ELIXA trial shows CV safety of Lixisenatide

August 31 2015

In patients with type 2 diabetes and acute coronary syndrome, the glucose-lowering medication lixisenatide did not increase or decrease the rate of cardiovascular (CV) events compared to placebo, according to results of the Evaluation of Lixisenatide in Acute Coronary Syndrome (ELIXA) trial.

The study, presented today at ESC Congress 2015, "demonstrates the cardiovascular safety of lixisenatide", reported Eldrin F. Lewis, MD, MPH, a member of the ELIXA trial's executive committee, a physician in the Cardiovascular Medicine Division at Brigham and Women's Hospital and an associate professor at Harvard Medical School, in Boston, USA.

The results of the ELIXA trial, originally presented in June at the American Diabetes Association, are the first to be reported on the CV safety outcomes of a glucagon-like peptide 1 (GLP-1) receptor agonist.

"Prior studies have established that patients with type 2 diabetes are at higher risk for incident cardiovascular disease than people who do not have type 2 diabetes, and some glucose-lowering drugs have been associated with increased risk of cardiovascular disease," said Dr. Lewis, explaining that this has prompted both the European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA) and to establish guidelines for clinical trials that would ensure cardiovascular safety in glucose-lowering therapies.

The ELIXA trial was powered to establish safety (non-inferiority) and

superiority of lixisendatide versus placebo. Although it was not able to establish the superiority of lixisenatide over placebo for CV safety, "the neutral effects on cardiovascular events are all within the limits of the EMA's and FDA's guidelines," commented Dr. Lewis. "In addition, lixisenatide provided a modest benefit in terms of weight gain."

The study included 6,068 patients (mean age 60.3 years) with type 2 diabetes and a history of myocardial infarction (83%) or hospitalisation for unstable angina (17%) within the past 180 days.

The patients were randomised to receive daily injections of either lixisenatide or placebo and followed for a minimum of 10 months to measure the primary outcome: a composite of cardiovascular death, heart attacks, stroke, and hospitalisation for unstable angina. Important additional outcome measures included all-cause death and heart failure hospitalisations.

This outcome occurred in 13.4 percent of the lixisenatide group compared to 13.2 percent of the placebo group, with the hazard ratio of 1.02 and a 95% confidence interval that was "well below the standard set by the FDA," noted Dr. Lewis.

Lixisenatide was also safe in patients with a history of heart failure. Among patients with a history of chronic heart failure prior to randomisation, approximately 10% had a hospitalisation for heart failure during follow-up, compared to 2.4% of patients without a history of chronic heart failure.

"The hazard ratio was similar between lixisenatide and placebo demonstrating similar CV safety of lixisenatide in this population," he said.

However, patients who were hospitalised for heart failure had a risk of

all-cause death that was 9-fold greater than those who were not hospitalised for heart failure. "This excess mortality suggests that these are important events to capture among patients with diabetes," said Dr. Lewis.

Provided by European Society of Cardiology