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FULL GUIDE

If you've been paying attention to the peptide space at all, you've heard the name. Retatrutide. Some people call it "The Triple Threat." Some call it "Super GLP-1." I call it the single most effective fat loss tool that currently exists on this planet — and the clinical data backs that up harder than anything I've ever seen.

This is the full guide. Mechanism, dosing, side effects, stacks, training, diet, everything. I went deep on the research for this one. Bookmark it.

What Retatrutide Actually Is

Retatrutide (LY-3437943) is a 39-amino acid peptide developed by Eli Lilly. It's a triple receptor agonist — meaning it activates three different hormone receptors simultaneously:

GLP-1 (Glucagon-Like Peptide-1) — This is the same receptor that Ozempic and Wegovy target. It crushes your appetite, slows gastric emptying (so food sits in your stomach longer and you feel full), and improves insulin sensitivity.

GIP (Glucose-Dependent Insulinotropic Polypeptide) — This is the second receptor that Mounjaro/Tirzepatide added. It enhances insulin secretion and — this is key — helps preserve lean muscle mass during weight loss.

GCG (Glucagon) — This is the third receptor. This is what makes Retatrutide different from everything else. Glucagon receptor activation directly increases your energy expenditure and ramps up fat oxidation. Your body literally burns more calories at rest and preferentially uses fat as fuel.

So the formula is simple: Eat Less + Burn More + Keep Muscle = Retatrutide.

Semaglutide hits one receptor. Tirzepatide hits two. Retatrutide hits all three. And the results reflect that.

The Clinical Data — This Is Not Bro Science

The landmark study was published in the New England Journal of Medicine in June 2023 (Jastreboff et al., cited over 1,000 times). This is the most prestigious medical journal in the world. 338 adults were enrolled in a Phase 2, double-blind, randomized, placebo-controlled trial over 48 weeks.

Here's what happened at 48 weeks. The placebo group lost just 2.1% of their body weight. The 1mg group lost 8.7%. The 4mg group lost 17.1%. The 8mg group lost 22.8%. And the 12mg group — the highest dose — lost 24.2% of their body weight in under a year.

Now look at the response rates at the 12mg dose: every single participant — 100% — lost at least 5% of their body weight. 93% lost over 10%. And 83% lost over 15%. Even the 8mg dose had 100% of participants hitting the 5% threshold and 91% hitting 10%.

For context — Semaglutide (Ozempic/Wegovy) gets you about 15% at 68 weeks. Tirzepatide (Mounjaro) gets you about 22%. Retatrutide hit 24.2% in less time. A 2025 meta-analysis

published in Baylor University Medical Center Proceedings confirmed: "Retatrutide demonstrates superior efficacy in both absolute and percentage weight reduction compared to tirzepatide."

This isn't even close.

It Doesn't Just Burn Fat — It Cleans Your Liver

This is the part most people don't talk about. A sub-study led by Dr. Arun Sanyal at Virginia Commonwealth University looked at what Retatrutide does to liver fat in obese patients with fatty liver disease (MASLD). The results were presented at the American Association for the Study of Liver Diseases meeting in November 2023.

98 obese adults. 48 weeks. Here's what happened:

At the 12mg dose, 93% of patients reduced their liver fat below 5% — meaning they no longer qualified as having fatty liver disease. The relative decrease in liver fat was 86%. Dr. Sanyal's exact words: "We could wipe out the fat very early in the course of this disease before it becomes a real threat to the liver."

Why does this matter for you? Because if you've been drinking, eating like shit, or carrying excess body fat for years, your liver is probably storing fat it shouldn't be. Fatty liver leads to inflammation, insulin resistance, metabolic dysfunction, and eventually serious liver disease. Retatrutide doesn't just help you lose weight — it actively reverses the metabolic damage.

Cardiovascular Benefits

Data presented at the European Society of Cardiology Congress in 2024 showed Retatrutide reduced non-HDL cholesterol by up to 26.9% at 48 weeks and significantly improved overall lipid and cardiovascular risk profiles. This is dose-dependent — higher doses showed greater improvements.

