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2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

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A new therapeutic class of agents acting on the RAAS and the neutral endopeptidase system has been developed [angiotensin receptor neprilysin inhibitor (ARNI)]. The first in class is LCZ696, which is a molecule that combines the moieties of valsartan and sacubitril (neprilysin inhibitor) in a single substance. By inhibiting neprilysin, the degradation of NPs, bradykinin and other peptides is slowed. High circulating A-type natriuretic peptide (ANP) and BNP exert physiologic effects through binding to NP receptors and the augmented generation of cGMP, thereby enhancing diuresis, natriuresis and myocardial relaxation and anti-remodelling. ANP and BNP also inhibit renin and aldosterone secretion. Selective AT1-receptor blockade reduces vasoconstriction, sodium and water retention and myocardial hypertrophy.187, 188

A recent trial investigated the long-term effects of sacubitril/valsartan compared with an ACEI (enalapril) on morbidity and mortality in patients with ambulatory, symptomatic HFrEF with LVEF ≤40% (this was changed to ≤35% during the study), elevated plasma NP levels (BNP ≥150 pg/mL or NT-proBNP ≥600 pg/mL or, if they had been hospitalized for HF within the previous 12 months, BNP ≥100 pg/mL or NT-proBNP ≥400 pg/mL), and an estimated GFR (eGFR) ≥30 mL/min/1.73 m^2 of body surface area, who were able to tolerate separate treatments periods with enalapril (10 mg *b.i.d.*) and sacubitril/valsartan (97/103 mg *b.i.d.*) during a run-in period.162 In this population, sacubitril/valsartan (97/103 mg *b.i.d.*) was superior to ACEI (enalapril 10 mg *b.i.d.*) in reducing hospitalizations for worsening HF, cardiovascular mortality and overall mortality.162 Sacubitril/valsartan is therefore