Summary of Clinical Trial Results

A study to look at whether gantenerumab was safe for long-term use in people with Alzheimer's disease (Open RoAD)

See the end of the summary for the full title of the study.

About this summary

Contents of the summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

- Members of the public and
- People who took part in the study (participants)

The Open RoAD study started in May 2020. It was stopped early in January 2023 because the medicine being studied did not work as well as expected in two other studies (called GRADUATE I and GRADUATE II studies) that were looking at the same medicine in people with early AD.

This summary of the study was written after the study was stopped and represents the results at the time the study was stopped, which have been fully analysed.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from those seen in other studies with the same medicine.

This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

Glossary

- Amyloid protein = a type of protein found in higher amounts in the brains of people with Alzheimer's disease. These proteins can come together to form plaques (or "amyloid plaques") that can damage the brain
- ARIA-E = build-up of fluid or swelling in the brain seen on brain scans, that can occur with or without symptoms
- ARIA-H = bleeding in the brain seen in brain scans, that can occur with or without symptoms
- Care partner = family member, friend or paid helper who regularly looks after someone with a condition
- Early Alzheimer's disease = mild cognitive impairment due to Alzheimer's disease or mild dementia due to Alzheimer's disease

- Mild cognitive impairment = when people have small changes in memory, thinking and problem-solving but these do not yet significantly affect their day-to-day activities
- Mild dementia due to Alzheimer's disease = a stage of the disease when people may still function independently, but they have significant changes in memory, thinking and problem-solving that affect their day-to-day activities
- Open-label study = a study where both researchers and people participants know the treatment which a person is receiving
- Study partner = someone who is directly involved in helping a person with a condition take part in a clinical study (this role can be performed by a family member or friend)

Thank you to the people who took part in this study

The people who took part in this study, and their families and care partners, have helped researchers to answer important questions about Alzheimer's disease and the experimental medicine studied – gantenerumab, such as whether long-term treatment with gantenerumab was safe for people living with Alzheimer's disease. Since the study was stopped early, learnings from this study are limited.

Key information about this study

- The study (known as the Open RoAD study) investigated a new medicine called gantenerumab, in people with Alzheimer's disease who had previously completed approximately five years of treatment with gantenerumab in either the SCarlet RoAD or Marguerite RoAD open-label extension studies.
- The Open RoAD study was done to see whether the study medicine, gantenerumab, was safe for people with Alzheimer's disease over a longer period of time for up to an additional four years.
- The Open RoAD study was stopped early because the main findings from two other studies looking at gantenerumab (GRADUATE I and GRADUATE II studies) showed that gantenerumab was not effective (unlikely to help people with early Alzheimer's disease).
- A total of 116 people from 17 countries who completed either of the SCarlet RoAD or Marguerite RoAD open-label extension studies entered the Open RoAD study.
- Out of the 116 people entering the study, 115 participants received at least one dose of gantenerumab.
- Of these 115 participants, 21 (18.3%) experienced at least one possible adverse reaction and no serious possible adverse reactions were reported. Most possible adverse reactions were well tolerated (meaning mild to moderate in severity) and the types of possible adverse reactions people experienced were similar to those seen in previous gantenerumab studies.

1. General information about this study

Why was this study done?

Studies have shown that people with Alzheimer's disease have abnormally high levels of amyloid protein, which gathers together to form small clusters (oligomers) and clumps (amyloid plaques) in the brain.

Alzheimer's disease progresses in stages, but everyone experiences it differently. Symptoms progress from mild cognitive impairment due to Alzheimer's disease in the early stages, through to dementia that severely affects daily living in the later stages of the disease.

The SCarlet RoAD and Marguerite RoAD open-label extension studies were done to test whether gantenerumab was well tolerated in people with early Alzheimer's disease when given for approximately 5 years.

The Open RoAD study was done to test whether gantenerumab would be well tolerated when it was continued to be given to people with Alzheimer's disease who had completed the SCarlet RoAD and Marguerite RoAD open-label extension studies for an additional 4 years. The study was stopped early when data from approximately 1.5 years had been collected.