So you're losing fat, cleaning your liver, AND improving your heart health. All from one weekly injection.

Body Composition — Does It Preserve Muscle?

This is the question every lifter asks. And the answer is encouraging.

A study published in *The Lancet Diabetes & Endocrinology* (June 2025) specifically looked at body composition changes with Retatrutide. The finding: Retatrutide significantly improved total body fat mass reduction compared with placebo and dulaglutide, with greater fat mass reduction versus lean mass loss. Business Insider reported in August 2025 that studies suggest Retatrutide "may be better at zeroing in on fat, preserving more lean muscle" compared to other GLP-1s.

The GIP receptor agonism is likely responsible for this. GIP has been shown to support lean mass preservation, and Retatrutide is 8.9x more potent at the GIP receptor than the body's own natural GIP.

That said — and I cannot stress this enough — you still need to train hard and hit your protein. No peptide replaces resistance training. If you take Retatrutide and sit on your ass eating 80g of protein a day, you will lose muscle. Period. The compound gives you the best possible environment for fat loss while preserving muscle, but YOU have to do the work.

Dosing Protocol

Retatrutide has a half-life of approximately 6 days, which means once-weekly subcutaneous injection. Here's the protocol based on clinical trial data and practical application:

Week 1 — Start at 0.5 to 1mg per week. This is your assessment phase. You're figuring out how your body responds. Don't rush this.

Weeks 2-3 — Move up to 2mg per week if side effects are manageable. Most people tolerate this well.

Weeks 4-6 — Increase to 2.5 to 3mg per week. This is where most people start seeing significant appetite suppression and noticeable fat loss.

Week 6 and beyond — If you're tolerating well and want aggressive fat loss, you can push to 3-4mg per week. Only do this if your body is handling the lower doses without major issues.

Why start low? The NEJM trial specifically tested different starting doses and found that starting at 2mg instead of 4mg significantly reduced gastrointestinal side effects. The GI issues are the main complaint — nausea, constipation, reduced appetite (which is kind of the point). Starting low lets your body adapt.

Injection frequency: Once per week, same day each week. Some people split into twice-weekly (e.g., 1.5mg Monday, 1.5mg Thursday) to smooth out side effects and maintain more consistent blood levels. Both approaches work.

Injection sites: Subcutaneous — stomach (around the belly button, rotating sides), outer thigh, or back of the arm. Rotate sites to avoid irritation.

Reconstitution (If Buying Lyophilized Powder)

If you're getting this as a lyophilized (freeze-dried) powder, you need to reconstitute it:

1. Use bacteriostatic water (bac water). Not sterile water, not saline — bac water. It contains a preservative that keeps the solution stable for multi-use.
2. Standard ratio: 5mg vial + 2mL bac water = 2.5mg/mL (so 0.4mL = 1mg).
3. Draw the bac water slowly into the vial. Let it run down the side — do not squirt it directly onto the powder. Swirl gently. Do not shake.
4. Use insulin syringes (29-31 gauge, 0.5mL or 1mL). These are the same ones used for any subcutaneous peptide injection.
5. Sterilize everything. Alcohol swab the vial tops and injection site every single time.
6. Store reconstituted solution in the refrigerator. Use within 28-30 days.

Side Effects and How to Handle Them

The NEJM trial data showed side effects are primarily gastrointestinal and dose-related. Most were mild to moderate. Here's what to expect and how to manage each one:

Nausea is the most common one. You'll feel queasy, especially after eating large meals. The fix is simple — start at a low dose and increase slowly. Eat smaller, more frequent meals instead of big ones. Ginger root extract helps a lot. If it's severe, ask your doctor about Ondansetron (Zofran).

Constipation happens because GLP-1 activation slows your digestion. Take a fiber supplement daily, add magnesium citrate (400-600mg before bed), and stay hydrated. This usually resolves as your body adjusts.

