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:	ARRY-371797 (PF-07265803)
Protocol Number:	C4411002 (ARRAY-797-301)
Dates of Study:	17 April 2018 to 13 October 2022
Title of this Study:	A Study of ARRY-371797 (PF-07265803) in Patients With Symptomatic Dilated Cardiomyopathy Due to a Lamin A/C Gene Mutation (REALM-DCM) [A Phase 3, Multinational, Randomized, Placebo-Controlled Study of ARRY-371797 (PF-07265803) in Patients With Symptomatic Dilated Cardiomyopathy Due to a Lamin A/C Gene Mutation (REALM-DCM)]
Date(s) of this Report:	21 September 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 dilated cardiomyopathy due to a mutation in the *LMNA* gene?

Dilated cardiomyopathy (DCM) happens when the heart becomes bigger and weaker than normal. This means it is not able to pump blood around the body as well as it should. There are many reasons why DCM can develop, but mutations or changes in DNA (genetic material) are an important cause of DCM. The participants in this study had a genetic form of DCM known as LMNA-related DCM. This type of DCM is caused by a mutation in DNA of the gene that makes the lamin A/C protein. This protein is important for the structure and function of many cells in the body including the cells that make up the heart.

Symptoms of LMNA-related DCM usually start in young to mid-adulthood and often the person develops arrhythmia. Arrhythmia is a condition where the heart does not beat normally and the person can be described as having an irregular heartbeat, or the heartbeat can be too fast or too slow. Over time, symptoms can get worse, and the person may also have problems with their heart values, heart failure or have an embolism (or blood clot), all of which can be life-threatening.

Drugs are often given to help reduce symptoms of LMNA-related DCM and a pacemaker might be used to help control the heartbeat. An implantable cardioverter defibrillator is commonly recommended to prevent deadly arrhythmias. An implantable cardioverter defibrillator is a device implanted into the body. It shocks the heart if it detects important arrhythmia.

Despite these treatments, LMNA-related DCM can be fatal, and some people may need a heart transplant.

What is ARRY-371797?

ARRY-371797 is an investigational drug. This means it has not been approved by the United States (US) Food and Drug Administration (FDA) or other regulatory agency for use in treating diseases, including DCM.

ARRY-371797 is a medicine that researchers are developing for use in DCM caused by a mutation in the LMNA gene. The researchers believed that ARRY-371797 may have been able to inhibit an important protein. Inhibiting means to stop something from working. This stops other proteins being made that are known to damage the cells in the heart.

What was the purpose of this study?

The main purpose of this study was to look at the effect of taking ARRY-371797 on participants' ability to do a 6-minute walking test.

Researchers wanted to know:

What effect did taking ARRY-371797 have on the distance participants walked in the 6-minute walking test?

What medical problems did participants have during the study?

What happened during the study?

How was the study done?

First, a study doctor checked each participant to make sure they were able to join the study. This is known as a screening period.

Participants were then divided into 2 groups:

- Participants in one group took ARRY-371797 400 mg twice a day
- Participant in the other group took placebo. A placebo does not have any medicine in it, but it looks just like the study medication.

Participant were assigned to each treatment group by chance alone. This is known as a “randomized” study, and it helps make the treatment groups balanced and more even to compare.

The study participants and researchers did not know who took ARRY-371797 and who took the placebo. This is known as a “blinded” study. Study participants were assigned to each group by chance alone.

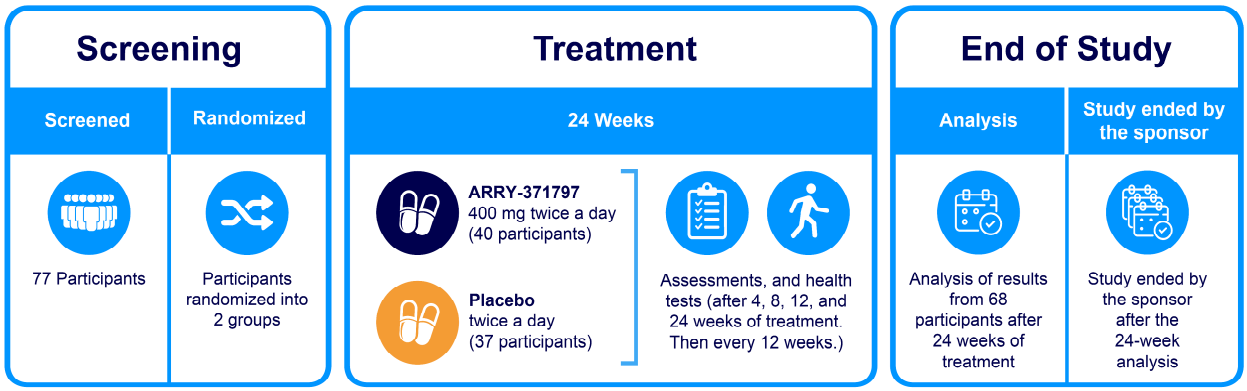
Participant were to visit the clinic at the start of the study and at Weeks 4, 8, 12, and 24, and then every 12 weeks.

