World Heart Journal
Volume 7, Number 1

ISSN: 1556-4002

Angiotensin-Receptor Neprilysin Inhibitor LCZ696; A Novel Therapy for Heart Failure

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Chronic heart failure (CHF) is characterized by evidence of cardiac systolic and/or diastolic dysfunction and clinical signs of dyspnea, palpitation, fatigue, and fluid retention [1-3]. Randomized clinical trials have shown that treatment with β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists, and mineralocorticoid receptor blockers reduces overall mortality and improves clinical symptoms of chronic HF [1-4]. These agents act by targeting detrimental pathways; activation of the renin–angiotensin–aldosterone system and sympathetic activation which may be called neurohumoral activation. The Food and Drug Administration (FDA) has already approved aldosterone antagonist eplerenone a new oral drug (hydralazine–isosorbide dinitrate) for patients with CHF and a reduced ejection fraction in 2005. This drug was recommended only for self-identified black patients who continued to have symptoms despite evidence-based treatment. In view of the high mortality and morbidity in HF patients, despite the use of the above treatments, there is a need for additional therapeutic options. Presence of nutrient deficiency such as omega-3 fatty acids, L-carnitine and coenzyme Q10 further complicates the response to treatment and outcome among these patients [6-8].

Some experts believe that this novel drug, LCZ696, a dual inhibitor of angiotensin II receptor and neprilysin, may prove to be the first disruptive agent to the heart-failure treatment algorithm, which has remained essentially unchanged for a decade [5]. In PARADIGM-HF (Prospective Comparison of ARNI [Angiotensin Receptor–Neprilysin Inhibitor] with ACEI [Angiotensin-Converting–Enzyme Inhibitor] was done to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial). The authors report that LCZ696, as compared with a target-dose enalapril-based regimen, significantly

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