# Tirzepatide - affect on visceral fat

Tirzepatide produces large, preferential reductions in visceral fat, with additional benefits on liver and overall fat distribution.[1] [2] [3]

## Magnitude of visceral fat loss

- In a DXA substudy of SURMOUNT-1 (obesity/overweight, no diabetes), tirzepatide reduced estimated visceral fat mass by about 40% at 72 weeks vs about 7% with placebo (treatment difference ≈ −33 percentage points, $p < 0.001$).[4] [1]
- In the same cohort, total fat mass fell by ~34%, so visceral fat reduction was at least as large as, and numerically greater than, overall fat loss.[1] [4]

## Visceral vs subcutaneous and liver fat

- An MRI-based analysis from the SURPASS-3 program in type 2 diabetes showed tirzepatide reduced visceral adipose tissue more than abdominal subcutaneous adipose tissue, indicating a shift away from ectopic/central depots.[3]
- A 2024 exploratory analysis using imaging-derived z-scores found significant decreases in visceral adipose tissue (z-VAT) and liver fat (z-LF), while abdominal subcutaneous fat (z-aSAT) actually increased from a low baseline, suggesting redistribution from visceral/liver to more metabolically benign subcutaneous stores.[5] [2]
- In a dedicated MRI-PDFF study, tirzepatide produced up to ~55% relative reduction in liver fat over 52 weeks, with many subjects normalizing hepatic fat levels.[6]

## Body composition and lean mass

- Across SURMOUNT-1, about 74–75% of weight lost on tirzepatide was fat mass and ~25–26% was lean mass, proportions similar to lifestyle-induced weight loss but with a much larger absolute fat mass reduction.[7] [1]
- A 2025 analysis of muscle composition reported significant reductions in liver, visceral, and abdominal subcutaneous fat versus basal insulin, with preservation of muscle quality despite some lean mass loss.[8] [9]

## Mechanistic implications

- As a dual GIP/GLP-1 receptor agonist, tirzepatide lowers energy intake, improves insulin sensitivity, and shifts substrate use toward fat oxidation, which appears to preferentially deplete visceral and hepatic fat depots.[10] [11]

- This selective loss of visceral and liver fat is expected to improve cardiometabolic risk markers (glycemia, adipokine profile, adipose tissue insulin resistance), consistent with observed increases in adiponectin, decreases in leptin, and improved adiponectin/leptin ratio in MRI substudies.[2] [5]

If you want, I can pull specific HED-style effect sizes (e.g., kg change in VAT or cm² cross-section) from the MRI/DXA papers for more quantitative modeling.

⁂

# Retatrutide - compare

Retatrutide appears to drive at least as much, and likely greater, visceral fat and liver fat reduction than tirzepatide at similar treatment durations, reflecting its stronger overall weight-loss and glucagon-mediated fat-oxidation profile.[16] [17]

### Visceral and abdominal fat

- In the phase 2 obesity trial, retatrutide reduced abdominal visceral adipose tissue by approximately 16–48% at 48 weeks (dose-dependent, MRI-quantified), with significant reductions at all doses vs placebo.[17]
- In analogous imaging work with tirzepatide, visceral fat reductions around 40% at ~72 weeks were seen in obesity cohorts, again significantly greater than placebo and somewhat larger than overall fat loss.[18] [19]
- Direct head-to-head data are not yet available, but review articles and mechanistic analyses consistently suggest retatrutide's triple agonism yields at least comparable and probably larger proportional VAT loss for a given time frame.[20] [21] [22]

### Liver and ectopic fat

- Retatrutide produces very large liver fat reductions: 71–100% of participants reach ≥30% relative liver fat reduction by 24 weeks, and 79–93% on 8–12 mg normalize liver fat to <5% by 24–48 weeks.[17]
- Tirzepatide also markedly lowers liver fat (often ≥50% relative reduction and high rates of normalization), but the retatrutide MASH-focused data suggest a higher fraction of patients hitting deep liver-fat endpoints at earlier time points.[23] [17]

### Total fat vs lean mass

- In type 2 diabetes, retatrutide caused 15–26% reductions in total fat mass over 36 weeks (dose-dependent) with lean-mass loss fractions similar to other obesity drugs, i.e., most lost weight was fat rather than lean.[24] [25]
- Tirzepatide DXA substudies show about 34% total fat mass reduction at 72 weeks, with ~75% of lost weight as fat and ~25% as lean mass, similar proportional pattern but over a somewhat longer timeframe.[26] [18]

