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 meglumine)

Protocol Number: B3461103

Dates of Study: 29 September 2022 to 18 December 2022

Title of this Study: A Study of the Capsule and Tablet Forms of Tafamidis and the Effect of Food on Tafamidis Tablet in Healthy Adults

[Final Report - A Phase 1, Open-Label, Randomized, Crossover, Single Dose Study to Determine the Bioequivalence of 12.2 mg Tafamidis Free Acid Tablets and Commercial 20 mg Tafamidis Meglumine Capsules Administered Under Fasted Conditions and the Effect of Food on Oral Bioavailability of 12.2 mg Tafamidis Free Acid Tablets in Healthy Adult Participants]

Date of this Report: 27 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. Transthyretin (TTR) is a protein normally made by the liver. TTR can break apart due to either a genetic mutation or with advanced age and clump together. This collection of fibers is called ‘amyloid’ and can build up in different organs such as the heart, kidneys, and nervous system.

Transthyretin amyloidosis (ATTR amyloidosis) is a condition where a person develops symptoms due to the buildup of abnormal amyloid in their tissues.

What is tafamidis?

Tafamidis (tuh-fuh-mi-dis) is an oral (by mouth) medication used in the treatment of ATTR amyloidosis.

It 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 for 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 find out if the tafamidis tablet form (“test”) acted similarly in the body compared to the commercial tafamidis capsule ("reference”). Researchers also wanted to see how the tafamidis tablet

acted in the body when taken with (a meal) or without food (on an empty stomach).

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 the tafamidis tablet act in the body compared to the tafamidis capsule?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested tafamidis on a group of participants aged 18 years or older to learn how the 2 tafamidis forms 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. During each washout period, treatment was not given to participants to allow time for drug removal from the body.

Participants were admitted to the study site at least 12 hours before receiving the first dose and were required to stay for 8 days in each period.

Researchers tested 3 treatments in the study:

- Treatment A: Single oral dose of 12.2 mg tafamidis tablet (without food)

- Treatment B: Single oral dose of 20 mg tafamidis capsule (without food)
- Treatment C: Single oral dose of 12.2 mg tafamidis tablet (with food)

Participants were assigned into 2 treatment sequences by chance:

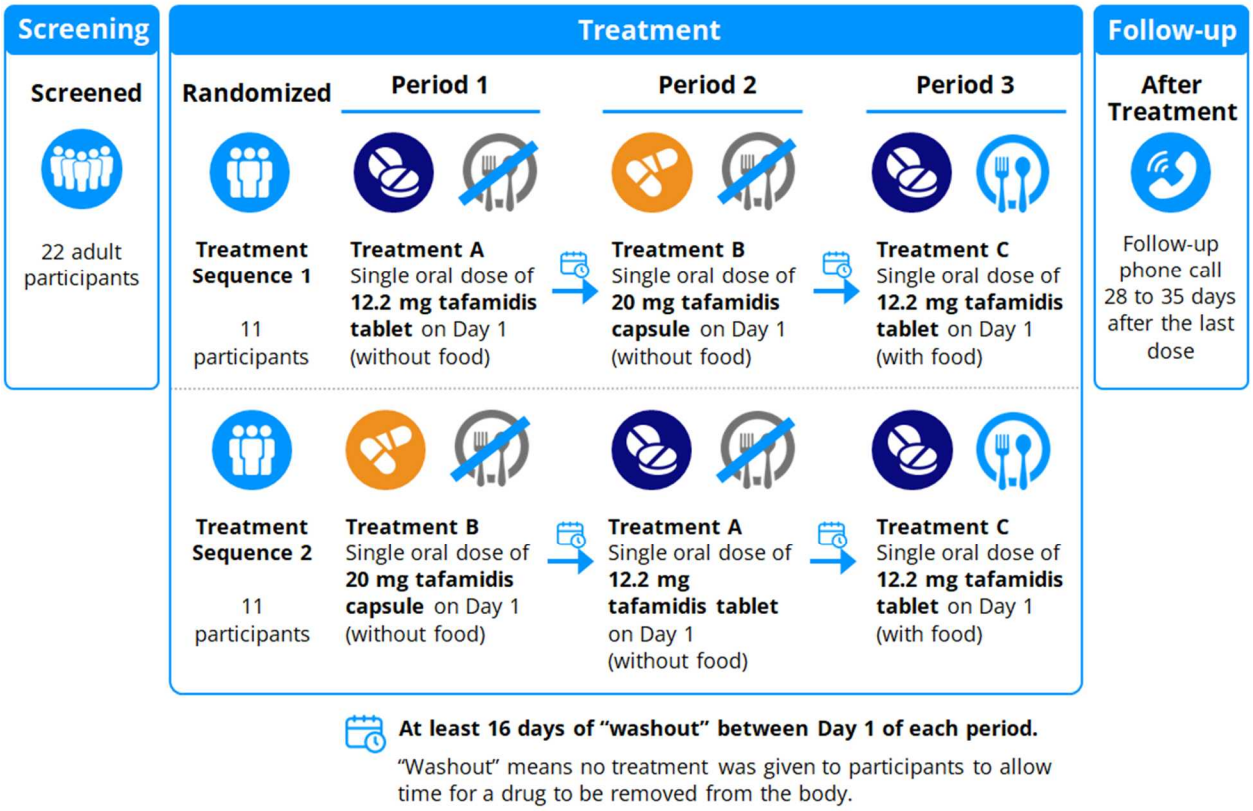
- Treatment Sequence 1: Treatment A on Period 1 Day 1 followed by Treatment B on Period 2 Day 1, and then Treatment C on Period 3 Day 1.
- Treatment Sequence 2: Treatment B on Period 1 Day 1, followed by Treatment A on Period 2 Day 1, and then Treatment C on Period 3 Day 1.

