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(s) Studied:	Vyndaqel® (tafamidis)
Protocol Number:	B3461102
Dates of Study:	29 August 2022 to 28 October 2022
Title of this Study:	A Single Dose Study to Test Two Tafamidis Tablet Formulations in Healthy Adult Participants [A Phase 1, Open-Label, Randomized, Crossover, Single Dose Study to Estimate the Relative Bioavailability of Variant 12.2 mg Tafamidis Free Acid Tablets and Proposed Commercial 12.2 mg Tafamidis Free Acid Tablets Administered Under Fasted Conditions in Healthy Adult Participants]
Date(s) of this Report:	09 October 2023

– 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.

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 abnormal amyloid in their 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 by the brand name Vyndaqel®) is a medication used in the treatment of ATTR amyloidosis. Tafamidis is an oral medication which works by keeping TTR from breaking apart and forming into amyloid fibers. Tafamidis slows down the buildup of amyloid fibers in different organs of the body. This helps slow down the rate at which the disease gets worse over time. Tafamidis is approved to be used in many countries in the treatment of transthyretin amyloid neuropathy (amyloid buildup in nerves) and transthyretin amyloid cardiomyopathy (amyloid buildup in heart muscle).

What was the purpose of this study?

The purpose of this study was to measure and compare how much tafamidis was in the participants' blood when given in two different formulations. A Test tafamidis formulation (Treatment A) was compared to

a proposed commercial (Reference) tafamidis formulation (Treatment B). 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 the drug helps to improve amyloidosis and only focused on how tafamidis moves through the body.

Researchers wanted to know:

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

What happened during the study?

How was the study done?

Researchers tested a single dose Test formulation of tafamidis tablet relative to the Reference formulation on a group of healthy participants to learn how tafamidis behaved in the body.

This study included 2 treatment periods. Each period lasted 8 days with at least 16 days of 'washout' between Day 1 in each period (no treatment given to participants on those days to allow time for a drug to be removed from the body).

Participants were admitted to 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. Participants were randomized into 2 treatment sequences:

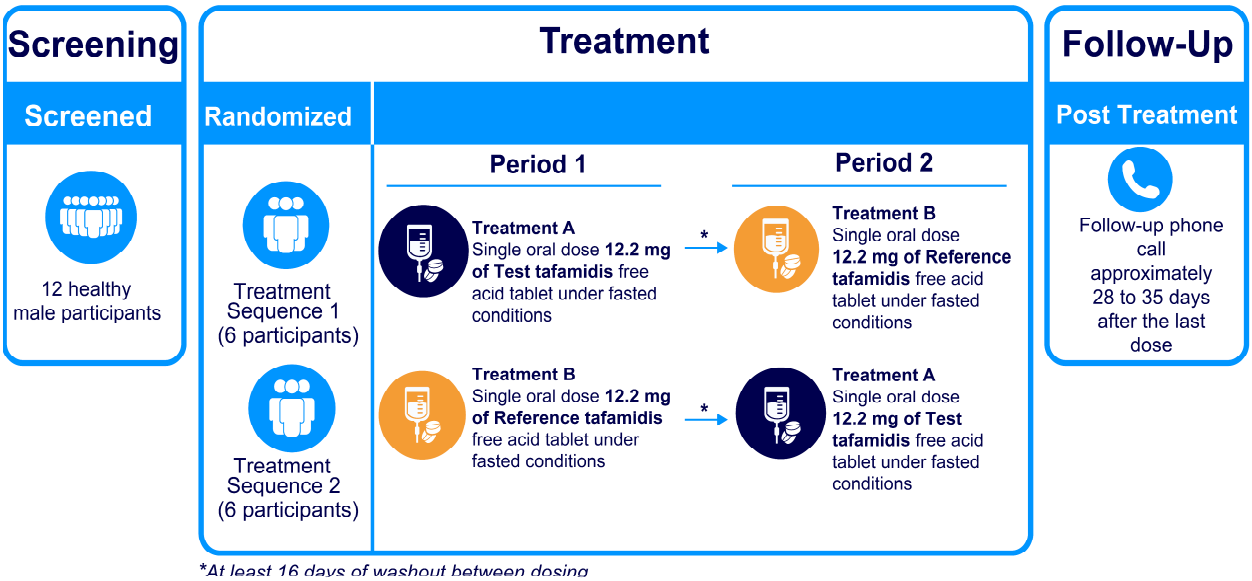
- Treatment Sequence 1: Treatment A on Period 1 Day 1 followed by Treatment B on Period 2 Day 1.
- Treatment Sequence 2: Treatment B on Period 1 Day 1 followed by Treatment A on Period 2 Day 1.

