Retatrutide and knee osteoarthritis: Trial results are not treatment approval

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Prelims: GLP-1, GIP, glucagon, clinical trials; Mains: GS-III biotechnology, GS-II health



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Why in the news

Published findings from two phase 3 retatrutide trials showed greater pain reductions than placebo in participants with painful knee osteoarthritis and obesity. TRIUMPH-4 also reported greater body-weight reduction. Retatrutide remains investigational in the sources reviewed. Positive trial results should not be described as regulatory approval, a treatment suitable for everyone, or a permanent cure.

What makes it different

Retatrutide is an agonist of three receptors: GIP, GLP-1 and glucagon. Calling it only a GLP-1 medicine gives an incomplete description. It was administered as a once-weekly injection under the skin. Drugs discussed in a broad category do not automatically share doses, indications or safety profiles.

Who was studied

TRIUMPH-4 and TRIUMPH-1-OA enrolled adults without diabetes who had painful knee osteoarthritis and a BMI of at least 27. They randomized 445 and 574 participants respectively. Results were assessed at week 68 in the first trial and week 80 in the second. Findings cannot therefore be applied directly to children, every painful joint or every form of arthritis.

Reading the results correctly

Both trials found greater improvements in WOMAC pain scores than placebo. The published abstract also reports body-weight results for TRIUMPH-4. A lower WOMAC pain score indicates improvement in reported pain; it does not by itself demonstrate cartilage regeneration. Interpretation requires attention to the selected population, duration, comparison group and statistical methods.

Safety and limitations

The published abstract reports that serious adverse events were more common with retatrutide than placebo, while the most common adverse events were gastrointestinal. Benefits and risks must be read together. Eli Lilly funded the studies. Funding disclosure supports transparency, but funding alone is not a reason either to accept or reject the findings.

This is educational information, not advice to buy the drug, self-medicate or change existing treatment.

Prelims practice question

Consider the following statements:

Statement-I: Retatrutide is an investigational agonist of GIP, GLP-1 and glucagon receptors.

Statement-II: Improvement in a pain score automatically proves cartilage regrowth and a permanent cure.

Choose the correct option:

(a) Both Statement-I and Statement-II are correct and Statement-II is the correct explanation for Statement-I

(b) Both Statement-I and Statement-II are correct, but Statement-II is not the correct explanation for Statement-I

(c) Statement-I is correct, but Statement-II is incorrect

(d) Statement-I is incorrect, but Statement-II is correct

▼ **Answer and explanation**

Correct answer: **(c)**. A clinical pain outcome and structural repair are different claims.

Sources

https://www.nejm.org/doi/full/10.1056/NEJMoa2610676
https://investor.lilly.com/news-releases/news-release-details/lilly-showcase-new-retatrutide-taltz-ixekizumab-and-zepbound

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Frequently asked questions

Which receptors does retatrutide act on, and how is it administered?

Retatrutide is an agonist of three receptors, GIP, GLP-1 and glucagon, so calling it only a GLP-1 medicine is incomplete. In the trials it was given as a once-weekly injection under the skin. Source (https://www.nejm.org/doi/full/10.1056/NEJMoa2610676)

Who was enrolled in TRIUMPH-4 and TRIUMPH-1-OA, and when were results assessed?

Both enrolled adults without diabetes who had painful knee osteoarthritis and a BMI of at least 27, randomising 445 and 574 participants respectively. Results were assessed at week 68 in the first trial and week 80 in the second. Source (https://www.nejm.org/doi/full/10.1056/NEJMoa2610676)

What did the trials find on safety, and who funded the studies?

The published abstract reports gastrointestinal events as the most common adverse events, with serious adverse events more frequent with retatrutide than placebo. The studies were funded by the manufacturer Eli Lilly, and the drug remains investigational without regulatory approval. Source (https://investor.lilly.com/news-releases/news-release-details/lilly-showcase-new-retatrutide-taltz-ixekizumab-and-zepbound)

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