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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-303 or COAV101A12302

Thank you!

Thank you to the parents and the babies who took part in the clinical trial for the drug **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 child was a participant and you 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.

Why was the research needed?

Researchers are looking for a way to treat **spinal muscular atrophy,** also called **SMA.**

Babies are born with SMA type 1 and symptoms usually start before they are 6 months old. Without treatment, many babies with SMA type 1 cannot hold their head up, never sit up without help, 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.

What is 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

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 the missing or nonworking gene to treat disease. When this trial started, AVXS-101 was not approved in the U.S. to treat babies with SMA type 1. While this trial was taking place, AVXS-101 was approved in the U.S. and in other countries to treat babies with SMA type 1.

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 at least 30 seconds at 18 months of age?
- How many of the babies were alive and did not need help breathing with permanent ventilation at 14 months of age?
- What medical problems did the babies have during the trial?

How long was this trial?

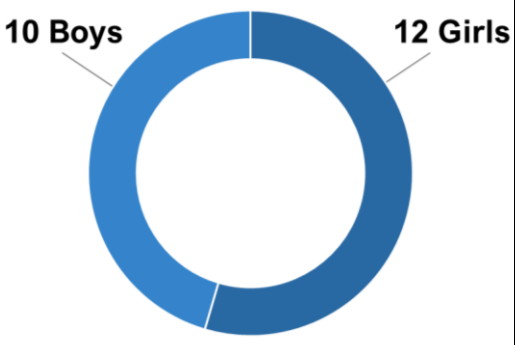
This trial started in October 2017 and ended in November 2019. This trial was designed so that each baby could take part until they were 18 months of age.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

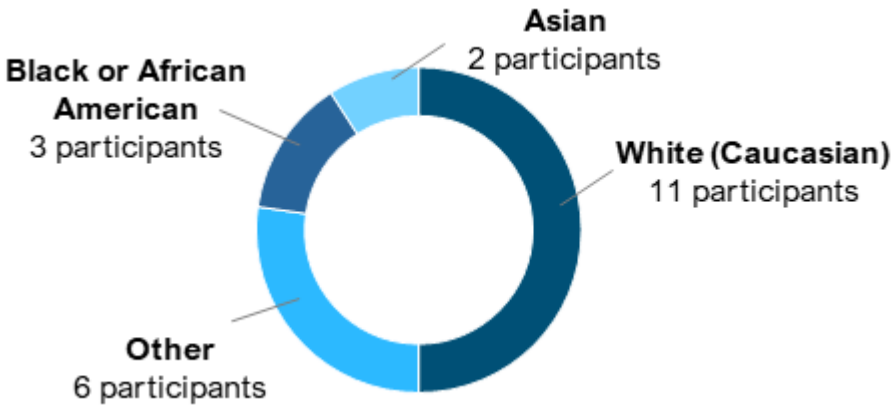
Who was in this trial?

22 babies with SMA type 1 were in this trial. All of the babies were less than 6 months of age when they joined this trial. Their average age was 4 months.

Babies' gender



Babies' race



The ethnicity of 4 babies was reported as Hispanic or Latino.

The babies could take part in this trial if they:

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

The babies took part at 16 trial sites in the United States.

What treatments did the babies receive?

The treatment in this trial was:

AVXS-101, also known as **onasemnogene abeparvovec** (pronounced on-a-SEM-noe-jeen a-be-PAR-voe-vek), which was given one time through a vein as a 30-60 minute intravenous (IV) infusion.

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

What happened during this trial?

Up to
1 month

During screening

Trial doctors checked the babies' health and genetic test results to make sure they could be in this trial. 22 babies took part in this trial.

1 dose

During treatment

The babies received AVXS-101 as one IV infusion which lasted about 30-60 minutes. After receiving the IV infusion, the babies and their family stayed at the hospital for 2 days so trial doctors could closely check their health.

Up to
18 months
of age

During follow-up

The babies had many follow-up visits for trial doctors to check their ability to sit up on their own and their health until they were 18 months of age. 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 called AVXS-101-LT-002.

What were the main results of this trial?

How many of the babies could sit up without help for at least 30 seconds at 18 months of age?

13 of 22 babies (59%) could sit up without help for at least 30 seconds at 18 months of age.

To find this out, the trial staff took videos of the babies' ability to sit up at each babies' 18-month trial visit. The researchers counted how many babies could sit up without help for at least 30 seconds.

How did these results compare with babies who did not receive AVXS-101?

Since by definition, babies with SMA type 1 are never able to sit up without help, the researchers compared these results against the chance that none of the babies would be able to sit up without help. The clinical trial team concluded that AVXS-101 had a meaningful effect on the babies' ability to sit up in this trial.

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

20 of 22 babies (91%) were alive and did not need help breathing with permanent ventilation at 14 months of age.

