**Association of tirzepatide with kidney parameters in people with obesity and prediabetes from SURMOUNT-1 over 176 weeks**

**Aim**: Obesity and type 2 diabetes (T2D) lead to kidney damage and decline in function over time. Tirzepatide (TZP), has been associated with kidney protective effects in people with T2D and with improvements in estimated glomerular filtration rate (eGFR) and urine albumin-creatinine ratio (UACR) in people with obesity or overweight after 72 weeks of treatment. The current analysis aimed to determine if improvements in kidney parameters persist over 176 weeks of TZP treatment in people with obesity and prediabetes.

**Methods:** SURMOUNT-1 was a 72-week, randomized Phase 3 study to evaluate the effects of TZP (5 mg, 10 mg, 15 mg) versus placebo in participants with obesity (BMI≥30 kg/m2) or overweight (BMI≥27 kg/m2) with weight-related comorbidities (excluding T2D). In the current post-hoc analysis, participants with prediabetes at randomization underwent an additional 104-week treatment follow-up period. UACR and eGFR (CKD-EPI Creatinine-Cystatin Equation 2021) were assessed for TZP (pooled 5/10/15 mg; n=762) or placebo (n=270). Change from baseline to week 176 was analyzed using mixed models for repeated measures with on-treatment data.

**Results:** Baseline mean eGFR was 97.1±17.6 ml/min per 1.73m2 and median UACR was 7.0 mg/g (interquartile range 4.0 – 12.0 mg/g). A significantly smaller decline in eGFR was observed with pooled TZP (-1.6±0.5 ml/min per 1.73m2) compared to placebo (-5.5±1.0 ml/min per 1.73m2) after 176 weeks (estimated treatment difference (ETD) of 3.9 ml/min per 1.73m2, p<0.001). A greater percentage decrease in UACR was observed with pooled TZP (-15.8±2.9%) compared to placebo (-3.9±6.4%) after 176 weeks (ETD of -12.4%, p=0.078).

**Conclusion**: In SURMOUNT-1 participants with prediabetes, overweight or obesity, and preserved eGFR at baseline, use of TZP was associated with an attenuated decline of eGFR over 3 years with a nonsignificant trend toward UACR reduction.