Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine Studied: Vyndaqel® (tafamidis)

Protocol Number: B3461114

Dates of Study: 27 February 2024 to 27 May 2024

Title of this Study: A Study to Learn How Different Formulations of Study Medication Tafamidis are Taken Up into the Blood in Healthy Adults

[A Phase 1, Open-Label, Randomized, Three-Treatment, Three-Period, Crossover, Single Dose Study to Estimate the Relative Bioavailability of 61 mg and 70 mg Tafamidis Free Acid Tablets to Commercial 61 mg Tafamidis Free Acid Capsule Administered Under Fasted Conditions in Healthy Adult Participants]

Date of this Report: 02 December 2024

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– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

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Why was this study done?

What is Amyloidosis?

Amyloidosis is a serious and life-threatening medical condition. People with this condition have higher than normal levels of an abnormal protein called 'amyloid' which builds up in various organs. Transthyretin (TTR) is a protein normally made by the liver. TTR can break apart due to either a genetic mutation or with advance age and clump together in fibers called amyloid. These fibers can accumulate in various organs including heart, kidneys, and nervous system.

Transthyretin amyloidosis (ATTR amyloidosis) is a condition where a person develops symptoms due to the accumulation of amyloid in their body tissues. Treatment for ATTR amyloidosis is focused on the goal of preventing further amyloid accumulation and maintenance of organ function.

What is tafamidis?

Tafamidis (tuh-fuh-mi-dis), also known as Vyndaqel® or Vyndamax®, is a medication approved for use in many countries for the treatment of transthyretin amyloid cardiomyopathy (ATTR-CM, which is amyloid fiber buildup in heart muscle). Tafamidis works by preventing TTR from breaking down and forming amyloid fibers. By doing this, tafamidis helps slow down the buildup of amyloid fibers in different organs of the body, which in turn slows down the worsening of the disease. Tafamidis is taken by mouth as a capsule to be swallowed. A new tafamidis tablet formulation is being developed to replace the current capsule formulation.

What was the purpose of this study?

The purpose of this study was to compare the amount of tafamidis in the participants' blood when given in two different formulations. Tafamidis

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tablet formulations were compared to a proposed commercial tafamidis capsule formulation when taken on an empty stomach. The tafamidis tablet formulations were referred to as 'Tests' and the capsule formulation was referred to as 'Reference'.

After tafamidis was swallowed, tafamidis entered the body and moved through the body. Tafamidis entered the blood and organs (for example, stomach, liver, and kidneys) when it moved through the body. Afterwards, tafamidis was removed from the body through urine and feces.

This study did not test if tafamidis helps to improve amyloidosis and only focused on how tafamidis moves through the body.

Researchers wanted to know:

- **How did the Test tafamidis tablets act in the body compared to the Reference tafamidis capsule?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested 2 different doses of the Test tafamidis tablets (Treatment A and C) and compared them with Reference tafamidis capsule (Treatment B) in a group of healthy participants to learn how tafamidis behaved in the body.

This study included 3 treatment periods. Each period lasted 8 days with at least 16 days of 'washout' between Day 1 in each period. Washout means

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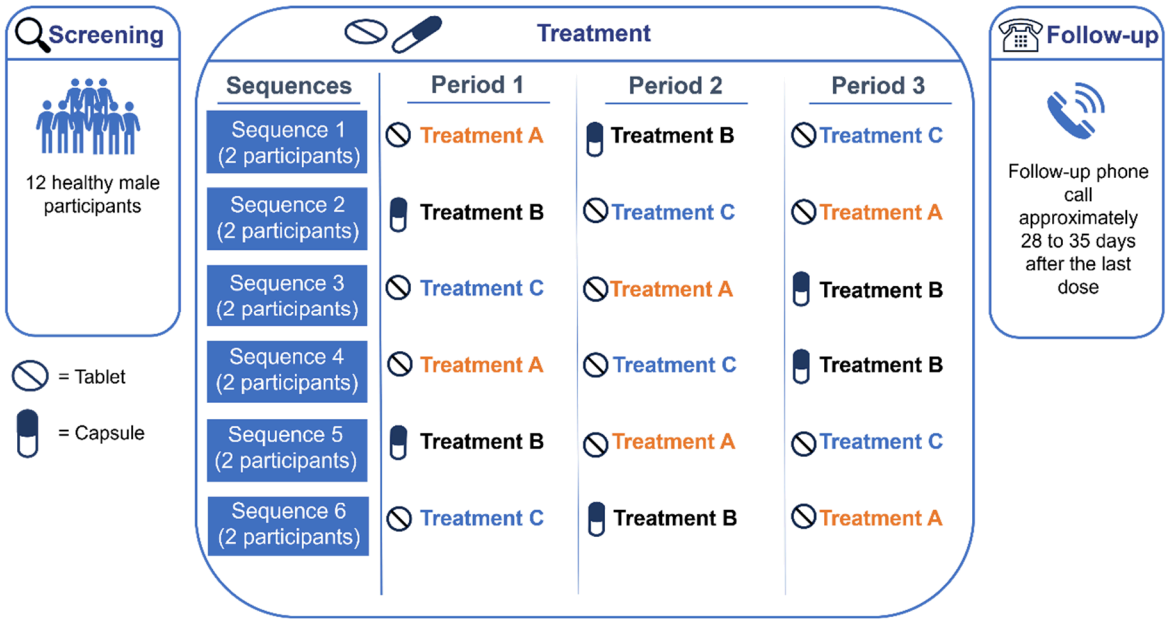
no treatment was given to participants on those days to allow time for the study medication to be removed from the body.