What was the study medicine?

A medicine called 'gantenerumab' was tested in the Open RoAD study.

- Gantenerumab is a type of monoclonal antibody, meaning that it is a kind of medicine that helps the immune system to specifically recognise and remove the harmful amyloid protein that is linked to Alzheimer's disease.
- Gantenerumab was given to people by injection at home or at a study site.

What did researchers want to find out?

- Researchers did this study to collect information on how safe the long-term use of gantenerumab is in people with Alzheimer's disease by checking how many people had possible adverse reactions

The main question that research doctors wanted to answer was:

- What are the possible adverse reactions of gantenerumab when given to people with Alzheimer's disease for up to an additional 4 years after completing their participation in the SCarlet RoAD and Marguerite RoAD open-label extension studies?

What kind of study was this?

This study was a 'Phase 3' study. This means that gantenerumab had been tested in a smaller number of people with Alzheimer's disease before the start of this study

In this study, it was planned that the people who had previously participated in the SCarlet RoAD or Marguerite RoAD open-label extension studies would continue to be given gantenerumab to investigate the possible adverse reactions of gantenerumab after long-term use in people with Alzheimer's disease.

This study was an 'open label' study. This means that both the people taking part in the study and the researchers knew all participants were receiving gantenerumab.

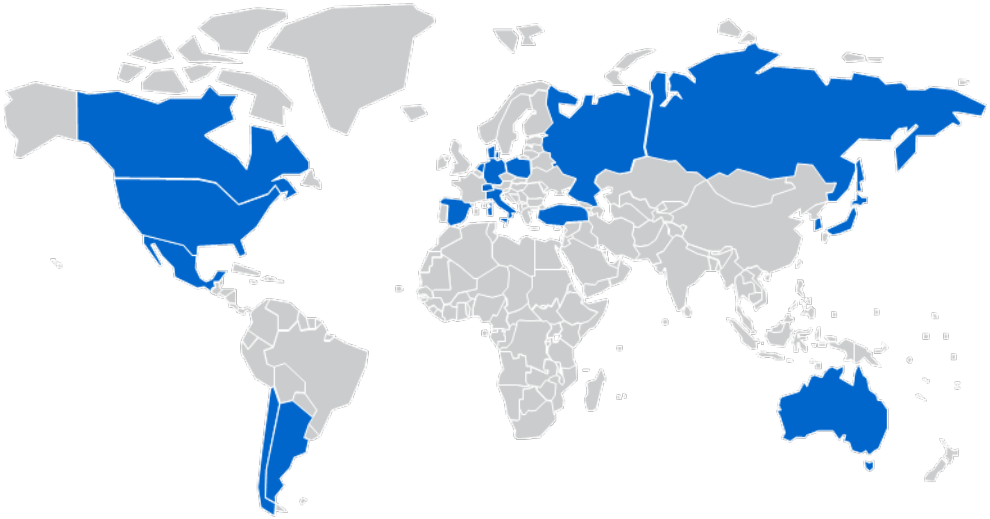
This study was a 'rollover' study. This means that only the participants from a previous related study, namely the SCarlet RoAD and Marguerite RoAD open-label extension studies, were offered the opportunity to participate in this study after the previous studies had been completed.

When and where did the study take place?

The Open RoAD study started in May 2020 and was stopped early because gantenerumab did not work as well as expected in two other studies (called GRADUATE I and GRADUATE II studies) that were looking at gantenerumab in people with early Alzheimer's disease. This summary presents the results of the study up until it was stopped in January 2023.

This study took place at 60 study centres across 18 countries in Asia, Australia, Europe, North America, and South America.