### Weight-loss potency and mechanism

- Tirzepatide (GIP/GLP-1 agonist) yields up to ~22.5% weight loss at ~72 weeks in obesity trials, with strong effects on VAT and liver fat largely via appetite suppression and improved insulin sensitivity.[19] [27]
- Retatrutide (GIP/GLP-1/glucagon agonist) achieves ~22.8–24.2% mean weight loss at 48 weeks in phase 2 obesity studies, a steeper trajectory, with glucagon receptor activation adding increased energy expenditure and hepatic fat oxidation that likely favors deeper visceral and hepatic fat depletion.[16] [17]

### Practical comparison

| Feature | Tirzepatide | Retatrutide |
|---|---|---|
| Receptor profile | GIP + GLP-1 dual agonist[27] | GIP + GLP-1 + glucagon triple agonist[17] |
| Max mean weight loss (trial) | ~22.5% at ~72 weeks[27] | ~24.2% at 48 weeks[16] |
| Visceral fat reduction (VAT) | ≈40% at ~72 weeks (MRI/DXA substudies)[18] [19] | 16–48% at 48 weeks (dose-dependent MRI)[17] |
| Liver fat normalization | High, many reach <5% liver fat[23] | ≥80–90% reach <5% liver fat at higher doses[17] |
| Mechanistic tilt | Strong appetite/insulin effects[27] | Appetite + increased fat oxidation/EE via glucagon[17] |
| Stage of development | Approved for T2D and obesity[27] | Phase 2 complete, further trials ongoing[21] [17] |

Net: both agents substantially deplete visceral and hepatic fat, but the current data suggest retatrutide's triple-agonist profile may deliver faster and somewhat deeper reductions in these ectopic depots, at the cost of still-emerging long-term safety and tolerability data.[21] [16] [17]

⁂

# Tirzepatide vs Retatrutide compare liver fat effect

Retatrutide produces larger and faster reductions in liver fat than tirzepatide, with more patients reaching complete or near-complete resolution of steatosis, though they have not been compared head-to-head.[36] [37]

### Tirzepatide: liver fat effects

- In the SURPASS-3 MRI substudy (type 2 diabetes, 52 weeks), tirzepatide 10–15 mg reduced liver fat content by about 8 percentage points from a baseline near 16%, corresponding to roughly a 47–55% relative reduction, versus ~3 percentage points with insulin degludec.[38] [39] [40]
- Many participants achieved normalization of liver fat (MRI-PDFF <5%), and improvements in MRI-cT1 suggested reduced hepatic inflammation/fibrosis risk.[41] [40]

### Retatrutide: liver fat effects

- In the 48-week phase 2 obesity study with a MASLD substudy, retatrutide achieved relative liver fat reductions of ≥30% in 71–100% of participants at 24 weeks, versus 4% with placebo.[37] [36]
- With 8 and 12 mg doses, 79–86% of participants had liver fat <5% at week 24, rising to 89–93% by week 48; mean relative liver fat reduction reached about 86% at 12 mg, one of the largest effects reported in MASLD/MASH trials.[36] [37]

### Direct comparison: what we can and cannot say

- Cross-trial, retatrutide's average relative liver fat reduction (~80–86% at 48 weeks) and very high normalization rates (>85%) appear greater than those reported for tirzepatide (~47–55% relative reduction, more modest but still substantial normalization rates).[40] [37] [36]
- However, populations and designs differ (obesity with MASLD vs type 2 diabetes cohorts, different baselines and time points), so we cannot claim definitive superiority without a head-to-head trial; best interpretation is that both are **very** effective for fatty liver, with current evidence favoring deeper and faster liver-fat clearance with retatrutide.[39] [37] [36]

### Mechanistic nuance

- Tirzepatide (GIP/GLP-1) reduces hepatic fat mainly via potent weight loss, improved insulin sensitivity, and reduced de novo lipogenesis.[38] [40]
- Retatrutide adds glucagon receptor agonism (GIP/GLP-1/GCG), which increases energy expenditure and directly promotes hepatic fatty acid oxidation, likely explaining the extra liver-fat lowering beyond what weight loss alone would predict.[37] [36]

If you share your situation (diabetes vs just fatty liver, BMI, other meds), I can translate these numbers into more personalized expectations and pros/cons for each agent.

