ForPatients
by Roche

Mature B-Cell Non-Hodgkin LymphomaMature B-Cell Lymphoma

A clinical trial to look at how well glofitamab works on its own, and in combination with standard cancer chemotherapy plus immunotherapy in children and young adults with B-cell non-Hodgkin lymphoma (B-NHL) after one or multiple standard therapies have not worked

A Study to Evaluate Glofitamab + Chemoimmunotherapy in Pediatric and Young Adult Participants With Relapsed/Refractory Mature B-Cell Non-Hodgkin Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Recruiting	9 Countries	NCT05533775 CO43810

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 I/II, Open-Label, Single-Arm, Two-Part Trial to Evaluate Safety, Tolerability, Pharmacokinetics, and Anti-Tumor Activity of Glofitamab in Monotherapy and in Combination With Chemoimmunotherapy in Pediatric and Young Adult Participants With Relapsed/Refractory Mature B-Cell Non-Hodgkin Lymphoma

Trial Summary:

The purpose of this study is to evaluate the safety and efficacy of glofitamab, as monotherapy and in combination with a standard chemoimmunotherapy regimen: rituximab, ifosfamide, carboplatin, and etoposide (R-ICE) in pediatric and young adult participants with relapsed and refractory (R/R) mature B-cell non-Hodgkin lymphoma (B-NHL).

Hoffmann-La Roche	Phase 1/Phase 2
Sponsor	Phase

NCT05533775 CO43810
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#6 Months & # 30 Years	No

1. Why is the iMATRIX GLO clinical trial needed?

B-cell non-Hodgkin lymphoma (B-NHL) is a common type of cancer that affects a type of immune cell called B cells. Current standard therapy works well for the first treatment of B-NHL in most children, but not all. For people who do not respond (also called relapsed/ refractory B-NHL), the current treatment is the combination of chemotherapy plus immunotherapy (chemoimmunotherapy): rituximab, ifosfamide, carboplatin, and etoposide (known as the R-ICE chemoimmunotherapy). However, R-ICE chemoimmunotherapy does not work well against first-time relapsed or refractory B-NHL in the majority of children. There is an urgent need for new treatments for first-time and multiple-time relapsed or refractory B-NHL. In adults, standard cancer chemoimmunotherapy has been shown to work better when given in combination with a new, experimental drug called glofitamab. This clinical trial will assess:

How well treatment with R-ICE plus glofitamab works in children and young adults with B-NHL that has not responded to one previous treatment, and

How well treatment with glofitamab alone works in children with B-NHL that has not responded to at least two previous treatments.

2. How does the iMATRIX GLO clinical trial work?

This clinical trial is recruiting children and young adults who have a health condition called B-cell non-Hodgkin lymphoma (B-NHL). People can take part if they have relapsed or refractory B-NHL.

The purpose of this clinical trial is to identify a recommended dose and to test the safety of glofitamab in combination with R-ICE, to understand how well glofitamab alone and in combination with R-ICE works against relapsed or refractory B-NHL, and to understand the way the body processes glofitamab.

The clinical trial is divided into two groups of participants (called ‘cohorts’) depending on their age and how many previous treatments for B-NHL they have received.

Cohort A:

People can join Cohort A if they are **aged 6 months to less than 30 years**, and have received **one previous treatment** for B-NHL.

Participants in Cohort A will receive glofitamab in combination with R-ICE therapy for at least two 21-day treatment cycles and if needed **up to three 21-day treatment cycles**, and will be assigned to one of two trial parts:

o **Part 1** is to find out the recommended dose of glofitamab for people under the age of 18 years

o **Part 2** will start after Part 1, and will assess how well the treatment works at the recommended dose, and will also include people aged up to 30 years

In both Parts 1 and 2, participants will need to stay in a hospital for days 1–10 and days 15–17 during treatment in Cycle 1, and for at least the first 3 days of treatment in cycles 2 and 3, to receive treatment and be seen by the clinical trial doctor.

Cohort B:

People can join Cohort B if they are **aged 6 months to less than 18 years**, and have received **two or more previous treatments** for B-NHL.