Participants were admitted to the clinical research unit at least 12 hours before receiving the first dose and were required to stay in the hospital for 8 days in each period. Each dose was taken on an empty stomach. Participants were randomly assigned into 1 of 6 treatment sequences as shown in Figure 1 below. They were assigned to each treatment by chance alone.

- Treatment A: Single dose of tafamidis 61 milligram (mg) tablet (Test).
- Treatment B: Single dose of commercially available tafamidis 61 mg capsule (Reference).
- Treatment C: Single dose of tafamidis 70 mg tablet (Test).

This was an open-label study, which means that the participants and the researchers knew which treatments the participants received. The study design is shown below:

Figure 1. Study Design



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Researchers took samples of blood from participants during the treatment phase and measured the amount of tafamidis in their blood. Researchers also checked the participants' health during the study and asked them how they were feeling.

Where did this study take place?

The Sponsor ran this study at 1 location in Belgium.

When did this study take place?

It began on 27 February 2024 and ended on 27 May 2024.

Who participated in this study?

The study included healthy participants who were aged 18 years or older. Participants with a body mass index (a measure of body weight in relation to height) of 16 to 32 kilograms per square meter (kg/m^2) and weighing more than 45 kg were eligible to take part in the study.

- A total of 12 men participated
- All participants were between the ages of 26 and 73 years.

All 12 participants finished the study.

How long did the study last?

The entire study took 3 months to complete.

When the study ended in May 2024, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

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What were the results of the study?

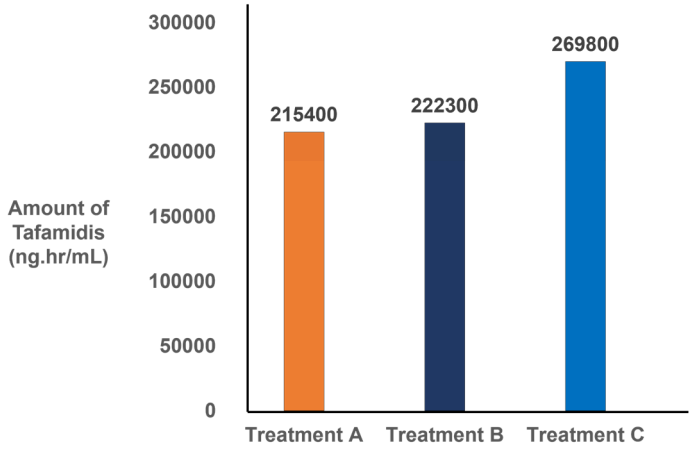
How did the Test tafamidis tablets act in the body compared to the Reference tafamidis capsule?

To answer this question the researchers compared the participants' blood test results after each treatment period.

What was the total amount of tafamidis in the blood after participants took the Test tablets and the Reference capsule?

The average estimated total amount of tafamidis in the blood from the time when tafamidis was taken until it was removed from the body is shown in Figure 2 below. The total amount of study medication in the blood overtime was measured in nanogram hours per milliliter, also called ng.hr/mL. Researchers considered the difference in the results between the Test tablets and Reference capsule formulations as minor.

