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 for patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine Studied: Vupanorsen (PF-07285557)

Protocol Number: C4491011

Dates of Study: 28 September 2020 to 06 December 2021

Title of this Study: A Study of Different Doses of Vupanorsen in Participants Who Have an Abnormal Level of Lipids (or Fats) in the Blood and Who Are Being Treated With a Class of Medicine Called Statins

[A Phase 2B Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Dose-Ranging Study to Assess the Efficacy, Safety, and Tolerability of Vupanorsen (PF-07285557) in Statin-Treated Participants With Dyslipidemia]

Date(s) of this Report: 09 September 2022

– 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 dyslipidemia?

Dyslipidemia is a condition in which the blood has an abnormal level of lipids (or fats) called cholesterol and triglycerides (TG). Levels of one or both lipids can be abnormal in dyslipidemia. High levels of cholesterol or TG increase the risk for heart disease (heart attack) or stroke. This is because fatty deposits in the blood vessels can build up and block the blood flow from the heart.

There are different types of cholesterol, which have different effects on the body. Non-high-density lipoprotein cholesterol (non-HDL-C) can tell how much cholesterols there are in the blood that can lead to heart disease or stroke. A high level of non-HDL-C means a higher risk of heart disease or stroke.

What is vupanorsen?

Vupanorsen is an injectable study medicine given through a needle inserted under the skin. It has not been approved for general use at the time of this study.

Researchers think that vupanorsen can lower the levels of non-HDL-C and TG in the blood. Researchers also think that taking vupanorsen for a longer period of time could help to lower the risk of heart disease.

What was the purpose of this study?

This study aimed to learn about the effects of vupanorsen after 24 weeks on the:

- Levels of non-HDL-C and TG in the blood
- Amount of fat in the liver

Researchers wanted to know:

1. **Did participants have a lower level of non-HDL-C after taking vupanorsen for 24 weeks?**
2. **Did participants have a lower level of TG after taking vupanorsen for 24 weeks?**
3. **Did participants have a change in the amount of liver fat after taking vupanorsen for 24 weeks?**

What happened during the study?

How was the study done?

In this study, researchers tested 7 doses of vupanorsen on a group of participants. Researchers then compared the results of participants taking vupanorsen to the results of participants taking a placebo. A placebo does not have any medicine in it, but it looks just like vupanorsen.

This was a "double-blind" study. This means the participants and researchers did not know which treatment the participants got.

Throughout the study, participants continued to take their statin medicine. Statins belong to a class of medicine that lowers the cholesterol levels in the blood.

- On Day 1 of the study, participants got assigned to a treatment group by chance, and they took their first dose of study treatment (vupanorsen or placebo).
- Participants then continued to take their assigned study treatment for 24 weeks. They took the study treatment either at home or at the study site.
- Participants returned to the study site for a follow-up visit 12 weeks after their last dose.

Figure 1. What happened during the study?

