

CBL-514: Is visceral fat reduction the real story?

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GLP-1 drugs shrink fat by changing appetite, and many patients regain it when treatment stops. CBL-514 takes a different route, an injection that makes fat cells themselves die, and new MRI data presented at EASD 2026 suggest it also reduces the deep visceral fat that drives metabolic risk.^{1,3}

KEY TAKEAWAYS

- **The Pivot:** CBL-514 is an injection that triggers fat cell death, and MRI data now show it reduces visceral fat as well as the subcutaneous fat measured in earlier trials.
- **The Data:** Visceral adipose tissue volume fell 12.01% with CBL-514 and rose 5.68% with placebo at 4 weeks after the last treatment, and was 10.45% lower versus 11.76% higher at 8 to 12 weeks, in 40 people.
- **The Action:** Treat this as an early signal from a small developer-run subgroup, since the weight regain claim is from rats and no metabolic benefit has been shown in humans.

CBL-514 selectively induces apoptosis, or programmed cell death, in adipocytes while leaving other cell types untouched. The idea is that fewer fat cells means less capacity to store fat again. Its developer, Caliway Biopharmaceuticals, has so far tested it as an injection into the lower abdomen, and the previously published phase 2 work measured subcutaneous fat, the layer beneath the skin that can be pinched.^{2,3}

In that earlier phase 2 trial, 69.6% of treated participants achieved a reduction of at least 150 mL in subcutaneous adipose tissue volume at the 8-week follow-up, compared with 0% of those given placebo. What was missing was evidence in humans on visceral adipose tissue (VAT), the fat wrapped around the internal organs that is highly metabolically active and a key driver of insulin resistance, type 2 diabetes, heart attack and stroke.^{2,3}

The Numbers

The new analysis used a subgroup of participants from 2 phase 2 trials, CBL-0204 and CBL-0205, who had MRI data. Baseline VAT included 41 participants, 23 on CBL-514 and 18 on placebo, while 40 had follow-up data at 8 to 12 weeks, 23 on CBL-514 and 17 on placebo. Participants had a BMI of 22 to 30 kg/m² and received up to 600 mg of CBL-514 or placebo into the lower abdomen every 3 weeks for up to 12 weeks, with the number of injections reduced as fat thickness fell.^{1,3}

Baseline VAT volume was similar between groups, at 563.85 mL with CBL-514 and 659.81 mL with placebo. Four weeks after the last treatment, mean VAT volume had fallen 12.01% from baseline with CBL-514 and risen 5.68% with placebo, a between-group difference of 17.69 percentage points. At the later follow-up, 8 weeks after the last treatment

in CBL-0205 and 12 weeks in CBL-0204, VAT was 10.45% below baseline with CBL-514 and 11.76% above baseline with placebo, a difference of 22.21 percentage points.^{1,3}

The placebo rise is part of the story. Visceral fat in the placebo group grew over the same weeks in which the treated group's shrank, so between a third and a half of the between-group gap comes from placebo drift rather than from loss in treated participants. The authors report the between-group figures as the headline, which is the fair comparison, but a reader looking for how much visceral fat a treated patient loses should use the 10% to 12% figure, not 22%.¹

Safety was described as generally good. Apart from mostly mild-to-moderate, transient injection-site reactions such as pain, swelling and redness, CBL-514 was well tolerated, and no serious adverse events were reported. The sex split of the VAT subgroup was uneven, at 74% female with CBL-514 and 56% female with placebo, which is worth remembering when a 23-person group is asked to represent a general population.^{1,3}

What the Data Can and Cannot Support

The claim that CBL-514 helps limit weight regain after stopping a GLP-1 receptor agonist rests on animal data. In rats, the combination with tirzepatide produced more weight loss than tirzepatide alone, and rats given both regained less weight after tirzepatide was stopped. That result was presented at the American Diabetes Association's 2026 annual meeting, and the authors say directly that research is needed in humans to prove it. The human data presented here involve no GLP-1 drug at all.^{1,3}

The trial population also limits what can be inferred. Participants had a BMI of 22 to 30 kg/m², so most were lean or overweight rather than living with obesity, and the phase 3 programme is designed to evaluate nonsurgical abdominal fat reduction, an endpoint with a large cosmetic component. No metabolic outcome, such as blood pressure, lipids or glycaemia, has been reported as improving with the VAT loss, and Professor Garvey himself frames those improvements as what should follow, not what has been shown.^{1,3}

Sample size and duration matter as well. The analysis covers 40 people, followed for 8 to 12 weeks after the final injection, in a subgroup defined by MRI availability. There is no full paper, and the abstract has not been submitted to a journal. Ling and 2 co-authors are employees of Caliva, and Ling holds company stock, while Professor Garvey and another declared author report advisory relationships with the company among many others.^{1,3}

Professor Garvey describes it as "a highly innovative approach to obesity pharmacotherapy that has produced some remarkable results in early human trials," and notes that liposuction and abdominoplasty address only subcutaneous fat and are more invasive. Recruitment for the first of 2 randomised, placebo-controlled phase 3 trials is under way, with first results expected at the end of next year. Those trials, not this subgroup, will show whether visceral fat loss translates into any clinical benefit.³

CLINICAL IMPLICATIONS

The reassuring parts of this result are the direction and the safety profile. Visceral fat fell in the treated group and rose in the placebo group, and no serious adverse events were reported,. If phase 3 confirms it, a locally injected drug that removes visceral fat cells would be a genuinely new mechanism in the field.

What clinicians should hold back on is the link to weight maintenance after GLP-1 therapy. That idea comes from a rat study, and the human trials so far enrolled mostly people in the BMI 22 to 30 range without any GLP-1 drug on board. Patients who ask about a fat-cell injection as a way to keep weight off after stopping semaglutide or tirzepatide should be told it is unproven.

The registration endpoint is also worth noting. Phase 3 is testing nonsurgical abdominal fat reduction, so a positive result may lead to a cosmetic indication first. Whether visceral fat loss of about 10% translates into lower blood pressure, better glycaemia or fewer cardiovascular events is a separate question that needs its own trial.

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REFERENCES

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