Participants were assigned to each sequence by chance alone:

- Treatment A: Single oral (by mouth) dose of Test tafamidis free acid tablet 12.2 milligrams (mg) under fasted (participants did not eat food overnight before each dose) conditions.
- Treatment B: Single oral dose of proposed commercial (Reference) tafamidis free acid tablet 12.2 mg under fasted conditions.

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



Researchers took samples of blood from participants during the treatment phase and measured the amount of tafamidis that was in their blood. Researchers then, compared the blood samples between periods 1 and 2. Researchers also checked the participants' health during the study and asked them how they were feeling.

Where did this study take place?

The Sponsor conducted this study at 1 location in Belgium.

When did this study take place?

The study started on 29 August 2022 and ended on 28 October 2022.

Who participated in this study?

The study included 12 healthy participants who met the inclusion criteria for things such as age, sex, and health status.

- All 12 participants in this study were men. The 'pre-natal' (before birth) safety of tafamidis was not known at the time of the study, only healthy non-childbearing women could be enrolled. This impacted the female participation in this study.
- All participants were between the ages of 26 and 57 years.

Of the 12 participants who started the study, 10 finished the study. One participant did not finish the study due to no longer meeting inclusion criteria.

One participant left before the study was over by his own choice.

How long did the study last?

The entire study took 8 weeks and 4 days to complete.

The Sponsor reviewed all the information collected and after the study ended in October 2022, created a report of the results. This is a summary of that report.

What were the results of the study?

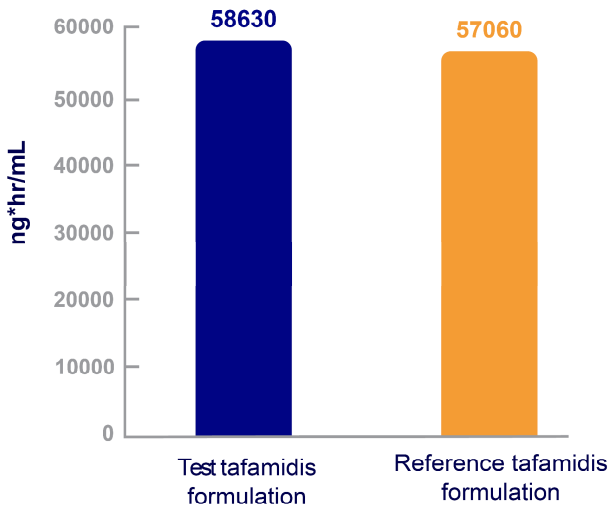
How did Test tafamidis tablet formulation act in the body compared to the Reference tafamidis tablet formulation?

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 Test and Reference tablet formulations of tafamidis?

