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Efficacy and safety of LCZ696 (sacubitril-valsartan) according to age: insights from PARADIGM-HF.

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Abstract

BACKGROUND:

The age at which heart failure develops varies widely between countries and drug tolerance and outcomes also vary by age. We have examined the efficacy and safety of LCZ696 according to age in the Prospective comparison of angiotensin receptor neprilysin inhibitor with angiotensin converting enzyme inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure trial (PARADIGM-HF).

METHODS:

In PARADIGM-HF, 8399 patients aged 18-96 years and in New York Heart Association functional class II-IV with an LVEF ≤40% were randomized to either enalapril or LCZ696. We examined the pre-specified efficacy and safety outcomes according to age category (years): <55 (n = 1624), 55-64 (n = 2655), 65-74 (n = 2557), and ≥75 (n = 1563).

FINDINGS:

The rate (per 100 patient-years) of the primary outcome of cardiovascular (CV) death or heart failure hospitalization (HFH) increased from 13.4 to 14.8 across the age categories. The LCZ696:enalapril hazard ratio (HR) was <1.0 in all categories (P for interaction between age category and treatment = 0.94) with an overall HR of 0.80 (0.73, 0.87), P < 0.001. The findings for HFH were similar for CV and all-cause mortality and the age category by treatment interactions were not significant. The pre-specified safety outcomes of hypotension, renal impairment and hyperkalaemia increased in both treatment groups with age, although the differences between treatment (more hypotension but less renal impairment and hyperkalaemia with LCZ696) were consistent across age categories.

INTERPRETATION:

LCZ696 was more beneficial than enalapril across the spectrum of age in PARADIGM-HF with a favourable benefit-risk profile in all age groups.