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 (PF-06291826)

Protocol Number: B3461028

Dates of Trial: 09 December 2013 to 07 February 2018

Title of this Trial: Does tafamidis help treat patients with transthyretin amyloid cardiomyopathy?

[A Multicenter, International, Phase 3, Double-Blind, Placebo-Controlled, Randomized Study to Evaluate the Efficacy, Safety, and Tolerability of Daily Oral Dosing of Tafamidis Meglumine (PF-06291826) 20 mg or 80 mg in Comparison to Placebo in Subjects Diagnosed With Transthyretin Cardiomyopathy (TTR-CM)]

Date of this Report: 23 August 2019

– 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 the site where you participated in the study.

WHY WAS THIS STUDY DONE?

People with transthyretin amyloid cardiomyopathy have higher than normal levels of a particular protein in their heart. This increases the risk of having heart problems, like heart failure.

Tafamidis is a study drug that is being tested for the treatment of transthyretin amyloid cardiomyopathy. Tafamidis is currently approved to treat transthyretin amyloid cardiomyopathy in Japan and the United States. Tafamidis is not approved to treat transthyretin amyloid cardiomyopathy in other countries because it is still being tested.

This study had 2 purposes:

- To understand the safety of tafamidis: to see what medical problems patients had during the study
- To look at controlling transthyretin amyloid cardiomyopathy: to see if patients taking tafamidis were less likely to have a stay in hospital and less likely to die earlier because of transthyretin amyloid cardiomyopathy

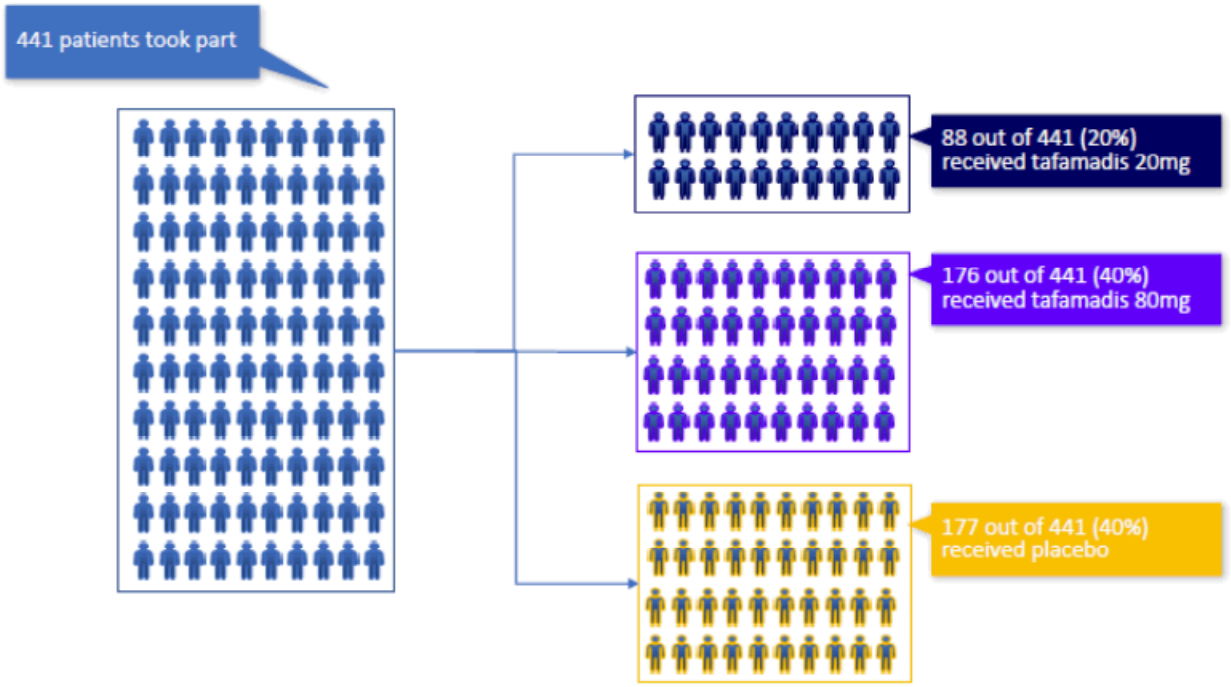
WHAT HAPPENED DURING THE STUDY?

