NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of mRNA COVID-19 vaccines in people with multiple sclerosis (MS) who are taking BAF312

Clinical trial protocol number: CBAF312ADE03

Thank you!

Thank you to the participants who took part in the clinical trial for the drug **BAF312**, also known as siponimod.

All of the participants helped the researchers learn more about how well mRNA COVID-19 vaccines work in people with **multiple sclerosis (MS)** who are taking **BAF312**. Novartis 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 participants understand their important role in medical research.

? **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.

Why was the research needed?

Researchers want to learn if mRNA COVID-19 vaccines work well in people with multiple sclerosis who are treated with BAF312.

mRNA COVID-19 vaccines help protect the body from COVID-19 by lowering the chance of severe COVID-19 infection:

- After getting a COVID-19 vaccine, the body's **immune system responds by creating antibodies** to the COVID-19 virus
- If a person is later infected with the virus, their immune system remembers to make antibodies to attack it

Antibodies are proteins that can help cells in the immune system find and attack possible threats, such as the COVID-19 virus.

Multiple sclerosis (MS) is a disease in which the immune system attacks the lining of nerves in the spine, brain, and eyes. MS causes many different symptoms – like muscle weakness and walking problems – that can come and go or get worse over time.

BAF312, also known as **siponimod** (pronounced sye-poe-ni-mod), is a drug that stops certain cells in the immune system from attacking the nerves in the brain and spinal cord:

- This type of drug is called an **immunosuppressant** because it suppresses (weakens or lowers) the immune system
- When this trial started, BAF312 was approved in Germany to treat a type of MS called secondary progressive MS (SPMS) that is active, which means MS is causing symptoms or changes on imaging tests

Trial purpose

The main purpose of this trial was to learn if people with MS had an immune system response to mRNA COVID-19 vaccines while continuing or pausing treatment with BAF312. The reason is because BAF312 stops certain immune system cells that help make antibodies.

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

- How many participants had antibodies to COVID-19 a week after getting their 2nd dose of the mRNA COVID-19 vaccine?
- What medical problems did the participants have during the trial?

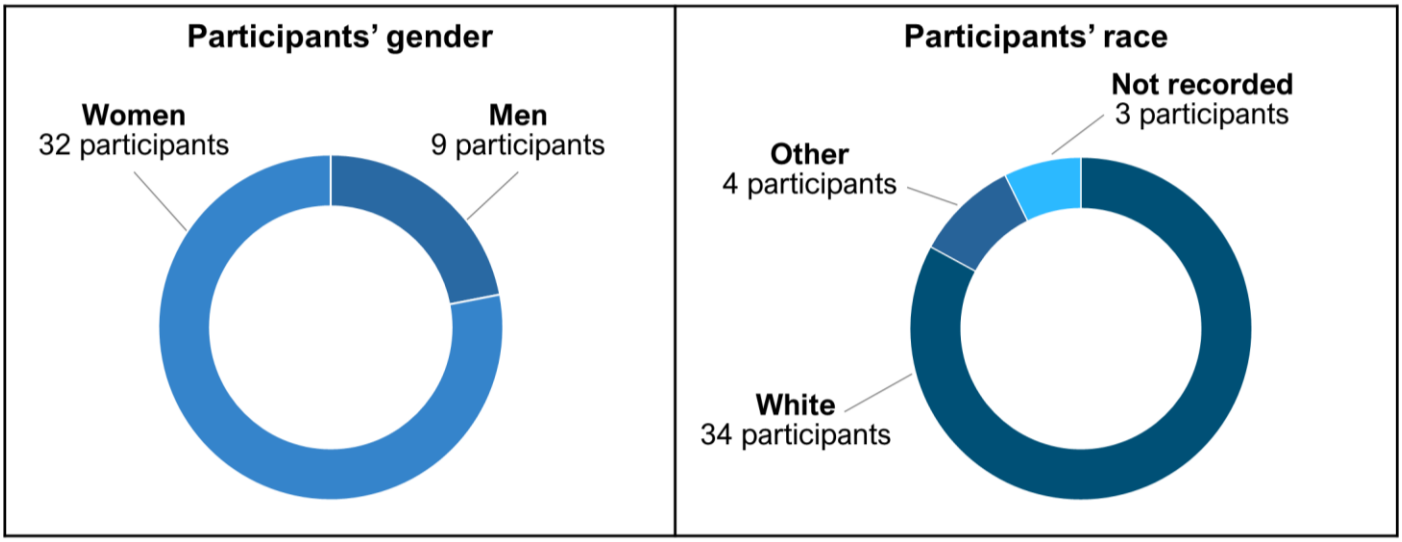
How long was this trial?

