Efficacy of LCZ696 in patients with heart failure and preserved ejection fraction

August 27 2012

The novel angiotensin receptor neprilysin inhibitor, LCZ696, demonstrated beneficial effects in heart failure patients with preserved ejection fraction (HFpEF), according to results of the PARAMOUNT (Prospective compArison of ARNI with ARB on Management Of heart failUre with preserved ejectioN fracTion) trial.

Approximately half of all heart failure patients have normal or nearly normal ejection fraction, a measure of their strength of cardiac contraction. However, while many studies have shown a benefit of pharmacological therapies in heart failure with reduced ejection fraction, so far, according to the latest ESC heart failure guidelines, no treatment has been shown to reduce mortality or morbidity in HFpEF.

The PARAMOUNT study, a phase II trial conducted in 308 patients in 13 countries, compared the effects of LCZ696, a new angiotensin receptor neprilysin inhibitor, and the ARB valsartan on the concentrations of natriuretic peptides. The natriuretic peptide investigated in this study, NT-proBNP, is a marker of cardiac wall stress, and levels are increased in patients with heart failure.

Study results presented here today showed that LCZ696 reduced levels of NT-proBNP by 23% when compared with valsartan. LCZ696 also reduced enlargement of the left atrium, another marker of adverse outcomes in heart failure, and improved the symptoms of heart failure.

According to the study's lead author Professor Scott Solomon, Professor

of Medicine at Harvard Medical School and Director of Noninvasive Cardiology at Brigham and Women's Hospital, Boston, LCZ696 acts by inhibiting both the angiotensin receptor and the enzyme responsible for the breakdown of the natriuretic peptides (neprilysin). LCZ696's dual mechanism of action thus acts to restore the altered neurohormonal balance in HFpEF. Earlier research has suggested that the clinical benefits derived from neprilysin inhibition may be best achieved if the renin-angiotensin system is simultaneously inhibited.

"LCZ696 is unique in simultaneously blocking the renin angiotensin system while augmenting the body's intrinsic natriuretic peptide system through neprilysin inhibition," said Professor Solomon. "These dual effects may be important in the treatment of HFpEF.

"LCZ696 in the PARAMOUNT study is the first compound to show both reductions in NT-proBNP and left atrial size in HFpEF patients, each powerful predictors of outcome in heart failure. The favorable effects of LCZ696 seen in patients with HFpEF in PARAMOUNT are encouraging, and further testing of this agent in this patient population is warranted."

Provided by European Society of Cardiology