NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of SEG101 on kidney function in people with long-term kidney disease due to sickle cell disease

Thank you!

Thank you to the participants who took part in the clinical trial for long-term kidney disease due to 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: CSEG101A2203

Drug studied: SEG101, also known as crizanlizumab

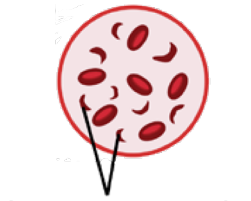
Sponsor: Novartis

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.

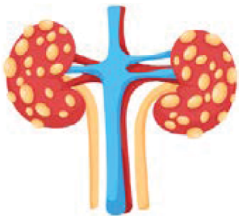
What was the main purpose of this trial?

The purpose of this trial is to learn about the effects of the combination of **SEG101** with regular treatment, and regular treatment alone on kidney function in people with long-term kidney disease caused due to **sickle cell disease (SCD)**.



Sickle-shaped RBCs

SCD is an inherited blood disorder that causes red blood cells (RBCs) to become sickle-shaped. This makes it difficult for the blood cells to pass through small blood vessels. In **SCD** blood vessels become damaged and sticky due to continuous irritation caused by the sickle-shaped RBCs. The blood cells tend to clump together.



A major complication associated with **SCD** is **sickle cell nephropathy (SCN)**. It causes kidney issues due to the distortion of the RBCs within the kidney's blood vessels and also due to blockages by the clumps of blood cells. People with **SCD** are at the risk of developing long-term kidney disease, also known as **chronic kidney disease (CKD)**. **CKD** is a condition in which the kidneys' ability to work properly gradually decreases over time. A common sign of **CKD** is the presence of excess protein in the urine that is not usually found when kidneys are healthy.

SEG101, may help prevent blockages of the blood vessels in people with SCD. **SEG101** works by blocking a protein, called **P-selectin**, which is present in the blood cells and on 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 many participants in each group had a decrease in albumin-to-creatinine ratio (ACR) of at least 30% or more after of 1 year of treatment?
  - ↳ The ACR is a test that detects protein levels in urine and is used to determine kidney function. A higher ACR value indicates poorer kidney function.
- 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 2019 and ended in March 2023. It was planned for participants to be in this trial for around 1 year and 5 months.

Researchers stopped recruiting participants early because of challenges in identifying the specific patient population experiencing long-term kidney disease caused by SCD. As a result, this trial included fewer participants than initially anticipated; 148 participants were anticipated.

Who was in this trial?

58 participants entered this trial. Participants' ages ranged from 19 to 61 years. Their average age was about 42 years.

