Cardiovascular Biomarkers and Long-term Outcomes in Patients with Type 2 Diabetes Mellitus Treated with Alogliptin vs. Placebo in the EXAMINE Trial

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Background

• Thorough evaluation of the cardiovascular (CV) safety of new drugs for diabetes mellitus (DM) is now mandated by the US FDA.
• Alogliptin, a dipeptidyl-peptidase 4 inhibitor, is one of a new drug class for treatment of DM.
• CV biomarkers may provide useful insight with respect to CV safety of new treatment for DM.
• B-type natriuretic peptide (BNP) and cardiac troponin (Tn) are both potent predictors of CV risk in unstable and stable pts.

Methods

• We evaluated the relationship between BNP and high sensitivity (hs) TnI and CV outcomes in a high risk population of patients with DM.

EXAMINE was a randomized, double-blind, placebo-controlled, multinational trial of alogliptin in pts with DM enrolled 15 to 90 days after an acute coronary syndrome (ACS).

• BNP and hsTnI (Abbott ARCHITECT) were measured in 5230 pts with baseline samples
  • BNP: Categorized by quartiles
  • hsTnI: Use of pre-specified cut-points

• Endpoints assessed were:
  • Major adverse CV events (MACE) : CV death, myocardial infarction, or stroke.
  • CV death or HF as an exploratory endpoint.

Results

Biomarkers and CV Outcomes

• BNP showed a significant graded relationship with CV outcomes at 18 mo (p-trend <0.001).
• Similarly, hsTnI showed a significant graded relationship w/ CV outcomes (p-trend <0.001).

Biomarkers and Alogliptin vs Placebo

• The rates of MACE were similar with alogliptin vs. placebo in the highest risk pts identified by:
  • BNP (Group 4: 19.9 vs. 22.2%; Fig below) or
  • hsTnI (Group 4: 18.3 vs. 20.6%).
• Results were for similar for CV death/HF for both BNP (17.5 vs. 19.4%) or hsTnI (14.3 vs. 14.9%).
• There was no evidence for heterogeneity in the HR for alogliptin vs. placebo for CV death/HF across BNP strata (p-interaction=0.71).

Conclusions

• Among pts with DM who were stable after a recent ACS, BNP & hsTnI identified pts at high risk of adverse CV outcomes.
• In this study, rates of MACE, & CV death or HF, were not increased with alogliptin vs. placebo, even in high risk pts with elevated CV biomarkers.

Disclosure:

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