ForPatients
by Roche

Non Hodgkin Lymphoma (NHL)

A study to evaluate the safety, efficacy, tolerability and pharmacokinetics of escalating doses of glofitamab (RO7082859) as a single agent and in combination with obinutuzumab, administered after a fixed, single dose pre-treatment of obinutuzumab (Gazyva®/ Gazyvaro™) in patients with relapsed/refractory B-cell non-Hodgkin's lymphoma

A Dose Escalation Study of Glofitamab (RO7082859) as a Single Agent and in Combination With Obinutuzumab, Administered After a Fixed, Single Pre-treatment Dose of Obinutuzumab in Participants With Relapsed/Refractory B-cell Non-hodgkin's Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Recruiting	13 Countries	NCT03075696 2016-001185-28 2023-505625-14-00 NP30179

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 Multicenter, Open-label, Phase I/II Study to Evaluate the Safety, Efficacy, Tolerability and Pharmacokinetics of Escalating Doses of Glofitamab (RO7082859) as a Single Agent and in Combination With Obinutuzumab Administered After a Fixed, Single Dose Pre-treatment of Obinutuzumab (Gazyva®/ Gazyvaro™) in Patients With Relapsed/Refractory B-cell Non-hodgkin's Lymphoma

Trial Summary:

This is a Phase I/II, multicenter, open-label, dose-escalation study designed to evaluate the efficacy, safety, tolerability and pharmacokinetics (PK) of a novel T-Cell bispecific (TCB), glofitamab, administered by intravenous (IV) infusion as a single agent and in combination with obinutuzumab, following pre-treatment with a one-time, fixed dose of obinutuzumab. This entry-into-human (EIH) study is divided in 3 parts: dose escalation (Parts I and II) and dose expansion (Part III). Single-participant dose-escalation cohorts will be used in Part I, followed by conversion to multiple participant dose-escalation cohorts (Part II), in order to define a tentative maximum tolerated dose (MTD) or optimal biological dose (OBD). The expansion cohorts (Part III) will be initiated when the tentative MTD/OBD is defined, to further evaluate the safety, PK and therapeutic activity of glofitamab.

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Phase 1/Phase 2
Phase

NCT03075696 2016-001185-28 2023-505625-14-00 NP30179
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	**#18 Years**	**No**

1. Why is this study needed?

B-cell non-Hodgkin lymphoma (B-cell NHL) is a blood cancer that affects a type of immune cell called B cells. It starts in lymphoid tissues and can spread to other organs. There are many different types of B-cell NHL.

People with B-cell NHL need better treatments. The cancer can return after improving for a while – a condition known as ‘relapsed’ cancer. Sometimes it does not respond to standard treatments or therapies – known as ‘refractory’ cancer.

This study is testing a medicine called glofitamab given on its own or combined with obinutuzumab. It is being developed to treat different types of B-cell NHL. Obinutuzumab is given before glofitamab, so it is known as a ‘pre-treatment’. The pre-treatment lowers the chance of an unwanted effect called ‘cytokine release syndrome’ (CRS), after being given glofitamab. CRS happens when the immune system reacts in an unusual way. During this reaction, substances called cytokines are released into the body. This can cause a variety of symptoms, such as a fever, nausea, headache and rash. After pre-treatment with obinutuzumab, glofitamab may work better against B-cell NHL if it is combined with obinutuzumab every time it is given.

When this study started in 2017, glofitamab was an experimental medicine. This means health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) had not yet approved glofitamab for the treatment of B-cell NHL. In 2023 due to results from this study, health authorities approved glofitamab given on its own after obinutuzumab pre-treatment for some types of B-cell NHL. Health authorities have not approved glofitamab in combination with obinutuzumab after pre-treatment has been given.

This study aims to test how well glofitamab given in combination with obinutuzumab after pre-treatment works against B-cell NHL. The study will also find the best doses of glofitamab and how often to give them, and what happens to glofitamab and obinutuzumab in the body.

