NOVARTIS

# Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of ofatumumab compared to placebo in people with relapsing multiple sclerosis

## Protocol number: COMB157G1301

## Thank You!

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. Thank you for taking part in this trial to study the drug ofatumumab. You helped researchers learn more about how well ofatumumab works in people with relapsing multiple sclerosis.

As a clinical trial participant, you belong to a large community of people around the world.Your invaluable contribution to medicine and healthcare is greatly appreciated.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. Researchers and health authorities, such as the Food and DrugAdministration (FDA) in the United States, the European Medicines Agency (EMA) in Europe, and the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan, 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 anyquestions about these trial results, please talk to the doctor or staff at your trial site.

# How long was this trial?

This trial started in March 2018 and ended in July 2020. The trial was designed to have two parts, known as the Core Part and the Extension Part, which together could last up to 72 weeks for individual participants.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments (ofatumumab or placebo) and created a report of the trial results.

This summary is based on that report.

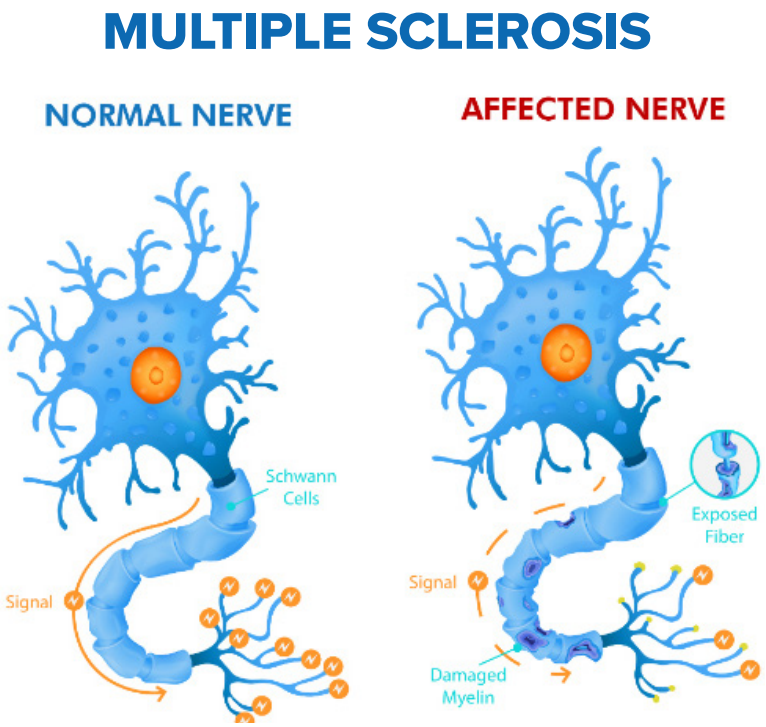
# Why was the research needed?

Multiple sclerosis (MS) is a condition that affects the brain and spinal cord. In patients with MS, the coating that protects the nerves, known as myelin, is damaged. This leads to nerve damage and the formation of areas of scar tissue known as lesions in the brain or spinal cord, which cause a range of symptoms. Brain lesions can be detected by magnetic resonance imaging (MRI).

Researchers were looking for a better way to treat a type of MS called relapsing MS. Patients with relapsing MS will have repeated attacks of neurological symptoms, called relapses.

The main purpose of this trial was to find out if ofatumumab was effective in reducing the number of brain lesions seen through MRI in patients with MS from Japan and outside Japan (i.e., Russia).

In people with MS, certain types of white blood cells can cause damage to the nervous system and lead to MS symptoms. Ofatumumab works to reduce the number of these white blood cells in the nervous system.



## Trial drugs

**The drugs given in this trial were:**

- **Ofatumumab:** an investigational drug being studied for the treatment of relapsing MS.

- **Placebo:** which looks like the trial drug but does not have any medicine in it. The use of placebo helps researchers to better understand the effect of a trial drug.

Both ofatumumab and placebo injections were given under the skin (subcutaneously) using a pre-filled syringe device.

