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.
Medicine Studied:	Osivelotor (also known as PF-07940367 or GBT021601)
Protocol Number:	C5351003 or GBT021601-013
Dates of Study:	22 December 2022 to 10 August 2023
Title of this Study:	A Study on the Safety, Absorption, and Elimination of Osivelotor (Radioactively Labeled With Carbon-14) [A Phase 1 Study to Assess the Mass Balance, Excretion, and Pharmacokinetics of [^{14}C]-GBT021601, an Oral Hemoglobin S Polymerization Inhibitor, in Healthy Participants]
Date of this Report:	07 August 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 sickle cell disease?

Sickle cell disease (SCD) is an inherited disorder wherein red blood cells are shaped like a crescent moon (sickle cells). Compared to round (normal) red blood cells, sickle cells are less able to carry oxygen around the body.

SCD causes anemia (a shortage of red blood cells), severe tiredness and attacks of pain, and frequent infections. SCD is a lifelong illness. Most people with SCD have a lower life expectancy.

What is osivelotor?

Osivelotor (also called PF-07940367 or GBT021601) is a tablet that is swallowed.

Researchers think that osivelotor may help treat SCD. Osivelotor is designed to help red blood cells deliver oxygen throughout the body and prevent the formation of sickle cells.

What was the purpose of this study?

The main goal of this study was to find out how osivelotor was taken up in the body, how it moved through the body, how it was broken down in the body, and how it was removed from the body.

In this study, osivelotor was made with a special radioactive label called **carbon-14 (^{14}C)**. Carbon-14 is harmless to humans and is commonly used in similar research studies. The use of a radioactive label is a standard way of tracing compounds such as osivelotor in the blood, urine, and feces. This helps researchers track a drug as it moves through and exits the body.

Researchers wanted to know:

How did osivelotor act in the body?

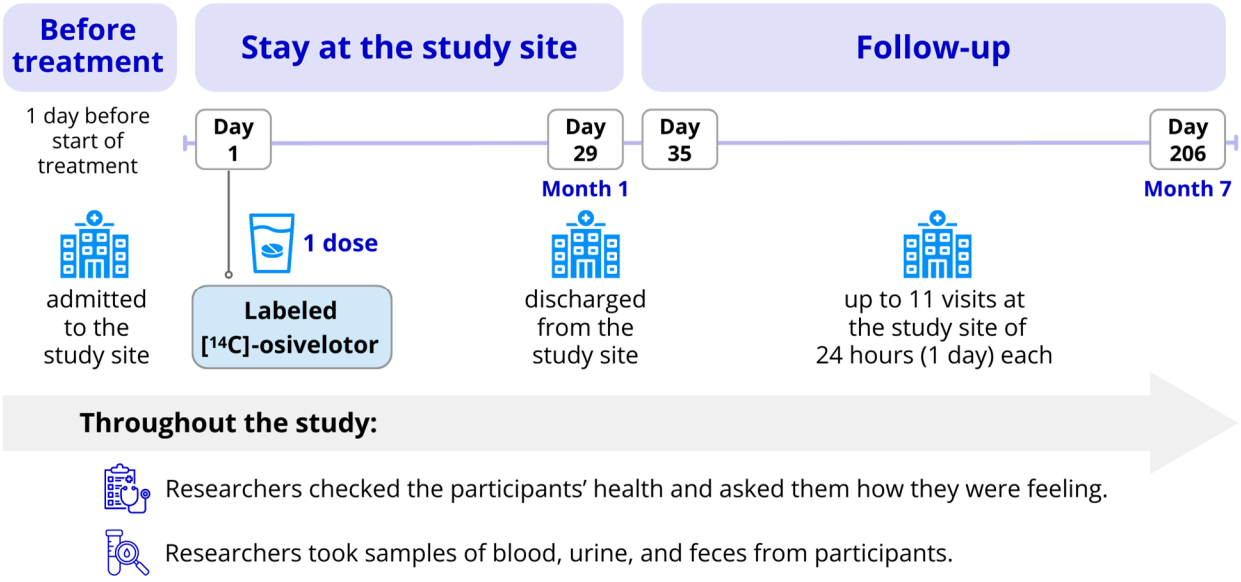
This study in healthy participants did not test if osivelotor helps to treat SCD.

What happened during the study?

How was the study done?

The figure below shows what happened in the study.

Figure 1. How was the study done?



Stay at the study site – Up to 1 month:

- Participants stayed at the study site from 1 day before dosing up to Day 29 (Month 1).
- After not eating for at least 10 hours overnight, they received 1 dose of labeled [^{14}C]-osivelotor 200 milligrams (mg) tablet mixed in liquid (oral solution) on Day 1 of the study.

The researchers and participants knew which medication was given in the study.

