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: 20-valent Pneumococcal Conjugate Vaccine (diphtheria CRM_{197} protein), Compound Number: PF-06482077

Protocol Number: B7471007

Dates of Trial: 12 December 2018 to 16 December 2019

Title of this Trial: Trial to Evaluate the Safety and Immunogenicity of a 20-valent Pneumococcal Conjugate Vaccine in Pneumococcal Vaccine-Naïve Adults

[Final Report: A Phase 3, Randomized, Double-Blind Trial to Evaluate the Safety and Immunogenicity of a 20-valent Pneumococcal Conjugate Vaccine in Pneumococcal Vaccine–Naïve Adults 18 Years of Age and Older]

Date of this Report: 4 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?

Streptococcus pneumoniae is a bacteria that can cause serious diseases, including infections of the lung (pneumonia), brain lining (meningitis), blood (bacteremia), or ear (otitis). These infections may be very serious in young children and older adults. *Streptococcus pneumoniae* is also known as *S. pneumoniae.* There are 100 types of *S. pneumoniae.*

This study is about a vaccine called the "20-valent pneumococcal conjugate vaccine", or 20vPnC. A vaccine is used to help prevent infection by helping the body to fight off germs. 20vPnC may help to prevent infections caused by *S. pneumoniae.* It is called "20-valent" because 20vPnC prevents 20 of the most common types of *S. pneumoniae.*

20vPnC is an investigational vaccine, which means that it has not been approved for general use and it is not yet known if it will protect against disease caused by *S. pneumoniae,* although studies are ongoing to assess how well 20vPnC works.

After a vaccine is injected into a person's body, the body responds to help fight infections and prevent diseases. The response to vaccines includes making "antibodies", which are proteins that fight infections and help to prevent diseases.

In the United States, the "13-valent pneumococcal conjugate vaccine", or 13vPnC, is currently approved for preventing *S. pneumoniae* diseases in children and adults. 13vPnC is made up of components to prevent diseases caused by 13 types of *S. pneumoniae.* 20vPnC has the same components found in 13vPnC, plus 7 additional components that may widen protection. The Pneumovax 23 vaccine, or PPSV23, is made up of components to prevent diseases caused by 23 types of *S. pneumoniae.*

The purpose of this study was to learn about the safety and about the antibody response to 20vPnC.

To learn about the antibody response, researchers asked these questions:

- For the 13 components found in both 13vPnC and 20vPnC, did participants aged 60 or older who received 20vPnC have antibody responses that were within a range considered to be comparable (noninferior) to those who received 13vPnC?

- For the 7 additional components found in both PPSV23 and 20vPnC, did participants aged 60 or older who received 20vPnC have antibody responses that were within a range comparable to those who received PPSV23?

To answer this question, the researchers measured the amount of antibodies in participants' blood 1 month after being vaccinated.

To learn about the safety of 20vPnC, researchers asked these questions:

- What percentage of participants had redness, swelling, or pain at the injection site within 10 days after being vaccinated?
- What percentage of participants had fever, headache, tiredness, muscle pain, or joint pain within 7 days after being vaccinated?
- What significant medical problems did participants have within 1 month after being vaccinated?
- Did participants have any newly diagnosed chronic medical problems or any serious medical problems within 6 months after being vaccinated?

WHAT HAPPENED DURING THE STUDY?

This study included 3 different age ranges of participants to learn about the safety and about the antibody response to 20vPnC. The main age range studied was participants 60 years old and above. The vaccines used in this study included 20vPnC, 13vPnC, PPSV23, and salt water (saline) placebo. A placebo is given in the same way as the vaccines used in study but does not have active ingredients. 20vPnC and 13vPnC looked the same; however, the saline and PPSV23 looked different and were injected by staff that were not involved in other aspects of the study. Participants were asked to turn their heads when the PPSV23 or saline was injected so they would not know which one they had received.

Participants were checked (screened) to make sure they were a good fit for the study. This study included adult men and women who:

- Were at least 18 years old
- Were considered to be healthy or with stable chronic disease by the study doctors

- Did not have a disease or take medicine that would be associated with a weakened immune system
- Never received any vaccine for *S. pneumoniae*
- Never had a disease caused by *S. pneumoniae*
- Never had a severe medical problem caused by a vaccine or an allergic reaction to any of the components in the vaccines used in this study

Participants of 3 different age ranges were entered into the study.

