Mounjaro: Is a dual agonist the new standard for CV protection?

Written by The Life Science Feed Editorial Team · Published 8 September 2026 · Edited by William Lopes

For years, clinicians have relied on GLP-1 receptor agonists to mitigate cardiovascular risk in patients with type 2 diabetes. But the emergence of dual GIP/GLP-1 receptor agonists like tirzepatide has raised questions about their comparative efficacy and whether they offer a distinct advantage. Now, Mounjaro has secured an expanded indication, confirming its role in cardiovascular event reduction.

KEY TAKEAWAYS

- The Pivot: Mounjaro (tirzepatide) now holds an indication for reducing major adverse cardiovascular events (MACE) in adults with type 2 diabetes.
- The Data: Tirzepatide significantly reduced MACE by 20% compared to placebo (HR 0.80; 95% CI, 0.71-0.90; P=.0004) in the SURPASS-CVOT trial.
- The Action: Clinicians should consider tirzepatide for type 2 diabetes patients who require both glycaemic control and cardiovascular risk reduction, particularly those with established cardiovascular disease or multiple risk factors.

Type 2 diabetes carries a substantial burden of cardiovascular disease, making therapies that address both glycaemic control and cardiovascular outcomes highly desirable. GLP-1 receptor agonists (GLP-1RAs) have become a cornerstone of treatment, demonstrating clear benefits in reducing major adverse cardiovascular events (MACE). But the arrival of tirzepatide, a dual GIP/GLP-1 receptor agonist, introduced a new contender into this therapeutic space.1

The SURPASS-CVOT trial, a study that aimed to determine if tirzepatide offered superior cardiovascular protection compared to placebo, evaluated tirzepatide's impact on cardiovascular outcomes. This trial enrolled patients with type 2 diabetes who had established cardiovascular disease or were at high risk for it. The primary endpoint was a composite of MACE, defined as cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. The trial aimed to determine if tirzepatide offered superior cardiovascular protection compared to placebo when added to standard care.1

The Cardiovascular Numbers

Tirzepatide significantly reduced the risk of MACE by 20% compared to placebo (HR 0.80; 95% CI, 0.71-0.90; P=.0004). This primary outcome included a reduction in cardiovascular death by 15% (HR 0.85; 95% CI, 0.72-1.00; P=.051) and non-fatal myocardial infarction by 32% (HR 0.68; 95% CI, 0.55-0.83; P18% (HR 0.82; 95% CI, 0.62-1.08; P=.16). These results confirm tirzepatide's efficacy in mitigating serious cardiovascular events in this high-risk population.1

A systematic review and network meta-analysis by Shokravi, Seth, and Mancini, published in Cardiovascular Diabetology, further explored tirzepatide's comparative efficacy.1 The analysis included data from SURPASS-CVOT

alongside trials of other GLP-1RAs. It concluded that tirzepatide demonstrated comparable cardiovascular benefits to existing GLP-1RAs, reinforcing its position as a viable option for cardiovascular risk reduction. This aligns with the broader understanding of how these incretin-based therapies influence cardiovascular health, a topic we have covered previously regarding GLP-1 receptor agonist use in youth with type 2 diabetes.

The safety profile of tirzepatide in SURPASS-CVOT was consistent with previous trials, primarily involving gastrointestinal adverse events such as nausea, vomiting, and diarrhoea. These events were generally mild to moderate and transient, leading to discontinuation rates similar to those observed with other GLP-1RAs. No new safety signals emerged from the cardiovascular outcomes trial. The drug's dual mechanism, targeting both GIP and GLP-1 receptors, offers a distinct pharmacological approach that appears to translate into robust clinical benefits without introducing unforeseen risks. For a deeper dive into the mechanisms and management of diabetes, the Oxford Handbook of Endocrinology and Diabetes provides a practical reference.

Still, the network meta-analysis highlighted that while tirzepatide's cardiovascular benefits are clear, its comparative effect against individual GLP-1RAs requires further direct head-to-head trials for definitive conclusions. The current evidence primarily establishes non-inferiority or comparable efficacy, rather than outright superiority over all existing GLP-1RAs for cardiovascular outcomes. This nuance is important for clinicians weighing treatment options, especially as the field continues to evolve with new therapies like mazdutide's dual agonism.

The trial was not powered to detect differences in specific subgroups, such as patients with different baseline eGFR levels or varying degrees of established atherosclerotic cardiovascular disease. That gap matters for precision medicine. While the overall benefit is clear, whether certain patient profiles derive disproportionately greater or lesser benefit remains an area for future investigation. This is a common challenge in large-scale CVOTs, where broad inclusion criteria ensure generalisability but can obscure subgroup-specific effects.

The approval of Mounjaro for cardiovascular event reduction solidifies its position as a comprehensive therapy for type 2 diabetes. It offers clinicians another powerful tool to manage not just glycaemia, but also the life-threatening cardiovascular complications that often accompany the disease. The next step will be to see how these findings influence guideline recommendations and real-world prescribing patterns, particularly in comparison to established GLP-1RAs that also carry strong cardiovascular indications.

CLINICAL IMPLICATIONS

The expanded indication for Mounjaro to reduce cardiovascular events in type 2 diabetes patients is not merely incremental; it confirms a dual agonist's place in the pantheon of cardioprotective diabetes therapies. Clinicians now have another robust option for patients who need more than just glycaemic control, particularly those with existing cardiovascular disease or multiple risk factors. This moves tirzepatide beyond a purely metabolic agent into a critical role in cardiovascular prevention.

The comparative efficacy data, while not always demonstrating outright superiority over every individual GLP-1RA, certainly positions tirzepatide as a strong contender. Its dual mechanism offers a distinct pathway to benefit, and the consistent safety profile means prescribers can integrate it into their practice with confidence. This approval will undoubtedly influence treatment algorithms, pushing for earlier consideration of tirzepatide in patients at high cardiovascular risk.

> For the pharmaceutical industry, this approval strengthens Eli Lilly's position in the lucrative diabetes and cardiovascular market. It intensifies competition within the incretin class, particularly against other GLP-1RAs with established cardiovascular benefits. The pressure will now be on for head-to-head trials to truly differentiate these agents, moving beyond non-inferiority to demonstrate superior outcomes in specific patient populations.
>
> Patients with type 2 diabetes stand to gain significantly. Access to another effective therapy that reduces the risk of heart attack, stroke, and cardiovascular death offers tangible improvements in long-term prognosis. The challenge will be ensuring equitable access and managing the cost implications, which remain a barrier for many patients despite the clear clinical benefits.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. 1. Shokravi A, Seth J, Mancini GBJ. Comparative efficacy of tirzepatide and glucagon-like peptide-1 receptor agonists on cardiovascular outcomes in patients with type 2 diabetes: a systematic review and network meta-analysis. Cardiovasc Diabetol 2026;25(1):123. https://pubmed.ncbi.nlm.nih.gov/41761267/

LICENCE & RIGHTS

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.

FOLLOW THE LIFE SCIENCE FEED