ForPatients
by Roche

Chronic Lymphocytic Leukemia

A clinical trial to compare how safe and effective different doses of mosunetuzumab on its own or in combination with other treatments are in people with chronic lymphocytic leukemia that has not responded to, or has come back after previous treatments

A Study Evaluating the Safety, Efficacy, and Pharmacokinetics of Mosunetuzumab and a Combined Regimen of Mosunetuzumab and Venetoclax in Participants With Relapsed or Refractory Chronic Lymphocytic Leukemia

Trial Status	Trial Runs In	Trial Identifier
Recruiting	8 Countries	NCT05091424 2022-501876-24-00 BO43243

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, efficacy, and pharmacokinetics of mosunetuzumab and a combined regimen of mosunetuzumab and venetoclax in patients with relapsed or refractory chronic lymphocytic leukemia

Trial Summary:

This study will assess the safety, tolerability, pharmaokinetics, and preliminary efficacy of mosunetuzumab (Lunsumio) monotherapy in participants with relapsed or refractory (R/R) chronic lymphocytic leukemia (CLL). This study will also allow participants who are currently progressing on a Bruton tyrosine kinase inhibitor (BTKi) and requiring salvage therapy as assessed by the treating physician to continue their BTKi throughout the screening period and for the first two cycles of mosunetuzumab. An additional arm (open to non-US participants only) has been added to assess the safety, tolerability, pharmacokinetics, and preliminary efficacy of mosunetuzumab in combination with venetoclax, a B-cell lymphoma 2 (BCL2) inhibitor.

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Phase 1
Phase

NCT05091424 2022-501876-24-00 BO43243
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the BO43243 clinical trial needed?

Chronic lymphocytic leukemia (CLL) is a type of blood cancer in which the bone marrow makes too many B-cells. B-cells are disease-fighting white cells in blood. The excess B-cells build up and stop the blood, bone marrow and lymph nodes working properly. Standard treatment for CLL includes medicines such as:

- Bruton's tyrosine kinase inhibitors (BTKi), such as ibrutinib and acalabrutinib. These work by blocking a protein called BTK in CLL cells so they cannot grow as quickly
- Venetoclax, which works by blocking the action of a protein called BCL2. This protein helps keep CLL cells alive. Venetoclax can be given on its own or with:
- Rituximab or obinutuzumab, which are known as 'immunotherapies'. This is a type of medicine that helps a person's own immune system attack cancer cells
- Chemotherapy – a medicine that kills cancer cells

Treatment can include stem cell transplant, but age or medical conditions prevent this for most people. Some people have CLL that does not respond to (known as 'refractory' CLL) or comes back after (known as 'relapsed' CLL) treatment with standard medicines. More treatments for people with CLL are needed when previous treatment has not worked. Mosunetuzumab is a type of immunotherapy. Mosunetuzumab attaches to a marker on some types of CLL cells and another marker on cancer-killing immune cells called T cells. This brings the CLL cells closer to T cells. Mosunetuzumab is an experimental drug – this means health authorities have not approved mosunetuzumab on its own or in combination with other treatments for treating CLL, but mosunetuzumab has been approved to treat follicular lymphoma.

This clinical trial aims to test mosunetuzumab at different doses on its own or in combination with BTKi. This is to understand how safe and how well it works in people with relapsed or refractory CLL and how the body changes and gets rid of mosunetuzumab.

2. How does the BO43243 clinical trial work?

This clinical trial is recruiting people with relapsed or refractory CLL.

People who take part in this clinical trial (participants) will be given increasing doses of the clinical trial treatment mosunetuzumab every week until the target dose is reached. This is either on its own (Group 1), or with BTKi (if they are currently treated with BTKi) until the target dose of mosunetuzumab is reached (Group 2). Treatment will end if their cancer gets worse or they have unacceptable unwanted effects. Participants will stay in the hospital for 2 days after each dose of mosunetuzumab and will be given a medicine called a corticosteroid to lower the chance of unwanted effects. Once the target

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doses are reached, mosunetuzumab will be given (without needing to stay in hospital after each dose) once every 3 weeks for about 1 year unless a participants' cancer gets worse, or they have unacceptable unwanted effects. Participants who are currently being treated with a BTKi will continue to be given it for up to 6 weeks from the start of mosunetuzumab treatment.

The clinical trial doctor will see participants at least every 3 weeks. These hospital visits will include checks to see how the participant responds to the treatment and any unwanted effects they may have. Participants will also be seen 1 month after the last dose of clinical trial treatment is given. Then, they will be followed up for as long as they agree to it, about every 3 months for 2 years, then every 6 months. The total time of participation in the clinical trial could be more than 3 years depending on the response to treatment. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the BO43243 clinical trial?

The main clinical trial endpoint (the main result measured in the trial) is the number and seriousness of unwanted effects with different doses of mosunetuzumab given alone or with BTKi.

The other clinical trial endpoints include:

- How many people have a reduction of their cancer after treatment
- How many participants have no CLL cells detectable in their blood or bone marrow 2–3 months after the final dose of treatment
- The time between the start of treatment and signs that disease getting worse
- How long people live
- The time between when a person starts the treatment and having a change in disease or treatment
- The number of people who do not have cancer on tests or scans after treatment
- How much time there is between the person's cancer first responding to treatment and the cancer getting worse
- How study treatment affects the immune system
- How the study treatment gets to different parts of the body, and how the body changes and gets rid of it

4. Who can take part in this clinical trial?

People can take part in this trial if they are over the age of 18 and have relapsed or refractory CLL after at least 2 treatments have failed, including a BTKi and/or venetoclax. People may not be able to take part in this trial if they have certain medical conditions including severe heart, lung or liver disease. People also may not be able to take part if they have had certain treatments including mosunetuzumab. Women cannot take part in this trial if they are pregnant or breastfeeding or are planning to become pregnant during or soon after the clinical trial.