2. Who can take part in the study?

People of 18 years of age or older with relapsed/refractory B-cell NHL can take part in the study. Participants may need to have a certain type of B-cell NHL to join the study. They may also need to have experienced a relapse, or to have not responded to at least 1 treatment before. Or, they have no standard treatment options available.

People may not be able to take part in this study if they have certain infections, such as hepatitis C virus or HIV. People with conditions such as kidney, liver, heart or autoimmune problems may not be able to take part. 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 28 days before pre-treatment is given.

Everyone who joins this study will be given:

- 1 or 2 obinutuzumab pre-treatments as a drip into the vein
- Glofitamab as a drip into the vein every 2 or 3 weeks, OR
- Glofitamab and obinutuzumab as drips into the vein every 3 weeks

Different groups of people will be given different doses of glofitamab. The dose and the number of pre-treatments will depend on when they join the study. The first doses of glofitamab may be given as ‘step up doses’. This means starting with a lower dose and then progressively increasing the dosage over time.

Everyone will be given up to 12 ‘cycles’ of treatment. A treatment cycle is the period of treatment and recovery time before the next set of treatment is given.

People who have CRS as an unwanted effect of glofitamab treatment may also be given tocilizumab. Tocilizumab is 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 regularly. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have follow-up visits after 1 month of completing the study treatment then every 3 months for as long as they agree to it, during which the study doctor will check on the participant’s wellbeing. Total time of participation in the study will be about 10 months plus follow-up visits. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so. Participants may restart glofitamab treatment in the follow-up period

if they meet certain criteria, such as NHL not getting worse or not having very severe unwanted effects.

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

The main results measured in the study to assess if the medicine has worked are:

- The number and seriousness of unwanted effects – to find the best dose of glofitamab to give on its own or in combination with obinutuzumab, and how often to give glofitamab, after 1 pre-treatment
- The number of people who do not have cancer on tests or scans after treatment
- How glofitamab gets to different parts of the body, and how the body changes and gets rid of it when given on its own or with obinutuzumab

Other key results measured in the study include:

- How pre-treatment gets to different parts of the body, and how the body changes and gets rid of it
- How the immune system is affected by glofitamab
- How many people have a positive response to the treatment, and how long the response lasts
- The time it takes from the start of treatment for a positive response to be seen
- How long people live, and how long people live without their cancer getting worse
- How a person's health and cancer symptoms impact their daily life and their ability to function and enjoy life

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.

Glofitamab, obinutuzumab and tocilizumab Participants will be told about the known unwanted effects of the study drugs, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects of glofitamab include CRS (which can cause a variety of symptoms, such as a fever, nausea, headache and rash; the person can also have a fast heartbeat, low blood pressure and trouble breathing), fever, low number of white blood cells and increased risk for infections such as infection of the lungs. Known unwanted effects of obinutuzumab include a reaction to the drip into the vein, low number of white or red blood cells, frequent watery stools, cough and difficulty falling asleep or staying asleep. Known unwanted effects of tocilizumab include an infection of the nose, throat, or sinuses, usually caused by a virus.

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, low blood pressure, fever, pain or discomfort in the head, 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:

- Depending upon study part, a history or status of: 1) a histologically-confirmed hematological malignancy that is expected to express cluster of differentiation (CD)20; 2) relapse after or failure to respond to at least one prior treatment regimen; and 3) no available treatment options that are expected to prolong survival (e.g., standard chemotherapy or autologous stem cell transplant [ASCT])
- Measurable disease, defined as at lease one bi-dimensionally measurable nodal lesion, defined as > 1.5 cm in its longest dimension, or at least one bi-dimensionally measureable extranodal lesion, defined as > 1.0 cm in its longest dimension
- Able to provide a fresh biopsy from a safely accessible site, per investigator determination, providing the patient has more than one measurable target lesion
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Life expectancy of >/=12 weeks
- AEs from prior anti-cancer therapy must have resolved to Grade less than or equal to (</=) 1
- Adequate liver, hematological and renal function
- Negative serologic or polymerase chain reaction (PCR) test results for acute or chronic Hepatitis B virus (HBV) infection
- Negative test results for Hepatitis C virus (HCV) and human immunodeficiency virus (HIV)
- Negative serum pregnancy test within 7 days prior to study treatment in women of childbearing potential. Women who are not of childbearing potential who are considered to be post-menopausal (at least 12 months of non-therapy amenorrhea) or surgically sterile (absence of ovaries and/or uterus) are not required to have a pregnancy test

