ForPatients
by Roche

Non Hodgkin Lymphoma (NHL)

A clinical trial to test CC-220 or CC-99282 in combination with mosunetuzumab, and CC-99282 in combination with glofitamab, in people with B-cell non-Hodgkin lymphoma.

A Study Evaluating the Safety, Pharmacokinetics, and Efficacy of Mosunetuzumab or Glofitamab in Combination With CC-220 and/or CC-99282 in Participants With B-Cell Non-Hodgkin Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Recruiting	5 Countries	NCT05169515 2023-505185-28-00 CO43805

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 Ib, Open-Label, Multicenter Study Evaluating the Safety, Pharmacokinetics, and Efficacy of Mosunetuzumab or Glofitamab in Combination With CC-220 and/or CC-99282 in Patients With B-Cell Non-Hodgkin Lymphoma

Trial Summary:

This study will evaluate the safety, efficacy, and pharmacokinetics of mosunetuzumab or glofitamab in combination with CELMoDs (CC-220 and/or CC-99282) in participants with B-cell NHL.

Hoffmann-La Roche	Phase 1
Sponsor	Phase

NCT05169515 2023-505185-28-00 CO43805
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the CO43805 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 will experience a relapse (their disease returns). New drug combinations could help people with relapsed or refractory NHL to live longer.

This clinical trial aims to test the safety and effectiveness of CC-220 or CC-99282 when combined with mosunetuzumab, or CC-99282 when combined with glofitamab, and to understand how the body processes these treatment combinations.

2. How does the CO43805 clinical trial work?

This clinical trial is recruiting people who have a health condition called B-cell NHL. People can take part if they have relapsed or refractory NHL.

People who take part in this clinical trial (participants) will be given the clinical trial treatment CC-220 or CC-99282 in combination with mosunetuzumab (Group A) OR CC-99282 in combination with glofitamab (Group B) for up to 12 cycles of treatment. A treatment cycle is the period of treatment and recovery time before the next dose of treatment is given. Participants will be seen by the clinical trial doctor every week during the first two to three cycles, and then every 3 or 4 weeks in the remaining treatment cycles. These hospital visits will include checks to see how the participant responds to the treatment and any side effects they may be having. Participants' total time in the clinical trial will be up to roughly 3 years, as they will be seen for follow-up appointments every 3 months for 2 years after they have finished treatment. Participants are free to stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the CO43805 clinical trial?

The main clinical trial endpoints (the main results that are measured in the trial to see if the drug has worked) are the type and number of dose-limiting toxicities (known as 'DLTs' - treatment side effects that are too severe to allow for an increase in the dose), and the number and seriousness of any other side effects.

Other clinical trial endpoints include:

- The number of participants who have no detectable cancer on scans (complete response rate)
- The number of participants with cancer that has shrunk or is not detectable on scans (overall response rate)
- The amount of time between cancer getting better to cancer progressing (duration of response)
- The amount of time between the start of treatment, to cancer first progressing, or a new treatment needed (progression-free and event-free survival)

- How long participants live (overall survival)

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 NHL that either failed to respond or relapsed after treatment with at least one or two previous lines of systemic therapy (treatment that travels through the bloodstream) depending on which treatment group they join. People may not be able to take part in this trial if they are pregnant or breastfeeding, have certain other medical conditions such as autoimmune, lung, liver or heart disease, or have previously received certain other treatments including mosunetuzumab, glofitamab or stem cell or organ transplant.

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

Everyone who joins this clinical trial will be put into groups depending on when they join and given either:

- **Group A**: Mosunetuzumab as an injection under the skin (subcutaneous) on Days 1, 8 and 15 of Cycle 1, then Day 1 of Cycles 2–12 and CC-220 as a capsule to be swallowed once a day on Days 1–21 of Cycles 2–12 OR CC-99282 as a capsule to be swallowed once a day on Days 1–14 of Cycles 2–12. Cycle 1 will last for 21 days and Cycles 2–12 will last for 28 days
- **Group B**: Glofitamab as an infusion into the vein on Days 8 and 15 of Cycle 1, then Day 1 of Cycles 2–12, and CC-99282 as a capsule to be swallowed once a day on Days 1–10 of Cycles 3–12. Each cycle will last for 21 days. People in this group will also need to have one pre-treatment dose of obinutuzumab as an infusion into the vein on Day 1 of Cycle 1

Participants may also receive tocilizumab as an infusion into the vein if they experience certain side effects 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. Potential participants will be told about the known side effects of mosunetuzumab, glofitamab, obinutuzumab, CC-220, CC-99282 and tocilizumab and, where relevant, also potential side effects based on human and laboratory studies or knowledge of similar drugs. Mosunetuzumab will be given as a subcutaneous injection (inserting a needle into the fatty layer between the skin and muscle); glofitamab, obinutuzumab and tocilizumab are each given as an intravenous infusion (inserting a needle into a vein, usually in the arm); CC-220 and CC-99282 are each given as capsules (to be swallowed). Participants will be told about any known side effects of subcutaneous injections, intravenous infusions and swallowing capsules.

