Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus (SAVOR) - TIMI 53

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European Society of Cardiology,
Amsterdam - September 2, 2013

NCT01107886; Funded by AstraZeneca and Bristol-Myers Squibb
Primary Objective

• To determine whether when added to background therapy, saxagliptin would be non-inferior to placebo for the composite endpoint of CV death, non-fatal MI, or non-fatal ischemic stroke (Upper 95% CI of HR < 1.3).

• And if non-inferiority were met, to determine if saxagliptin would be superior to placebo.
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**Documented Type 2 Diabetes**

N = 16,492

- Established CV Disease or Multiple Risk Factors

**RANDOMIZED 1:1 DOUBLE BLIND**

- **SAXAGLIPTIN** 5 mg/d
  - 2.5 mg/d if eGFR < 50 ml/min

- **PLACEBO**

  - All other DM Rx per treating MD

**Follow up Visits**

- Q6 months

**Final Visit**

**Primary EP**

- CV Death, MI, Ischemic Stroke

**Duration**

- Event driven (n=1040)
- Median duration 2.1y
- LTFU 0.2%
- W/C 2.4%

**Major Secondary EP**

- CV death, MI, ischemic stroke, or hosp.
- for heart failure, unstable angina, or coronary revascularization
Primary Endpoint

HR 1.00
95% CI 0.89-1.12
p<0.001 (non-inferiority)
p=0.99 (superiority)

Placebo 7.2%
Saxagliptin 7.3%

Placebo 8212 7983 7761 7267 4855
Saxagliptin 8280 8071 7836 7313 4920

Months
Conclusions

• When added to standard of care in patients with T2DM at high CV risk, saxagliptin neither reduced nor increased the risk of the primary composite endpoint of CV death, MI, or ischemic stroke.
Conclusions

• In addition, saxagliptin:
  - Improved glycemic control
  - Decreased the need for insulin and other diabetes medications
  - Increased hypoglycemic events, but not hospitalization for hypoglycemia
  - Prevented progression of microalbuminuria
  - Did not increase risk of pancreatitis or pancreatic cancer
Conclusions (Heart Failure)

• The higher incidence of hospitalization for heart failure was unexpected, but it was a pre-defined, adjudicated endpoint.

• It merits further evaluation given the history of other diabetic agents and heart failure.

• Additional analyses are ongoing, and preliminary data suggest that the risk is highest in those with elevated baseline clinical risk for heart failure and/or elevated BNP levels.
Implications

• SAVOR-TIMI 53 highlights the importance of performing large trials with clinical cardiovascular endpoints for diabetes drugs.

• Further research is needed to explore the relationship between HbA1c and cardiovascular outcomes.