Plain Language Clinical Study
Summary

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 Studied: Oxbryta® (voxelotor, also known as PF-06759497 or GBT440)

Protocol Number: GBT440-034 (C5341022)

Dates of Study: 06 June 2018 to 12 November 2024

Title of this Study: Study to Assess the Effect of Long-Term Treatment With Voxelotor in Participants Who Have Completed Treatment in Study GBT440-031 (034OLE)

[An Open Label Extension Study of Voxelotor (GBT440) Administered Orally to Participants With Sickle Cell Disease Who Have Participated in Voxelotor Clinical Trials]

Date of this Report: 29 July 2025

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– Thank You –

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

This summary will describe the study results. Do you have any questions about the study or the results? If so, please contact the doctor or staff at your or your child's study site.

Why was this study done?

What is sickle cell disease?

Sickle cell disease (SCD) is a condition where red blood cells are shaped like a "sickle" (crescent moon) instead of being round. These sickle cells break down more quickly and can block blood flow. This makes it harder for the blood to carry oxygen around the body, leading to problems such as anemia (low levels of hemoglobin). Hemoglobin is a protein in the red blood cells that carries oxygen throughout the body.

What is voxelotor?

Voxelotor (VOX-el-oh-tor), also known as Oxbryta®, is a study medicine given as a tablet and is designed to prevent the formation of sickle cells.

In this study, researchers wanted to learn about the long-term effects of voxelotor as a treatment for SCD.

What was the purpose of this study?

The main purpose of this study was to find out whether voxelotor could safely treat SCD for a long time.

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Researchers wanted to know:

- **Can voxelotor safely treat SCD for a long time?**
- **What medical problems did participants have during the study?**

This study was stopped early and was not completed as planned.

What happened during the study?

How was the study done?

This study included participants who completed the previous study of voxelotor (GBT440-031, also called "HOPE" study). All participants continued to take voxelotor 1500 mg once per day, regardless of treatment taken in the earlier "HOPE" study (placebo, voxelotor 900 mg, or voxelotor 1500 mg). A placebo does not have any medicine in it, but it looks just like the study medicine. The participants and researchers knew that all participants were taking voxelotor in this study.

The study planned to allow participants to continue taking voxelotor until it became available in their country, they chose to stop being part of the study, or the Sponsor chose to end the study.

After the Sponsor chose to end the study, the participants had to stop taking voxelotor. Participants and their parents/caregivers, who were still in the study, returned to the study site for 2 follow-up visits: within 2 weeks and then within 28 days after taking their last dose.

Where did this study take place?

The Sponsor ran this study at 48 locations in Canada, Egypt, France, Italy, Kenya, Lebanon, the Netherlands, Oman, Türkiye, the United Kingdom, and the United States.

When did this study take place?

It began on 06 June 2018 and ended on 12 November 2024 when the final results were collected.

Who participated in this study?

The study included participants with SCD who had completed the earlier study of voxelotor (GBT440-031 or "HOPE" study).

- Of the 179 participants who took part in this study, 178 took at least 1 dose of voxelotor.
- A total of 78 boys/men and 100 girls/women participated.
- All participants were between the ages of 13 and 61 years when they started this study.

Of the 179 participants who started the study, 46 finished the study as planned.

A total of 133 participants did not finish the study. The most common reason (57 participants, 32%) was that the Sponsor stopped the study early.

How long did the study last?

Study participants were in the study for different lengths of time, depending on how long they took voxelotor in this study.

- 132 out of 178 participants (74%) took voxelotor for at least 48 weeks,
- 81 out of 178 participants (46%) took voxelotor for at least 3 years (or 168 weeks), and
- 55 out of 178 participants (31%) took voxelotor for at least 5 years (or 264 weeks).

The study ran for about 6 years and was not completed as planned because the Sponsor stopped the study early.

On 25 September 2024, the Sponsor decided that voxelotor would no longer be available where it was previously approved. The Sponsor also stopped this study and all ongoing clinical studies on voxelotor. This decision was due to safety concerns based on the information available at that time from other voxelotor studies.

When the study ended in November 2024, the Sponsor reviewed all information collected. The Sponsor then created a report of the results. This is a summary of that report.

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What were the results of the study?

Can voxelotor safely treat SCD for a long time?

To answer this question, researchers looked at any medical problems, including those related to SCD, that participants had during the study. Researchers also checked whether voxelotor could help increase the hemoglobin levels in the blood and keep the hemoglobin levels steady.

Overall,

- Participants aged 12 years and older with SCD were able to tolerate voxelotor well. The medical problems seen in this study were similar to those seen in the earlier "HOPE" study (GBT440-031).
- Participants who took a placebo in the earlier "HOPE" study had increased hemoglobin levels after taking voxelotor in this study. Participants who took voxelotor since the earlier "HOPE" study and through this study continued to show stable hemoglobin levels in this study. These results lasted through the whole study.

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 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 medicine might have on a participant.

The medical problems that participants had during the study were sorted into 2 groups:

"SCD-related" – any medical problems caused by SCD, for examples:

- **"Sickle cell anemia with crisis"** – a sudden pain that happens when the sickled red cells in blood vessels lead to a blockage. As a result, the blood flow and oxygen delivery to areas of the body are prevented, causing painful crises.
- **"Acute chest syndrome"** – a severe SCD complication that causes chest pain and trouble breathing
- Lung infection ("pneumonia")
- Painful erection ("priapism")
- Death of bone cells ("osteonecrosis")

"Non-SCD-related" – all other medical problems not listed above as SCD-related.

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Figure 1 below shows the number of participants who had at least 1 medical problem in the study.

Figure 1. How many participants had medical problems?

