NEWSLETTER 21

Tirzepatide Across the Cardiovascular Continuum

From HFpEF to cardiorenal protection with a dual GLP-1/GIP agonist

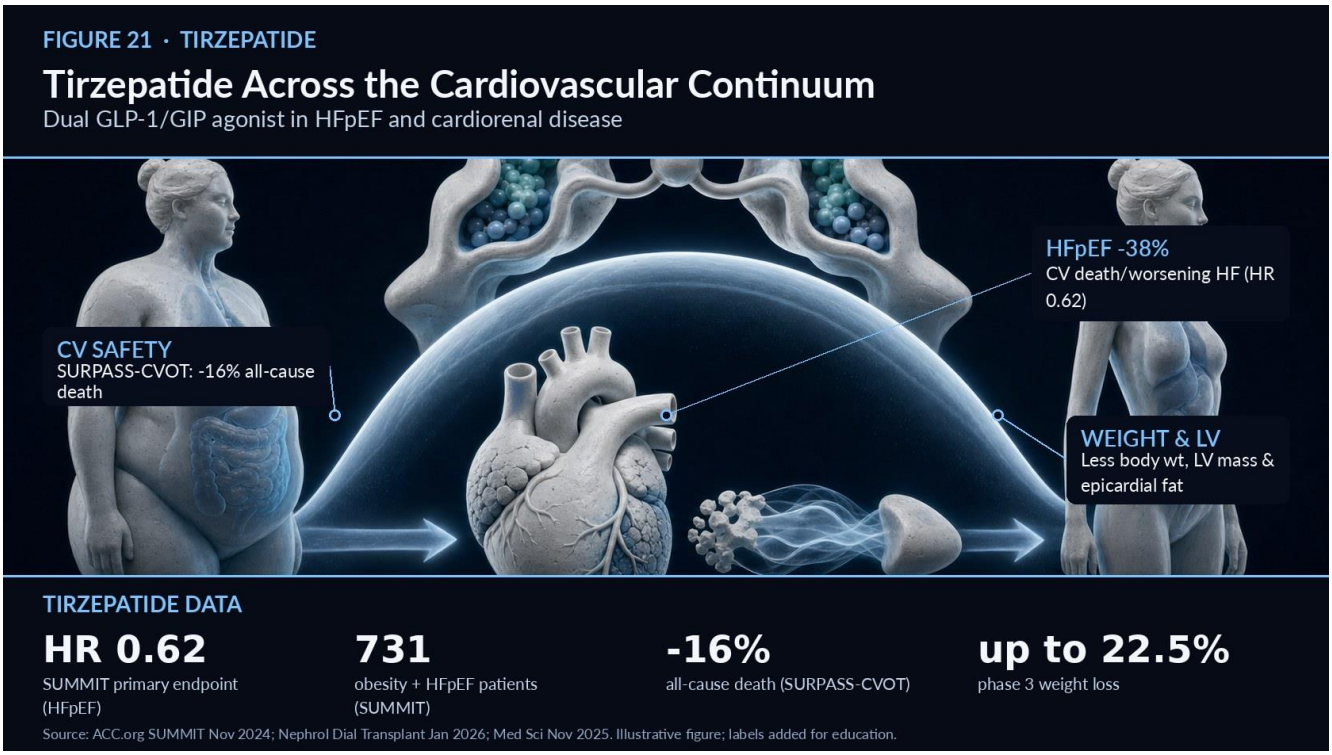

Figure 21. Tirzepatide Across the Cardiovascular Continuum — mechanism overview (illustrative; labels added for education).

Tirzepatide, a dual GLP-1/GIP receptor agonist, has generated some of the most striking recent cardiovascular data. The SUMMIT trial randomised 731 patients with obesity (BMI > 30) and HFpEF—364 to tirzepatide up to 15 mg weekly and 367 to placebo—across 129 centres in nine countries, with a median follow-up of about two years.[1]

The primary endpoint was met convincingly. Cardiovascular death or worsening heart-failure events occurred in 36 versus 56 patients (HR 0.62, 95% CI 0.41–0.95, P = 0.026), a 38% relative reduction in a phenotype—obesity-related HFpEF—with historically few effective therapies.[1]

Beyond events, tirzepatide improved symptoms and structure. It improved the Kansas City Cardiomyopathy Questionnaire clinical summary score and 6-minute walk distance at 52 weeks, produced 11.6% greater body-weight loss, and lowered high-sensitivity CRP; a *JACC* imaging substudy showed decreased LV mass (−11 g) and paracardiac adipose tissue (−45 mL).[1] These changes suggest genuine reverse remodelling, not merely symptomatic relief.

Cardiovascular safety and mortality data are reassuring. SURPASS-CVOT confirmed tirzepatide's cardiovascular safety, with MACE-3 non-inferior to dulaglutide (HR 0.92) and a 16% reduction in all-cause mortality (HR 0.84, 95% CI 0.75–0.94).[3]

The imaging substudy is what elevates SUMMIT beyond a symptom trial. Reductions in left-ventricular mass and paracardiac adipose tissue suggest tirzepatide reverses some of the cardiac remodelling that drives obesity-

related HFpEF, rather than merely easing symptoms.[1] Coupled with SURPASS-CVOT's confirmation of cardiovascular safety and a 16% all-cause mortality reduction, the data position the dual GLP-1/GIP agonist as a disease-modifying option in a heart-failure phenotype that has long lacked effective therapies.[3]

The metabolic potency is central to its cardiorenal promise: tirzepatide achieves up to 22.5% weight loss in phase 3 trials, with cardiorenal implications across the CKM spectrum.[2] The 2026 CKM guideline accordingly recommends adding GLP-1-based therapies—a class that includes dual agonists like tirzepatide—in HFmrEF/HFpEF patients with obesity or other CKM risk factors.[5] For clinicians treating the growing population of patients with obesity-driven heart failure and metabolic disease, tirzepatide represents a therapy that simultaneously addresses weight, symptoms, and hard cardiovascular outcomes.

References

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