⁂

# Clinical trials comparing tirzepatide retatrutide liver enzymes

There are no completed human clinical trials that directly compare tirzepatide vs retatrutide head-to-head for liver enzymes yet; available data come from separate trials plus one planned outcomes study.[52] [53]

### Tirzepatide trials: ALT/AST

- In SURPASS-3 MRI (type 2 diabetes, 52 weeks), tirzepatide significantly reduced liver fat and improved ALT and AST compared with insulin degludec; participants who normalized liver fat tended to show greater enzyme improvements.[54] [55] [56]
- Summaries of this substudy report clinically meaningful drops in ALT (on the order of 20–30% from baseline) and smaller but favorable changes in AST, consistent with reduced

steatosis and inflammation.[57] [56]

### Retatrutide trials: ALT/AST

- In the phase 2 obesity/MASLD substudy, retatrutide produced very large reductions in MRI-measured liver fat, but ALT and AST changes were modest and not consistently different from placebo across all doses.[58] [52]
- AASLD 2025 data note that while >85% of subjects on 8–12 mg had steatosis resolution by liver fat criteria, ALT and AST "did not change consistently versus placebo," suggesting discordance between liver fat and enzyme shifts in the short–medium term.[58]

### Comparative interpretation

- Cross-trial, tirzepatide shows clearer, more consistent ALT/AST improvements parallel to liver-fat reduction in diabetes cohorts, whereas retatrutide shows much larger liver-fat reductions but relatively flat average ALT/AST vs placebo so far.[56] [52] [58]
- A master protocol (SYNERGY-OUTCOMES, NCT07165028) is planned to evaluate both agents in high-risk MASLD and will track liver outcomes and lab measures, but it is not a classic randomized head-to-head ALT/AST comparison between the two drugs.[53] [59]

### Key takeaways for liver enzymes

- Tirzepatide: proven liver-fat reduction plus consistent ALT/AST improvement in SURPASS-3 MRI and related analyses.[55] [57] [56]
- Retatrutide: extremely strong liver-fat clearance with high steatosis resolution rates, but current human trial reports show ALT/AST changes that are variable and not reliably superior to placebo, despite improved fat and metabolic markers.[52] [58]

If you tell me your current ALT, AST, and whether you have confirmed MASLD/MASH, I can suggest which pattern (stronger enzyme response vs deeper fat clearance) might align better with your goals.

⁂

# compare effects on brown and beige fat

Evidence for both drugs on **brown** and **beige** fat is mostly preclinical or from ongoing trials, and there are no head-to-head human data yet.[67] [68]

### Tirzepatide

- In obese mice, tirzepatide increased thermogenesis in brown and beige adipose tissue, with higher UCP1 expression and enhanced fat utilization, indicating activation of thermogenic fat depots.[69] [70]
- A dedicated human trial (TABFAT, NCT06893211) is now testing tirzepatide's effect on brown fat activity and beige fat markers (UCP1 and other browning genes in subcutaneous

fat) over 24 weeks using PET/CT, MRI, and biopsy; results are pending, so human proof of BAT/beige activation is not yet established.[71] [72] [67]

### Retatrutide

- Retatrutide's glucagon agonism is expected to raise energy expenditure and thermogenesis, and animal data on glucagon show stimulation of brown fat activity, but human retatrutide studies have mainly focused on weight, liver fat, and metabolic markers rather than direct BAT/beige readouts.[68] [73]
- Reviews emphasize that while glucagon can activate brown fat in animals, human experiments so far show only modest increases in energy expenditure that have not clearly translated into large, measured BAT activation in clinical settings.[73] [68]

### Comparative view

- Tirzepatide: direct preclinical evidence of brown and beige fat activation plus an active human imaging/biopsy trial specifically designed to quantify these effects.[70] [67] [69]
- Retatrutide: stronger theoretical and animal-based rationale for thermogenesis via glucagon, but no published human data yet that directly measure BAT volume/activity or beige markers for this drug.[68] [73]

So right now, tirzepatide has **more targeted mechanistic data** on brown/beige fat (especially in mice and via the TABFAT trial design), whereas retatrutide likely enhances thermogenesis indirectly through glucagon signaling but lacks equally direct human BAT/beige measurements in published trials.

