

## BACKGROUND

- Left atrial (LA) enlargement may reflect elevated LA pressure and be associated with worse outcomes in heart failure and mildly reduced or preserved ejection fraction (HFmrEF/HFpEF).
- There are few reports on how LA size affects the response to neurohumoral modulation therapies.
- This study aimed to examine the efficacy of finerenone based on LA size at baseline in patients with HFmrEF/HFpEF enrolled in the FINEARTS-HF trial

## METHODS

- FINEARTS-HF was a randomized, double-blind, multicenter, event-driven trial, investigating the efficacy and safety of the non-steroidal mineralocorticoid receptor antagonist finerenone, compared to placebo in patients with HFmrEF/HFpEF.
- Key inclusion criteria were NYHA functional class II-IV, treatment with a diuretic for  $\geq 30$  days before randomization, a LVEF  $\geq 40\%$  with evidence of structural heart disease and an elevated natriuretic peptide level (NT-proBNP  $>300$  pg/mL [or BNP  $>100$  pg/mL] for patients in sinus rhythm or NT-proBNP  $>900$  pg/mL or BNP  $>300$  pg/mL for patients in atrial fibrillation).
- Structural heart disease was defined as meeting at least one of the following criteria: LA enlargement was defined as a left atrial diameter (LAD) of  $\geq 3.8$  cm, a left atrial area (LAA) of  $\geq 20$  cm<sup>2</sup>, or a left atrial volume index (LAVI) of  $>30$  mL/m<sup>2</sup>. Left ventricular hypertrophy was defined as a left ventricular mass index (LVMI) of  $\geq 115$  g/m<sup>2</sup> in males or  $\geq 95$  g/m<sup>2</sup> in females, or a septal or posterior wall thickness of  $\geq 1.1$  cm.
- Investigators were instructed to record the LAD, LAA, and LAVI on the electronic case report form as echocardiographic parameters, using the most recent measurements obtained within 12 months prior to screening.
- Among the 6,001 patients enrolled in the FINEARTS-HF trial, those with available measurements of LA size were stratified into quartiles. LAD was the most frequently measured parameter and was therefore used as the primary measure for assessment. If LAD was unavailable, LAVI, the second most frequently measured parameter, was used. In cases where both LAD and LAVI were unavailable, LAA was used.
- The primary outcome was the composite of cardiovascular death and total (first and recurrent) HF events.

