Saxagliptin, Alogliptin, and Cardiovascular Outcomes

Besides showing futility in the use of dipeptidyl peptidase 4 (DPP-4) inhibitors to reduce cardiovascular outcomes, the studies by Scirica et al.1 and White et al.2 (Oct. 3 issue) have raised concerns regarding increased rates of heart failure associated with these agents.

The Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus (SAVOR)–Thrombolysis in Myocardial Infarction (TIMI) 53 (SAVOR-TIMI 53) trial, reported by Scirica et al., showed a 27% increase in hospitalization for heart failure among patients with diabetes who received saxagliptin as compared with patients with diabetes who received placebo (3.5% vs. 2.8%; hazard ratio, 1.27; 95% confidence interval [CI], 1.07 to 1.51; P=0.007).

Outcomes with respect to heart failure were not mentioned at all in the Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care (EXAMINE) trial reported by White et al., although 28% of patients had congestive heart failure at baseline.2

Clinically oriented readers would have wished to see figures for incident (not total) heart failure as an outcome in both trials, as well as rates of cardiovascular events among patients with preexisting heart failure, to clarify this safety aspect of DPP-4 inhibitor therapy, especially since there has been some uncertainty about the use of another DPP-4 inhibitor, vildagliptin, in patients with heart failure.3

Furthermore, interactions of DPP-4 inhibitors with heart failure cannot be totally ruled out, since levels of brain natriuretic peptides, which may be 100 times as high in patients with heart failure as in patients without heart failure, are known substrates of the enzyme DPP-4.4

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