NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the suitable dose of SEG101 and its safety in children and adolescents with sickle cell disease who had painful episodes (vaso-occlusive crises)

Thank you!

Thank you to the children and adolescents who took part in the clinical trial for **sickle cell disease with painful episodes**. 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: CSEG101B2201, also known as the **SOLACE Kids study**

Novartis drug studied: **SEG101**, also called **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 results.

What was the main purpose of this trial?

The purpose of this trial was to learn more about the suitable dose of **SEG101**, also called **crizanlizumab**, and its safety in children and adolescents with **sickle cell disease** who have had painful episodes requiring a hospital visit. To find the suitable dose of **SEG101**, researchers looked at how much **SEG101** was in the blood of participants after receiving their first dose and after multiple doses.

Normal red blood cells are flexible and round so that they can travel through small blood vessels to deliver oxygen to various parts of the body. **Sickle cell disease** is a genetic condition that is passed down from parents, causing red blood cells to become stiff and shaped like a crescent or sickle. This makes it difficult for the blood cells to pass through small blood vessels. Eventually, blood cells stick to the blood vessels and block them, causing severely painful episodes, which are also called **vaso-occlusive crises (VOCs)**.

SEG101 may help prevent **VOCs** in people with **sickle cell disease**. It works by blocking a protein called **P-selectin**, which is present on blood cells and blood vessels and causes them to stick together. **SEG101** is approved in some countries to reduce the number of **VOCs** in adults and adolescents aged 16 years and older with **sickle cell disease**.

Trial drug
SEG101 also called crizanlizumab
Pronounced as criz-AN-liz-U-mab

The trial's 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 **SEG101** able to block the P-selectin protein?
- 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 October 2018 and ended in November 2024. The participants were in the trial for up to 2 years and 3 months.

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

Who was in this trial?

117 participants with **sickle cell disease** received treatment in this trial – 61 boys and 56 girls. Participants' ages ranged from 2 to less than 18 years. Their average age was 11 years. The number of participants by race is shown below.

Race

- 7 American Indian or Alaska Native
- 10 Asian
- 66 Black or African American
- 30 White
- 4 Multiple races

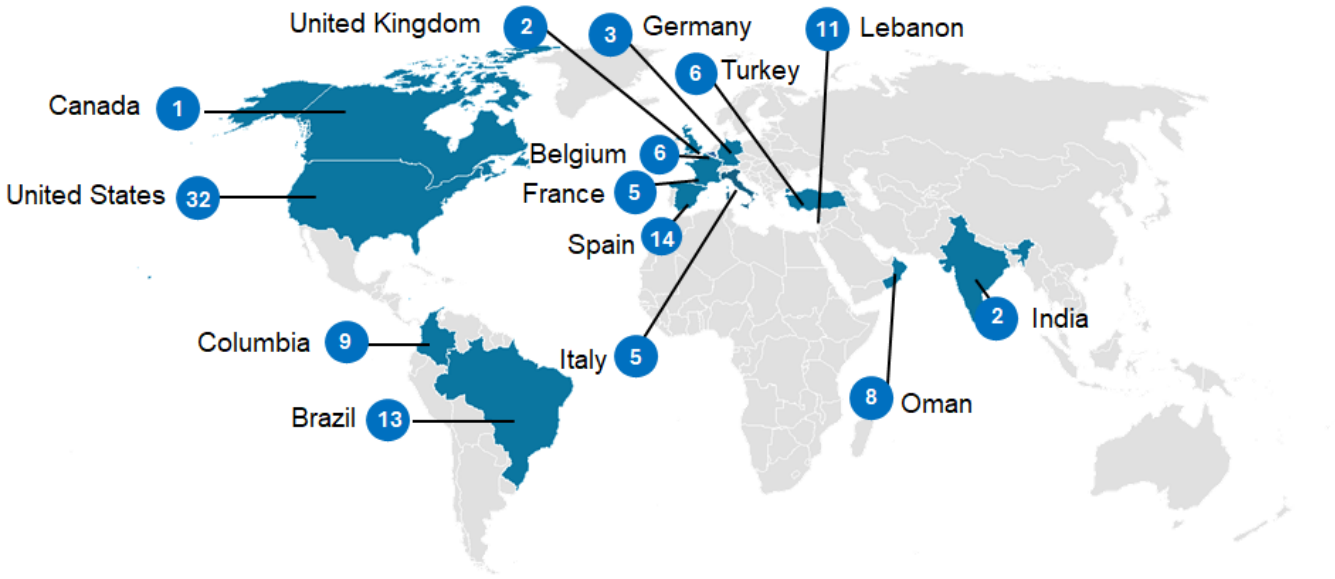
Participants could take part in this trial if they:

