ForPatients
by Roche

Relapsed or Refractory Follicular Lymphoma

A study to evaluate efficacy and safety of mosunetuzumab in combination with lenalidomide in comparison to rituximab in combination with lenalidomide in patients with follicular lymphoma

A Study Evaluating the Efficacy and Safety of Mosunetuzumab in Combination With Lenalidomide in Comparison to Rituximab in Combination With Lenalidomide With a US Extension of Mosunetuzumab in Combination With Lenalidomide in Participants With Follicular Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	15 Countries	NCT04712097 2023-505807-21-00 GO42909

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:

Phase III Randomized, Open-Label, Multicenter Study Evaluating Efficacy and Safety of Mosunetuzumab in Combination With Lenalidomide in Comparison to Rituximab in Combination With Lenalidomide With a Non-Randomized Single Arm US Extension of Mosunetuzumab in Combination With Lenalidomide in Patients With Follicular Lymphoma After at Least One Line of Systemic Therapy

Trial Summary:

This study will evaluate the efficacy and safety of mosunetuzumab in combination with lenalidomide (M + Len) compared to rituximab in combination with lenalidomide (R + Len) in participants with relapsed or refractory (R/R) follicular lymphoma (FL) who have received at least one line of prior systemic therapy.

Para descargar el folleto en Español aquí

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT04712097 2023-505807-21-00 GO42909
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

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All	#18 Years	No

1. Why is the Celestimo clinical trial needed?

Lymphoma is a type of blood cancer that starts in white blood cells, which are an essential part of our immune system. Follicular lymphoma (FL) is a slow-growing (also sometimes called indolent) form of non-Hodgkin lymphoma (NHL). Standard treatments include radiotherapy, chemotherapy and immunotherapy. Immunotherapies help the body to use its own immune system to fight the cancer. 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. An immunotherapy called rituximab (that also attaches to CD20 on cancer cells) is an approved standard treatment for FL in combination with another drug called lenalidomide. Lenalidomide can stop cancer cells developing and help the immune system attack cancer cells. Lenalidomide in combination with mosunetuzumab has not been approved by health authorities, and may work well against relapsed or refractory FL.

This clinical trial aims to compare the effects, good or bad, of mosunetuzumab plus lenalidomide with rituximab plus lenalidomide in people with previously treated FL.

2. How does the Celestimo clinical trial work?

This clinical trial is recruiting people with relapsed or refractory FL. People can take part if they need treatment for their FL and have cancer cells that test positive for the CD20 marker. People who take part in this clinical trial (participants) will be given the clinical trial treatment mosunetuzumab plus lenalidomide OR rituximab plus lenalidomide for about 1 year unless their cancer worsens. 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 side effects they may have. After the last dose, participants will be seen by the clinical trial doctor every 3 months for up to 5 years from the time of enrollment or for as long as they agree to it. In addition, participants' medical records will be checked for up to 5 years after the last participant has enrolled. The total time of participation in the clinical trial will be up to 8 and a half years depending on when they start the trial. Participants can stop trial treatment and leave the clinical trial at any time.

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

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

- The length of time between the start of the trial and participants' cancer getting worse (progression-free survival)
- The number of participants whose cancer shrinks or disappears on scans (objective response rate)

The other clinical trial endpoints include:

- The number of participants whose cancer disappears on scans (complete response rate) and the length of time this lasts if cancer then gets worse (duration of complete response)
- How long participants live (overall survival)
- The length of time between cancer getting better, then getting worse (duration of response)
- The length of time between the start of trial treatment and cancer symptoms, levels of tiredness and ability to do daily physical tasks getting worse or a new treatment for FL being given
- The number and seriousness of any side effects
- How the body breaks down and gets rid of the trial treatment and its effects on the immune system

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 had systemic treatment (a treatment that travels through the bloodstream) for FL before. People may not be able to take part in this trial if they have certain other types of cancer or medical conditions. These include autoimmune, heart, liver and lung diseases, certain infections, and being pregnant or breastfeeding. People who have had lenalidomide or certain other treatments before may not be able to take part.

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

Treatment will be given in cycles – a treatment cycle is the treatment and recovery time before the next dose is given. Everyone who joins this clinical trial will be split into two groups randomly (like flipping a coin) with an equal chance of being placed in either group and given either:

- **Mosunetuzumab plus lenalidomide**
    - Mosunetuzumab as an infusion into the vein 3 times during Cycle 1, and then once during each of Cycles 2–12
    - Lenalidomide as a pill (to be swallowed) once a day for the first 21 days of every cycle (11 cycles in total), starting from Day 1 of Cycle 2
- **OR rituximab plus lenalidomide**

- Rituximab as an infusion into the vein 4 times during Cycle 1, and then once during Cycles 3, 5, 7, 9 and 11
- Lenalidomide as a pill (to be swallowed) once a day for the first 21 days of every cycle (12 cycles in total), starting from Day 1 of Cycle 1

Everyone who joins this clinical trial extension in the United States will be given **mosunetuzumab** plus **lenalidomide** in the same way as described above.