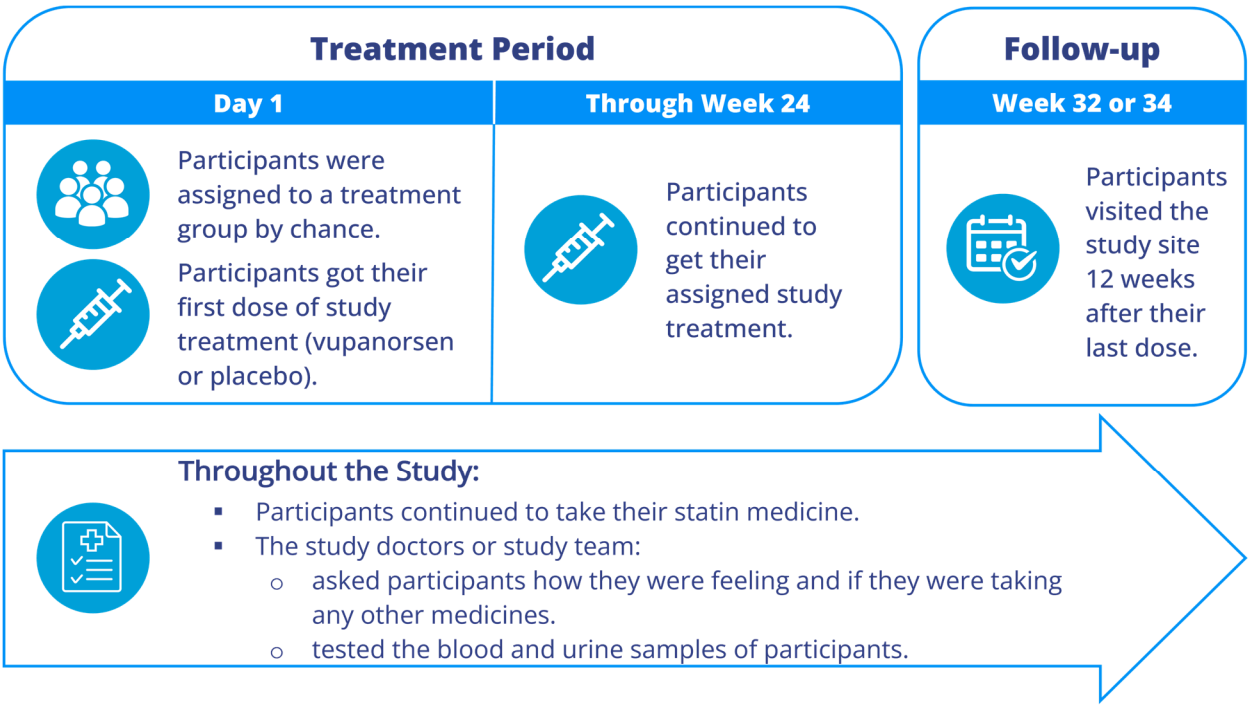


Figure 2. What were the treatment groups?

Placebo	Vupanorsen						
once a month or once every 2 weeks	80 mg once a month	60 mg once every 2 weeks	120 mg once a month	80 mg once every 2 weeks	160 mg once a month	120 mg once every 2 weeks	160 mg once every 2 weeks
44 participants	23 participants	24 participants	23 participants	45 participants	45 participants	46 participants	36 participants

Where did this study take place?

The Sponsor ran this study at 55 study sites in 3 countries (Canada, Poland, and United States of America).

When did this study take place?

It began 28 September 2020 and ended 06 December 2021.

Who participated in this study?

The study included participants who were 40 years old or above, had abnormal levels of cholesterol and TG in the blood, and were on a stable dose of a statin. The study did not allow those who had medical conditions such as an active liver disease or high blood pressure that could not be controlled with treatment.

In total, 160 men and 126 women joined the study. All participants were between the ages of 40 and 88 years.

Participants were to be treated for 24 weeks. Of the 286 participants who started the study, 226 finished the treatment period.

Sixty (60) participants did not finish the treatment period. The most common reason was because of a medical problem they had during the study. Other reasons were:

- A study doctor decided it was best for a participant to stop being in the study.
- Participants left by their choice before the study was over.
- Participants took medicines that were not allowed during the study.

How long did the study last?

Participants were in the study for about 36 weeks. The entire study took about 1 year and 2 months to finish.

When the study ended in December 2021, 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?

To answer the first 2 questions, researchers looked at the participants' blood test results during the study to see the levels of non-HDL-C and TG.

