofitamab, atezolizumab, obinutuzumab, polatuzumab vedotin and tocilizumab, and possible side effects based on human and laboratory studies or knowledge of similar drugs. Participants will be told about any known side effects of infusions into the vein (intravenous infusions).

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Histologically-confirmed hematologic malignancy that is expected to express CD20 (Relapsed after or refractory to respond to at least one prior treatment regimen; no available treatment options that are expected to prolong survival or patients refusing chemotherapy or autologous stem cell transplant (SCT))
- Dose-escalation: Grades 1-3b relapsed or refractory (R/R) follicular lymphoma (FL) or marginal zone lymphoma (MZL) (nodal; extra-nodal; or splenic), diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL), high-grade B-cell lymphoma (HGBCL) with MYC and BCL2 and/or BCL6 rearrangements (double-hit lymphoma), HGBCL not otherwise specified (NOS), DLBCL arising from FL (transformed FL)
- Dose-expansion: R/R LBCL, including DLBCL NOS, DLBCL arising from FL (transformed FL), PMBCL, HGBCL with MYC and BCL2 and/or BCL6 rearrangements (i.e., double-hit and triple-hit lymphomas), and HGBCL NOS
- At least one measurable target lesion
- Fresh pre-treatment biopsy, but if this cannot be taken, a previous archived biopsy from metastatic lesion can be taken as replacement if it is not older than 6 months and not confounded by major events (progression, treatment)
- Eastern Cooperative Oncology Group (ECOG) performance status of 0-2

- Adequate organ function (liver, hematological, renal)
- Negative test results for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV)

Inclusion Criteria Specific to Imaging Substudy

- At least two measurable target lesions
- Able to provide two fresh tumor biopsies (baseline and on-treatment)

Exclusion Criteria:

- Participants with Chronic Lymphocytic Leukemia (CLL), acute lymphoblastic leukemia (ALL), lymphoblastic lymphoma, Richter's transformation, CD20-positive ALL, Burkitt lymphoma, or lymphoplasmacytic lymphoma
- Current > Grade 1 peripheral neuropathy (only for participants being treated in the polatuzumab vedotin arm)
- Patients with known active infection, or reactivation of a latent infection within 4 weeks prior to Obinutuzumab (Gpt) infusion
- Patient with history of confirmed progressive multifocal leukoencephalopathy (PML)
- History of leptomeningeal disease
- Current or past history of central nervous system (CNS) lymphoma
- Current or past history of CNS disease
- Major surgery or significant traumatic injury </=28 days prior to Gpt infusion
- Significant cardiovascular disease or significant pulmonary disease
- Active or history of autoimmune disease or immune deficiency (with exceptions, e.g. hypothyroidism and Diabetes mellitus Type 1)
- History of idiopathic pulmonary fibrosis, organizing pneumonia (e.g. bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- Treatment with any other standard anti-cancer radiotherapy / chemotherapy including investigational therapy within 4 weeks prior to Gpt infusion
- Prior solid organ transplantation
- Prior allogenic stem cell transplant (SCT)
- Autologous SCT within 100 days prior to Gpt infusion
- Documented refractoriness to an obinutuzumab-monotherapy regimen
- Prior treatment with anti-cancer/lymphoma therapies and systemic immunotherapeutic/ immunostimulating agents within 4 weeks or 5 half-lives of the drug, whichever is shorter, prior to Gpt infusion
- Any history of immune related >/= Grade 3 adverse events (AE) with the exception of endocrinopathy managed with replacement therapy
- Ongoing corticosteroid use >25 milligrams/day of prednisone or equivalent within 4 weeks prior to and during study treatment
- Treatment with systemic immunosuppressive medication
- Administration of a live, attenuated vaccine within 4 weeks prior to Gpt infusion or anticipation that such a live attenuated vaccine will be required during the study or within 5 months after last dose of study treatment

Exclusion Criteria Specific to Imaging Substudy

- Circulating lymphoma cells, defined by out of range (high) absolute lymphocyte count and/or the presence of abnormal/malignant cells in the peripheral blood differential signifying circulating lymphoma cell

- Participants who have had splenectomy or functional asplenia that could compromise protocol objectives