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: Bivalent rLP2086 (PF-05212366)

Protocol Number: B1971035

Dates of Trial: 31 August 2015 to 21 August 2017

Title of this Trial: Study of the immunogenicity, safety, and tolerability of PF-05212366 in healthy toddlers aged 12 to less than 18 Months and 18 to less than 24 months

[A Phase 2, Randomized, Controlled, Observer-Blinded Study Conducted to Describe the Immunogenicity, Safety, and Tolerability of a *Neisseria meningitides* Serogroup B Bilvalent recombinant Lipoprotein 2086 Vaccine (Bivalent rLP2086) When Administered to Healthy Toddlers Aged 12 to less than 18 Months or 18 to less than 24 Months]

Date of this Report: 02 FEB 2019

– Thank You –

Pfizer, the Sponsor, would like to thank you for your child's 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?

This study was done to find out if an experimental vaccine might prevent meningococcal B disease. Meningococcal disease is an infection that causes the tissues that surround the brain and spinal cord to become swollen and inflamed. It is caused by a germ called "meningococcus."

There are different types of the meningococcal germ: types A, B, C, and Y. The type B meningococcal germ causes more meningococcal disease than any other type of meningococcal germ. While the likelihood of getting meningococcal B disease is very low, children under the age of 4 years are more likely to get it than any other age group.

Vaccines are given to prevent people from getting infections, and they work by helping people to fight off germs. While there are vaccines available to prevent other types of meningococcal disease, there isn't one available worldwide to prevent meningococcal B disease.

The vaccine given in this study is an injectable called bivalent rLP2086. This study tested bivalent rLP2086 to see if it will help people fight off the meningococcal B germ and provide protection (immunity) against the disease. This could only be done by testing the vaccine in healthy people who have never had an infection with meningococcal disease before.

As this disease is most common in babies and toddlers, the vaccine was tested in this age group. This study was done to see if toddlers made immune system proteins, called antibodies, after receiving bivalent rLP2086. Antibodies help the body to fight off diseases, in this case, group B meningococcal disease. Researchers also wanted to see what side effects toddlers have after receiving bivalent rLP2086 compared to a pediatric hepatitis A virus (HAV) vaccine. Bivalent rLP2086 is being compared to HAV because HAV is already widely used and the side effects of HAV are well known.

WHAT HAPPENED DURING THE STUDY?

This study compared 3 groups of children to find out if toddlers made immune system proteins, called antibodies, after taking bivalent rLP2086, and how the side effects compared to taking HAV plus placebo. A placebo does not have any medicine in it, but looks just like the medicine.

Children in both age groups were put into 1 of 3 study groups by chance alone. This is known as a "randomized" study, and is done to reduce differences between the study groups. Reducing differences between groups makes comparing the groups more fair.

In 2 of the 3 groups, children received the experimental vaccine bivalent rLP2086. One group received a 60 μg dose of bivalent rLP2086, and the second group received a 120 μg dose. The third group received HAV and a placebo. About 64% (6 out of 10) of children received bivalent rLP2086 and 33% (3 of 10) received HAV plus placebo. Researchers used a placebo to see if the study medicine is safe and works better than not taking anything.

The study included children who were aged 12 months to less than 24 months.

This study was done in two stages. In Stage 1, your child was followed for about 18 months. During Stage 1, each child received 3 injections, at one of two different dose levels (60 μg or 120 μg) of investigational bivalent rLP2086, or HAV and placebo. The injections were given at:

- Visit 1 (Day 1)
- Visit 4 (Month 2). Children who were randomized to receive HAV received a placebo (sterile saline) injection at this visit.
- Visit 6 (Month 6)

Only children who were originally randomized to the bivalent rLP2086 group in Stage 1 were eligible to be enrolled in Stage 2 of the study. In Stage 2, your child was followed for about 2 years. This stage measured how long the immune response lasted after the third vaccination with bivalent rLP2086.

While patients were only in the the study for about 18 months, stage 1 of the study took 2 years to complete. Patients joined the study at 1 of 25 locations in Australia, Czechia, Finland, and Poland. It began 31 August 2015 and is ongoing. 396 children participated. All children were between the ages of 12 months and 24 months.

