NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of ETB115 in East Asian adults and children with severe aplastic anemia

Thank you!

Thank you to the participants who took part in the clinical trial for **severe aplastic anemia (SAA)**. Every participant helped the researchers learn more about the trial drug **ETB115**, also called **eltrombopag**.

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: CETB115G2201

Novartis drug studied: **ETB115**, also called **eltrombopag**

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 results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **ETB115**, given with standard treatments, for East Asian adults and children with severe aplastic anemia (SAA). Standard treatments are the usual treatments that doctors use for people with SAA. Standard treatments may not always work to treat SAA, or symptoms may come back over time.

Severe aplastic anemia (SAA) is a disease in which bone marrow does not make enough blood cells. Bone marrow is the tissue inside of bones that helps make:

- **Red blood cells**, which contain a protein called hemoglobin that carries oxygen
- **White blood cells**, such as neutrophils, which are part of the immune system and help the body fight infection and other diseases
- **Platelets**, which help blood to clot and stop bleeding

Aplastic anemia can range from mild to severe based on the number of blood cells in the body.

People with SAA often feel weak and tired, get more infections, and have bruising and bleeding that can be hard to stop.

ETB115, also called **eltrombopag**, is a drug created to signal bone marrow to make more blood cells.

When this trial was planned, **ETB115 was approved to be given with standard treatments as a first treatment for adults and children with SAA in some countries**, such as the United States. However, it had **not been approved as a first treatment for SAA in certain Asian** countries and locations.

Standard treatments for SAA are immunosuppressive therapies and include:

- **Cyclosporine** which lowers the activity of the immune system, so it does not attack bone marrow cells
- **r-ATG**, also called **rabbit anti-thymocyte globulin**, which kills certain cells in the immune system, so they do not attack bone marrow cells

Trial drug
ETB115 also called eltrombopag

Pronounced as
el-traam-buh-pag

Immunosuppressive therapies are medicines that lower the activity of the immune system

The trial's purpose was to answer these main questions:

- How many participants had all 3 of their blood cell counts go up after 6 months of taking ETB115 with standard treatments?
  - The blood cell counts included red blood cells, white blood cells, and platelets
- 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 November 2020 and ended in December 2024. Each participant was in the trial for up to 3 years. The participants started this trial on different dates.

Who was in this trial?

36 adults and children with SAA received treatments in this trial – 15 males and 21 females. Participants' ages ranged from 9 to 72 years. Their average age was 35 years.

The participants could take part in this trial if they were East Asian and:

- Had not previously received immunosuppressive therapies as standard treatments for SAA
- Did not have certain other blood-related health conditions
- Had not had a blood clot in the past 6 months

The participants took part in:

- China | 26 participants
- Japan | 5 participants
- Republic of Korea | 3 participants
- Taiwan | 2 participants

What treatments did the participants receive?

The treatments in this trial were:

ETB115, which was taken by mouth each day as tablets. Based on their age, a participant's dose started at:

- 37.5 milligrams (mg) a day for children 6 to 11 years old
- 75 mg a day for participants 12 years old or older

Trial doctors could lower a participant's dose, if needed based on a participant's platelet count or medical problems. Participants could take **ETB115** for up to 1 year.

Cyclosporine, which was taken by mouth 2 times a day as capsules or a liquid. Each participant's dose started at 3 to 6 mg per kilogram of body weight. Trial doctors could adjust a participant's dose as needed. Participants could take **cyclosporine** for up to 2 years.

r-ATG, which was given through a needle in a vein for the first 5 days of trial treatment. On each of the 5 days, participants received 2.5 to 3.5 mg per kilogram of body weight.

Along with the treatments above, participants could take other treatments if needed, such as **transfusions**.

The participants, researchers, and trial staff knew that all participants took **ETB115** with **cyclosporine** and **r-ATG**.

Transfusions give a person blood through a vein to replace red blood cells, platelets, or both that the bone marrow isn't making.

What happened during this trial?

Before ETB115 treatment — 1 month

The trial staff checked to make sure the participants could be in this trial.

During ETB115 treatment — Up to 1 year

36 participants received **ETB115** with standard treatments **cyclosporine** and **r-ATG**:

- Participants started at 37.5 or 75 mg of **ETB115** a day based on their age
- Trial doctors could lower a participant's dose, if needed

Participants could receive **ETB115** with **cyclosporine** for 6 months. If the trial doctor thought the participant was benefiting from treatment at 6 months, the participant could continue taking **ETB115** with **cyclosporine** for another 6 months.

After ETB115 treatment — Up to 2 years

Participants could continue taking **cyclosporine** for another year.

Trial staff checked the participants for:

- Any medical problems for up to 1 month after their last dose of **ETB115**
- Blood cell counts for about 2 years after their last dose of **ETB115**

Trial staff checked the participants' general health throughout the trial.

What were the main results of this trial?

How many participants had all 3 of their blood cell counts go up after 6 months of taking ETB115 with standard treatments?

6 out of 36 participants (17%) had all 3 of their blood cell counts go up after 6 months of taking **ETB115** with standard treatments.

To learn this, the trial staff measured the participants' red blood cell, white blood cell, and platelet counts. The trial staff kept track of how many participants had all 3 types of blood cell counts go up within 6 months.

