

## 223-OR: Emulation of the Study of Tirzepatide Compared with Dulaglutide on Major Cardiovascular Events in Participants with Type 2 Diabetes (SURPASS-CVOT) FREE

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**Introduction and Objective:** SURPASS-CVOT is an ongoing, randomized, active-controlled trial evaluating the effect of tirzepatide vs. dulaglutide on major adverse cardiovascular events (MACE) in people with type 2 diabetes (T2D) and atherosclerotic cardiovascular disease (ASCVD). We aimed to emulate the SURPASS-CVOT trial using insurance claims data.

**Methods:** Using claims from a private health plan (06/2022 to 08/2024), we identified 15,775 pairs of 1:1 propensity score (PS)-matched adults initiating tirzepatide or dulaglutide, stratified by baseline SGLT2i use. Our primary outcome was MACE (myocardial infarction, stroke, or mortality). We estimated hazard ratios (HRs) and 95% confidence intervals (CI), adjusting for 125 covariates. We also conducted HbA<sub>1c</sub>-adjusted analyses among those with HbA<sub>1c</sub> values (54% of population).

**Results:** Over a median follow up of ~6 months, tirzepatide was associated with a 37% reduction in MACE vs. dulaglutide (**Table**). Results were consistent in the HbA<sub>1c</sub>-adjusted analysis (HR, 0.77; 95% CI, 0.62 to 0.95) and, in both analyses, irrespective of SGLT2i use.

**Conclusion:** In this observational study emulating SURPASS-CVOT, tirzepatide appeared superior to dulaglutide in preventing MACE events. This study may also inform the design and conduct of future observational studies evaluating GLP-1-based treatments.

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Table 1: Baseline characteristics and outcomes in the 1:1 propensity score matched population

