PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Study Number: GS-US-454-6075

Date of Study: August 2021 to December 2024

Short Study Title: Study of Semaglutide, and Cilofexor/Firsocostat, Alone and in Combination, in Adults With Cirrhosis Due to Nonalcoholic Steatohepatitis (NASH)

Study Nickname: WAYFIND

Date of this Plain Language Summary: September 2025

The information in this summary does not include any information available after this date.

Thank you

Thank you to the participants who contributed to the clinical study for **Cilofexor/Firsocostat (CILO/FIR). CILO** is also known as **GS-9674**, while **FIR** is known as **GS-0976**.

Gilead Sciences sponsored this study in collaboration with Novo Nordisk. We believe it is important to share the results with 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.

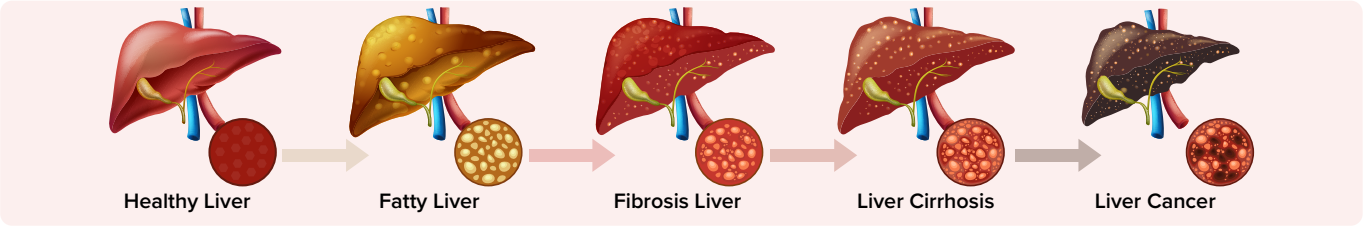
General information about the study

What is Nonalcoholic Steatohepatitis (NASH)?

Nonalcoholic Steatohepatitis (NASH) is a severe form of nonalcoholic fatty liver disease (NAFLD). In NASH, there is buildup of fat in the liver causing inflammation and liver damage in people who do not consume too much alcohol. That is why is it called “nonalcoholic fatty liver disease".

Over time, NASH may lead to liver scarring (fibrosis). If left untreated, it can progress to severe liver scarring (cirrhosis) or life-threatening conditions like liver failure or liver cancer.

The graphics below show stages of liver damage.



NASH can develop in overweight or obese people or those with diabetes. A diet high in fat and sugar can also be a factor, and family history may play a role. For these reasons, NASH is now also called metabolic dysfunction-associated steatohepatitis (MASH). Normally, the body produces insulin to help the cells in the body absorb sugar. In Type 2 diabetes, the body may not be able to use insulin properly, or may not make enough of it. This can lead to sugar building up in the blood. The extra sugar may be stored as fat in various parts of the body, including the liver. That may lead to NASH. Semaglutide (SEMA) is an approved medicine for Type 2 diabetes and supports weight loss. It is also approved to treat MASH in patients with moderate-to-advanced liver scarring.

Cilofexor/Firsocostat (CILO/FIR) is a fixed-dose combination of two drugs, cilofexor and firsocostat, also being studied for NASH.

Currently, there are very few treatments available for NASH. There is an unmet need for effective therapies, especially for patients with cirrhosis. Researchers believe that combining drugs may be more effective than using a single drug to treat NASH with cirrhosis. In this study, the researchers wanted to see if people with cirrhosis due to NASH could benefit from a combination of SEMA and CILO/FIR.

This is a **Phase 2** clinical study. This means that researchers tested SEMA, CILO/FIR and their combination in a small number of people with NASH and cirrhosis.

What was the purpose of the study?

The main purpose of this study was to see if the study drug—SEMA combined with CILO/FIR—could help improve liver fibrosis in participants with NASH, compared to placebo.

A placebo looks like a treatment but does not have any drug in it.

The main question the researchers wanted to answer in this study was:

- **How many participants who took SEMA with CILO/FIR showed improvement in liver fibrosis without worsening NASH, compared to participants who took placebo?**

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

Who took part in the study?

- **457 participants** with NASH and cirrhosis around the world took part in the study.

People could take part in the study if they:

Were between the ages of 18 to 80 years

Had confirmed NASH with cirrhosis, confirmed by looking at liver tissue (liver biopsy)

Had Body Mass Index (BMI) of 23 mg/m² or above, indicating they were overweight

The study participants were between the ages of **27** and **80** years.

The participants from each country are shown below (Number (%) of participants).