Participants took a 6-minute walking test at the study visits, which measured the number of meters that participants could walk in 6 minutes. Researchers also checked the participants’ health during the study and asked them how they were feeling.

An analysis was conducted of the 6-minute walking test results for the first 68 participants who completed their Week 24 assessment (or who stopped participating in the study before 24 weeks of treatment).

A diagram showing what happened in the study is provided in Figure 1.

Figure 1: Study Plan



Where did this study take place?

The Sponsor ran this study at 31 locations in 6 countries in Europe, North America, and the US.

When did this study take place?

It began 17 April 2018 and ended 13 October 2022.

Who participated in this study?

The study included participants who had genetic DCM due to a mutation in the *LMNA* gene. The participants also met the inclusion/exclusion criteria for things such as age, condition type, severity, prior treatments, etc.

- A total of 44 men participated
- A total of 33 women participated
- All participants were between the ages of 23 and 72 years

Participants were to be treated for 24 weeks. Of the 77 participants who started the study, 51 participants completed 24 weeks of study treatment.

The reasons why the 77 participants left the study were as follows:

- 61 participants left because the sponsor terminated the study (this was the most common reason)
- 6 participants left by their own choice
- 5 participants left because of an unspecified reason
- 3 participants died (no death was believed to be related to study medications)
- 2 participants were lost to follow-up (this means that they could not be contacted)

How long did the study last?

Study participants were in the study for a variable length of time. The entire study took around 4 years and 6 months until the Sponsor stopped the study due to "futility". This was because no benefits were seen in the group treated with ARRY-371797 compared to placebo. Researchers believed that adding more participants to the study would be unlikely to change that result.

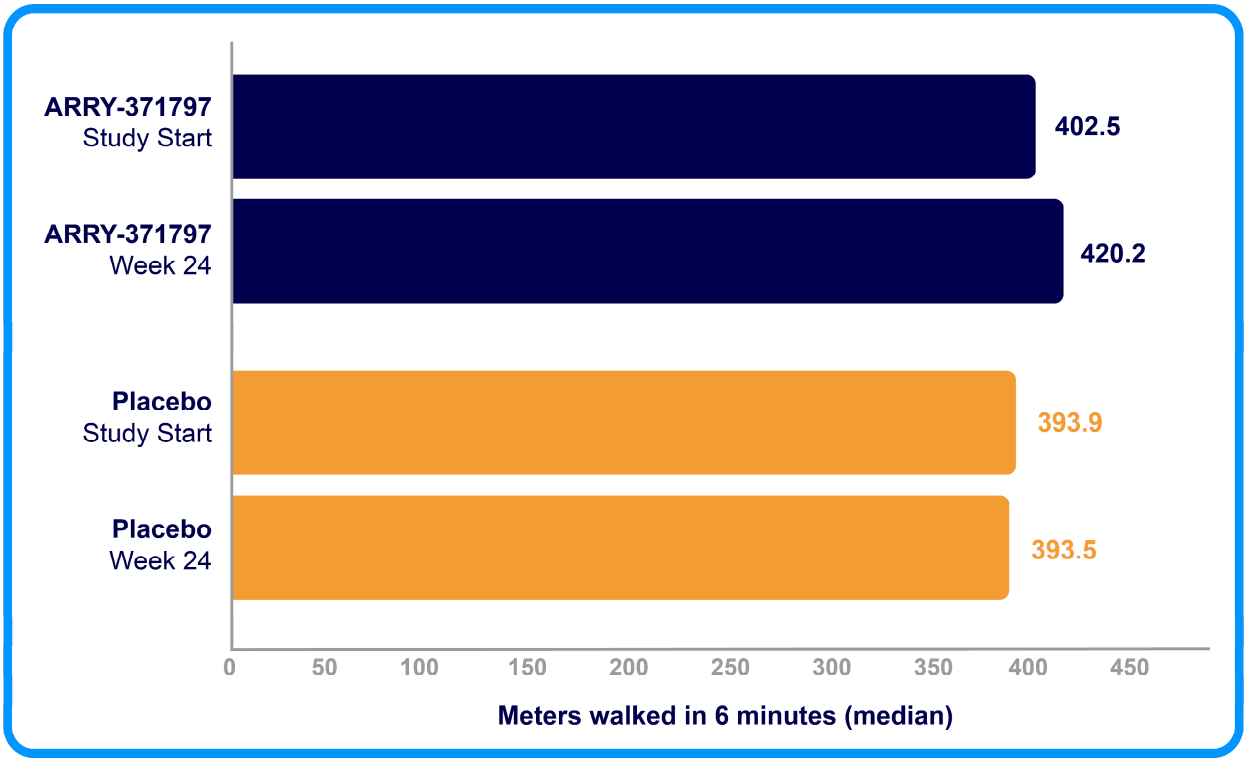
When the study ended in October 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

What effect did taking ARRY-371797 have on the distance participants walked in the 6-minute walking test?

Researchers measured how many meters participants walked in 6 minutes (the 6-minute walking test). The results are shown in Figure 2. The median is the middle number of a set of values when these values are arranged from smallest to largest.