## Trial purpose

This trial was done to learn more about the effects and safety of ofatumumab in patients with relapsing MS from Japan and outside Japan (i.e., Russia).

The main question the researchers wanted to answer in this trial was:
How well does ofatumumab work in reducing brain lesions seen on MRI scans in patients with MS?

Another question the researchers wanted to answer in this trial was:
Is the effect of treatment with ofatumumab similar in participants from Japan and outside Japan (i.e., Russia)?

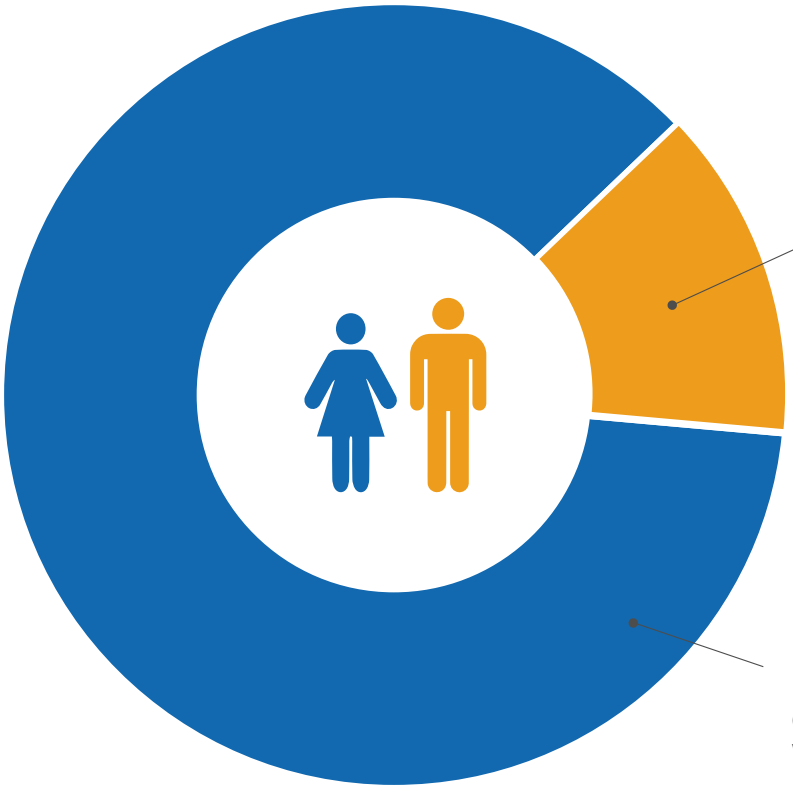
# Who was in this trial?

Participants could take part in this trial if they:

- were 18 to 55 years of age and had relapsing MS;
- had active disease with at least one relapse in the past 2 years prior to taking part in the study and a brain MRI scan indicating active MS in the past 1 year prior to trial participation;
- were neurologically stable for 1 month prior to the trial;
- did not have any disease of the immune system other than MS.

A total of **64 participants from two countries** (32 participants from Japan and 32 participants from Russia) took part in this trial.

The average age of participants in this trial was 35.2 years. A total of 85.9% of the trial participants, or 55 out of 64, were female. A total of 50% of participants were Asian and 50% of participants were White. Participants' age ranged from 18 to 55 years.



**14,1%**
**OF PARTICIPANTS WERE MALE**
**(9 out of 64)**

**85,9%**
**OF PARTICIPANTS WERE FEMALE**
**(55 out of 64)**

# What kind of trial was this?

This trial had a Core Part and an Extension Part. The Core Part of the trial was double-blind. This means that none of the participants, trial doctors, or trial staff knew what treatment participants were receiving. Some trials are done this way to ensure fairness towards all treatments because knowing what treatment each participant is getting can affect the results of the trial.

The Extension Part of the trial was open-label. This means that the participants, trial doctors, and trial staff knew what treatment participants were receiving.

