# PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

**Study Sponsor:** Gilead Sciences

**Gilead Study Number:** CB8025-21838

**Dates of Study:** November 2021 to February 2025

**Short Study Title:** How Seladelpar Works in People With Primary Biliary Cholangitis and Liver Impairment

**Date of this Plain Language Summary:** February 2026
The information in this summary does not include any information available after this date.

## Thank you

Thank you to the participants who took part in this clinical study for **seladelpar**, brand names: **Livdelzi**, **Lyvdelzi**.

Gilead Sciences sponsored this study. This summary is prepared for study participants and the general public.

If you participated in the study and have questions about the results, please speak with a doctor or staff member at the study site.

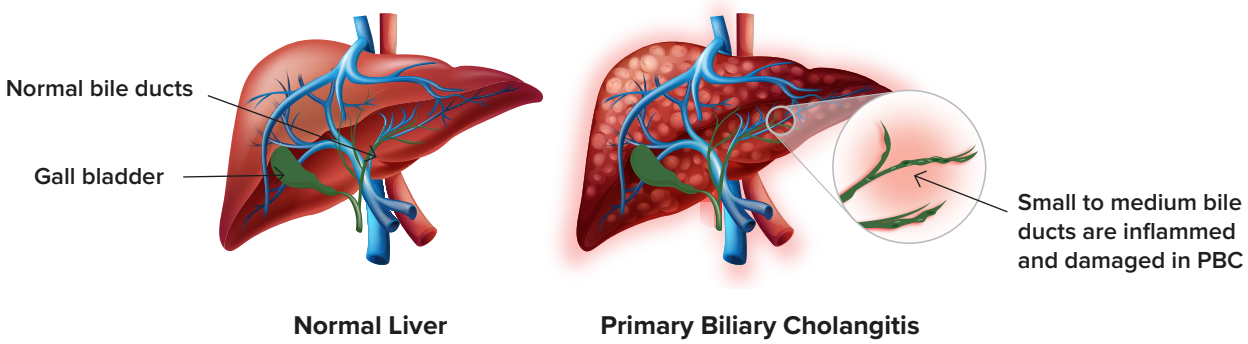
Always talk to a doctor or healthcare provider before making any treatment changes.

This document is a short summary of this study written for a general audience. Links to scientific summaries of this study can be found at the end of this document.

# General information about the study

## What is primary biliary cholangitis?

**Primary biliary cholangitis (PBC)** is an autoimmune liver disease. The immune system (the body's defense system) attacks the bile ducts by mistake. Bile ducts are tiny tubes that carry bile, which helps digest food and absorb vitamins. When bile ducts are damaged, bile cannot flow properly and builds up in the liver. This can cause problems in the liver. If PBC is left untreated, it may lead to scarring, cirrhosis (severe scarring of the liver), or even liver failure.




PBC mostly affects middle-aged women. Common treatments for PBC do not work for everyone. **Seladelpar** is a new treatment approved in the United States for people with PBC.

This study focused on how seladeplar works in people with **PBC who have liver impairment**. Liver impairment means the liver isn't working as well as it should. The liver normally helps break down and remove medicines from the body. If the liver is impaired, medicines may stay in the body longer or work differently. This study observed how liver impairment affects the way the body processes seladelpar in people with PBC.

This is a **Phase 1 clinical study**. This means that researchers looked at how seladelpar behaves in the body in a small group of participants.

## What was the purpose of the study?

The main purpose of this study was to learn more about the levels of seladelpar in the body, how it works, and how safe it is in people living with PBC who also had liver impairment.

## The main questions the researchers wanted to answer in this study were:

- How much seladelpar and its **breakdown products** were found in participants' blood and urine after taking the medicine?

  **Breakdown products** are substances formed when the body breaks down a drug.

- How did liver-related blood test results change after taking seladelpar during Part B of the study?
- How many participant had **unwanted medical events** during the study?

  **Unwanted medical events** can happen during a study, and they may or may not be caused by the study drug. In this summary, we use 'side effects' to describe the unwanted medical events that study doctors thought might have been caused by the study drug, seladelpar.

