NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the immune response to COVID-19 vaccination in people with relapsing multiple sclerosis treated with ofatumumab

Thank you!

Thank you to the participants who took part in the clinical trial for relapsing multiple sclerosis. Every participant helped the researchers learn more about the trial drug **ofatumumab**, also called **OMB157**.

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: COMB157GDE01
Drug studied: **OMB157**
also known as **ofatumumab**
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 findings.

What was the main purpose of this trial?

The main purpose of this trial was to learn about the immune response to **COVID-19** (coronavirus disease 2019) vaccination in people with **relapsing multiple sclerosis** or **RMS** treated with **ofatumumab**. To find this out, researchers compared the immune response to **COVID-19** vaccines in participants receiving the vaccine before starting **ofatumumab** or during ongoing **ofatumumab** treatment.

What is an immune response?

Immune response is the process of the body's defences against infection. The body produces specific cells and proteins (antibodies) to fight-off the infection. **Cellular immune response** is one of the steps in this process.

Multiple sclerosis or **MS**, is a condition of the brain and spinal cord. In **MS**, myelin, the layer that protects the nerves, is damaged. This leads to nerve damage and the formation of lesions in the brain or spinal cord. Hence, this makes it difficult for the brain to communicate with rest of the body. **RMS** is a type of **MS** in which patients have repeated attacks or flares, called relapses.

Ofatumumab is a medicine that is approved in United States and European Union for the treatment of **RMS**. There was a major concern that treatment with **ofatumumab** may reduce the immune response to certain **COVID-19** vaccines.

Trial drug
Ofatumumab

Pronounced as
OH-fa-TUE-mue-mab

COVID-19 is a contagious disease caused by the virus SARS-CoV-2. It mainly affects the lungs and causes breathing issues.

The trial purpose was to answer these main questions:

- How many participants treated with **ofatumumab** developed a cellular immune response against **COVID-19** after receiving the vaccine?
- What adverse events did the participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial started in May 2021 and ended in June 2023. It was planned for the participants to be in the trial for about 1 year and 7 months after receiving the first dose of the **COVID-19** vaccine.

Who was in this trial?

34 participants from Germany took part in this trial. Participants' ages ranged from 21 to 79 years. Their average age was 42 years. The number of participants by gender and race are shown below.

Gender

11 Men	23 Women

Race

32 White	2 Missing

The participants could take part in this trial if they:

- were on **ofatumumab** or were allowed to start **ofatumumab** for the treatment of **relapsing multiple sclerosis** or **RMS**, as prescribed by their doctors,
- were willing and eligible to receive a **COVID-19** vaccine (initial vaccination or booster shot).

What treatments did the participants receive?

The treatments in this trial were:

Ofatumumab, 20 mg once a month, received as an injection under the skin.

COVID-19 vaccine, received on routine based on the approved dose for vaccine.

In this trial, all the participants and clinical trial team knew what treatment each participant took.

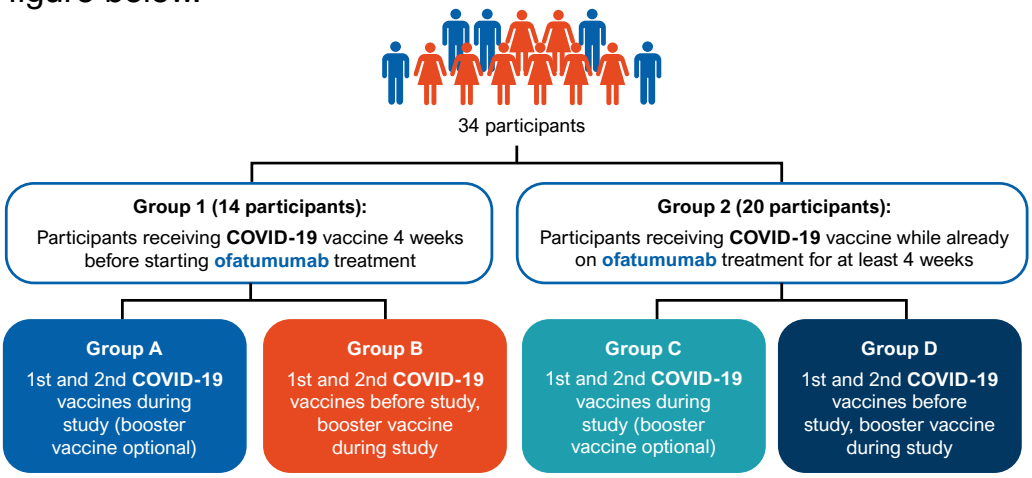
What happened during this trial?

