NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of AVXS-101 in babies with spinal muscular atrophy (SMA) type 1

Clinical trial protocol number: AVXS-101-CL-306 or COAV101A12304

Thank you!

Thank you to the parents and their babies who took part in the clinical trial for the treatment **AVXS-101**, also known as **onasemnogene abeparvovec.**

All of the parents and babies helped the researchers learn more about how AVXS-101 works in babies with **spinal muscular atrophy (SMA)**. AveXis, a Novartis company, sponsored this clinical 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 parents and babies understand their important role in medical research.

If your baby participated in the trial and you have questions about the results, please talk to the doctor or staff at your trial site.

Why was the research needed?

Researchers are looking for a way to treat **spinal muscular atrophy,** also called **SMA.** SMA is a group of conditions that causes the body to lose motor neurons. **Motor neurons** are the nerve cells in the spinal cord that control muscle movement in the arms, legs, chest, face, throat, and tongue. In SMA, the motor neurons die and can't tell the muscles how to work. The muscles become weak and cause problems with:

- Moving parts of the body
- Breathing
- Swallowing

Babies are born with SMA type 1 and symptoms usually start before they are 6 months of age. Without treatment, many babies with SMA type 1 cannot hold their head up or sit up and may not live past age 2.

SMA type 1 is caused by a missing or nonworking survival motor neuron 1 (*SMN1*) gene. *SMN1* is needed for motor neurons to live. When the *SMN1* gene isn't working, motor neurons die and can't control muscles.

AVXS-101 is a gene therapy designed to treat babies with SMA by correcting the missing or nonworking *SMN1* gene. **Gene therapy** is a treatment that corrects or replaces a missing or nonworking gene to treat disease. When this trial started, AVXS-101 was approved in the U.S. to treat babies with SMA type 1. During this trial, more countries approved AVXS-101 to treat babies with SMA type 1, including Taiwan.

Trial purpose

The purpose of this trial was to learn more about the safety and effects of AVXS-101 in babies with SMA type 1. This included effects on their ability to sit up on their own, which is a key milestone in child development.

The main questions the researchers wanted to answer in this trial were:

- How many of the babies could sit up without help for 10 seconds at least once by 18 months of age?
- How many of the babies were alive and did not need help breathing at 14 months of age?
- What medical problems did the babies have during the trial?

Trial treatment

The treatment given in this trial was:

AVXS-101, which was given once through a vein as a one-hour intravenous (IV) infusion.

How long was this trial?

The trial started in May 2019 and ended in June 2021. It was designed so that each baby would receive treatment before they were 6 months of age and take part until they were 18 months of age.

The researchers did not enroll as many babies as planned. This trial was designed to have 6 or more babies take part. But, the sponsor stopped enrollment early after 2 babies had joined. The reason for stopping enrollment was difficulty finding babies with SMA who could join the trial. The decision to stop enrollment was not due to safety or how well AVXS-101 might work.

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

Who was in this trial?

2 babies with SMA type 1 were in this trial. When they joined the trial, the babies were about 1 month of age.

The babies' genders were:

Both babies' races were reported as Asian.

The babies could take part in this trial if they:

- Had SMA type 1 based on genetic test results
- Were able to swallow or were receiving feeding support
- Could usually breathe without help or with some help from a breathing machine
- Had no other serious health problems

They took part at 1 hospital site in Taiwan.

What kind of trial was this?

This was an open-label trial, which meant that the parents and clinical trial team knew that the babies received AVXS-101.

What happened during this trial?

Up to one month before treatment

During screening

After the babies' parents gave their written consent, trial doctors checked the babies' health to make sure they could be in this trial.

1 dose

During treatment

The babies received AVXS-101 as one IV infusion which lasted about one hour.

After receiving the IV infusion, they stayed with their family at the hospital site for 2 days so the researchers could closely check their health.

Until 18 months of age

During follow-up

The babies had many follow-up visits for trial doctors to check their health until they were 18 months of age. During the COVID-19 pandemic, some visits were done by phone, video chat, or home visit. The researchers checked the babies' ability to sit up by themselves and their general health.

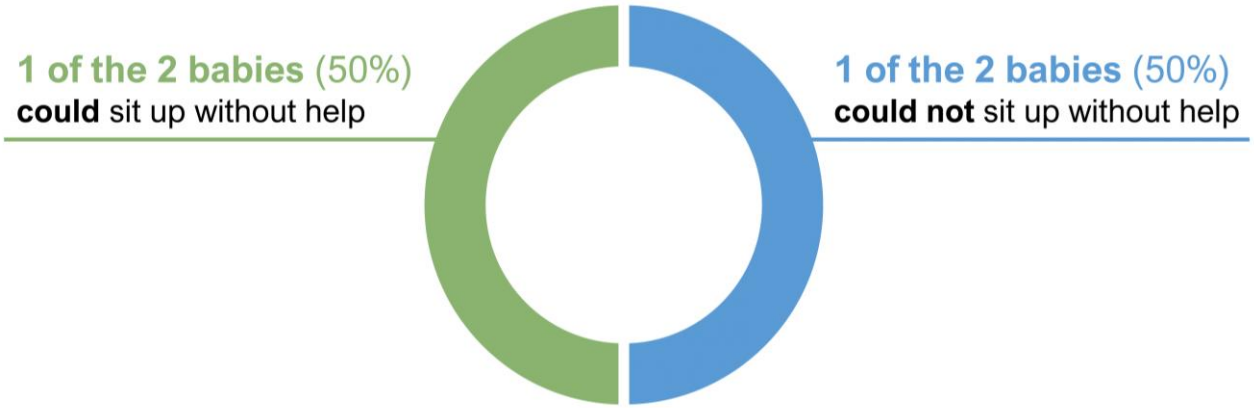
After the end of their follow-up visits, the researchers asked the parents if they wanted their babies to join a separate, long-term follow-up trial.

