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 vaccine 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: Tick-Borne Encephalitis (TBE) Vaccine (Compound Number: PF-06830414)

Protocol Number: B9371039

Dates of Study: 18 January 2021 to 21 February 2022

Title of this Study: A Study to Learn if TBE Vaccine was Safe in Healthy Japanese People 1 Year of Age and Older, and if TBE Vaccine Produced an Immune Response Against a Germ called Tick-Borne Encephalitis Virus

[A Phase 3, Single-Arm, Open-Label Study to Evaluate the Immunogenicity, Safety, and Tolerability of a Tick-Borne Encephalitis Vaccine in Healthy Japanese Participants 1 Year of Age and Older]

Date(s) of this Report: 17 March 2023

– Thank You –

If you or your child participated in this study, Pfizer, the Sponsor, would like to thank you or your child for your participation.

This summary will describe the study results. If you or your child 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 Tick-borne encephalitis (TBE)?

TBE is a disease caused by infection by the TBE virus (a type of germ). It is spread to humans by the bite of a small, spider-like creature called a tick. Ticks that spread this virus can be found in most of Europe, Russia, and parts of Asia, including parts of Japan. Not all ticks spread TBE, only those infected with the virus. TBE virus is part of a family of viruses known as flavivirus.

TBE infection affects the central nervous system (the brain and spinal cord). Many people with TBE infection do not show any symptoms. Some people may experience headache, fever, feeling/being sick, tiredness, confusion, loss of coordination, and/or seizures. In the most severe cases, TBE infection can lead to death.

What is a vaccine and an antibody response?

Vaccines can help the body prevent an infection or a disease. After a person gets a vaccine, the body makes "antibodies", which are proteins that fight off infections. This is known as the body's "immune response".

What is TBE vaccine?

TBE vaccine (PF-06830414) is an injectable vaccine that was tested in this study. It is also known by the brand names TicoVac® and TicoVac Junior® and is approved for use in people aged 1 year and older in many European countries, Russia, and the United States. The TBE vaccine is given as 3 doses. Each dose is given by injection into a muscle. There are 2 different dose levels of TBE vaccine. A dose of 0.5 milliliters (mL) is given to people aged 16 years and older, and a dose of 0.25 mL is given to children aged from 1 year to 15 years.

TBE vaccine was an investigational vaccine in this study because it has not been approved for use in Japan.

What was the purpose of this study?

The main purpose of this study was to learn about the safety and about the body's immune response to the TBE vaccine, in healthy Japanese children and adults aged 1 year and older.

Researchers wanted to know:

1. **Did participants who received 3 doses of TBE vaccine have a strong immune response against the virus that can cause TBE?**
2. **How many participants had redness, swelling, or pain at the injection site within 7 days after each vaccination?**
3. **How many participants aged 3 years and older had fever, tiredness, headache, vomiting, diarrhea, muscle pain, or joint pain within 7 days after each vaccination?**
4. **How many participants aged 1 and 2 years old had fever, decreased appetite, drowsiness, and irritability within 7 days after each vaccination?**
5. **How many participants had medical problems during the study?**

What happened during the study?

How was the study done?

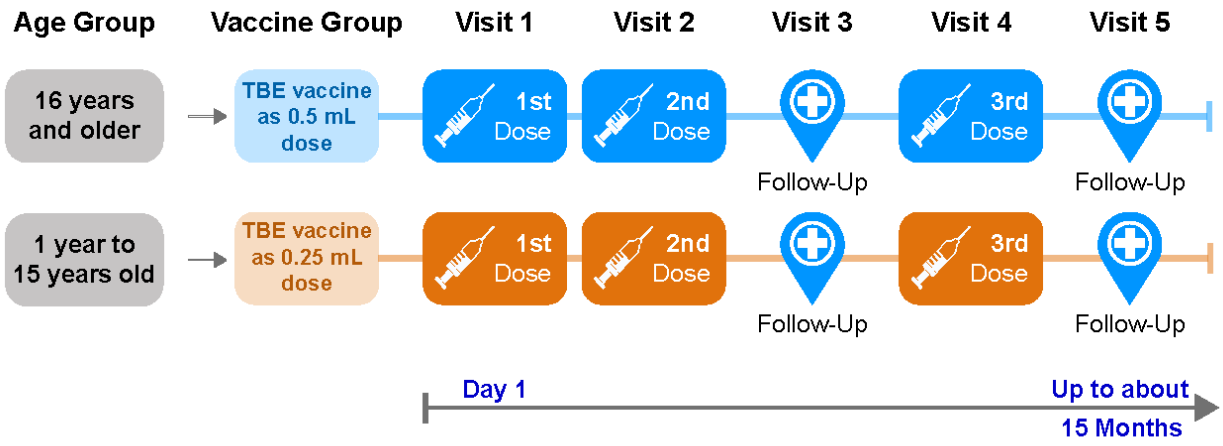
Healthy Japanese participants aged 1 year and older, and their parents or guardians as needed, were invited to join this study.