Before treatment [Up to 4 weeks]

Trial doctors checked the participants' health and **relapsing multiple sclerosis** or **RMS** to make sure they could be in this clinical trial.

During treatment [Up to 19 months]

All participants received **COVID-19** vaccination. They started **ofatumumab** treatment before or after vaccination depending on their treatment group (Group 1 or Group 2), as shown in the figure below.



To analyze the immune response against **COVID-19**, participants in Groups **A** and **C** were followed-up at Week 1, Month 1, Month 6, Month 12 , and Month 18 after the second dose of vaccine and participants in Groups **B** and **D** were followed-up at Months 1, 6 and 12 after the booster vaccine.

Trial doctors checked the participants' health and **RMS** throughout the trial.

After treatment [1 month]

- Participants' health was monitored during this period.

What was the main result of this trial?

When a vaccine is given, it triggers 2 reactions in the body:

1. Specific immune cells are developed that detect and fight a specific type of agent that can cause disease in the body. This is called **cellular immune response**.
2. **Antibodies** are developed that bind and eliminate specifically one type of agent that can cause disease in the body.

In other words, specific immune cells and antibodies are two different kinds of mechanism to defend the body against an infection.

In this trial, both reactions towards the **COVID-19** vaccine were investigated so that the following questions could be answered:

How many participants treated with ofatumumab developed a cellular immune response against COVID-19 after receiving the vaccine?

One month after receiving the second dose or the booster vaccination, the percentage of participants who developed cellular immune response against **COVID-19** was 80% in **Group A**, 88% in **Group B**, 100% in **Group C**, and 47% in **Group D**.

To find this out, researchers assessed the percentage of participants achieving cellular immune response against **COVID-19**, 1 month after receiving their second dose or booster vaccination.

Percentage of participants who developed cellular immune response against COVID-19 in each group

Group 1
(Receiving **COVID-19** vaccine 4 weeks before **ofatumumab** treatment)

Group 2
(Receiving **COVID-19** vaccine while already on **ofatumumab** treatment for at least 4 weeks)

(After 1st and 2nd vaccination) 4 out of 5* participants

(After booster) 7 out of 8 participants

(After 1st and 2nd vaccination) 4 out of 4* participants

(After booster) 7 out of 15 participants

*For two participants, cellular immune response could not be measured.

What were the other results of this trial?

How many participants treated with ofatumumab developed antibodies against COVID-19 after receiving the vaccines?

One week after receiving the second dose of vaccine, 100% of participants in **Group A** and 40% of participants in **Group C** developed antibodies against **COVID-19**. One month after the second dose of vaccine, 100% of participants in **Group A** and 25% of participants in **Group C** developed antibodies against **COVID-19**. One month after booster vaccination, all participants in Groups **A** and **B**, and 67% of participants in **Group C** and 93% in **Group D** developed antibodies against **COVID-19**.

What adverse events did the participants have?

During a trial, all medical problems, also known as **adverse events**, are recorded, whether or not they are thought to be caused by the trial treatment.

Many trials are needed to know if a trial treatment causes medical problems or adverse events.

This section is a summary of the adverse events that happened from the start of treatment up to 1 month after the last treatment in this trial.

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.

32 (94%) participants had adverse events. 2 (6%) participants had adverse events that were considered serious.
No participants died in this trial. 1 (3%) participant left the trial due to an adverse event.

