Patient-Reported Outcomes in Patients with Type 2 Diabetes Treated with Tirzepatide or Placebo (SURPASS-1)

Kristina Boye, Maria Yu, Clare J. Lee, Huzhang Mao, Xuewei Cui, Laura Fernández Landó, Vivian Thieu

Eli Lilly and Company, Indianapolis, USA
All authors are employees and shareholders of Eli Lilly and Company
Tirzepatide: Dual GIP/GLP-1 Receptor Agonist

Molecular Attributes

- Tirzepatide is a multi-functional peptide based on the native GIP peptide sequence, modified to bind to both GIP and GLP-1 receptors
- Tirzepatide is a 39 amino acid linear peptide and includes a C20 fatty diacid moiety
- *In vitro*, it has higher potency to native GIP and is less potent to native GLP-1
- Tirzepatide has a mean half-life of ~5 days, enabling once-weekly dosing


GIP=glucose-dependent insulintropic polypeptide; GLP-1 RAs=glucagon-like peptide-1 receptor agonists
SURPASS-1 Study

Key Inclusion Criteria
- T2D
- HbA1c ≥7.0% to ≤9.5% at screening
- BMI ≥23 kg/m^2 with stable weight
- Naïve to T2D injectable therapy

Key Exclusion Criteria
- T1D
- History of pancreatitis
- eGFR <30 mL/min/1.73 m^2
- Use of any oral antihyperglycemic medication in the 3 months prior to screening

Key Study Findings at 40 weeks\(^1\)
- Tirzepatide 5, 10, and 15 mg demonstrated superior and clinically meaningful HbA1c reduction versus placebo; 31-52% of patients achieved a HbA1c of <5.7%
- Tirzepatide 5, 10, and 15 mg demonstrated superior and clinically meaningful body weight loss versus placebo; 31-47% of patients achieved ≥10% weight loss
- Tirzepatide was well tolerated; the most common adverse events were gastrointestinal and mild to moderate in severity

\(^1\)Rosenstock J et al. 2021 [Abstract] ADA - 81st Annual Scientific Sessions. See related oral presentation 100-OR on Saturday June 26th 4:00pm
Objective
■ To evaluate the effect of tirzepatide treatment versus placebo in patient-reported outcomes measuring health status and health-related quality of life, self-perceptions impacted by body weight, and ability to perform activities of daily living in SURPASS-1

Outcomes
■ Patient-reported outcome measures were assessed at baseline and Week 40
  – EQ-5D-5L
  – Impact of Weight on Self-Perception Questionnaire (IW-SP)
  – Ability to Perform Physical Activities of Daily Living Questionnaire (APPADL)
■ Higher patient-reported outcome scores indicate better outcomes

Methods
■ Included patients randomized who received at least 1 dose of study drug (modified intent-to-treat [mITT] population)
■ Analyses conducted on the mITT efficacy analyses set which excluded patients who discontinued study drug due to inadvertent enrolment and excluded data after initiating rescue antihyperglycemic medication or prematurely stopping study drug
■ Change from baseline at 40 weeks was analysed using analysis of covariance with baseline value, country, baseline HbA1c group (≤8.5%, >8.5%) and prior use of oral antihyperglycemic medication (Yes, No) as independent variables. Last postbaseline observation was carried forward
EQ-5D-5L Index scores of each of the 3 tirzepatide groups significantly improved from baseline, indicating better overall health-related quality of life, with the greatest improvement seen with tirzepatide 15 mg.

- There was minimal change seen in the placebo group.

- There were no statistically significant differences on the mean change of the EQ-5D-5L Index score compared with placebo.
EQ VAS scores of each of the 3 tirzepatide groups significantly improved from baseline, indicating better overall health-related quality of life, with the greatest improvement seen with tirzepatide 15 mg.

There was minimal change seen in the placebo group.

Compared with placebo, all 3 doses of tirzepatide significantly improved the VAS scores.

**EQ visual analogue scale (EQ VAS) (Scale 0 – 100)**
- Measures records the patient’s health-related quality of life on a vertical visual analogue scale

ETD: LSM (95% CI). *p<.05 from baseline. †p<.05 vs placebo. n=number of patients with baseline and ≥1 postbaseline value. ETD=estimated treatment difference; LSM=least square means; PBO=placebo; SE=standard error; TZP=tirzepatide
IW-SP scores for each of the 3 tirzepatide groups and placebo significantly improved from baseline indicating better self-perception.

Compared with placebo, tirzepatide 10 mg and 15 mg significantly improved the total IW-SP scores. No significant differences were observed when tirzepatide 5 mg was compared with placebo.

IW-SP Questionnaire (Score 0 - 100)
- Measures patients' self-perception relating to their body weight
- Includes 3 items: feel unhappy with appearance due to weight; feel self-conscious in public due to weight; feel unhappy due to comparing weight with others

ETD: LSM (95% CI). *p<.05 from baseline. †p<.05 vs placebo. n=number of patients with baseline and ≥1 postbaseline value. ETD=estimated treatment difference; LSM=least square means; PBO=placebo; SE=standard error; TZP=tirzepatide
APPADL scores for the 3 tirzepatide groups significantly improved from baseline with the highest improvement seen with tirzepatide 15 mg, indicating better self-reported ability to perform physical activities of daily living.

- There was no significant change seen in the placebo group.
- However, tirzepatide had no statistically significant difference on the mean change in APPADL scores compared with placebo.

**APPADL Questionnaire (Score 0 - 100)**
- Measures self-reported ability to perform tasks of daily living
- Includes difficulty in 7 items: getting up from floor/ground; getting down to floor/ground; standing; climbing stairs; household chores/yard work; moderate physical activity; strenuous physical activity
Summary and Conclusion

- There was improvement in overall health and weight-related quality of life measures from baseline to Week 40 in the tirzepatide 5 mg, 10 mg, and 15 mg groups.

- In addition to clinically meaningful reductions in HbA1c and body weight, compared with placebo:
  - Improvements in EQ VAS indicate that patients’ overall assessment of their health improved with tirzepatide 5, 10, and 15 mg.
  - Improvements in IW-SP scores indicate that patients’ body weight-related self-perception improved with tirzepatide 10 mg and 15 mg.

- Limitations:
  - The patient-reported outcome instruments assessed overall health-related quality of life and the patient-associated impact related to weight loss. Additional quality of life concepts were not assessed.
  - More patients from the placebo arm than each of the tirzepatide arms had their postbaseline measurement on rescue therapy and thus were excluded from the analyses, which might have introduced bias.

- Conclusion: These patient-reported outcomes may help clinicians more fully understand patient perspectives regarding patients’ quality of life after starting tirzepatide treatment.