## RESULTS

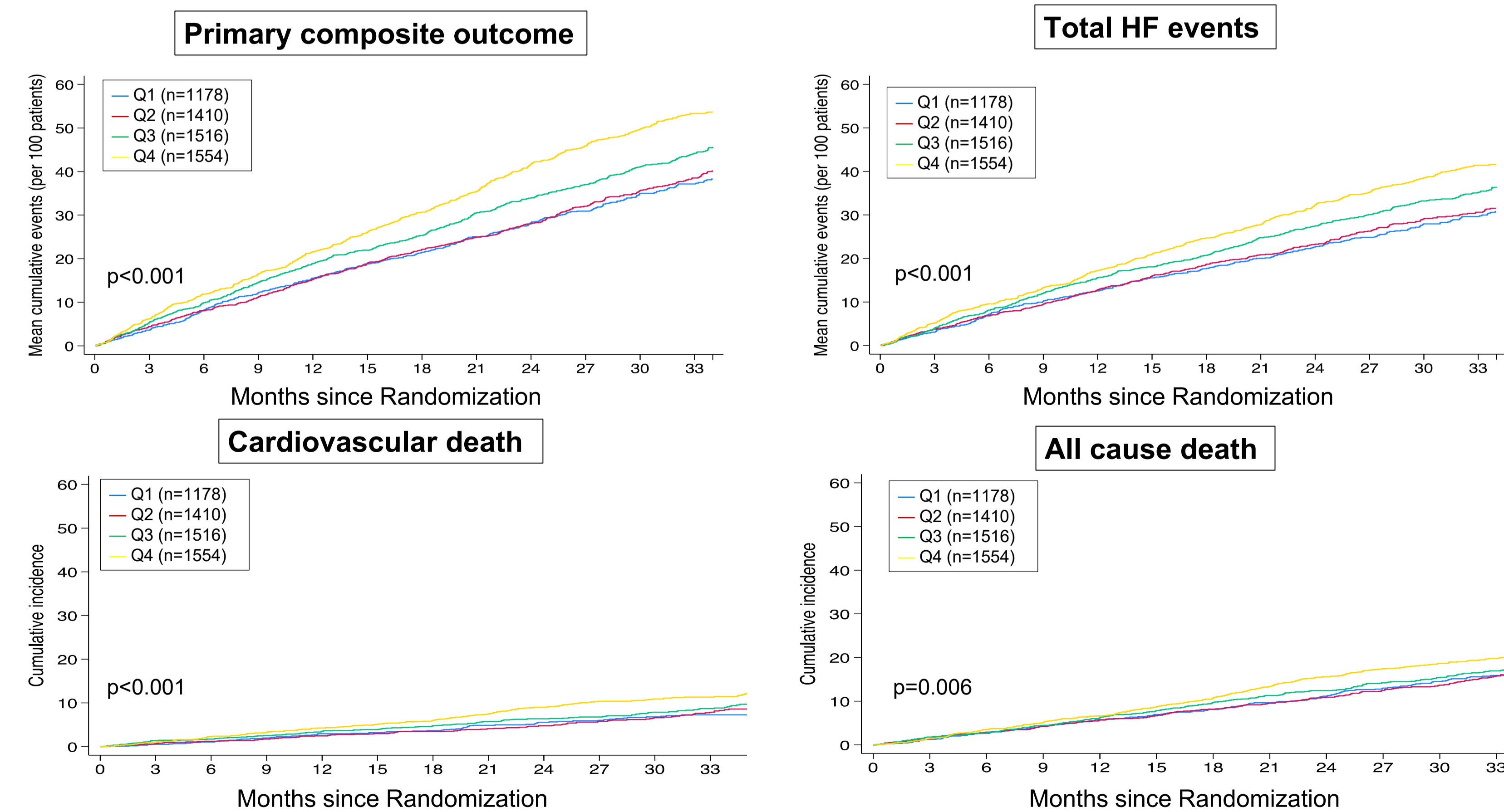
- The values for each LA parameter, stratified by quartile, are as follows:
- Patients in lowest quartile (Q1) had an LAD of  $< 4.1$  cm, an LAA of  $< 22.0$  cm<sup>2</sup>, and an LAVI of  $< 36.0$  mL/m<sup>2</sup>.
  - Patients in quartile 2 (Q2) had an LAD of  $\geq 4.1$  cm and  $< 4.5$  cm, an LAA of  $\geq 22.0$  cm<sup>2</sup> and  $< 25.4$  cm<sup>2</sup>, and an LAVI of  $\geq 36.0$  mL/m<sup>2</sup> and  $< 44.0$  mL/m<sup>2</sup>.
  - Patients in quartile 3 (Q3) had an LAD of  $\geq 4.5$  cm and  $< 5.0$  cm, an LAA of  $\geq 25.4$  cm<sup>2</sup> and  $< 30.0$  cm<sup>2</sup>, and an LAVI of  $\geq 44.0$  mL/m<sup>2</sup> and  $< 55.5$  mL/m<sup>2</sup>.
  - Patients in highest quartile (Q4) had an LAD of  $\geq 5.0$  cm, an LAA of  $\geq 30.0$  cm<sup>2</sup>, and an LAVI of  $\geq 55.5$  mL/m<sup>2</sup>.