# What happened during this trial?

Participants went through a **Screening** Period to confirm that they could take part in the trial. Participants who qualified entered the 24-week double-blind treatment period **(Core Part)** where they were randomly (by chance) put into 2 groups. This process is called randomization.
The participants were to receive either:

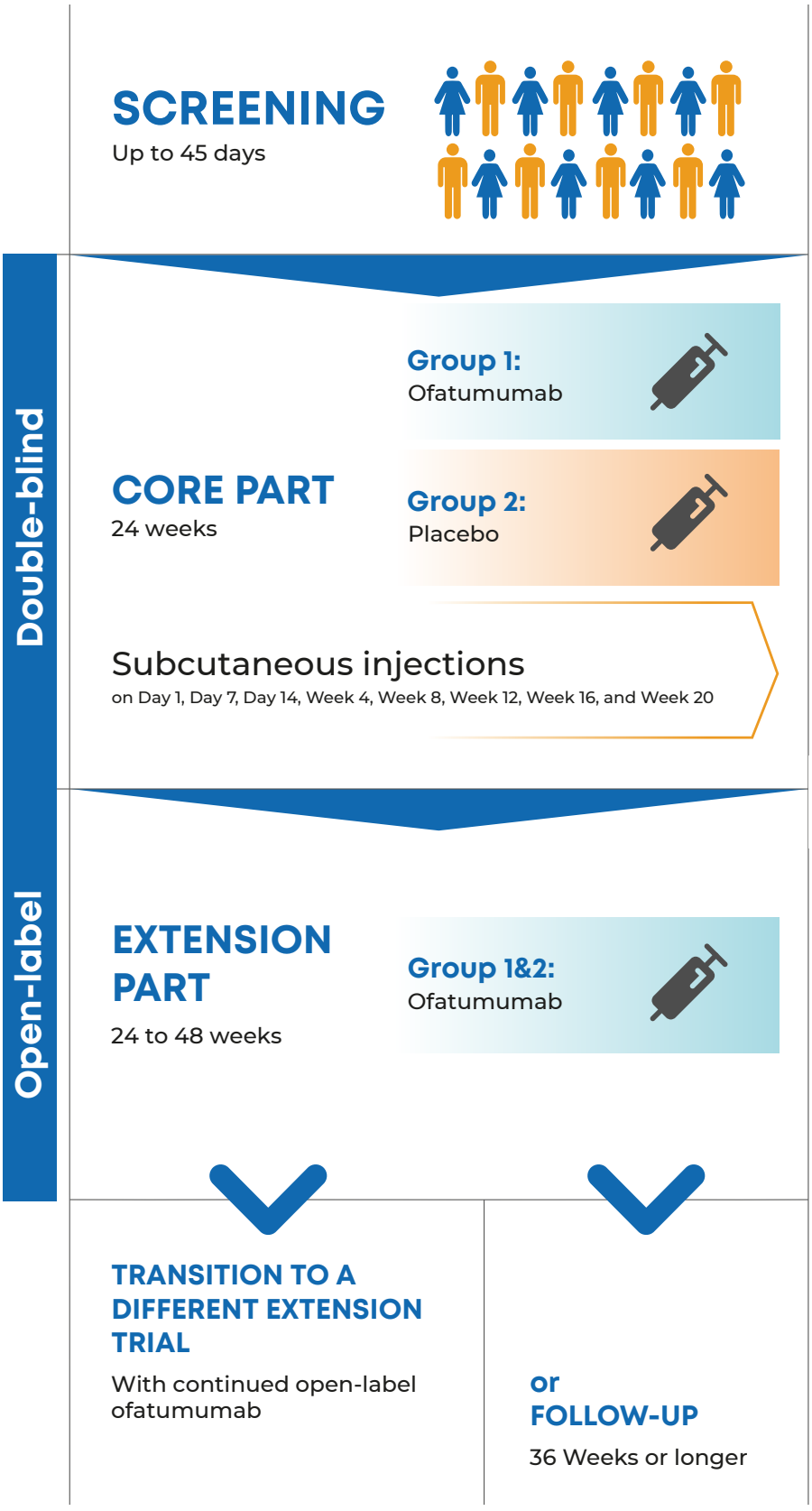
**Group 1:** ofatumumab injection administered via pre-filled syringe at a dose of 20 milligrams (mg).
**Group 2:** placebo injection administered via pre-filled syringe.

