Clinical Trial Results

TRIAL SPONSOR:

Otsuka Pharmaceutical Development & Commercialization, Inc.

TREATMENT STUDIED:

AVP-786

PROTOCOL NUMBER:

20-AVP-786-307

SHORT TRIAL TITLE:

A Study to Learn How AVP-786 Works and How Safe It Is In People with Agitation due to Alzheimer's Dementia

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Clinical Trial Results

Thank you!

Thank you to the participants who took part in the clinical trial for AVP-786. All the participants helped the researchers learn more about using AVP-786 to help treat people with agitation due to Alzheimer's dementia.

Otsuka Pharmaceutical Development & Commercialization, Inc. also called OPDC, sponsored this trial and thinks it is important to share the results with the participants and the public. Otsuka reviewed the results of the trial when it ended. This is a summary of that trial. An independent organization called Xogene helped prepare this summary of the trial results.

We hope this helps the participants understand and feel proud of their important role in medical research. If you participated in the trial and have questions about the results, please speak with a doctor or staff at a trial site.

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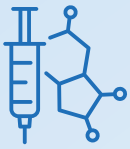
OVERVIEW OF THIS TRIAL

Why was the research needed?

Researchers are looking for a better way to treat people with agitation due to Alzheimer's dementia. Before a treatment is available to all patients, researchers study it in clinical trials to learn how it works and how safe it is.



What treatments did the participants receive?

The participants in this trial received AVP-786 or a placebo.
A placebo looks like a treatment but does not have any medicine in it.

What were the results of this trial?

The main questions the researchers wanted to answer in this trial were:

- **Did treatment with AVP-786 lower how often participants felt agitated?**
  Because the trial was stopped early, researchers could not make any conclusions about the effect AVP-786 had on agitation due to Alzheimer's dementia.
- **What medical issues did the participants have during the trial?**
  The most common medical issues that the doctors thought may be related to AVP-786 were **dizziness**, **falling**, and **difficulty walking (gait disturbance)**.

More details about the results of this trial are included later in this summary.

Where can I learn more about this trial?

You can find more information about this trial on the websites listed on the last page. If a full report of the trial results is available, it can be found on those websites.

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What is happening with this trial now?

The trial started in September 2020 and ended in June 2024. Each participant was in the trial for up to 5 months.

The trial included 236 participants from the United States and Europe. Of those, 99 participants were from the United States and 137 participants were from Europe.

The trial ended earlier than planned after a business decision made by Otsuka.

Why was the research needed?

Researchers are looking for a different way to treat people with agitation due to Alzheimer's dementia. Before a treatment is available to all patients, researchers study it in trials to learn how it works and how safe it is.

Dementia is a word used to describe problems with memory and thinking that make daily life difficult. **Alzheimer's disease** is the most common type of dementia. It happens when abnormal proteins build up in the brain, slowly causing damage to nerve cells. This damage can make it harder for people to think, remember, and do everyday tasks.

One common symptom of Alzheimer's disease is **agitation**. People with agitation may feel restless, confused, or upset, which leads to behaviors like yelling, pacing, and being aggressive. These symptoms often get worse over time.

Some medications may help ease agitation for a short time, but they can cause unwanted side effects. Researchers are studying new treatments to provide better options. Finding ways to control symptoms could improve care and lead to better outcomes.

AVP-786 is a medication that contains 2 drugs: deudextromethorphan hydrobromide (d6-DM), and quinidine sulfate (Q). Researchers believe AVP-786 could help treat agitation.

In this trial, researchers wanted to learn about the safety of AVP-786 and its effects on agitation in participants with Alzheimer's dementia.

The main questions the researchers wanted to answer in this trial were:

- Did treatment with AVP-786 lower how often participants felt agitated?
- What medical issues did the participants have during the trial?

To answer these questions, the researchers asked for the help of men and women with agitation due to Alzheimer's dementia. Everyone in the trial was between 56 to 89 years of age when they joined. Each participant had a reliable caregiver that helped them take the medications.

This was a Phase 3 trial, meaning researchers tested AVP-786 in a large group of participants to better understand its effects and safety. Phase 3 trials are one of the final steps before a treatment can be considered for approval.

What treatments did the participants receive?

The participants in this trial received AVP-786 or a placebo.

A placebo looks like a treatment but does not have any medicine in it. The researchers used a placebo to help make sure the effects of AVP-786 they found in the trial were actually caused by it.

> **In this summary, "trial treatment" means anything the participants received as a part of the trial. This includes AVP-786 and the placebo. AVP-786 is the treatment that the researchers wanted to learn more about.**

This was a "double blind" trial. This means none of the participants, doctors, or other trial staff knew what treatment each participant received.

Some trials are done this way because knowing what treatment the participants are taking can affect the results of the trial. When Otsuka reviewed the results of the trial, they knew what treatment each participant received so they could create a report of the results.