- were between 2 to less than 18 years of age
- had confirmed **sickle cell disease** with at least 1 vaso-occlusive crisis (VOC) requiring a hospital visit in the past 12 months before joining the trial
- were either on a stable **standard-of-care** treatment and planned to continue the same treatment during the trial, or had not taken medicines for **sickle cell disease** for at least 6 months before joining the trial

Standard-of-care is the usual treatment or medicine given to people with a specific condition or disease.

In this study, participants were allowed to receive **hydroxyurea**/**hydroxycarbamide** as standard-of-care treatment for **sickle cell disease** if considered appropriate by their doctors.

117 participants from 14 countries received treatment. The below map shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatment in this trial was **SEG101**.

Participants were put into 3 groups depending on their age:

- **Group 1**: 12 to less than 18 years of age
- **Group 2**: 6 to less than 12 years of age
- **Group 3**: 2 to less than 6 years of age

Participants received 5 or 8.5 milligrams of **SEG101** per kilogram of their body weight (mg/kg) as an infusion into a vein. Participants received the treatment on the first day of Week 1 and Week 3, followed by once every 4 weeks for up to 2 years or until they stopped participating in the trial for any reason.

The participants, researchers, and trial staff knew what treatment the participants were receiving.

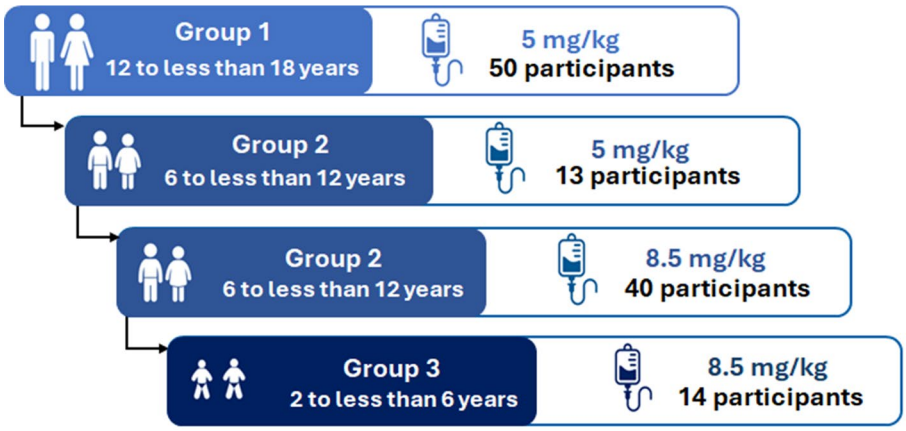
What happened during this trial?

Before treatment — Up to 1 month

The trial staff checked to make sure the children and adolescents could be in this trial.

During treatment — Up to 2 years

All participants received **SEG101**.



Participants received **SEG101** along with their stable **standard-of-care** treatment, if applicable, for up to 2 years or until they stopped participating in the trial for any reason.

Once a suitable dose of **SEG101** was found for an age group, the next group was enrolled. Initially, researchers gave participants in **Group 1** and **Group 2** the dose of 5 mg/kg. Based on the trial results, the dose was eventually increased to 8.5 mg/kg for another group of participants in **Group 2** and all the participants in **Group 3**.

Researchers collected blood and urine samples from the participants at certain times during the trial.

After treatment — Up to 3.5 months

Trial staff checked participants' general health and for any medical problems for up to 3.5 months after their last dose of trial treatment.

This check was not done for the participants who continued the treatment after this trial.

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 in all age groups:

- **SEG101** reached its highest level in the blood just after participants received it as an infusion.
- the levels of the drug remained high for up to 4 hours after the first 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** in the blood was minimal after continued use.

