Objectives and End Points of EXAMINE

- **Primary objective**: To demonstrate that major CV event rates are not higher with alogliptin than with placebo in type 2 diabetes patients with recent ACS who are receiving standard of care for diabetes and secondary CV prevention
  - **Primary end point**: composite of first occurrence of CV death, nonfatal MI, and nonfatal stroke

**Secondary Objectives:**

**Superiority assessment**: If non-inferiority proven, to demonstrate that major CV event rates were lower on alogliptin than with placebo

**Secondary end point**: Evaluate the time from randomization to the first occurrence of the expanded MACE:
  - Composite of CV death, nonfatal MI, nonfatal stroke, and urgent revascularization due to UA

- **Major exploratory end points**: all CV deaths, all-cause mortality

Abbreviations: ACS, acute coronary syndrome; CV, cardiovascular; MI, myocardial infarction; UA, unstable angina.
DECLARATION OF INTEREST

- Consulting/Royalties/Owner/ Stockholder of a healthcare company
Study Patients

• Diagnosis of type 2 diabetes and receiving antihyperglycemic therapy (single or combination therapies)

• Acute coronary syndrome* within 15 to 90 days before randomization

• Receiving local standard of care for type 2 diabetes care and secondary CV prevention (excluded were DPP-4 inhibitors and GLP-1 agonists)

• Patients with unstable cardiovascular conditions or those on dialysis within 14 days of planned randomization were excluded

  • Myocardial infarction or hospitalized unstable angina
Non-Inferiority Met for All End Points

- Primary end point
- Secondary end point
- All CV deaths
- All-cause mortality

Hazard Ratio

- Alogliptin Better
- Placebo Better

Non-inferiority

* One-sided repeated CI using alpha=0.01.
Summary of All Major Findings

• Rates of major adverse cardiovascular events were similar with alogliptin compared with placebo in patients with type 2 diabetes and recent acute coronary syndromes

• This observation occurred in the following context:
  – Significantly lower HbA$_{1c}$ level (–0.36%) with alogliptin
  – High overall CV event rate (11% over the median follow-up of 18 months)
  – High levels of standard of care for both diabetes and cardiovascular prevention

• Outcomes were similar for the secondary end point (composite of CV death, nonfatal MI, nonfatal stroke, urgent revascularization due to UA)
Summary (2)

- Rates of cardiovascular and all-cause mortality were similar in the alogliptin and placebo groups.
- Similar rates of withdrawal due to adverse events in the alogliptin and placebo groups.
- Other adverse events of interest:
  - No differences between alogliptin and placebo groups in:
    - Incidence of Hypoglycemia.
    - Reported malignancies (including pancreatic cancer).
    - Renal function.
  - Low and similar frequencies of acute and chronic pancreatitis were observed.
Conclusion:
In patients with type 2 diabetes and recent acute coronary syndrome, major adverse cardiovascular event rates for the DPP-4 inhibitor alogliptin were not increased compared with placebo.