1 Did participants have a lower level of non-HDL-C after taking vupanorsen for 24 weeks?

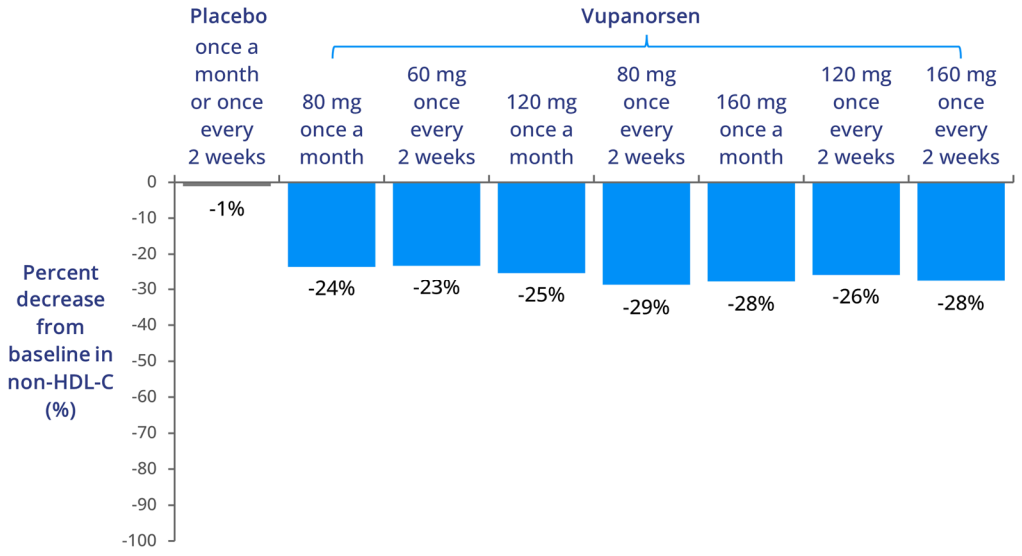
Yes. Researchers found that participants had a lower level of non-HDL-C after taking vupanorsen for 24 weeks compared to before starting treatment (baseline).

Then, researchers looked at how much the levels of non-HDL-C decreased at 24 weeks compared to baseline. This is called the "percent decrease from baseline" in non-HDL-C.

Did vupanorsen lower the level of non-HDL-C compared to placebo?

Yes. Researchers found a larger percent decrease from baseline in non-HDL-C among participants who took vupanorsen (all tested doses) for 24 weeks compared to those who took placebo. Researchers found that the results are not likely due to chance. The tested doses of vupanorsen may help to lower the level of non-HDL-C in the blood.

Figure 3. How much was the percent decrease from baseline in the level of non-HDL-C after 24 weeks of treatment?



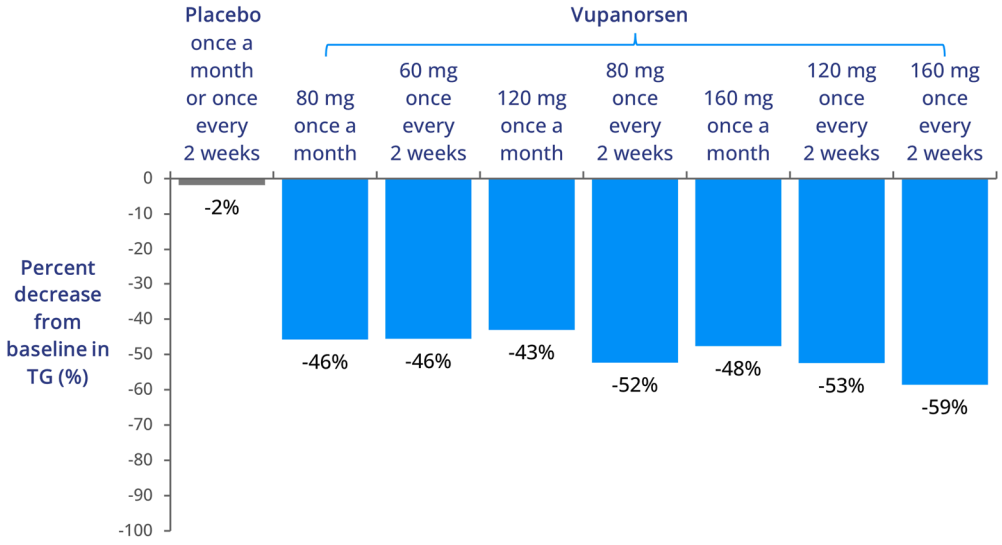
2 Did participants have a lower level of TG after taking vupanorsen for 24 weeks?

Yes. Researchers found that participants had a lower level of TG after taking vupanorsen for 24 weeks compared to baseline.

Did vupanorsen lower the level of TG compared to placebo?