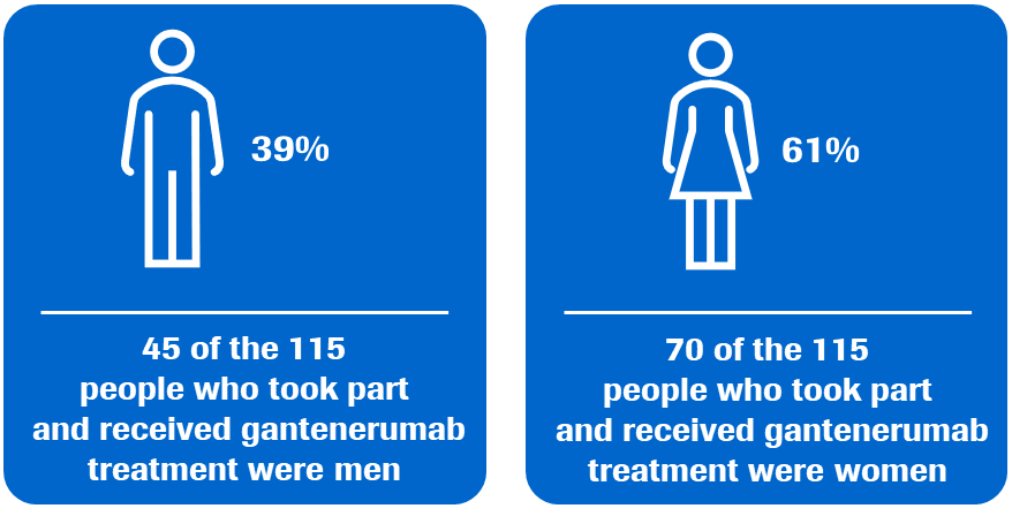
The following map shows the countries where any part of this study took place. The countries were:



- Argentina
- Australia
- Canada
- Chile
- Denmark
- Germany
- Italy
- Japan
- Korea, Republic of
- Mexico
- Netherlands
- Poland
- Russia
- Spain
- Switzerland
- Turkey
- United States

2. Who took part in this study?

A total of 115 adults with Alzheimer's disease took part in the Open RoAD study and received gantenerumab during the study.



People could take part in the study if they:

- had completed the SCarlet RoAD and Marguerite RoAD open-label extension studies.
- were in frequent contact with a dedicated study partner who could provide information on the person's progress.

People could not take part in the study if they:

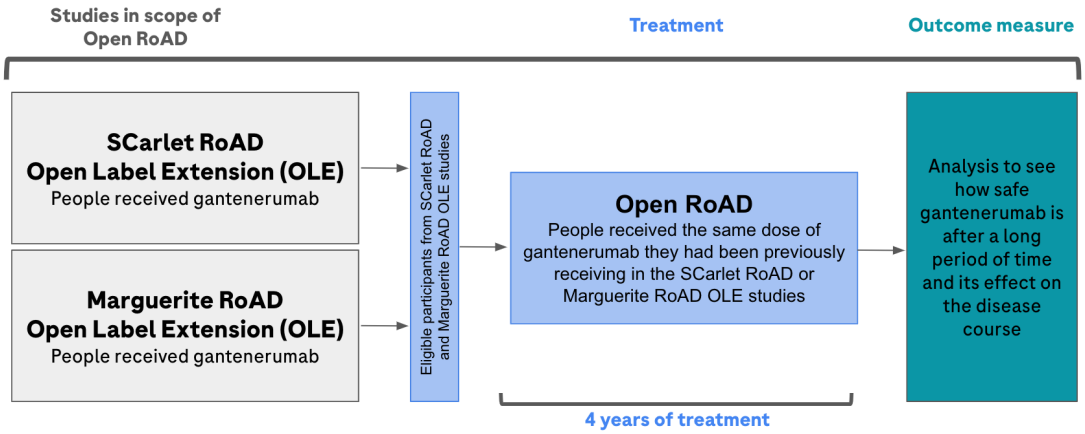
- left the SCarlet RoAD and Marguerite RoAD studies before the original or open-label extension parts of the study were completed;
- had other diseases caused by abnormal function of their brain; or
- had other diseases such as cancers, as well as heart, liver, immune, and metabolic diseases that were not already well controlled.

3. What happened during the study?

The Open RoAD study was intended for all people with Alzheimer's disease who finished the SCarlet RoAD and Marguerite RoAD open-label extension studies to continue taking gantenerumab for up to 4 additional years.

