ForPatients
by Roche

Follicular Lymphoma

A clinical trial to look at the safety and effectiveness of mosunetuzumab plus lenalidomide for treating follicular lymphoma

A Study Evaluating the Safety, Pharmacokinetics, and Efficacy of Mosunetuzumab + Lenalidomide (+Len), and the Safety, Tolerability, and Pharmacokinetics of SC Versus IV Mosunetuzumab + Len in Participants With Follicular Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Recruiting	5 Countries	NCT04246086 2023-507236-20-00 CO41942

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/II, open-label, multicenter study with a non-randomized stage evaluating the safety, pharmacokinetics, and efficacy of mosunetuzumab plus lenalidomide (+len) and a randomized stage evaluating the safety, tolerability, and pharmacokinetics of SC versus IV mosunetuzumab+len in patients with follicular lymphoma

Trial Summary:

This study will evaluate the safety, efficacy, pharmacokinetics, and immunogenicity of mosunetuzumab (Mosun) + lenalidomide (Len) (Mosun + Len) in participants with follicular lymphoma (FL). This study will also compare the pharmacokinetics, pharmacodynamics, safety, efficacy, and immunogenicity of IV mosunetuzumab + len vs subcutaneous (SC) mosunetuzumab + len.

Hoffmann-La Roche	Phase 1/Phase 2
Sponsor	Phase

NCT04246086 2023-507236-20-00 CO41942
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the CO41942 clinical trial needed?

Follicular lymphoma is a type of blood cancer that is the most common form of low-grade, or slow-growing, non-Hodgkin lymphoma. This type of lymphoma typically starts in the lymph nodes, which are small organs that are part of the body's immune system. Standard treatments include radiotherapy, chemotherapy and immunotherapy. Immunotherapy is a type of medicine that helps a person's own immune system attack cancer cells. However, FL often comes back after treatment (relapses) and it becomes more difficult to treat with each relapse. Treatments can stop working (known as 'refractory' FL) and for people who have had two or more previous therapies, treatment options are currently limited. New treatments are needed to slow or prevent FL getting worse and the chance of relapses.

Mosunetuzumab is a type of immunotherapy approved by health authorities for treating relapsed or refractory FL in people who have had at least two treatments before. Mosunetuzumab attaches to a marker called CD20 that is on some types of cancer cells. This brings them closer to cancer-killing immune cells. Lenalidomide is a cancer drug that can stop cancer cells developing and help the immune system attack cancer cells. Lenalidomide is approved for treating FL in combination with rituximab. Lenalidomide in combination with mosunetuzumab has not been approved by health authorities, and may work well against relapsed/refractory FL. This clinical trial aims to test the safety and effectiveness of mosunetuzumab in combination with lenalidomide and to understand how the body processes the combination in people with FL.

2. How does the CO41942 clinical trial work?

This clinical trial is recruiting people with FL. People who take part in this clinical trial (participants) will be given the clinical trial treatment mosunetuzumab plus lenalidomide for up to 1 year. The clinical trial doctor will see them regularly. These hospital visits will include checks to see how the participant responds to the treatment and any unwanted effects they may have. After being given their last dose, participants will be contacted by the clinical trial staff approximately every 6 months, for up to 5 years from the start of the trial as long as they agree to it, or until their cancer gets worse or they start a new treatment for FL. The total time of participation in the clinical trial will depend on how the participant responds to treatment but could be from 1 day to about 5 years. Participants can stop trial treatment and leave the clinical trial at any time.

3.What are the main endpoints of the CO41942 clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see if the drug has worked) are the number and seriousness of any unwanted effects that occur while on treatment.

The other clinical trial endpoints include:

- The number of people who do not have cancer on tests or scans after treatment
- How many participants have a specific level of reduction in the size of their tumour

- How much time there is between the participant's cancer first responding to treatment and the cancer getting worse
- The time between when a person has no signs of cancer and when the cancer worsens
- How the treatment gets to different parts of the body, and how the body changes and gets rid of it
- How treatment affects the immune system

4. Who can take part in this clinical trial?

People can take part in this trial if they are aged 18 years or older, have been diagnosed with FL but have not been treated (1## line therapy) or if they have relapsed/refractory FL after previous treatment with immunotherapy.