Yes. Researchers found a larger percent decrease from baseline in TG among participants who took vupanorsen (all tested doses) for 24 weeks compared to those who took placebo. Researchers found that the results are not likely due to chance. The tested doses of vupanorsen may help to lower the level of TG in the blood.

Figure 4. How much was the percent decrease from baseline in the level of TG after 24 weeks of treatment?



To answer the 3rd question, participants had a magnetic resonance imaging (MRI) scan to measure the amount of liver fat. They had an MRI scan at baseline and after taking study treatment for 24 weeks.

3 Did participants have a change in the amount of liver fat after taking vupanorsen for 24 weeks?

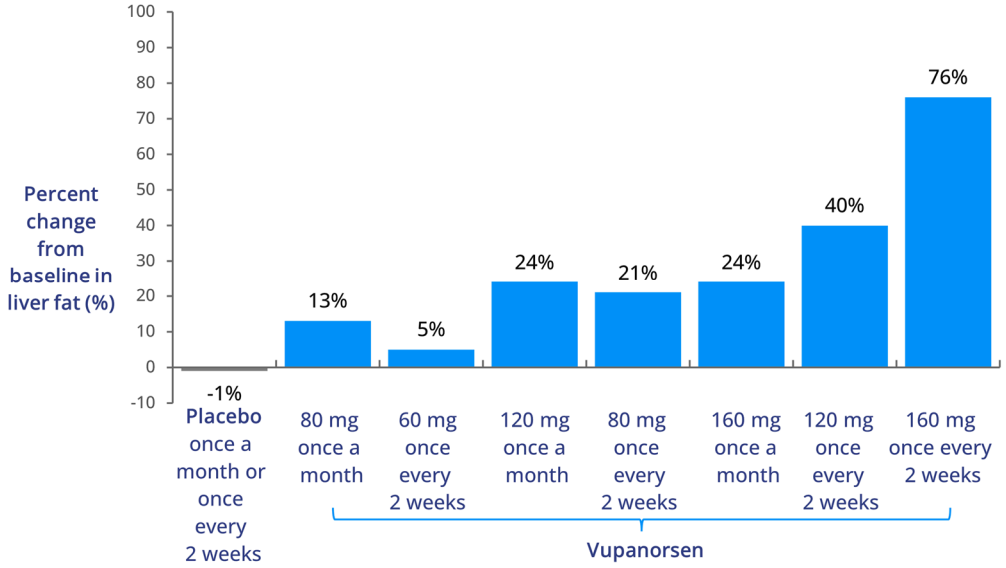
Yes. Researchers found an increased amount of liver fat among participants who took the higher tested doses of vupanorsen for 24 weeks compared to baseline.

Did vupanorsen change the amount of liver fat compared to placebo?

Yes. Compared to those who took placebo, researchers found a larger percent increase from baseline in the amount of liver fat among participants who took the higher tested doses of vupanorsen for 24 weeks. These doses of vupanorsen were:

- 120 mg once a month
- 80 mg once every 2 weeks
- 160 mg once a month
- 120 mg once every 2 weeks
- 160 mg once every 2 weeks

Figure 5. How much was the percent change in the amount of liver fat after 24 weeks of treatment?



The results in this summary do not mean that everyone in this study had these results. This is a summary of just some of the main results of this study, and it describes the average results. Other studies with vupanorsen 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 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.

Overall, 195 out of 286 participants (68%) in this study had at least 1 medical problem. A total of 42 out of 286 participants (15%) stopped taking the study treatment because of a medical problem they had during the study.

Table 1 lists the most common medical problems – those reported by at least 10% of participants in any group.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1

- Table 1 lists the most common medical problems that were reported during the study. It lists all medical problems reported by at least 10% of participants in any group.
- The **1st** column tells how many of the 44 participants taking placebo reported each medical problem. Next to this number is the percentage of the 44 participants taking placebo who reported the medical problem.
- The **2nd** to **8th** columns tell how many participants taking different doses of vupanorsen reported each medical problem. The **2nd** column tells how many of the 23 participants taking vupanorsen 80 mg once a month reported each medical problem. Next to this number is the percentage of the 23 participants taking vupanorsen 80 mg once a month who reported the medical problem.
- Using these instructions, you can see that 1 out of the 23 participants (4%) taking vupanorsen 80 mg once a month reported redness over the injection area. None of the 44 participants (0%) taking a placebo reported redness over the injection area.