- 60 years of age and older (3009 participants)
- 50 through 59 years of age (445 participants)
- 18 through 49 years of age (448 participants)

Next, participants in the 3 age ranges were assigned to vaccine groups by chance alone, and received the following vaccinations:

60 years and older:

- Vaccine Group 1: 20vPnC at Visit 1 and placebo at Visit 2 one month later (1507 participants)
- Vaccine Group 2: 13vPnC at Visit 1 and PPSV23 at Visit 2 one month later (1490 participants)

50 through 59 years of age:

- Vaccine Group 1: 20vPnC at Visit 1 (334 participants)
- Vaccine Group 2: 13vPnC at Visit 1 (111 participants)

18 through 49 years of age:

- Vaccine Group 1: 20vPnC at Visit 1 (335 participants)
- Vaccine Group 2: 13vPnC at Visit 1 (112 participants)

This was a "randomized" study, which means that participants were assigned to groups based on chance alone. Randomization is done to make the groups similar so that differences in antibody response or safety are most likely due to the different vaccines participants received.

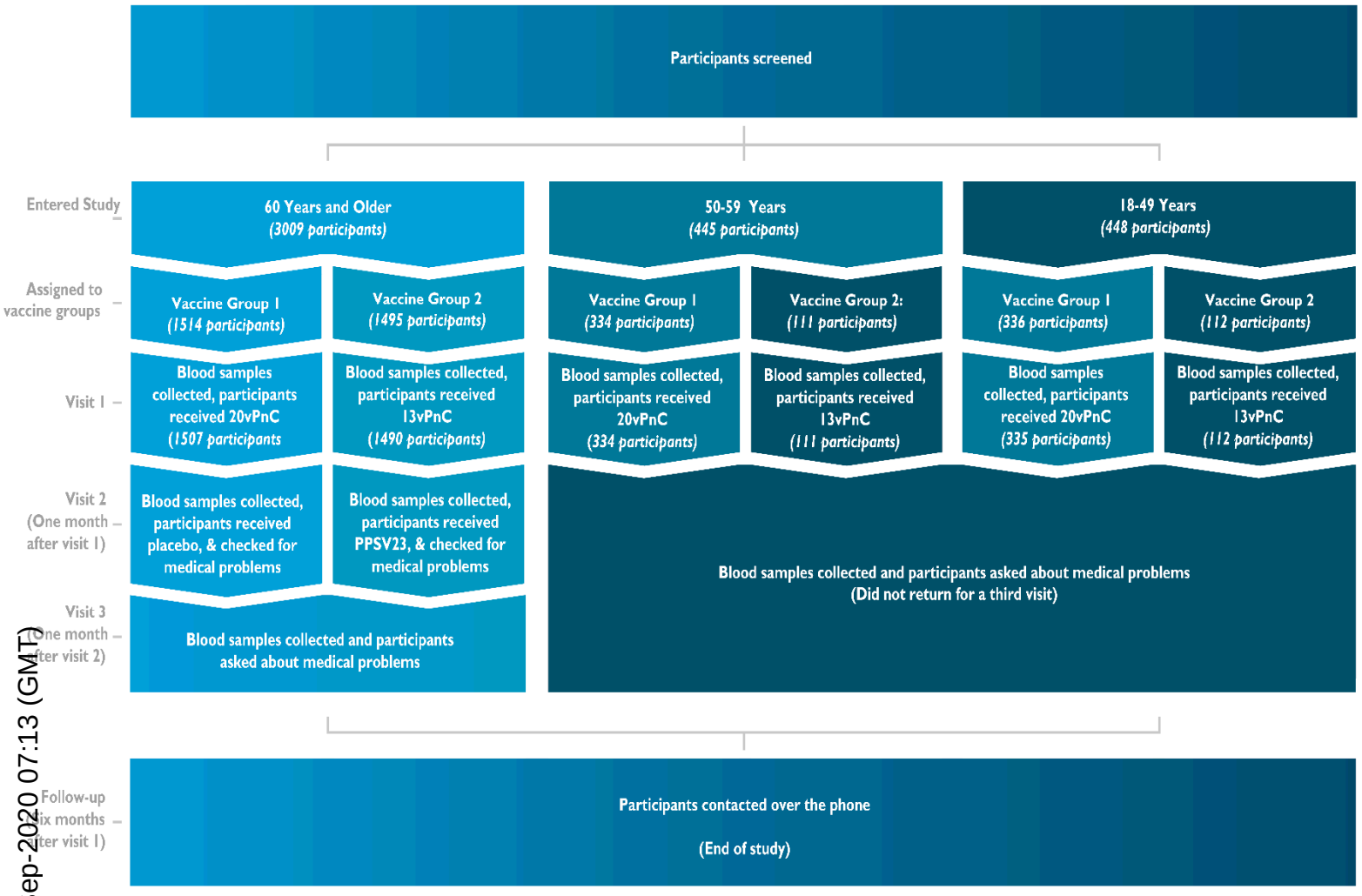
This study was also "double-blinded". This means that participants and study staff members who administered the vaccine did not know who was given which vaccine. This was done to make sure that the study results were not influenced in any way.