People may not be able to take part in this trial if their cancer is 'high-grade' (fast growing) when the clinical trial starts, or at any time in the past, and it cannot have spread to the brain or spinal cord, or they have received certain previous treatments for their cancer including lenalidomide in the past year. People must not have any other significant medical conditions or be pregnant or breastfeeding.

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

This clinical trial is in two stages – a non-randomised stage and a randomised stage.

Non-randomised stage

- Mosunetuzumab given as increasing doses as either a drip into a vein (for participants with relapsed/refractory FL) or as a drip under the skin (for participants with untreated FL), AND
- Lenalidomide given as a tablet to take by mouth

Randomised stage

Everyone who joins this clinical trial stage will be placed into 1 of 2 groups. Participants will have a 1 in 3 chance of being in Group A, and a 2 in 3 chance of being in Group B.

- Group A: Mosunetuzumab given as drip into a vein, and lenalidomide given as a tablet to take by mouth
- Group B: Mosunetuzumab given as a drip under the skin, and lenalidomide given as a tablet to take by mouth

In both stages, mosunetuzumab will be given weekly for 3 weeks then once a month for 11 months. Lenalidomide is taken on Days 1–21 of a 28-day treatment cycle for 11 cycles. Treatments in this clinical trial will be given for as long as they can help, up to a maximum of 12 cycles of treatment (approximately 1 year). Participants with newly diagnosed FL (1## line therapy) who respond to treatment then have the option to be given further

mosunetuzumab as maintenance treatment. It will be given as a drip under the skin every 2 months for a year and a half. Participants who have certain unwanted effects may also receive a treatment called tocilizumab, given as a drip into a vein.

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 an unwanted effect of a drug or medical treatment used in this clinical trial. Unwanted 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 unwanted effects of mosunetuzumab plus lenalidomide and tocilizumab, and possible unwanted effects based on human and laboratory studies or knowledge of similar drugs. Participants will be told about any known unwanted effects of being given a drip into a vein, a drip under the skin and of 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:

- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2
- R/R FL after treatment with at least one prior systemic lymphoma therapy, which includes prior immunotherapy or chemoimmunotherapy
- Previously untreated participants with FL must require systemic therapy assessed by investigator based on the Groupe d'Etude des Lymphomes Folliculaires (GELF) criteria and have a Follicular Lymphoma International Prognostic Index (FLIPI) score of 2-5
- Histologically documented FL of Grade 1, 2, or 3a, and that expresses CD20 at time of diagnosis as determined by the local laboratory
- Fluorodeoxyglucose avid lymphoma (i.e., positron emission tomography (PET) positive lymphoma)

- At least one bi dimensionally measurable nodal lesion (>1.5 cm in its largest dimension by PET-computed tomography (CT) scan), or at least one bi dimensionally measurable extranodal lesion (>1.0 cm in its largest dimension by PET-CT scan)
- Availability of a representative tumor specimen and the corresponding pathology report for confirmation of the diagnosis of FL
- Adequate hematologic function (unless due to underlying lymphoma, per the investigator) as defined by the protocol
- Negative HIV test at screening, with the following exception: Individuals with a positive HIV test at screening are eligible provided they are stable on antiretroviral therapy for at least 4 weeks, have a CD4 count # 200/mL, have an undetectable viral load, and have not had a history of opportunistic infection attributable to AIDS within the last 12 months
- Normal laboratory values (unless due to underlying lymphoma) as defined by the protocol
- Agreement to comply with all local requirements of the Len risk minimization plan
- For women of childbearing potential: agreement to remain abstinent or use two adequate methods of contraception, including at least one method with a failure rate of < 1% per year, for at least 28 days prior to Day 1 of Cycle 1, during the treatment period, and for at least 12 months after the final dose of glofitamab, 28 days after the last dose of Len, 18 months after the last dose of G, 3 months after the final dose of tocilizumab, and 3 months after the final dose of Mosun. Women must refrain from donating eggs during this same period
- For men: agreement to remain abstinent or use contraceptive measures and agreement to refrain from donating sperm, with female partners of childbearing potential or pregnant female partners, men must remain abstinent or use a condom during the treatment period and for at least 2 months after the final dose of glofitamab, 28 days after last dose of Len, 18 months after the last dose of G, 3 months after the final dose of tocilizumab, and 3 months after the final dose of Mosun

