CLINICAL TRIAL RESULTS

Sponsor: Pfizer, Inc.

Medicine Studied: PF-06425090

Protocol Number: B5091003

Dates of Trial: 28 July 2014 to 28 December 2015

Title of this Trial: A study to find out if 3 injections with a vaccine (given over the course of 30 days) to prevent infection with *Clostridium difficile* (*C difficile*) is safe and well tolerated in healthy people who were 50 to 85 years of age.

[A Phase 2, placebo-controlled, randomized, observer-blinded trial to evaluate the safety, tolerability, and immunogenicity of a *Clostridium difficile* vaccine administered as a 3-dose regimen in healthy adults aged 50 to 85 years.]

Date of this Report: 19 May 2017

– 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.

This summary of results represents a single trial only.

WHY WAS THIS STUDY DONE?

C difficile is a type of bacteria that can cause serious infections. It often shows up as antibiotic-associated diarrhea and is the most commonly recognized cause of infectious diarrhea in healthcare settings. The number of *C difficile* cases has increased recently, including in hospitals and nursing homes, possibly because of stronger strains of *C difficile* bacteria and increased use of antibiotics.

There is no approved vaccine to prevent primary *C difficile* infection. The investigational vaccine used in this study, PF-06425090, is an injection that helps the body produce an immune system response and potentially defend against a *C difficile* infection.

- The purpose of this trial was to find a safe dose of the PF-06425090 vaccine that caused few or no negative medical problems. This is why 2 different dose amounts were studied. Some volunteers received 3 injections of 100 µg (100 micrograms). Others received 3 injections of 200 µg. A third group received 3 injections of a solution with no active medication in it (placebo).
    - The placebo group was used to compare against the effects seen in volunteers who received the 2 different dose amounts of PF-06425090 vaccine (100 µg and 200 µg).
    - A previous study has already shown that the PF-06425090 vaccine can produce an immune system response against *C difficile* in humans.
- This study was divided into 3 stages:
    - The first 2 stages tested the 2 dose amounts of PF-06425090 vaccine (100 µg and 200 µg) and placebo in volunteers who were between 50 and 64 years of age (Stage 1) and 65 to 85 years of age (Stage 2).
    - Based on the findings in Stage 2, a third stage was planned to compare 3 injections of the most effective (best immune response) and well tolerated dose of PF-06425090 vaccine (either 100 µg or 200 µg) with placebo in volunteers who were 65 to 85 years of age.

WHAT HAPPENED DURING THE STUDY?

This study compared 2 different doses of PF-06425090 vaccine with placebo in volunteers who were 50 to 64 year of age (Stage 1) and then in volunteers who were 65 to 85 years of age (Stage 2).

The study was run at 12 sites across the United States. It began on 28 July 2014 and ended on 28 December 2015. The entire study took 17 months to complete because volunteers began at different times. Stage 1 was completed before Stage 2 started.

Volunteers were put into 1 of 3 groups (100 µg or 200 µg of PF-06425090 vaccine, or placebo) by chance alone. This is known as a "randomized" study. This is done to make the groups more similar for things like age and the number of men and women. Reducing differences between the groups makes the groups more even to compare.

In this study, the volunteers were "randomized" at a 3:3:1 ratio. This means for every 3 volunteers who received 100 µg of PF-06425090 vaccine, 3 different volunteers received the 200 µg dose, and 1 other volunteer received placebo.

In total, 184 volunteers took part. 42 volunteers started Stage 1, 27 volunteers were men and 15 were women. 142 volunteers started Stage 2, 56 were men and 86 were women. An additional volunteer was randomized to one of the groups, but never received any injections.