Follow-up – Up to 6 months:

During follow-up, participants had regular check-ups at the study site up to 11 times, from Day 35 (after Month 1) up to Day 206 (Month 7).

- The number of follow-up visits depended on how much of the labeled [^{14}C]-osivelotor was found in the urine and feces.
- For each follow-up visit, participants stayed at the study site for 24 hours (1 day).

Throughout the study:

- Researchers checked the participants' health and asked them how they were feeling.
- Researchers took samples of blood, urine, and feces from participants from Day 1 (after dosing) up to 7 months. This was done because it is expected to take about 1 month to reduce the amount of osivelotor by half in the blood.

Where did this study take place?

The Sponsor ran this study at 1 location in the Netherlands.

When did this study take place?

It began on 22 December 2022 and ended on 10 August 2023.

Who participated in this study?

The study included healthy adults who were 18 to 55 years old.

- A total of 7 male (77.8%) and 2 female (22.2%) participants took part in the study.
- Participants were 21 to 46 years old. The average age was 34 years.

Of the 9 participants who started the study:

- 6 participants (66.7%) finished the study.
- 3 participants (33.3%) did not finish the study because they left before the study was over by their choice.

How long did the study last?

Each participant was in the study for up to 7 months. The entire study took about 8 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?

How did osivelotor act in the body?

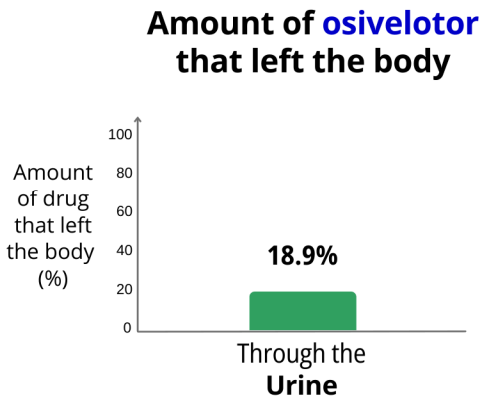
In this summary, the **study medication** means either of the following:

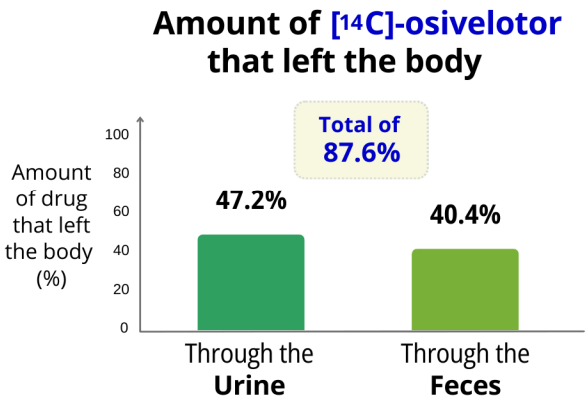
- **"Osivelotor"** or **"unlabeled osivelotor"**: Osivelotor without a radioactive label.
- **"[^{14}C]-osivelotor"** or **"labeled [^{14}C]-osivelotor"**: Osivelotor that is radioactively labeled with carbon-14 (^{14}C).

During the study, researchers measured how much of the **study medication** left the body through the **urine** or **feces** of participants after they took [^{14}C]-osivelotor.

How much of osivelotor and [^{14}C]-osivelotor left the body?

The figure below shows the **amounts** of osivelotor and [^{14}C]-osivelotor that left the body after participants took [^{14}C]-osivelotor.





Osivelotor

- **18.9%** of unlabeled osivelotor left the body through the **urine**.

[^{14}C]-osivelotor

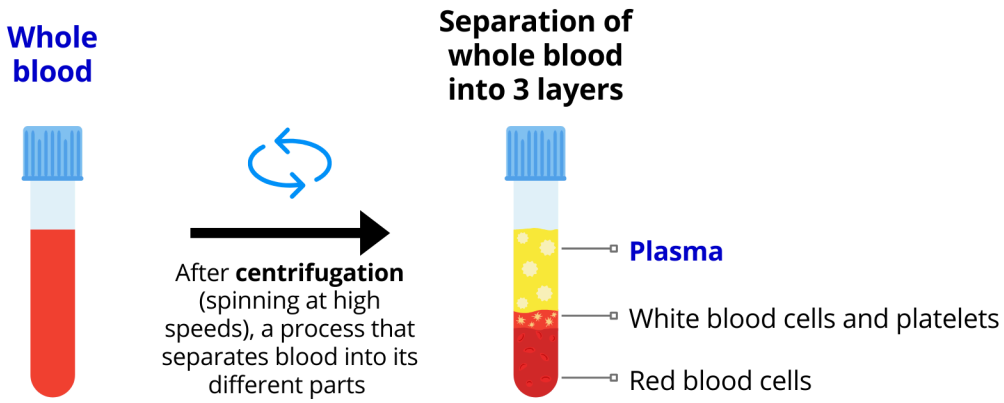
- **47.2%** of [^{14}C]-osivelotor left the body through the **urine**.
- **40.4%** of [^{14}C]-osivelotor left the body through the **feces**.

