

## HEART FAILURE

## Another new PARADIGM in treatment for heart failure?

The investigators conducting the PARADIGM-HF trial previously reported that LCZ696, an angiotensin–neprilysin receptor inhibitor, significantly reduced mortality in patients with heart failure compared with the current standard treatment with enalapril, an angiotensin-converting-enzyme inhibitor. Now, presenting additional data at the AHA Scientific Sessions 2014 in Chicago, IL, USA, and published in *Circulation*, the PARADIGM-HF investigators report

that LCZ696 is also more effective than enalapril at preventing the clinical progression of heart failure.

In 8,399 patients with heart failure who were randomly assigned to receive a daily dose of 400 mg LCZ696 or 20 mg enalapril, those who received the angiotensin–neprilysin receptor inhibitor were less likely to require intensified treatment (520 versus 604; HR 0.84, 95% CI 0.74–0.94,  $P=0.003$ ), or be hospitalized for worsening heart failure (851 versus 1,079; rate ratio 0.77, 95% CI 0.67–0.89,  $P<0.001$ ). Patients receiving LCZ696 also had fewer visits to the emergency department (102 versus 150;  $P=0.001$ ), and were less likely to require intensive care if hospitalized (549 versus 623;  $P=0.019$ ) compared with those in the enalapril group.

The time to first hospitalization for heart failure was also significantly longer in patients receiving LCZ696 than in those receiving enalapril. This difference was seen as early as 30 days after initial randomization (HR 0.60, 95% CI 0.38–0.94,  $P=0.027$ ). “The advantage of LCZ696 over

enalapril in preventing clinical deterioration was apparent early in the trial and persisted for the duration of double-blind therapy,” explain the investigators.

Furthermore, those patients who received LCZ696 had lower levels of the biomarkers NT-proBNP and troponin compared with those receiving enalapril, indicating that these patients had reduced cardiac wall stress and cardiac injury. These differences were apparent within 4 weeks of treatment and were maintained when patients were assessed again 8 months later ( $P<0.0001$  for the difference at both time points).

The investigators conclude that “the effect of LCZ696 to stabilize the course of heart failure is likely to have important ramifications for both quality of life and resource utilization in this disorder”.

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**Original article** Packer, M. et al. Angiotensin receptor neprilysin inhibition compared with enalapril on the risk of clinical progression in surviving patients with heart failure. *Circulation* doi:10.1161/CIRCULATIONAHA.114.013748