## RESULTS

**Table : Baseline characteristics according to LA size (quartile) in the FINEARTS-HF**

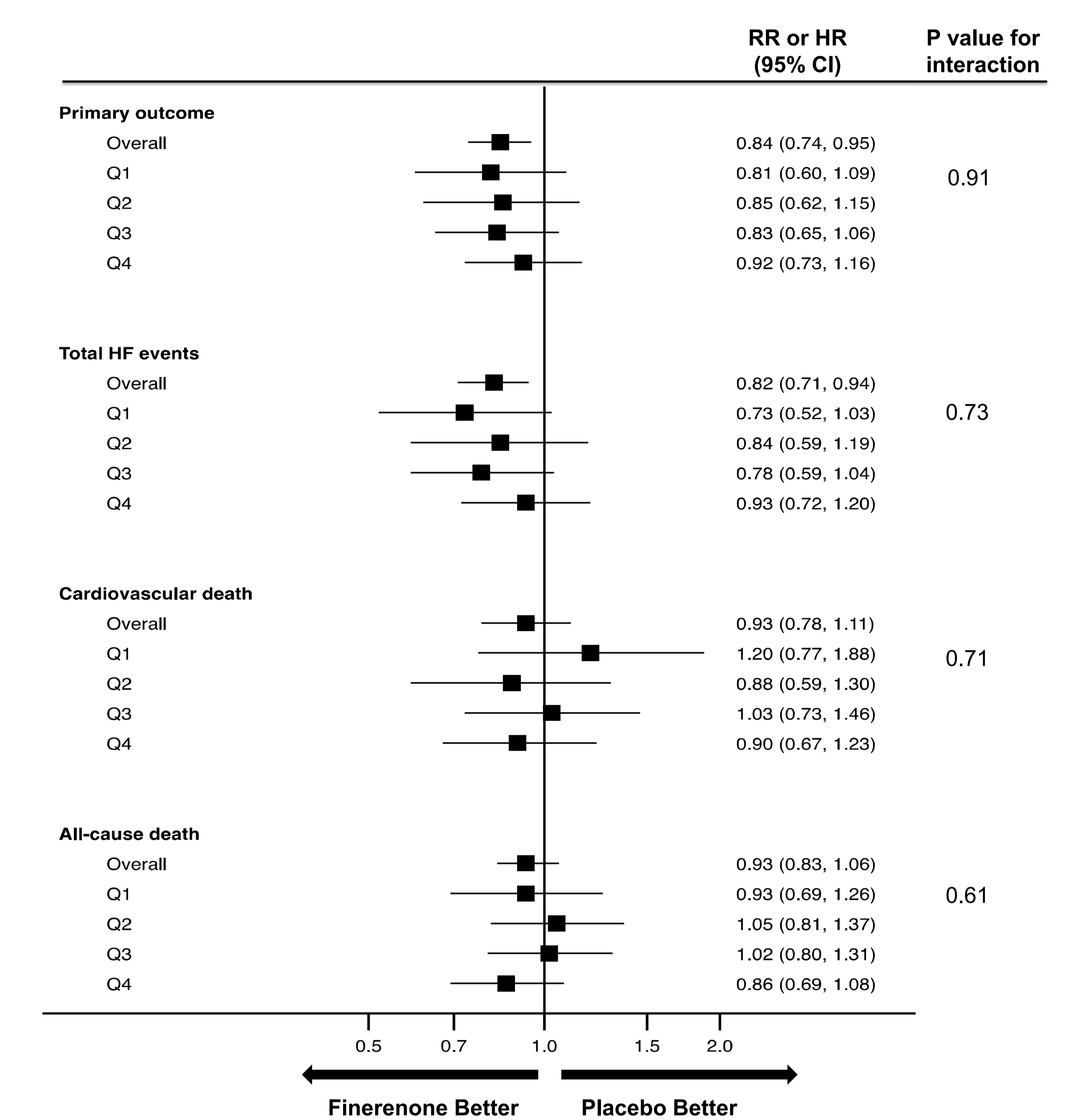
	Lowest quartile (Q1) (n = 1178)	Quartile 2 (Q2) (n = 1410)	Quartile 3 (Q3) (n=1516)	Highest quartile (Q4) (n=1554)	p-value
Age (years)	71.1 $\pm$ 10.4	71.8 $\pm$ 9.7	72.3 $\pm$ 9.4	72.4 $\pm$ 9.3	0.002
Male – no (%)	552 (46.9)	717 (50.9)	860 (56.7)	958 (61.7)	<0.001
NYHA functional class III/IV – no (%)	321 (27.3)	436 (30.9)	476 (31.4)	537 (34.6)	0.004
KCCQ total symptom score	68.4 $\pm$ 24.4	67.6 $\pm$ 23.5	66.6 $\pm$ 23.9	65.8 $\pm$ 23.9	0.02
Systolic blood pressure (mmHg)	129.3 $\pm$ 15.3	129.0 $\pm$ 15.2	130.1 $\pm$ 15.4	128.8 $\pm$ 15.7	0.10
Body mass index (kg/m <sup>2</sup> )	28.6 $\pm$ 5.7	29.9 $\pm$ 6.3	30.1 $\pm$ 6.1	30.8 $\pm$ 6.2	<0.001
eGFR (ml/min/1.73m <sup>2</sup> )	63.0 $\pm$ 20.4	62.8 $\pm$ 20.1	61.8 $\pm$ 19.4	61.5 $\pm$ 19.2	0.12
NT-proBNP (pg/mL)	651 (300-1624)	804 (372-1708)	1119 (520-1994)	1359 (789-2354)	<0.001
<b>Echocardiography findings</b>					
LVEF (%)	53.5 $\pm$ 8.1	52.9 $\pm$ 7.6	52.5 $\pm$ 7.8	51.7 $\pm$ 7.9	<0.001
LVEF $\geq 50\%$ – no (%)	795 (67.7)	925 (65.7)	968 (63.9)	914 (58.9)	<0.001
Left atrium dimension (cm)	3.7 $\pm$ 0.4	4.3 $\pm$ 0.1	4.7 $\pm$ 0.1	5.5 $\pm$ 0.7	<0.001
