

1

Time to insulin in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS)**S.S. Engel**¹, M.A. Bethel², J. Garg³, S.R. Stevens³, Y. Lokhnygina³, R.G. Josse⁴, J.B. Green³, E.D. Peterson³, R.R. Holman², on behalf of the TECOS Study Group;¹Merck & Co., Inc., Rahway, USA, ²University of Oxford, UK, ³Duke Clinical Research Institute, Durham, USA, ⁴University of Toronto, Canada.

Background and aims: TECOS was a randomized, placebo-controlled trial assessing the impact of sitagliptin on cardiovascular outcomes when added to usual care in patients with type 2 diabetes (T2DM). Among those not using insulin at baseline (n=11,263), we report the risk for progression to insulin during follow-up.

Materials and methods: TECOS enrolled 14,671 participants with HbA1c 6.5-8.0% on monotherapy with metformin (MET), pioglitazone, sulfonylurea (SU) or insulin, or dual combination with two oral agents or insulin with MET. They were randomized double-blind to sitagliptin or placebo, with subsequent diabetes management by the participants' usual care physician. Time to initiation of insulin was estimated using a Cox proportional hazards model.

Results: 5739 and 5472 participants were on mono- (MET 4435 [77%], SU 1246 [22%]) and dual- (SU + MET 5152 [94%]) oral agent therapy, respectively. Monotherapy patients had similar mean age (66 vs 65 years) but shorter median T2DM duration (6 vs 11 years), compared to dual therapy patients. MET monotherapy users were slightly younger (65 vs 68 years), had shorter T2DM duration (6 vs 8 years), similar HbA1c (7.1% vs 7.2%) and higher eGFR (77.4 vs 70.7) compared to SU monotherapy users. Overall, 4.7% of MET monotherapy users, 11.0% of SU monotherapy users and 17.2% of MET + SU users initiated insulin over a median duration of 3.1 years. Randomization to sitagliptin delayed the time to progression to insulin when added to MET monotherapy (1.3 vs 2.0 events per 100 pyrs; HR 0.67 [95% CI 0.51-0.89]) or SU + MET dual therapy (5.1 vs 7.8 events per 100 pyrs; 0.64 [0.56-0.73]), but not to SU monotherapy (4.0 vs 4.2 events per 100 pyrs; 0.96 [0.68-1.34]).

Conclusion: Among a cohort of international clinical trial participants with T2DM well controlled with MET or SU mono- or dual oral agent therapy, the rate of initiation of insulin was higher among SU users (as mono- or dual therapy). Randomization to sitagliptin treatment delayed progression to insulin among MET and MET + SU users.

Clinical Trial Registration Number: NCT00790205

Supported by: Merck & Co., Inc., Kenilworth, NJ, USA

Disclosure: S.S. Engel: Employment/Consultancy; Merck & Co., Inc.