ForPatients
by Roche

Lymphoma

A clinical trial to compare how well glofitamab on its own works versus standard treatment in people with mantle cell lymphoma that has come back after or has not responded to treatment

A Study to Evaluate Glofitamab as a Single Agent vs. Investigator's Choice in Participants With Relapsed/Refractory Mantle Cell Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Recruiting	12 Countries	NCT06084936 2023-503206-37-00 GO43878

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 Glofitamab as a Single Agent Versus Investigator's Choice in Patients With Relapsed/Refractory Mantle Cell Lymphoma

Trial Summary:

The purpose of this study is to evaluate the efficacy of glofitamab monotherapy compared with an investigator's choice of either rituximab plus bendamustine (BR), or lenalidomide with rituximab (R-Len) in patients with relapsed or refractory (R/R) mantle cell lymphoma (MCL).

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT06084936 2023-503206-37-00 GO43878
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the GO43878 clinical trial needed?

Mantle cell lymphoma (MCL) is a rare type of cancer that starts in white blood cells called lymphocytes. Lymphocytes help protect the body from infection. They travel around the body through a network known as the lymphatic system. This includes the spleen, thymus, tonsils, and beanshaped glands called lymph nodes. In MCL, lymphocytes called B cells become abnormal and cannot fight infections. Abnormal B cells collect in the lymph nodes and spleen. This causes lymph nodes to swell and form cancerous tumours. The standard treatments for MCL include so-called 'systemic' treatments such as chemotherapy (for example, bendamustine, or **B**), immunotherapy (medicines that help the body to use its immune system to fight the cancer) and targeted therapy (treatment that affects only the cancer cells so that healthy cells have less risk of being harmed) such as lenalidomide (**Len**), rituximab (**R**) and BTK inhibitors. But MCL often does not respond to treatment (known as 'refractory' disease) or comes back after treatment (known as 'relapsed' disease). Stem cell transplant is a cure, but people with MCL are rarely well enough to be given this procedure. New treatments are needed for people with relapsed/refractory MCL. Glofitamab is an experimental drug (health authorities have not approved it for treating MCL). It attaches to a protein called CD20 found on some types of MCL cells and can join to another protein on cancer-killing immune system cells. This brings them closer together, so immune cells destroy the MCL cells. This clinical trial aims to compare how well **glofitamab** works versus standard treatment (**BR** or **R-Len**) in people with relapsed/ refractory MCL.

2. How does the GO43878 clinical trial work?

This clinical trial is recruiting people with relapsed/refractory MCL. People can take part if they have been given at least one treatment including a BTK inhibitor and systemic treatment combination. People who take part in this clinical trial (participants) will be given **glofitamab** (for up to about 9 months) or the doctors choice of **BR** (for up to 6 months) or **R-Len** (for as long it can help them). Treatment will be stopped if cancer gets worse; participants can then choose to swap from **BR** or **R-Len** to glofitamab treatment. The clinical trial doctor will see them regularly - at least every 3–4 weeks. Participants will also be seen 6 weeks and 3 months after the final dose of treatment. These hospital/clinical trial doctor visits will include checks to see how participants respond to treatment and any side effects they may have. The total time in the clinical trial will be from 7 months to over 2 years, plus a follow-up every 3 months for as long as the participant agrees. Participants can stop trial treatment and leave the trial at any time.

3. What are the main endpoints of the GO43878 clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see if the drug has worked) is the length of time between the start of the trial and participants' cancer getting worse (known as 'progression-free survival', or PFS). The other clinical trial endpoints include:

- How many participants' have no signs of cancer after treatment (complete response rate)
- How many participants' tumours get smaller or disappear after treatment (objective response rate)
- How long participants live (overall survival)
- Changes in health-related quality of life

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 18 years old and have relapsed/ refractory MCL. People may not be able to take part in this trial if they have:

- Previously received certain treatments, including glofitamab or if they can have, or already had, a stem cell transplant
- Cancer that has spread to the brain or spinal cord
- Certain other medical conditions such as heart, liver or auto-immune disease, infections, pregnancy or breastfeeding, or people planning to conceive during the trial or up to a year after the final dose of treatment (depending on which treatment is given). People must also not donate/store sperm or eggs during these periods.

