NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn the amount of SEG101 in the blood after receiving it and its effects in people with sickle cell disease who previously had painful episodes (vaso-occlusive crises)

Thank you!

Thank you to the participants who took part in the clinical trial for vaso-occlusive crisis (VOC) in people with sickle cell disease. Every participant helped the researchers learn more about the trial drug **SEG101**, also called crizanlizumab.

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: CSEG101A2202

Drug studied: SEG101 (crizanlizumab)

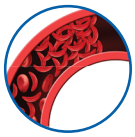
Sponsor: Novartis

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 purpose of this trial was to learn the amount of **SEG101** in the blood after receiving it and its effects in people with sickle cell disease who previously had painful episodes called vaso-occlusive crises (VOCs).



Regular red blood cells are flexible and round so that they can travel through small blood vessels to deliver oxygen to all parts of the body. **Sickle cell disease** is an inherited blood disorder that causes red blood cells to become sickle shaped. This makes it difficult for the blood cells to pass through small blood vessels. Also, in sickle cell disease blood vessels become damaged and sticky due to continuous irritation. This leads to blood cells sticking to the blood vessels and blocking them, causing severe painful episodes called VOCs.

SEG101 may help prevent VOCs in people with sickle cell disease. SEG101 works by blocking a protein, called **P-selectin**, which is present in blood cells and blood vessels and causes them to stick together.

Trial drug
SEG101 also called crizanlizumab

Pronounced as
criz-AN-liz-U-mab

The trial purpose was to answer these main questions:

- How much SEG101 was in the blood of participants after their first dose and after multiple doses?
- Was the tested dose able to block P-selectin protein?
- What adverse events did the participants have during this trial?
  - An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in December 2017 and ended in June 2023. It was planned that participants would be in the trial as long as they were benefiting from the treatment.

Who was in this trial?

57 participants received treatment in this trial. Participants' ages ranged from 16 to 65 years. Their average age was about 29 years.

All the participants were from the United States of America.

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

Age group

- 3 **Under 18 years**
- 54 **18 years or above**

Gender

- 26 **Men**
- 31 **Women**

Race

- 56 **Black** or **African American**
- 1 **White and Black** or **African American**

The participants could take part in this trial if they:

- had confirmed sickle cell disease and had at least 1 VOC in the past 12 months before joining the trial
- were receiving hydroxyurea/hydroxycarbamide for at least 6 months before joining the trial and planned to continue during the trial

What treatment did the participants receive?

All participants received **SEG101** as an infusion into a vein. The trial looked at 2 doses of SEG101:

- **SEG101 5 mg/kg*:** Researchers used this dose to answer the main questions of this trial. It became available in the market while the trial was still ongoing.
- **SEG101 7.5 mg/kg:** Researchers used this dose to further their understanding of how SEG101 affects participants when they receive a dose higher than SEG101 5 mg/kg.

*mg/kg is a unit to measure the dose of SEG101. It means milligrams (mg) of SEG101 per kilogram (kg) of a participant's body weight.

Researchers enrolled participants in the **SEG101 5 mg/kg** dose group first followed by the **SEG101 7.5 mg/kg** dose group.

Each participant, the trial doctors, and the trial staff knew what treatment participants were receiving.

What happened during the trial?

Before treatment

Up to 5 weeks

Trial doctors checked participants' overall health to ensure they could be in this trial. 57 participants joined the trial.

During treatment

About 3 and a half years

SEG101 5 mg/kg: 45 participants received 5 mg of SEG101 per kg of their body weight

SEG101 7.5 mg/kg: 12 participants received 7.5 mg of SEG101 per kg of their body weight

All participants received the trial drug on the first day of Weeks 1 and 3 followed by once every 4 weeks until they stopped participating in the trial for any reason. Participants received SEG101 for about 3 and a half years during the trial.

Trial doctors monitored the overall health of the participants throughout the trial.