This trial was designed so that each participant could take part for up to 14 months. The trial started in April 2021 and ended in August 2022.

The researchers completed this trial. 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?

41 participants with MS were in this trial. Participants' ages ranged from 22 to 71 years. Their average age was 52 years.



The participants had a type of MS in which their symptoms were getting worse. The types of MS included:

- **Relapsing-remitting multiple sclerosis (RRMS)**, in which MS symptoms go away (remission) and come back (relapse)
- **Secondary progressive multiple sclerosis (SPMS)**, in which MS symptoms get worse over time and relapses happen less often

The participants could take part in this trial if they:

- Were already receiving BAF312, another MS treatment, or no MS treatment as part of their regular health care
- Didn't have COVID-19 antibodies in their blood

Participants took part at 10 trial sites in Germany.

What treatments did the participants receive?

The treatments in this trial were:

BAF312, which was taken once a day by mouth as pills. Based on their regular doctor's recommendations, participants either paused taking BAF312 or continued taking it while getting the 2 mRNA COVID-19 vaccines doses.

No MS treatment, or other MS treatments, which included:

- Dimethyl fumarate
- Glatiramer acetate
- Interferons
- Teriflunomide

Participants either took these treatments as pills by mouth or received them as injections.

mRNA COVID-19 vaccine, which participants received as 2 doses, about a month apart, made using mRNA (either the Pfizer or Moderna vaccine). Participants could get a booster dose after their 2nd dose.

In this trial, the participants and clinical trial team knew what treatment each participant took. Participants who were taking BAF312 or other MS treatments were already taking them as part of their regular health care. Some participants were not taking any MS treatment as part of their regular care.

What happened during this trial?

Up to **1 month**

Before getting the mRNA COVID-19 vaccine

Trial doctors checked participants' health and MS treatments to make sure they could be in this clinical trial.

41 participants took part in this trial.

About **1 month**

While getting the mRNA COVID-19 vaccine

Based on a participant's regular MS treatment and their regular doctor's recommendation, the participants were assigned to **1 of 3 groups:**

Group	Trial treatment	Type of MS
Group 1 **17** participants	**Continued BAF312** while getting 2 mRNA COVID-19 vaccine doses	SPMS
Group 2 **4** participants	**Paused BAF312** while getting 2 mRNA COVID-19 vaccine doses	SPMS
Group 3 **20** participants	**Continued other MS treatments or no MS treatment** while getting 2 mRNA COVID-19 vaccine doses	Mostly RRMS

The participants could receive an mRNA COVID-19 vaccine booster after their 2nd dose based on the guidelines of their local health authority.

Researchers checked the participants antibodies to COVID-19 and general health throughout the trial.

Up to **1 year**

After getting the mRNA COVID-19 vaccine

Participants returned to their trial site 1 week, 1 month, and 6 months after their 2nd dose of the mRNA COVID-19 vaccine for researchers to check their antibodies to COVID-19. If they had a booster dose, they returned again 1 month after the booster.

Trial staff also called participants 1 year after their 2nd dose to ask about their health.

What were the main results of this trial?