- Did the participants' general laboratory tests and health measurements change after taking seladelpar?

Researchers also wanted to know if there were any side effects that participants had during the study.

# Who took part in the study?

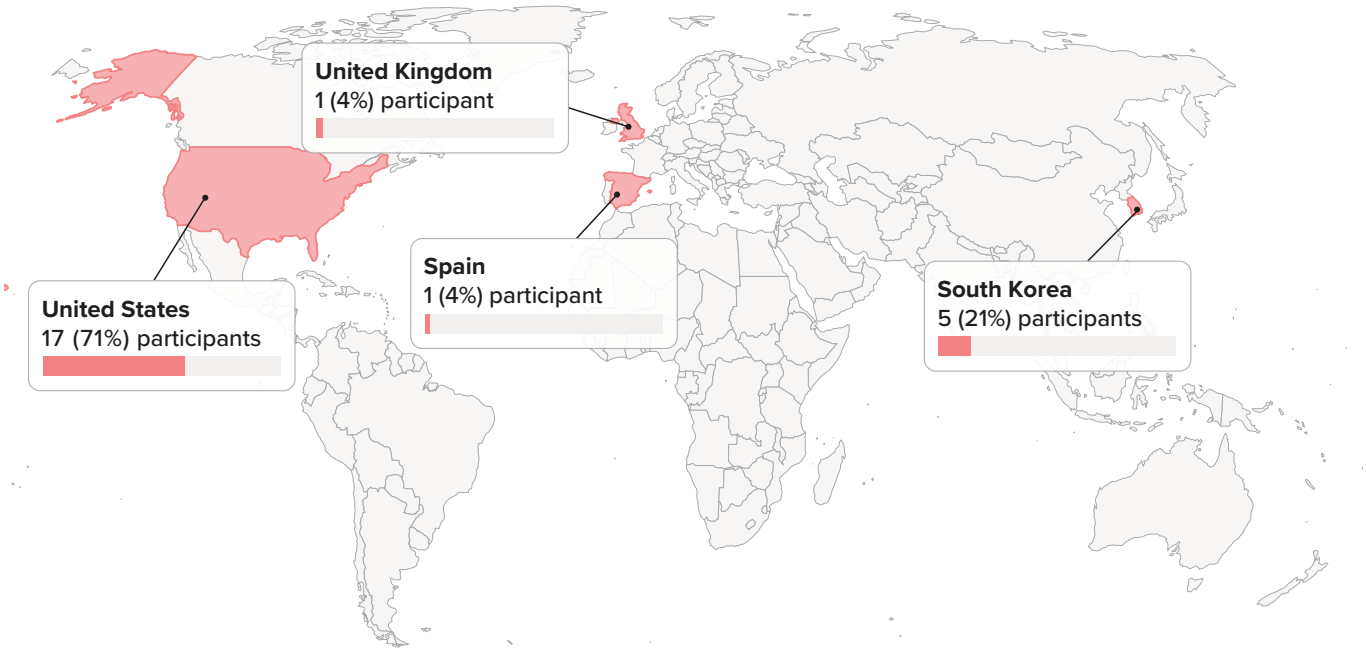
**24 participants** living with PBC and liver impairment in the United States, South Korea, Spain, and the United Kingdom took part in the study.

**People could take part in the study if they:**

- Were 18 to 80 years old
- Were living with PBC
- Had suitable test results that confirmed liver impairment

Participants were **33 to 75 years old** when they joined the study.

The map below shows how many study participants were from each country.

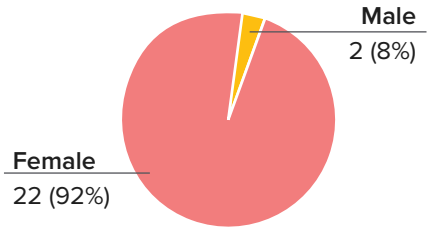



The sex, race, and ethnicity of participants are shown below.

| Race | Number of participants (%) |
|---|---|
| White | 17 (71%) |
| Asian | 7 (29%) |

| Ethnicity | Number of participants (%) |
|---|---|
| Not Hispanic or Latino | 18 (75%) |
| Hispanic or Latino | 6 (25%) |

**Sex**



# What happened during the study?

This was an **open-label** study, which means each participant knew what treatment they were taking, and the doctors and the study staff also knew.