Reduced appetite — this is literally the mechanism working. You genuinely won't want to eat. But you **MUST** still hit your protein targets. Set alarms if you have to. This is the most dangerous side effect for lifters because it's easy to massively undereat without realizing it.

Dehydration is common because you're losing fat faster and eating less (which means less water from food). Drink 3-4 liters of water daily minimum and add electrolytes — sodium, potassium, magnesium.

Fatigue and lethargy hit especially in the first 2-3 weeks when your caloric intake drops suddenly. Keep carbs moderately high. Don't crash diet on top of this compound. Taurine at 2-5g per day helps with energy.

Injection site irritation — some redness, slight burning or itching at the injection site. Rotate your injection sites every time. Use 29-31 gauge needles and let the alcohol dry completely before injecting.

Elevated heart rate — the NEJM trial showed a slight dose-dependent increase in heart rate that peaks around week 24 and then declines on its own. Monitor it. If it's concerning, consult your doctor. It's self-resolving in most cases.

Important note on nausea: The clinical trial data showed that starting at 2mg (instead of jumping to 4mg) significantly reduced nausea. Don't be a hero. Start low. Your body will adapt.

Optimal Stacks

Retatrutide is powerful on its own, but these compounds can complement it:

MK-677 (Ibutamoren): Growth hormone secretagogue. Helps preserve and even build lean mass while in a caloric deficit. This is probably the best stack partner for Retatrutide if your goal is body recomposition. 10-25mg daily.

L-Carnitine (Injectable): Improves fat oxidation during cardio. Pairs perfectly with Retatrutide's glucagon-driven fat burning. 500mg-1g injected before fasted cardio.

Testosterone (TRT Range): If you're a male on TRT or considering it, maintaining optimal testosterone while running Retatrutide ensures you preserve maximum muscle mass during aggressive fat loss. This is not about supraphysiological doses — just keeping your test in a healthy range.

Berberine: Natural compound that further improves insulin sensitivity. 500mg 2-3x daily with meals. No injection required. Stacks well for metabolic optimization.

Glutathione: Since Retatrutide is already cleaning up your liver fat, adding glutathione supports the detoxification process by binding to the toxins and heavy metals being mobilized. I wrote a full guide on glutathione in this community — go read it.

Training While On Retatrutide

This is where people fuck it up. They take Retatrutide, their appetite disappears, they stop eating enough, they stop training hard, and they end up skinny-fat. Don't be that person.

Resistance Training: 4-6 days per week. Moderate to high volume. The goal is to give your body every reason to hold onto muscle while it's burning fat. Compound movements. Progressive overload. Don't switch to some light "toning" routine because you're in a deficit.

Cardio: 3-5x per week. Mix of LISS (low-intensity steady state — walking, incline treadmill, cycling) and 1-2 HIIT sessions. The glucagon receptor activation from Retatrutide is already increasing your energy expenditure, so you don't need to go crazy on cardio. Use it as a tool, not a punishment.

Diet: This is critical. Your appetite will be crushed, but you still need to eat strategically.

Protein — 1g per pound of bodyweight. Non-negotiable. If you weigh 200lbs, you're eating 200g of protein. Set reminders if you have to. Protein shakes count.

Carbs — Keep them moderate. Don't go keto on top of Retatrutide unless you want to feel like death. Carbs fuel your training and keep your energy up.

Fats — Low to moderate. You're already burning fat like crazy — you don't need to eat a ton of it.

Calories — You'll naturally be in a deficit because your appetite is suppressed. Aim for a 500-750 calorie deficit. Do NOT crash diet. If you're eating under 1,500 calories as a 200lb male, you're doing it wrong.

Track your macros. I know it's annoying. Do it anyway. The appetite suppression makes it dangerously easy to undereat, and if you undereat protein while in a massive deficit, you WILL lose muscle. Retatrutide gives you the best possible fat-to-muscle loss ratio, but only if you feed the machine.

Expected Results Timeline

Weeks 1-2: Appetite starts dropping. You'll notice you're thinking about food less. Some nausea is normal. Scale might not move much yet.