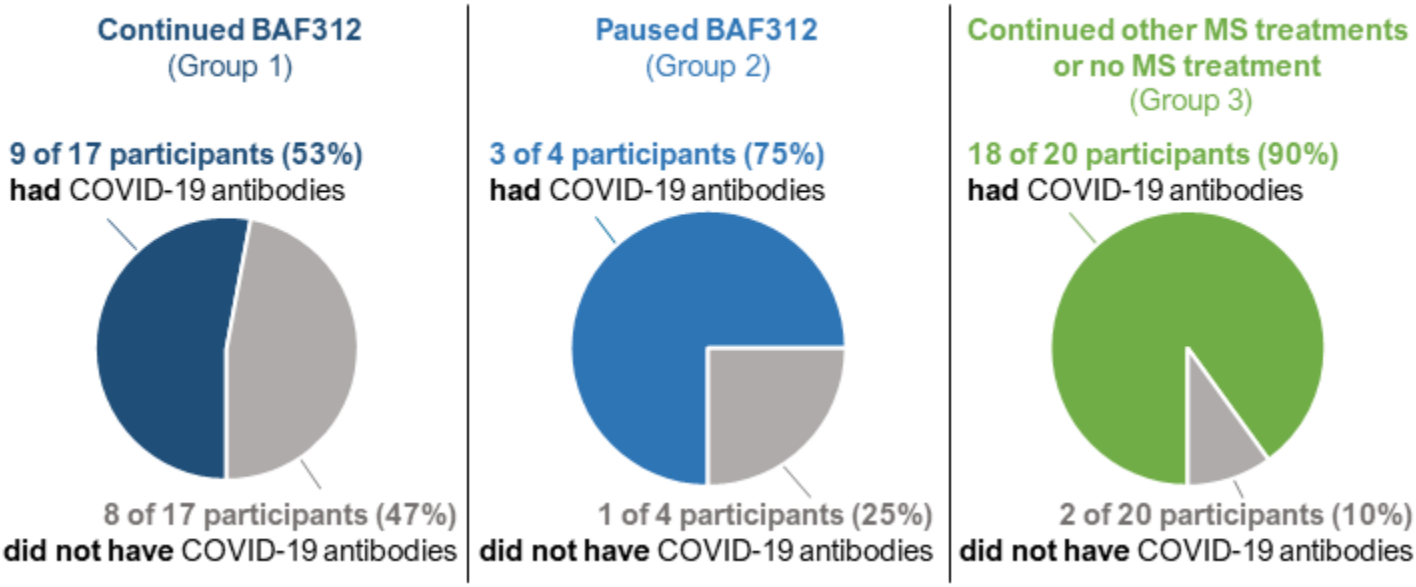
How many participants had antibodies to COVID-19 a week after getting their 2nd dose of the mRNA COVID-19 vaccine?

More than half of participants in each group had antibodies to COVID-19 a week after getting their 2nd dose of the mRNA COVID-19 vaccine.

To learn this, the trial staff took blood samples from participants a week after they got their 2nd dose of the mRNA COVID-19 vaccine. Researchers **checked each blood sample for antibodies to the COVID-19 virus.**

Because of the small number of participants in Group 2, those who paused BAF312, the researchers could not be sure the results were meaningful.

Participants who had antibodies to COVID-19 a week after getting their 2nd dose of the mRNA COVID-19 vaccine



What were the other results of this trial?

How did participants' levels of antibodies to COVID-19 change over time after getting the vaccine?

Participants in all 3 groups had:

- Higher levels of antibodies to COVID-19 1 month after the 2nd dose
- The levels go down 6 months after the 2nd dose

For participants in each group who had a booster dose, antibody levels were highest 1 month after getting the booster dose.

What medical problems did the participants 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 up to 1 month after the participant's last visit. 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 any 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.

How many participants had adverse events?

	Continued BAF312 (Group 1) 17 participants	Paused BAF312 (Group 2) 4 participants	Continued other MS treatments or no MS treatment (Group 3) 20 participants
Participants who had at least 1 adverse event	**10** of 17 59%	**3** of 4 75%	**16** of 20 80%
Participants who had at least 1 serious adverse event	**1** of 17 6%	**1** of 4 25%	**1** of 20 5%
Participants who stopped taking their MS treatment due to an adverse event	**1** of 17 6%	**0** of 4 0%	**0** of 20 0%

What were the serious adverse events?

There were no deaths reported during this trial.

