Clinical Trial Results Summary

NOVARTIS

The safety of CGF166 and its effects on hearing in people with severe-to-profound hearing loss

Thank you!

Thank you to the participants who took part in the clinical trial for the trial drug **CGF166**. All of the participants helped the researchers learn more about how safe CGF166 is and how well it could work.

Novartis sponsored this trial and believes it is important to share the results learned from this trial with the participants and the public. An independent organization helped Novartis prepare this summary of the trial results.

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

Trial information

Trial number: CCGF166X2201
Trial drug studied: CGF166
Sponsor: Novartis

This trial at a glance

What was the purpose of this trial?

Read more on **page 3**

The purpose of this trial was to learn about:

- The safety of CGF166 in people with severe-to-profound hearing loss
- If CGF166 increased the participants' hearing

Who was in this trial?

Read more on **page 4**

- 22 men and women began this trial
- The participants were 18 to 73 years old and had severe-to-profound hearing loss in one or both ears

What treatments did the participants receive?

Read more on **page 4**

- Each participant received one dose of CGF166 in one ear. A surgeon used a small needle to inject CGF166 into the cochlea, which is part of the inner ear.
- Each participant was assigned 1 of 4 dose levels of CGF166

What were the main results of this trial?

Read more on **pages 5-7**

- Most of the participants had medical problems during this trial. The most common medical problem was slight hearing loss based on hearing tests. Some amount of hearing loss is expected for participants that undergo ear surgery.
- There was no meaningful increase in the participants' hearing after they received CGF166.

Read about other results of this trial on **page 8**

You can find **more information** about this trial by going to the websites listed on **page 9**.

What was the purpose of this clinical trial?

The purpose of this trial was to learn about the safety of the trial drug CGF166 and if it could increase the hearing of people with severe-to-profound hearing loss. This level of hearing loss ranges from being unable to hear speech to being unable to hear any sound, including loud noises.

The main cause of hearing loss is damage to **sensory hair cells** in the cochlea. These hair-like cells allow people to hear. Over time, loud noises and aging can permanently damage these cells and cause hearing loss. When this happens, the body cannot replace the damaged hair cells.

CGF166 is a gene therapy designed to treat hearing loss. It delivers a gene called **Atonal** to the cells around the damaged hair cells. Researchers believe that Atonal could change these cells into new hair cells. These new hair cells might increase a person's hearing.

Before a trial drug can be approved for doctors to use in patients, researchers do many trials to find out how safe it is and how it works.

What is a gene therapy?

A gene therapy is a treatment that replaces or adds a gene inside the body to treat a disease or condition.

For more information, visit: medlineplus.gov/genesandgenetherapy.html

The main questions this trial was designed to answer:

- What medical problems did the participants have during this trial? Keeping track of the medical problems helped to learn about the safety of CGF166.
- Did CGF166 increase the participants' hearing?

How long was this trial?

This trial started in June 2014 and ended in December 2019.

The participants took part in the trial for up to 2 years. 3 participants did not complete this trial.

Who was in this trial?

22 participants were in this trial – 15 men and 7 women. The participants were 18 to 73 years old. Their average age was 50.

Every participant in this trial had severe-to-profound hearing loss. Early in the trial, the participants who joined had hearing loss in both ears. Later in the trial, participants with hearing loss in one or both ears could join.

The participants in this trial could **not** have:

- A cochlear implant in their ear that would receive CGF166
- Any health condition that would make the surgery to receive CGF166 unsafe for them

This trial took place in the United States.

Visit novctrd.com for more information about:

- Who could and could not be in this trial
- The participants in this trial, such as their age, gender, and race
- The reasons why participants left this trial

Use trial number **CCGF166X2201** to find the scientific summary.

What treatments did the participants receive?

