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: Vyndaqel® (Tafamidis meglumine)

Protocol Number: B3461026 (Fx1B-303)

Dates of Trial: 22 September 2009 to 20 November 2019

Title of this Trial: A Trial to Measure the Safety and Efficacy of Vyndaqel Treatment in Patients With Transthyretin Amyloid Cardiomyopathy

[Open-Label Safety and Efficacy Evaluation of FX-1006A in Patients With V122I or Wild-Type Transthyretin (TTR) Amyloid Cardiomyopathy]

Date(s) of this Report: 25 September 2020

― 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 cardiomyopathy is a type of heart disease that is caused by a certain kind of protein building up in the heart muscle. This protein is called transthyretin, or “TTR”. TTR is normally made by your liver and carries things like hormones and Vitamin A throughout your body. In patients with transthyretin amyloid cardiomyopathy, TTR breaks apart and clumps together in fibers called “amyloid”. These amyloid fibers build up in the heart muscle and cause it to become stiff, eventually resulting in heart failure. Researchers are looking for new treatments that can help patients with transthyretin amyloid cardiomyopathy live longer.

Tafamidis meglumine (also known as Vyndaqel® and another form of tafamidis, Vyndamax®) is a drug that is now approved in the United States and other countries to treat transthyretin amyloid cardiomyopathy. Tafamidis was still an investigational drug when this study began. Tafamidis works by keeping TTR from breaking apart and forming into amyloid fibers. Researchers think that this slows down the buildup of amyloid fibers in the heart muscle, which helps slow down the rate at which the heart disease gets worse over time.

This study was an extension of the Study Fx1B-201, which treated transthyretin amyloid cardiomyopathy patients with tafamidis for 12 months. The main purpose of the current study was to measure how safe tafamidis treatment is over a longer period of time. Another purpose of this study was to give patients who took part in Study Fx1B-201 access to tafamidis treatment for up to 10 additional years. To measure the safety of long-term tafamidis treatment, the researchers in this study asked:

- What medical problems and serious medical problems did patients have while taking tafamidis?
- How long did patients live while taking tafamidis?
WHAT HAPPENED DURING THE STUDY?

This study followed 31 patients for up to 10 years to see what medical problems they had while taking tafamidis. This was an open-label study, which means that the patients and researchers knew that the patients were taking tafamidis. All patients took 20 mg of tafamidis by mouth once daily.

The study included men and women with transthyretin amyloid cardiomyopathy who had completed Study Fx1B-201 and had not received a heart or liver transplant. A diagram of the study is shown below.

Patients could have been in the study for up to 10 years. The entire study took 10 years and 2 months to complete. The Sponsor ran this study at 5 locations in the United States. It began on 22 September 2009 and ended on 20 November 2019. Twenty-eight (28) men and 3 women participated. All patients were between the ages of 69 and 88.
Patients were to be treated until the end of the study, or until the patient withdrew from the study or passed away. Of the 31 patients who started the study, 2 finished 10 years of study treatment. Twenty-nine (29) patients did not finish the study. Nineteen (19) patients did not finish the study because they passed away. Eight (8) patients left before the study was over by their choice, and 2 patients left because a doctor decided it was best for a patient to stop being in the study.

When the study ended in November 2019, 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?

What medical problems did patients have while taking tafamidis?

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 the side effects of an experimental drug might be.

All 31 patients in this study had at least 1 medical problem. A total of 2 patients stopped taking tafamidis because of medical problems and did not start again. The most common medical problems are listed below.

<table>
<thead>
<tr>
<th>Medical Problem</th>
<th>Tafamidis 20 mg (31 Patients Treated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fell down</td>
<td>15 (48%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>11 (36%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>11 (36%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>11 (36%)</td>
</tr>
<tr>
<td>Feeling very tired</td>
<td>10 (32%)</td>
</tr>
</tbody>
</table>
What serious medical problems did patients have while taking tafamidis?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems. Twenty-nine (29) patients (94%, or 29 out of 31 patients) had serious medical problems. The researchers in this study think that most of the serious medical problems were not related to taking tafamidis. Four (4) serious medical problems were reported for 3 patients that may have been related to taking tafamidis (1 patient had a blood clot in the lung, 1 patient reported feeling faint, and 1 patient had an irregular heart rhythm and kidney failure). A total of 23 patients passed away during this study, mostly due to heart-related medical problems. The most common serious medical problems are listed below.

<table>
<thead>
<tr>
<th>Serious Medical Problem</th>
<th>Tafamidis 20 mg (31 Patients Treated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>9 (29%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>Fell down</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>Health problems got worse</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Transthyretin amyloid cardiomyopathy got worse</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Infection of skin and soft tissue underneath</td>
<td>4 (13%)</td>
</tr>
</tbody>
</table>
How long did patients live while taking tafamidis?

To answer this question, the researchers measured how long patients lived while taking tafamidis before they passed away. They calculated the ‘median’ time lived, which is the time point when half (50%) of the patients in the study were still alive and half had passed away for any reason (such as a medical problem or an accident). For patients who passed away for any reason during the study, the median amount of time they lived was 4 years.

The researchers also looked at the patients who passed away from heart-related medical problems and calculated how long they had lived. For patients who passed away from heart-related medical problems during the study, the median amount of time they lived was 6 years.

Because all patients in this study took tafamidis, this study was not intended to show that one treatment was better than another. Tafamidis is now an option for treating patients with transthyretin amyloid cardiomyopathy.

This does not mean that everyone in this study had these results. Other studies may produce different results. 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 NCT00935012
www.pfizer.com/research/research_clinical_trials/trial_results Use the protocol number B3461026

Further clinical trials with tafamidis are planned. 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!