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A Study of TAK-105 in Healthy Adults

THANK YOU!

Thank you to all of the participants who took part in this study.

Takeda sponsored this study and thinks it is important to share the results of the study with the study participants and the public.

This summary reports the main results of this study.

Key points of the study:

TAK-105 is being studied as a potential treatment for nausea and vomiting. The main purpose of the study was to check the safety of TAK-105 when given to healthy adults. In this study, participants were given either TAK-105 or placebo as an injection under the skin in increasing doses. Researchers checked how much TAK-105 could be given to the participants without them having any medical problems.

This study showed that TAK-105 was tolerated by the healthy participants. This study was planned to be conducted in 6 parts, however due to safety findings only 2 parts of the study were conducted. The study was considered completed based on the completion of these 2 parts.

Why was this study done?

Nausea and vomiting are common symptoms associated with many diseases or as medical problems from various medicines. Gamma-aminobutyric acid (GABA) is a brain messenger that sends a signal to the brain to control vomiting. Glucose-dependent insulinotropic polypeptide receptors (GIPR), when activated, support GABA to send signals to control and stop vomiting.

This study medicine, TAK-105, helps activate GIPR, which researchers believe could help prevent nausea and vomiting. TAK-105 may help prevent nausea and vomiting for a longer period, which may reduce the frequency at which participants receive treatment. Therefore, this saves the participants from taking many doses of the medicine.

What are medical problems?

Medical problems are any new or worsening problems that the participants had after they took the study medications. They may or may not be related to the study drug.

In this study, researchers wanted to learn about the safety of TAK-105. Participants were treated with TAK-105 at increasing doses to check how much medicine could be given to participants without causing any medical problems. The main aim of the study was to check if healthy adults would have any medical problems from taking TAK-105 when compared to a placebo. A placebo looks like TAK-105 but has no medicine in it. A placebo helps researchers learn about the real effects of the treatment. Researchers also wanted to check how much TAK-105 could be given without causing any medical problems.

What were the main questions?

In this study, the researchers wanted to learn about the safety of TAK-105 in healthy participants. This was done by giving TAK-105 at increasing doses to find out how much could be given to the participants without them having any medical problems. The following was the main questions asked by the researchers:

- **How many participants had medical problems during the study?**

How was the study done?

What type of study was this?

Clinical studies are done as part of the development of a new treatment. The type of clinical study depends on the stage, or phase, of development. These studies are called Phase 1 to Phase 4 studies.

- This was a Phase 1 study where a small number of healthy people received the potential medicine or treatment. This was done to check its safety.
- This was a double-blinded study. This meant that none of the participants, doctors, or other study clinic staff knew which treatment each participant received. This is done because knowing what treatment the participants are receiving could affect the results of the study.

What treatments were studied?

Participants were assigned to their treatment group by chance (randomly). This helped to make the treatment groups as similar as possible.

The participants received 1 of the following treatments:

- TAK-105, given as a subcutaneous injection, which is an injection under the skin.
- Placebo, given as a subcutaneous injection.

A placebo looks the same as TAK-105 but has no medicine in it. This helped the researchers learn about the real effects of the treatment.

What happened during the study?

The study doctors checked that each participant met the study rules before they joined the study.

The study was planned to be conducted in 6 parts. However, based on the review of the safety data collected during the study, the sponsor decided to discontinue the study. The study Parts 3, 4, 5, and 6 were not conducted after the completion of the ongoing Parts 1 and 2 of the study.

PART 1

- Part 1 of the study included up to 8 groups.
- Participants were assigned to any one of the 8 groups to receive a single dose of TAK-105 or placebo. Participants had a higher chance of receiving TAK-105 as compared to the placebo.
- Each group received a different dose of TAK-105.
- At the start, they received a smaller dose followed by increasing doses within each group.
- Participants' vital signs, including heart rate and blood pressure, along with other blood tests were done a day before the medicine was given.
- On Day 1, the participants were given a single dose of either TAK-105 or placebo after a minimum of 8 hours of fasting.
- After they were treated, they were required to stay in the clinic for 8 days to monitor their safety.
- Their vital signs were also checked after the medicine was given. The researchers also took blood and urine samples to check for any changes in the participant's well-being.
- Participants had follow-up visits on Days 15, 29, 45, and 60.