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

Gender

- 21 **Men**
- 37 **Women**

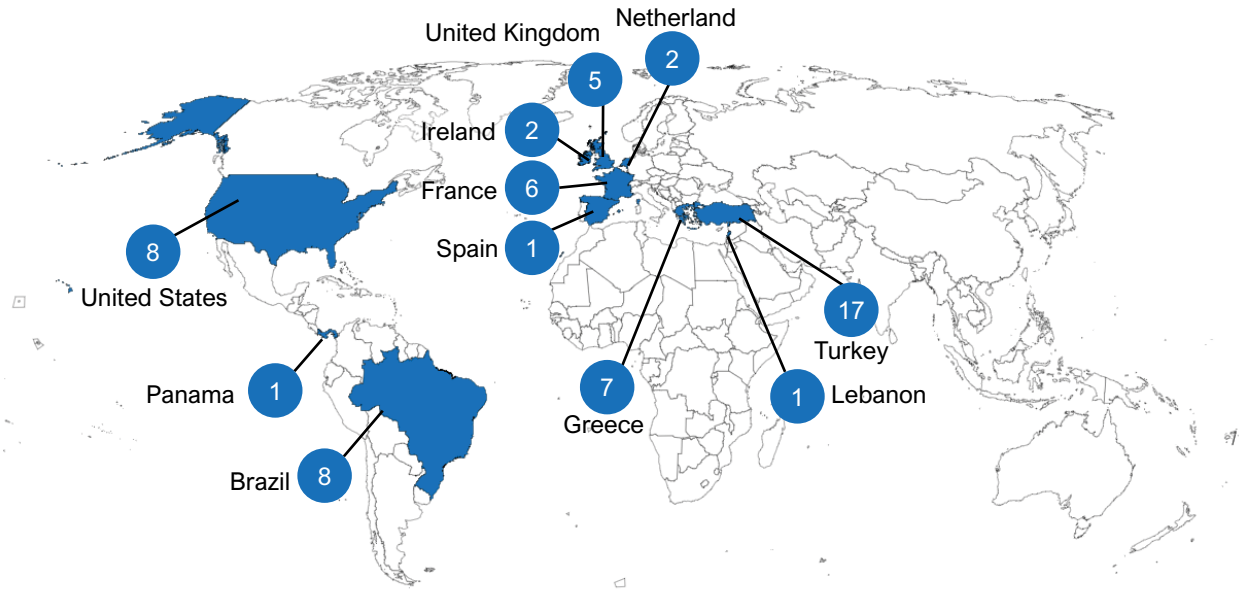
Race

- 30 **Black** or **African American**
- 27 **White**
- 1 **Multiple**

The participants could take part in this trial if they:

- were 16 years of age or older
- had a confirmed SCD-related long-term kidney disease
- had mild-to-moderate kidney function

58 participants from 11 countries entered this trial, but 1 participant did not receive treatment during this trial. The map below shows the number of participants who took part in each country.



What treatment did the participants receive?

The treatments given in this trial were:

SEG101 5 milligram per kilogram of the participant's body weight (mg/kg), given as an infusion directly into a vein which lasted about 30 minutes on Day 1 of Week 1 and Week 3, and then on Day 1 of every 4 weeks for a total period of 1 year.

Regular treatment included regularly prescribed medicines for SCD and CKD throughout the trial.

In this trial, each participant, the trial doctors, and the trial staff knew what treatment participants were receiving.

What happened during the trial?

Before treatment — Up to 28 days

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

During treatment — 1 year

58 participants joined the trial. 1 participant did not receive treatment because it was challenging to access the veins.

Participants were randomly assigned to one of the two groups:

Group 1 (30 participants): SEG101 + Regular treatment

Participants received **SEG101** 5 mg/kg for 1 year in addition to their regular treatment on:

- Day 1 on Week 1 and Week 3
- and then on Day 1 every 4 weeks

Group 2 (28 participants): Regular treatment alone

- Participants continued to receive their regular treatment as prescribed.

After treatment — Up to 15 weeks

At the end of 1 year of treatment, participants had two safety follow-ups:

- Participants who chose to receive **SEG101** commercially outside of this trial, were followed up via phone, 30 days after the last dose in this trial.
- Participants who did not receive **SEG101** commercially outside of this trial were required to complete a follow-up at the site, up to 15 weeks after the last dose.

What was the main result of this trial?

How many participants in each group had a decrease in albumin-to-creatinine ratio (ACR) of at least 30% or more after 1 year of treatment?

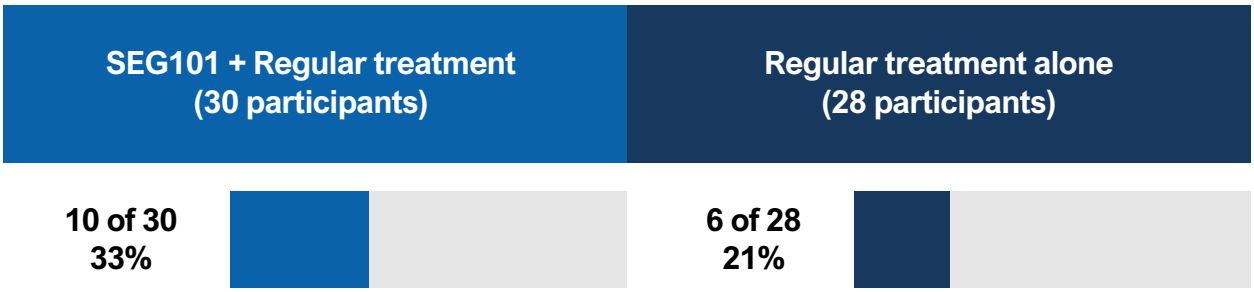
10 out of 30 participants treated with **SEG101** and their **regular treatment** and 6 out of 28 participants who took their **regular treatment alone** had at least a 30% decrease in **ACR** after 1 year of treatment.