This study compared patients who received tafamidis with patients who received placebo, to understand if tafamidis helped patients with transthyretin amyloid cardiomyopathy. A placebo does not have any medicine in it, but looks just like the medicine being studied.

This was a randomized trial, meaning patients were put randomly (by chance) into 1 of 3 groups:

- Group 1: received a study drug called tafamidis at a dose of 20 milligrams (mg)
- Group 2: received a study drug called tafamidis at a dose of 80 mg
- Group 3: received a placebo that didn't contain any drug

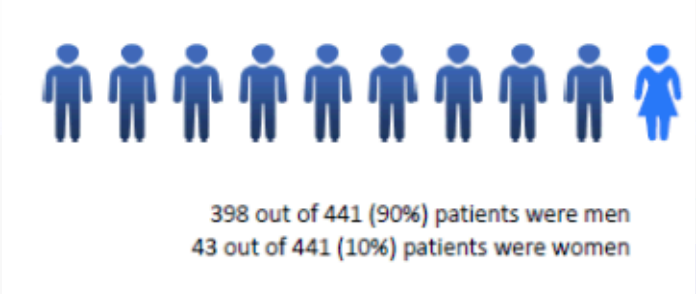
Putting patients into groups randomly makes comparing the groups more fair.



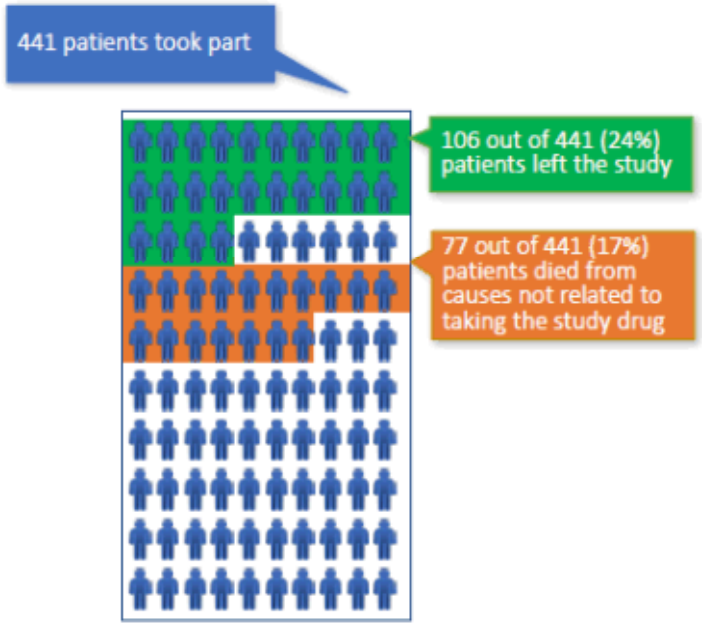
The study included patients who had a history of heart failure due to transthyretin amyloid cardiomyopathy. The patients and researchers did not know who took tafamidis and who took the placebo. This is known as a "blinded" study. This means that neither the patients nor doctors knew which drug the patients actually got.

The study began 09 December 2013 and ended 07 February 2018. While patients were in the study for 2.5 years (30 months), the entire study took about 4.5 years to complete. At the end of this study, all patients were offered the possibility to continue tafamidis treatment in a separate study to help researchers collect more data on the safety of tafamidis.

The Sponsor ran this study at 48 locations in 13 countries around the world. 398 men and 43 women participated. All patients were between the ages of 46 and 89.



Patients were to be treated for 30 months (2.5 years). Of the 441 patients who started the study, 258 finished the study. 183 patients did not finish the study by their choice or a doctor decided it was best for a patient to stop the study, or because they died from causes not related to taking the study drug.



When the study ended in February 2018, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

Was tafamidis more effective than placebo for treating patients with transthyretin amyloid cardiomyopathy?