3 participants had serious adverse events. 1 participant had 2 serious adverse events. The table below shows the **serious adverse events**.

	Continued BAF312 (Group 1) 17 participants	Paused BAF312 (Group 2) 4 participants	Continued other MS treatments or no MS treatment (Group 3) 20 participants
A type of UTI Escherichia urinary tract infection	**1** of 17 6%	**0** of 4 0%	**0** of 20 0%
Sinus infection Acute sinusitis	**0** of 17 0%	**0** of 4 0%	**1** of 20 5%
A stomach virus Gastroenteritis rotavirus	**0** of 17 0%	**0** of 4 0%	**1** of 20 5%
A brain disorder that causes seizures Epilepsy	**0** of 17 0%	**1** of 4 25%	**0** of 20 0%

What were the most common other adverse events?

29 participants had other adverse events.

The table below shows the **other adverse events** that happened in **4** or more of all participants (about 10% or more).

	Continued BAF312 (Group 1) 17 participants	Paused BAF312 (Group 2) 4 participants	Continued other MS treatments or no MS treatment (Group 3) 20 participants
COVID-19	**4** of 17 24%	**0** of 4 0%	**5** of 20 25%
Pain where the vaccine is given Injection site pain	**3** of 17 18%	**0** of 4 0%	**2** of 20 10%
Pain in the arms or legs Pain in extremity	**2** of 17 12%	**1** of 4 25%	**2** of 20 10%
Low number of a type of white blood cell Lymphopenia	**3** of 17 18%	**1** of 4 25%	**0** of 20 0%

How has this trial helped?

This trial helped researchers learn if people with MS who are taking BAF312 create antibodies in response to mRNA COVID-19 vaccines. They learned that:

- More than half of participants in each group had antibodies to COVID-19 a week after getting their 2nd vaccine dose - the researchers could not be sure the results from Group 2, those who paused BAF312 treatment, were meaningful because there were so few participants in that group
- For participants in each group who had a booster dose, their levels of antibodies to COVID-19 went up to the highest levels 1 month after the booster

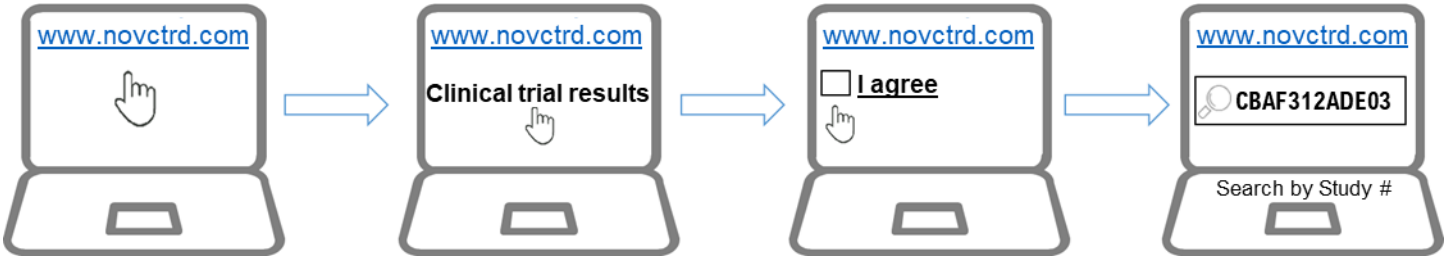
The researchers concluded that the difference between the groups was not large enough to recommend pausing BAF312 while getting mRNA COVID-19 vaccines.

There are no plans for future trials of BAF312 in people with MS who get mRNA COVID-19 vaccines. When this trial started, BAF312 was approved in Germany to treat a type of MS called secondary progressive MS (SPMS) that is active.

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 **NCT04792567** in the search field.
- www.clinicaltrialsregister.eu. Use the EudraCT identifier **2020-005752-38** in the search field.

Full clinical trial title: An open-label multicenter study to assess response to SARS-CoV-2 modRNA vaccines in participants with secondary progressive multiple sclerosis treated with Mayzent (siponimod) (AMA-VACC)

Thank you

Thank you for taking part in this trial. As a clinical trial participant, 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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