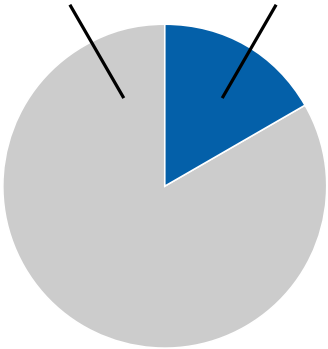
Researchers considered a participants' blood cell count to have gone up if **all 3** of these happened:

- Platelet count went up to at least 100 billion per (L) of blood
- Hemoglobin (a protein in red blood cells) went up to at least 100 grams per liter (g/L) of blood
- Neutrophils (a type of white blood cell) went up to at least 1 billion per (L) of blood

Number of participants who had all 3 of their blood cell counts go up

30 out of 36 participants (83%) **did not have** their blood cell counts go up after 6 months of taking **ETB115**

6 out of 36 participants (17%) **had** their blood cell counts go up after 6 months of taking **ETB115**



What were the other results of this trial?

How many participants had changes in their blood cell counts after 1 year of taking ETB115 with standard treatments?

After 1 year of taking **ETB115** with standard treatments, out of all 36 participants:

- 11 participants (31%) had all 3 of these blood cell counts go up: platelets, hemoglobin, and neutrophils. These participants' blood cell counts stayed about the same until the end of the trial.
- 24 participants (67%) had at least 2 of their blood cell counts go up

To learn this, the researchers looked at participants' blood cell counts many times during the trial.

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 trial treatment until 1 month after the last dose of **ETB115**.

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.

All 36 participants had adverse events, including serious and other adverse events. 14 participants had adverse events that were considered serious. 1 participant died.

The researchers concluded there were no new safety concerns for **ETB115** in this trial.

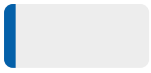
How many participants had adverse events?

	ETB115 with standard treatments 36 participants
Had **any adverse event, including serious and other**	**36 of 36** 
Had at least 1 **serious adverse event**	**14 of 36** 
Died	**1 of 36**

What serious adverse events did the participants have?

14 participants had serious adverse events. 1 participant died.

The table below shows the most common serious adverse events.

	ETB115 with standard treatments 36 participants
High level of uric acid in blood Hyperuricemia	**4 of 36** 11% 
Serious complication of an infection Sepsis	**3 of 36** 8% 
Low level of potassium in blood Hypokalemia	**2 of 36** 6%

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

The table below shows the most common other adverse events.

	ETB115 with standard treatments 36 participants
Low level of potassium in blood Hypokalemia	18 of 36 50%
High level of uric acid in blood Hyperuricemia	14 of 36 39%
Blood sugar went up Blood glucose increased	13 of 36 36%
Possible sign of liver damage Alanine aminotransferase increased	13 of 36 36%
Fever Pyrexia	12 of 36 33%

What was learned from this trial?

Researchers learned about the effects of **ETB115** with standard treatments for East Asian adults and children with severe aplastic anemia (SAA).

The researchers concluded that, out of 36 participants:

- 6 participants (17%) had all 3 of their blood cell counts go up after 6 months of taking **ETB115** with standard treatments
- 11 participants (31%) had all 3 of their blood cell counts go up after 1 year of taking **ETB115** with standard treatments. These participants' blood cell counts stayed higher until the end of the trial.
- 24 participants (67%) had at least 2 of their blood cell counts go up after 1 year of taking **ETB115** with standard treatments

There were no new safety concerns for **ETB115** in this trial.

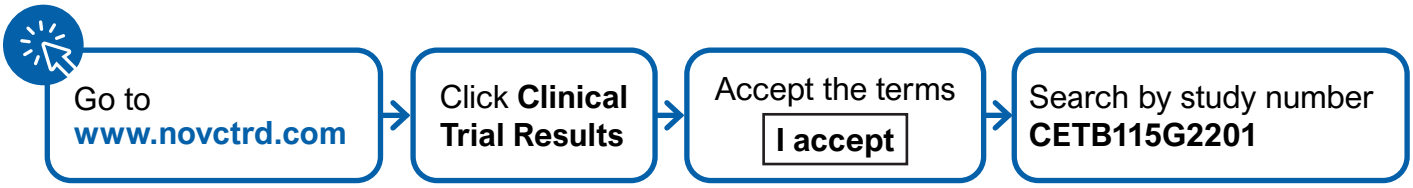
Based on the results of this trial, health insurance plans in certain countries and locations started to cover (pay for) **ETB115** for people with SAA.

When this summary was written, the sponsor had no plans for future trials of **ETB115** in people with SAA.

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:



For more information about this trial, go to this website:

- **clinicaltrials.gov** – search using the number **NCT04328727**

Other trials of **ETB115** may appear on the public website above. When there, search for **ETB115** or **eltrombopag**.

Full clinical trial title: A non-randomized, open label, multi-center, Phase II study to assess the safety and efficacy of eltrombopag in combination with rabbit anti-thymocyte globulin (r-ATG) and cyclosporine A (CsA) in East-Asian patients with treatment naive severe aplastic anemia (REACTS)

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