NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of OAV101 in children with spinal muscular atrophy who had not been treated before

Thank you!

Thank you to the children and families who took part in the clinical trial for spinal muscular atrophy. All the children helped the researchers learn more about the trial drug **OAV101**, also called onasemnogene abeparvovec.

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: COAV101B12301

Novartis drug studied: **OAV101**, also called onasemnogene abeparvovec

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 about the effects of **OAV101** for children with spinal muscular atrophy who had not been treated before.

Spinal muscular atrophy (SMA) is a group of conditions that cause the body to lose motor neurons. Motor neurons are the nerve cells that control muscle movement in the body, including the arms, legs, chest, face, throat, and tongue. In SMA, motor neurons die and can't tell the muscles to work. The muscles become weak and cause problems with:

- Moving parts of the body
- Breathing
- Swallowing

SMA 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. The children in this trial had 2 copies of the *SMN1* gene that did not work. The children could sit on their own but could not walk.

What is a gene?

A **gene** is a section of DNA that stores the instructions for a cell. **DNA** is like a special code inside cells that tells cells what to do and how to grow. Each gene has a job, like telling a muscle how to move or hair to grow.

OAV101, also called onasemnogene abeparvovec, is a gene therapy designed to treat SMA by correcting the missing or nonworking *SMN1* gene. **Gene therapy** is a treatment that works by replacing or adding a gene inside a person's cells to treat a disease or condition.

Trial drug

OAV101 also called onasemnogene abeparvovec

Pronounced as

ON-a-SEM-noe-jeen A-be-PAR-voe-vek

The trial's purpose was to answer these main questions:

- Did children's ability to move improve 1 year after receiving OAV101?
- 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 February 2022 and ended in April 2025. Each child was in the trial for up to about a year and a half.

Who was in this trial?

126 children with SMA received treatment in this trial – 62 boys and 64 girls. Children's ages ranged from 2 to 16 years. Their average age was 6 years.

The number of children by race is shown below.

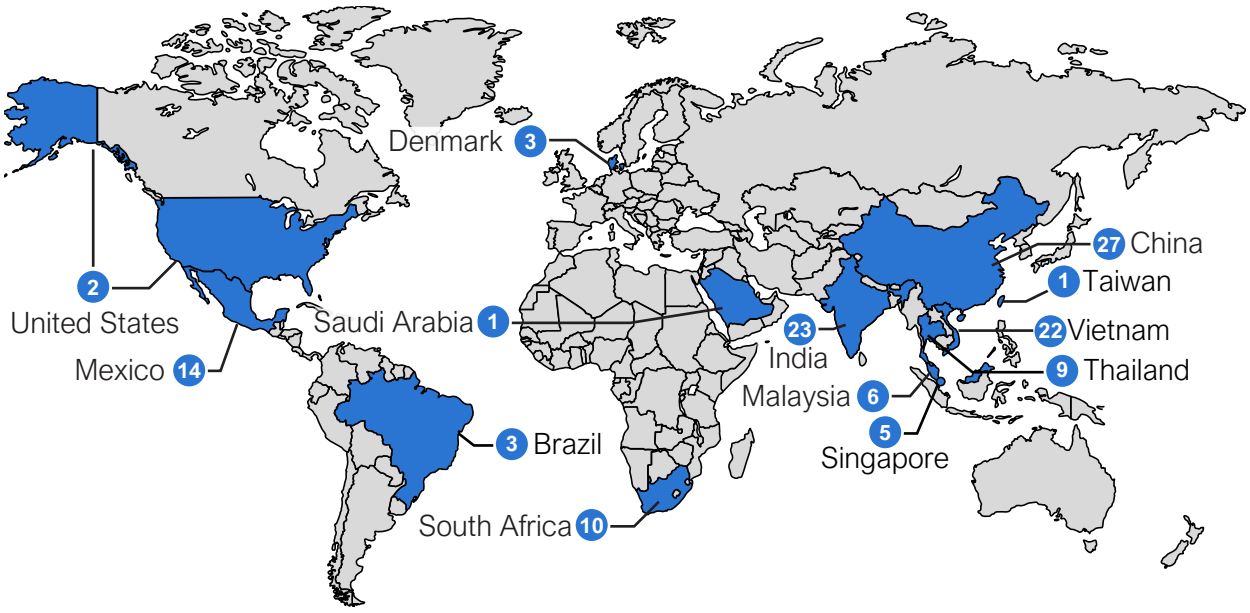
Race

7 American Indian or Alaska Native	74 Asian
9 Black or African American	14 White
22 Unknown or Not reported	

Children could take part in this trial if they had SMA and:

- Were between 2 and 17 years old
- Had blood test results and spine measurements that met certain requirements
- Could sit by themselves, but could not walk
- Had never received treatments for SMA, such as nusinersen or risdiplam

126 children from 13 countries received treatment in the trial. The map below shows the number of children who took part in each country.



What treatments did the children receive?

The treatments in this trial were:

OAV101, which was given one time as an intrathecal (IT) injection. An **IT injection** is given through the lower back and into the fluid around the spinal cord.

A **sham procedure**, which was a needle prick in the skin in the lower back one time. The **sham procedure** did not inject anything into the body.

Researchers used a **sham procedure** to better understand the effect of the trial drug. Using a **sham procedure** meant that neither the researchers or participants knew when they were receiving the trial drug.

Researchers used a computer to randomly assign children to a treatment group, in which they received the trial treatments in a certain order. This trial had 2 parts.

In **Part 1**, children were assigned by chance to 1 of 2 groups:

- **Group 1** received **OAV101**
- **Group 2** received a **sham procedure**

In Part 1, for every 3 children who received **OAV101**, 2 children received the **sham procedure**.

In **Part 2**, children in both groups from Part 1 who continued the trial received the other treatment:

- **Group 1** received a **sham procedure**
- **Group 2** received **OAV101**

By the end of Part 2, both groups received both trial treatments.

The children and their families, researchers, and trial staff did not know what treatment group the participants were assigned. A separate team of trial staff gave children **OAV101** or the **sham procedure**. Some trials are done this way because knowing what treatment the participants receive can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

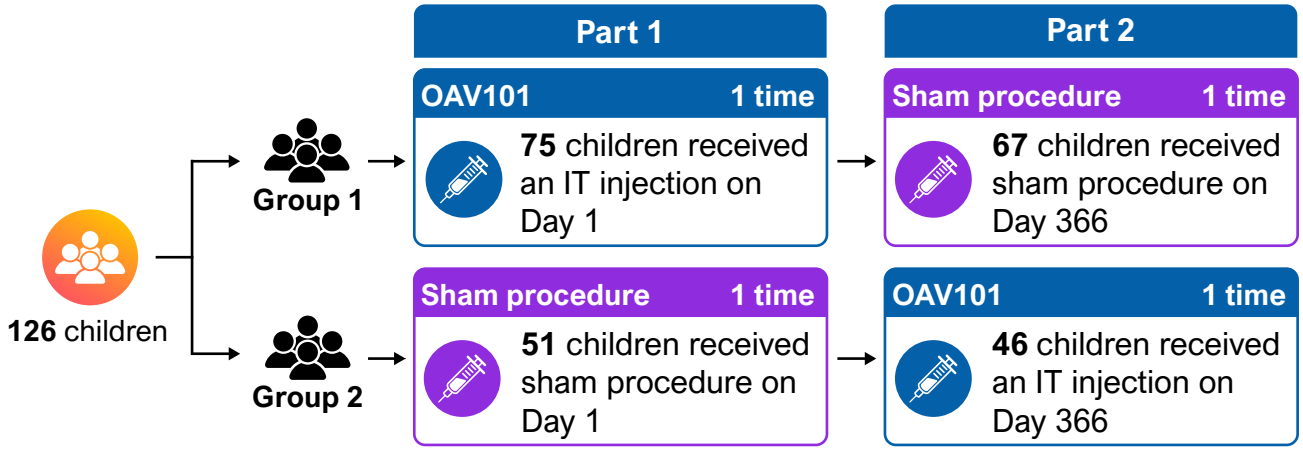
What happened during this trial?

Before treatment — Up to 2 months

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

During treatment — 1 year

126 children received treatment in 1 of 2 groups. Each group received treatment during 2 parts. The graphic below shows which treatment the groups received during each part.



Trial staff checked children's health for about one year during Part 1. At the end of Part 1, trial staff checked if they could continue to Part 2.