A total of **87.6%** of [^{14}C]-osivelotor left the body over **29 weeks**.

In this study, researchers also looked at how the **study medication** acted in the participants' **blood** (also called **whole blood**) and **plasma** after they took [^{14}C]-osivelotor.

- **Whole blood** contains plasma and other blood cells.
- **Plasma** is the clear yellow liquid part of the blood. Plasma carries blood components and other substances throughout the body.

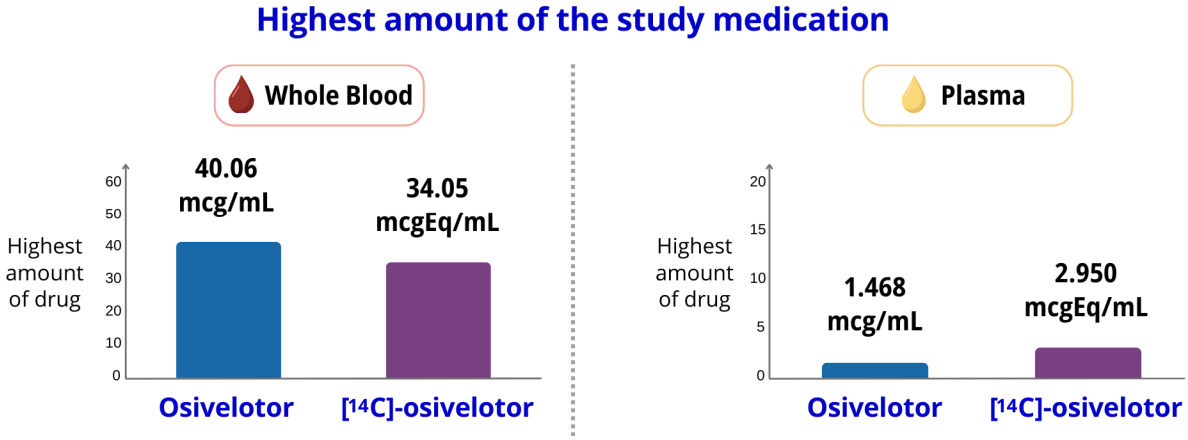
The figure below shows the blood's 3 layers when a machine called a centrifuge spins the blood samples at high speeds.



What were the amounts of osivelotor and [^{14}C]-osivelotor in the blood after participants took [^{14}C]-osivelotor?

The amounts of study medication in the blood and plasma were measured in micrograms per milliliter (also called **mcg/mL**) and microgram equivalents per mL (also called **mcgEq/mL**).

The figure below shows the **highest amounts** of osivelotor and [^{14}C]-osivelotor after participants took [^{14}C]-osivelotor.



Whole Blood

The highest amount of osivelotor in the blood was about **118%** of the highest amount of [^{14}C]-osivelotor.

- Osivelotor: **40.06 mcg/mL**
- [^{14}C]-osivelotor: **34.05 mcgEq/mL**

It took **24 hours** for osivelotor and [^{14}C]-osivelotor to reach their highest amounts in the blood.

Plasma

The highest amount of osivelotor in the plasma was about **50%** of the highest amount of [^{14}C]-osivelotor.

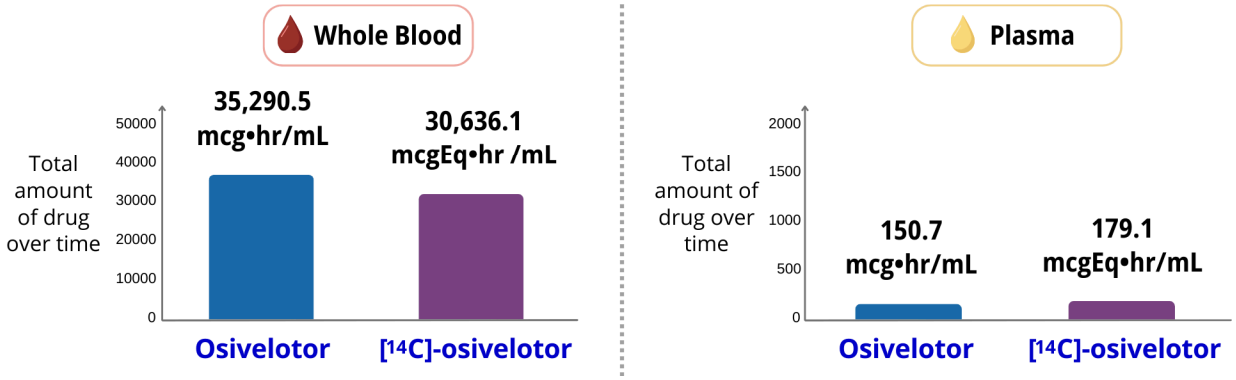
- Osivelotor: **1.468 mcg/mL**
- [^{14}C]-osivelotor: **2.950 mcgEq/mL**

It took **1 hour** for osivelotor and [^{14}C]-osivelotor to reach their highest amounts in the plasma.