For every 3 participants who took part in the trial, 2 received ofatumumab and 1 received placebo. During the Core Part, participants were given ofatumumab injections on Day 1, Day 7, Day 14, and at Week 4, Week 8, Week 12, Week 16, and Week 20. Participants who were in the placebo group were given injections that looked like the ofatumumab injections but did not have any medicine in them.

After the Core Part, participants transitioned to the **Extension Part** lasting at least 24 weeks but not longer than 48 weeks. During the Extension Part, all participants from Group 1 and Group 2 received ofatumumab treatment.

MRI was used to assess MS lesions in the brain at Screening, throughout the Core and Extension Parts and at the end of the study.

The Extension Part continued until the last patient was transitioned to a different extension study or to the Post-treatment Follow-up period of this study. In the Post-treatment Follow-up period, participants were followed for up to 36 weeks or until their white blood cell levels returned to normal or the level they entered the study with, whichever occurred first after stopping study treatment.


SCREENING
Up to 45 days
Double-blind
Group 1:
Ofatumumab
CORE PART
24 weeks
Group 2:
Placebo
Subcutaneous injections
on Day 1, Day 7, Day 14, Week 4, Week 8, Week 12, Week 16, and Week 20
Open-label
EXTENSION PART
24 to 48 weeks
Group 1&2:
Ofatumumab
TRANSITION TO A DIFFERENT EXTENSION TRIAL
With continued open-label ofatumumab
or
FOLLOW-UP
36 Weeks or longer

# What were the key results of this trial?

This is a summary of the average results for all participants in different treatment groups. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. A detailed presentation of the results can be found on the websites listed at the end of this summary.

## How well does ofatumumab work in reducing brain lesions seen on MRI scans?

Researchers found that participants who received ofatumumab during the Core Part had 93.6% less active brain lesions on MRI scans when compared to participants that received placebo.

# What were other results of this trial?

The researchers also wanted to know the answer to the following question:

## Is the effect of treatment with ofatumumab similar in participants from Japan and in participants outside Japan?

Researchers found that participants from Japan who received ofatumumab in the Core Part had similar benefits to participants from outside Japan (i.e., Russia), with reduced numbers of active brain lesions on MRI scans when compared to placebo.

# 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. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. When new drugs are being studied, researchers keep track of all adverse events participants have.

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

## How many participants had adverse events?

Medical problems that happen in clinical trials are called “adverse events”.

In the **Core Part** of this trial, 23 out of 43 participants (53.5%) who received ofatumumab (Group 1) and 15 out of 21 participants (71.4%) who received placebo (Group 2) reported at least 1 adverse event. In the **Extension Part** of the trial, 23 out of 40 participants (57.5%) in Group 1 and 11 out of 19 participants (57.9%) in Group 2 reported at least 1 adverse event. None of the participants died during the study.

An adverse event is an unwanted sign, symptom, or disease 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 drug.

### Number of Participants (%) with Adverse Events

| | Core Part | | Extension Part | |
|---|---|---|---|---|
| | Group 1 Ofatumumab (Out of 43 participants) | Group 2 Placebo (Out of 21 participants) | Group 1 Continuing Ofatumumab (Out of 40 participants) | Group 2 Ofatumumab (after Placebo in Core Part) (Out of 19 participants) |
| At least 1 adverse event | 23 (53.5%) | 15 (71.4%) | 23 (57.5%) | 11 (57.9%) |
| At least 1 serious adverse event | 1 (2.3%) | 0 (0%) | 1 (2.5%) | 0 (0%) |
| Stopped drug due to adverse event | 0 (0%) | 0 (0%) | 2 (5%) | 0 (0%) |

# What was the most common non-serious adverse event?

Injection-related reaction, which is a bodily reaction to a medication injection, was the most common non-serious adverse event that happened in participants in both treatment groups in this study.

