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: B7471006

Dates of Trial: 12 February 2019 to 12 February 2020

Title of this Trial: Trial to Evaluate the Safety and Immunogenicity of a 20-Valent Pneumococcal Vaccine in Adults 65 Years of Age or Older With Prior Pneumococcal Vaccination

[Final Report: A Phase 3, Randomized, Open-Label Trial to Evaluate the Safety and Immunogenicity of a 20-valent Pneumococcal Conjugate Vaccine in Adults ≥65 Years of Age With Prior Pneumococcal Vaccination]

Date of this Report: 25 November 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.

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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 is intended to prevent 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, 2 vaccines are currently approved for preventing *S. pneumoniae* diseases. Pneumovax 23 vaccine, or PPSV23, is an older vaccine made up of components to prevent diseases caused by 23 types of *S. pneumoniae.* It has some limitations. The "13-valent pneumococcal conjugate vaccine", or 13vPnC, is made up of similar, but more active, components to prevent diseases caused by 13 types of *S. pneumoniae.* 20vPnC has the same components found in 13vPnC, plus 7 additional active components that may widen protection.

It is currently recommended that upon consultation with their health practitioner, adults 65 years and above in the United States receive 1 dose of 13vPnC, followed by 1 dose of PPSV23 1 year later.

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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 this question:

- One month after receiving 20vPnC, did participants aged 65 or older who had previously received 13vPnC and/or PPSV23 have antibody responses against the 20 types of *S. pneumoniae* contained in the vaccine?

To learn about the safety of 20vPnC in adults aged 65 or older who previously received 13vPnC and/or PPSV23, researchers asked these questions:

- What percentage of participants had significant medical problems within 1 month after being vaccinated?
- 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 percentage of participants had newly diagnosed chronic medical problems or serious medical problems within 6 months after being vaccinated?

WHAT HAPPENED DURING THE STUDY?

This study was done to learn about the safety and the antibody response to 20vPnC in participants 65 years old and older. The vaccines used in this study included 20vPnC, 13vPnC, and PPSV23.

This study included adult men and women who:

- Were at least 65 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 had a disease caused by *S. pneumoniae*

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- 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
- Had previously been vaccinated with 13vPnC and/or PPSV23

Participants were placed into 3 categories based on which vaccines they had previously received:

- Category 1: Received PPSV23 between 1 and 5 years before the study started, but had never received 13vPnC (375 participants)
- Category 2: Received 13vPnC at least 6 months before the study started, but had never received PPSV23 (375 participants)
- Category 3: Received 13vPnC followed by PPSV23 1 year later, and the PPSV23 dose had been received at least 1 year before the study started (125 participants)

Next, participants in Category 1 and Category 2 were assigned by chance alone to receive the following study vaccines:

- Category 1: 1 dose of either 20vPnC (253 participants) or 13vPnC (122 participants)
- Category 2: 1 dose of either 20vPnC (248 participants) or PPSV23 (127 participants)

A control group is a group of participants who do not receive the vaccine being studied. In this study, 13vPnC and PPSV23 were used as the controls to look at safety of 20vPnC because they are commonly used in this age group.

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.

The participants who had been vaccinated with both 13vPnC and PPSV23 in the past (Category 3, 125 participants) received 20vPnC only.

This study was also "open-label". This means that participants and study staff members who administered the vaccine knew who was given which vaccine.