Figure 2: Median number of Meters Walked in 6 Minutes



Was there a difference in the distance walked after treatment with ARRY-371797 compared to placebo?

The researchers have decided that these results were likely the result of chance. This means the study results did not show any clinically meaningful difference (there was no real-life difference to participants) between taking ARRY-371797 and taking placebo in the effect on the distance walked.

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.

A total of 69 out of 77 (89.6%) participants in this study had at least 1 medical problem. No participants left the study because of medical problems. The most common medical problems – those reported by more than 10% of participants – are described below.

Below are instructions on how to read Table 1 and Table 2.

Instructions for Understanding Table 1 and Table 2.

- The **1st** column of Table 1 and Table 2 lists medical problems that were commonly reported during the study. All medical problems reported by more than 10% of participants are listed in Table 1, and all serious medical problems reported by more than 1 participant are listed in Table 2.
- The **2nd** column tells how many of the 40 participants taking ARRY-371797 reported each medical problem. Next to this number is the percentage of the 40 participants taking ARRY-371797 who reported the medical problem.

- The **3rd** column tells how many of the 37 participants taking a placebo reported each medical problem. Next to this number is the percentage of the 37 participants taking a placebo who reported the medical problem.
- Using these instructions, you can see that in Table 1, 8 out of the 40 (20.0%) participants taking the study medication reported ventricular tachycardia (a very fast heartbeat). A total of 11 out of the 37 (29.7%) participants taking a placebo reported ventricular tachycardia.

Table 1. Commonly reported medical problems by study participants

Medical Problem	ARRY-371797 (40 Participants)	Placebo (37 Participants)
Ventricular tachycardia (very fast heartbeat)	8 out of 40 participants (20.0%)	11 out of 37 participants (29.7%)
Atrial fibrillation (irregular heartbeat, uncoordinated contractions in upper chambers of the heart)	7 out of 40 participants (17.5%)	6 out of 37 participants (16.2%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**ARRY-371797 (40 Participants)**	**Placebo (37 Participants)**
Diarrhea (loose stools)	12 out of 40 participants (30.0%)	4 out of 37 participants (10.8%)
Nausea (feeling about to vomit)	7 out of 40 participants (17.5%)	5 out of 37 participants (13.5%)
Positive COVID (coronavirus disease) test	11 out of 40 participants (27.5%)	7 out of 37 participants (18.9%)
Dizziness	9 out of 40 participants (22.5%)	4 out of 37 participants (10.8%)
Headache	4 out of 40 participants (10.0%)	6 out of 37 participants (16.2%)
Dyspnea (shortness of breath)	1 out of 40 participants (2.5%)	7 out of 37 participants (18.9%)
Hypotension (low blood pressure)	4 out of 40 participants (10.0%)	4 out of 37 participants (10.8%)

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.

A total of 31 out of 77 participants (40.3%) had serious medical problems. Serious medical problems reported by more than 1 out of the total 77 participants are shown in Table 2.

Table 2. Commonly reported serious medical problems by study participants

Medical Problem	ARRY-371797 (40 Participants)	Placebo (37 Participants)
Ventricular tachycardia (very fast heartbeat)	5 out of 40 participants (12.5%)	5 out of 37 participants (13.5%)
Ventricular fibrillation (irregular heartbeat, uncoordinated contractions in lower chambers of the heart)	2 out of 40 participants (5.0%)	3 out of 37 participants (8.1%)
Atrial fibrillation (irregular heartbeat, uncoordinated contractions in upper chambers of the heart)	1 out of 40 participants (2.5%)	2 out of 37 participants (5.4%)

Table 2. Commonly reported serious medical problems by study participants		
Medical Problem	**ARRY-371797 (40 Participants)**	**Placebo (37 Participants)**
Atrial flutter (rapid contraction of upper chambers of the heart)	1 out of 40 participants (2.5%)	1 out of 37 participants (2.7%)
Acute cardiac failure (heart is suddenly not pumping enough to get blood around the body)	1 out of 40 participants (2.5%)	2 out of 37 participants (5.4%)
Cardiac failure (heart is not pumping properly but blood is still getting around the body)	0	3 out of 37 participants (8.1%)
Acute kidney injury (kidneys suddenly stop working properly)	1 out of 40 participants (2.5%)	1 out of 37 participants (2.7%)

A total of 4 participants in the ARRY-371797 group had a serious medical problem that researchers believed was related to the study medication. These serious medical problems were diarrhea (loose stools), hemorrhagic diarrhea (diarrhea with bleeding), decreased ejection fraction (decreased amount of blood that is pumped out of the heart in one beat), and urticaria (itchy rash).

A total of 6 participants died during the study (3 in the ARRY-371797 group and 3 in the placebo group). Researchers do not believe any of the deaths reported by participants were related to study medications.

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 C4411002

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

www.clinicaltrials.gov	Use the study identifier NCT03439514
www.clinicaltrialsregister.eu	Use the study identifier 2017-004310-25

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!