Summary of Clinical Trial Results

A study of a new medicine (semorinemab) in patients with moderate Alzheimer's disease

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

About this summary

This is a summary of the results of a clinical trial (called a "study" in this document).

This summary is written for:

- Members of the public
- People who took part in the study

This summary is based on information known at the time of writing.

The study started in January 2019 and finished in August 2023. This summary was written after the study had ended.

A single study cannot tell us all there is to know about the risks and benefits of a medicine. It takes many people in several studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

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Contents of the summary

Thank you to the people who took part in this study

The people who took part in this study have helped researchers answer important questions about moderate Alzheimer's disease and the study medicine, semorinemab.

Key information about this study

- This study was done to see if a new medicine called "semorinemab" could help people with Alzheimer's disease.
- In the first part of the study, people got either semorinemab or a placebo. A placebo looks like the real medicine but doesn't have any actual medicine in it.
- After finishing the first part, everyone could join the second part, where they all got semorinemab.
- The study had 272 people from four different countries.
- People took two tests to check brain function and how well they could do daily activities – before and after the treatments. Only one of these tests showed that semorinemab helped a little.
- No one had any serious side effects that were thought to be caused by the treatments. In the first part, 27 people had mild side effects that were thought to be caused by the treatments (14 people on placebo and 13 on semorinemab). In the second part, 20 people had mild side effects that were thought to be caused by semorinemab.

1. General information about this study

Why was this study done?

Understanding Alzheimer's Disease
Around the world, about 50 million people have dementia, and the most common cause of dementia is Alzheimer's disease. In the United States, about 6.7 million people are affected by Alzheimer's.

People with Alzheimer's have changes in their brain cells. There are two main problems: "plaques" and "tangles."

What are Plaques and Tangles?
Plaques are sticky clumps of protein pieces that build up between nerve cells. These clumps contain a protein called "beta-amyloid."

Tangles are twisted strands of protein found inside cells. These strands have a protein called "tau." Normally, tau protein helps keep the strands straight, but in people with Alzheimer's, the tau protein gets twisted up. When these tangles form, they mess up the smooth flow of supplies inside the cells, causing the cells to die.

Stages and Treatments
Doctors diagnose Alzheimer's disease based on how well a person can function and think. They use the term "functional and cognitive decline" to describe changes from what is normal. Some medicines can help improve symptoms for a while, but they do not stop the disease from getting worse.

A New Medicine: Semorinemab
Semorinemab is a new medicine. This study was done to see if semorinemab could be used to treat Alzheimer's disease. People who joined the study had moderate Alzheimer's disease.

What was the medicine being studied?

This study looked at 2 treatments:

- **Semorinemab** is a new medicine that might help people with Alzheimer's disease. It is a special kind of medicine that sticks to the "tau" protein outside cells. This could stop tau proteins from making tangles inside the cells.
- Some people got a "**placebo**" treatment. The placebo looked like semorinemab but didn't have any real medicine in it. By comparing what happened to people who got semorinemab with those who got placebo, researchers could see how well the real medicine worked.

What did researchers want to find out?

Researchers did this study to compare semorinemab with the placebo – to see how well semorinemab worked.

The main questions that researchers wanted to answer were:

1. Did people with moderate Alzheimer's disease do better on memory and function tests after getting semorinemab compared to those who got a fake treatment (placebo)?
2. Was semorinemab safe and easy for people to handle compared to the fake treatment (placebo)?

What kind of study was this?

There are several ways to describe this study.

Phase 2 study
Phase 2 studies check if the medicine works for people with the disease. Semorinemab was tested on healthy people first, in Phase 1 studies, and found to be safe, before it was given to patients in the Phase 2 study.

Randomized study
A computer picked at random who got the real medicine and who got the fake one (placebo). Neither the researchers nor the people in the study could choose.

Double-blind study
Nobody knew who was getting the real medicine and who was getting the placebo, not even the researchers. This is called a double-blind study.

Placebo-controlled study
Some people got the real medicine, and some got a fake treatment (placebo). This helped to show how well the real medicine worked compared to the placebo.

Parallel-group study
This type of study compares two or more treatments at the same time. People were randomly put into different treatment groups, and at the end, the results of these groups were compared.

When and where did the study take place?

The study started in January 2019 and finished in August 2023. This summary was written after the study had ended.

The study took place at 49 study centers – across four countries: United States (31 study sites), Spain (6 study sites), Poland (7 study sites), and France (5 study sites).

2. Who took part in this study?

Two hundred and seventy-two people took part in this study. Among these, 176 (65%) were female and 96 (35%) were male. People were between 51 and 86 years old.

People could take part in the study if: they met all the following:

- They were between 50 and 85 years old.
- Doctors believed they had symptoms for dementia due to Alzheimer's disease.
- They tested positive for Alzheimer's disease through a brain scan (PET scan) or spinal tap (lumbar puncture) to look for proteins associated with Alzheimer's disease.
- Memory tests indicated Alzheimer's disease of moderate severity.

People could not take part in the study if they met any of the following:

- They could not tolerate brain imaging procedures (magnetic resonance imaging – MRI), PET scan, or spinal tap.
- They received care and lived in a nursing home.
- They had a planned procedure or surgery that would interfere with the study.
- They had a serious medical condition or abnormal blood test results.
- They had other types of brain or mental health disorders.