The total amounts of drug over time in the blood and plasma were measured in microgram hours per milliliter (also called **mcg•hr/mL**) and microgram equivalent hours per mL (also called **mcgEq•hr/mL**).

The figure below shows the estimated **total amounts** of osivelotor and [^{14}C]-osivelotor after participants took [^{14}C]-osivelotor.

Total amount of the study medication over time



Whole Blood

The total amount of osivelotor from when the participants took [^{14}C]-osivelotor to the time when its lowest amount was detected in the blood was about **115%** of the total amount of [^{14}C]-osivelotor.

- Osivelotor: **35,290.5 mcg•hr/mL**
- [^{14}C]-osivelotor: **30,636.1 mcgEq•hr/mL**

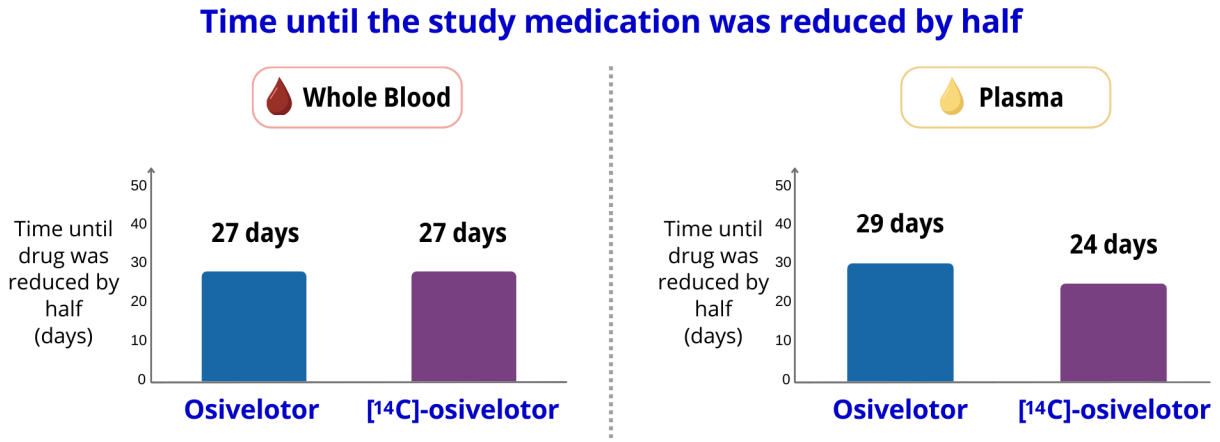
Plasma

The total amount of osivelotor from when the participants took [^{14}C]-osivelotor to the time when its lowest amount was detected in the plasma was about **84%** of the total amount of [^{14}C]-osivelotor.

- Osivelotor: **150.7 mcg•hr/mL**
- [^{14}C]-osivelotor: **179.1 mcgEq•hr/mL**

How long did it take for the amounts of osivelotor and [^{14}C]-osivelotor in the blood to be reduced by half after participants took [^{14}C]-osivelotor?

The figure below shows **how long it took for the study medication to be reduced by half** in the blood and plasma after participants took [^{14}C]-osivelotor.



Whole Blood

- It took **27 days** for osivelotor to be reduced by half in the blood.
- It took **27 days** for [^{14}C]-osivelotor to be reduced by half in the blood.

Plasma

- It took **29 days** for osivelotor to be reduced by half in the plasma.
- It took **24 days** for [^{14}C]-osivelotor to be reduced by half in the plasma.

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 unknown 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, 4 out of 9 participants (44.4%) in this study reported at least 1 medical problem. No participant left the study because of medical problems they experienced during the study.

The most common medical problem in the study – reported by at least 2 participants – was headache. A mild **headache** was reported by 2 out of 9 participants (22.2%) during the study. Researchers thought the reported headache in 1 participant may have been related to osivelotor. No other participant had a medical problem that researchers thought could be related to osivelotor.

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.

No participant had serious medical problems or 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 **C5351003 or GBT021601-013**

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

www.clinicaltrials.gov	Use the study identifier **NCT05718687**
www.clinicaltrialsregister.eu	Use the study identifier **2022-003108-34**

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!