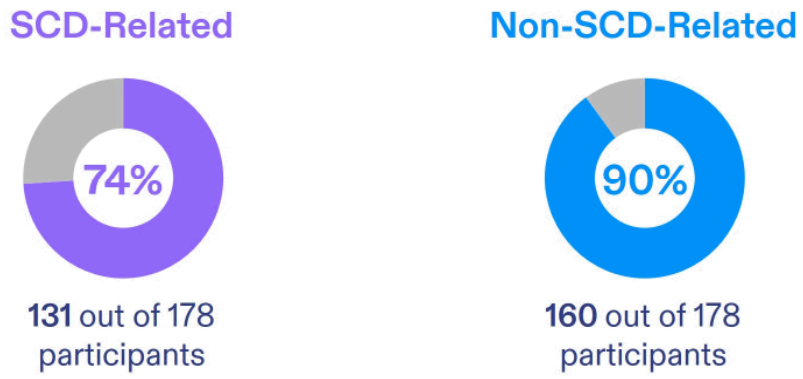
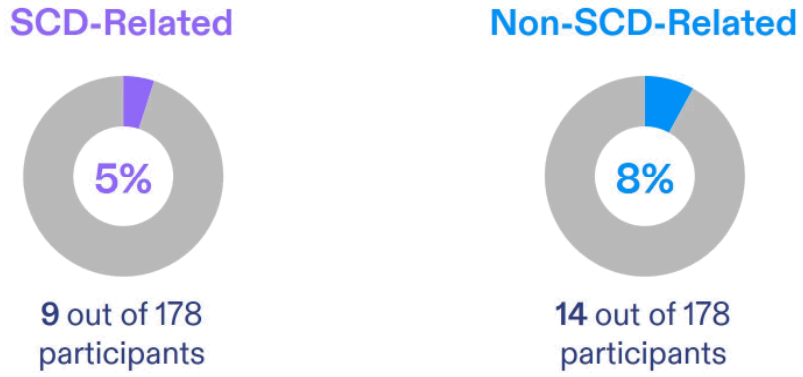


Figure 2 below shows the number of participants who stopped taking voxelotor because of medical problems.

Figure 2. How many participants stopped taking voxelotor because of medical problems?



Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column lists the commonly reported medical problems in the study. All medical problems in the table below were reported by 15% of participants or more.
- The **2nd** column shows the total number and percentage of participants in the study who reported each medical problem.
- Using these instructions, you can see that 125 out of the 178 participants (70%) who took voxelotor reported sickle cell anemia with crisis.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Voxelotor (178 Participants)
Sickle cell anemia with crisis	125 out of 178 participants (70%)
Headache	40 out of 178 participants (22%)
Pain in the legs or arms ("pain in extremity")	34 out of 178 participants (19%)
Joint pain ("arthralgia")	32 out of 178 participants (18%)

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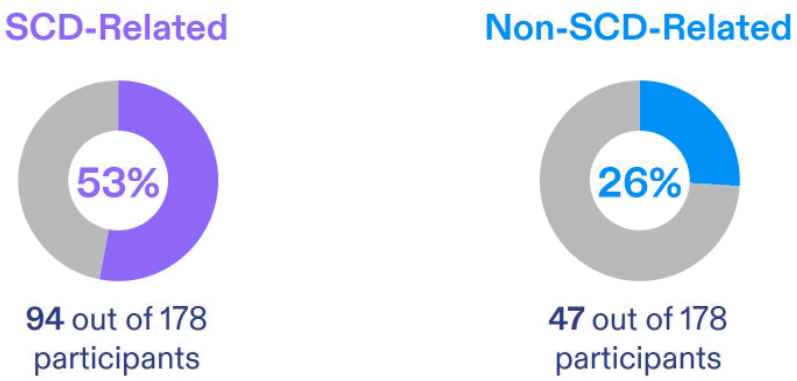
Table 1. Commonly reported medical problems by study participants	
Medical Problem	**Voxelotor (178 Participants)**
Nose and throat infection (upper respiratory tract infection)	31 out of 178 participants (17%)
Nausea	29 out of 178 participants (16%)
Back pain	28 out of 178 participants (16%)
Pain	27 out of 178 participants (15%)

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.

Figure 3 below shows the number of participants who had at least 1 serious medical problem in the study.

Figure 3. How many participants had serious medical problems?



Below are instructions on how to read Table 2.

Instructions for Understanding Table 2.

- The **1st** column lists the commonly reported serious medical problems in the study. All serious medical problems in the table below were reported by 5% of participants or more.
- The **2nd** column shows the total number and percentage of participants in the study who reported each serious medical problem.
- Using these instructions, you can see that 88 out of the 178 participants (49%) who took voxelotor reported sickle cell anemia with crisis.

Table 2. Commonly reported serious medical problems by study participants	
Serious Medical Problem	**Voxelotor (178 Participants)**
Sickle cell anemia with crisis	88 out of 178 participants (49%)
Acute chest syndrome	19 out of 178 participants (11%)
Anemia	9 out of 178 participants (5%)

A total of 4 out of 78 male participants (5%) had a serious medical problem of painful erection.

A total of 10 participants died because of medical problems in the study. None of the deaths were considered related to voxelotor. Of the 10 participants:

- 3 participants died because of sickle cell anemia with crisis,
- 1 participant died because of acute chest syndrome, and
- 6 participants died because of other medical problems. These medical problems were “COVID-19” (contagious illness caused by SARS-CoV-2), fever, “sepsis” (a condition wherein the body responds improperly to an infection), anemia, “cardiac arrest” (the heart stopped beating), and difficulty breathing.

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 **C5341022 (GBT440-034)**

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

www.clinicaltrials.gov	Use the study identifier **NCT03573882**
https://euclinicaltrials.eu	Use the study identifier **2017-004045-25**

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 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!

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