After treatment

Up to 15 weeks after the last dose

Trial doctors checked the overall health of the participants.

Participants who were benefiting from the treatment in both dose groups could choose to continue the treatment outside of this trial.

- Participants in **SEG101 5 mg/kg** group could continue the treatment as it became available in the market.
- Participants in **SEG101 7.5 mg/kg** group could join another trial, CSEG101A2401B, and continue receiving the same treatment.

What were the main results of this trial?

How much SEG101 was in the blood of participants after their first dose and after multiple doses?

Researchers found that:

- SEG101 5 mg/kg reached its highest level in the blood just after participants received it as an infusion.
- The levels of drug remained high for 6 hours after the first dose and after multiple doses.
- The highest amount of SEG101 in the blood was similar after the first dose and multiple doses. This means that the build-up of SEG101 5 mg/kg in the blood was minimal after continued use.

To answer this, researchers took participants' blood samples before and after SEG101 5 mg/kg doses and studied the levels of SEG101 in their blood.

The researchers found that after receiving a 5 mg/kg dose for the first time and after multiple times, the amount of SEG101 in participants' blood:

Reached the highest level just after participants received it

Remained high for 6 hours

Reached the same high level every time

Showed minimal build up after multiple doses

Was the tested dose able to block P-selectin protein?

Researchers found that SEG101 5 mg/kg almost completely blocked P-selectin protein for the 4 weeks between each dose.

What is P-selectin protein?

P-selectin is the protein present in blood cells and blood vessels that causes them to stick together. This leads to a vaso–occlusive crisis.

To answer this, researchers took participants' blood samples before and after SEG101 5 mg/kg doses and studied the levels of blocked P-selectin for a year.

Researchers found that after receiving SEG101 5 mg/kg, the percentage of the P-selectin protein that remained blocked was:

97% **For 2 weeks after the first dose**

86-98% **For 4 weeks after each of the following doses**

What were the other results of this trial?

How often did participants have vaso-occlusive crises (VOCs) in a year that required a hospital visit?

Participants who received **SEG101 5 mg/kg**, had about 4 VOCs in a year that required a hospital visit before the start of treatment and about 3 such VOCs in a year during treatment.

Those who received **SEG101 7.5 mg/kg** had about 2 VOCs in a year that required a hospital visit before the start of treatment and about 1 such VOC in a year during treatment.

In both dose groups, participants had about 1 VOC less in a year during treatment than before the start of treatment.

How often did participants have VOCs in a year that could be treated at home?

Participants who received **SEG101 5 mg/kg** or **SEG101 7.5 mg/kg** had about 1 VOC in a year that could be treated at home during treatment.

Did the participants develop antibodies against SEG101?

No participant developed antibodies against SEG101 during the trial.

Antibodies are normally made by our immune system to fight off infections or anything that does not belong in our own body. Sometimes the immune system makes antibodies against the treatment that can stop it from working. To check if this happened, researchers studied the participants' blood samples.

What adverse events did the participants have?

Trial doctors keep track of all **adverse events** that happen in trials, 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 up to 15 weeks 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.

How many participants had adverse events?

All 57 participants had adverse events. 28 out of 57 (49%) participants had adverse events that were considered serious. 2 out of 57 (4%) participants died while on treatment, one in each dose group. 3 out of 57 (5%) participants stopped treatment due to an adverse event. The researchers concluded that there were no new safety concerns about SEG101 from this trial.

Participants who:	**SEG101 5 mg/kg** 45 participants	**SEG101 7.5 mg/kg** 12 participants
Had at least 1 serious adverse event	**22 of 45** 49%	**6 of 12** 50%
Had at least 1 adverse event	**45 of 45** 100%	**12 of 12** 100%
Stopped treatment due to an adverse event	**2 of 45** 4%	**1 of 12** 8%
Died during the trial	**1 of 45** 2%	**1 of 12** 8%

What serious adverse events did the participants have?

