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.

Vaccine Studied: PF-07845104 (Influenza saRNA Vaccine)

Protocol Number: C4861001

Dates of Study: 28 April 2022 to 04 August 2023

Title of this Study: A Study to Assess the Safety of a Self-Amplifying RNA Vaccine Against Influenza in Healthy Participants

[A Phase 1, Placebo-Controlled, Randomized, Observer-Blind, Dose Finding Study to Evaluate the Safety, Tolerability, and Immunogenicity of Self-Amplifying RNA Vaccine Preparations Against Influenza in Healthy Individuals]

Date of this Report: 18 December 2024

– 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 influenza?

Influenza, also known as flu, is caused by a virus that infects the respiratory system. This includes the nose, throat, and lungs. Symptoms include runny or stuffy nose, sore throat, cough, headache, fever, chills, and muscle pain or body aches.

One way to prevent influenza is to receive a vaccine. Vaccines help the body to fight off infection and disease.

What is saRNA influenza vaccine?

Self-Amplifying RNA (saRNA) influenza vaccines are specially designed to copy themselves, using a type of ribonucleic acid (RNA) from certain viruses that can replicate on their own. This means that lower doses of the vaccine are needed, compared to regular RNA vaccines, to achieve the same effect. RNA is present in all living cells, and it helps the cell to make proteins.

In this study, 9 different saRNA vaccine preparations were used. Each preparation had some changes in the composition of the RNA features that could affect how the vaccine works. These were used at 3 different dose levels (low, medium, and high doses). The saRNA vaccine preparations were referred to as saRNA Vax Preps.

The vaccine was given as an injection into the muscle in the upper arm. The vaccine used in this study had not been approved for use at the time the study was done.

What was the purpose of this study?

The purpose of this study was to learn if a new type of influenza vaccine, called saRNA Vax Prep, is safe in healthy participants. Some participants also received 1 of 2 licensed quadrivalent influenza vaccines (QIV) or a

placebo. A placebo does not have any vaccine in it, but it looks just like the study vaccine.

Researchers wanted to know:

- **Did participants have any local reactions (redness, swelling, or pain at the injection site) within 10 days of vaccination?**
- **Did participants have any systemic events (fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain) within 10 days of vaccination?**
- **Did participants have any abnormal laboratory test results within 7 days of vaccination?**
- **Did participants have any abnormal electrocardiogram (ECG) results, within 7 days of vaccination, that were considered medically important?**
- **Did participants have any medical problems or serious medical problems after vaccination?**

What happened during the study?

How was the study done?

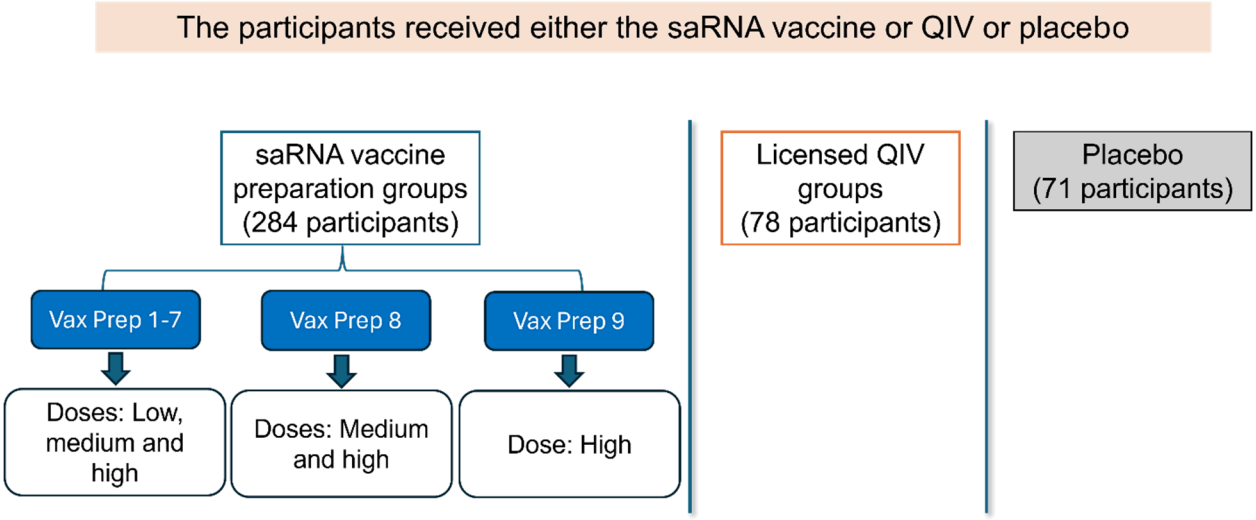
Researchers tested different saRNA Vax Prep for influenza in a group of study participants to learn about the safety of the saRNA Vax Prep, compared to placebo or 2 licensed QIV.

Participants were randomly assigned to receive either a single dose of saRNA Vax Prep or placebo. Alternatively, depending on when the

participants joined the study, they received a licensed QIV as a comparator. Participants were to be vaccinated only on Day 1 of the study.

The study participants and researchers did not know who received the saRNA Vax Prep and who received the placebo or QIV. This is known as a "blinded" study. Figure 1 below shows the details of all the vaccines the participants received.