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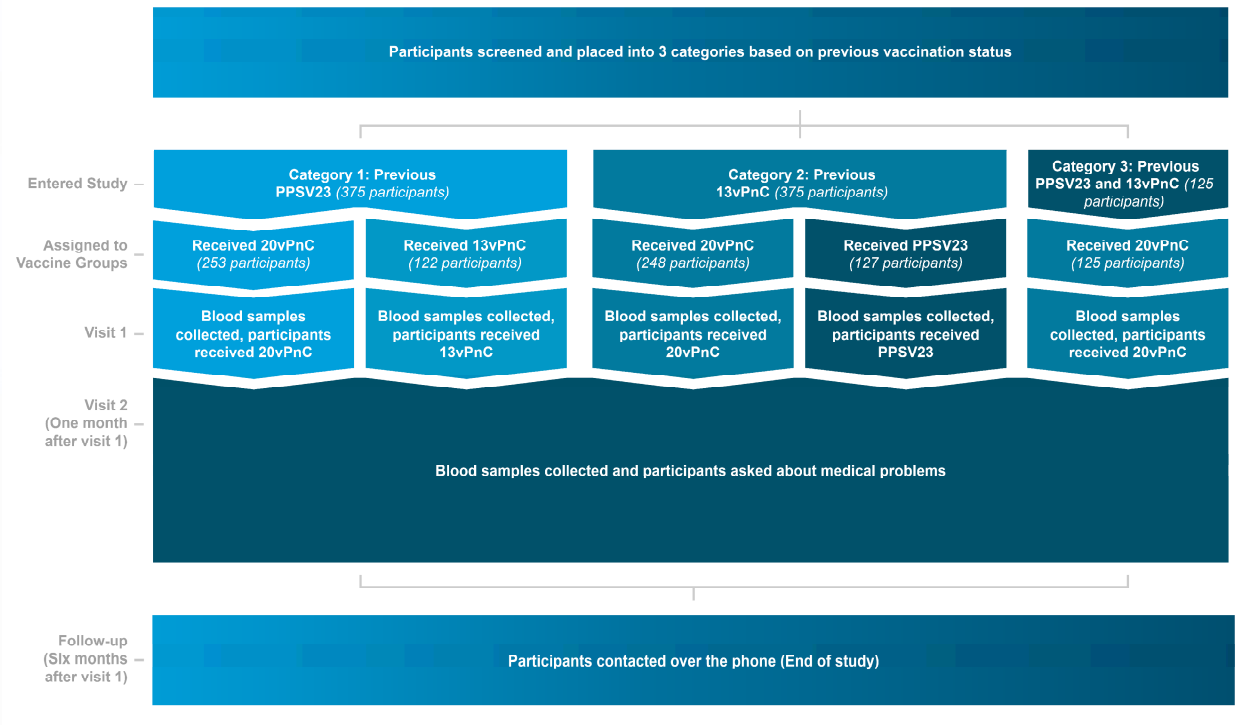
However, the researchers who did the antibody testing did not know this information until after the antibody testing was completed.

Participants were expected to participate in 3 study visits. At the first visit, participants were checked (screened) to make sure they were a good fit for the study, blood samples were collected, and then participants received study vaccine. The second visit was done about 1 month after the first visit. Participants were checked for medical problems and blood samples were collected. In the participants who received 20vPnC, the researchers measured the amount of antibodies in the blood. The third visit (follow-up) was done over the phone about 6 months after the first visit. The participants were asked about medical problems and whether they had received any other vaccines besides the study vaccines.

The figure below shows what happened during the study.



While participants were in this study for about 6 months, the entire study took 1 year to complete as participants entered the study at different times. The Sponsor ran this study at 33 locations in the United States and 8 locations in Sweden. It began 12 February 2019 and ended 12 February 2020. 398 men (46%) and 475 women

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(54%) received the study vaccines. All participants were between the ages of 65 and 92 years.

Of the 875 participants who joined the study, 865 (99%) completed it. A total of 10 participants (1%) 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 leave the study.

Throughout the course of the study, the Sponsor reviewed the data. When the study ended in February 2020 and after antibody testing was completed on the participants who received 20vPnC, the Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

One month after receiving 20vPnC, did participants aged 65 or older who had previously received 13vPnC and/or PPSV23 have antibody responses against the 20 types of *S. pneumoniae* contained in the vaccine?

To evaluate antibody response, the researchers measured the amount of antibodies in participants' blood 1 month after receiving 20vPnC.

The researchers found that, 1 month after receiving 20vPnC, antibody responses were present against all 20 vaccine components in study participants regardless of whether they had previously received 13vPnC, PPSV23, or both. Based on these results, the researchers have decided that the results are not likely the result of chance. The antibody response suggests that 20vPnC may be an option for preventing *S. pneumoniae* diseases.

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.

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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 percentage of participants had significant medical problems within 1 month after being vaccinated?

69 out of 873 participants in this study (8%) had at least 1 significant medical problem within 1 month after being vaccinated. Among participants who were vaccinated with 20vPnC, 19 out of 253 participants in Category 1 (received PPSV23 prior to the study) (8%), 12 out of 246 participants in Category 2 (received 13vPnC prior to the study) (5%), and 13 out of 125 participants in Category 3 (received 13vPnC and PPSV23 prior to the study) (10%) had significant medical problems within 1 month after being vaccinated. No single significant medical problem occurred in 4 or more participants during this time. No participants 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 generally similar regardless of vaccine received prior to the study, and was similar among participants who received 20vPnC or the control vaccine within each category, 13vPnC or PPSV23. The tables below show the percentage of participants with these reactions.