Left atrial area (cm <sup>2</sup> )	22.2 $\pm$ 7.3	24.9 $\pm$ 5.6	27.0 $\pm$ 5.6	31.3 $\pm$ 7.9	<0.001
Left atrial volume index (mL/m <sup>2</sup> )	36.0 $\pm$ 13.0	42.1 $\pm$ 13.0	49.1 $\pm$ 13.7	62.3 $\pm$ 24.1	<0.001
Left ventricular mass index (g/m <sup>2</sup> )	111 $\pm$ 36	120 $\pm$ 42	124 $\pm$ 44	133 $\pm$ 50	<0.001
Left ventricular interventricular septum thickness (cm)	1.2 $\pm$ 0.4	1.2 $\pm$ 0.3	1.2 $\pm$ 0.4	1.2 $\pm$ 0.3	<0.001
Left ventricular posterior wall thickness (cm)	1.1 $\pm$ 0.3	1.1 $\pm$ 0.2	1.1 $\pm$ 0.4	1.1 $\pm$ 0.2	0.01
<b>Medical history – no (%)</b>					
Hypertension	1,026 (87.1)	1,251 (88.7)	1,382 (91.2)	1,368 (88.0)	0.005
Diabetes mellitus	460 (39.3)	609 (43.4)	642 (42.4)	589 (37.9)	0.008
Myocardial infarction	348 (29.5)	391 (27.7)	381 (25.1)	338 (21.8)	<0.001
AF (history)	405 (34.4)	639 (45.3)	903 (59.6)	1,141 (73.4)	<0.001
Any prior hospitalization for HF	733 (62.2)	856 (60.7)	899 (59.3)	934 (60.1)	0.47
<b>Treatments – no (%)</b>					
Beta-blocker	960 (81.4)	1,208 (85.5)	1,305 (85.9)	1,353 (87.0)	0.007
ACEi or ARB	911 (77.3)	1,129 (80.1)	1,210 (79.8)	1,251 (80.5)	0.007
ARNI	129 (11.0)	116 (8.2)	114 (7.5)	122 (7.9)	0.008
SGLT2i	173 (14.7)	191 (13.6)	191 (12.6)	200 (12.9)	0.40
Loop diuretics	982 (83.4)	1,212 (86.0)	1,342 (88.5)	1,400 (90.1)	<0.001