At the start of the study, the study doctors checked each participant's health and medical history to make sure they were a good fit. They also ran tests to check how much liver impairment each participant had.

The study was conducted in 2 parts, **Part A and Part B**.

**Part A**

In Part A, all **24 participants** were placed into 1 of 4 treatment groups based on their liver impairment. Participants in Groups 1 and 2 were also checked for **portal hypertension (PHT)**.

**What is PHT?**

PHT is high blood pressure in the vein that carries blood to the liver. Checking for PHT helps doctors detect early signs of liver problems.

Each group had **6 participants**. All participants received a single dose of **seladelpar 10 milligrams (mg)** on Day 1 of the study.

- **Group 1**: Participants with mild liver impairment without PHT
- **Group 2**: Participants with mild liver impairment but with signs of PHT
- **Group 3**: Participants with moderate liver impairment
- **Group 4**: Participants with severe liver impairment

After receiving seladelpar, participants stayed at the clinic for at least 12 hours. Study doctors monitored their health and collected blood and urine samples. They measured seladeplar and its breakdown products in the blood and urine. They repeated these tests over 4 days and checked how the liver was working. Doctors also watched participants for any medical issues.

Participants had a follow-up phone call on Day 7 after they received seladelpar to see how they were doing.

**Part B**

Before receiving seladelpar in Part B, study doctors checked participants' health to make sure they could safely continue. They ran tests to confirm each participant's liver impairment and see if they could continue to be part of Groups 2 and 3.

**12 participants** from Groups 2 and 3 who completed Part A of the study entered Part B. Participants from these groups had early signs of liver problems and mild to moderate liver impairment, that doctors thought might benefit from longer treatment with seladelpar. Participants in Groups 1 and 4 either had mild or severe liver impairment so doctors did not expect them to benefit from longer treatment.

In Part B, participants did not take seladelpar for the first 14 days. This was to allow their bodies to clear the seladelpar received in Part A before they started taking it again in Part B.

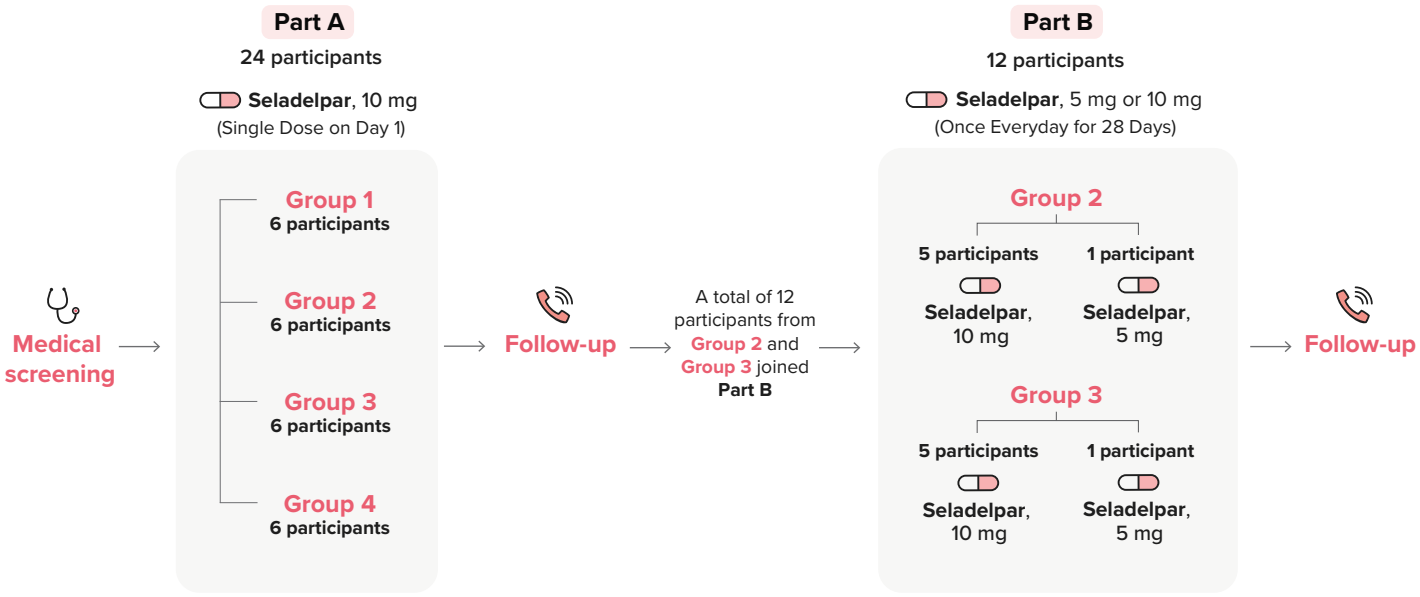
The study doctors looked at the Part A results for participants to decide their dose for Part B. In each group, 5 participants received **10 mg** and 1 participant received **5 mg** of seladelpar, once every day, for up to 28 days.