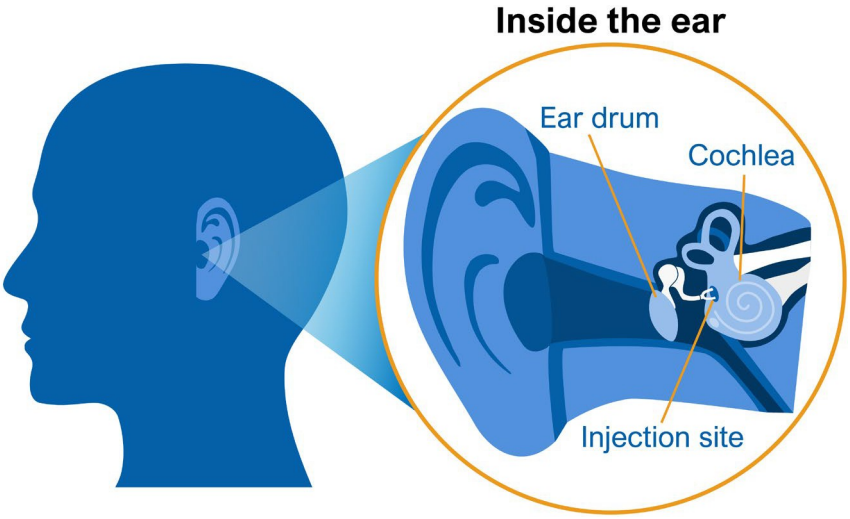
Each participant received 1 of 4 dose levels of CGF166. For each dose level, the clinical trial team compared the safety results and effects on hearing. The participants and trial staff knew which dose level of CGF166 a participant received.

To lower the chance for medical problems, the clinical trial team assigned the lowest of the 4 dose levels first. The team reviewed its safety results before moving to the next highest dose level.

The participants received CGF166 through a new method called an **intra-labyrinthine (IL) infusion.** A surgeon made a small cut near the participant's ear drum and used a laser to create a tiny hole in their cochlea. The surgeon guided a small needle through the hole to inject CGF166. For this surgery, a participant went under general anesthesia, which means they were put to sleep.

This trial was the first time a human received an IL infusion. After any type of inner ear surgery, there is a chance that a person may have slight hearing loss. Before the participants joined this trial, the clinical trial team informed them that the IL infusion could cause slight hearing loss.

Where did a participant receive CGF166?



What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

What medical problems did the participants have during this trial?

Medical problems that happen during trials are called “adverse events”. An **adverse event** is any unwanted sign or symptom that participants have during a trial. An adverse event is 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. Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they think the adverse events might not be related to the trial treatments.

Trial doctors looked for adverse events when they checked the participants’ health at the trial site. The participants also reported adverse events. This section includes the adverse events that happened during and after a participant received the IL infusion of CGF166.

Participants who had adverse events

Participants who had:	CGF166 22 participants
Serious adverse events	0% 0 of 22
Other adverse events	73% 16 of 22
Left this trial due to adverse events	0% 0 of 22

What serious adverse events did participants have?

During and after trial treatment, no serious adverse events were reported, including deaths.

What other adverse events did participants have?

Most of the participants had adverse events during this trial. The table below shows the adverse events that happened to **2 or more participants**. Other adverse events were reported by fewer participants.

	CGF166 22 participants
Slight hearing loss Hypoacusis	32% 7 of 22
Dizziness	18% 4 of 22
Feeling of moving or spinning Vertigo	14% 3 of 22
Muscle pain Myalgia	9% 2 of 22

- The most common adverse event was slight hearing loss based on a hearing test. Some amount of hearing loss is expected for participants that undergo ear surgery.
- All participants who had slight hearing loss reported they didn't notice any loss in hearing.

For more information about the adverse events the participants in this trial had, visit novctrd.com. Use trial number **CCGF166X2201** to find the scientific summary.

Did CGF166 increase the participants' hearing?

There was no meaningful increase in the participants' hearing after they received CGF166.

To find this out, the clinical trial team used pure tone audiometry to measure the participants' hearing before and after they received CGF166. **Pure tone audiometry** is the standard way to measure a person's hearing. During this test, a participant wore 2 types of headphones and listened for an electronic beep that was played at different volumes.