The researchers used a computer program to randomly choose the treatment each participant received. This helped make sure the treatments were chosen fairly and comparing the results of the treatments was as accurate as possible.

The treatment period lasted 12 weeks. During the first week of treatment, all participants received placebo. This was done because previous studies showed that some participants have a strong response to treatment in the first week, even when taking a placebo. By having all participants start with a placebo, researchers could better understand how some participants respond to placebo alone.

After the first week, participants were assigned to 1 of 3 treatment groups.
The chart below shows the treatment plan for the participants:

	WEEK 1	WEEK 2 TO 12		
	241 participants received a placebo	76 participants received a placebo	83 participants received AVP-786-18	77 participants received AVP-786-42.63
	Placebo was taken as capsules by mouth	Placebo was taken as capsules by mouth	AVP-786 capsules by mouth containing 18 mg of d6-DM and 4.9 mg of Q	AVP-786 capsules by mouth containing 42.63 mg of d6-DM and 4.9 mg of Q
	Twice a day	Twice a day	Twice a day	Twice a day

d6-DM = deudextromethorphan hydrobromide
Q = quinidine sulfate

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What happened during the trial?

The chart below shows what happened during the trial:

Before the participants received treatment

- The doctors checked to make sure the patients could join the trial.
- Participants visited the trial site once.

4 weeks

During the trial

All participants visited the trial site 8 times.

Participants received treatment with:

- AVP-786-18,
- AVP-786-42.63
- or placebo

12 weeks

End of trial

- Participants visited the trial site 30 days after their last dose.
- The doctors asked participants about medications they were taking and any medical issues they had.

16 weeks

Throughout the trial, the doctors:

- Performed physical exams.
- Asked participants about medications they were taking and any medical issues they had.
- Took blood and urine samples.
- Checked the participants' heart health using an electrocardiogram, also called an ECG.
- Did tests to measure participants' thinking, memory, and behavior.
- Checked diary cards given to the caregivers.

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What were the results of the trial?

This is a summary of the main results from this trial. The individual results of each participant might be different and are not in this summary.

The results from several trials are needed to decide how well treatments work and which are safest. Other trials may provide new information or different results. Always talk to a doctor before making any treatment changes.

Did treatment with AVP-786 lower how often participants felt agitated?

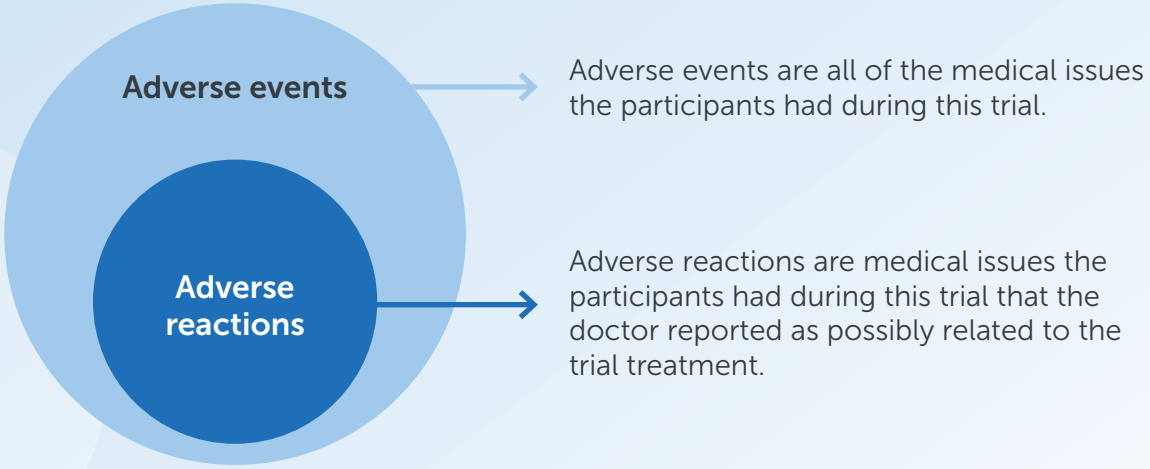
To answer this question, researchers used a tool called the **Cohen-Mansfield Agitation Inventory (CMAI).** The CMAI is a scale that checks how often participants are agitated. It tracks 29 agitated behaviors. Each one is scored from 1 to 7 based on how often the behaviors happen.

Researchers wanted to check if AVP-786 could lower how often participants had agitated behaviors compared to placebo. However, since the trial was stopped early, researchers were not able to make any conclusions about the effect AVP-786 had on agitation due to Alzheimer's dementia.

What medical issues did the participants have during the trial?

This section is a summary of the medical issues that the participants had during this trial. An **adverse event** is **any** medical issue that a participant has during a trial. Doctors keep track of all adverse events that happen in trials, whether or not these may be related to the trial treatments.

In this summary, an **adverse reaction** is an adverse event that **doctors think may be related** to the trial treatments. The results from several trials may be needed to decide if a treatment causes an adverse reaction.