PART 2

- Part 2 was conducted before completion of Part 1. The doses of TAK-105 were chosen based on a dose that was lower than the highest dose being tested during Part 1 of the study.
- Part 2 included up to 3 groups.
- Participants were given multiple doses of TAK-105 or placebo.
- Each group received a different dose of TAK-105.
- Participants' vital signs, including heart rate and blood pressure, along with other blood tests were done a day before the medicine was given.
- They received an injection of either TAK-105 or placebo on Days 1, 8, 15, and 22 after a minimum of 8 hours of fasting.
- The participants stayed in the clinic for 48 hours after the last dose was given. This was done to monitor safety and how well the participants would tolerate the medicine.
- Their vital signs were also checked after the medicine was given. The researchers took blood and urine samples to check for any changes in the participant's well-being.
- Participants had follow-up visits on Days 30, 37, 51, 67 and 82.

During Parts 3 to 5, participants were supposed to receive either TAK-105 or placebo in different dosing patterns. Part 6 was planned for the testing of a new formulation of TAK-

105. However, these parts of the study were not conducted. The overall duration of the study was 22 months.

Before treatment	During Treatment	After Treatment
Check-up including checks on their general health, medical history, and vital signs	The study was done in 2 parts. Part 1: Participants were given a single dose of TAK-105 or placebo: 42 participants took TAK-105 14 participants took a placebo Part 2: Participants were given multiple doses of TAK-105 or placebo: 18 participants took TAK-105 6 participants took a placebo	Check-up including recording medical problems, vital signs, as well as other laboratory tests.

Who took part in the study?

Potential participants could take part if:

- They were 18 to 55 years of age.
- They were healthy.
- They were non-smokers.

Potential participants could not take part if:

- They had participated in another clinical study within 4 weeks before the start of the study.
- They had a history of several allergies or other medical conditions.

All 80 participants who joined the study were treated.

They were from 20 to 55 years old when they joined the study.

How many participants took part?	
80 participants joined the study 80 participants were treated	
Which treatment group were the participants in?	
56 participants were in the Part 1 of the study	24 participants were in the Part 2 of the study
49 men 7 women	19 Men 5 women
20 to 55 years old	23 to 55 years old

Where was the study done?

This study took place in 3 study clinics in the United States.

When was the study done?

The study started in August 2021 and ended in June 2023. The overall study duration was up to 1 year and 10 months.

What were the study results?

This summary gives the main results of this single study. Other studies may give different results. Researchers look at the results of many studies to decide which medicines work best and are safest for patients. Always speak with your doctor before changing your treatment.

The researchers wanted to answer the following question:

- **How many participants had medical problems during the study?**

Researchers collected information on all medical problems participants experienced after receiving a dose of TAK-105 or placebo. Medical problems may or may not be caused by the study medication.

The table below shows how many participants from each group experienced medical problems.

Number of participants experiencing medical problems in Part 1		
	TAK-105 (42 participants)	**Placebo** (14 participants)
Any medical problem	26 participants (62%)	6 participants (43%)

Number of participants experiencing medical problems in Part 2		
	TAK-105 (18 participants)	**Placebo** (6 participants)
Any medical problem	15 participants (83%)	6 participants (100%)

Were there any medical problems?

In a clinical study, the study doctors record all medical problems the participants have during the study. They do this whether or not they think these problems were caused by the study treatment. These medical problems are called **adverse events**. If the study doctors think some of these medical problems might be caused by the study treatment, they are called **side effects**.

The medical problems shown here are from a total of 80 participants who received study treatment.

Possible side effects in this study may be different to the side effects shown on package leaflets of approved medicines. Other studies of the same treatment may report different side effects. It takes the results of many studies to understand if medical problems may be caused by a treatment.

How many participants had medical problems?

During this study, 32 out of 56 participants (57%) in Part 1 and 21 out of 24 participants (88%) in Part 2 had medical problems that occurred within 30 days after getting the last dose of the treatment.

2 out of 24 participants (8%) in Part 2 stopped study treatment early due to medical problems.

Information on Medical Problems (Part 1)		
	TAK-105 (42 participants)	**Placebo** (14 participants)
How many participants had medical problems?	26 participants (62%)	6 participants (43%)
How many participants stopped the study treatment due to medical problems?	0	0

Information on Medical Problems (Part 2)		
	TAK-105 (18 participants)	**Placebo** (6 participants)
How many participants had medical problems?	15 participants (83%)	6 participants (100%)
How many participants stopped the study treatment due to medical problems?	1 participant (6%)	1 participant (17%)

Medical problems that happened in at least 4% of the participants in Part 1 are shown here.