The table below summaries the most common non-serious adverse events that occurred in at least 5% of participants in one treatment group.

For a full list of the non-serious adverse events that occurred in this trial, please visit the websites listed at the end of this summary.

### Number of Participants (%) with most common non-serious Adverse Events

| | Core Part | | Extension Part | |
|---|---|---|---|---|
| | **Group 1 Ofatumumab** (Out of 43 participants) | **Group 2 Placebo** (Out of 21 participants) | **Group 1 Continuing Ofatumumab** (Out of 40 participants) | **Group 2 Ofatumumab** (after Placebo in Core Part) (Out of 19 participants) |
| **Injection-related reaction (bodily reaction to a medication injection)** | 9 (20.9%) | 4 (19%) | 1 (2.5%) | 4 (21.1%) |
| **Nasopharyngitis (nose and throat infection)** | 6 (14%) | 4 (19%) | 7 (17.5%) | 4 (21.1%) |
| **Oral herpes** | 4 (9.3%) | 0 (0%) | 2 (5%) | 0 (0%) |
| **Tension headache (feeling of a tight band around the head)** | 4 (9.3%) | 3 (14.3%) | 2 (5%) | 0 (0%) |
| **Back pain** | 3 (7%) | 1 (4.8%) | 0 (0%) | 1 (5.3%) |
| **Rash** | 1 (2.3%) | 0 (0%) | 3 (7.5%) | 0 (0%) |
| **Constipation** | 0 (0%) | 3 (14.3%) | 1 (2.5%) | 1 (5.3%) |
| **Insomnia (difficulty sleeping)** | 0 (0%) | 3 (14.3%) | 1 (2.5%) | 0 (0%) |

# What was the most common serious adverse event?

Serious adverse events occurred in 2 participants who received ofatumumab in this study. The events were acute heart failure and chronic inflammatory demyelinating polyradiculoneuropathy, which is a disorder in which the patient's immune system attacks myelin that protects the nerves.

### How many participants stopped trial drug due to adverse events?

During the trial, 2 of the participants who received ofatumumab in the Core Part and in the Extension Part stopped ofatumumab early due to an adverse event, one due to acute heart failure and one due to a positive test for viral hepatitis (a liver inflammation).

# How was this trial useful?

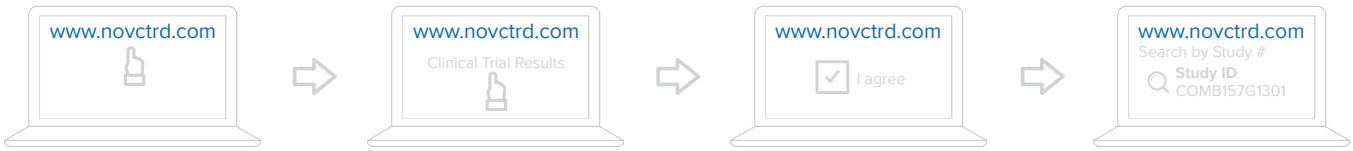
This trial helped researchers learn how well ofatumumab works and if it is safe in participants with relapsing MS.

Researchers found that, compared to placebo, treatment with ofatumumab resulted in a clear benefit to participants from both Japan and Russia.
The treatment with ofatumumab was well tolerated and the medical problems in this study were consistent with what was seen in the completed larger trials, COMB157G2301 and COMB157G2302.

This clinical trial was used to support approval for ofatumumab in Japan. 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 the following websites:
www.clinicaltrials.gov Use the NCT identifier NCT03249714 in the search field.

**Full clinical trial title:** A 24-week, randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate the efficacy, safety, and pharmacokinetics of ofatumumab in patients with relapsing multiple sclerosis followed by an extended treatment of at least 24 weeks with open-label ofatumumab.

## Thank You!

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researches answer important health questions and test new medical treatments.

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

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