Exclusion Criteria:

- Any history of Grade 3b FL
- Suspicion or clinical evidence of transformed lymphoma at enrollment by investigator assessment
- Any history of disease transformation and/or diffuse large B-cell lymphoma (DLBCL)
- Documented refractoriness to an obinutuzumab monotherapy containing regimen in glofitamab-containing treatment combination
- Active or history of central nervous system (CNS) lymphoma or leptomeningeal infiltration
- Documented refractoriness to lenalidomide, defined as no response (partial response (PR) or complete response (CR)) within 6 months of therapy
- Prior standard or investigational anti-cancer therapy as specified by the protocol
- Clinically significant toxicity (other than alopecia) from prior treatment that has not resolved to Grade <=2 prior to Day 1 of Cycle 1
- Known history of idiopathic pulmonary fibrosis, organizing pneumonia (e.g. bronchiolitis obliterans), drug-induced pneumonitis or evidence of active pneumonitis on screening chest CT scan
- Treatment with systemic immunosuppressive medications, including, but not limited to, prednisone, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents within 2 weeks prior to Day 1 of Cycle 1
- History of solid organ transplantation
- History of severe allergic or anaphylactic reaction to humanized, chimeric or murine MAbs
- Known sensitivity or allergy to murine products
- Known hypersensitivity to biopharmaceuticals produced in Chinese hamster ovary cells or any component of the glofitamab, Mosun, G, Len, or thalidomide formulation, including mannitol
- History of erythema multiforme, Grade >=3 rash, or blistering following prior treatment with immunomodulatory derivatives
- Known history of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis or evidence of active pneumonitis on screening chest CT scan

- Known active bacterial, viral, fungal, or other infection, or any major episode of infection requiring treatment with IV antibiotics within 4 weeks of Day 1 of Cycle 1
- Known or suspected chronic active Epstein-Barr virus infection or hemophagocytic syndrome
- Known history of macrophage activating syndrome (MAS) or hemophagocytic lymphohistiocytosis (HLH)
- Active Hepatitis B and Hepatitis C infection or autoimmune disease requiring treatment
- Prior allogenic hematopoietic stem cell transplant
- Known history of HIV positive status
- History of progressive multifocal leukoencephalopathy
- Administration of a live, attenuated vaccine within 4 weeks before first dose of study treatment or anticipation that such a live attenuated vaccine will be required during the study
- Other malignancy that could affect compliance with the protocol or interpretation of results
- Prior allogenic hematopoietic stem cell transplant (HSCT)
- Contraindication to treatment for thromboembolism prophylaxis
- Grade >=2 neuropathy
- Evidence of any significant, uncontrolled concomitant disease that could affect compliance with the protocol or interpretation of results, including, but not limited to significant cardiovascular disease or significant pulmonary disease
- Major surgical procedure other than for diagnosis within 28 days prior to Day 1 of Cycle 1 Day 1 or anticipation of a major surgical procedure during the course of the study
- Clinically significant history of liver disease, including viral or other hepatitis, current alcohol abuse, or cirrhosis
- Inadequate hematologic function
- Any of the following abnormal laboratory values
- Pregnant or lactating or intending to become pregnant during the study
- Life expectancy < 3 months
- Unable to comply with the study protocol, in the investigator's judgment
- History of illicit drug or alcohol abuse within 12 months prior to screening, in the investigator's judgment
- Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator's or Medical Monitor's judgment, precludes the patient's safe participation in and completion of the study, or which could affect compliance with the protocol or interpretation of results