NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of JBH492 in people with chronic lymphocytic leukemia and non-Hodgkin's lymphoma

Thank you!

Thank you to the participants who took part in the clinical trial for **chronic lymphocytic leukemia (CLL)** and **non-Hodgkin's lymphoma (NHL)**. Every participant helped the researchers learn more about the trial drug **JBH492**.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CJBH492A12101
Drug studied: JBH492
Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings.

What was the main purpose of this trial?

The main purpose of this trial was to find the recommended dose of **JBH492** for further testing in people with **CLL** or **NHL**. The recommended dose is the amount of a drug that helps treat the disease while keeping the chance of medical problems as low as possible.

Chronic lymphocytic leukemia (CLL) is a type of cancer that starts in the bone marrow and affects blood cells called **lymphocytes**. The bone marrow is the tissue found in the center of most bones, where new blood cells are made. Normally, lymphocytes help the body fight infections. But in people with **CLL**, lymphocytes become abnormal and stop working properly, which weakens the immune system.

Non-Hodgkin's lymphoma (NHL) is another type of cancer that affects lymphocytes. It starts in the lymphatic system, which is part of the body's immune system and helps fight infections. In **NHL**, abnormal lymphocytes grow out of control and form tumors in lymph nodes or other organs.

Current treatments for **CLL** and **NHL** do not always work, or they may stop working over time. This is called **refractory disease**. Sometimes cancer comes back after treatment - this is called a **relapse**. That is why researchers are looking for new treatment options.

The trial drug, **JBH492**, is designed to find and destroy cancer cells. This trial was the first time that **JHB492** was tested in people. The researchers tested increasing doses of **JBH492** in different groups of participants to find the recommended dose that could be safely used for further study. Researchers also carefully checked all the medical problems that happened during the trial and identified any that could cause changes in dosing. This type of research is called a **dose escalation trial**, which is an early step in testing a new drug.

The main questions that researchers wanted to answer in this trial were:

- What was the recommended dose of **JBH492** for further testing?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in September 2020 and ended in September 2024. The participants received trial treatments as long as their doctors thought the treatment was helping them, and they were not having serious medical problems.

The trial ended earlier than planned due to a business decision by the sponsor. This decision was not due to any safety concerns with **JBH492**.

When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

25 participants with **CLL** and **NHL** received treatment in this trial.

Participants' ages ranged from 43 to 85 years. Their average age was 66 years.

The number of participants by gender and race are shown below.