Participants stayed at the clinic for at least 12 hours on Days 1 and 28 after receiving seladelpar. For the other doses, they could visit the clinic or take the medication at home. Study doctors continued to check their health, collect blood and urine samples, and monitor liver tests for 31 days.

Participants had a follow-up phone call 14 days after they received the last dose of seladelpar.

Including the screening, treatment period, and the follow-up phone calls, the study lasted about 5 weeks for Part A, and about 8 weeks for Part B.

The graphic below shows how the study was done.




# What were the results of the study?

This is a summary of the main results from this study. The individual results of each participant might be different and are not in this summary. A detailed presentation of the results can be found on the websites listed at the end of this summary.

### How much seladelpar and its breakdown products were found in participants' blood and urine after taking the medicine?

To answer this question, the researchers collected blood and urine samples from the participants before and after they took seladelpar. They wanted to better understand how the body processes seladelpar.

**Part A** (Single dose of seladelpar 10 mg)

- Participants with severe liver impairment (Group 4) had higher levels of seladelpar in their blood compared to participants with moderate liver impairment (Group 3) and mild liver impairment (Groups 1 and 2).
- For all participants, seladelpar reached its highest level in the blood quickly (about 1 to 1.5 hours) and half of it was removed from the body within about 4 to 4.5 hours.
- Only a very small amount of seladelpar was removed through urine across all groups.
- The breakdown products of seladelpar generally stayed in the blood longer in participants with severe liver impairment (Group 4). It took more time for them to reach their highest levels and for it to be removed from the body.

**Part B** (Multiple doses of seladelpar 10 mg or 5 mg)

- The results were similar between participants who received multiple doses of seladelpar 5 mg or 10 mg.
- When participants took seladelpar once a day for 28 days, the medicine did not build up in their bodies over time.
- The way the body processed seladelpar on Day 28 was similar to Day 1, showing consistent effects with daily use.
- For all participants, seladelpar reached its highest level in the blood (about 1 to 3 hours) and half of it was removed from the body within about 4 to 5 hours.

Overall, the seladelpar levels were found to be higher in participants with severe liver impairment (Group 4) as compared to participants with mild liver impairment (Group 1). As liver impairment becomes severe, the body broke down the medicine more slowly leading to higher levels in the blood. This information will help researchers to find the right dose for participants with different levels of liver impairment.

## How did liver-related blood test results change after taking seladelpar during Part B of the study?

To answer this question, the researchers collected blood samples from the participants before and after they took seladelpar. They wanted to see how treatment affected normal liver function. The blood tests looked at signs of bile duct damage and other signs of liver impairment.

Researchers looked at the changes in the blood test results from the start of Part B until Day 28.

Researchers found improvements in some liver-related blood test results after 28 days of seladelpar treatment. But these improvements could not be confirmed because Part B included only a few participants and their results were very different.

## How many participant had unwanted medical events during the study?

The researchers kept track of any unwanted medical events that the participants had during the study.