Participants 60 years of age and older were expected to participate in 3 study visits. At the first visit, blood samples were collected first and then participants received either 20vPnC or 13vPnC. The second visit was done about 1 month after the first visit. Blood samples were collected before the participants received either saline placebo or PPSV23, and they were checked for medical problems. The third visit was done about 1 month after the second visit. Blood samples were collected and participants were asked about medical problems.

Participants 18 to 59 years of age were expected to participate in 2 study visits. At the first visit, blood samples were collected first and then participants received either 20vPnC or 13vPnC. The second visit was done about 1 month after the first visit. Blood samples were collected and participants were asked about medical problems.

All participants were also contacted over the phone about 6 months after Visit 1. The participants were asked about medical problems and whether they had received any other vaccines besides the study vaccines.

The figure on the following page shows what happened during the study.



While participants were in this study for about 6 months, the entire study took more than a year to complete as participants entered the study at different times. The Sponsor ran this study at 61 locations in the United States and Sweden. It began 12 December 2018 and ended 16 December 2019. 1558 men (40%) and 2331 women (60%) received the study vaccines. All participants were between the ages of 18 and 91 years.

Of the 3902 participants who joined the study, 3690 (95%) completed it. A total of 212 participants (5%) left the study early. The most common reasons for leaving early were the participant's choice or because a doctor decided it was best for them to stop the study.

Throughout the course of the study, the Sponsor reviewed the data. When the study ended in December 2019 and after antibody testing was completed, the Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

For the 13 components found in both 13vPnC and 20vPnC, did participants aged 60 or older who received 20vPnC have antibody responses that were within a range considered to be comparable (noninferior) to those who received 13vPnC?

To evaluate antibody response, the researchers measured the amount of antibodies in participants' blood 1 month after being vaccinated with 13vPnC or 20vPnC.

The researchers found that antibody levels for each of these 13 vaccine components in participants after 20vPnC were within a range considered to be comparable (noninferior) to those in participants after 13vPnC. Therefore, the participants who received 20vPnC had comparable antibody responses to the participants who received 13vPnC. Based on these results, the researchers have decided that the results are not likely the result of chance. 20vPnC may be an option for preventing *S. pneumoniae* diseases.

For the 7 additional components found in both PPSV23 and 20vPnC, did participants aged 60 or older who received 20vPnC have antibody responses that were within a range comparable to those who received PPSV23?

To evaluate antibody response, the researchers measured the amount of antibodies in participants' blood 1 month after being vaccinated with PPSV23 or 20vPnC.

The researchers found that antibody levels for 6 of the 7 additional vaccine components after 20vPnC were within a range considered to be comparable (noninferior) to those in participants after PPSV23. Therefore, the participants who received 20vPnC had antibody responses that were comparable to the participants who received PPSV23 for these 6 components, and in fact had higher antibody levels.

For 1 of these 7 additional vaccine components, antibody levels were found to be in a slightly lower range in participants who received 20vPnC compared to those who received PPSV23. However, the researchers still expected 20vPnC to produce an adequate antibody response for this component. Based on these results, the researchers have decided that the results are not likely the result of chance. 20vPnC may be an option for preventing *S. pneumoniae* diseases.

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 PARTICIPANTS HAVE DURING THE STUDY?

The researchers recorded any significant 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 study vaccine or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By

looking at significant medical problems across many treatment groups in many studies, doctors try to understand what the side effects of an experimental drug (in this case experimental vaccine) might be.

What significant medical problems did participants have within 1 month after being vaccinated?

For participants 60 years of age and older, 314 out of 2997 (10%) had at least 1 significant medical problem within 1 month after being vaccinated with 20vPnC or 13vPnC, including 148 out of 1507 (10%) participants in Vaccine Group 1 and 166 out of 1490 (11%) participants in Vaccine Group 2. 11 participants (1%) in Vaccine Group 1 and 8 participants (1%) in Vaccine Group 2 left the study due to medical problems. The table below shows the most common significant medical problems in the participants 60 years of age and older.