13 children did not continue to Part 2.

After Part 2 treatment — Up to 3 months

Trial staff checked children for any medical problems for up to 3 months after treatment in Part 2.

At the end of this trial, children were invited to join another trial called COAV101A12308 to learn about the safety and effects of **OAV101** over a longer period of time.

Trial staff checked the children's general health throughout the trial.

What were the main results of this trial?

Did children's ability to move improve 1 year after receiving OAV101?

Children's ability to move improved in those who received **OAV101** compared to children who received the **sham procedure** 1 year after treatment in Part 1. Overall, children's movement score was about 2 points higher 1 year after receiving **OAV101** compared to before treatment.

To learn this, the trial staff used the **Hammersmith Functional Motor Scale-Expanded (HFMSE)** to score children's movements. The HFMSE is a test that measures the ability of a child with SMA who is 2 years or older to do 33 movements including:

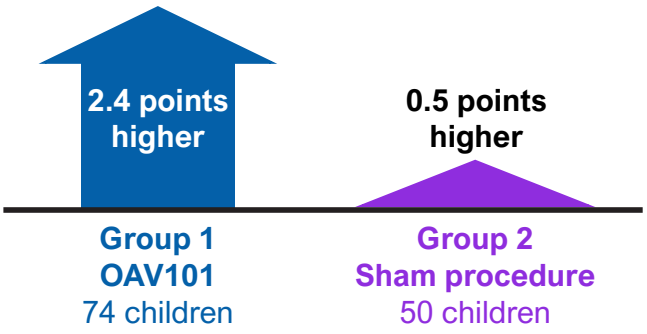
- Sitting up
- Rolling over
- Crawling
- Lifting their head up
- Standing
- Stepping and walking

The HFMSE score can range from 0 (not able to complete any movements in the HFMSE) to 66 (able to complete all movements in the HFMSE). Researchers compared the average HFMSE score of children from before treatment to 1 year after treatment in Part 1. **A higher score means the child can do more movements.**

Change in HFMSE score 1 year after treatment in Part 1

The change in average HFMSE score for children who received **OAV101** was higher than children who received the **sham procedure**. The graph below does not include 2 children who did not have HFMSE results after treatment.

Average change in HFMSE score compared to before treatment



What were the other results of this trial?

Did OAV101 affect another measure of movement?

Children who received **OAV101** could move their arms and hands more 1 year after treatment in Part 1 compared to children who received a **sham procedure**.

To learn this, the researchers checked how well children could move their hands and arms to do certain tasks, such as pick up a cup or open a lid.

What medical problems, also called adverse events, happened 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 about 3 months after their last 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.

In **Part 1**: 120 of 126 children had adverse events, including serious and other adverse events.

- 38 children had adverse events that were considered serious
- 19 children had **adverse events of special interest**, which are adverse events that researchers expect could happen based on other trials
- 32 children had adverse events that researchers thought could be related to the trial treatment, including throwing up, headache, and fever
- 1 child left the trial due to an adverse event
- No children died

Overall: 104 of 121 children who received **OAV101** in either part had adverse events, including serious and other adverse events.

- 34 children had adverse events that were considered serious
- 21 children had **adverse events of special interest**
- 36 children had adverse events that researchers thought could be related to the trial treatment
- No children died

The researchers concluded there were no new safety concerns for **OAV101** in this trial.

The tables on the next pages show adverse events that happened during Part 1 and overall. In the tables, "overall" shows the adverse events that all 121 children had after they received **OAV101** in either Part 1 (75 children) or Part 2 (46 children).

How many children had adverse events?

	Part 1		Overall
	OAV101 75 children	**Sham procedure** 51 children	**OAV101** 121 children who received **OAV101** in either part
Had **any adverse event**	**74 of 75** 99%	**46 of 51** 90%	**104 of 121** 86%
Had at least 1 **serious adverse event**	**21 of 75** 28%	**17 of 51** 33%	**34 of 121** 28%
Had an **adverse event of special interest**	**12 of 75** 16%	**7 of 51** 14%	**21 of 121** 17%
Had an **adverse event related to trial treatment**	**27 of 75** 36%	**5 of 51** 10%	**36 of 121** 30%
Left the trial due to an adverse event	**0 of 75**	**1 of 51**	

What serious adverse events did the children have?