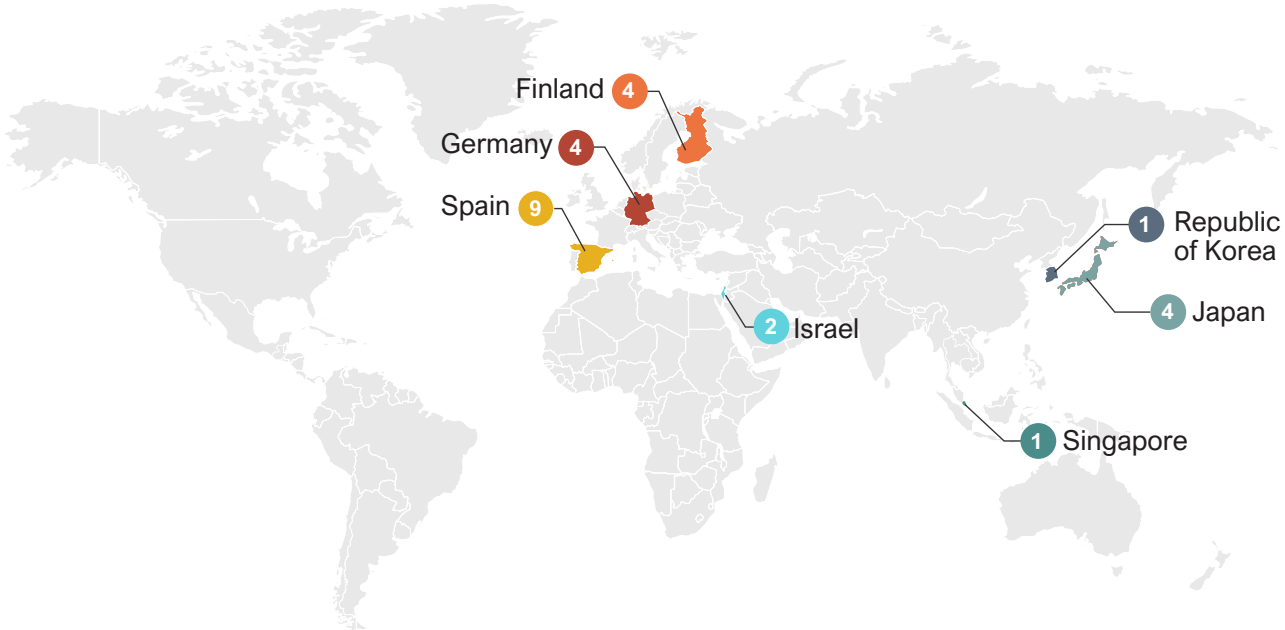
Gender

17 Men	8 Women

Race

17 White	6 Asian	2 Black or African American

25 participants from **7 countries** received treatment. The map below shows the number of participants who took part in each country.



Participants **could take part** in this trial if they:

- Were at least 18 years old
- Had confirmed relapsed or refractory **CLL** or **NHL**
- Did not respond to at least 2 previous standard treatments

What treatments did the participants receive?

Researchers studied the following treatment in a 21-day (3-week) cycle. A cycle is a treatment period that is repeated.

JBH492: Researchers first started with a dose of **0.4 milligrams per kilogram of body weight (mg/kg)**.

- **JBH492** was given as an intravenous (IV) infusion, which is a slow drip through a tube directly into a vein.
- Participants received the infusion once every 3 weeks, on Day 1 of each cycle.
- Researchers increased the dose for each new group of participants based on how their bodies responded to the drug. The doses ranged from 0.4 mg/kg to 3.6 mg/kg.

The participants, researchers, and trial staff knew which treatment and doses the participants received.

What happened during this trial?

Before treatment

Up to 28 days

Trial doctors checked the participants' health to make sure they could be in this clinical trial.

During treatment

For as long as participants benefited from treatment

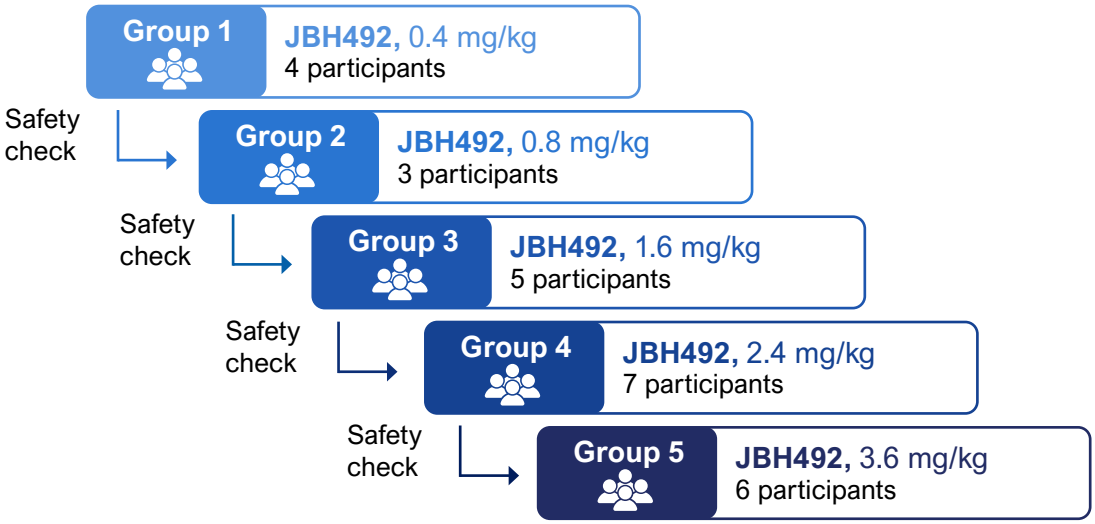
The trial was originally planned to be done in 2 parts – the first part is **Dose Escalation** and the second part is **Dose Expansion**. However, as the trial ended early, the Dose Expansion was not done.