Participants were put into either of the following vaccine groups, based on age:

- 16 years and older group: received a 0.5 mL dose of TBE vaccine
- 1 year to 15 years old group: received a 0.25 mL dose of TBE vaccine

The figure below shows that participants received 3 doses of TBE vaccine. The first dose (Dose 1) was given at Visit 1 (Day 1). The second dose (Dose 2) was given at Visit 2 which happened 3 to 5 weeks after the first dose. Visit 3 (follow-up) happened 3 to 5 weeks after the second dose. The third dose (Dose 3) was given at Visit 4 which happened 5 months to 1 year after the second dose. Visit 5 (follow-up) happened 3 to 5 weeks after the third dose.

Figure 1. Study Design



Blood samples were taken during Visits 1, 3, 4, and 5. During each visit, researchers checked the participants' health and asked them or their parent or guardian, how they were feeling. The participant, or their parent or guardian also kept diaries to record how the participants were doing for 7 days after each vaccination.

Researchers measured the amount of antibodies against TBE virus in the participants' blood samples. They compared the amount of antibodies before and after getting TBE vaccine and used this to measure each participant's immune response. A "strong" immune response meant that the amount of antibodies in the participant's

blood had reached a certain level that the researchers believed was likely to give protection against infection with the TBE virus.

Where did this study take place?

The Sponsor ran this study at 6 locations in Japan.

When did this study take place?

It began 18 January 2021 and ended to 21 February 2022.

Who participated in this study?

The study included Japanese participants aged 1 year and older who:

- Were assessed as healthy by study doctors.
- Had not been infected with TBE virus, or other flaviviruses before joining this study.
- Had not received any other vaccine for TBE virus or for other flaviviruses (apart from Japanese encephalitis virus) before joining this study.

Overall, 165 participants joined the study and received at least 1 dose of TBE vaccine.

In the 16 years and older group:

- A total of 45 men were vaccinated
- A total of 55 women were vaccinated
- Participants were between the ages of 16 and 75 years old

In the 1 year to 15 years old group:

- A total of 46 boys were vaccinated
- A total of 19 girls were vaccinated
- Participants were between the ages of 1 and 15 years old

Of the 100 participants in the 16 years and older group, all participants (100%) received at least 2 doses of TBE vaccine, and 99 participants (99%) received all 3 doses. One participant in this age group did not complete the study because they were lost to follow-up before getting the third dose. Lost to follow-up means the participant stopped coming to study visits and could not be contacted by the study site staff.

Of the 65 participants in the 1 year to 15 years old group, all participants (100%) received all 3 doses and completed the study.

How long did the study last?

Participants could have been in the study between about 7 and 15 months. The entire study took about 13 months to actually complete.

When the study ended in February 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?

Did participants who received 3 doses of TBE vaccine have a strong immune response against the virus that can cause TBE?

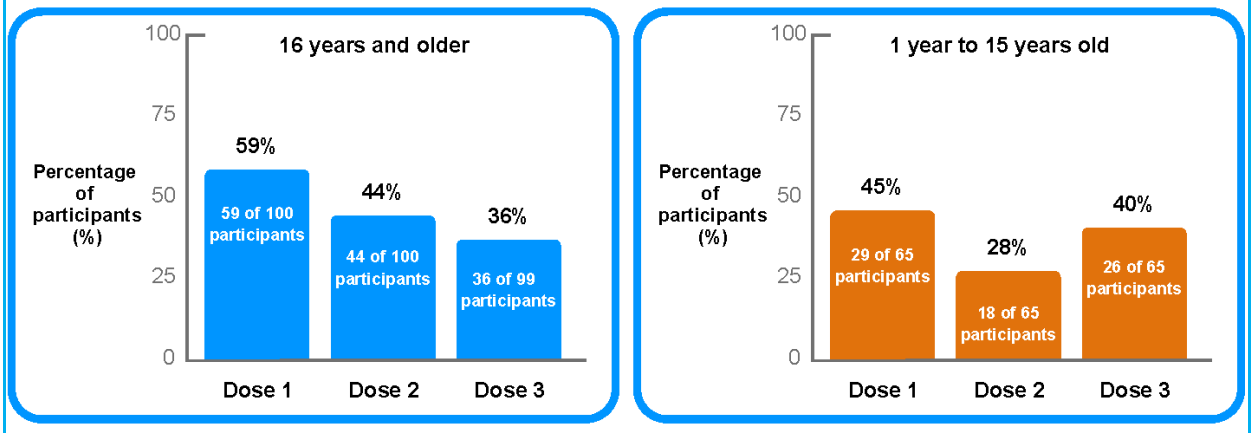
- In the 16 years and older group, 97 out of 99 participants (98%) had a strong immune response measured at 1 month after Dose 3.
- In the 1 year to 15 years old group, all 65 participants (100%) had a strong immune response measured at 1 month after Dose 3.

