ForPatients
by Roche

Non Hodgkin Lymphoma (NHL)B-cell Non-Hodgkin Lymphoma

A clinical study for people with B-cell non-Hodgkin lymphoma that looks at how safe and how well mosunetuzumab works when given in combination with polatuzumab vedotin

A Study to Evaluate the Safety and Efficacy of Mosunetuzumab (BTCT4465A) in Combination With Polatuzumab Vedotin in B-Cell Non-Hodgkin Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	5 Countries	NCT03671018 2023-506986-74-00 GO40516

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, multicenter, phase Ib/II study evaluating the safety, tolerability, pharmacokinetics, and efficacy of mosunetuzumab (BTCT4465A) in combination with polatuzumab vedotin in patients with B cell non-Hodgkin lymphoma

Trial Summary:

This study will evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of intravenous (IV) or subcutaneous (SC) mosunetuzumab in combination with polatuzumab vedotin in participants with diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), and mantle cell lymphoma (MCL). It will consist of a dose finding portion followed by an expansion phase for second line or later (2L+) participants with relapsed or refractory (R/R) DLBCL and 2L+ R/R FL. In addition, subcutaneous mosunetuzumab in combination with polatuzumab vedotin will be evaluated in participants with at least 2 prior lines of systemic therapy (3L+) for the treatment of R/R mantle cell lymphoma (MCL) and in participants with 2L+ R/R DLBCL.

Hoffmann-La Roche
Sponsor

Phase 1/Phase 2
Phase

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Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

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All	# 18 Years	No

1. Why is the GO40516 clinical study 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 will experience a relapse (their disease returns). New drug combinations could help people with relapsed or refractory NHL to live longer. Mosunetuzumab is a drug that attaches to a protein called CD20 that is found on some types of NHL cells. It can join to another protein on cancer-killing cells of the immune system. This brings them closer together so immune cells can destroy the NHL cells. Mosunetuzumab, when given on its own, is approved for the treatment of a type of NHL called follicular lymphoma (FL). This clinical study aims to test the safety and effects (good or bad) of mosunetuzumab when given with polatuzumab vedotin (another medicine used to treat NHL) in people with different types of NHL. The study will also compare how well mosunetuzumab plus polatuzumab vedotin works versus a drug combination that is routinely used, called rituximab plus polatuzumab vedotin.

2. How does the GO40516 clinical study work?

This clinical study is recruiting people with the following types of NHL: FL, diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL). People can take part if their lymphoma did not respond to or got worse after at least one (for those with FL or DLBCL) or two (for those with MCL) previous treatments.

The study is split into 3 parts.

- Part 1 aims to find:
    - the safest and most effective dose of mosunetuzumab to give as an infusion into the vein (intravenous, or IV) with polatuzumab vedotin, and
    - how often to give it (schedule) in participants with relapsed/refractory DLBCL or FL
- After researchers find out the best dose and schedule to use, Part 2 of the study will look at:
    - how safe and effective this selected dose and schedule is in more people with relapsed/refractory DLBCL or FL, and
    - how safe and effective mosunetuzumab is when given as an injection under the skin (subcutaneous, or SC) with IV polatuzumab vedotin in participants with MCL
- Part 3 will compare how well SC mosunetuzumab plus polatuzumab vedotin works versus IV rituximab plus polatuzumab vedotin in participants with relapsed/refractory DLBCL

- participants who join Part 3 will have an equal chance of being in either treatment group
- participants in the rituximab group whose cancer stays the same or worsens during or after 6 months of treatment, may be given SC mosunetuzumab for a further 6 months (plus IV polatuzumab vedotin)

People who take part in this clinical study (participants) will be given the clinical study treatment mosunetuzumab or rituximab plus polatuzumab vedotin. This will be for up to 6 months to 1 year, depending on which part of the study they join and how well they respond to treatment. Participants who initially respond well to treatment then their NHL comes back, may be given study treatment again. The clinical study doctor will see the participant regularly throughout the study. These visits will include checks to see how the participant responds to the treatment and any side effects they may have. Participants will see the clinical study doctor for scans approximately every 3 months for the first year. Additional scans will be done every 6 months for the next 2 years. Then the scans will be done yearly for the next 3 years until the participant`s cancer worsens, they leave the study, or they start a new lymphoma treatment. The total time of participation in the clinical study will be about 6 years. Participants can stop study treatment and leave the clinical study at any time.