What were the main results of this trial?

This is a summary of the overall results for all participants. More details on the results can be found on the websites listed at the end of this summary.

How many of the babies could sit up without help for 10 seconds at least once by 18 months of age?

By 18 months of age, 1 of the 2 babies (50%) could sit up without help at least once. The researchers concluded that this was consistent with the results of past trials of AVXS-101.



To find this out, the trial staff took videos of the babies' ability to sit up at the trial visits. The researchers kept track of how many babies could sit up without help for at least 10 seconds by 18 months of age.

How many of the babies were alive and did not need help breathing at 14 months of age?

Both babies (100%) were alive and did not need help breathing at 14 months of age.

To find this out, the trial staff kept track of how many babies were alive and did not need permanent ventilation at 14 months of age. **Permanent ventilation** is breathing support with a machine that either:

- Required tracheostomy (surgery to create a hole in the neck to connect the breathing tube to the windpipe)
- Was needed for at least 16 hours a day for 14 days in a row or longer when not sick with another illness

What medical problems did the babies have during the trial?

Medical problems that happen in clinical trials are called "**adverse events**".

A lot of research is needed to know whether a drug causes an adverse event. So, when new drugs are being studied, researchers keep track of all adverse events the participants have, whether or not they are thought to be caused by the trial treatment.

This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

An **adverse event** is an unwanted sign or symptom that participants have during a trial. An adverse event is considered "**serious**" when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial treatment.

What were the serious adverse events?

There were no deaths reported during this trial. 1 of the 2 babies (50%) had a serious adverse event:

- **Trouble swallowing** (dysphagia)

What were the most common non-serious adverse events?

Both babies (100%) had adverse events that were not considered serious. The most common non-serious adverse event that both babies had was:

- **Baby doesn't gain weight or grow as expected for their age** (failure to thrive)

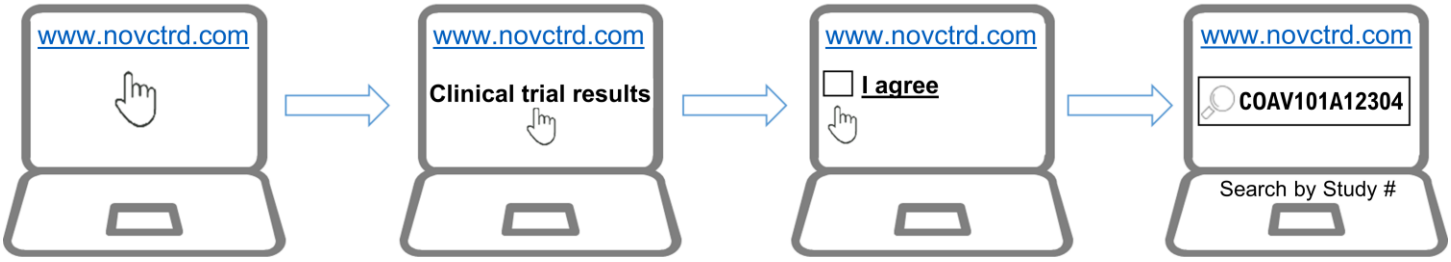
How has this trial helped?

This trial helped researchers learn how well AVXS-101 works and if it is safe to use in babies with SMA type 1. Because of the small number of babies in this trial, the researchers could not be sure if these results were meaningful. They concluded that the results were consistent with results from past clinical trials of AVXS-101. There were no safety concerns for the participants in this trial.

Please remember, this summary only shows the results of one clinical trial. Other clinical trials may have different results. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

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).



You can find more information about this trial on these websites:

- www.clinicaltrials.gov. Use the NCT identifier **NCT03837184** in the search field.
- www.clinicaltrialsregister.eu. Use the EudraCT identifier **2019-002611-26** in the search field.

Full clinical trial title: Phase 3, Open-Label, Single-Arm, Single-Dose Gene Replacement Therapy Clinical Trial for Patients with Spinal Muscular Atrophy Type 1 With One or Two SMN2 Copies Delivering AVXS-101 by Intravenous Infusion

Thank you

Thank you to the babies and their parents for taking part in this trial. As a clinical trial participant, you and your baby belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

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