Participants in Cohort B will receive glofitamab alone for up to **twelve 21-day treatment cycles**

Participants will need to stay in a hospital for days 1–3, 8–10, and 15–17 during treatment in Cycle 1, for at least the first 3 days of treatment in Cycle 2, and for at least the first day of treatment from Cycle 3, to receive treatment and be seen by the clinical trial doctor.

In both cohorts, the number of treatment cycles that participants will be given will depend on how well their cancer responds to treatment and whether they stop treatment because of side effects.

All participants will receive increasingly higher doses (also called ‘step up doses’) of glofitamab in Cycle 1 and target doses from Cycle 2.

After finishing the trial treatment, participants will be seen by the clinical trial doctor approximately every 3 months. These hospital visits will include checks to see how the participant is responding to the treatment and any side effects they may be having. Participants’ total time in the clinical trial will be around one year. Participants are free to stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the iMATRIX GLO clinical trial?

The main clinical trial endpoints (the main results that are measured in the trial to see if the medicine has worked) are:

1) the percentage of participants in Cohort A who have no detectable cancer after up to three cycles of treatment (complete response rate)

2) to assess the safety of glofitamab, as measured by the number and type of side effects that participants experience

3) an assessment of the way the body processes glofitamab.

The other clinical trial endpoints (for both cohorts) include the percentage of participants who have either no detectable cancer or who have cancer that has reduced in size by at least 50% compared with the beginning of the trial (objective response rate), and how long participants live (overall survival).

4. Who can take part in this clinical trial?

People can take part in this trial if they have been diagnosed with B-NHL that has returned or has not responded to either one (for Cohort A) or two or more (for Cohort B) previous cancer treatments, and if they are aged between 6 month and 18 years (for Cohort A Part 1 and Cohort B), or between 6 months and 30 years (for Cohort A Part 2).

People may not be able to take part in this trial if they have certain medical conditions or have previously received certain treatments. Women cannot take part in this trial if they are pregnant or breastfeeding or are planning to become pregnant soon after the clinical trial.

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

Everyone who joins this clinical trial will be given:

Obinutuzumab pre-treatment as an infusion (into the vein) on days 1 and 2 of Cycle 1. This drug is given to reduce the risk of side effects.

Cohort A will be given:

Ifosfamide, carboplatin, and etoposide (ICE) as an infusion on days 3, 4 and 5 of Cycle 1

Glofitamab (step-up dose) as an infusion on days 8 and 15 of Cycle 1

Glofitamab (target dose) as an infusion on Day 1 of cycles 2 and 3

Rituximab-ICE as an infusion on days 5, 6, 7 and 8 of cycles 2 and 3

Cohort B will be given:

Glofitamab (step-up dose) as an infusion on days 8 and 15 of Cycle 1

Glofitamab (target dose) as an infusion on Day 1 of Cycle 2 and all subsequent cycles

Some participants will be given tocilizumab as an infusion if certain side effects (called ‘cytokine release syndrome’) are experienced by the participant during or following glofitamab treatment.

Some participants will be given chemotherapy drugs into the fluid around the spine (intrathecal) before or after they are given obinutuzumab or glofitamab, depending on the type of B-NHL they have.

This is an open-label clinical trial, which means that all participants and trial doctors will know which treatments they are receiving.

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, although it may not be greater than the risks related to routine medical care or the natural progression of the health condition. Potential participants 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. These will all be described in an informed consent document (a document that provides people with the information they need to make a decision to volunteer for a clinical trial) and assent documents (documents providing information about the clinical trial designed for patients below 18 years of age). A potential participant should also discuss these with members of the research team and with their usual healthcare provider. Anyone interested in taking part in a clinical trial should know as much as possible about the trial and feel comfortable asking the research team any questions about the 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 and even life-threatening, and can vary from person to person.

Obinutuzumab, Ifosfamide, Carboplatin, Etoposide, Rituximab, Glofitamab and Tocilizumab

Potential participants will be told about the known side effects of obinutuzumab, ifosfamide, carboplatin, etoposide, rituximab, glofitamab and tocilizumab, and where relevant, also potential side effects based on human and laboratory studies or knowledge of similar drugs.