⁂


1. https://pmc.ncbi.nlm.nih.gov/articles/PMC11965027/
2. https://pubmed.ncbi.nlm.nih.gov/38528819/
3. https://www.sciencedirect.com/science/article/pii/S0003426624000763
4. https://www.thecardiologyadvisor.com/news/tirzepatide-significantly-reduces-fat-mass-preserves-lean-mass/
5. https://www.diva-portal.org/smash/get/diva2:1849827/FULLTEXT01.pdf
6. https://www.worldgastroenterology.org/publications/news-you-can-use/tirzepatide-shows-potential-to-improve-fatty-liver-associated-fibrosis-in-diabetes-insights-from-the-surpass-3-mri-substudy
7. https://pubmed.ncbi.nlm.nih.gov/39996356/
8. https://www.thelancet.com/journals/landia/article/PIIS2213-8587(25)00027-0/fulltext
9. https://pmc.ncbi.nlm.nih.gov/articles/PMC10861994/
10. https://www.cardiomenderweightloss.com/blog/does-tirzepatide-burn-fat/
11. https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2023.1230206/full
12. https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.15566
13. https://diabetesjournals.org/diabetes/article-xml/72/Supplement_1/758-P/149195
14. https://www.sciencedirect.com/science/article/pii/S0753332226000892
15. https://dom-pubs.onlinelibrary.wiley.com/doi/abs/10.1111/dom.15566

16. https://pubmed.ncbi.nlm.nih.gov/37366315/
17. https://pmc.ncbi.nlm.nih.gov/articles/PMC11271400/
18. https://pmc.ncbi.nlm.nih.gov/articles/PMC11965027/
19. https://www.sciencedirect.com/science/article/pii/S0003426624000763
20. https://pmc.ncbi.nlm.nih.gov/articles/PMC12456317/
21. https://pmc.ncbi.nlm.nih.gov/articles/PMC12190491/
22. https://welllifemedctr.com/tirzepatide-or-retatrutide-which-glp-1-medication-is-more-effective-for-obesity-and-diabetes/
23. https://www.worldgastroenterology.org/publications/news-you-can-use/tirzepatide-shows-potential-to-improve-fatty-liver-associated-fibrosis-in-diabetes-insights-from-the-surpass-3-mri-substudy
24. https://pubmed.ncbi.nlm.nih.gov/40609566/
25. https://www.thelancet.com/journals/landia/article/PIIS2213-8587(25)00092-0/abstract
26. https://pubmed.ncbi.nlm.nih.gov/39996356/
27. https://pmc.ncbi.nlm.nih.gov/articles/PMC10861994/
28. https://academic.oup.com/ndt/advance-article/doi/10.1093/ndt/gfaf230/8305911
29. https://amramedical.com/knowledge-hub/revealing-the-true-impact-of-drug-therapies-for-metabolic-diseases-through-weight-invariant-fat-distribution-assessment-using-amras-z-scores/
30. https://www.linkedin.com/posts/drkhizerjunaidy_obesity-diabesity-retatrutide-activity-7405449032904540160-HUwx
31. https://revolutionhealth.org/blogs/news/retatrutide-vs-tirzepatide-for-weight-loss-and-metabolic-health
32. https://www.sciencedirect.com/science/article/pii/S2667368125000646
33. https://www.tydewellness.com/learn/tirzepatide-vs-retatrutide-comparing-weight-loss-efficacy-and-safety/
34. https://revolutionhealth.org/blogs/news/visceral-fat-health-risks-treatment-retatrutide-mots-c
35. https://pmc.ncbi.nlm.nih.gov/articles/PMC11420505/
36. https://www.nature.com/articles/s41591-024-03018-2
37. https://pmc.ncbi.nlm.nih.gov/articles/PMC11271400/
38. https://www.thelancet.com/journals/landia/article/PIIS2213-8587(22)00070-5/abstract
39. https://www.sciencedirect.com/science/article/abs/pii/S2213858722000705
40. https://www.worldgastroenterology.org/publications/news-you-can-use/tirzepatide-shows-potential-to-improve-fatty-liver-associated-fibrosis-in-diabetes-insights-from-the-surpass-3-mri-substudy
41. https://diabetesjournals.org/diabetes/article/72/Supplement_1/758-P/149195/758-P-Changes-in-Liver-and-Abdominal-Fat-in
42. https://diabetesonthenet.com/wp-content/uploads/Distilled-1_SURPASS3-MRI.pdf
43. https://revolutionhealth.org/blogs/news/retatrutide-vs-tirzepatide-for-weight-loss-and-metabolic-health
44. https://awakeniv.com/retatrutide-vs-tirzepatide/
45. https://www.prnewswire.com/news-releases/lillys-tirzepatide-led-to-greater-improvements-in-liver-fat-content-compared-to-insulin-degludec-in-adults-with-type-2-diabetes-in-surpass-3-mri-sub-study-301388229.html

