Summary of Clinical Trial Results

A study comparing different tools for looking at the brain in people with Alzheimer's disease: tau radiotracers for brain imaging with Positron Emission Tomography (PET)

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 October 2020 and finished in July 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 radiotracer. 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 radiotracer.

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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 Alzheimer's disease and the tau radiotracers tested in this study.

Key information about this study

- This study looked at three different radiotracers used for looking at the brain in pictures (brain scans) of people with and without Alzheimer's disease.
- The radiotracers were: [^{18}F]GTP1, [^{18}F]PI-2620, and [^{18}F]MK-6240. They were given to people through an IV. These radiotracers reversibly stick to "tau protein", found in the brain in people with Alzheimer's disease.
- The study included 50 people at one study center in the USA.
- Researchers found brain scan results for the different radiotracers were very similar. They were good at finding tau in the brain, except in one area (the hippocampus).
- There were no serious side effects or deaths reported during the study. Two people had non-serious side effects that researchers thought were caused by the radiotracers.
- This study showed that brain scans with all three radiotracers were safe and provided similar information.

1. General information about this study

Why was this study done?

Understanding Alzheimer's disease and tau protein
In our healthy brains, tau proteins make sure that the nerve cells (neurons) in our brain stay strong and work properly. They do this by stabilizing microtubules, which are important for the shape of the nerve cells and helps them do their job.

What happens in Alzheimer's disease
When someone has Alzheimer's disease, the tau proteins go through an unhealthy change called hyperphosphorylation. This makes them fall off the microtubules. When they fall off, they start to stick together in clumps. These clumps twist and turn into something called "neurofibrillary tangles."

Neurofibrillary tangles are bad news
As more and more neurofibrillary tangles pile up in a nerve cell, this can eventually cause the cell to die. The more tangles there are, the worse the brain works, which leads to problems with memory and thinking.

Tau protein is a biomarker
A biomarker is something doctors can measure to learn about a disease. Tau protein is an important biomarker for Alzheimer's disease. By measuring tau, doctors can see if someone has Alzheimer's, how far it has progressed, and if treatments are working.

How can you see tau proteins
Doctors take pictures of the brain using Positron Emission Tomography (PET) scans to look at tau proteins. This scan uses something called a radiotracer.

What Is a Radiotracer
Radiotracers contain a small amount of radiation, at a safe level, which allows us to see them on a brain scan. A radiotracer is a chemical that doctors inject into your body through a vein (IV). It travels around your body and is designed to reversibly stick to a protein. Tau radiotracers stick to tau proteins, and the area lights up in brain scans. It helps doctors see how much tau protein is present, and where it is located.

Why was this study done

There are different kinds of radiotracers that can find tau proteins. This study compared three different radiotracers to see if they produced similar pictures of the brain. Knowing whether different radiotracers will provide similar information will help doctors decide which ones can be used in large clinical trials, where many patients undergo PET scans, potentially with different radiotracers. Overall, radiotracers allow for a better look at the brain to find out if study medicines are effective. This will help find better treatments faster in large studies.

What was the medicine being studied?

Radiotracers are given to people through an IV and then doctors use a PET scan to take pictures of the brain.

- They help doctors see clumps of tau protein in the brain.
- They move quickly through the body, give clear pictures, and then are removed (eliminated) from the body.
- Because these were made for tau proteins, they do not stick well to other parts of the body.
- They can show doctors which areas of the brain have disease present.

The three different radiotracers used in this study were:

- **[^{18}F]PI-2620**, also known as [^{18}F]MNI-960.
- **[^{18}F]GTP1**, also known by other names: [^{18}F]G02941054, [^{18}F]MNI-798, and [^{18}F]RO6880276).
- **[^{18}F]MK-6240**, also known as [^{18}F]MNI-946.

What did researchers want to find out?

Researchers did this study to learn whether certain brain radiotracers provide the same information.

People:

- This study looked at healthy people and people with Alzheimer's disease.

Radiotracers:

- Researchers looked at three different radiotracers in this study. They compared [^{18}F]GTP1 to [^{18}F]PI-2620 and [^{18}F]MK-6240.

Understanding **SUVR** (Standardized Uptake Value Ratio):

- What Is SUVR? SUVR is a way to measure how much of a radiotracer is taken up by different parts of the brain. It helps doctors compare the amount of radiotracer in one area to another.
- How Is SUVR calculated? It is calculated by dividing the amount of tracer in the target area by the amount in a reference area. This helps compare tracer uptake across different people or different brain regions.

Understanding **ROI** (Region of Interest):

- What Is an ROI? ROI is a specific area in the brain that researchers focus on during imaging studies.

- ROIs in this study: Researchers looked at areas in the brain known to have tau deposits, like the hippocampus and entorhinal cortex. By studying these areas, they can understand more about where and how much tau is present.
- **Braak ROIs**: These are specific areas of the brain named after a scientist named Braak. Researchers study these areas to understand brain diseases better.

The main questions that researchers wanted to answer were:

1. How does the distribution of tau protein look when comparing the three radiotracers?
2. Were the radiotracers safe for people? Did they cause any side effects?

What kind of study was this?

Phase 1 study
One or more Phase 1 studies are carried out to find out basic information about a new medicine. A medicine has therapeutic effects on a disease. Radiotracers for PET imaging are not "medicines," but are "radiopharmaceuticals," a specialized category that combines features of medicines and diagnostic tools. Diagnostic tools are used in medical practice to learn about what the disease is. Radiopharmaceuticals are regulated by the government similarly to medicines.