3. What happened during the study?

People who met the study requirements could join. The study had two parts. First was the "double-blind treatment" period. After that came the "open-label extension" period.

Double-blind treatment:

- A computer randomly chose the treatment for each person. 136 people got semorinemab, and another 136 got a fake treatment (placebo). No one, not even the study staff, knew who got which treatment.
- People received their treatment through an IV (a tube in their vein).
    - For the first 3 doses, they got treated once every two weeks.
    - Starting with the fourth dose, they got treated once every 4 weeks.
- People were treated for 48 weeks. If they didn't miss any doses, they were in "Group 1."
- In they missed one or more doses during the 48 weeks, their treatment was extended to 60 weeks, and they were in "Group 2."

Measuring the effect of the treatments:

- Study staff gave people two different tests to measure brain function. These were given before the treatments started and after the double-blind treatments were over, during Week 49 for Group 1 and Weeks 49 and 61 for Group 2.
    - One test was called "**ADAS-Cog11**." It checks how well different parts of the brain are working in people with Alzheimer's disease.
    - The other test was called "**ADCS-ADL**." It checks how well people can do daily activities.

Open-label extension

- People who finished the double-blind treatment could join the open-label extension study. They received semorinemab once every 4 weeks for up to 96 weeks. 199 people joined this part of the study.

4. What were the results of the study?

Question 1: Did people with moderate Alzheimer's disease do better on memory and function tests after getting semorinemab treatment compared to those who got a fake treatment (placebo)?

ADAS-Cog11: At Week 49 and Week 61, people who got semorinemab had fewer thinking and memory problems that those who got the fake treatment (placebo).

ADCS-ADL: Semorinemab did not slow down how quickly people lost their ability to do everyday activities. This was checked from the start of the study to Week 49 for Group 1 and to Weeks 49 and 61 for Group 2.

Question 2: Was semorinemab safe and easy for people to handle compared to the fake treatment (placebo)??

Overall, people did well with semorinemab. It was safe to use and didn't cause unexpected problems. The side effects were what the researchers expected and were similar for both treatments in the study. However, there were more side effects (infusion related reactions) during semorinemab infusions than placebo infusions, but these were not serious. Side effects are discussed in detail in Section 5.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see Section 8).

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happened during the study.

- If they were seen in this study, they are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Everybody in a study will not have all the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflet.
- Serious and common side effects are listed in the following sections if they were seen in this study.

Serious side effects

A side effect is considered “serious” if it is life-threatening, needs hospital care, or causes lasting problems. There weren’t any serious side effects from semorinemab or the fake treatment (placebo) that were thought to be caused by these treatments.

Deaths during the study:

- Six people (2%) died while on the study but none of the deaths were caused by the study treatment.
    - One person who received semorinemab during the double-blind period died from an unknown reason.
    - Three people who got fake treatment (placebo) during the double-blind period died – two for unknown reasons and one due to COVID-19.
    - Two people who received semorinemab during the open-label period died due to COVID-19.

Stopping treatment because of side effects:

- Some people stopped their treatment because of side effects.
    - 6 people (5%) who got fake treatment (placebo)
    - 7 people (5%) who got semorinemab

Most common side effects

During the study, 14 people (11%) who got the fake treatment (placebo) and 13 people (10%) who got semorinemab had side effects. These side effects were not serious but were thought to be caused by the study treatment.

Here are the most common side effects. Some people had more than one side effect and are counted on more than one line in the table below:

Side effect	**People treated with semorinemab who had this side effect**	**People treated with placebo who had this side effect**
Taking a fall	14 people (10%)	19 people (14%)
An infection in any part of the urinary tract (urinary tract infection or UTI)	11 people (8%)	16 people (12%)
Feeling worried, nervous, or scared (anxiety)	9 people (7%)	12 people (9%)
Headache	11 people (8%)	9 people (7%)
Infusion related reaction	14 people (10%)	5 people (4%)
A persistent feeling of sadness and loss of interest that can affect daily functioning (depression)	10 people (7%)	7 people (5%)

Other side effects

You can find information about other side effects (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?

The information presented here is from a single study of 272 people with moderate Alzheimer's disease. These results helped researchers learn more about Alzheimer's disease and semorinemab.

A single study cannot tell us all there is to know about the risks and benefits of a medicine. It takes many people in several studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

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7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at semorinemab were planned.

8. Where can I find more information?

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

- https://clinicaltrials.gov/study/NCT03828747
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2018-003398-87/results
- https://forpatients.roche.com/en/trials/neurodegenerative-disorder/ad/a-study-of-mtau9937a-in-patients-with-moderate-alzheime-94595.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: "Randomized Phase II Study of the Safety and Efficacy of Semorinemab in Participants with Mild-to-Moderate Alzheimer Disease: Lauriet". The authors of the scientific paper are C. Monteiro, B. Toth, F. Brunstein, A. Bobbala, S. Datta, and others. The paper is published in the journal "Neurology," volume number 101(14), on pages e1391-e1401.

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/About.html
- 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 study 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 organized and paid for this study?

This study was organized and paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

- The full title of this study is:
  A phase II, multicenter, randomized, double-blind, placebo-controlled, parallel-group, efficacy, and safety study of MTAU9937A in patients with moderate Alzheimer's disease
- The study is known as "Lauriet."
- The protocol number for this study is GN40040.
- The ClinicalTrials.gov identifier for this study is NCT03828747.
- The EudraCT number for this study is 2018-003398-87.