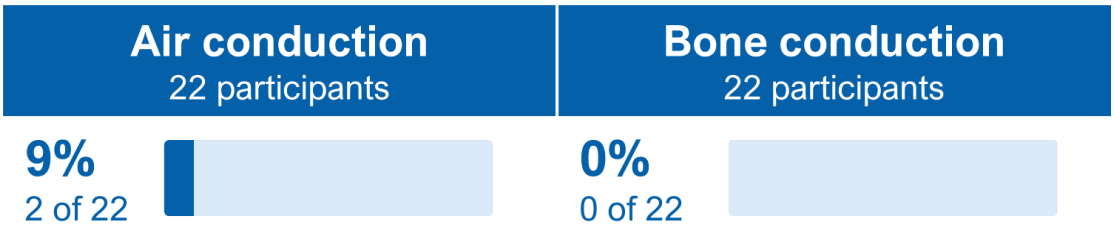
Air conduction headphones go over the ears to send sounds through the ear and eardrum to reach the inner ear.

The team found that most of the participants showed no increase in how well they could hear through air conduction after receiving CGF166. 2 participants could hear a few beeps at a lower volume.

Bone conduction headphones sit above the ear to send sounds through bones in the head to reach the inner ear, without passing through the eardrum.

The team found that none of the participants showed any increase in how well they could hear through bone conduction after receiving CGF166.

Participants who could hear beeps at a lower volume after treatment



What other results were learned?

The clinical trial team also measured:

- Any changes in the participants' sense of balance, which the inner ear also controls
- The participants' hearing in other ways
- The participants' ability to recognize speech

Trial staff compared participants' results from before and after they received CGF166. The team concluded that CGF166 had no meaningful effect on any of these measures.

What was learned from this trial?

This was the first trial to learn about the safety of CGF166 and how well it could work for people with severe-to-profound hearing loss. It was also the first time that people received a gene therapy directly into the inner ear.

The clinical trial team found that CGF166 didn't increase the participants' hearing. They found this was the case for any dose level. The team also learned that an IL infusion is a new possible way to inject a treatment directly into the inner ear. The team also found no serious safety concerns for the participants in this trial.

This type of trial learned about the safety of a trial drug and how well it works in a small number of participants. This may help researchers find new ways to treat hearing loss in the future.

ⓘ The results presented here are for one trial. One trial cannot give a complete picture of the benefits and risks of a trial drug. The results of many trials are needed to find out which treatments can be used for people with hearing loss. This summary shows only the main results from this trial. Other trials may provide new information or different results.

Where can I learn more about this and future clinical trials?

This is a summary of the results for one trial.

You can find detailed results and more information about this clinical trial on the Novartis Clinical Trial Results website:

1. Visit novctrd.com
2. Click on “Clinical Trial Results” at the top right of the page
3. Read and scroll down, then click “I accept” to agree to use the information and the website
4. Select “Study number” from the drop-down menu
5. Type **“CCGF166X2201”** in the search box and click search

If you would like to view the website in a language other than English, you can click the “Google Translate” button on the top right of the page.

If you were in this trial and have questions about the results, please speak with the doctor or staff at your trial site.

This trial was registered on the following website:

- ClinicalTrials.gov – https://clinicaltrials.gov/

  To find this trial, type **CCGF166X2201** in the **Other terms** search box

Full trial title:

A three-part, multicenter, open label, single dose study to assess the safety, tolerability, and efficacy of intra labyrinthine (IL) CGF166 in patients with severe-to-profound hearing loss

If more trials are planned, they will appear on the public websites listed above. When there, search for **CGF166.**

Thank you!

Novartis would like to thank all of the people who participated in this clinical trial. The participants made this clinical trial possible and helped researchers answer important health questions and learn about a possible medical treatment. Many volunteers and many clinical trials are needed to advance medical science.

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