Figure 1: Types of vaccines the participants received



All participants were given an electronic study diary and were asked to record details of any local reactions (redness, swelling, or pain at the injection site) or systemic events (fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain) in it. This information was collected for 10 days after vaccination.

Researchers also collected blood samples from participants for laboratory tests on Day 1, at Week 1, Week 2, and Week 4, and at Month 6. Routine ECGs were collected at the start of the study, Day 1, Day 3, Week 1, and Week 2. An ECG machine looks at the heart activity.

Researchers then compared the results of the study participants taking the saRNA Vax Prep to the results of the study participants taking placebo or licensed QIV.

Where did this study take place?

The Sponsor ran this study at 15 locations in the United States.

When did this study take place?

It began on 28 April 2022 and ended on 04 August 2023.

Who participated in this study?

The study included healthy participants as determined by their medical history, physical examination, and by the researchers.

- A total of 173 men participated
- A total of 260 women participated
- All participants were between the ages of 18 and 49 years.

Participants were to be vaccinated only on Day 1 of the study.

Of the 440 participants who started the study, 7 did not receive a vaccine. Among the remaining 433 participants, 284 in the saRNA Vax Prep groups, 78 in the licensed QIV groups, and 71 in the placebo group finished the study.

Of the vaccinated participants, 64 did not finish the study because:

- the participant no longer wanted to continue in the study
- no contact could be made on follow-up.

How long did the study last?

Study participants were in the study for about 7 months. The entire study took about 15 months to complete.

When the study ended in August 2023, 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?

The below is a summary of just some of the main results of this study. This does not mean that everyone in this study had these results. Other studies may have different results.

Did participants have any local reactions within 10 days of vaccination?

Pain at the injection site was the most common local reaction reported in all the saRNA Vax Prep groups, the licensed QIV groups, and the placebo group. With increasing doses of the saRNA vaccines, there was an increase in the overall local reactions.

Did participants have any systemic events within 10 days of vaccination?

Of the different types of systemic events, tiredness and headache were the most common events reported in all the saRNA Vax Prep groups, the licensed QIV groups, and the placebo group. With increasing doses of the saRNA vaccines, there was an increase in the overall systemic events.

Did participants have any abnormal laboratory test results within 7 days of vaccination?

- In the saRNA Vax Prep groups, the most common abnormalities observed in laboratory tests were low levels of neutrophils and higher than normal number of monocytes (types of white blood cells that fights infection), and an increase in C-reactive protein (a marker of inflammation).
- Majority of these abnormalities were observed 2 to 4 days after vaccination and resolved by 1 week.
- In the placebo or the licensed QIV groups, fewer participants had laboratory test abnormalities.

Did participants have any abnormal ECG results within 7 days of vaccination that were considered medically important?

No events of confirmed inflammation of heart muscle (myocarditis) or inflammation of the membrane around the heart (pericarditis) were observed in the saRNA Vax Prep groups, the licensed QIV groups or the placebo group.

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.

Forty-three (43) out of 284 (15%) participants in the saRNA Vax Prep groups, 13 out of 78 (17%) participants in the licensed QIV groups, and 9 out of 71 (13%) participants in the placebo group in this study had at least 1 medical problem. Of which, 12 participants in the saRNA Vax Prep groups, 4 participants in the licensed QIV groups, and 1 participant in the placebo group reported medical problems that were believed to be caused by the study treatment. No participants left the study because of medical problems. The most common medical problems – those reported by more than 1% of participants – are described below.

- 10 out of 284 (4%) participants in the saRNA Vax Prep groups, 0 out of 78 (0%) participants in the licensed QIV groups, and 0 out of 71 (0%) participants in the placebo group were reported to have low levels of neutrophils, a type of white blood cell that fights infection.
- 5 out of 284 (2%) participants in the saRNA Vax Prep groups, 3 out of 78 (4%) participants in the licensed QIV groups, and 0 out of 71 (0%) participants in the placebo groups were reported to have increase in C reactive protein (a marker of inflammation).
- 2 out of 284 (1%) participants in the saRNA Vax Prep groups, 2 out of 78 (3%) participants in the licensed QIV groups, and 2 out of 71 (3%) participants in the placebo group were reported to have positive COVID 19 tests.
- 0 out of 284 (0%) participants in the saRNA Vax Prep groups, 2 out of 78 (3%) participants in the licensed QIV groups, and 0 out of 71 (0%) participants in the placebo group were reported to have inflammation of the sinuses.

- 0 out of 284 (0%) participants in the saRNA Vax Prep groups, 2 out of 78 (3%) participants in the licensed QIV groups, and 0 out of 71 (0%) participants in the placebo group were reported to have increase in white blood cell.

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.

One (1) participant in the saRNA Vax Prep groups experienced a serious medical problem of breakdown of muscles, a problem that can lead to kidney damage. The researchers determined that this serious medical problem was not caused by the study treatment. No serious medical problems were reported in the licensed QIV groups or the placebo group.

No participants died during the 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.pfizer.com/research/research_clinical_trials/trial_results

Use the protocol number **C4861001**

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

www.clinicaltrials.gov

Use the study identifier **NCT05227001**

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!