Because the study was stopped early, people only received gantenerumab for up to 1.5 years after completing the Scarlet RoAD and Marguerite RoAD open-label extension studies. People in the study had a follow-up visit 4 weeks after their last dose of gantenerumab.

Study design of the Open RoAD study



4. What were the results of the study?

Question: What are the possible adverse reactions of gantenerumab when given to people with Alzheimer's disease for up to an additional 4 years after completing their participation in the SCarlet RoAD and Marguerite RoAD open-label extension studies?

The Open RoAD study investigated the safety of gantenerumab by recording the number of possible adverse reactions, and particularly the number of serious possible adverse reactions, that people had during the study.

- The study showed that gantenerumab was well tolerated.
- Gantenerumab was given as an injection under the skin and some people reported reactions at the site of the injection such as redness, rash or swelling.
- All types of possible adverse reactions reported during this study were similar to those reported in other studies of gantenerumab (for example, headaches and falls).

Please see the next section (Section 5) for full details of the possible adverse reactions people had during the Open RoAD study

5. What were the possible adverse reactions?

Possible adverse reactions are medical problems (such as feeling dizzy) that happened during the study.

- They are described in this summary because the study doctors believed these possible adverse reactions were related to the treatments in the study.
- Not all of the people in this study had all of the possible adverse reactions.
- Possible adverse reactions may be mild to very serious and can be different from person to person.
- It is important to be aware that the possible adverse reactions reported here are from this single study. Therefore, the possible adverse reactions shown here may be different from those seen in other studies.
- Serious and common possible adverse reactions are listed in the following sections.

Overall, 21 out of 115 people (18.3%) who received gantenerumab in Open RoAD experienced at least one possible adverse reaction. In total, 217 possible adverse reactions were reported.

Most possible adverse reactions were mild or moderate meaning that they were easy to treat if necessary, and people recovered quickly.

Serious possible adverse reactions

A possible adverse reaction is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

During the Open RoAD study, there were no serious possible adverse reactions reported (considered to be related to the study treatment by the study doctors).

A total of 2 people died during the study data collection period. None of the deaths that occurred were considered by study doctors to be caused by treatment with gantenerumab.

During the study, a total of 3 out of 115 people (5.1%) stopped taking gantenerumab but this was not related to possible adverse reactions.

Possible adverse reactions

Most possible adverse reactions were mild or moderate, meaning that they were easy to treat if necessary, and people recovered quickly.

The adverse reactions of gantenerumab treatment include injection site reactions and amyloid-related imaging abnormalities (ARIA).

An injection site reaction is a reaction at the place where a medicine is injected under the skin, and can include redness, rash or swelling. A total of 20 in 115 (17.4%) people in the Open RoAD study experienced injection site reactions.

Amyloid-related imaging abnormalities (ARIA) are findings in the brain during magnetic resonance imaging (MRI) scans, sometimes experienced by people receiving gantenerumab and drugs similar to gantenerumab. These can occur with and without the person having any symptoms.

There are two types of ARIA: 1) ARIA-E, which involves transient build-up of fluid in the brain, and 2) ARIA-H, which is small bleeding in or on the surface of the brain.

None of the 115 participants in the Open RoAD study experienced an ARIA-E or ARIA-H possible adverse reaction.

Other possible adverse reactions

You can find information about other possible adverse reactions (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

While the Open RoAD study was stopped early because gantenerumab did not work as well as expected in GRADUATE I and GRADUATE II, this study showed that taking gantenerumab every four weeks over a long period of time was well tolerated.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

No other studies of gantenerumab are planned at this time.

8. Where can I find more information?

You can find more information about this study on the websites listed below:

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/neurodegenerative-disorder/ad/a-study-to-evaluate-the-safety-and-tolerability-of-long-88018.html
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- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the research doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “A Study to Evaluate the Safety and Tolerability of Long-term Administration of Gantenerumab in Participants With Alzheimer's Disease”.

The study is known as Open RoAD.

- The protocol number for this study is: WN41874.
- The ClinicalTrials.gov identifier for this study is: NCT04339413.
- The EudraCT number for this study is: 2019-004431-23.

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