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:

- Age >/= 18 years
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2
- History of one of the following histologically documented hematologic malignancies that are expected to express the CD20 antigen: In the Dose Escalation phase, participants must have relapsed after or failed to respond to at least two prior lines of systemic therapy. In the Dose Expansion phase, participants with FL Grades 1-3a must have relapsed after or failed to respond to at least one prior line of systemic therapy and must require systemic therapy. Participants with DLBCL/transformed FL must have relapsed after or failed to respond to at least one prior systemic treatment regimen.
- Participants with DLBCL/transformed FL who have received only one prior line of therapy must: Not be considered a candidate for autologous stem cell transplantation (ASCT) due to age, performance status, comorbidities and/or insufficient response to prior treatment, or have refused ASCT; or be ineligible for or unable to receive chimeric antigen receptor T-cell (CAR-T) therapy due to reasons defined by the protocol
- Fluorodeoxyglucose-avid lymphoma (i.e. PET-positive lymphoma)
- At least one bi-dimensionally measurable nodal lesion (> 1.5 cm in its largest dimension by diagnostic quality CT or PET/CT scan), or at least one bi-dimensionally measurable extranodal lesion (> 1.0 cm in its largest dimension by diagnostic quality CT or PET/CT scan)
- Availability of a representative tumor specimen and the corresponding pathology report for confirmation of the diagnosis of NHL
- A fresh pretreatment biopsy during screening period, excisional or incisional, is preferred
- Adequate hematologic function without growth factors or blood product transfusion within 14 days of first dose of study drug administration
- Normal laboratory values
- All participants and health care providers will be trained and counseled on pregnancy prevention. For female participants of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception during the treatment period and for 3 months after the final dose of

mosunetuzumab, at least 18 months after pre-treatment with obinutuzumab or 2 months after the last dose of glofitamab, 28 days after the last dose of CC-220, 28 days after the last dose of CC-99282, 3 months after the last dose of tocilizumab (if applicable), whichever is longer
- For male participants: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom, and agree to refrain from donating sperm during the treatment period and for at least 3 months after pre-treatment with obinutuzumab or 2 months after the last dose of glofitamab, 28 days after the last dose of CC-220, 28 days after the last dose of CC- 99282, 2 months after the final dose of tocilizumab (if applicable), whichever is longer

Exclusion Criteria:

- Pregnancy or breastfeeding, or intention of becoming pregnant during the study (female participants of childbearing potential must have a negative serum pregancy test result within 14 days prior to initiation of the study treatment) or within 3 months after the final dose of mosunetuzumab, at least 3 months after pre-treatment with obinutuzumab or 2 months after the last dose of glofitamab, whichever is longer, 28 days after the last dose of CC-220, 28 days after the last dose of CC-9282, 3 months after the final dose of tocilizumab, whichever is longer
- Participant has received prior therapy with cereblon (CRBN)-modulating drug (e.g., lenalidomide, avadomide/CC-122, pomalidomide) </= 4 weeks prior to starting CC-220 and/or CC-99282
- Inability to swallow pills, or persistent diarrhea or malabsorption >= Grade 2 National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), despite medical management
- QTc interval of > 470 ms
- The following treatments prior to study entry: mosunetuzumab, glofitamab, or other CD20/CD3-directed bispecific antibodies; allogenic stem cell therapy (SCT); solid organ transplantation
- Treatments (investigational or approved) within the following time periods prior to initiation/first dose of study treatment: radiotherapy within 2 weeks; autologous SCT within 100 days; chimeric antigen receptor (CAR) T-cell therapy within 30 days; prior anti-lymphoma treatment with monoclonal antibodies or antibody-drug conjugates within 4 weeks; use of radioimmunoconjugates within 12 weeks; systemic immunosuppressive medications within 2 weeks; any other anti-cancer therapy, whether investigational or approved, including but not limited to chemotherapy, within 4 weeks or 5 half-lives of the drug, whichever is shorter
- Live, attenuated vaccine within 4 weeks before first dose of study treatment, or in whom it is anticipated that such a live attenuated vaccine will be required during the study period or within 5 months after the final dose of study treatment
- Current or past history of central nervous system (CNS) lymphoma or leptomeningeal infiltration
- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibody therapy (or recombinant antibody-related fusion proteins)
- 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, granulomatosis with polyangiitis, Sjögren's syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis
- Major surgery or significant traumatic injury < 28 days prior to enrollment (excluding biopsies) or anticipation of the need for major surgery during study treatment
- Clinically significant toxicities from prior treatment have not resolved to Grade </= 1 (per US national cancer institute (NCI) common terminology criteria for adverse events (CTCAE) v5.0) prior to the first study drug administration with exceptions defined by the protocol
- Evidence of any significant, concomitant disease (e.g. cardiovascular, pulmonary, liver, CVA or stroke, ILD, PML, infection, HLH etc) that could affect compliance with the protocol or interpretation of results
- For participants enrolled into glofitamab cohort: documented refractoriness to an obinutuzumab monotherapy-containing regimen (defined as disease that did not achieve response (PR or CR) or progressed within 6 months of the last dose of an obinutuzumab-containing regimen)

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