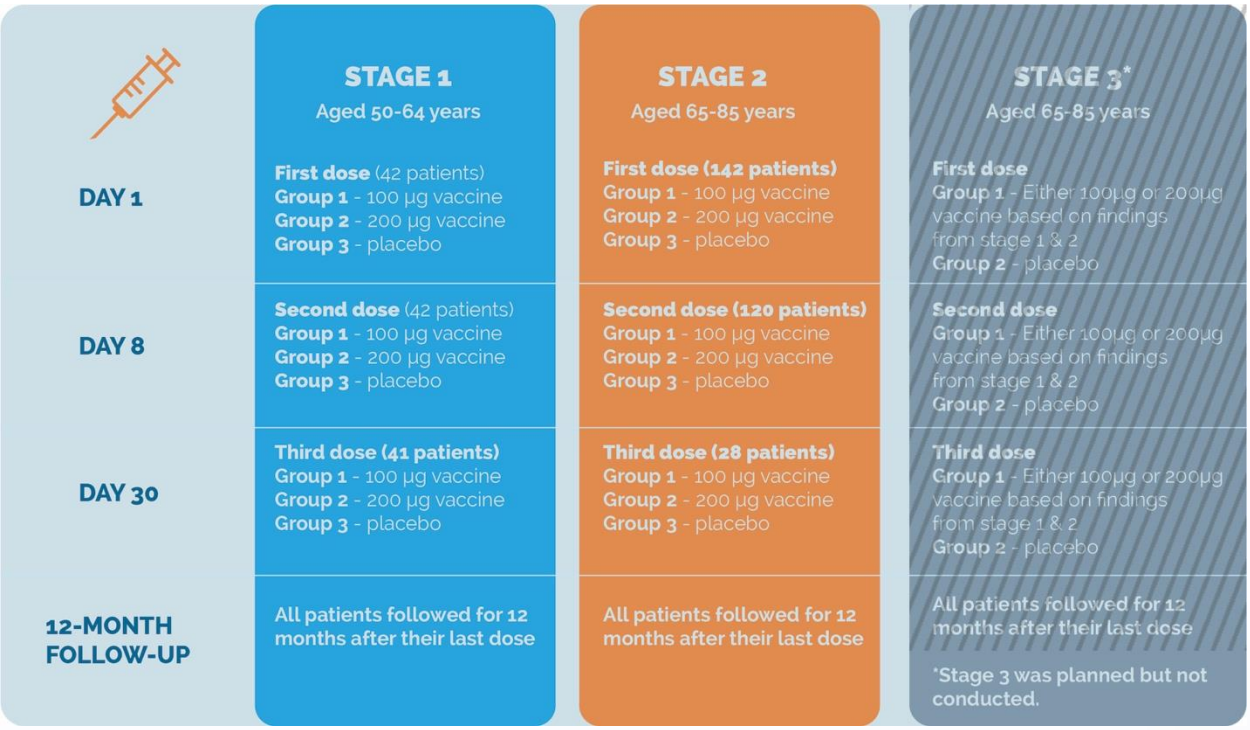
The study included:

- People considered healthy following a medical examination
- People with a long-term condition if it was stable
- Women no longer able to have children (for example, they had been through the menopause or had surgery to remove their reproductive organs)

Over the course of 30 days, volunteers received either 3 doses of 100 µg vaccine, 3 doses of 200 µg vaccine or 3 doses of placebo on Day 1, Day 8, and Day 30. All volunteers were followed for at least 12 months after their last injection.

The volunteers and researchers did not know who was in each group. Only the person who prepared the vaccine for injection knew who received which dose of vaccine or placebo. This is called an "observer-blinded study."

Stage 3 was planned but did not happen. Vaccinations were stopped in Stage 2 after several volunteers who were 65 to 85 years of age had severe redness at the site of their injection.



In Stage 1, involving volunteers who were 50 to 64 years of age:

- 18 volunteers were in the 100 µg vaccine group;
- 18 volunteers were in the 200 µg vaccine group;
- 6 volunteers were in the placebo group;
    - In total, 42 volunteers received dose 1, 42 volunteers received dose 2, and 41 volunteers received dose 3.

In Stage 2, involving volunteers who were 65 to 85 years of age:

- 62 volunteers were in the 100 µg vaccine group;
- 60 volunteers were in the 200 µg vaccine group;
- 21 volunteers were in the placebo group;
    - In total, 142 volunteers received dose 1, 120 volunteers received dose 2, and 28 volunteers received dose 3.

As 7 volunteers had severe injection site redness in Stage 2 of the study, vaccinations were stopped. This is why only 28 volunteers received the third dose. Stage 3 of this trial did not happen.

Out of the 184 volunteers in the study, 14 withdrew before it was completed (5 from Stage 1 and 9 from Stage 2). 1 volunteer in Stage 2, who received 2 doses of 200 µg PF-06425090 vaccine, withdrew after he had a heart attack and later died. The study doctor determined the heart attack was not as a result of the vaccine.

WHAT WERE THE RESULTS OF THE STUDY?

Was PF-06425090 vaccine safe and acceptable (with no serious medical problems) in volunteers 50 to 85 years of age at either the 100 µg or 200 µg dose? That was the main reason for this study (known as the primary endpoint). A group who received 3 doses of a placebo vaccine was used as a comparison.