Most Common Significant Medical Problems (Reported by At Least 4 Participants in a Group) 1 Month After 20vPnC or 13vPnC – 60 Years of Age and Older

	Vaccine Group 1 20vPnC + Placebo (1507 Participants)	Vaccine Group 2 13vPnC + PPSV23 (1490 Participants)
Infection of the nose, throat, and airways	12 (1%)	8 (1%)
Joint pain	6 (less than 1%)	1 (less than 1%)
Fall	5 (less than 1%)	7 (less than 1%)
Cough	5 (less than 1%)	5 (less than 1%)
Viral infection	5 (less than 1%)	0 (0%)
Sinus infection	4 (less than 1%)	6 (less than 1%)

Inflammation of the tubes that carry air to the lungs	**4 (less than 1%)**	**3 (less than 1%)**
Common cold	**2 (less than 1%)**	**7 (less than 1%)**
Diarrhea	**2 (less than 1%)**	**4 (less than 1%)**
Tiredness	**2 (less than 1%)**	**4 (less than 1%)**
High blood pressure	**1 (less than 1%)**	**7 (less than 1%)**
Lung disease that causes breathing problems	**0 (0%)**	**4 (less than 1%)**
Acid reflux disease	**0 (0%)**	**4 (less than 1%)**

For participants 50 through 59 years of age, 43 out of 445 (10%) had at least 1 significant medical problem within 1 month after being vaccinated, including 34 out of 334 (10%) participants in Vaccine Group 1 and 9 out of 111 (8%) participants in Vaccine Group 2. The table below shows the most common significant medical problems in participants 50 through 59 years.

Most Common Significant Medical Problems (Reported in At Least 4 Participants in a Group) 1 Month After 20vPnC or 13vPnC – 50 to 59 Years of Age		
	Vaccine Group 1 20vPnC (334 Participants)	**Vaccine Group 2 13vPnC (111 Participants)**
Infection of the nose, throat, and airways	**4 (1%)**	**3 (3%)**
Fall	**4 (1%)**	**0 (0%)**

For participants 18 through 49 years of age, 64 out of 447 (14%) had at least 1 significant medical problem within 1 month after being vaccinated, including 51 out of 335 (15%) participants in Vaccine Group 1 and 13 out of 112 (12%) participants in Vaccine Group 2. The table below shows the most common significant medical problems in participants 18 through 49 years of age.

Most Common Significant Medical Problems (Reported in At Least 4 Participants in a Group) 1 Month After 20vPnC or 13vPnC – 18 to 49 Years of Age

	Vaccine Group 1 20vPnC (335 Participants)	Vaccine Group 2 13vPnC (112 Participants)
Infection of the nose, throat, and airways	**7 (2%)**	**1 (1%)**
Flu	**7 (2%)**	**1 (1%)**
Common cold	**6 (2%)**	**2 (2%)**

No participants 59 years of age and younger left the study due to medical problems.

What percentage of participants had redness, swelling, or pain at the injection site within 10 days after being vaccinated?

The percentage of participants with redness, swelling, or pain at the injection site within 10 days after being vaccinated was similar for both vaccine groups in each age range. The tables on the following page show the percentage of participants with these reactions.

Percentage of Participants With Redness, Swelling, or Pain at Injection Site Within 10 Days After Being Vaccinated with 20vPnC or 13vPnC – 60 Years of Age and Older		
	Vaccine Group 1 20vPnC + Placebo (1505 Participants)	Vaccine Group 2 13vPnC + PPSV23 (1483 Participants)
Redness at injection site	110 (7%)	92 (6%)
Swelling at injection site	113 (8%)	118 (8%)
Pain at injection site	834 (55%)	803 (54%)

Percentage of Participants with Redness, Swelling, or Pain at Injection Site Within 10 Days After Being Vaccinated with 20vPnC or 13vPnC – 50 to 59 Years of Age		
	Vaccine Group 1 20vPnC (331 Participants)	Vaccine Group 2 13vPnC (111 Participants)
Redness at injection site	27 (8%)	6 (5%)
Swelling at injection site	29 (9%)	12 (11%)
Pain at injection site	240 (73%)	77 (69%)

Percentage of Participants with Redness, Swelling, or Pain at Injection Site Within 10 Days After Being Vaccinated with 20vPnC or 13vPnC – 18 to 49 Years of Age		
	Vaccine Group 1 20vPnC (335 Participants)	Vaccine Group 2 13vPnC (112 Participants)
Redness at injection site	30 (9%)	11 (10%)
Swelling at injection site	39 (12%)	14 (13%)
Pain at injection site	272 (81%)	92 (82%)

What percentage of participants had fever, headache, tiredness, muscle pain, or joint pain within 7 days after being vaccinated?