When and where did the study take place?

The study started in October 2020 and finished in July 2023. This summary was written after the study had ended.

The study took place at one study center in one country – the USA.

2. Who took part in this study?

Fifty people joined this study. They were between 64 to 82 years old. There were 22 males (44%) and 28 females (56%).

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

- Provided a written informed consent form
- Females in the study were not pregnant and could not become pregnant
- Males in the study agreed to use birth control and refrain from donating sperm
- People with normal brain function were 65 to 90 years old and had at least one close relative with Alzheimer's disease
- People with Alzheimer's disease were 50 to 90 years old and met the brain test scores for the disease
- Other tests were also used for staging people into groups with different levels of brain function, including clinical dementia rating, mini-mental state exam, beta-amyloid PET imaging, and brain MRI imaging

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

- History of or current drug or alcohol abuse
- Any health condition from a list of conditions that were not allowed
- They participated in another study in the last 3 months
- They had been exposed to radiation that was over the annual limit
- Women who were pregnant, lactating, or breastfeeding

3. What happened during the study?

This was a research study to test different radiotracers to see tau proteins in the brain using PET scans. The study was open-label, which means everyone knew what was being tested.

Study Steps:

- Screening: Researchers asked questions and did medical tests. People who were interested in joining the study and who met all the study conditions could then join the study.
    - Tests included memory and thinking tests, checking vital signs, ECG, physical exam, and brain MRI.
    - A separate PET scan to check for a protein in the brain (beta-amyloid [Aβ] deposits) was done for people with Alzheimer's, and sometimes for healthy people.
- Tau PET Scans:
    - Each person had either two or three tau PET scans with different tracers.
    - People in the study received the tracer via an IV injection.
    - Follow-up safety calls were made 4 days after each scan.
    - The second scan was done within 1 to 45 days after the first, usually within 14 days.

People in the study:
Each group had five people with normal thinking abilities and more people with mild to moderate Alzheimer's. All participants went to one clinical site for the study.

Study Groups:

- Group 1: These people had two PET scans: one with [^{18}F]PI-2620 and one with [^{18}F]GTP1, in no specific order.
- Group 2: These people also had two PET scans: one with [^{18}F]GTP1 and one with [^{18}F]MK-6240, in no specific order.
- People from Group 1 could join Group 2 if they could do the [^{18}F]MK-6240 scan within 45 days of their [^{18}F]GTP1 scan and stayed within safe radiation limits.

4. What were the results of the study?

Question 1: How does the distribution of tau protein look when comparing the three radiotracers?

Comparing Brain Scans

- Similar results between tracers for seeing tau proteins: Researchers found that the SUVR values (which show how much tracer is in different brain areas) of [^{18}F]GTP1 were very similar to those of [^{18}F]PI-2620 and [^{18}F]MK-6240 in almost all brain regions they looked at. The only exception was the Braak II area, which includes the hippocampus, an important part of the brain for memory.
- Different off-target signals: Each tracer had different "off-target signals." This means that sometimes the tracers showed up in places they weren’t supposed to. These differences can make it harder to accurately measure how much tracer is in nearby brain regions.

Question 2: Were the radiotracers safe for people? Did they cause any side effects?

Before this study, doctors had already been using the three radiotracers. However, this study was the first time all three radiotracers were compared to each other.

Researchers found all three radiotracers were safe to use, which was the same as what doctors outside of this study had observed. There were some side effects, and these are described in the next section.

Section 4 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.
- Not everyone in a study will 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 radiotracer 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 were no serious side effects in this study.

There were no side effects that caused anyone to stop the study or change the brain scan procedure in any way to accommodate any side effects.

There were no deaths in this study due to side effects.

Most common side effects

Two people (4%) got side effects that were not serious but were caused by the study treatment.

- One person who received [^{18}F]GTP1 radiotracer felt dizzy.
- One person who received [^{18}F]MK-6240 radiotracer had a headache.

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 50 people, some of whom were healthy and others had Alzheimer's. These results helped researchers learn more about radiotracers used for looking at the brain in people with Alzheimer's.

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7. Are there plans for other studies?

At the time of writing this summary, other studies to compare the three radiotracers were not 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/NCT04566003
- https://forpatients.roche.com/en/trials/neurodegenerative-disorder/ad/evaluation-comparing-two-tau-pet-radiotracers---18f-pi--90861.html

If you would like to find out more about the results of this study, the relevant scientific publications are:

- Sanabria Bohorquez S, Constantinescu C, Manser PT, et al. In vivo head-to-head comparison of [18F]GTP1 and [18F]PI2620 in Alzheimer's disease. Alzheimers Dement 2022; 18(Suppl. 6):e063513.
- Tonietto M, Constantinescu C, Sanabria Bohorquez S, et al. In vivo head-to-head comparison of [18F]GTP1 and [18F]MK6240 in Alzheimer's disease. J Prev Alzheimers Dis 2022; 9:S132–3.
- Tonietto M, Constantinescu CC, Sanabria Bohorquez S, et al. In vivo head-to-head comparison of [18F]GTP1, [18F]PI2620, and [18F]MK6240 in Alzheimer's disease. 2023. 14th Human Amyloid Imaging Conference Program Book, 46–7.

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:
Phase 1 evaluation comparing tau PET radiotracers, [^{18}F]GTP1 and [^{18}F]PI-2620 or [^{18}F]MK-6240 in subjects with normal cognition or prodromal to moderate Alzheimer's disease.

- The protocol number for this study is GN42801.
- The ClinicalTrials.gov identifier for this study is NCT04566003.