**Tirzepatide in adults with type 1 diabetes: a phase 2 randomised controlled clinical trial**

**Background**

Overweight and obesity are prevalent in type 1 diabetes (T1D) and contribute to cardiovascular risk. Tirzepatide, a dual gastric inhibitory polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, has not been studied in T1D.

**Methods**

Adults with T1D were randomised 1:1 to weekly subcutaneous tirzepatide (2.5mg for 4 weeks, 5.0mg thereafter) or placebo for 12 weeks. The primary endpoint was change in body weight at 12 weeks.

**Results**

Twenty-two of 24 adults with T1D (mean±SD; 41±10 years, BMI 33.7±3.2 kg/m2, HbA1c 7.3±1.2%, total daily dose of insulin median 69.1 units/day [interquartile range 41.9 to 86.7 units/day], 42% female, 13 insulin pump, 11 multiple daily injection) completed the study. After 12 weeks, tirzepatide was associated with significant reductions in body weight vs placebo (mean difference -8.7 kg, 95% confidence interval [CI] -12.0 to -5.5 kg; p<0.0001), representing 8.8% weight loss. Reduction in fat mass was -7.2 kg [95% CI -10.5 to -3.9 kg] vs placebo; p=0.0002, whilst fat-free mass was -1.8 kg [95% CI -3.75 to +0.1 kg] vs placebo; p=0.06). Tirzepatide improved HbA1c (mean difference -0.35% [95% CI -0.7 to 0.0%] vs placebo; p=0.05) and total daily insulin dose (insulin dose -35.1% from baseline vs placebo, 95% CI -46.5 to -21.3%; p=0.0002). Overall energy intake was reduced (mean difference -429 kcal/d [95% CI -852 to -5 kcal/d] vs placebo; p=0.05). Energy expenditure assessed by indirect calorimetry, and self-reported physical activity level (International Physical Activity Questionnaire Short Form) did not change. There were significant adverse events in either group.

**Conclusion**

In the first randomised trial of tirzepatide in T1D, tirzepatide was associated with favourable changes in weight and marked insulin dose reductions. Studies are required to assess the mechanisms for rapid tirzepatide-driven metabolic impacts in T1D. ANZCTR, ACTRN12624000111572.