The trial staff kept track of how many babies were alive and did not need help breathing with 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, unless the baby was sick

Of the 22 babies, 1 was not alive and 1 needed permanent ventilation at 14 months of age.

How did these results compare with babies who did not receive AVXS-101 in an earlier observational study?

The researchers compared these results to a past observational study of babies with SMA type 1. The observational study was called the Pediatric Neuromuscular Clinical Research (PNCR) Network study. The comparison group from the PNCR study included 23 babies who had the same genetic results and received standard of care because there was no SMA type 1 therapy available at the time.

In the PNCR comparison group, 6 of the 23 babies (26%) were alive and did not need permanent ventilation at 14 months of age. The clinical trial team concluded that AVXS-101 had a meaningful effect in this trial.

What were the other results of this trial?

The researchers also looked at other possible effects of AVXS-101. The researchers kept track of how many of the babies were able to thrive, which means they could eat and grow as expected. 9 of the 22 babies (41%) were able to thrive at 18 months of age. Babies were considered **able to thrive** if at 18 months of age they:

- Did not need a feeding tube
- Could swallow thin liquids, such as formula
- Were a normal weight for their age and gender

They also kept track of how many of the babies needed to use a machine to help them breathe by opening and pushing air through their lungs. This machine is called a **bilevel positive pressure airway (BiPAP) machine.** 18 of the babies (82%) did not use a BiPAP machine at 18 months of age.

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 until the babies were 18 months of age. 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 was 1 death reported during this trial. The death was due to a stop in breathing related to SMA (respiratory arrest).

10 of the 22 babies (45%) had serious adverse events.

The table below shows the **serious adverse events** that happened in **2** or more of the 22 babies (**9%** or more):

	Number out of 22 babies Percent
Fluid in the lungs prevents oxygen flow Respiratory distress	4 babies 18%
A type of lung infection Bronchiolitis	2 babies 9%
A type of lung infection Pneumonia	2 babies 9%
Lung infection from RSV Respiratory syncytial virus bronchiolitis	2 babies 9%
Lungs can't get enough oxygen into the blood Respiratory failure	2 babies 9%

What were the most common non-serious adverse events?

All 22 babies had adverse events that were not considered serious.

The table below shows the **non-serious adverse events** that happened in **6** or more of the 22 babies (**27%** or more):

	Number out of 22 babies Percent
Fever Pyrexia	**12 babies** 55%
Infection in the nose, throat, or upper airways Upper respiratory tract infection	**11 babies** 50%
Trouble passing stool Constipation	**9 babies** 41%
Spine twists and curves to the side Scoliosis	**9 babies** 41%
Cough	**7 babies** 32%
High blood level of a protein, which is mostly in the liver Aspartate aminotransferase increased	**6 babies** 27%
Fluid in the lungs prevents oxygen flow Respiratory distress	**6 babies** 27%

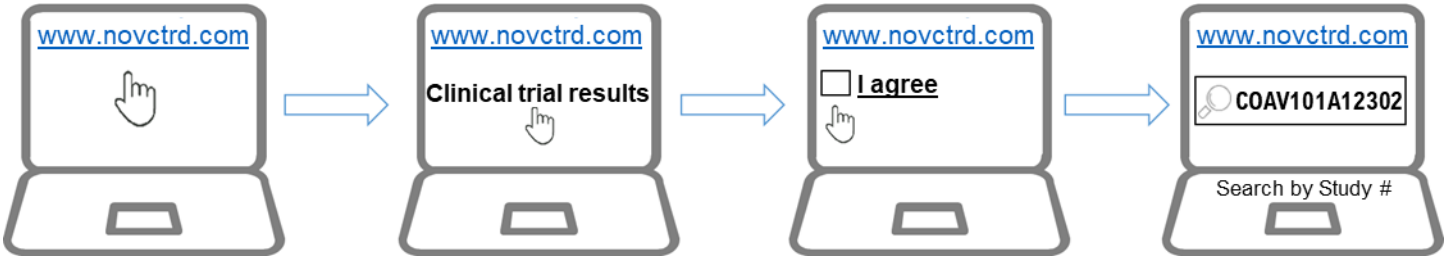
How has this trial helped?

This trial helped researchers learn how well AVXS-101 works and if it is safe to use in babies with SMA type 1 who were younger than 6 months of age. Researchers concluded that more than half of the babies in this trial were able to sit up at 18 months of age. Most babies were alive and did not need permanent ventilation at 14 months of age. Researchers also found no new safety concerns.

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:



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

- www.clinicaltrials.gov. Use the NCT identifier **NCT03306277** in the search field.
- www.clinicaltrialsregister.eu. Use the EudraCT identifier **2020-000095-38** 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, your baby and you 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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Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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