To answer this, researchers took participants' blood samples before and after **SEG101** doses and measured the levels of **SEG101** in their blood to determine the following:

- Highest amount of **SEG101** in the blood
- Total amount of **SEG101** in the blood over a period of time

The researchers found that after receiving a 5 mg/kg or 8.5 mg/kg dose for the first time and after multiple times, the amount of **SEG101** in participants' blood:

reached its maximum amount just after participants received it	remained high for 4 hours	reached the same high amount every time	showed minimal build-up after multiple doses over a period of time

Based on the total and highest amount of **SEG101** in participants' blood, researchers concluded that **SEG101** **5 mg/kg** was the suitable dose for **Group 1** (12 to less than 18 years of age) and **SEG101** **8.5 mg/kg** was the suitable dose for **groups 2** and **3** (2 to less than 12 years of age).

Was SEG101 able to block the P-selectin protein?

Researchers found that for all age groups, **SEG101** 5 mg/kg or 8.5 mg/kg almost completely blocked P-selectin protein for the 4 weeks between the doses.

To answer this, researchers took participants' blood samples before and after **SEG101** 5 mg/kg or 8.5 mg/kg doses and studied the levels of blocked **P-selectin** for a year.

Researchers found that after receiving **SEG101** 5 mg/kg and 8.5 mg/kg doses, the percentage of the P-selectin protein that remained blocked in all age groups was:

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.

98-100% **For 2 weeks after the first dose**

95-100% **For 4 weeks after each of the subsequent doses**

What were the other results of this trial?

How often did participants have vaso-occlusive crises (VOCs) that required a hospital visit while on trial treatment?

In each group, participants had the following number of VOCs that required hospital visit in a year:

- **Group 1**: participants had 3 VOCs in a year before treatment and 2 VOCs in a year after the start of treatment
- **Group 2 (5 mg/kg)**: participants had 1 VOCs in a year before and after the start of treatment
- **Group 2 (8.5 mg/kg)**: participants had 2 VOCs in a year before treatment and 1 VOCs in a year after the start of treatment
- **Group 3**: participants had 1 VOCs in a year before and after the start of treatment

How often did participants have VOCs that they treated at home while on trial treatment?

- Participants in **groups 1**, **2 (8.5 mg/kg)**, and **3** had about 1 VOC in a year that they treated at home during treatment.
- Participants in **group 2 (5 mg/kg)** had about 3 VOCs in a year that they treated at home during treatment.

How many days did participants stay in a hospital for any reason while on trial treatment?

On average, participants stayed for about 15 days a year in a hospital for any reason during treatment.

What adverse events did the participants have 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 treatment until 3.5 months after the last dose of the trial treatment.

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 participants need hospital care, or results in death

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

Researchers found that:

- almost all the participants (112 of 117) had adverse events.
- 59 participants had adverse events that were considered serious.
- 2 participants left the trial due to an adverse event.
- 1 participant died during the trial. This was not considered to be related to the trial treatment by the trial doctors.

The adverse events that happened in this trial were similar to those seen in previous **SEG101** trials. There were no new safety concerns for **SEG101** in this trial.

How many participants had adverse events?

	Group 1 5 mg/kg 50 participants	Group 2		Group 3 8.5 mg/kg 14 participants
		5 mg/kg 13 participants	8.5 mg/kg 40 participants	
Had at least 1 **adverse event**, including serious and non-serious	**47 of 50**	**13 of 13**	**38 of 40**	**14 of 14**
Had at least 1 **serious adverse event**	**18 of 50**	**9 of 13**	**20 of 40**	**12 of 14**
Left the trial due to an adverse event	**1 of 50**	**0**	**0**	**1 of 14**
Died	**1 of 50**	**0**	**0**	**0**

What serious adverse events did the participants have?

59 participants had serious adverse events.

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

	Group 1 5 mg/kg 50 participants	Group 2		Group 3 8.5 mg/kg 14 participants
		5 mg/kg 13 participants	8.5 mg/kg 40 participants	
COVID-19 infection	**4 of 50** 8%	**0**	**1 of 40** 3%	**2 of 14** 14%
Fever Pyrexia	**2 of 50** 4%	**2 of 13** 15%	**1 of 40** 3%	**4 of 14** 29%
Low levels of red blood cell Anaemia	**2 of 50** 4%	**1 of 13** 8%	**5 of 40** 13%	**1 of 14** 7%
Lung infection Pneumonia	**1 of 50** 2%	**1 of 13** 8%	**4 of 40** 10%	**3 of 14** 21%

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.