Figure 2: Average Estimated Total Amount of Tafamidis in the Blood, From When it Was Taken Until it Was Removed From the Body

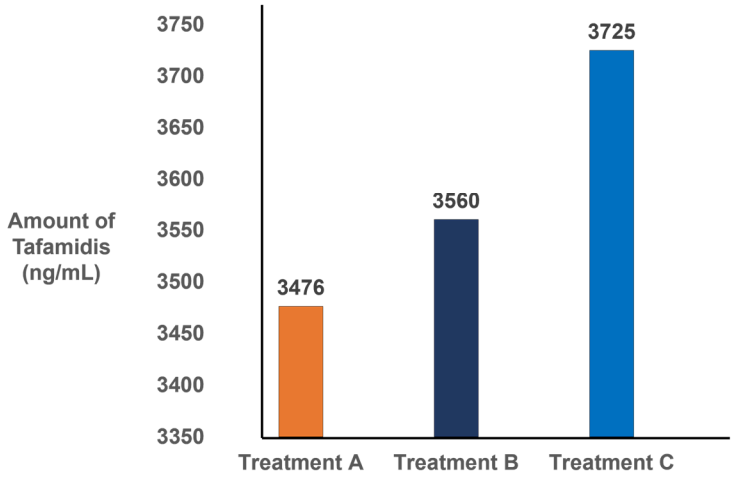


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What was the highest amount of tafamidis in the blood after participants took the Test tablets and the Reference capsule?

The average highest amount of tafamidis in the blood after participants took a single dose of the Test tablets and the Reference capsule is shown in Figure 3 below. The amount of study medication in the blood was measured in nanograms per milliliter, also called ng/mL. In this study, the highest amount of tafamidis measured in the blood was similar between the tablets and capsule formulations. Researchers considered the differences in the results as minor.

Figure 3: Average Highest Amount of Tafamidis in the Blood



The study found that tafamidis tablets and capsule behaved similar in the body. This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

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What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

Two (2) out of 12 (17%) participants in each group who received Treatment A or Treatment B and 3 out of 12 (35%) participants who received Treatment C in this study had at least 1 medical problem. None of the participants left the study because of medical problems. All the medical problems reported by the participants are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by participants are listed.
- The **2nd** column tells how many of the 12 participants taking Test tafamidis tablet 61 mg reported each medical problem. Next to this number is the percentage of the 12 participants taking Test tafamidis tablet 61 mg who reported the medical problem.

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- The **3rd** column tells how many of the 12 participants taking Reference tafamidis capsule reported each medical problem. Next to this number is the percentage of the 12 participants taking Reference tafamidis capsule who reported the medical problem.
- The **4th** column tells how many of the 12 participants taking Test tafamidis tablet 70 mg reported each medical problem. Next to this number is the percentage of the 12 participants taking Test tafamidis tablet 70 mg who reported the medical problem.
- Using these instructions, you can see that 0 out of the 12 (0%) participants taking Test tafamidis tablet 61 mg reported back pain.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Treatment A Test tafamidis tablet 61 mg (12 Participants)	Treatment B Reference tafamidis capsule 61 mg (12 Participants)	Treatment C Test tafamidis tablet 70 mg (12 Participants)
Back pain	0 out of 12 participants (0%)	1 out of 12 participants (8%)	1 out of 12 participants (8%)
Inflammation of the nose and throat	1 out of 12 participants (8%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)
Diarrhea	0 out of 12 participants (0%)	1 out of 12 participants (8%)	0 out of 12 participants (0%)

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Table 1. Commonly reported medical problems by study participants

Medical Problem	Treatment A Test tafamidis tablet 61 mg (12 Participants)	Treatment B Reference tafamidis capsule 61 mg (12 Participants)	Treatment C Test tafamidis tablet 70 mg (12 Participants)
Headache	1 out of 12 participants (8%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)
Muscle cramps	0 out of 12 participants (0%)	0 out of 12 participants (0%)	1 out of 12 participants (8%)
Stomach pain	0 out of 12 participants (0%)	0 out of 12 participants (0%)	1 out of 12 participants (8%)
Vomiting	0 out of 12 participants (0%)	1 out of 12 participants (8%)	0 out of 12 participants (0%)

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Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

No participants in this study had serious medical problems.

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Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **B3461114**

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT06273839**
www.euclinicaltrials.eu	Use the study identifier **2023-509241-12-00**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!

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