The table below shows the most common serious adverse events that happened in **5% or more** participants in either group.

	SEG101 5 mg/kg 45 participants	SEG101 7.5 mg/kg 12 participants
A blood clot in a blood vessel of the lungs Pulmonary embolism	**3 of 45** 7%	**0**
Brain injury	**0**	**1 of 12** 8%
COVID-19 illness	**3 of 45** 7%	**1 of 12** 8%
Fever Pyrexia	**1 of 45** 2%	**1 of 12** 8%
Gunshot wound	**0**	**1 of 12** 8%
Heart failure Cardiac arrest	**0**	**1 of 12** 8%
High level of a liver enzyme called transaminase Hypertransaminasemia	**0**	**1 of 12** 8%
Inflammation of the appendix Appendicitis	**0**	**1 of 12** 8%
Low number of blood cells Cytopenia	**0**	**1 of 12** 8%
Low number of red blood cells to carry oxygen around the body Anemia	**0**	**1 of 12** 8%
Lung infection Pneumonia	**3 of 45** 7%	**0**
Permanent damage to a bone tissue Osteonecrosis	**1 of 45** 2%	**1 of 12** 8%
Severe allergic reaction Anaphylactic reaction	**0**	**1 of 12** 8%
Stone in the gallbladder Cholelithiasis	**0**	**1 of 12** 8%
Sudden kidney damage Acute kidney injury	**1 of 45** 2%	**1 of 12** 8%
Sudden liver damage Ischemic hepatitis	**0**	**1 of 12** 8%

What other adverse events did the participants have?

All participants had other adverse events. The table below shows the most common other adverse events that happened in **15% or more** participants in either group.

	SEG101 5 mg/kg 45 participants	SEG101 7.5 mg/kg 12 participants
Anxiety	**2 of 45** 4%	**2 of 12** 17%
Constipation	**3 of 45** 7%	**2 of 12** 17%
COVID-19 illness	**5 of 45** 11%	**2 of 12** 17%
Diarrhea	**4 of 45** 9%	**2 of 12** 17%
Feeling sick Nausea	**6 of 45** 13%	**2 of 12** 17%
Fever Pyrexia	**13 of 45** 29%	**3 of 12** 25%
Headache	**12 of 45** 27%	**2 of 12** 17%
Infection of the nose and throat Upper respiratory tract infection	**10 of 45** 22%	**2 of 12** 17%
Joint pain Arthralgia	**8 of 45** 18%	**2 of 12** 17%
Low levels of potassium in the blood Hypokalemia	**12 of 45** 27%	**2 of 12** 17%
Road traffic accident	**5 of 45** 11%	**2 of 12** 17%
Vomiting	**4 of 45** 9%	**3 of 12** 25%
Yellowing of the white part of the eyes Ocular icterus	**1 of 45** 2%	**2 of 12** 17%

What was learned from this trial?

Researchers learned the amount of SEG101 in the blood after receiving it and its effects in people with sickle cell disease who previously had vaso-occlusive crises (VOCs).

- SEG101 5 mg/kg reached its highest level in the blood just after participants received it as an infusion. The levels remained high for 6 hours after the first dose and after multiple doses.
- SEG101 5 mg/kg almost completely blocked P-selectin protein for the 4 weeks between each dose.
- Researchers did not find any new safety concerns with the use of SEG101 in this trial.

Findings from this trial may be used in other studies with SEG101.

Other trials with SEG101, including CSEG101A2401B, are ongoing.

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 the following website:

- **www.clinicaltrials.gov** search using the number **NCT03264989**

If more trials are planned, they will appear on the public website above. When there, search for SEG101, crizanlizumab, sickle cell disease, vaso-occlusive crisis.

Full clinical trial title: A phase II, multicenter, open-label study to assess PK/PD of SEG101 (crizanlizumab), with or without hydroxyurea/hydroxycarbamide, in sickle cell patients with vaso-occlusive crisis (SOLACE-adults)

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