3. What are the main results measured in the GO40516 clinical study?

The main results measured (the main study endpoints) are the:

- Dose of IV mosunetuzumab plus IV polatuzumab vedotin that is the safest and most effective
- Number of participants with a reduction in their cancer, or with no cancer on scans

The other clinical study endpoints include:

- How long participants maintain a reduction in their cancer, or no cancer on scans
- The amount of time between the start of study treatment and participants' cancer getting worse or a different cancer treatment being given
- How long participants live
- How the body absorbs and gets rid of mosunetuzumab
- The effects of mosunetuzumab and polatuzumab vedotin on the immune system

4. Who can take part in this clinical study?

People aged 18 years or older with relapsed/refractory FL, DLBCL or MCL can take part. They must also have had a type of medicine called anti-CD20 for lymphoma before. People may not be able to take part in this study if they are able to have a stem cell transplant, or have had certain treatments before, including mosunetuzumab (or similar drugs) or polatuzumab vedotin. People with lymphoma that affects the brain or spinal

cord, or medical conditions like heart or lung disease or certain infections cannot take part. People cannot be pregnant or breastfeeding.

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

Everyone who joins this clinical study will be given either:

- Mosunetuzumab, given as an infusion (into the vein) or as an injection (under the skin) every 3 weeks for 8–17 cycles (a cycle is the period of treatment and recovery time before the next dose of treatment is given and each cycle lasts 3 weeks)
- OR rituximab, given as an infusion (into the vein) every 3 weeks for 8 cycles
- AND polatuzumab vedotin, given as an infusion (into the vein) every 3 weeks for 6 cycles

Participants may also receive tocilizumab as an infusion into the vein if they experience certain side effects during the clinical study. This is an open-label study, which means everyone involved, including the participant and the clinical study doctor, will know the clinical study treatment the participant has been given.

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

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the study. Most studies 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 NHL. People who would like to participate will be told about any risks and benefits of taking part in the clinical study, 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 study).

Risks associated with the clinical study drugs

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

Participants will be told about the known side effects of mosunetuzumab, polatuzumab vedotin, rituximab, 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) and injections under the skin (subcutaneous injections).

Potential benefits associated with the clinical study

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

Inclusion Criteria:

- ECOG PS of 0, 1, or 2
- Histologically confirmed FL, DLBCL, or MCL
- Must have received at least one prior systemic treatment regimen containing an anti-CD20-directed therapy for DLBCL or FL
- For MCL, participants must have received at least two prior systemic treatment regiments, which include 1) anti-CD20-directed therapy, 2) BTK inhibitor, and 3) anthracycline or bendamustine
- Relapsed to prior regimen(s) after having a documented history of response (complete response [CR], CR unconfirmed [CRu], or partial response [PR]) of >/= 6 months in duration from completion of regimen(s); or, refractory to any prior regimen, defined as no response to the prior therapy, or progression within 6 months of completion of the last dose of therapy
- 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
- Adequate hematologic, renal, and hepatic function

Exclusion Criteria:

- Prior treatment with mosunetuzumab or other CD20-directed bispecific antibodies
- Prior treatment with polatuzumab vedotin
- Current > Grade 1 peripheral neuropathy
- Prior use of any monoclonal antibody, radioimmunoconjugate or antibody-drug conjugate (ADC) within 4 weeks before first dose of study treatment
- Treatment with any chemotherapeutic agent, or treatment with any other anti-cancer agent (investigational or otherwise) within 4 weeks or 5 half-lives of the drug, whichever is shorter, prior to first dose of study treatment
- Treatment with radiotherapy within 2 weeks prior to the first dose of study treatment
- Autologous stem-cell transplantation (SCT) within 100 days prior to first study treatment administration
- Prior treatment with chimeric antigen receptor T-cell (CAR-T) therapy within 30 days before first study treatment administration
- Prior allogeneic SCT
- Prior solid organ transplantation
- Known or suspected history of hemophagocytic lymphohistiocytosis (HLH)
- Patients with history of confirmed progressive multifocal leukoencephalopathy (PML)
- Current or past history of central nervous system (CNS) lymphoma or CNS disease
- History of autoimmune disease