Medical Problems in at Least 4% of the Participants in Part 1		
	TAK-105 (42 participants)	**Placebo** (14 participants)
Rapid heartbeat (Tachycardia)	14 participants (33%)	3 participants (21%)
Inflammation of the skin at the site of medical device (medical device site dermatitis)	1 participant (2%)	2 participants (14%)
Dizziness	3 participants (7%)	0
Headache	3 participants (7%)	0
Abnormally fast heartbeats (supraventricular extrasystoles)	2 participants (5%)	0
Condition in which the lower chambers of the heart (ventricles) beat very quickly, but the increased heartbeat stops on its own within 30 seconds (non-sustained ventricular tachycardia)	2 participants (5%)	0
Nausea	2 participants (5%)	0
Irritation of the skin at the site of medical device (medical device site irritation)	2 participants (5%)	0

In Part 1, the most common medical problems were rapid heartbeat, inflammation of the skin at the site of medical device, dizziness, and headache.

Medical problems that happened in at least 8% of the participants in Part 2 are shown here.

Medical Problems in at Least 8% of the Participants in Part 2		
	TAK-105 (18 participants)	**Placebo** (6 participants)
Inflammation of the skin at the site of medical device (medical device site dermatitis)	10 participants (56%)	4 participants (67%)
Rapid heartbeat (tachycardia)	5 participants (28%)	1 participant (17%)
Headache	4 participants (22%)	0
Constipation	2 participants (11%)	1 participant (17%)
Rapid or irregular heartbeats (palpitation)	2 participants (11%)	0
Condition in which the lower chambers of the heart (ventricles) beat very quickly, but the increased heartbeat stops on its own within 30 seconds (non-sustained ventricular tachycardia)	2 participants (11%)	0
Low blood glucose levels (hypoglycemia)	2 participants (11%)	0
Dizziness on standing or sitting up (dizziness postural)	2 participants (11%)	0

In Part 2, the most common medical problems were inflammation of the skin at the site of medical device, rapid heartbeat, headache, and constipation.

How many participants had serious medical problems?

Some medical problems are called serious if they cause death, threaten life, cause ongoing health problems, or lead to serious complications, or need a hospital stay or a longer stay in hospital.

During this study, 3 out of 56 participants (5%) in Part 1 and 3 out of 24 participants (13%) in Part 2 had serious medical problems that occurred within 30 days after getting the last dose of the treatment.

Serious medical problems that happened in 1 or more participants in Part 1 are shown here.

Serious medical problems in 1 or more participants in Part 1		
	TAK-105 (42 participants)	**Placebo** (14 participants)
Condition in which the lower chambers of the heart (ventricles) beat very quickly, but the increased heartbeat stops on its own within 30 seconds (non-sustained ventricular tachycardia)	2 participants (5%)	0
Fainting (syncope)	1 participant (2%)	0

Serious medical problems that happened in 1 or more participants in Part 2 are shown here.

Serious medical problems in 1 or more participants in Part 2		
	TAK-105 (18 participants)	**Placebo** (6 participants)
Condition in which the lower chambers of the heart (ventricles) beat very quickly, but the increased heartbeat stops on its own within 30 seconds (non-sustained ventricular tachycardia)	2 participants (11%)	0
Fainting (syncope)	0	1 participant (17%)

How has this study helped?

This study has helped researchers learn about the safety of TAK-105 in healthy adults. Researchers found that TAK-105 was tolerated at different doses by the healthy participants.

The results from several studies are needed to decide which treatments work best and are safest. This summary only shows the main results from this 1 study. Other studies may provide new information or give different results.

There are no plans for further studies with TAK-105.

Where can I learn more about this study?

Title of this study:	A Randomized, Double-Blind, Sponsor-Open, Placebo-Controlled, Phase 1 Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of TAK-105 in Healthy Subjects
Study number:	TAK-105-1001
United States study number:	NCT04964258

More information about the study results is available here:

United States	www.clinicaltrials.gov Search this website using the study number NCT04964258
Takeda website	https://www.clinicaltrials.takeda.com/ Use the detailed search using the Study Identifier TAK-105-1001

Takeda sponsored this study.

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June 2024