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Efficacy and Safety of Tirzepatide Versus Semaglutide in a Hispanic or Latino Population: A Prespecified Subgroup Analysis of SURPASS-2

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Tirzepatide, a dual GIP/GLP-1 receptor agonist, demonstrated clinically meaningful reductions in HbA1c and body weight that were significantly greater compared with semaglutide in patients with type 2 diabetes on background metformin. In a pre-specified subgroup analysis, we evaluated the efficacy and safety of tirzepatide in the Hispanic or Latino population of SURPASS-2.

In this open-label, 40-week, Phase 3 study (N=1878; mean baseline HbA1c 8.28%; BMI 34.2 kg/m^2; Hispanic or Latino ethnicity 70%) participants were randomized 1: 1: 1: 1 to tirzepatide (5, 10, 15 mg; doses were double-blinded) or semaglutide (1 mg). Efficacy analyses included all randomised patients who received ≥1 treatment dose (modified intention-to-treat [mITT] population) while patients were on treatment without rescue therapy and excluding patients who discontinued study drug due to inadvertent enrollment (efficacy estimand). Safety analyses were performed in the mITT population, including all data from the start of treatment to the end of the safety follow-up. The least square mean (LSM) change from baseline was calculated within each subgroup using a mixed model for repeated measurements (MMRM) with country, baseline value, treatment group, visit, and treatment-by-visit interaction as the fixed effect, and patient as the random effect. MMRM for weight change also included baseline HbA1c group (≤8.5%, >8.5%) as a covariate.

In patients of Hispanic or Latino ethnicity, the LSM change from baseline in HbA1c at 40 weeks was -2.11%, -2.46%, and -2.47% with tirzepatide 5, 10, and 15 mg, respectively, and -1.93% with semaglutide (all $p<0.001$). The respective changes in patients not of Hispanic or Latino ethnicity were

-2.03%, -2.14%, -2.43%, and -1.69% (all p<0.001). Reductions in HbA1c were significantly greater for all tirzepatide doses compared with semaglutide in patients of both Hispanic or Latino and non-Hispanic or Latino ethnicity (all p≤0.027). In Hispanic or Latino patients, body weight change was -6.9 kg with tirzepatide 5 mg, -9.7 kg with 10 mg, -10.5 kg with 15 mg, and -5.6 kg with semaglutide (all p<0.001). In non-Hispanic or Latino patients, the changes from baseline in body weight were -9.9 kg, -11.6 kg, -17.1 kg, and -7.5 kg, for the tirzepatide doses and semaglutide, respectively, (all p<0.001). In both subgroups, reductions in body weight were significantly greater than semaglutide with all tirzepatide doses (all p≤0.013).

The most common adverse events were gastrointestinal in the tirzepatide and semaglutide arms, including nausea (Hispanic or Latino 11-17% and 13%; non-Hispanic or Latino 32-36% and 29%), diarrhoea (10-13% and 10%; 15-24% and 17%) and vomiting (4-7% and 7%; 10-16% and 12%).

Consistent with the primary SURPASS-2 results, in a Hispanic or Latino population with type 2 diabetes, tirzepatide demonstrated greater reductions from baseline in HbA1c and body weight than the selective GLP-1 receptor agonist semaglutide, with a comparable safety profile.

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