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DIPEPTIDYL PEPTIDASE-4 INHIBITORS AND CARDIOVASCULAR OUTCOMES: META-ANALYSIS OF RANDOMIZED CLINICAL TRIALS WITH 55,141 PARTICIPANTS

Poster Contributions
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Background: The association between glucose-lowering in subjects with diabetes mellitus and major cardiovascular (CV) outcomes is weak; indeed, some oral hypoglycaemic agents are associated with increased CV events. Dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors) are a new class of oral hypoglycemic agent that may have beneficial CV effects. We performed a meta-analysis to appraise the CV safety and efficacy of DPP-4 inhibitors.

Methods: Comprehensive search of MEDLINE, EMBASE and clinicaltrials.gov, for published and unpublished prospective trials comparing DPP-4 inhibitors with placebo and active comparators in participants with Type 2 diabetes mellitus. Inclusion criteria were a minimum of 100 participants, minimum duration 24 weeks, in English and reporting on at least one of the outcomes examined.

Results: 50 trials were included, enrolling 55,141 participants and mean follow-up 45.3 weeks. DPP-4 inhibitors compared to all comparators (placebo and active) showed no difference in all-cause mortality (n=50,982, RR 1.01, 95% CI 0.91-1.13, p=0.83), CV mortality (n=48,151, RR 0.97, 95% CI 0.85-1.11, p=0.70, acute coronary syndrome (n=53,034 RR 0·97, 95% CI 0.87-1.08, p=0.59) or stroke (n=42,737, RR 0.98, 95% CI 0.81-1.18, p=0.80). There was statistically significant increase in heart failure outcomes (n=39,953, RR 1.16, 95% CI 1.01-1.33, p=0.04).

Conclusions: Treatment with DPP4-inhibitors compared with placebo shows no increase in risk with regards to all-cause mortality, CV mortality, acute coronary syndrome and stroke, but a nominally statistically significant trend towards increased risk of HF outcomes. These findings suggest there is no cardiovascular harm (or benefit) with DPP-4 inhibitors; further large-scale CV outcome studies with these agents will help resolve the issue of excess HF risk.