The percentage of participants with fever, headache, tiredness, muscle pain, or joint pain within 7 days after being vaccinated was similar for both vaccine groups in each age range. A fever is a body temperature that is 38.0 degrees Celsius or higher (100.4 degrees Fahrenheit or higher). The tables on the following page show the percentage of participants with these reactions.

Percentage of Participants With Fever, Headache, Tiredness, Muscle Pain, or Joint Pain Within 7 Days After Being Vaccinated with 20vPnC or 13vPnC – 60 Years of Age and Older		
	Vaccine Group 1 20vPnC + Placebo (1505 Participants)	Vaccine Group 2 13vPnC + PPSV23 (1483 Participants)
Fever	14 (1%)	12 (1%)
Tiredness	454 (30%)	455 (31%)
Headache	324 (22%)	345 (23%)
Muscle pain	588 (39%)	553 (37%)
Joint pain	190 (13%)	203 (14%)

Percentage of Participants With Fever, Headache, Tiredness, Muscle Pain, or Joint Pain Within 7 Days After Being Vaccinated with 20vPnC or 13vPnC – 50 to 59 Years of Age		
	Vaccine Group 1 20vPnC (331 Participants)	Vaccine Group 2 13vPnC (111 Participants)
Fever	5 (2%)	1 (1%)
Tiredness	130 (39%)	40 (36%)
Headache	107 (32%)	40 (36%)
Muscle pain	165 (50%)	55 (50%)
Joint pain	51 (15%)	23 (21%)

Percentage of Participants With Fever, Headache, Tiredness, Muscle Pain, or Joint Pain Within 7 Days After Being Vaccinated with 20vPnC or 13vPnC – 18 to 49 Years of Age		
	Vaccine Group 1 20vPnC (335 Participants)	Vaccine Group 2 13vPnC (112 Participants)
Fever	4 (1%)	2 (2%)
Tiredness	143 (43%)	49 (44%)
Headache	130 (39%)	38 (34%)
Muscle pain	223 (67%)	83 (74%)
Joint pain	45 (13%)	20 (18%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

Did participants have any newly diagnosed chronic medical problems or any serious medical problems within 6 months after being vaccinated?

There were 69 participants 60 years of age and older (2%) with newly diagnosed chronic medical problems within 6 months after being vaccinated, including 34 out of 1507 (2%) participants in Vaccine Group 1 and 35 out of 1490 (2%) participants in Vaccine Group 2.

There were 2 participants 50 through 59 years of age (less than 1%) who had newly diagnosed chronic medical problems within 6 months after being vaccinated, including 1 out of 334 (less than 1%) participants in Vaccine Group 1 and 1 out of 111 (1%) participants in Vaccine Group 2.

There were 2 participants 18 through 49 years of age (less than 1%) who had newly diagnosed chronic medical problems within 6 months after being vaccinated, including 2 out of 335 (1%) participants in Vaccine Group 1 and 0 out of 112 (0%) participants in Vaccine Group 2.

In participants 60 years of age and older, 65 out of 2997 (2%) had serious medical problems within 6 months after being vaccinated, including 36 out of 1507 (2%) participants in Vaccine Group 1 and 29 out of 1490 (2%) participants in Vaccine Group 2. None of the serious medical problems were thought to be related to the study vaccine by the study doctors. One participant 60 years of age or older died during this study. This death was not considered to be related to the study vaccine.

In participants 50 through 59 years of age, 2 out of 445 (less than 1%) had serious medical problems within 6 months after being vaccinated, including 1 out of 334 (less than 1%) participants in Vaccine Group 1 and 1 out of 111 (1%) participants in Vaccine Group 2. None of the serious medical problems were thought to be related to the study vaccine by the study doctors. No participants 50 through 59 years of age died during this study.

In participants 18 through 49 years of age, 3 out of 447 (1%) had serious medical problems within 6 months after being vaccinated, including 2 out of 335 (1%) participants in Vaccine Group 1 and 1 out of 112 (1%) participants in Vaccine Group 2. None of the serious medical problems were thought to be related to the study vaccine by the study doctors. No participants 18 through 49 years of age died during this study.

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.clinicaltrials.gov	Use the study identifier **NCT03760146**
www.clinicaltrialsregister.eu	Use the study identifier **2018-004279-11**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients. Further clinical trials with 20vPnC are planned.

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!