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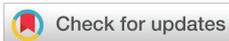
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## Research Article

# Sacubitril/Valsartan versus enalapril in nonischemic heart failure in Paradigm-Hf trial

## Abstract

**Background:** We compared the angiotensin receptor–neprilysin inhibitor LCZ696 (sacubitril/valsartan) with enalapril in patients who had nonischemic heart failure with a reduced ejection fraction.

**Methods:** In this double-blind trial, we randomly assigned 8442 patients with class II, III, or IV heart failure and an ejection fraction of 40% or less to receive either LCZ696 (at a dose of 200 mg twice daily) or enalapril (at a dose of 10 mg twice daily), in addition to recommended therapy. The primary outcome was a composite of death from cardiovascular causes or hospitalization for heart failure, but the trial was designed to detect a difference in the rates of death from cardiovascular causes.

**Results:** The trial was stopped early, according to prespecified rules, after a median follow up of 27 months, because the boundary for an overwhelming benefit with LCZ696 had been crossed. The ischemic patients were 5036 (60%) patients and non-ischemic patients were 3363 (40%) patients. In ischemic and in non-ischemic group the LCZ696 was superior to enalapril for reduce primary outcome and CV death ( $P < 0.001$ ). In LCZ696 group: the primary outcome had occurred in 339 patients (20.16 %) in the non-ischemic group and 575 patients (22.9 %) in the ischemic group ( $P: 0.03$ ). A total of 199 patients (11.8%) in non-ischemic group and 359 patients in ischemic group (14.3%) died from cardiovascular causes ( $P: 0.01$ ), and no significant difference between in CV death and primary outcome in enalapril group in the ischemic and non-ischemic patients

**Conclusions:** LCZ696 was superior to enalapril in reducing the risks of cardiovascular death and hospitalization for heart failure in ischemic and non-ischemic heart failure.

## Introduction

In PRADIGM–HF trial, A 8442 patients (mean age  $63.8 \pm 11.4$  years) with class II, III, or IV heart failure and an ejection fraction of 40% or less to receive either LCZ696 (at a dose of 200 mg twice daily) or enalapril (at a dose of 10 mg twice daily), in addition to recommended therapy.

Both groups received optimal medical therapy (93% on a beta blocker, 56.6 % on a mineralocorticoid antagonist) and 21.6 % of both groups receiving CRT or ICD. Over a median follow-up of 27 months. The primary outcome was a composite of death from cardiovascular causes or hospitalization for heart failure. The trial was stopped early, according to prespecified rules, after a median follow up of 27 months, because the boundary for an overwhelming benefit with LCZ696 had been crossed. At the time of study closure, the primary outcome had occurred in 914 patients (21.8%) in the LCZ696 group and 1117 patients (26.5%) in the enalapril group ( $P < 0.001$ ). A total of 711

patients (17.0%) receiving LCZ696 and 835 patients (19.8%) receiving enalapril died ( $P < 0.001$ ); of these patients, 558 (13.3%) and 693 (16.5%), respectively, died from cardiovascular causes ( $P < 0.001$ ). As compared with enalapril, LCZ696 also reduced the risk of hospitalization for heart failure by 21% ( $P < 0.001$ ) and decreased the symptoms and physical limitations of heart failure ( $P = 0.001$ ). The causes of heart failure in this trial was 60% ischemic and 40% non- ischemic [1].

The non-ischemic causes were idiopathic (N:1595), hypertension (N:968), infective/viral (N:185), alcoholic (N:158), valvular (N:110), Diabetic (N:66), drug related (N:30), Peripartum -related (N:14) and others (N:237) [2].

## Method

In this article we analysis the The primary outcome was a composite of death from cardiovascular causes or hospitalization for heart failure and Cardiovascular death



death between ischemic and idiopathic non-ischemic patients in PARADIGM Trial.

### Result

The ischemic patients were 5036 (60%) patients and non-ischemic patients were 3363 (40%) patients. In ischemic and in non-ischemic group the sacubitril/valsartan was superior to enalapril for reduce primary outcome and Cardiovascular death death (Table 1).

In a follow-up of 27 months the number needed to treat to prevent primary end points was 22 patients and to prevent one CV death was 37 patients in ischemic group

In non-ischemic group the number needed to treat to prevent primary end points was 21 patients and to prevent one CV death was 26 patients.

In LCZ696 group: the primary outcome had occurred in 339 patients (20.16 %) in the non-ischemic group and 575 patients (22.9 %) in the ischemic group (P: 0.03). A total of 199 patients (11.8%) in non-ischemic group and 359 patients in ischemic

group (14.3%) died from cardiovascular causes (P: 0.01). and no significant difference between in CV death and primary outcome in enalapril group in the ischemic and nonischemic patients (Table 2).

### Discussion

In our study involving patients with nonischemic and ischemic chronic heart failure and a reduced ejection fraction, the inhibition of both the angiotensin II receptor and neprilysin with LCZ696 was more effective in reducing the risk of death from cardiovascular causes or hospitalization for heart failure than enalapril. But LCZ696 more effective in nonischemic than ischemic causes.

**Table 2:** LCZ696 and Enalapril in ischemic and non-ischemic heart failure.

	LCZ696 Group			Enalapril Group		
	Ischemic	nonischemic	P value	Ischemic	Nonischemic	P Value
Primary outcome	575 -22.94%	339 (20.16%)	0.03	697 -27.55%	420 (24.97%)	0.07
CV death	359 (14.32%)	199 (11.84%)	0.01	430 -16.99%	263 -15.64%	0.2

**Table 1:** Primary outcome in ischemic and non-ischemic heart failure.

	Ischemic (5036)		p	Non-Ischemic ( 3363)		P
	Enalapril (2530)	LCZ696 (2506)		Enalapril (1682)	LCZ 696 (1681)	
Primary outcome	697 (27.55%)	575 (22.94%)	0.0002	420 (24.97%)	339 (20.16%)	0.0008
CV Death	430 (16.99%)	359 (14.32%)	0.008	263(15.64%)	199 (11.84%)	0.001

### References

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