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New trial results support treatment with Inspra (eplerenone) within first 24 hours of symptoms, in addition to standard therapy, in patients with acute STEMI without heart failure.

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Primary Composite Efficacy Endpoint Met in REMINDER trial

(BUSINESS WIRE)--Pfizer Inc. (NYSE: PFE) today announced results from the REMINDER trial showing statistically significant risk reductions in the primary composite efficacy endpoint. The composite endpoint was defined as the time to first event of cardiovascular (CV) mortality, re-hospitalization or extended initial hospital stay due to diagnosis of heart failure (HF), sustained ventricular tachycardia or fibrillation, ejection fraction (EF) ?40% after 1 month, or an elevation of BNP/ NT-proBNP after 1 month.

The results were presented for the first time during the Late Breaker Clinical Trial session at the 62nd Annual Scientific Session of the American College of Cardiology in San Francisco today.

The REMINDER trial was a randomized, double-blind trial, involving 1,012 patients with acute ST-segment elevation myocardial infarction (STEMI) without a history of HF or EF <40% and without signs of HF. Patients received, preferably before myocardial reperfusion, either eplerenone (25-50 mg OD) or placebo in addition to standard therapy. Treatment was initiated within the first 24 hours of symptom onset (preferably within first 12h).

The REMINDER trial demonstrated a statistically significant 42.9% relative risk reduction in the primary endpoint with $p < 0.0001$ (95% confidence interval [CI] 0.439, 0.742) in patients with acute STEMI when eplerenone was initiated within the first 24 hours of onset of symptoms. Overall, the adverse events reported in the REMINDER trial were consistent with those already known for eplerenone, primarily hyperkalemia.

Eplerenone is not approved for use in the patient population studied in the REMINDER trial in any market.

The improvement in outcome was mainly driven by a significant reduction of the BNP / NT-proBNP biomarker component at 1 month. BNP/NT-proBNP has been shown to be an important marker for short- and long-term prognosis in patients with myocardial infarction in the presence or absence of preserved ejection fraction. An elevation of BNP / NT-proBNP after 1 month was observed less frequently in the eplerenone group 81(16.0%) than in the placebo group 131(25.9%) (adjusted HR, 0.584; 95% CI 0.441-0.773; p=0.0002).

Over the course of the study, the incidence of hyperkalemia (elevated potassium defined as serum potassium levels exceeding 5.5 mEq/L) occurred in 5.6% vs. 3.2% (p=0.09) in the eplerenone and placebo groups, respectively. Hypokalemia (serum potassium level below 3.5 mEq/L) occurred more frequently in the placebo group with 1.4% vs. 5.5% (p=0.0002) in the eplerenone and placebo groups, respectively. The rates of other

adverse events were similar in both groups.

Commenting on the findings, the chair of the REMINDER Steering Committee Professor Gilles Montalescot, Institute of Cardiology, Centre Hospitalier Pitié-Salpêtri?re, Paris, France said: “Eplerenone improved the outcome of patients presenting with acute STEMI and without concomitant heart failure. This benefit was obtained in a low-risk population that was well treated, without serious adverse drug effect. Adding eplerenone to standard therapy as early as within the first 24 hours of symptoms reduced heart failure-related morbidity.”

About the REMINDER trial

The REMINDER trial was a randomized, double-blind trial, involving 1012 patients with acute STEMI without a history of HF or EF <40% and without signs of HF.

The REMINDER trial was conducted in 11 countries: Canada, Czech Republic, France, Germany, Greece, Hungary, Netherlands, Poland, Slovakia, Spain, UK.

The primary objective of the REMINDER trial was to assess the efficacy of Inspra 25 -50 mg once daily, compared to placebo, in the early treatment of acute ST-segment elevation myocardial infarction (STEMI) within 24 hours (preferably within the first 12h).

The mean follow-up time was 10.5 months.

The study was funded by Pfizer.

About INSPRA®

INSPRA® (eplerenone) is a steroid nucleus-based mineralcorticoid receptor (MR) antagonist with a higher degree of selectivity than spironolactone.

Important Prescribing Information

In the United States, Inspra® (eplerenone) is indicated to improve survival of stable patients with left ventricular (LV) systolic dysfunction (ejection fraction less than or equal to 40%) and clinical evidence of congestive heart failure (CHF) after an acute myocardial infarction (MI). Eplerenone is also indicated for the treatment of hypertension. Eplerenone may be used alone or in combination with other antihypertensive agents.

Eplerenone is contraindicated in all patients with serum potassium greater than 5.5 mEq/L at initiation, creatinine clearance less than or equal to 30 mL/min, or concomitant administration of strong CYP3A4 inhibitors. Eplerenone is also contraindicated for the treatment of hypertension in patients with type 2 diabetes with microalbuminuria, serum creatinine greater than 2.0 mg/dL in males or greater than 1.8 mg/dL in females, creatinine clearance less than 50 mL/min, or concomitant administration of potassium supplements or potassium sparing diuretics.

Serum potassium should be measured before initiating eplerenone therapy, within the first week, and at one month after the start of treatment or dose adjustment. Serum potassium should be assessed periodically thereafter, especially in patients at risk for the development of hyperkalemia such as elderly patients with renal insufficiency and patients with type 2 diabetes and microalbuminuria.

Most common adverse reactions (greater than 2% and more frequent than with placebo) in patients with CHF Post-MI: hyperkalemia and increased creatinine. Most common adverse reactions (greater than or equal to 2% and more frequent than with placebo) in hypertensive patients: dizziness, diarrhea, coughing, fatigue and flu-like

symptoms.

In the European Union, eplerenone is indicated, in addition to standard optimal therapy, to reduce the risk of cardiovascular mortality and morbidity in adult patients with NYHA class II (chronic) heart failure and left ventricular systolic dysfunction (LVEF ?30%). Eplerenone is also indicated to reduce the risk of cardiovascular mortality and morbidity in stable patients with left ventricular dysfunction (LVEF ?40%) and clinical evidence of heart failure after recent myocardial infarction.

In Japan, eplerenone is approved for the treatment of hypertension.

For additional product information in the US, visit:
http://media.pfizer.com/files/products/uspi_inspra.pdf

UK prescribing information is available at:
http://www.medicines.org.uk/EMC/medicine/16746/SPC/Inspra+25mg+%26+50+mg+film-coated+tablets/

Other countries should refer to local prescribing information.

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DISCLOSURE NOTICE: The information contained in this release is as of March 10, 2013. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about a potential additional indication for Inspra, including its potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; whether and when supplemental drug applications may be filed with regulatory authorities for this potential additional indication for Inspra; decisions by regulatory authorities regarding whether and when to approve any supplemental drug applications that may be filed for this potential additional indication for Inspra as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; and competitive developments.

A further list and description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2012, and in its reports on Form 10-Q and Form 8-K.

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