Pfizer Logo

Adding INSPRA® (eplerenone) to Standard Therapy Significantly Reduces the Risk of CV Mortality and Morbidity in Patients With Chronic Heart Failure With Mild Symptoms, Study Shows

Saturday, November 13, 2010 - 10:30pm

Rates of Heart Failure Hospitalization, All-Cause Hospitalization, and All-Cause Mortality also Significantly Reduced

"It is encouraging to see a clinical trial deliver results that are sufficiently strong to meet strict pre-defined stopping criteria. Patients such as those enrolled in EMPHASIS-HF typically have a poor prognosis and today's results should therefore provide real encouragement for doctors and patients alike."

CHICAGO--(BUSINESS WIRE)--Pfizer Inc. (NYSE: PFE) today announced results from the EMPHASIS-HF trial(1) showing a statistically significant reduction in risk of cardiovascular (CV) death or heart failure (HF) hospitalization for patients with chronic heart failure with mild symptoms treated with Inspra® (eplerenone) versus those given placebo in addition to standard HF therapy. The results were presented to physicians attending the American Heart Association Scientific Sessions in Chicago and were simultaneously published online in the *New England Journal of Medicine*.

The EMPHASIS-HF trial demonstrated a statistically significant 37% relative risk reduction for the eplerenone group ($p<0.0001$) compared to placebo in the primary composite endpoint of death from CV causes or HF hospitalization. There were also statistically significant reductions in other secondary endpoints of all-cause mortality (24%; $p=0.008$), CV mortality (24%; $p=0.012$), all-cause hospitalization (23%, $p<0.0001$) and HF hospitalization (42%; $p<0.0001$).

Heart failure can lead to a reduction in the quality of life, frequent admissions to hospital and a greatly shortened life expectancy, despite the availability of several effective treatments(2). Dr. Faiez Zannad, Professor of Therapeutics and cardiologist at the CHU (University Hospital) of the Henri Poincare University of Nancy, France and co-chair of the EMPHASIS-HF Steering Committee said: "It is encouraging to see a clinical trial deliver results that are sufficiently strong to meet strict pre-defined stopping criteria. Patients such as those enrolled in EMPHASIS-HF typically have a poor prognosis and today's results should therefore provide real encouragement for doctors and patients alike."

The primary objective of the EMPHASIS-HF trial was to evaluate the efficacy and safety of eplerenone plus standard HF therapy versus placebo plus standard HF therapy on the cumulative incidence of the composite endpoint of CV death or HF hospitalization. Patients enrolled in the study had New York Heart Association (NYHA) Class II chronic systolic heart failure with mild symptoms.

No new safety information emerged as a result of this study. As anticipated, there was a higher incidence of hyperkalemia (elevated potassium, defined as serum potassium level >5.5mmol/L.) among patients assigned to eplerenone compared to placebo (11.8% vs 7.2%, respectively; p<0.001). In contrast, the incidence of hypokalemia (low potassium, defined as serum potassium level <3.5mmol/L.) was lower in the eplerenone group compared to placebo (7.5% vs 11.0%, respectively; p=0.002).

In May 2010, recruitment to the EMPHASIS-HF trial was halted early after the second pre-specified interim analysis showed that the study's pre-defined stopping rules had been met and a significant difference (two-sided P<0.001 in favor of eplerenone) in the primary endpoint was evident.

Eplerenone is not authorised for use in the patient population studied in the EMPHASIS-HF trial in any individual market.

About the EMPHASIS-HF trial

EMPHASIS HF (A6141079) is a phase 3B, multinational (2,737 patients from 272 centres in 29 countries), randomized, double-blind placebo-controlled, parallel-group trial. It is conducted in a NYHA II chronic systolic heart failure population, which is a distinct population from the EPHESUS study population (patients with left ventricular dysfunction (LVEF less than or equal to 40 %) and clinical evidence of heart failure after recent myocardial infarction). In Europe, the current approved indication for eplerenone is based on the EPHESUS study population.

The primary objective of this trial is to evaluate the efficacy and safety of eplerenone plus standard heart failure (HF) therapy - including an angiotensin converting enzyme (ACE) inhibitor and/or an angiotensin receptor blockers (ARB), plus a beta–blocker – versus placebo plus standard HF therapy on the cumulative incidence of cardiovascular (CV) mortality and HF hospitalization (a composite primary endpoint). The mean follow-up time was 21.1 months.

Patients were to be randomized (1:1) to receive eplerenone 25 mg once daily (OD) or matching placebo. At four weeks, the dose of study drug could be increased to 50 mg OD (two 25mg tablets of eplerenone or two matching placebo tablets once daily) based on serum potassium level. The trial was designed to enroll 3100 patients and to continue until a total of 813 adjudicated primary endpoint events were reported.

In May 2010, Pfizer announced that it planned to halt recruitment to the EMPHASIS-HF trial early on the recommendations of the trial's independent Executive Steering Committee (ESC). The recommendations follow a second interim analysis by the independent Data Safety Monitoring Committee (DSMC) of the EMPHASIS-HF trial confirming the study has reached its primary efficacy endpoint early according to the protocol pre-defined stopping rules.

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. Eplerenone is thought to be a more selective blocker at the mineralcorticoid receptor since there is evidence that some of the effects result from a blockade of cortisol stimulation of the MR-receptor.

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 EU, eplerenone is indicated to reduce the risk of cardiovascular mortality and morbidity in stable patients with left ventricular dysfunction (LVEF less than or equal to 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: \files\pressrelease_assets\pdf\ShowLabeling.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.

Pfizer Inc.: Working together for a healthier world™

At Pfizer, we apply science and our global resources to improve health and well-being at every stage of life. We strive to set the standard for quality, safety and value in the discovery, development and manufacturing of medicines for people and animals. Our diversified global health care portfolio includes human and animal biologic and small molecule medicines and vaccines, as well as nutritional products and many of the world's best-known consumer products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as the world's leading biopharmaceutical company, we also collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more about our commitments, please visit us at www.pfizer.com

DISCLOSURE NOTICE: The information contained in this release is as of November 14, 2010. 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; decisions by regulatory authorities regarding whether and when to approve any supplemental drug applications that may be filed for this additional indication for Inspra as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of any such additional indication; 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, 2009 and in its reports on Form 10-Q and Form 8-K.

References

(1) Zannad, F; McMurray, J.J.V; and Drexler, H; et al. Eplerenone in patients with systolic heart failure and mild symptoms. New England Journal of Medicine 2010 [10.1056/nejmoa1009492 nejm.org]

(2) McMurray, J.J.V; Andersson, F.L; and Stewart, S; et al. Resource utilization and costs in the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) programme Eur Heart J (2006) 27 (12): 1447-1458.

Pfizer Inc. Media: Andrew Thomas, +44-7814-528928 Investor: Jennifer Davis, +1-212-733-0717