46. https://www.aasld.org/the-liver-meeting/triple-hormone-receptor-agonist-retatrutide-resolves-steatosis-85-subjects-masld
47. https://everestregenerative.com/motherhood-is-a-transformative-experience-bringing-immens/
48. https://fattyliver.ca/blog/f/the-year-everything-changed-for-masld-and-mash
49. what-are-the-synergies-between-zNUin5TlRjCz_0izjvNEng.md
50. https://pubmed.ncbi.nlm.nih.gov/35468325/
51. https://www.sciencedirect.com/science/article/pii/S2213858722000705
52. https://pmc.ncbi.nlm.nih.gov/articles/PMC11271400/
53. https://clinicaltrials.gov/study/NCT07165028
54. https://www.sciencedirect.com/science/article/abs/pii/S2213858722000705
55. https://diabetesjournals.org/diabetes/article/72/Supplement_1/758-P/149195/758-P-Changes-in-Liver-and-Abdominal-Fat-in
56. https://pubmed.ncbi.nlm.nih.gov/35468325/
57. https://medical.lilly.com/us/products/answers/what-were-the-effects-of-mounjaro-tirzepatide-on-the-liver-abdominal-adipose-tissue-and-muscle-fat-content-in-the-surpass-3-mri-substudy-151659
58. https://www.aasld.org/the-liver-meeting/triple-hormone-receptor-agonist-retatrutide-resolves-steatosis-85-subjects-masld
59. https://www.clinicaltrials.gov/study/NCT07165028
60. https://pubmed.ncbi.nlm.nih.gov/39212900/
61. https://www.sciencedirect.com/science/article/pii/S1525001625002989
62. https://revolutionhealth.org/blogs/news/retatrutide-vs-tirzepatide-for-weight-loss-and-metabolic-health
63. https://www.patientcareonline.com/view/study-novel-triagonist-retatrutide-resolved-steatosis-in-over-85-of-patients-with-masld-and-obesity
64. https://instalab.com/answers/retatrutide-vs-tirzepatide
65. https://pubmed.ncbi.nlm.nih.gov/38858523/
66. https://www.xiahepublishing.com/m/2310-8819/JCTH-2024-00123
67. https://pmc.ncbi.nlm.nih.gov/articles/PMC12374325/
68. https://pmc.ncbi.nlm.nih.gov/articles/PMC12190491/
69. https://pmc.ncbi.nlm.nih.gov/articles/PMC9396640/
70. https://dom-pubs.onlinelibrary.wiley.com/doi/abs/10.1111/dom.16294
71. https://clinicaltrials.gov/study/NCT06893211
72. https://www.centerwatch.com/clinical-trials/listings/NCT06893211/effect-of-tirzepatide-on-brown-adipose-tissue-in-obesity
73. https://www.sciencedirect.com/science/article/pii/S0092867424006433
74. https://revolutionhealth.org/blogs/news/retatrutide-vs-tirzepatide-for-weight-loss-and-metabolic-health
75. https://pmc.ncbi.nlm.nih.gov/articles/PMC11271400/
76. https://academic.oup.com/jes/article/9/Supplement_1/bvaf149.169/8297754
77. https://www.nature.com/articles/s44324-025-00054-5

78. https://everestregenerative.com/motherhood-is-a-transformative-experience-bringing-immens/
79. https://www.clinicaltrials.gov/study/NCT06893211
80. https://www.sciencedirect.com/science/article/pii/S0753332226000892
81. https://pubmed.ncbi.nlm.nih.gov/40847412/