ForPatients
by Roche

Chronic Lymphocytic Leukemia

A study to test how safe, effective and how body's responds to the combination of mosunetuzumab and pirtobrutinib together to treat patients with relapsed or refractory chronic lymphocytic leukemia and small lymphocytic lymphoma

A phase Ib open-label, multicenter study evaluating the safety, efficacy, and pharmacokinetics of mosunetuzumab in combination with pirtobrutinib in patients with relapsed or refractory chronic lymphocytic leukemia and small lymphocytic lymphoma

Trial Status	Trial Runs In	Trial Identifier
Recruiting	6 Countries	2024-514152-32-00 BO45287

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 in combination with pirtobrutinib in patients with relapsed or refractory chronic lymphocytic leukemia and small lymphocytic lymphoma

Trial Summary:

Study BO45287 is testing an experimental combination of two medicines—mosunetuzumab and pirtobrutinib—in patients with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). The study focuses on people whose cancer has come back (relapsed) or did not respond (refractory) to at least one previous treatment. The main purpose of this study is to find out how safe the combination is, how well it works to reduce cancer, and how the body processes each medicine. This is an open-label study, meaning both the doctors and participants know which treatments are being given.

The study is divided into two parts:

- Part 1 (Dose-escalation): Researchers will test different doses of mosunetuzumab with pirtobrutinib to identify the safest doses.
- Part 2 (Dose-expansion): Participants may be randomly assigned to receive either the combination at specific doses or pirtobrutinib alone to compare the results.

Participants take pirtobrutinib as a daily pill and receive mosunetuzumab as an injection under the skin starting at Week 9. Mosunetuzumab is given using "step-up dosing",where the dose is gradually increased to help the body adjust. Researchers will measure success

by looking at the number of side effects, how many people have a reduction in their cancer, and how long participants live without their disease getting worse.

F. Hoffmann-La Roche Ltd
Sponsor

Phase 1b
Phase

2024-514152-32-00 BO45287
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
Males and females	**At least 18 years old**	**No**

1. Why is this study needed?

Chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL) are types 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 and SLL includes medicines such as:

- Bruton's tyrosine kinase inhibitors (BTKi), such as ibrutinib and acalabrutinib. These work by blocking a protein called BTK that helps cancer cells grow.
- Venetoclax blocks a protein called BCL2 that helps cancer cells survive. Venetoclax can be given on its own or with:
    - Immunotherapy (such as rituximab or obinutuzumab), that help a person's own immune system attack cancer cells or chemotherapy - a medicine that kills cancer cells

Some people have CLL or SLL that does not respond to treatment (known as 'refractory') or comes back after treatment (known as 'relapsed') with standard medicines. More treatments for people with relapsed or refractory CLL or SLL are needed.

This study is testing 2 medicines called mosunetuzumab (an immunotherapy) and pirtobrutinib (a BTKi). They are being developed to treat CLL and SLL after previous treatment has not worked. Mosunetuzumab and pirtobrutinib is an experimental combination of medicines. This means health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not approved this combination for treating CLL or SLL. Mosunetuzumab, given on its own, has been approved to treat another type of blood cancer called follicular lymphoma. Pirtobrutinib, also given on its own, has been approved to treat CLL and SLL and another type of blood cancer called mantle cell lymphoma.

This study aims to test mosunetuzumab at different doses together with pirtobrutinib, and pirtobrutinib alone as standard treatment. This is to understand how safe the treatments are, how well they work, and how the body processes each medicine in people with relapsed or refractory SLL or CLL.

2. Who can take part in the study?

People of at least 18 years of age with relapsed or refractory SLL or CLL can take part in the study. They must have had at least 1 treatment before, including a BTKi or venetoclax. Their CLL or SLL must also have a protein called ‘CD20’ on it – this will be checked using a blood test before a person can join the study.

People may not be able to take part in this study if they have been given certain treatments before, including mosunetuzumab, pirtobrutinib or similar drugs. People may not take part if they have certain health problems, such as liver, heart or lung diseases or certain infections. People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

People will be screened to check if they are able to participate in the study. The screening period will take place from 1 month before the start of treatment.

Everyone who joins this study will be given pirtobrutinib as a pill to be swallowed every day. From Week 9 they will also be given mosunetuzumab as an injection under the skin. All participants will be given mosunetuzumab weekly starting with a lower dose and then progressively increasing the dosage over time until the target dose is reached. This is known as ‘step-up dosing’. Participants will stay in the hospital for at least 2 nights after each step-up dose of mosunetuzumab during the first two dosing schedules in the first part of the study (dose-escalation). Once the target dose of mosunetuzumab is reached, it will be given every 3 weeks. If participants experience an unwanted effect of mosunetuzumab treatment called ‘cytokine release syndrome’, they may also receive tocilizumab as a drip into the vein. Cytokine release syndrome (CRS) happens when the immune system reacts in an unusual way to an infection or cancer immunotherapy.

After safe doses are identified in the first part of the study, participants in the second part (dose-expansion) will be randomly assigned (like flipping a coin) into 1 of 4 groups. They will receive 1 of 3 different doses of mosunetuzumab together with pirtobrutinib, or pirtobrutinib alone (once daily).

This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

During this study, the study doctor will see participants regularly. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have follow-up visits every 3 months, starting about 8–12 weeks after completing the treatment, for up to 2 years. After this, follow-up visits will occur every 6 months until their cancer worsens. Once the cancer worsens, they will have follow-up visits every 3 months. Total time of participation in the study is more than 2 years. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main result measured in the study to assess which dose of mosunetuzumab is best to use with pirtobrutinib is the number of people who have to pause, stop, or have a lower dose due to unwanted effects. This study also looks at how many people have a reduction of their cancer after treatment. Other key results measured in the study include:

- How long people live
- How long people live without their cancer getting worse or needing a new treatment
- The number of people who do not have cancer on tests or scans after treatment
- The number and seriousness of unwanted effects
- How study treatment gets to different parts of the body, and how the body changes and gets rid of it
- How mosunetuzumab affects the immune system

5. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future.

It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study drugs:
Participants may have unwanted effects of the drugs used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects. Participants will be told about the known unwanted effects of mosunetuzumab, pirtobrutinib and tocilizumab, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines.

Known unwanted effects of **mosunetuzumab** include a reaction on the skin where it has been pricked with a needle to give a treatment, increased risk of infections, and a condition that can occur when a large number of cancer cells break down quickly, leading to chemical changes in the blood – called ‘tumour lysis syndrome’. Known unwanted effects of **pirtobrutinib** include feeling tired or weak, bruising, cough, muscle and bone pain, wanting to throw up, frequent watery stools, swelling, infections, fever, and pain or discomfort in the head. Known unwanted effects of **tocilizumab** include infection of the nose, throat or sinuses, usually caused by a virus. Known unwanted effects of injections under the skin include redness, swelling or rash on the skin where it has been pricked with a needle to give a treatment. Known unwanted effects of drips into the vein include throwing up, wanting to throw up, a feeling of coldness that makes the body shiver, low blood pressure, fever, pain or discomfort in the head, frequent watery stools, shortness of breath and cough.

The study medicines may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.