Results were based on volunteers' reports in electronic diaries (e-diaries) and medical problems noted by the study doctors. Among volunteers who were 50 to 64 years of age, who received either 100 µg or 200 µg doses of PF-06425090 vaccine, pain or redness of the skin at the injection site was the most common medical problem. In nearly all cases these medical problems were mild and no volunteers withdrew from the study.

Among volunteers who were 65 to 85 years of age, redness around the vaccination area (injection site erythema) was the most common medical problem. 6 volunteers, out of the total of 121 in the 2 vaccine groups, experienced severe redness. None of them withdrew from the study as a result of the reaction. However, following this finding, the Sponsor decided not to carry out Stage 3 of the study. All volunteers were followed for 12 months after their last injection and no other safety concerns were noted.

WHAT MEDICAL PROBLEMS DID VOLUNTEERS HAVE DURING THE STUDY?

The researchers recorded any medical problems the volunteers had during the study. Volunteers 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 drug the volunteer 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.

In this study, in volunteers 50 to 64 years of age, 5 out of 18 who received the 100 µg vaccine, and 9 out of 18 who received 200 µg had at least 1 non-serious medical problem. In volunteers 65 to 85 years of age, 22 out of 61 who received the 100 µg vaccine and 22 out of 60 who received 200 µg had at least 1 non-serious medical problem. The most common are listed below.

Most Common Non-Serious Medical Problems (Reported by More Than 1 Volunteer in Each Group)

	Placebo Group	100 µg Vaccine Group	200 µg Vaccine Group
50 to 64 years old	**6 volunteers**	**18 volunteers**	**18 volunteers**
Injection site redness (erythema)	0	1 (6%)	3 (17%)
65 to 85 years old	**21 volunteers**	**61 volunteers**	**60 volunteers**
Injection site bruising	0	2 (3%)	0
Injection site redness (erythema)	0	2 (3%)	5 (8%)
Injection site pain	0	1 (2%)	2 (3%)
Upper respiratory tract infection	0	0	2 (3%)
Fall	1 (5%)	2 (3%)	2 (3%)
Muscle strain	0	0	2 (3%)
Headache	1 (5%)	2 (3%)	0
High blood pressure	0	1 (2%)	3 (5%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. In total, 14 volunteers (8%) had serious medical problems. 10 of the volunteers received either 100 µg or 200 µg of PF-06425090 vaccine and 4 of the volunteers received placebo. None of the serious medical problems were considered by the study doctors or Sponsor to be related to the vaccine.

- Serious medical problems among volunteers who were 50 to 64 years of age:
  - 1 in the placebo group;
  - 2 in the 100 µg vaccine group;
  - None in the 200 µg vaccine group.
- Serious medical problems among volunteers who were 65 to 85 years of age:
  - 3 in the placebo group;
  - 2 in the 100 µg vaccine group;
  - 6 in the 200 µg vaccine group.

One volunteer died during the study of a heart attack, but the study doctors and Sponsor did not consider this to be related to the PF-06425090 vaccine.

Serious Medical Problems (Experienced by Volunteers 50 to 64 Years of Age)

Medical Problem	Placebo Group (6 volunteers)	100 µg Vaccine Group (18 volunteers)	200 µg Vaccine Group (18 volunteers)
Any serious medical problem	1 (17%)	2 (11%)	0
Skin and bone infections	0	1 (6%)	0
Tumors (neoplasms)	1 (17%)	1 (6%)	0

Serious Medical Problems (Experienced by Volunteers 65 to 85 Years of Age)			
Medical Problem	**Placebo Group (21 volunteers)**	**100 µg Vaccine Group (61 volunteers)**	**200 µg Vaccine Group (60 volunteers)**
Any serious medical problem*	3 (14%)	2 (3%)	6 (10%)
Heart (cardiac) issues	1 (5%)	0	3 (5%)
Liver or gallbladder (hepatobiliary) issues	0	1 (2%)	1 (2%)
Infections (abscess)	0	0	1 (2%)
Fractures and falls	1 (5%)	0	1 (2%)
Muscle or bone pain	1 (5%)	0	1 (2%)
Tumors (neoplasms)	0	0	1 (2%)
Seizure	0	0	1 (2%)
Issues with equipment	0	1 (2%)	1 (2%)
Low blood pressure	0	0	1 (2%)

* Some volunteers experienced more than 1 serious medical problem

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 **NCT02117570**).

Please remember that researchers look at the results of many studies to find out which medicines work best and are safest 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!