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

Everyone in this clinical trial will join 1 of 2 treatment groups and will be given:

- **Group 1** – Increasing doses of mosunetuzumab only, as an injection under the skin (subcutaneous injection) weekly until the target dose is reached, then every 3 weeks for about 1 year
- **Group 2** – Increasing doses of mosunetuzumab, given in the same way as Group 1, AND continued treatment with a BTKi (taken as prescribed) for up to 6 weeks from the start of mosunetuzumab treatment

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

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 unwanted effects (an unwanted effect of a drug or medical treatment) from the drugs 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 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 subcutaneous injections and a drip into a vein given slowly.

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:

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- Have a diagnosis of CLL requiring treatment according to the International Workshop on CLL (iwCLL) criteria (Hallek et al 2018)
- Eastern Cooperative Oncology Group (ECOG) performance score (PS) of # 2
- Adequate bone marrow (BM) function independent of growth factor or transfusion support, within 2 weeks of screening, at screening as defined by the protocol unless cytopenia is clearly due to marrow involvement of CLL
- Adequate liver function unless directly attributable to the participant's CLL
- Life expectancy > 6 months
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods that result in a failure rate of < 1% per year, and agreement to refrain from donating eggs during the treatment period and for at least 3 months after the last dose of mosunetuzumab and 3 months after the last dose of tocilizumab (if applicable)
- For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom, and agreement to refrain from donating sperm as defined by the protocol

Inclusion Criteria Specific to Arm B:

- Participants must have been taking a BTKi for at least 12 months, have demonstrated evidence of progressive disease while receiving the BTKi and require additional salvage therapy as assessed by their treating physician. Participants should be able to continue their previously prescribed BTKi at a stable dose throughout the study screening period and for the first two cycles of mosunetuzumab administration

Inclusion Criteria Specific to Arm C:

- Non-US participants only

Exclusion Criteria:

- Pregnant or breastfeeding, or intending to become pregnant during the study or within 3 months after the final dose of mosunetuzumab and tocilizumab or within 30 days after the final dose of venetoclax (if applicable)
- Participants who have received any of the following treatments prior to study entry: treatment with mosunetuzumab or other CD20/CD3-directed bispecific antibodies; allogenic stem cell transplant
- Participants who have received any of the following treatments, whether investigational or approved, within the respective time periods prior to initiation of study treatment: radiotherapy within 2 weeks prior to the first dose of study treatment; autologous stem cell transplant within 100 days prior to first study treatment; CAR T-cell therapy within 30 days before first study treatment; prior use of any monoclonal antibodies, radioimmunoconjugates, or antibody-drug conjugates for anti-CLL treatment within 4 weeks before first dose of study treatment; systemic immunosuppressive medications (including but not limited to cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents) within 2 weeks prior to the first dose of study treatment; any other anti-cancer therapy, whether investigational or approved, including but not limited to chemotherapy within 4 weeks prior to initiation of study treatment (except for participants enrolled in Arm B, where overlapping therapy is permitted; other prior cancer immunotherapy not explicitly defined by the protocol is to be discussed with the medical monitor to determine eligibility
- Received a live, attenuated vaccine within 4 weeks before the first dose of study treatment, or in whom it is anticipated that such a vaccine will be required during the study period or within 5 months after the final dose of study treatment
- Transformation of CLL to aggressive non-Hodgkin's lymphoma (NHL)
- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibody therapy (or recombinant antibody-related fusion proteins)

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- Contraindication to tocilizumab
- History of prior malignancy except for conditions defined by the protocol
- Participants with infections requiring intravenous (IV) treatment with antibiotics or hospitalization within the last 4 weeks prior to enrollment or known active bacterial, viral (including SARS-CoV-2), fungal, mycobacterial, parasitic, or other infection (excluding fungal infections of nail beds) at study enrollment
- Evidence of any significant concomitant disease that could affect compliance with the protocol or interpretation of results
- Recent major surgery within 4 weeks prior to first study treatment administration, with the exception of protocol-mandated procedures (e.g., tumor biopsies and bone marrow biopsies)
- Positive SARS-CoV-2 test within 7 days prior to enrollment

Exclusion Criteria Specific to Arm C:

- Have received venetoclax therapy within 12 months prior to first study treatment administration
- Participants with known infection with HIV or human T-cell leukemia virus 1 (HTLV1)
- HIV testing will be performed in countries where mandatory testing by health authorities is required
- HTLV testing is required in participants from endemic countries
- Participants with uncontrolled autoimmune hemolytic anemia or immune thrombocytopenia
- Participants who have received the following: strong and moderate CYP3A inhibitors within 7 days prior to the initiation of study treatment; strong and moderate CYP3A inducers within 7 days prior to the initiation of study treatment; steroid therapy for anti-neoplastic intent with the exception of inhaled steroids for asthma, topical steroids, or replacement/stress corticosteroids within 7 days prior to the first dose of study drug administration
- Have consumed grapefruit, grapefruit products, Seville oranges (including marmalade containing Seville oranges), or star fruit within 3 days prior to the first dose of study drug and throughout venetoclax administration
- Inability to swallow a large number of tablets
- Malabsorption syndrome or other condition that precludes enteral route of administration
- Known allergy to both xanthine oxidase inhibitors and rasburicase

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