Table 1. Most common medical problems in the study

Placebo	Vupanorsen						
once a month or once every 2 weeks	80 mg once a month	60 mg once every 2 weeks	120 mg once a month	80 mg once every 2 weeks	160 mg once a month	120 mg once every 2 weeks	160 mg once every 2 weeks
44 participants	23 participants	24 participants	23 participants	45 participants	45 participants	46 participants	36 participants
Redness over the skin where the needle was injected (or injection site)							
0 out of 44 (0%)	1 out of 23 (4%)	1 out of 24 (4%)	2 out of 23 (9%)	2 out of 45 (4%)	1 out of 45 (2%)	3 out of 46 (7%)	4 out of 36 (11%)
Reaction at the injection site							
0 out of 44 (0%)	1 out of 23 (4%)	3 out of 24 (13%)	4 out of 23 (17%)	4 out of 45 (9%)	4 out of 45 (9%)	6 out of 46 (13%)	8 out of 36 (22%)
Reaction at the prior injection site after the last injection (or a "recall reaction" of the injection site)							
0 out of 44 (0%)	0 out of 23 (0%)	2 out of 24 (8%)	1 out of 23 (4%)	2 out of 45 (4%)	0 out of 45 (0%)	5 out of 46 (11%)	3 out of 36 (8%)
A high level of a liver enzyme called alanine aminotransferase (ALT)							
2 out of 44 (5%)	0 out of 23 (0%)	0 out of 24 (0%)	0 out of 23 (0%)	1 out of 45 (2%)	1 out of 45 (2%)	4 out of 46 (9%)	9 out of 36 (25%)
A high level of a liver enzyme called aspartate aminotransferase (AST)							
1 out of 44 (2%)	0 out of 23 (0%)	0 out of 24 (0%)	0 out of 23 (0%)	0 out of 45 (0%)	0 out of 45 (0%)	2 out of 46 (4%)	4 out of 36 (11%)
A high level of a set of liver enzymes called transaminases							
0 out of 44 (0%)	0 out of 23 (0%)	0 out of 24 (0%)	0 out of 23 (0%)	2 out of 45 (4%)	0 out of 45 (0%)	1 out of 46 (2%)	6 out of 36 (17%)

Placebo	Vupanorsen						
once a month or once every 2 weeks	80 mg once a month	60 mg once every 2 weeks	120 mg once a month	80 mg once every 2 weeks	160 mg once a month	120 mg once every 2 weeks	160 mg once every 2 weeks
44 participants	23 participants	24 participants	23 participants	45 participants	45 participants	46 participants	36 participants
Back pain							
2 out of 44 (5%)	1 out of 23 (4%)	2 out of 24 (8%)	0 out of 23 (0%)	6 out of 45 (13%)	1 out of 45 (2%)	0 out of 46 (0%)	0 out of 36 (0%)
Pain in a limb							
1 out of 44 (2%)	0 out of 23 (0%)	3 out of 24 (13%)	0 out of 23 (0%)	3 out of 45 (7%)	0 out of 45 (0%)	2 out of 46 (4%)	0 out of 36 (0%)

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.

Overall, 19 out of 286 participants (7%) had a serious medical problem during the study. The list below shows the most common serious medical problems reported by at least 2 participants in the total group.

- 2 participants who took vupanorsen 80 mg once every 2 weeks had a medical condition that got worse.
    - Narrowing of spaces within the spine in 1 participant
    - Brain tumor in 1 participant
- 1 participant who took placebo and 1 participant who took vupanorsen 60 mg once every 2 weeks had a urinary tract infection (UTI).

The study doctors did not think any of the serious medical problems were caused by the study treatment. There were other serious medical problems across the treatment groups, but these happened in fewer participants.

No participant 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 **C4491011**

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

www.clinicaltrials.gov	Use the study identifier **NCT04516291**
www.clinicaltrialsregister.eu	Use the study identifier **2020-002796-35**

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!