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

Everyone who joins this clinical trial will be split into two groups randomly (like flipping a coin) and given treatment as an infusion (into a vein) of either **glofitamab** (experimental group) every 3 weeks (called treatment 'cycles') for up to 12 cycles, or the doctors choice of **BR** or **R-Len** (control group) every 4 weeks. **BR** will be given for up to 6 cycles and **R-Len** will be given for as long it can benefit participants. Participants will have an equal chance of being placed in either the experimental group or the control group. If a participant experiences a potential side effect called 'cytokine release syndrome' (when the body's immune cells are activated and release large amounts of inflammatory substances throughout the body), they may receive another medicine called tocilizumab. Before being given glofitamab for the first time, participants will be given another drug called obinutuzumab, to reduce the risk of side effects. 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 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 bendamustine glofitamab, lenalidomide, obinutuzumab, rituximab and tocilizumab and possible side effects based on laboratory studies or knowledge of similar drugs. Bendamustine, glofitamab, obinutuzumab, rituximab and tocilizumab will be given as infusions into a vein (intravenous infusions); lenalidomide will be given as a tablet (to be swallowed). Participants will be told about any known side effects of intravenous infusions and swallowing tablets.

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:

- Life expectancy at least 12 weeks
- Histologically-confirmed MCL, with documentation of either overexpression of cyclin D1 or the presence of t(11:14)
- Relapsed (disease progression after the last treatment regimen) or refractory (failure to achieve a partial or complete response from the last treatment regimen) disease
- At least 1 line of prior systemic therapy including a BTK inhibitor and additional systemic therapy option
- Confirmed availability of tumor tissue, unless deemed unsafe per investigator assessment
- At least one bi-dimensionally measurable (defined as at least 1.5 cm) nodal lesion, or one bi-dimensionally measurable (at least 1 cm) extranodal lesion, as measured on CT scan
- Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2
- Negative HIV test at screening
- Adequate hematological function

Exclusion Criteria:

- Pregnancy or breastfeeding, or intention of becoming pregnant during the study or within 3 months after the final dose of tocilizumab, 2 months after the final dose of glofitamab, whichever is longer
- Leukemic, non-nodal MCL
- 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 or rituximab, and either bendamustine or lenalidomide
- Prior treatment with glofitamab or other bispecific antibodies targeting both CD20 and CD3
- Prior treatment with CAR-T cell therapy
- Treatment with systemic therapy or BTK inhibitors, or any investigational agent for the purposes of treating cancer within 2 weeks or 5 half-lives (whichever is shorter) prior to first study treatment
- Primary or secondary CNS lymphoma at the time of recruitment or history of CNS lymphoma

- Current or history of CNS disease, such as stroke, epilepisy, CNS vasculitis, or neurodegenerative disease
- History of other malignancy that could affect compliance with the protocol or interpretation of results
- Significant or extensive cardiovascular disease
- Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection at study enrollment or any major episode of infection within 4 weeks prior to the first study treatment
- Suspected or latent tuberculosis
- Positive test for hepatitis B virus (HBV) or hepatitis C virus (HCV)
- Known or suspected chronic active Epstein-Barr viral infection (EBV)
- Known or suspected history of hemophagocytic lymphohistiocytosis (HLH)
- Known history of progressive multifocal leukoencephalopathy (PML)
- Adverse events from prior anti-cancer therapy that have not resolved to Grade 1 or better
- 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 or allogenic stem cell transplant
- Eligibility for stem cell transplantation (SCT)
- Active autoimmune disease requiring treatment
- Prior treatment with systemic immunosuppressive medications within 2 weeks or five half-lives (whichever is shorter) prior to the first dose of study treatment
- Corticosteroid therapy within 2 weeks prior to first dose of study treatment
- Recent major surgery (within 4 weeks before the first study treatment) other than for diagnosis
- Clinically significant history of cirrhotic liver disease