CLINICAL TRIAL 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 medicine 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: Tafamidis meglumine

Protocol Number: B3461023

Dates of Trial: 5 August 2009 to 8 July 2020

Title of this Trial: Safety And Efficacy Evaluation Of Fx-1006A In Subjects With Transthyretin Amyloidosis

[Open-Label Safety and Efficacy Evaluation of Tafamidis Meglumine in Subjects With Transthyretin Amyloidosis (ATTR Amyloidosis)]

Date of this Report: 9 June 2021

– Thank You –

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your study site.

WHY WAS THIS STUDY DONE?

Transthyretin amyloid polyneuropathy (ATTR-PN) is a rare and life-threatening medical condition which worsens over time. There are about 10,000 people in the world known to have ATTR-PN. People with this condition have a particular protein, known as transthyretin amyloid, in their nerves. This can lead to problems with the nervous system, such as weakness, numbness, or pain in the hands and feet (known as "neuropathy") and difficulty walking. ATTR-PN is caused by a genetic mutation (change) in the transthyretin (TTR) gene. The most common genetic mutation that causes ATTR-PN is called "Val30Met".

Tafamidis is a study drug approved in some countries to treat adult patients with ATTR-PN to delay neurologic symptoms. The researchers in this study were interested in learning more about the long-term safety and effects of tafamidis.

This study had several purposes:

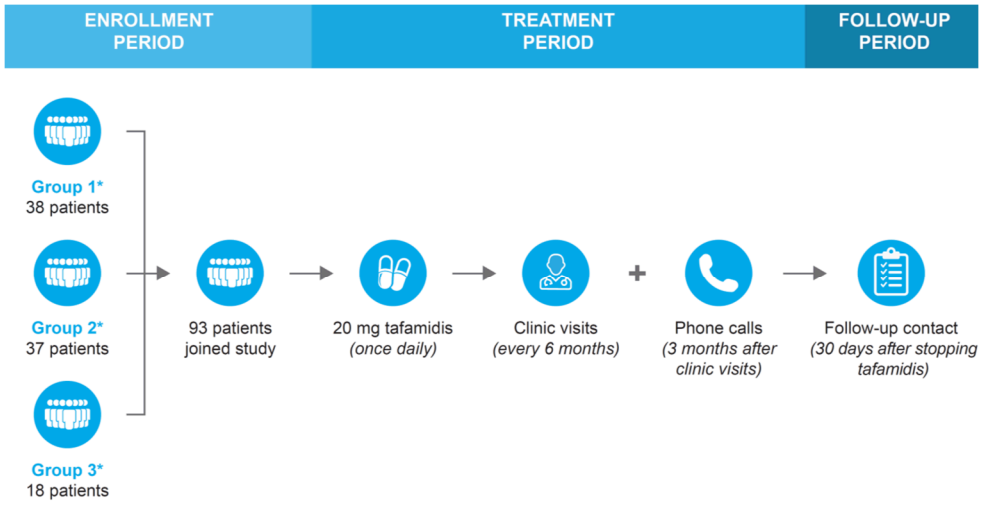
- To continue to study if tafamidis is safe and the potential effects of tafamidis in patients with ATTR-PN over the long-term.
- To continue to provide tafamidis to patients with ATTR-PN who had participated in previous clinical trials for tafamidis and were benefiting from taking it.

WHAT HAPPENED DURING THE STUDY?

This study included adult patients with ATTR-PN who had participated in prior studies with tafamidis and never had a heart or liver transplant.

All patients in this study received tafamidis 20 milligrams, taken once per day every day by mouth. Patients were asked to attend clinic visits every 6 months, and were contacted by phone 3 months after each clinic visit. There was also a follow-up contact 30 days after patients stopped taking tafamidis to check for any medical problems. This was an "open-label" study, which means that both the patients and researchers knew what medicine was being given.

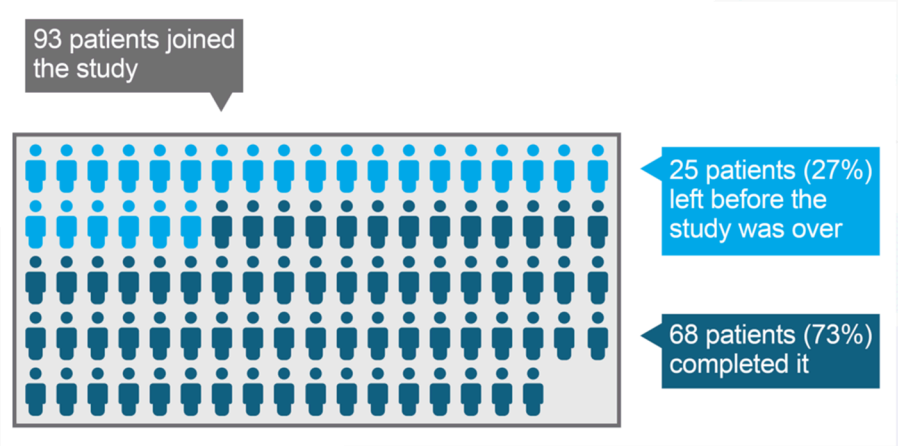
The figure below shows what happened during this study.



*Patients completed prior studies with tafamidis. See description of groups on page 6.

There was no specific amount of time that patients were required to stay in the study, but the time from when the first patient started to when the last patient ended was about 11 years. The Sponsor ran this study at 9 locations in North America, South America, and Europe. It began 5 August 2009 and ended 8 July 2020. 47 patients (51%) were women and 46 patients (49%) were men. All patients were between the ages of 26 and 78 years old when they started in this study.