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

How many participants had adverse events?

Participants who:	Group 1		Group 2	
	Group A 6 participants	**Group B** 8 participants	**Group C** 5 participants	**Group D** 15 participants
Had at least 1 adverse event	**6 of 6** 100%	**6 of 8** 75%	**5 of 5** 100%	**15 of 15** 100%
Had at least 1 serious adverse event	**0 of 6** 0%	**0 of 8** 0%	**1 of 5** 20%	**1 of 15** 7%
Stopped treatment due to an adverse event	**0 of 6** 0%	**0 of 8** 0%	**0 of 5** 0%	**1 of 15** 7%
Died during the trial	**0 of 6** 0%	**0 of 8** 0%	**0 of 5** 0%	**0 of 15** 0%

What serious adverse events did the participants have?

2 participants had serious adverse events. No participants died.

The table below shows the most common serious adverse events that happened in any of the treatment groups.

	Group 1		Group 2	
	Group A 6 participants	**Group B** 8 participants	**Group C** 5 participants	**Group D** 15 participants
Multiple sclerosis relapse Multiple sclerosis relapse	**0 of 6** 0%	**0 of 8** 0%	**1 of 5** 20%	**0 of 15** 0%
Non-cancerous tumor of the nerve Neurilemmoma benign	**0 of 6** 0%	**0 of 8** 0%	**0 of 5** 0%	**1 of 15** 7%

What other adverse events did the participants have?

32 participants had other adverse events.

The table below shows the other adverse events that happened in **2 or more** participants in any of the treatment groups.

	Group 1		Group 2	
	Group A 6 participants	**Group B** 8 participants	**Group C** 5 participants	**Group D** 15 participants
COVID-19 COVID-19	2 of 6 33%	2 of 8 25%	5 of 5 100%	9 of 15 60%
Common cold Nasopharyngitis	1 of 6 17%	0 of 8 0%	3 of 5 20%	3 of 15 20%
Headache Headache	3 of 6 50%	2 of 8 25%	4 of 5 80%	3 of 15 20%
High blood pressure Hypertension	0 of 6 0%	0 of 8 0%	0 of 5 0%	2 of 15 13%
Pain at the site of injection Injection site pain	3 of 6 50%	0 of 8 0%	1 of 5 20%	0 of 15 0%
Pain in hands and feet Pain in extremity	3 of 6 50%	1 of 8 13%	2 of 5 40%	1 of 15 7%
Reaction caused after receiving a treatment by infusion Infusion related reaction	0 of 6 0%	2 of 8 25%	0 of 5 0%	0 of 15 0%
Scratch on skin Skin abrasion	0 of 6 0%	0 of 8 0%	0 of 5 0%	2 of 15 13%
Stomach flu Gastroenteritis	0 of 6 0%	0 of 8 0%	2 of 5 40%	0 of 15 0%

What was learned from this trial?

Researchers learned about the immune response to **COVID-19** vaccination in people with **relapsing multiple sclerosis** or **RMS** treated with **ofatumumab**. However, the results need to be considered with caution due to the small number of participants in the trial.

- The researchers concluded that people with **RMS** treated with **ofatumumab** can develop immune response against **COVID-19** within one month after the full vaccination cycle, regardless of whether they were vaccinated before or after **ofatumumab** treatment.
- No new safety concerns were observed during this trial.

At the time this report was created, there were no plans for future trials with **ofatumumab** in people with **RMS**.

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:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Agree to the terms ☑ **I agree** → Search for **COMB157GDE01**

For more information about this trial, go to any of these websites:

- **clinicaltrials.gov** – search using the number **NCT04869358**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2021-000307-20**

Other trials will appear on the public websites above. When there, search for **OMB157** and/or **ofatumumab**.

Full clinical trial title: Tracking the immune response to SARS-CoV-2 modRNA vaccines in an open-label multicenter study in participants with relapsing multiple sclerosis treated with ofatumumab s.c. (KYRIOS)

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