Based on these results, the researchers have decided that the results are not likely the result of chance. The TBE vaccine when given as 3 doses may produce a strong immune response in Japanese people aged 1 year and older and may help to protect against TBE infection.

How many participants had redness, swelling, or pain at the injection site within 7 days after each vaccination?

The participants, or their parents or guardians, checked for any redness, swelling, or pain at the area where the vaccine was injected. These "injection site reactions" were recorded in the participant diaries. The graphs in Figure 2 show the percentage of participants with at least 1 injection site reaction within 7 days after each dose of TBE vaccine. All of the injection site reactions were reported as mild or moderate.

Figure 2. Percentage of participants with at least 1 injection site reaction (any redness, swelling, or pain at the injection site) within 7 days after each dose



The most common single reaction after any dose of TBE vaccine was pain at the injection site.

In participants 16 years and older, pain at the injection site ranged from 36 participants (36%) to 59 participants (59%) across the 3 doses.

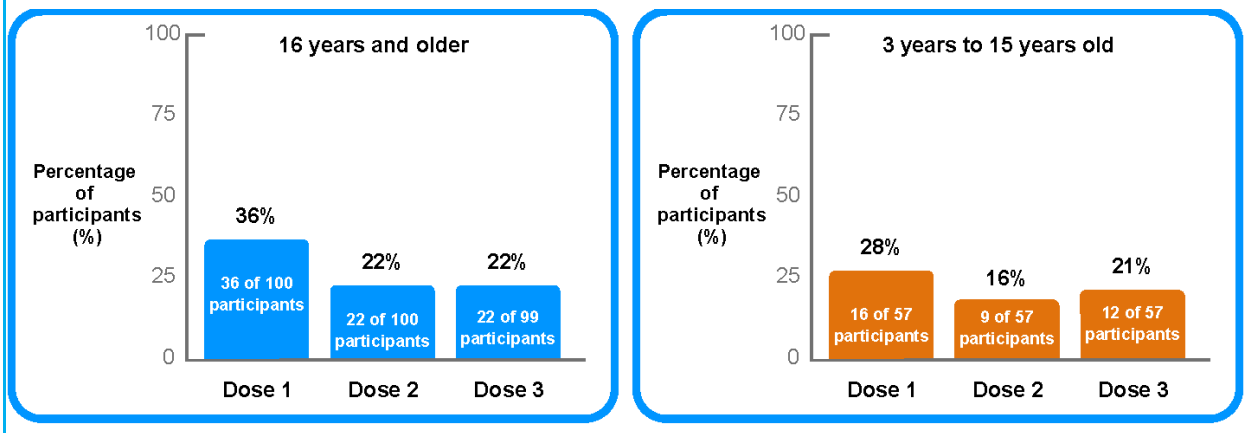
In participants 1 year to 15 years old, pain at the injection site ranged from 17 participants (26%) to 28 participants (43%) across the 3 doses.

After each dose of TBE vaccine, the researchers looked at 2 sets of "symptoms" based on the participant's age group. In the group aged 3 years and older (57 participants aged 3 years to 15 years old and 100 participants aged 16 years and older), the symptoms recorded in the participant diaries were fever, tiredness, headache, vomiting, diarrhea, muscle pain, or joint pain. In the group aged 1 and 2 years (8 participants), the symptoms recorded were fever, decreased appetite, drowsiness, and irritability.

How many participants aged 3 years and older had fever, tiredness, headache, vomiting, diarrhea, muscle pain, or joint pain within 7 days after each vaccination?

The graphs in Figure 3 show the percentage of participants aged 3 years and older with at least 1 of these symptoms within 7 days after each dose of TBE vaccine. Most of the symptoms in the age groups shown were reported as mild or moderate.