The table below shows the number of participants with unwanted medical events in each study group.

| Unwanted Medical Events | | | | | | |
|---|---|---|---|---|---|---|
| | Part A | | | | Part B | |
| | **Group 1** (out of 6 participants) | **Group 2** (out of 6 participants) | **Group 3** (out of 6 participants) | **Group 4** (out of 6 participants) | **Group 2** (out of 6 participants) | **Group 3** (out of 6 participants) |
| | Number of participants (%) | | | | | |
| How many participants had unwanted medical events? | 0 | 2 (33%) | 1 (17%) | 0 | 2 (33%) | 3 (50%) |

Researchers also wanted to learn more about these unwanted medical events.

They looked at:

- **How severe the events were:**

  The severity of an event shows how strong the symptom feels (mild, moderate, or severe).

  They found that all events in the study were mild or moderate, except for **1 participant** in Group 2 of Part B, who had unwanted medical events of **inflammation of the lining of bronchial tubes, which carry air to and from your lungs** (bronchitis) and **whole-body swelling** (generalized oedema). These events were severe and required medical care.

- **Which events might have been caused by seladelpar (called side effects):**

  They found that, out of all the unwanted medical events, only 1 event, report by **1 participant** in Group 3, Part B, was considered a side effect. This means the study doctors thought seladelpar might have caused it.

  The event was **indigestion** (dyspepsia), which was not serious in nature. More details about what “serious” means are provided in the section “What side effects did participants have during the study?”

### Unwanted medical events of interest

Doctors watch some unwanted medical events more closely because they are important for safety. These are called events of interest.

During this study, 2 participants had unwanted medical events of interest during **Part B**:

- 1 participant in Group 2 had **fluid in the belly, which caused bloating and discomfort** (ascites)
- 1 participant in Group 3 had **high blood levels of urea caused by kidney problems** (blood urea increased)

The doctors believed these two events were not caused by seladelpar.

### Did the participants' general laboratory tests and health measurements change after taking seladelpar?

To answer this question, researchers looked at participants' health measurements and did laboratory tests before and after the participants took seladelpar. These tests include:

- Blood tests to check both liver function and blood cells
- Urine tests
- Blood clotting tests to see how well and how fast blood clots

Researchers checked if the changes in the participants' health measurements and test results were abnormal, meaning they were out of the normal reference range.

**They did not find any concerning changes during the study.**

## What side effects did participants have during the study?

In this summary, "**side effects**" are defined as unwanted medical events that the study doctors thought might be caused by the study treatment.

The results from several studies are usually needed to help decide if a treatment actually causes a side effect.

A side effect is considered "**serious**" if it:

- results in death
- is life-threatening
- considered by the study doctor to be medically important
- causes lasting problems
- requires hospital care
- causes a birth defect

Below is the summary of side effects that occurred during the study:

**None of the participants had any serious side effects or died due to any side effects during the study.**

**No participants stopped taking the study treatment because of side effects.**

One participant in Group 3, Part B, had **indigestion** (dyspepsia). This was the only side effect seen in the study. This side effect was not serious in nature and did not meet the definition of 'serious side effects' mentioned above in this summary.

## How has this study helped researchers?

The researchers learned more about how liver impairment affects the way the body breaks down seladelpar. They also learned more about the safety of seladelpar in people living with PBC and liver impairment.

The results from several studies are needed to help decide which treatments work and are safe. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Gilead Sciences does plan to have further clinical studies with seladelpar.

## Where can I learn more about this study?

You can find more information about this study on the websites listed below.

| Organization (Website) | Study Identifier |
|---|---|
| **United States National Institutes of Health (NIH)** www.clinicaltrials.gov | ClinicalTrials.gov ID: NCT04950764 |
| **Gilead Website** www.gileadclinicaltrials.com | CB8025-21838 |

Please note that information on these websites may be presented in a different way from this summary.

**Full Study Title:** The Effect of Hepatic Impairment on The Pharmacokinetics of Seladelpar: An Open-Label Study Following Oral Dosing of Seladelpar to Subjects With Primary Biliary Cholangitis (PBC) and Hepatic Impairment

To learn more about clinical trials in general, please visit this page on www.clinicaltrials.gov website.

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*Thank you*

Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

GILEAD