Due to the small number of participants in each group, researchers did not see a meaningful difference between the two groups.

The **ACR** is a test that detects protein levels in urine and is used to determine kidney function. It calculates the albumin (a protein) to creatinine (a waste product) ratio in a urine sample. A higher ACR value indicates poorer kidney function.

To answer this question, researchers took urine samples from participants to perform an **ACR test**.

Number (percentage) of participants who had at least a 30% decrease in ACR after 1 year of treatment



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 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 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?

45 out of the total 57 treated participants had adverse events. 4 participants had adverse events that were considered serious.1 participant stopped the treatment with **SEG101** due to an adverse event. No new safety concerns were identified with the use of **SEG101** in this trial.

Participants who:	SEG101 + Regular treatment 29 participants	Regular treatment alone 28 participants
Had at least 1 serious adverse event	**2 of 29** 7%	**2 of 28** 7%
Had at least 1 other adverse event	**25 of 29** 86%	**20 of 28** 71%
Stopped treatment due to an adverse event	**1 of 29** 3%	**0**
Died during the trial	**0**	**0**

What serious adverse events did the participants have?

The table below shows the serious adverse events that happened in at least 1 participant in any group.

	SEG101 + Regular treatment 29 participants	Regular treatment alone 28 participants
A condition where sickle-shaped RBCs block blood flow to organs and tissue, requiring urgent medical care Sickle cell anaemia with crisis	**1 of 29** 3%	**1 of 28** 4%
Overactive thyroid gland Hyperthyroidism	**0**	**1 of 28** 4%
Flu Influenza	**1 of 29** 3%	**0**
Inability of lungs to supply oxygen to the blood Acute respiratory failure	**0**	**1 of 28** 4%

What other adverse events did the participants have?

45 participants had other adverse events. The table below shows the other adverse events that happened in **15% or more** participants in any group.

	SEG101 + Regular treatment 29 participants	Regular treatment alone 28 participants
COVID-19 illness	**7 of 29** 24%	**4 of 28** 14%
Headache	**6 of 29** 21%	**4 of 28** 14%
Flu Influenza	**5 of 29** 17%	**4 of 28** 14%
Feeling sick Nausea	**4 of 29** 14%	**5 of 28** 18%
Joint pain Arthralgia	**5 of 29** 17%	**3 of 28** 11%
Vomiting	**1 of 29** 3%	**7 of 28** 25%

What was learned from this trial?

Researchers studied the effects of **SEG101** in decreasing **albumin-to-creatinine ratio (ACR)** in people with long-term kidney disease due to sickle cell nephropathy.

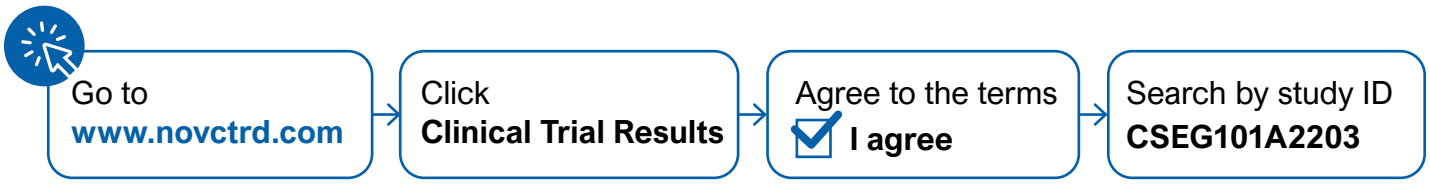
As researchers stopped recruiting participants in this trial early with a small number of participants versus required, there were not enough participants to draw a meaningful conclusions.

There were no new safety concerns with the use of **SEG101**. Findings from this trial may be used in other ongoing studies with **SEG101**.

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 the following websites:

- **www.clinicaltrials.gov** - search using the number **NCT04053764**
- **clinicaltrialsregister.eu/ctr-search/search** - search using the number **2018-003608-38**

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

Full clinical trial title: A Phase II, multicenter, randomized, open label two arm study evaluating the effect of crizanlizumab + standard of care and standard of care alone on renal function in sickle cell disease patients ≥ 16 years with chronic kidney disease due to sickle cell nephropathy (STEADFAST)

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