Dose Escalation

In this part, trial doctors wanted to find out the recommended dose of **JBH492** for further testing. They tested different doses of **JBH492** in separate groups of participants.

Researchers started by giving 0.4 mg/kg of **JHB492** to a few participants. After checking the safety of this dose, researchers gave a higher dose of 0.8 mg/kg to the next group. This continued until the safety of each dose had been checked.

A total of 25 participants received treatment during this trial.



Participants continued treatment until their condition got worse, they had adverse events that made it unsafe to continue, or they or their trial doctor chose to stop the treatment.

After treatment

Up to 5 months after the last dose

Participants were monitored for up to 5 months after their last dose to check for any adverse events.

Trial doctors checked participants for their overall health throughout the trial.

What were the main results of this trial?

What was the recommended dose of JBH492 for further testing?

The trial ended early and as a result researchers could not find the recommended dose of **JBH492** for further testing.

To find the recommended dose of **JBH492**, researchers closely monitored participants for **dose-limiting toxicities (DLTs)** during the first treatment cycle.

DLTs are medical problems that:

- Trial doctors believe may be related to the trial treatment
- Are serious enough to require lowering the dose or pausing treatment

The table below shows how many participants had DLTs during the first treatment cycle. The results cover 23 out of 25 participants because only those who completed the first cycle and had results available were included.

Participants who had DLTs

Participants who:	Group 1 3 participants	Group 2 3 participants	Group 3 5 participants	Group 4 7 participants	Group 5 5 participants
Had DLTs during the first treatment cycle	0 of 3 **(0%)**	0 of 3 **(0%)**	1 of 5 **(20%)**	0 of 7 **(0%)**	0 of 5 **(0%)**

- 1 participant from Group 3 had a DLT. It was a low number of platelets, which are cells that help the blood to clot.

Researchers also checked how many participants had to pause or reduce their dose of **JBH492** due to adverse events during the treatment period.

Participants who had to pause or reduce their dose due to adverse events

Participants who:	Group 1 4 participants	Group 2 3 participants	Group 3 5 participants	Group 4 7 participants	Group 5 6 participants
Paused or reduced their dose during treatment	0 of 4 **(0%)**	0 of 3 **(0%)**	0 of 5 **(0%)**	3 of 7 **(43%)**	2 of 6 **(33%)**

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of the treatment up to 5 months after the last dose.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

A total of **24 out of 25 participants (96%)** had adverse events.

- **8 out of 25 participants (32%)** had adverse events that were considered serious.
- **2 out of 25 participants (8%)** left the trial due to an adverse event.
- **8 out of 25 participants (32%)** died due to any cause.

There were no unexpected safety concerns with **JBH492**.

How many participants had adverse events?

The table below shows how many participants had adverse events during the trial.

Summary of adverse events

Participants who:	Group 1 4 participants	Group 2 3 participants	Group 3 5 participants	Group 4 7 participants	Group 5 6 participants
Had any adverse event, including serious and other	4 of 4 (100%)	3 of 3 (100%)	5 of 5 (100%)	7 of 7 (100%)	5 of 6 (83%)
Had at least 1 serious adverse event	1 of 4 (25%)	1 of 3 (33%)	0 of 5 (0%)	2 of 7 (29%)	4 of 6 (67%)
Left the trial due to an adverse event	0 of 4 (0%)	0 of 3 (0%)	0 of 5 (0%)	0 of 7 (0%)	2 of 6 (33%)
Died due to any cause	1 of 4 (25%)	1 of 3 (33%)	0 of 5 (0%)	3 of 7 (43%)	3 of 6 (50%)

What serious adverse events did the participants have?

The table below shows all the serious adverse events that happened during the trial. Each serious adverse event happened in 1 participant.