To answer this question, the researchers looked at 2 separate measures:

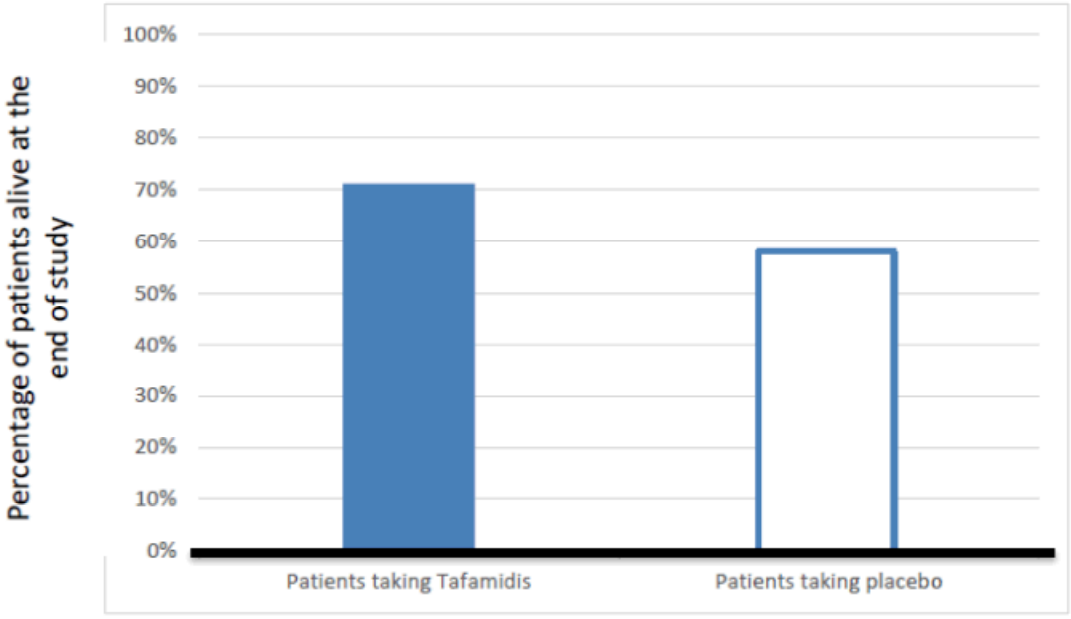
- How many patients were alive at the end of study?
- During the study, how many times was each patient hospitalized for heart problems?

The researchers used a method to determine whether tafamidis treatment was more effective than placebo. This method evaluated mortality (how many patients were

alive at the end of the study) and heart-related hospitalizations, giving higher priority to mortality.

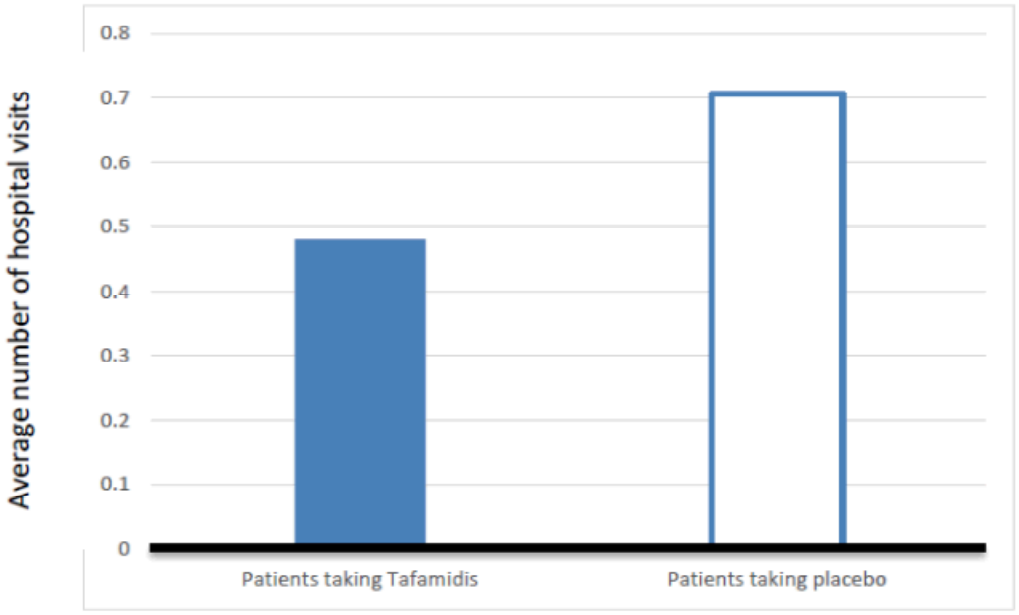
In the chart below you can see how many patients were alive at the end of the study. The higher the bar rises above the thick black line, the more patients survived.