Weeks 2-4: Appetite suppression is fully kicked in. You're eating less without trying. First visible fat loss — face gets leaner, waist starts tightening. Insulin sensitivity improving.

Weeks 4-8: This is where it gets real. Significant visible body fat reduction. Clothes fitting differently. Energy levels stabilize. Strength in the gym should be maintained if protein and training are on point.

Weeks 8-16: Full recomposition mode. Fat is melting. If you're training hard and hitting protein, you'll look dramatically different. The clinical data shows 15-25% bodyweight loss is typical at higher doses over this timeframe.

Weeks 16-48: Continued fat loss with diminishing returns as you get leaner. The NEJM trial showed weight loss hadn't fully plateaued even at 48 weeks at the 12mg dose. This is a marathon, not a sprint.

Who Should NOT Use Retatrutide

Be smart about this. Do not use if you have a history of medullary thyroid carcinoma or MEN-2 syndrome — this is a contraindication for all GLP-1 class drugs. Do not use if you are pregnant or breastfeeding. Do not use if you have severe gastrointestinal disorders like Crohn's or severe gastroparesis. Do not use if you are already severely underweight — this is a fat loss tool, not an anorexia accelerator. And do not use if you have a history of pancreatitis — GLP-1 agonists have been associated with rare cases.

Always consult a medical provider if you're unsure. I'm not a doctor. I'm telling you what the research says and what works in practice. But your health is your responsibility.

The Comparison — Why Retatrutide Wins

Semaglutide (Ozempic/Wegovy) only hits the GLP-1 receptor. One receptor. It gets you about 15% weight loss over 68 weeks. Muscle preservation is moderate, and it has some liver fat reduction but nothing dramatic.

Tirzepatide (Mounjaro/Zepbound) hits two receptors — GLP-1 and GIP. The dual action gets you about 22% weight loss over 72 weeks. Muscle preservation is better because of the GIP component, and liver fat reduction is significant.

Retatrutide hits all three — GLP-1, GIP, and GCG. It achieved 24.2% weight loss in just 48 weeks — more weight loss in less time than either competitor. The body composition data shows the best fat-to-muscle loss ratio of the three, likely because of the 8.9x GIP potency. And the liver data is in a completely different league — 93% of participants reversed their fatty liver disease. The glucagon receptor is the difference maker. It's actively increasing your metabolic rate while the other two receptors handle appetite and muscle preservation.

Where to Get It

You can find Retatrutide listed as "GLP-RT Peptide" on V&L Labs. Quality is legit, they ship fast, and I've used their products personally.

👉 [Get GLP-RT Peptide from V&L Labs](#)

Use code CS or connor for 10% off your order.

Want a Full Protocol Built For You?

Retatrutide is a tool. A powerful one. But it works best when it's part of a complete system — training, nutrition, supplementation, peptides, recovery, all dialed in together. If you want me to build that system for you personally, I do 1-on-1 coaching where we map everything out based on YOUR body, YOUR goals, and YOUR lifestyle.

👉 [Book a coaching call at connorsinann.ca](#)

We'll get on a call, assess where you're at, and build the full plan. No templates. No generic advice. Just a real protocol built for you.

The Bottom Line

Retatrutide is arguably the most powerful fat loss compound ever developed. The New England Journal of Medicine data speaks for itself — 24.2% body weight loss, 93% liver fat reversal, favorable body composition, improved cardiovascular markers. All from one injection per week. But here's the thing — it's not magic. It's a tool. The best tool available, but still a tool. You still need to train. You still need to hit your protein. You still need to be disciplined. Retatrutide removes the hardest part of fat loss — the hunger, the cravings, the constant battle with food — and lets you focus on execution.

Done smart: you get an elite-level body transformation that would take most people years to achieve naturally.

Done lazy: you end up skinny-fat with no muscle and a slower metabolism.

Your call.

Drop your questions below. I'll answer everything.

— Connor