Serious adverse events	Group 1 4 participants	Group 2 3 participants	Group 3 5 participants	Group 4 7 participants	Group 5 6 participants
Breakdown of red blood cells caused by immune system Autoimmune hemolytic anemia	0 of 4 (0%)	0 of 3 (0%)	0 of 5 (0%)	0 of 7 (0%)	1 of 6 (17%)
Vision blurred	0 of 4 (0%)	0 of 3 (0%)	0 of 5 (0%)	0 of 7 (0%)	1 of 6 (17%)
Leakage of medicine from a vein into the surrounding tissue Extravasation	0 of 4 (0%)	0 of 3 (0%)	0 of 5 (0%)	0 of 7 (0%)	1 of 6 (17%)
Overall decline in physical health General physical health deterioration	0 of 4 (0%)	0 of 3 (0%)	0 of 5 (0%)	1 of 7 (14%)	0 of 6 (0%)
Condition where immune system attacks own cells, with serious inflammation Hemophagocytic lymphohistiocytosis	0 of 4 (0%)	0 of 3 (0%)	0 of 5 (0%)	0 of 7 (0%)	1 of 6 (17%)
Severe infection in belly area Abdominal sepsis	1 of 4 (25%)	0 of 3 (0%)	0 of 5 (0%)	0 of 7 (0%)	0 of 6 (0%)
Infection caused by medical device Device related infection	0 of 4 (0%)	1 of 3 (33%)	0 of 5 (0%)	0 of 7 (0%)	0 of 6 (0%)
Kidney stones Calculus urinary	0 of 4 (0%)	0 of 3 (0%)	0 of 5 (0%)	1 of 7 (14%)	0 of 6 (0%)
Blockage in the intestine Intestinal obstruction	0 of 4 (0%)	0 of 3 (0%)	0 of 5 (0%)	0 of 7 (0%)	1 of 6 (17%)
Hole in the intestine Intestinal perforation	0 of 4 (0%)	0 of 3 (0%)	0 of 5 (0%)	0 of 7 (0%)	1 of 6 (17%)

What other (not including serious) adverse events did the participants have?

The table below shows the most common other adverse events that happened during the trial.

Other adverse events

	Group 1 4 participants	Group 2 3 participants	Group 3 5 participants	Group 4 7 participants	Group 5 6 participants
Low levels of red blood cells Anemia	1 of 4 (25%)	1 of 3 (33%)	3 of 5 (60%)	1 of 7 (14%)	2 of 6 (33%)
Increased liver protein Aspartate aminotransferase increased	0 of 4 (0%)	0 of 3 (0%)	2 of 5 (40%)	2 of 7 (29%)	3 of 6 (50%)
Increased liver protein Alanine aminotransferase increased	0 of 4 (0%)	0 of 3 (0%)	2 of 5 (40%)	2 of 7 (29%)	3 of 6 (50%)
Low levels of blood platelets Thrombocytopenia	0 of 4 (0%)	1 of 3 (33%)	2 of 5 (40%)	2 of 7 (29%)	1 of 6 (17%)
Increased level of lactate dehydrogenase in the blood, which can be a sign of tissue or organ damage Blood lactate dehydrogenase increased	1 of 4 (25%)	0 of 3 (0%)	2 of 5 (40%)	1 of 7 (14%)	1 of 6 (17%)
Dry eye	1 of 4 (25%)	0 of 3 (0%)	0 of 5 (0%)	2 of 7 (29%)	2 of 6 (33%)

What was learned from this trial?

This trial helped researchers learn about the effects of **JBH492** in people with **chronic lymphocytic leukemia (CLL)** and **non-Hodgkin's lymphoma (NHL)**.

Researchers found that:

- Because the trial ended early, researchers were not able to find the recommended dose of **JBH492** to use for future trials.
- There were no unexpected safety concerns with **JBH492**.

When this summary was written, the sponsor had no plans for future trials of **JBH492** in people with **CLL** and **NHL**.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website, www.novctrd.com.

Follow these steps to find the scientific summary:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Accept the terms **I accept** → Search for **CJBH492A12101**

For more information about this trial go to this website:

clinicaltrials.gov – search using the number **NCT04240704**

clinicaltrialsregister.eu – search using the number **2019-002666-12**

Other trials with **JBH492** appear on the public websites above. When there, search for **JBH492**.

Full clinical trial title: A phase I/Ib open-label, multi-center dose escalation study of JBH492 in patients with relapsed/refractory chronic lymphocytic leukemia (CLL) and Non-Hodgkin's Lymphoma (NHL)

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