NOVARTIS PHARMACEUTICALS

LCZ696 in Heart Failure (HF) Backgrounder

Fast facts

- LCZ696, an investigational twice a day tablet, is a first of its kind medicine that has a dual action on the neurohormonal systems of the heart, enhancing the body's natural defenses against heart failure (HF) while simultaneously blocking receptors exerting harmful effects[1,2,3,4]
- HF is a debilitating and potentially life-threatening disease in which the heart is unable to pump enough blood[5,6]
- 900,000 people in the UK have HF[6], facing a high risk of death and poor quality of life, despite currently available medicines[7]
- Every year HF costs the world economy over $45 billion and consumes almost 2% of the National Health Service (NHS) budget in the UK which equates to approximately £1.9 billion[8,9,10,11,12,13,14,15,16]
- LCZ696 is thought to reduce the strain on the failing heart, by enhancing the body's natural defenses against HF while simultaneously blocking pathways associated with the failure of the heart[1,2]
- The PARADIGM-HF study of LCZ696 is the largest study ever done in heart failure, with 8,442 patients with HF with reduced ejection fraction (HF-REF) having taken part[1,17]
- In March 2014, the study was stopped early when it was confirmed that those given LCZ696 were significantly less likely to die from CV causes[1,18]

What makes LCZ696 different?

LCZ696 is a new compound that is the result of a decade of research in collaboration with leading international cardiologists. LCZ696 is a first of its kind medicine that acts to enhance the protective neurohormonal system of the heart (NP system) while simultaneously suppressing the harmful system (the RAAS)[1,2,3]. Older medicines only work on the harmful system. In this way, LCZ696 is thought to reduce the strain on the failing heart[1,3].

What is the evidence for LCZ696 so far?

The Phase II PARAMOUNT study showed the efficacy and tolerability of LCZ696 in patients with heart failure with preserved ejection fraction (HF-PEF). The results showed that LCZ696 reduced stress on the heart – measured by levels of the biomarker NT-proBNP - and indicated it may reverse an indicator of structural damage. The incidence of serious adverse events was low in patients treated with LCZ696, and no higher than in those treated with widely used ARB, valsartan[3].

Initiated in December 2009, the Phase III randomized, double-blind PARADIGM-HF study was designed to see if LCZ696 could increase survival 15% over and above what can be achieved with ACE-inhibitor enalapril in addition to current best treatment in patients with heart failure with reduced ejection fraction (HF-REF)[1]. In March 2014 PARADIGM-HF was stopped early when it was confirmed that those given LCZ696 were significantly less likely to die from CV causes[1,18]. The full results will be presented at the European Society of Cardiology congress in August 2014.

In July 2014 a second Phase III study, PARAGON-HF in patients with HF-PEF, began[19].

When might LCZ696 be available?

Novartis expects to file the application for marketing authorization with the US FDA by the end of 2014 and in the EU in early 2015. As HF is a serious condition with an urgent need for new treatments, the FDA has granted LCZ696 Fast Track designation, which can expedite the review of new medicines intended to treat serious or life-threatening conditions[20].

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