| Patient characteristics, n (%)                           | Overall cohort                 |                                |                      | HbA <sub>1c</sub> -adjusted cohort* |                                |                      |
|----------------------------------------------------------|--------------------------------|--------------------------------|----------------------|-------------------------------------|--------------------------------|----------------------|
|                                                          | Tirzepatide<br>(N= 15,775)     | Dulaglutide<br>(N= 15,775)     | Abs Std diff†        | Tirzepatide<br>(N= 8,578)           | Dulaglutide<br>(N= 8,578)      | Abs Std diff†        |
| Age, years, mean (SD)                                    | 67.50 (8.99)                   | 67.52 (8.92)                   | 0.002                | 68.06 (8.55)                        | 68.19 (8.50)                   | 0.015                |
| Female                                                   | 8,052 (51.0%)                  | 8,077 (51.2%)                  | 0.004                | 4,385 (51.1%)                       | 4,380 (51.1%)                  | 0.000                |
| Race and ethnicity                                       |                                |                                |                      |                                     |                                |                      |
| Asian                                                    | 300 (1.9%)                     | 297 (1.9%)                     | 0.000                | 174 (2.0%)                          | 191 (2.2%)                     | 0.014                |
| Black                                                    | 2,159 (13.7%)                  | 2,200 (13.9%)                  | 0.006                | 1,140 (13.3%)                       | 1,161 (13.5%)                  | 0.006                |
| Hispanic                                                 | 2,140 (13.6%)                  | 2,174 (13.8%)                  | 0.006                | 1,286 (15.0%)                       | 1,295 (15.1%)                  | 0.003                |
| White                                                    | 9,574 (60.7%)                  | 9,526 (60.4%)                  | 0.006                | 5,320 (62.0%)                       | 5,319 (62.0%)                  | 0.000                |
| Medical history                                          |                                |                                |                      |                                     |                                |                      |
| Class I or II obesity (BMI 30-39.9 kg/m <sup>2</sup> )   | 4,627 (29.3%)                  | 4,593 (29.1%)                  | 0.004                | 2,646 (30.8%)                       | 2,601 (30.3%)                  | 0.011                |
| Class III obesity (BMI ≥40 kg/m <sup>2</sup> )           | 4,712 (29.9%)                  | 4,666 (29.6%)                  | 0.007                | 2,652 (30.9%)                       | 2,653 (30.9%)                  | 0.000                |
| Hypertension                                             | 14,106 (89.4%)                 | 14,086 (89.3%)                 | 0.003                | 7,786 (90.8%)                       | 7,782 (90.7%)                  | 0.003                |
| Diabetic retinopathy                                     | 1,698 (10.8%)                  | 1,724 (10.9%)                  | 0.003                | 945 (11.0%)                         | 935 (10.9%)                    | 0.003                |
| Diabetic neuropathy                                      | 5,610 (35.6%)                  | 5,620 (35.6%)                  | 0.000                | 3,189 (37.2%)                       | 3,141 (36.6%)                  | 0.012                |
| Diabetic nephropathy                                     | 4,293 (27.2%)                  | 4,309 (27.3%)                  | 0.002                | 2,550 (29.7%)                       | 2,545 (29.7%)                  | 0.000                |
| Myocardial infarction                                    | 1,580 (10.0%)                  | 1,598 (10.1%)                  | 0.003                | 833 (9.7%)                          | 872 (10.2%)                    | 0.013                |
| Heart failure                                            | 3,262 (20.7%)                  | 3,234 (20.5%)                  | 0.005                | 1,763 (20.6%)                       | 1,762 (20.5%)                  | 0.002                |
| Ischemic stroke                                          | 2,468 (15.6%)                  | 2,418 (15.3%)                  | 0.008                | 1,353 (15.8%)                       | 1,349 (15.7%)                  | 0.003                |
| Obstructive sleep apnea                                  | 4,886 (31.0%)                  | 4,743 (30.1%)                  | 0.020                | 2,728 (31.8%)                       | 2,677 (31.2%)                  | 0.013                |
| Number of glucose-lowering medications at CED, mean (SD) | 1.19 (0.84)                    | 1.18 (0.81)                    | 0.012                | 1.23 (0.84)                         | 1.24 (0.81)                    | 0.012                |
| Medications                                              |                                |                                |                      |                                     |                                |                      |
| Metformin                                                | 9,705 (61.5%)                  | 9,710 (61.6%)                  | 0.002                | 5,397 (62.9%)                       | 5,387 (62.8%)                  | 0.002                |
| Insulin                                                  | 5,423 (34.4%)                  | 5,381 (34.1%)                  | 0.006                | 2,745 (32.0%)                       | 2,794 (32.6%)                  | 0.013                |
| Beta blockers                                            | 8,442 (53.5%)                  | 8,373 (53.1%)                  | 0.008                | 4,573 (53.3%)                       | 4,604 (53.7%)                  | 0.008                |
| Antiplatelets                                            | 2,929 (18.6%)                  | 2,979 (18.9%)                  | 0.008                | 1,591 (18.5%)                       | 1,547 (18.0%)                  | 0.013                |
| Statins                                                  | 13,174 (83.5%)                 | 13,133 (83.3%)                 | 0.005                | 7,241 (84.4%)                       | 7,279 (84.9%)                  | 0.014                |
| HbA <sub>1c</sub> , %, mean (SD)                         | 7.71 (1.61)                    | 7.97 (1.65)                    | 0.159                | 7.58 (1.28)                         | 7.59 (1.25)                    | 0.008                |
| eGFR, mL/min/1.73 m <sup>2</sup> , mean (SD)             | 74.01 (21.67)                  | 73.74 (22.15)                  | 0.012                | 73.91 (21.51)                       | 73.55 (21.82)                  | 0.017                |
| Primary Analysis                                         | No. of Events<br>(IR/1,000 PY) | No. of Events<br>(IR/1,000 PY) | HR<br>(95% CI)       | No. of Events<br>(IR/1,000 PY)      | No. of Events<br>(IR/1,000 PY) | HR<br>(95% CI)       |
| Major adverse cardiovascular events‡                     | 275 (28.36)                    | 384 (45.87)                    | 0.63<br>(0.54, 0.73) | 163 (30.73)                         | 183 (40.05)                    | 0.77<br>(0.62, 0.95) |

Patient characteristics were measured during the 12 months prior (and including) treatment initiation date. HbA<sub>1c</sub> was available in 54% of individuals and eGFR was available in 56% of individuals.

\*Restricted to individuals with laboratory results available and adjusting by baseline HbA<sub>1c</sub> level via propensity score-matching.

†Values >0.1 indicate meaningful imbalance.

‡Myocardial infarction, stroke, or mortality

Abbreviations: Abs Std diff: absolute standard differences; BMI: body mass index; CED: cohort entry date; CI: confidence interval; eGFR: estimated glomerular filtration rate; HbA<sub>1c</sub>: glycated hemoglobin; HR: hazard ratio; IR: incidence rate; PY: person-years; SD: standard deviation

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Disclosure

J. Ostrominski: None. J. Ortega-Montiel: None. H. Tesfaye: None. C. Alix: None. D.J. Wexler: Other Relationship; Novo Nordisk. J.M. Paik: None. E. Patorno: Research Support; National Institute of Diabetes and Digestive and Kidney Diseases, Patient-Centered Outcomes Research Institute, Food and Drug Administration (FDA), Boehringer-Ingelheim. Other Relationship; UpToDate.

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