The role of dual angiotensin receptor and neprilysin inhibition in the treatment of heart failure

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The main major change in 2016 western heart failure guidelines in pharmacological treatment is angiotensin receptor neprilysin inhibitor (ARNI) for heart failure. According to PARADIGM HF trial, ARNI was enrolled in the guidelines quickly. Both, ECS guideline and ACC/AHA/HFSA guideline update have the ARNI class I indication for heart failure treatment. Natriuretic peptides have potential beneficial actions in heart failure by decreasing sympathetic outflow, natriuresis/diuresis and decreasing renin secretion, decreasing blood pressure, increasing endothelial permeability, decreasing fibrosis, decreasing hypertrophy, and so on. Natriuretic peptides are degraded by neprilysis which also degrades angiotension II. Dual angiotensin receptor and neprilysin inhibition could get the most benefit for the treatment of heart failure. LCZ696 simultaneously inhibiting neprilysin (via LBQ657) and blocking AT1 receptors (via valsartan) is the first ARNI. In PARADIGM HF trial, LCZ696 was superior to ACE inhibition alone by overall 20% reduction in risk of CV death, 21% reduction in risk of hospitalization for heart failure, and overall 16% reduction in risk of all-cause death. This robust finding provides strong evidence that combined inhibition of the angiotensin receptor and neprilysin is superior to inhibition of the RAS alone in patients with chronic heart failure.