

Early worsening of diabetic retinopathy after initiation of tirzepatide in individuals with type 2 diabetes

Adam Buckley¹, Garry D Tan^{2,3}, Marta Gruszka-Goh⁴, Peter H Scanlon⁴, Imran Ansari¹, Sara Suliman¹

1 Imperial College London Diabetes Centre, Abu Dhabi, United Arab Emirates

2 OCDEM, Oxford University Hospitals NHS Foundation Trust

3 Oxford NIHR Biomedical Research Centre

4 Gloucestershire Hospitals NHS Foundation Trust

Aims: Early Worsening of Diabetic Retinopathy (EWDR) has been reported with subcutaneous semaglutide administration. Whether EWDR is associated with initiating tirzepatide is unknown.

Methods: Single-centre retrospective cohort study of clinical data. 4116 tirzepatide-exposed patients were matched 2:1 with 8223 controls for sex, baseline retinopathy status, diabetes duration, baseline HbA1c, and followed for up to 550 days. Endpoints were onset of new proliferative retinopathy or worsening of retinopathy grade, assessed through routine digital retinal photography.

Results: Tirzepatide treated patients, (mean baseline HbA1c $7.2 \pm 1.4\%$), showed significantly increased hazard of new proliferative retinopathy both in univariate analysis (hazard ratio (HR) 1.70, 95%CI (1.11-2.61), $p < 0.05$) and after adjustment for mean post-treatment HbA1c, pre-treatment retinopathy grade, diabetes duration, mean arterial pressure, LDL-C, treatment with insulin, and pre-existing microalbuminuria (HR 1.58 (1.2-2.47), $p < 0.05$). Pre-proliferative DR (R2M1, R2M0) at baseline was associated with the greatest increase in hazard of proliferative retinopathy (HR 111.6 (41.7-298.7) $p < 0.0001$, 132.1 (31.1-561.1) $p < 0.0001$, respectively). In people with no retinopathy or background retinopathy, tirzepatide was not significantly associated with EWDR. Higher mean dose of tirzepatide was not associated with increased hazard of either endpoint. Individuals with R0M0 at baseline in the highest quartile for mean tirzepatide dose were at reduced hazard for new retinopathy (HR 0.61 (0.42-0.88), $p < 0.01$).

Conclusions: Tirzepatide treatment is associated with the development of proliferative retinopathy (R3). The risk appears lowest in those with no retinopathy or only background retinopathy at baseline. Enhanced monitoring following tirzepatide initiation may be indicated for individuals at high pre-treatment risk of proliferative retinopathy.