38 children in Part 1 and 34 children overall who received **OAV101** had serious adverse events.

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

	Part 1		Overall
	OAV101 75 children	**Sham procedure** 51 children	**OAV101** 121 children who received **OAV101** in either part
Lung infection Pneumonia	**9 of 75** 12%	**7 of 51** 14%	**16 of 121** 13%
Infection in the airways or lungs Lower respiratory tract infection	**2 of 75** 3%	**4 of 51** 8%	**2 of 121** 2%
Throwing up Vomiting	**3 of 75** 4%	**0 of 51** 0%	**5 of 121** 4%

What other (not including serious) adverse events did the children have?

The table below shows the most common other adverse events that happened.

	Part 1		Overall
	OAV101 75 children	**Sham procedure** 51 children	**OAV101** 121 children who received **OAV101** in either part
Infection in the nose, throat, and airways Upper respiratory tract infection	26 of 75 35%	15 of 51 29%	34 of 121 28%
Fever Pyrexia	19 of 75 25%	12 of 51 24%	23 of 121 19%
Cough	11 of 75 15%	11 of 51 22%	15 of 121 12%
Trouble passing stool Constipation	11 of 75 15%	11 of 51 22%	15 of 121 12%
Throwing up Vomiting	13 of 75 17%	6 of 51 12%	18 of 121 15%

What were the adverse events of special interest?

19 children in Part 1 and 21 children overall who received **OAV101** had **adverse events of special interest**, which are adverse events that researchers expect could happen based on other trials. In this trial, examples included liver problems and low number of cells that help blood to clot (platelets).

The table below shows the adverse events of special interest that researchers looked for during this trial.

	Part 1		Overall
	OAV101 75 children	**Sham procedure** 51 children	**OAV101** 121 children who received **OAV101** in either part
Possible signs of liver damage based on blood tests Hepatotoxicity	7 of 75 9%	5 of 51 10%	10 of 121 8%
Low number of cells that help blood to clot Transient thrombocytopenia	4 of 75 5%	2 of 51 4%	9 of 121 7%
Signs and symptoms of possible damage to nerve cells that branch out from the spine Signs and symptoms that may be suggestive of dorsal root ganglia toxicity	2 of 75 3%	1 of 51 2%	3 of 121 2%

What was learned from this trial?

Researchers learned about the effects of **OAV101** in children with spinal muscular atrophy (SMA) who had not been treated before.

The researchers concluded that compared to those who received the **sham procedure**:

- Children's ability to move improved in those who received **OAV101** 1 year after treatment in Part 1
- Children could move their arms and hands more 1 year after receiving **OAV101** in Part 1

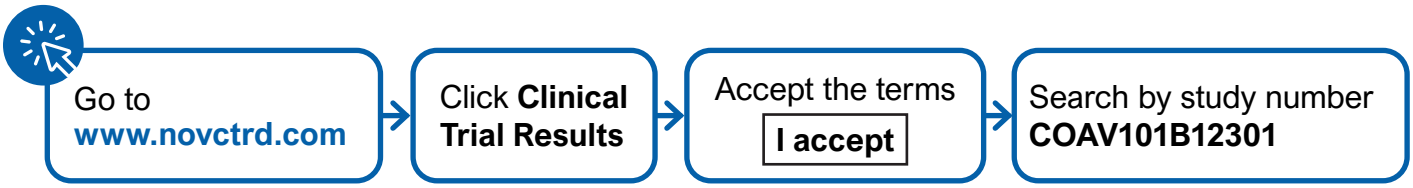
The researchers concluded there were no new safety concerns for **OAV101** in this trial.

When this summary was written, a long-term follow-up trial COAV101A12308 was ongoing for children and adults with SMA who completed this and other trials of **OAV101**.

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 **NCT05089656**
- **clinicaltrialsregister.eu** – search using the number **2021-003474-31**

Other trials of **OAV101** may appear on the public websites above. When there, search for **OAV101** or onasemnogene abeparvovec.

Full clinical trial title: A randomized, sham-controlled, double-blind study to evaluate the efficacy and safety of intrathecal OAV101 in Type 2 spinal muscular atrophy (SMA) patients who are ≥ 2 to < 18 years of age, treatment naive, sitting, and never ambulatory

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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