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Percentage of Participants With Redness, Swelling, or Pain at Injection Site Within 10 Days After Being Vaccinated With 20vPnC or 13vPnC – Category 1		
	20vPnC (253 Participants)	13vPnC (121 Participants)
Redness at injection site	20 (8%)	3 (3%)
Swelling at injection site	25 (10%)	8 (7%)
Pain at injection site	127 (50%)	52 (43%)

Percentage of Participants with Redness, Swelling, or Pain at Injection Site Within 10 Days After Being Vaccinated With 20vPnC or PPSV23 – Category 2		
	20vPnC (245 Participants)	PPSV23 (126 Participants)
Redness at injection site	21 (9%)	16 (13%)
Swelling at injection site	23 (9%)	18 (14%)
Pain at injection site	150 (61%)	71 (56%)

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Percentage of Participants With Redness, Swelling, or Pain at Injection Site Within 10 Days After Being Vaccinated With 20vPnC – Category 3	
	20vPnC (125 Participants)
Redness at injection site	**6 (5%)**
Swelling at injection site	**5 (4%)**
Pain at injection site	**66 (53%)**

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 regardless of vaccine received prior to the study, and was similar among participants who received 20vPnC or the control vaccines 13vPnC or PPSV23. In Category 2 participants (previously received 13vPnC only prior to the study), a higher percentage of participants who received PPSV23 (46%) had muscle pain than participants who received 20vPnC (34%). A fever is a body temperature that is 38.0 degrees Celsius or higher (100.4 degrees Fahrenheit or higher). The tables below show the percentage of participants with these reactions.

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Percentage of Participants With Fever, Headache, Tiredness, Muscle Pain, or Joint Pain Within 7 Days After Being Vaccinated With 20vPnC or 13vPnC – Category 1		
	20vPnC (253 Participants)	13vPnC (121 Participants)
Fever	2 (1%)	0 (0%)
Tiredness	73 (29%)	27 (22%)
Headache	45 (18%)	22 (18%)
Muscle pain	81 (32%)	38 (31%)
Joint pain	17 (7%)	13 (11%)

Percentage of Participants With Fever, Headache, Tiredness, Muscle Pain, or Joint Pain Within 7 Days After Being Vaccinated With 20vPnC or PPSV23 – Category 2		
	20vPnC (245 Participants)	PPSV23 (126 Participants)
Fever	0 (0%)	2 (2%)
Tiredness	76 (31%)	42 (33%)
Headache	33 (14%)	27 (21%)
Muscle pain	83 (34%)	58 (46%)
Joint pain	29 (12%)	20 (16%)

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Percentage of Participants With Fever, Headache, Tiredness, Muscle Pain, or Joint Pain Within 7 Days After Being Vaccinated With 20vPnC – Category 3	
	20vPnC (125 Participants)
Fever	**0 (0%)**
Tiredness	**41 (33%)**
Headache	**24 (19%)**
Muscle pain	**47 (38%)**
Joint pain	**21 (17%)**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

What percentage of participants had newly diagnosed chronic medical problems or serious medical problems within 6 months after being vaccinated?

In participants who received PPSV23 only, prior to joining the study, 6 out of 375 (2%) had newly diagnosed chronic medical problems within 6 months after being vaccinated, including 5 out of 253 participants (2%) who received 20vPnC and 1 out of 122 participants (1%) who received 13vPnC.

In participants who received 13vPnC only, prior to joining the study, 10 out of 373 3%) had newly diagnosed chronic medical problems within 6 months after being vaccinated, including 7 out of 246 participants (3%) who received 20vPnC and 3 out of 127 participants (2%) who received PPSV23.

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In participants who received both 13vPnC and PPSV23, prior to joining the study, 5 out of 125 (4%) had newly diagnosed chronic medical problems within 6 months after being vaccinated with 20vPnC.

4 out of 375 participants (1%) who received PPSV23 only, prior to joining the study, had serious medical problems within 6 months after being vaccinated, including 2 out of 253 participants (1%) who received 20vPnC and 2 out of 122 participants (2%) who received 13vPnC.

8 out of 373 participants (2%) who received 13vPnC only, prior to joining the study, had serious medical problems within 6 months after being vaccinated, including 6 out of 246 participants (2%) who received 20vPnC and 2 out of 127 participants (2%) who received PPSV23.

2 out of 125 participants (2%) who received 13vPnC and PPSV23, prior to joining the study, had serious medical problems within 6 months after being vaccinated with 20vPnC.

Fainting was the most common serious medical problem, which happened in 2 out of 624 participants (less than 1%) who received 20vPnC. None of the serious medical problems were thought to be related to the study vaccine by the study doctors. No participants 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.

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For more details on your study protocol, please visit:

www.clinicaltrials.gov	Use the study identifier **NCT03835975**
www.clinicaltrialsregister.eu	Use the study identifier **2018-004278-91**

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!

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