



# Retatrutide and Fatty Liver

Why Metabolic Doctors Are Watching  
the TRIUMPH Trials

By Dr. Cyrus, MD • February 2026

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Evidence-based | Provider-reviewed | No BS

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# The Disease Nobody Sees

One in three adults has it. Most do not know.

# 1 in 3

adults have fatty liver disease (MASLD)

*Prevalence has climbed from 25% to 38% of the global population*

Metabolic dysfunction-associated steatotic liver disease — MASLD, formerly called NAFLD — has quietly become one of the most common chronic diseases in the world. Unlike most diseases at this scale, fatty liver has no obvious symptoms in its early stages. No pain. No fatigue. No warning signs.

By the time symptoms appear, the disease has often progressed from simple fat accumulation to active inflammation (MASH), fibrosis, and in the worst cases, cirrhosis or liver cancer. It is now one of the fastest-growing indications for liver transplantation in the United States.

*The first FDA-approved medication for MASH — resmetirom — arrived in March 2024. But retatrutide is producing liver fat reduction data that has hepatologists calling it "top of the class" among everything currently being studied.*

# The Glucagon Advantage: Targeting the Liver Directly

Semaglutide and tirzepatide both reduce liver fat through weight loss and insulin-sensitizing effects. But they work primarily through appetite suppression. What they do not do — at least not robustly — is directly increase the rate at which the liver burns its existing fat stores.

This is where the **glucagon receptor** changes the equation. Glucagon receptor activation in the liver tells it: **stop storing fat and start burning it.**

## Increases Fat Oxidation

The liver actively burns stored fat for energy rather than continuing to accumulate it

## Decreases Lipogenesis

Stops the creation of new fat in the liver, cutting off the supply at the source

## Improves Glycogen Mobilization

Better regulation of liver energy storage and glucose management

## Reduces Hepatic Inflammation

Directly reduces the inflammatory processes that drive progression from MASLD to MASH

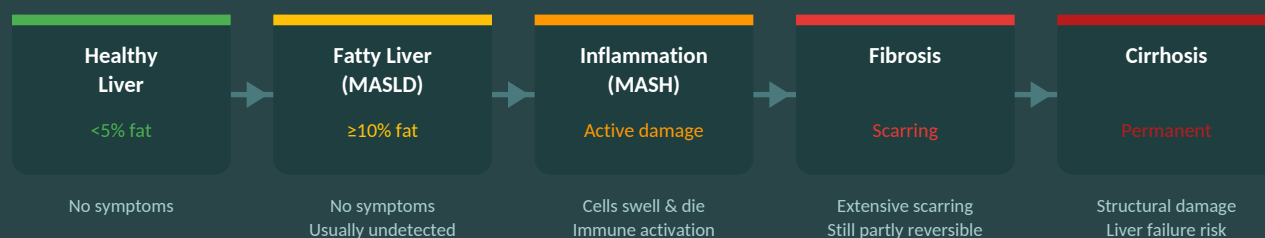
*Retatrutide does not just reduce the flow of new fat into the liver — it actively accelerates the removal of fat that is already there. This is the mechanism that makes it fundamentally different from semaglutide or tirzepatide for liver disease.*

# The Progression — and Where Treatment Intervenes

Your liver is not just a filter. It is a metabolic factory — processing nutrients, regulating blood sugar, producing cholesterol, and manufacturing proteins. When excess calories and insulin resistance cause fat to accumulate, the consequences cascade through every system in your body.

## Fatty Liver Disease: The Progression Nobody Sees

*Every arrow is a window of opportunity. Earlier intervention = more reversible damage.*



### INTERVENTION WINDOW: Reversible with treatment

**Retatrutide Phase 2: 93% of patients on 12mg had liver fat below 5%**

*Effectively moving patients from MASLD back to Healthy Liver*

*MASLD affects 38% of the global population. One of the fastest-growing indications for liver transplant.*

# What the Data Shows

The retatrutide Phase 2 trial included a MASLD substudy of 98 participants with at least 10% liver fat, measured by MRI. The results, published in **Nature Medicine** and presented at the AASLD annual meeting, were striking.



Nine out of ten patients on the higher doses no longer met diagnostic criteria for fatty liver disease by the end of the study. Zero percent of placebo patients achieved this threshold.

## The Metabolic Cascade

The liver fat data is impressive on its own. But the metabolic improvements that accompanied it tell an even more important story.

Marker	Change vs. Placebo	What It Means
Fasting Insulin	↓ 37-71%	Dramatically reduced insulin resistance
HOMA-IR	↓ 36-69%	Standard insulin resistance marker
Adiponectin	↑ 30-99%	Metabolic health and insulin sensitivity marker
Triglycerides	↓ 35-40%	Reduced cardiovascular risk factor
Leptin	↓ 30-56%	Reflects reduced fat stores

# Tests Worth Discussing with Your Provider

Standard blood panels often miss early fatty liver disease. Liver enzymes (ALT and AST) can be normal even with significant fat accumulation. If you think fatty liver might be relevant to you, here are the tests worth discussing.

## ALT and AST

Liver enzymes that indicate cellular damage. The most commonly available first step, though normal values do not rule out fatty liver.

*Available on any standard blood panel. Elevated values warrant further investigation.*

## FIB-4 Score

A calculated index using age, AST, ALT, and platelet count that estimates the likelihood of liver fibrosis. Requires no additional blood tests beyond a standard panel.

*Underused in primary care. Your provider can calculate this from existing lab values.*

## FibroScan

A noninvasive ultrasound-based test that measures liver stiffness (correlating with fibrosis) and can also quantify liver fat. The gold standard for noninvasive assessment.

*Increasingly available in gastroenterology and hepatology practices.*

## MRI-PDFF

The most accurate noninvasive measurement of liver fat content. This is what was used in the retatrutide clinical trials.

*Typically reserved for research or complex clinical cases due to cost.*

*You do not need all of these. Starting with a FIB-4 calculation (which your provider can do with existing lab values) and a FibroScan if indicated gives you a reliable picture of where you stand.*

## Sources & References

This guide draws on peer-reviewed clinical trial data, hepatology conference presentations, and published epidemiological research.

### Retatrutide MASLD Substudy

Phase 2 MASLD substudy: liver fat reduction by MRI-PDFF in 98 participants. Nature Medicine. 2024.

### AASLD Liver Meeting

Sanyal AJ, et al. Retatrutide liver fat data presentation. American Association for the Study of Liver Diseases annual meeting. 2023.

### MASLD Epidemiology

Younossi ZM, et al. Global epidemiology of MASLD/NAFLD — updated prevalence estimates. Hepatology. 2023.

### ADA 2023 Symposium

American Diabetes Association Scientific Sessions. Triple agonism and hepatic fat reduction. 2023.

### Triple Agonism Review

Glucagon, GLP-1, and GIP receptor agonism: mechanisms and metabolic implications. PMC review. 2025.

### Resmetirom Approval

FDA approval of resmetirom (Rezdiffra) for MASH — first approved treatment for metabolic liver disease. March 2024.

### Retatrutide Phase 2

Jastreboff AM, Kaplan LM, Frias JP, et al. Triple-hormone-receptor agonist retatrutide for obesity. New England Journal of Medicine. 2023;389(6):514-526.

*All clinical data referenced in this guide was current as of February 2026. Retatrutide is an investigational medication not yet approved by the FDA. Fatty liver that is diagnosed early is highly reversible. Fatty liver that progresses to cirrhosis is not.*



## Ready to Take the First Step?

Talk to a licensed provider about your metabolic health —  
including liver fat, insulin resistance, and whether  
weight loss treatment may help.

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