If a participant experiences a potential side effect called 'cytokine release syndrome' (CRS), they may receive another drug called **tocilizumab** given as an infusion into the 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

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. Participants will be told about the known side effects of mosunetuzumab, lenalidomide, 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 swallowing pills.

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

- Histologically documented CD20+ FL (Grades 1-3a)
- Requiring systemic therapy assessed by investigator based on tumor size and/or Groupe d'Etude des Lymphomes Folliculaires (GELF) criteria
- Received at least one prior systemic lymphoma therapy, which included prior immunotherapy or chemoimmunotherapy
- Availability of a representative tumor specimen and the corresponding pathology report at the time of relapse/persistence for confirmation of the diagnosis of FL. Pretreatment sample of at least 1 core-needle, excisional or incisional tumor biopsy is required. Cytological or fine-needle aspiration samples are not acceptable. Fresh pretreatment biopsy is preferred. Patients who are unable to undergo biopsy procedures may be eligible for study enrollment if an archival tumor tissue sample (preferably from the most recent relapse/persistence) as paraffin blocks or at least 15 unstained slides, or in accordance with local regulatory requirements, can be sent to the Sponsor.
- Adequate hematologic function (unless due to underlying lymphoma, per the investigator)
- Agreement to comply with all local requirements of the lenalidomide risk minimization plan, which includes the global pregnancy prevention program.
- For women of childbearing potential: Agreement to remain abstinent (refrain from heterosexual intercourse) or use 2 adequate methods of contraception, including at least 1 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 (including periods of treatment interruption), and for at least 28 days after the last dose of lenalidomide, 3 months after the final dose of tocilizumab (if applicable), mosunetuzumab, and 12 months after final dose of rituximab. Women must refrain from donating eggs during this same period.
- For men: Agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures and agreement to refrain from donating sperm, as defined: 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 28 days after last dose of lenalidomide, 3 months after the final dose of tocilizumab (if applicable), mosunetuzumab and 12 months after the final dose of rituximab. Men must refrain from donating sperm during this same period.

Exclusion Criteria:

- Grade 3b FL
- Any history of disease transformation and/or diffuse-large B cell lymphoma (DLBCL)
- Documented refractoriness to lenalidomide, defined as no response (partial response or complete response) or relapse within 6 months of therapy
- Active or history of CNS lymphoma or leptomeningeal infiltration
- Prior standard or investigational anti-cancer therapy as specified: Lenalidomide exposure within 12 months prior to Day 1 of Cycle 1; Chimeric antigen receptor T cell therapy within 30 days prior to Day 1 of Cycle 1; Radioimmunoconjugate within 12 weeks prior to Day 1 of Cycle 1; Monoclonal antibody or antibody-drug conjugate within 4 weeks prior to Cycle 1 Day 1; Treatment with any 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
- Clinically significant toxicity (other than alopecia) from prior treatment that has not resolved to Grade </= 1 (per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 5.0) prior to Day 1 of Cycle 1
- Treatment with systemic immunosuppressive medications, including, but not limited to prednisone (> 20 mg), 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 monoclonal antibodies
- Known sensitivity or allergy to murine products

- Known hypersensitivity to biopharmaceuticals produced in Chinese hamster ovary (CHO) cells or any component of the mosunetuzumab, rituximab, tocilizumab, lenalidomide, or thalidomide formulation, including mannitol
- History of erythema multiforme, Grade >/= 3 rash, or blistering following prior treatment with immunomodulatory derivatives
- History of interstitial lung disease, drug-induced pneumonitis, and autoimmune pneumonitis
- 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 (EBV) infection
- Known or suspected history of hemophagocytic lymphohistiocytosis
- Clinically significant history of liver disease, including viral or other hepatitis, or cirrhosis
- Active Hepatitis B infection
- Active Hepatitis C infection
- Known history of HIV positive status
- History of progressive multifocal leukoencephalopathy (PML)
- 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
- Active autoimmune disease requiring treatment
- 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, Wegener's granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis
- Prior allogeneic stem cell transplantation
- Contraindication to treatment for thromboembolism prophylaxis
- 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 (e.g., New York Heart Association Class III or IV cardiac disease, myocardial infarction within the previous 6 months, unstable arrhythmia, or unstable angina) or significant pulmonary disease (such as obstructive pulmonary disease or history of bronchospasm)
- 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
- Pregnant or lactating or intending to become pregnant during the study
- Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator'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