United States	349 **(76%)**	Japan	17 **(4%)**
Canada	32 **(7%)**	Australia	16 **(4%)**
France	29 **(6%)**	Spain	14 **(3%)**

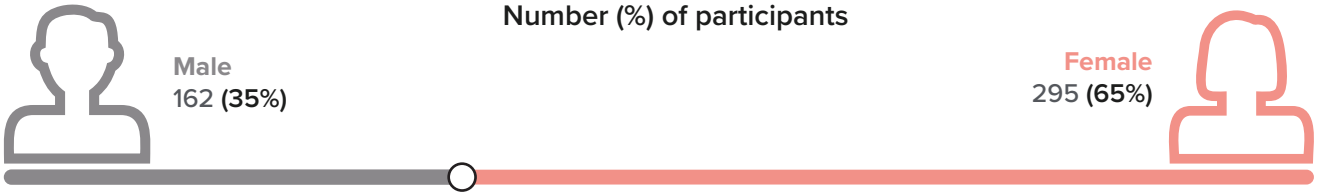
The race of participants is shown below (Number (%) of participants).

White	376 **(82%)**	Not Collected	13 **(3%)**
Asian	38 **(8%)**	Black or African American	9 **(2%)**
Other or More Than One Race	14 **(3%)**	American Indian or Alaska Native	7 **(2%)**

The ethnicity of participants is shown below (Number (%) of participants).

Not Hispanic or Latino	350 **(77%)**	Hispanic or Latino	100 **(Below 22%)**
Not Collected	7 **(2%)**		

Sex of participants is shown below
Number (%) of participants



What happened during the study?

This was a **randomized**, **double-blind**, and **double-dummy** study.

Randomized means the researchers used a computer program to put participants into treatment groups by chance. This helped make sure the treatments were chosen fairly.

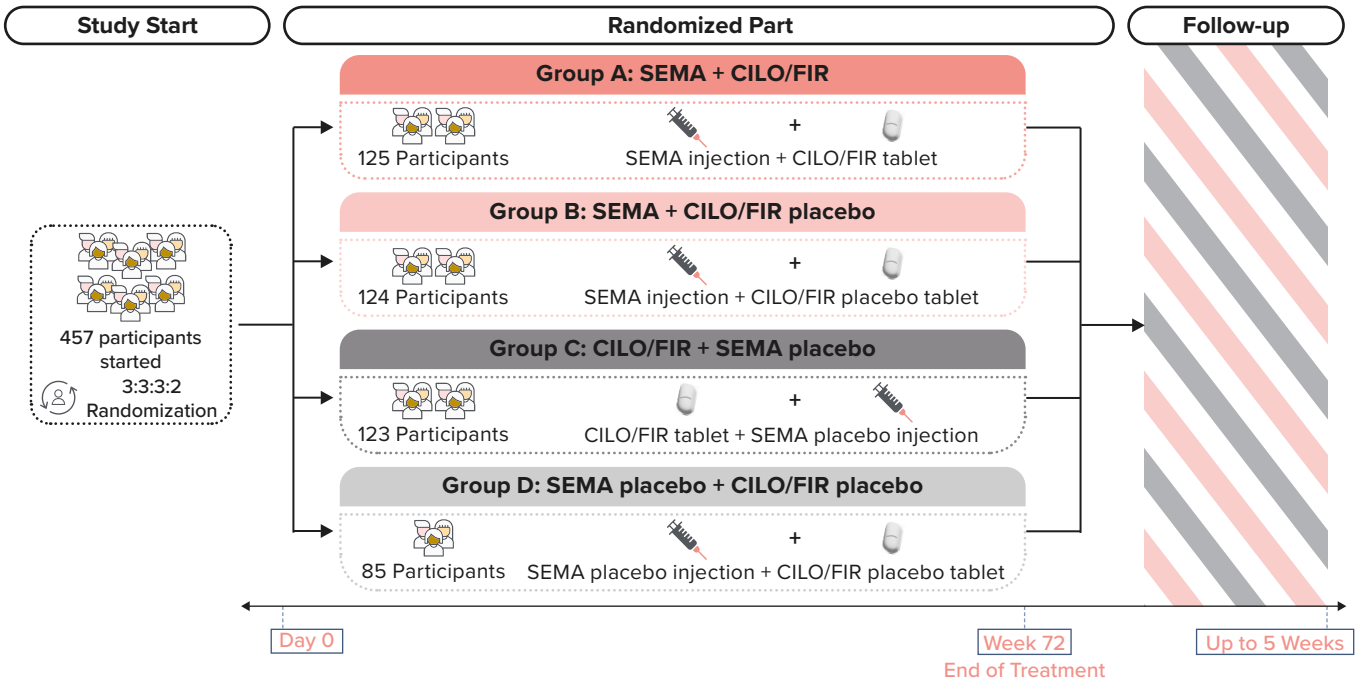
Double-blind means none of the participants, doctors or other study staff, and the sponsor personnel knew what treatment each participant took. This was done to make sure that the study results were not influenced in any way. Participants were monitored closely for any side effects, and safety measures were in place to address any safety concerns.

Double-dummy means 2 placebos were used. In this study 2 placebos were used, one looked like SEMA, the other looked like CILO/FIR. This ensured blinding across all treatment groups.