- 186 out of 264 patients (70%) taking tafamidis were alive at the end of the study. This is shown by the blue column (bar) on the left.
- 101 out of 177 patients (57%) taking placebo were alive at the end of the study. This is shown by the white column (bar) on the right.



In the chart below you can see how many times patients were hospitalized for heart problems during the study. The higher the bar rises above the thick black line, the greater the number of hospital stays.

- On average, patients taking tafamidis were hospitalized for heart problems 0.48 times per year. This is shown by the blue column (bar) on the left.
- On average, patients taking placebo were hospitalized for heart problems 0.7 times per year. This is shown by the white column (bar) on the right.



The results of these 2 measures show that in this study, tafamidis was more effective than placebo for treating patients with transthyretin amyloid cardiomyopathy. The researchers have concluded that these results are not likely the result of chance, meaning that they were likely the result of the study drug.

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.

WHAT MEDICAL PROBLEMS DID PATIENTS 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 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 the side effects of an experimental drug might be.

412 out of 441 patients (93%) in this study had at least 1 medical problem. In this study, the percentage of patients with medical problems was similar in each group:

- Tafamidis 20 mg: 99% (87 out of 88 patients)
- Tafamidis 80 mg: 98% (173 out of 176 patients)
- Placebo: 99% (175 out of 177 patients)

Some of the medical problems were determined to be related to the study drug. In this study, more patients in the placebo group had medical problems that were determined to be related to the study drug, compared to patients in the tafamidis groups.

- Tafamidis 20 mg: 39% (34 out of 88 patients)
- Tafamidis 80 mg: 45% (79 out of 176 patients)
- Placebo: 51% (90 out of 177 patients)

The most common medical problems are listed on the following page.

Most Common Medical Problems (Reported by More Than 15% of Patients)			
Medical Problem	Tafamidis 20 mg (88 Patients treated)	Tafamidis 80 mg (176 Patients treated)	Placebo (177 Patients treated)
Fall	24 (27%)	38 (22%)	40 (23%)
Shortness of breath	21 (24%)	27 (15%)	51 (29%)
Heart failure	18 (20%)	20 (11%)	33 (19%)
Swelling in legs and ankles	17 (19%)	29 (16%)	31 (18%)
Tiredness	16 (18%)	29 (16%)	33 (19%)
Dizziness	16 (18%)	25 (14%)	32 (18%)
Cough	16 (18%)	20 (11%)	30 (17%)
Constipation	14 (16%)	25 (14%)	30 (17%)
Irregular heartbeat (atrial fibrillation)	13 (15%)	28 (16%)	31 (18%)
Extra fluid in the blood	11 (13%)	18 (10%)	27 (15%)
Diarrhea	10 (11%)	22 (13%)	39 (22%)
Acid buildup in joints	10 (11%)	17 (10%)	29 (16%)
Nausea	9 (10%)	20 (11%)	36 (20%)
Pain in the arms or legs	6 (7%)	27 (15%)	20 (11%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems. 339 out of 441 patients (77%) had serious medical problems. A total of 12 patients (3%) had serious medical problems that were determined to be related to study treatment, including 3 patients in the tafamidis 20 mg group, 3 patients in the tafamidis 80 mg group, and 6 patients in the placebo group.

Additionally, information about whether a patient was alive or not was collected at 30 months after the study began. A total of 144 patients died during this time period, including 77 deaths during the study and 67 deaths during the follow-up period. None of these deaths were determined to be related to study treatment.

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 this study protocol, please visit:

www.clinicaltrials.gov	Use the study identifier **NCT01994889**
www.clinicaltrialsregister.eu	Use the study identifier **2012-002465-35**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **B3461028**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients. Findings from this trial will be used to seek approval for using tafamidis for patients with transthyretin amyloid cardiomyopathy.

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!