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

This was an open-label study. This means that the participants and the researchers knew who took 2 tafamidis forms.

Figure 1 below shows what happened during the study.

Figure 1: What happened during the study?



Where did this study take place?

The study took place at 1 location in Canada.

When did this study take place?

The study started on 29 September 2022 and ended on 18 December 2022.

Who participated in this study?

The study included healthy adult participants aged 18 years and older who met the eligibility criteria such as overall health status. Participation in the

study is only allowed for female participants who are no longer able to have children.

- A total of 18 men and 4 women participated.
- All participants were between the ages of 18 and 67 years.

Overall, 22 participants started the study and received at least 1 dose of tafamidis.

A total of 20 participants completed the study. Two (2) participants left the study before it was over after they finished the study treatment phase. These participants could not be contacted for follow-up.

How long did the study last?

Study participants were in the study for about 11 weeks. The entire study took about 3 and a half months to complete.

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

What were the results of the study?

How did the tafamidis tablet act in the body compared to the tafamidis capsule?

What was the highest amount of tafamidis in the blood after participants took a 12.2 mg tablet or a 20 mg capsule without food?

The highest amount of tafamidis in the blood is called C_{max}. The C_{max} was measured in nanograms per milliliter, also called ng/mL.

The C_{max} of tafamidis in the blood after participants took tafamidis tablet and capsule without food was as follows:

- 1,046 ng/mL for the 12.2 mg tablet
- 1,291 ng/mL for the 20 mg capsule

Among healthy adults in this study, the C_{max} of tafamidis tablet was 19% lower than the C_{max} of tafamidis capsule.

What was the total amount of tafamidis in the blood after participants took a 12.2 mg tablet or a 20 mg capsule without food?

The estimated total amount of tafamidis in the blood after participants took tafamidis is called AUC_{inf}. AUC_{inf} was measured in nanogram hours per milliliter, also called ng•hr/mL. The ng•hr/mL is a unit used to measure total amount of drug over time in the blood.

The AUC_{inf} of tafamidis in the blood after participants took tafamidis tablet and capsule without food was as follows:

- 60,670 ng•hr/mL for the 12.2 mg tablet
- 67,690 ng•hr/mL for the 20 mg capsule

Among healthy adults in this study, the AUC_{inf} of tafamidis tablet was comparable to the AUC_{inf} of tafamidis capsule.

Based on these results, the researchers concluded that the 2 forms 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 unknown 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.

Overall, all 22 participants took both the tafamidis forms without food and 21 of 22 participants took the tablet with food.

- 7 out of 22 participants (32%) reported at least 1 medical problem after they took tafamidis tablet without food.
- 5 out of 22 participants (23%) reported at least 1 medical problem after they took tafamidis capsule without food.
- 9 out of 21 participants (43%) reported at least 1 medical problem after they took tafamidis tablet with food.

No participant left the study because of a medical problem they had during the study.

Headache was the most common medical problem reported in

- 4 out of 22 participants (18%) after they took tafamidis tablet without food

- 2 out of 22 participants (9%) after they took tafamidis capsule without food
- 4 out of 21 participants (19%) after they took tafamidis tablet with food

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 participant had serious medical problems or died during the study.

The 2 tafamidis forms 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 **B3461103**

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

www.clinicaltrials.gov

Use the study identifier **NCT05498701**

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!