Exclusion Criteria:

- Inability to comply with protocol mandated hospitalizations and restrictions
- Participants with chronic lymphocytic leukemia (CLL), Burkitt lymphoma and lymphoplasmacytic lymphoma
- Participants with a known or suspected history of hemophagocytic lymphohistiocytosis (HLH)

- Participants with acute bacterial, viral, or fungal infection at baseline, confirmed by a positive blood culture within 72 hours prior to obinutuzumab infusion or by clinical judgment in the absence of a positive blood culture
- Participants with known active infection, or reactivation of a latent infection, whether bacterial, viral, fungal, mycobacterial, or other pathogens or any major episode of infection requiring hospitalization or treatment with IV antibiotics within 4 weeks of dosing
- Prior treatment with systemic immunotherapeutic agents, including, but not limited to, radio-immunoconjugates, antibody-drug conjugates, immune/cytokines and monoclonal antibodies (e.g., anti-cytotoxic T-lymphocyte-associated protein 4 [anti-CTLA4], anti-programmed death 1 [anti-PD1] and anti-programmed death ligand 1 [anti-PDL1]) within 4 weeks or five half-lives of the drug, whichever is shorter, before obinutuzumab infusion on Cycle 1 Day -7
- History of treatment-emergent immune-related AEs associated with prior immunotherapeutic agents
- Documented refractoriness to an obinutuzumab-containing regimen
- Treatment with standard radiotherapy, any chemotherapeutic agent, or treatment with any other investigational anti-cancer agent, including chimeric antigen receptor therapy (CAR-T) within 4 weeks prior to obinutuzumab infusion
- Prior solid organ transplantation
- Prior allogeneic SCT
- Autologous SCT within 100 days prior to obinutuzumab infusion
- Participant with history of confirmed progressive multifocal leukoencephalopathy (PML)
- Current or past history of central nervous system (CNS) lymphoma
- Current or past history of CNS disease, such as stroke, epilepsy, CNS vasculitis, or neurodegenerative disease. Participants with a past history of stroke that have not experienced a stroke or transient ischemic attack in the past 2 years and have no residual neurologic deficits are allowed.
- Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results, including diabetes mellitus, history of relevant pulmonary disorders and known autoimmune diseases
- Participants with another invasive malignancy in the last 2 years (with the exception of basal cell carcinoma and tumors deemed by the Investigator to be of low likelihood for recurrence)
- Significant or extensive history of cardiovascular disease such as New York Heart Association Class III or IV or Objective Class C or D cardiac disease, myocardial infarction within the last 6 months, unstable arrhythmias, or unstable angina
- Administration of a live, attenuated vaccine within 4 weeks before obinutuzumab infusion or anticipation that such a live attenuated vaccine will be required during the study
- Received systemic immunosuppressive medications (including but not limited to cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents) within two weeks prior to obinutuzumab infusion. Treatment with corticosteroid </= 25 mg/day prednisone or equivalent is allowed. Inhaled and topical steroids are permitted.
- Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that would contraindicate the use of an investigational drug
- History of autoimmune disease, including but not limited to myocarditis, pneumonitis, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus, erythematosus, rheumatoid arthritis, inflammatory bowel disease, vascular thrombosis associated with antiphospholipid syndrome, Wegener's granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis. Participants with a remote history of, or well controlled autoimmune disease, may be eligible to enroll after consultation with the Medical Monitor
- In Part III DLBCL dexamethasone cohort, patients with a history of hypersensitivity to dexamethasone or systemic corticosteroids will be excluded