A total of 457 participants were randomized in a 3:3:3:2 ratio into four treatment groups.

- Participants started with a low dose of SEMA 0.24 mg (or placebo) and gradually increased to the full dose (2.4 mg) over 16 weeks. They gave themselves an injection under the skin once a week using a prefilled pen. A pen is a medical device used to inject medicine under the skin.
- Participants took a CILO 30 mg/FIR 20 mg tablet (or a placebo) by mouth once a day.

The graphics below show the treatment plan.



All participants took treatment up to 72 weeks and were followed for safety up to 5 weeks after the end of treatment.

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.

Of 457 participants, 453 took the study drug and were included in the results below. This included 124 participants in Group A (SEMA + CILO/FIR), 122 in Group B (SEMA + CILO/FIR placebo), 123 in Group C (CILO/FIR + SEMA placebo), and 84 in Group D (SEMA placebo + CILO/FIR placebo).

How many participants who took SEMA with CILO/FIR (Group A) showed improvement in liver fibrosis without worsening NASH, compared to participants who took placebo (Group D)?

Researchers checked all four treatment groups to see if liver fibrosis had improved in participants after 72 weeks of treatment. They did tests and scans from time to time.

After 72 weeks, they found:

- **Group A (SEMA + CILO/FIR):** 17 out of 124 (14%) participants showed improvement in liver fibrosis.
- **Group D (SEMA placebo + CILO/FIR placebo):** 7 out of 84 (8%) participants showed improvement in liver fibrosis.

Even though more participants showed improvement with the SEMA + CILO/FIR treatment (Group A), the researchers could not conclude that the treatment caused the improvement. **The study's main purpose—comparing Group A to Group D—was not met.**

The results of liver fibrosis improvement in Group B and Group C are not included in this summary because they were not part of the main question of the study.

What side effects did participants have during the study?

Unwanted medical events can happen to the study participants when they take a study drug. In this summary, "**side effects**" are defined as unwanted medical events that the study doctors thought might be caused by the study drug.

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

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

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

The table below shows how many participants had side effects during the study.

Overall Side Effects

	Group A SEMA + CILO/FIR (Out of 124 participants)	**Group B** SEMA + CILO/FIR placebo (Out of 122 participants)	**Group C** CILO/FIR + SEMA placebo (Out of 123 participants)	**Group D** SEMA placebo + CILO/FIR placebo (Out of 84 participants)	**Total** (Out of 453 participants)
	Number (%) of participants				
How many participants had any side effects?	75 (60%)	69 (57%)	53 (43%)	41 (49%)	238 (53%)
How many participants stopped taking the study treatment because of the side effects?	10 (8%)	6 (5%)	4 (3%)	2 (2%)	22 (5%)

What were the serious side effects?

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

What were the non-serious side effects?

The table below shows the most common non-serious side effects reported in at least 10% of total participants, during the study.

These side effects were not serious in nature and did not meet the definition of 'serious side effects' mentioned in the section above in this summary.

Non-Serious Side Effects

	Group A SEMA + CILO/FIR (Out of 124 participants)	**Group B** SEMA + CILO/FIR placebo (Out of 122 participants)	**Group C** CILO/FIR + SEMA placebo (Out of 123 participants)	**Group D** SEMA placebo + CILO/FIR placebo (Out of 84 participants)	**Total** (Out of 453 participants)
	Number (%) of participants				
Feeling sick to the stomach (Nausea)	50 (40%)	38 (31%)	20 (16%)	16 (19%)	124 (27%)
Fewer bowel movements (Constipation)	20 (16%)	16 (13%)	8 (7%)	5 (6%)	49 (11%)
Feeling less hungry (Decreased appetite)	18 (15%)	17 (14%)	5 (4%)	5 (6%)	45 (10%)
Frequent, loose watery stools (Diarrhoea)	14 (11%)	16 (13%)	7 (6%)	7 (8%)	44 (10%)

There were other non-serious side effects, but those occurred in fewer participants. Some participants may have had more than 1 non-serious side effect.

? How has this study helped researchers?

The researchers learned more about the safety and effectiveness of SEMA and CILO/FIR in people with NASH and cirrhosis.

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 not plan to have further clinical studies with SEMA + CILO/FIR or CILO/FIR alone in NASH.

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
European Medicines Agency www.clinicaltrialsregister.eu	EudraCT Number: 2021-001445-12
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	ClinicalTrials.gov Number: NCT04971785
Gilead Website www.gileadclinicaltrials.com	GS-US-454-6075

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

Full Study Title: A Phase 2, Randomized, Double-Blind, Double-Dummy, Placebo-Controlled Study Evaluating the Safety and Efficacy of Semaglutide, and the Fixed-Dose Combination of Cilofexor and Firsocostat, Alone and in Combination, in Subjects with Compensated Cirrhosis (F4) due to Nonalcoholic Steatohepatitis (NASH)

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

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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.

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