**Figure : Cumulative incidence of clinical outcomes according to quartile of LA size**



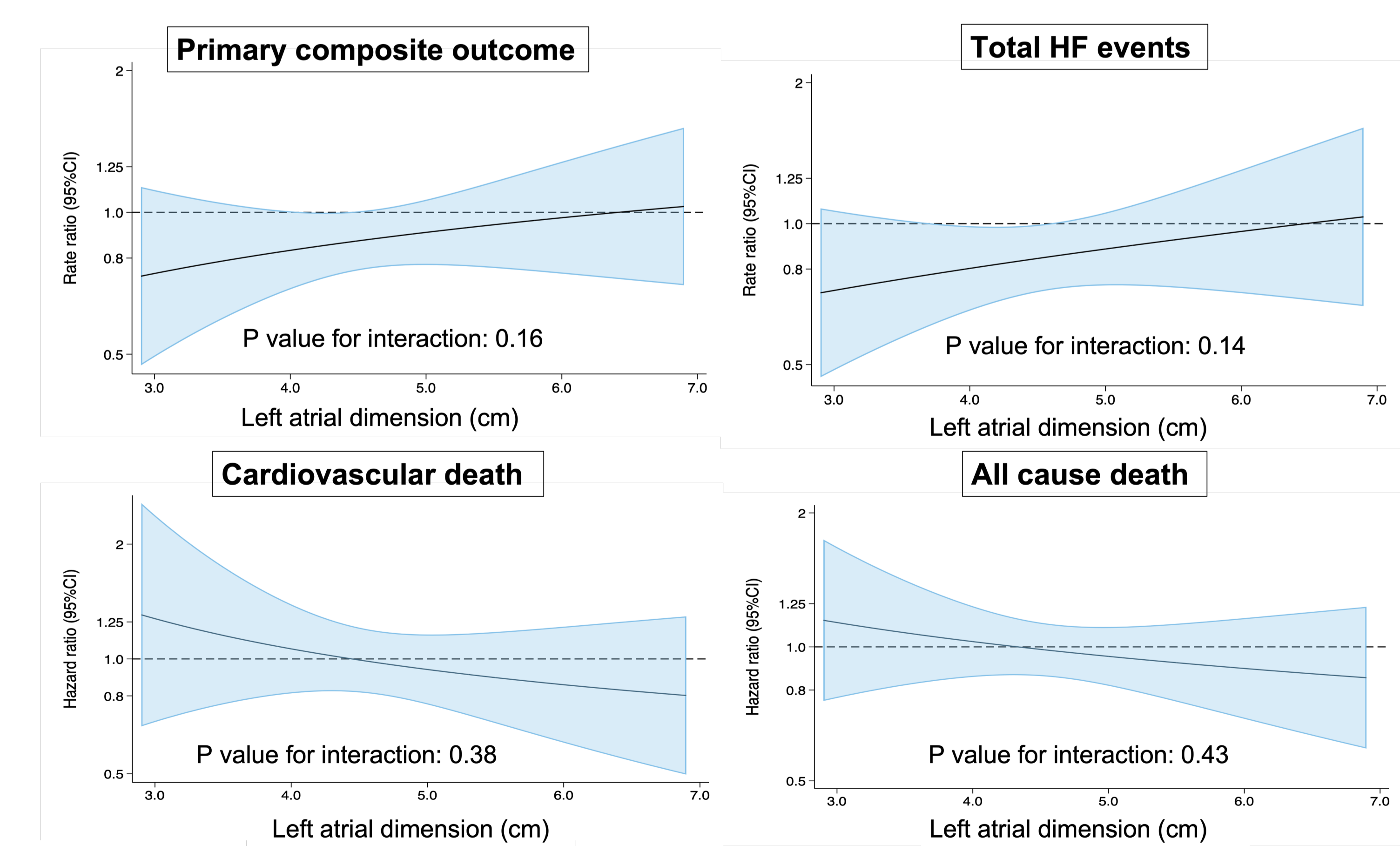
The risk of the primary composite outcome, the components of primary composite outcome, and all cause death increased with LA size.

**Figure : Effect of finerenone compared to placebo according to LA size**



No test for LA size-by-treatment interaction was significant.

**Figure : Effect of finerenone compared to placebo according to LA diameter**



The treatment effect of finerenone was maintained across the spectrum of LA diameter when assessed as a continuous variable.

## CONCLUSION

In FINEARTS-HF, finerenone was efficacious, irrespective of LA size, in patients with HFmrEF/HFpEF.