Figure 3. Percentage of participants 3 years and older with at least 1 symptom (fever, tiredness, headache, vomiting, diarrhea, muscle pain, or joint pain) within 7 days after each dose



In participants 16 years and older, the most common symptoms after Dose 1 were muscle pain in 19 participants (19%), tiredness in 16 participants (16%), and headache in 13 participants (13%). After Dose 2, headache in 10 participants (10%) was the most common symptom. After Dose 3, headache and tiredness, each in

11 participants (11%) were the most common symptoms.

In participants 3 years to 15 years old, the most common symptoms after Dose 1 were headache and tiredness, each in 6 participants (11%), and diarrhea in 5 participants (9%). After Dose 2, fever and diarrhea, each in 4 participants (7%) were the most common symptoms. After Dose 3, fever in 6 participants (11%), and headache and diarrhea, each in 5 participants (9%) were the most common symptoms.

How many participants aged 1 and 2 years old had fever, decreased appetite, drowsiness, and irritability within 7 days after each vaccination?

In the group 1 year and 2 years old, participants with at least 1 symptom of fever, decreased appetite, drowsiness, or irritability within 7 days after each dose of TBE vaccine were as follows:

- 5 out of 8 participants (63%) had at least 1 symptom after Dose 1.
- 1 out of 8 participants (13%) had at least 1 symptom after Dose 2.
- 2 out of 8 participants (25%) had at least 1 symptom after Dose 3.

All of the symptoms in this age group were reported as mild or moderate. Symptoms reported in at least 2 participants aged 1 year and 2 years old were as follows: After Dose 1, fever, drowsiness, and irritability were reported in 2 participants each. After Dose 2, there were no occurrences of 2 or more participants reported with symptoms. After Dose 3, drowsiness was reported in 2 participants.

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 of TBE vaccine 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 vaccine, another vaccine, or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many vaccine groups in many studies, doctors try to understand what effects a study vaccine might have on a participant.

From Dose 1 up to 1 month after Dose 3, 41 out of 165 participants in this study had at least 1 medical problem:

- 16 years and older group: 14 out of 100 participants (14%)
- 1 year to 15 years old group: 27 out of 65 participants (42%)

None of the participants in either age group left the study because of medical problems. Table 1 shows the most common medical problems - those reported for 2 or more participants in either age group from Dose 1 up to 1 month after Dose 3.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by 2 or more participants in either age group from Dose 1 up to 1 month after Dose 3 are listed.
- The **2nd** column tells how many of the participants 16 years and older given TBE vaccine were reported to have each medical problem. Next to this

number is the percentage of participants in this age group who reported the medical problem.

- The **3rd** column tells how many of the participants 1 year to 15 years old given TBE vaccine were reported to have each medical problem. Next to this number is the percentage of participants in this age group who reported the medical problem.
- Using these instructions, you can see that 3 out of 100 participants (3%) in the 16 years and older group were reported with common cold. A total of 11 out of 65 participants (17%) in the 1 year to 15 years old group were reported with common cold.

Table 1. Most common medical problems in the study

Medical Problem	16 years and older (100 Participants)	1 year to 15 years old (65 Participants)
Common cold	3 out of 100 participants (3%)	11 out of 65 participants (17%)
Infection of the stomach or bowels (gastroenteritis)	1 out of 100 participants (1%)	8 out of 65 participants (12%)
Fall	2 out of 100 participants (2%)	1 out of 65 participants (2%)
Eye infection (conjunctivitis)	0	3 out of 65 participants (5%)
Itchy and dry skin condition (eczema)	0	3 out of 65 participants (5%)

Infection of the stomach or bowels (viral gastroenteritis)	1 out of 100 participants (1%)	2 out of 65 participants (3%)
Infection of the nose, sinuses, throat, voice box, or windpipe	1 out of 100 participants (1%)	2 out of 65 participants (3%)
Lung condition (asthma)	0	2 out of 65 participants (3%)
Inflammation of the nose, sinuses, throat, voice box, or windpipe	0	2 out of 65 participants (3%)

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.

From Dose 1 up to 1 month after Dose 3, 3 out of 165 participants (2%) had serious medical problems:

- 1 out of 100 participants (1%) in the 16 years and older group had stomach pain.
- 1 out of 100 participants (1%) in the 16 years and older group had inflammation of the bowel, caused by lack of blood flow.
- 1 out of 65 participants (2%) in the 1 year to 15 years old group had diarrhea.

None of these serious medical problems were considered to be related to the study vaccine.

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 **B9371039**

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

www.clinicaltrials.gov

Use the study identifier **NCT04648241**

Please remember that researchers look at the results of many studies to find out which vaccines can work and are safe for patients.

Again, if you or your child 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!