Children were supposed to be treated until all vaccinations had been given. Of the 396 children who started the study, 381 completed the study. 15 did not finish the study.

All 15 children left before the study was over by their parent's choice or because a doctor decided it was best for the child to stop the study.

In August 2017, 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 the vaccine produce an immune response?

Yes. On average, the vaccine produced an immune response in all groups of the study.

The first goal of the study was to see what would happen to the children's immune response to the meningococcal B vaccine 4 weeks after the last vaccination. Researchers measured the levels of 4 types of an immune system protein (called MnB antibody) and determined whether the vaccine produced an immune response. Researchers wanted to know how many children had an immune response to the vaccine.

Researchers looked at two different age groups when looking at the results: children aged 12 to less than 18 months, and children aged 18 to 24 months.

In the 60 µg dose group, 92% of the children aged 12 to 18 months produced an immune response, and 90% of the children aged 18 to 24 months produced an immune response.

In the 120 µg dose group, 87% of the children aged 12 to 18 months produced an immune response, and 86% of the children aged 18 to 24 months produced an immune response.

Percent of Patients That Produced an Immune Response		
Age Group	Vaccine Group 60 µg dose (44 Children Treated)	Vaccine Group 120 µg dose (220 Children Treated)
12 to 18 Months	92%	87%
18 to 24 Months	90%	86%

How did the side effects of taking bivalent rLP2086 compare to taking HAV plus placebo?

The second main goal of the study was to see how the side effects of taking bivalent rLP2086 compared to taking HAV plus placebo.

Overall, children receiving rLP2086 had more reactions than those receiving HAV. However, these reactions were non-serious medical problems, which meant children could continue the study even after experiencing these reactions. The table in the next section describes some of these reactions.

There was no major difference in the type or severity of reactions between the different age groups. The researchers determined that both the 60 µg and 120 µg dose of bivalent rLP2086 are safe for children aged 12 to 24 months.

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 PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the children had during the study. Children 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 vaccine, or by another medicine the child was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many study groups in many studies, doctors try to understand what the side effects of an experimental vaccine might be.

365 out of 396 patients (92%) in this study had at least 1 medical problem . The most common medical problems reported by participants in this study are listed below.

Most Common Medical Problems (Reported by More Than 5% of Patients)			
Medical Problem	Vaccine Group 60 µg dose (44 Children Vaccinated)	Vaccine Group 120 µg dose (220 Children Vaccinated)	HAV plus Placebo (132 Children Vaccinated)
Tenderness at injection site	35 (80%)	160 (73%)	41 (31%)
Irritability	31 (70%)	176 (80%)	69 (52%)
Redness at injection site	30 (68%)	137 (62%)	28 (21%)
Drowsiness	23 (52%)	127 (58%)	40 (30%)
Loss of appetite	22 (50%)	142 (65%)	50 (38%)
Swelling at injection site	17 (39%)	103 (47%)	20 (15%)
Fever	16 (36%)	82 (37%)	20 (15%)
Sore throat	6 (14%)	18 (8%)	15 (11%)
Nose and throat infection	6 (14%)	58 (26%)	34 (26%)
Lung infection (Bronchitis)	5 (11%)	22 (10%)	11 (8%)

Viral nose and throat infection	**5 (11%)**	**45 (20%)**	**23 (17%)**
Stomach infection	**4 (9%)**	**29 (13%)**	**11 (8%)**
Ear infection	**3 (7%)**	**27 (12%)**	**20 (15%)**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

31 patients (8%) had serious medical problems. 2 patients in the 60 µg dose group, 15 patients in the 120 µg dose group, and 5 patients in the HAV/placebo group had some type of infection. No patients died during the study. The researchers determined that the serious medical problems were not related to the experimental vaccine.

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 **NCT02534935**
www.clinicaltrialsregister.eu	Use the study identifier **2011-004400-38**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **B1971035**

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 your child's participation. We do research to try to find the best ways to help patients, and you helped us to do that!