All of these drugs will be given as an intravenous (into a vein) infusion. Participants will be told about any known side effects of intravenous infusion.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial, but the information that is collected may help other people who have a similar medical condition in the future.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatients page or follow this link to ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT05533775

Inclusion Criteria:

- Age 6 months to < 18 years at the time of signing Informed Consent for Part 1 and Cohort B of the study, and age 6 months to # 30 years old at the time of signing Informed Consent for Part 2 of the study
- Histologically re-confirmed diagnosis, via tissue biopsy, or bone marrow aspirate, pleural effusion, or ascites, prior to study entry of aggressive mature B-NHL that expresses CD20 (reconfirmed by IHC or flow cytometry if IHC is not possible), including BL, BAL (mature B-cell leukemia FAB L3), DLBCL, and PMBCL, at the time of first R/R disease for Cohort A and second or greater R/R disease for Cohort B
- Refractory or relapsed disease (i.e., prior treatment was ineffective or intolerable) following first-line standard-of-care chemoimmunotherapy for Cohort A and following at least two prior systemic chemoimmunotherapy regimens and who have exhausted all available established therapies for Cohort B
- Measurable disease, defined as: At least one bi-dimensionally measurable nodal lesion, defined as > 1.5 cm in its longest dimension, or at least one bi dimensionally measurable extranodal lesion, defined as > 1.0 cm in its longest dimension; or percentage of bone marrow involvement with lymphoma cells defined by cytomorphological analysis of bone marrow aspirates
- Adequate performance status, as assessed according to the Lansky or Karnofsky Performance Status scales: Participants < 16 years old: Lansky Performance Status # 50%; Participants # 16 years old: Karnofsky Performance Status # 50%
- Adequate bone marrow, liver, and renal function
- Negative test results for acute or chronic hepatitis B virus (HBV), hepatitis C virus (HCV)
- Negative HIV test at screening, with the following exception: Individuals with a positive HIV test at screening are eligible provided they are stable on anti-retroviral therapy for at least 4 weeks, have

a CD4 count #200/uL, have an undetectable viral load, and have not had a history of opportunistic infection attributable to AIDS within the last 12 months
- Negative SARS-CoV-2 antigen or PCR test within 7 days prior to enrollment
- Participants and/or caregivers who are willing and able to complete clinical outcome assessments throughout the study using either paper or interviewer methods

Exclusion Criteria:

- Isolated CNS disease of mature B-NHL without systemic involvement, and primary CNS lymphoma
- Receipt of glofitamab prior to study enrollment
- Ongoing adverse events from prior anti-cancer therapy that were not resolved to Grade # 1 (exceptions: alopecia, Grade 2 peripheral neuropathy)
- Grade # 3 adverse events, with the exception of Grade 3 endocrinopathy managed with replacement therapy
- Participants with active infections which are not resolved prior to Day 1 of Cycle 1
- Prior solid organ transplantation
- Known or suspected history of hemophagocytic lymphohistiocytosis (HLH), or chronic active Epstein-Barr viral infection (CAEBV)
- Active autoimmune disease requiring treatment
- History of severe allergic or anaphylactic reactions to monoclonal antibody therapy (or recombinant antibody-related fusion proteins) or known sensitivity or allergy to murine products, except if the participant was able to safely receive it after initial administration (consider consultation with Medical Monitor)
- History of confirmed progressive multifocal leukoencephalopathy
- Current or past history of uncontrolled non-malignant CNS disease, such as stroke, epilepsy, CNS vasculitis, or neurodegenerative disease
- Evidence of significant and uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results
- Major surgery or significant traumatic injury < 28 days prior to the obinutuzumab pretreatment infusion (excluding biopsies) or anticipation of the need for major surgery during study treatment
- Administration of a live, attenuated vaccine within 4 weeks before the start of study treatment (obinutuzumab pretreatment) or at any time during the study treatment period and within 12 months after end of study treatment
- Participants with 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