	Group 1 5 mg/kg 50 participants	Group 2 5 mg/kg 13 participants	Group 2 8.5 mg/kg 40 participants	Group 3 8.5 mg/kg 14 participants
Back pain	**11 of 50** 22%	**2 of 13** 15%	**9 of 40** 23%	**4 of 14** 29%
COVID-19 infection	**11 of 50** 22%	**1 of 13** 8%	**4 of 40** 10%	**2 of 14** 14%
Fever Pyrexia	**12 of 50** 24%	**5 of 13** 38%	**16 of 40** 40%	**5 of 14** 36%
Headache	**19 of 50** 38%	**4 of 13** 31%	**10 of 40** 25%	**3 of 14** 21%
Joint pain Arthralgia	**11 of 50** 22%	**1 of 13** 8%	**7 of 40** 18%	**1 of 14** 7%
Negative COVID-19 test SARS-CoV-2 test negative	**12 of 50** 24%	**3 of 13** 23%	**0**	**0**
Pain in hands and legs Pain in extremity	**11 of 50** 22%	**3 of 13** 23%	**10 of 40** 25%	**3 of 14** 21%
Stomach pain Abdominal pain	**10 of 50** 20%	**5 of 13** 38%	**12 of 40** 30%	**1 of 14** 7%
Vomiting	**14 of 50** 28%	**2 of 13** 15%	**4 of 40** 10%	**1 of 14** 7%

What was learned from this trial?

Researchers learned about the suitable doses of **SEG101** and its safety in children and adolescents with **sickle cell disease** who also had painful episodes requiring a hospital visit.

The researchers concluded that:

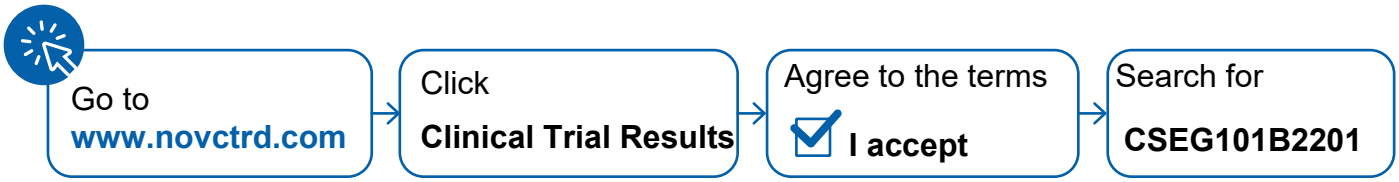
- based on the amounts of **SEG101** in participants' blood, **SEG101 5 mg/kg** was the suitable dose for adolescents 12 to less than 18 years of age, and **SEG101 8.5 mg/kg** was the suitable dose for children 2 to less than 12 years of age
- **SEG101 5 mg/kg** or **8.5 mg/kg** almost completely blocked P-selectin protein for the 4 weeks between the doses across all age groups
- on average, participants had 1 less vaso-occlusive crisis (VOC) in a year during treatment than before the start of treatment
- the adverse events that happened in this trial were similar to those seen in previous **SEG101** trials. There were no new safety concerns for **SEG101** in this trial.

Results of this trial are helping researchers plan future trials for **SEG101** in people with **sickle cell disease**. Other trials are ongoing with **SEG101** in people with **sickle cell disease**.

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 any of these websites:

- clinicaltrials.gov– search using the number **NCT03474965**
- clinicaltrialsregister.eu/ctr-search/search - search using the number **2017-001747-12**

Other trials of **SEG101** may appear on the public websites above. When there, search for **SEG101** or **crizanlizumab**.

Full clinical trial title: A phase 2, Multicenter, Open-Label Study to Assess Appropriate Dosing and to Evaluate Safety of Crizanlizumab, with or without Hydroxyurea/Hydroxycarbamide, in Sequential, Descending Age Groups of Pediatric Sickle Cell Disease Patients with Vaso-Occlusive Crisis

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