An adverse event or adverse reaction is considered "serious" when it leads to death, is life-threatening, causes lasting problems, or requires hospital care. An adverse event or adverse reaction is also "serious" if it is medically important enough to require treatment to prevent any of those issues.

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How many participants had adverse events during the trial?

SUMMARY OF ADVERSE EVENTS			
	Placebo (out of 76 participants)	**AVP-786-18** (out of 83 participants)	**AVP-786-42.63** (out of 77 participants)
How many participants had adverse events?	 33% (25 participants)	 46% (38 participants)	 44% (34 participants)
How many participants had serious adverse events?	 5% (4 participants)	 6% (5 participants)	 6% (5 participants)
How many participants stopped receiving trial treatment because of adverse events?	 1% (1 participant)	 4% (3 participants)	 10% (8 participants)

What serious adverse events were reported?

The most common serious adverse events were dizziness and lung infection (pneumonia).

What were the most common reported adverse events?

The most common adverse events were falling, dizziness, urinary tract infection, and tiredness (fatigue).

Researchers checked vital signs, performed lab and heart tests, and measured participants' mood, memory, sleepiness, and physical function using different tools.

They did not find any safety risks in AVP-786 compared to placebo.

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What medical issues did the doctors think were related to the trial treatment?

This section is a summary of the medical issues the participants had during the trial that the doctors **thought may be related** to the trial treatments. These medical issues are called **adverse reactions.**

The adverse reactions listed below were reported by the doctors. They may or may not be related to the treatments in the trial. The results from several trials may be needed to decide if a treatment causes an adverse reaction.

How many participants had adverse reactions during the trial?

SUMMARY OF ADVERSE REACTIONS			
	Placebo (out of 76 participants)	**AVP-786-18** (out of 83 participants)	**AVP-786-42.63** (out of 77 participants)
How many participants had adverse reactions?	 8% (6 participants)	 8% (7 participants)	 16% (12 participants)
How many participants had serious adverse reactions?	 0% (0 participants)	 1% (1 participant)	 0% (0 participants)
How many participants stopped receiving trial treatment because of adverse reactions?	 0% (0 participants)	 1% (1 participant)	 5% (4 participants)

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What serious adverse reactions were reported?

There were 2 serious adverse reactions during this trial.

- 1 out of 60 participants (1%) in the AVP-786-18 group reported dizziness and falling.
- There were no deaths caused by adverse reactions.

What were the most common reported adverse reactions?

The adverse reactions below happened in 2 or more of participants. There were other adverse reactions, but those happened in fewer participants.

MOST COMMON ADVERSE REACTIONS			
	Placebo (out of 76 participants)	**AVP-786-18** (out of 83 participants)	**AVP-786-42.63** (out of 77 participants)
Dizziness	 4% (3 participants)	 1% (1 participant)	 4% (3 participants)
Fall	 0% (0 participants)	 2% (2 participants)	 4% (3 participants)
Difficulty walking (gait disturbance)	 0% (0 participants)	 1% (1 participant)	 4% (3 participants)
Feeling dizzy or lightheaded when standing or sitting up due to a drop in blood pressure (orthostatic hypotension)	 0% (0 participants)	 1% (1 participant)	 1% (1 participant)
Sleepiness (somnolence)	 0% (0 participants)	 0% (0 participants)	 3% (2 participants)
Decreased appetite	 1% (1 participant)	 0% (0 participants)	 1% (1 participant)

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How has this trial helped patients and researchers?

This trial helped researchers learn more about how AVP-786 works and its safety in people with agitation due to Alzheimer's dementia. The results from several trials are needed to decide which treatments work best and are safest. This summary shows only the main results from this one trial. Other trials may provide new information or different results.

Because the trial ended earlier than planned, researchers were not able to make any conclusions about how well AVP-786 works to treat agitation. No new safety concerns were found.

Further clinical trials with AVP-786 are not planned.

Where can I learn more about this trial?

You can find more information about this trial on the websites listed below. If a full report of this trial's results is available, it might be on these websites:

https://clinicaltrials.gov/study/NCT04464564

https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2023-504991-31-00

FULL TRIAL TITLE: A Phase 3, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy, safety, and tolerability of AVP-786 (deudextromethorphan hydrobromide [d6-DM]/quinidine sulfate [Q]) for the treatment of agitation in patients with dementia of the Alzheimer's type

PROTOCOL NUMBER: 20-AVP-786-307

NATIONAL CLINICAL TRIAL NUMBER: NCT04464564

EU CLINICAL TRIAL NUMBER: 2023-504991-31-00

OPDC, Inc., sponsored this trial and has its headquarters at 2440 Research Boulevard, Rockville, Maryland, 20850, United States. The phone number for general information is +1 (844) 687-8522.

Thank you!

Participants in clinical trials belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

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