Patients could be treated for up to 10 years or until tafamidis became available by prescription in their country. Patients who left the study when they got a prescription for tafamidis were called completers. Of the 93 patients who started the study, 68 patients (73%) were completers. 25 patients (27%) left before the study was over by their choice or a doctor decided it was best for a patient to stop the study, or because they passed away.



When the study ended in July 2020, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the patients had during the study. Patients could have had medical problems for reasons not related to the study (for example, caused by another illness they have or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the patient 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 the side effects of an experimental drug might be.

86 out of 93 patients (93%) had at least 1 medical problem, including 35 out of 38 patients (92%) with Val30Met who received tafamidis only in their previous study, 33 out of 37 patients (89%) with Val30Met who received placebo followed by tafamidis in their previous study, and 18 out of 18 patients (100%) without Val30Met who received tafamidis in their previous study.

A total of 6 patients (7%) left the study due to medical problems, including 3 patients (8%) with Val30Met who received tafamidis in their previous study, 1 patient (3%) with Val30Met who received placebo followed by tafamidis in their previous study, and 2 patients (11%) without Val30Met who received tafamidis in their previous study.

The most common medical problems are listed below.

Most Common Medical Problems (Reported by At Least 10% of Patients)

Medical Problem	Tafamidis 20 mg (93 Patients Treated)
Urinary tract infection	16 (17%)
Fall	13 (14%)

Burn	**12 (13%)**
Flu	**11 (12%)**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

25 out of 93 patients (27%) had at least 1 serious medical problem, including 6 out of 38 patients (16%) with Val30Met who received tafamidis in their previous study, 9 out of 37 patients (24%) with Val30Met who received placebo followed by tafamidis in their previous study, and 10 out of 18 patients (56%) without Val30Met who received tafamidis in their previous study.

A total of 11 out of 93 patients (12%) died during the study or the follow-up period, including 3 patients with Val30Met who received tafamidis in their previous study (8%), 1 patient with Val30Met who received placebo followed by tafamidis in their previous study (3%), and 7 patients without Val30Met who received tafamidis in their previous study (39%). None of these deaths were considered to be related to tafamidis by the study doctors.

The table below shows the most common serious medical problems.

Most Common Serious Medical Problems (Reported by 2 or More Patients)	
Serious Medical Problem	**Tafamidis 20 mg (93 Patients Treated)**
Heart failure	**4 (4%)**
Chest pain	**3 (3%)**
Serious complication of infection	**3 (3%)**
Urinary tract infection	**3 (3%)**
Vomiting	**2 (2%)**

Worsened medical condition	**2 (2%)**
Build-up of protein in heart, nerves, or other organs (amyloidosis)	**2 (2%)**
Lung infection	**2 (2%)**
Fall	**2 (2%)**
Fluid build-up in the space surrounding the lungs	**2 (2%)**
Temporary loss of blood flow to the brain	**2 (2%)**

Overall, the study results suggest that long-term treatment with tafamidis 20 milligrams, taken once per day every day by mouth, was well-tolerated in patients with ATTR-PN. No new safety concerns were identified during this study.

WHAT WERE THE RESULTS OF THE STUDY?

To answer the study questions, the researchers looked at 3 groups of patients. The groups were based on whether patients had the Val30Met mutation and when tafamidis was started:

- Group 1: 38 patients with the Val30Met mutation who received tafamidis for 30 months in their previous studies.
- Group 2: 37 patients with the Val30Met mutation who received placebo for 18 months followed by 12 months of tafamidis in their previous studies. A placebo does not have any active ingredients in it, but it looks just like the study drug.
- Group 3: 18 patients without the Val30Met mutation who received tafamidis for 12 months in their previous study.

- In patients with the Val30Met mutation, those in the tafamidis only group (Group 1) had less worsening of neuropathy impairment in the legs and feet at Month 66, compared to those in the placebo followed by tafamidis group (Group 2). Results show the benefits of earlier treatment with tafamidis.
- In patients with the Val30Met mutation, the ability to perform activities of daily living (such as personal hygiene and feeding) slightly improved from Month 30 to Month 66 for those in the tafamidis only group (Group 1). The ability to perform activities of daily living slightly worsened from Month 30 to Month 66 for those in the placebo followed by tafamidis group (Group 2).
- In patients with the Val30Met mutation, the ability to walk worsened more for those in the placebo followed by tafamidis group (Group 2) at Year 6, compared to those in the tafamidis only group (Group 1). After Year 6, there were not enough patients with the Val30Met mutation in the study to draw further conclusions on changes in ability to walk.
- In patients with the Val30Met mutation who received tafamidis only (Group 1), quality of life showed little change from the beginning of the study to Month 30, then worsened from Month 30 to Month 66. In patients with the Val30Met mutation who received placebo followed by tafamidis (Group 2), quality of life worsened from the beginning of the study to Month 18, then improved from Month 42 to Month 66 (after tafamidis was started at Month 18).
- After Month 66, there were not enough patients with the Val30Met mutation in the study to draw further conclusions about the effects of tafamidis.
- There were no patients without the Val30Met mutation treated with placebo in previous studies. This makes it more difficult to understand the effects of tafamidis in Group 3. Impairment in the lower limbs, ability to perform activities of daily living and quality of life generally worsened over time in Group 3.
- In patients without the Val30Met mutation (Group 3), ability to walk worsened more quickly at Year 5 compared to those patients with the Val30Met mutation, and did not change further by Year 9.

Over time, patients were able to be prescribed tafamidis by their doctor or left the study. The earlier that patients in this study started taking tafamidis, the more they

benefited from treatment. Tafamidis may be an option for treating patients with ATTR-PN, and starting tafamidis treatment early may be beneficial.

This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

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.

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

www.clinicaltrials.gov Use the study identifier **NCT00925002**

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

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