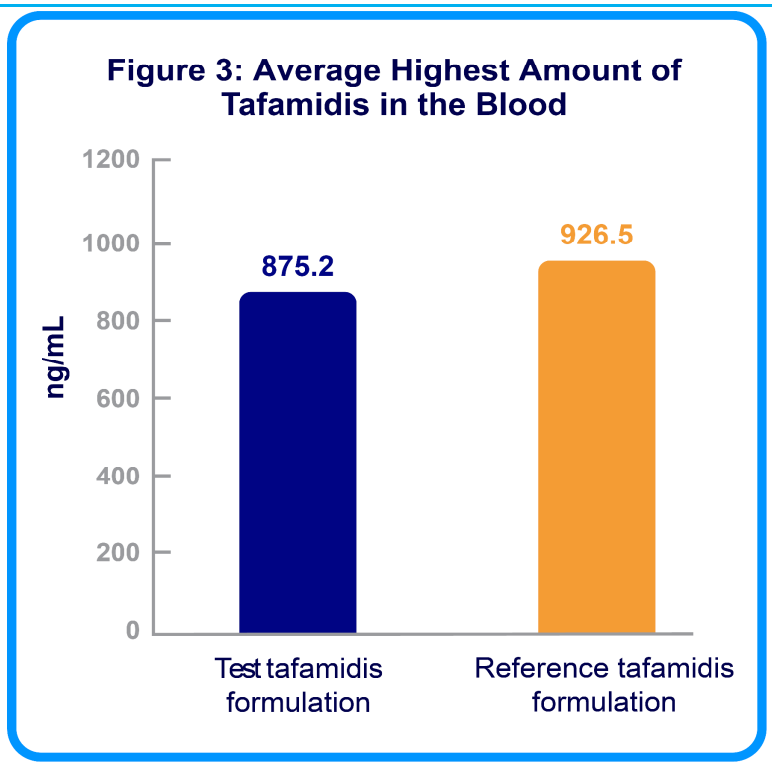
The average estimated total amount of tafamidis in the blood from the time when tafamidis was taken until it was removed from the body is shown in Figure 2. The total amount of drug in the blood overtime was measured in nanogram hours per milliliter, also called ng.hr/mL. Researchers considered the difference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



What was the highest amount of tafamidis in the blood after participants took two different formulations of tafamidis?

The average highest amount of tafamidis in the blood after participants took a single dose of two different tafamidis formulations is shown in Figure 3. The amount of drug in the blood was measured in nanogram per milliliter, also called ng/mL. In this study, the highest amount of tafamidis measured in the blood were similar between the two formulations. Researchers considered the differences in the results as minor.



Based on these results, the researchers concluded that the two formulations 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.

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.

Six (6) out of 11 participants (54.5%) who received Treatment A and 4 out of 12 participants (33.3%) who received Treatment B in this study had at least 1 medical problem. Three (3) medical problems each in both treatment groups (A and B) were caused due to the study treatment. None of the participants left the study because of medical problems. All of 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 11 participants taking Test tafamidis formulation reported each medical problem. Next to this number is the percentage of the 11 participants who reported the medical problem.
- The **3rd** column tells how many of the 12 participants taking Reference tafamidis formulation reported each medical problem. Next to this number is the percentage of the 12 participants who reported the medical problem.
- Using these instructions, you can see that 2 out of the 11 participants (18.2%) taking study Treatment A reported back pain.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Treatment A** **Test tafamidis formulation (11 Participants)**	**Treatment B** **Reference tafamidis formulation (12 Participants)**
Diarrhea	1 out of 11 participants (9.1%)	0 out of 12 participants (0%)
Flu-like symptoms	1 out of 11 participants (9.1%)	0 out of 12 participants (0%)
Bruising at the site where a needle is inserted	0 out of 11 participants (0%)	1 out of 12 participants (8.3%)
Bleeding from a wound	1 out of 11 participants (9.1%)	0 out of 12 participants (0%)
Back pain	2 out of 11 participants (18.2%)	0 out of 12 participants (0%)
Headache	1 out of 11 participants (9.1%)	2 out of 12 participants (16.7%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Treatment A** **Test tafamidis formulation (11 Participants)**	**Treatment B** **Reference tafamidis formulation (12 Participants)**
Cough	1 out of 11 participants (9.1%)	1 out of 12 participants (8.3%)
Acne	0 out of 11 participants (0%)	1 out of 12 participants (8.3%)
Dry skin	2 out of 11 participants (18.2%)	0 out of 12 participants (0%)

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, and no participants died during the study. The Test and Reference tafamidis formulations were generally safe and well-tolerated in healthy adult participants.

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 **B3461102**

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

www.clinicaltrialsregister.eu	Use the study identifier **2022-001833-35**

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!