Effect of the Cardiac Myosin Activator Omecamtiv Mecarbil on Ventricular Arrhythmias, Cardiac Arrest, and Sudden Death in HFrEF: the GALACTIC-HF Trial

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Chicago, 16 November, 2024

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GALACTIC-HF

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DISCLOSURES

Alberto Foà has no relevant disclosures

Funding: the Global Approach to Lowering Adverse Cardiac Outcomes through Improving Contractility in Heart Failure (**GALACTIC-HF**) trial was funded by Amgen, Cytokinetics and Servier.

GALACTIC-HF

BACKGROUND

- Omecamtiv mecarbil (OM) is a novel selective cardiac myosin activator with unique characteristics: increases cardiac contractility without altering the intracellular calcium concentration

- In the GALACTIC-HF trial, OM has been shown to benefit individuals with HFrEF but the clinical experience of cardiac myosin activators and risk of life-threatening ventricular arrhythmias is limited

- We investigated the effects of OM on incidence of ventricular arrhythmia (VT or VF), cardiac arrest, and sudden death (SD) in the GALACTIC-HF trial

GALACTIC-HF

METHODS

- GALACTIC-HF is a placebo-controlled trial that tested OM in participants with symptomatic chronic HF and LVEF ≤ 35%
- Ventricular arrhythmia (VA) and cardiac arrest were investigator-reported adverse events, SD was centrally adjudicated
- The effect of OM, compared with placebo, on the composite of the first occurrence of serious VA, cardiac arrest, or SD was examined using Cox proportional hazards models
- Subgroups of interest were participants with LVEF ≤ the median and patients with severe HF according to the ESC-HFA criteria*

*All the following: NYHA class III/IV; LVEF ≤ 30%; one HF hospitalization within the previous 6 months or participants hospitalized at the time of trial enrollment

GALACTIC-HF

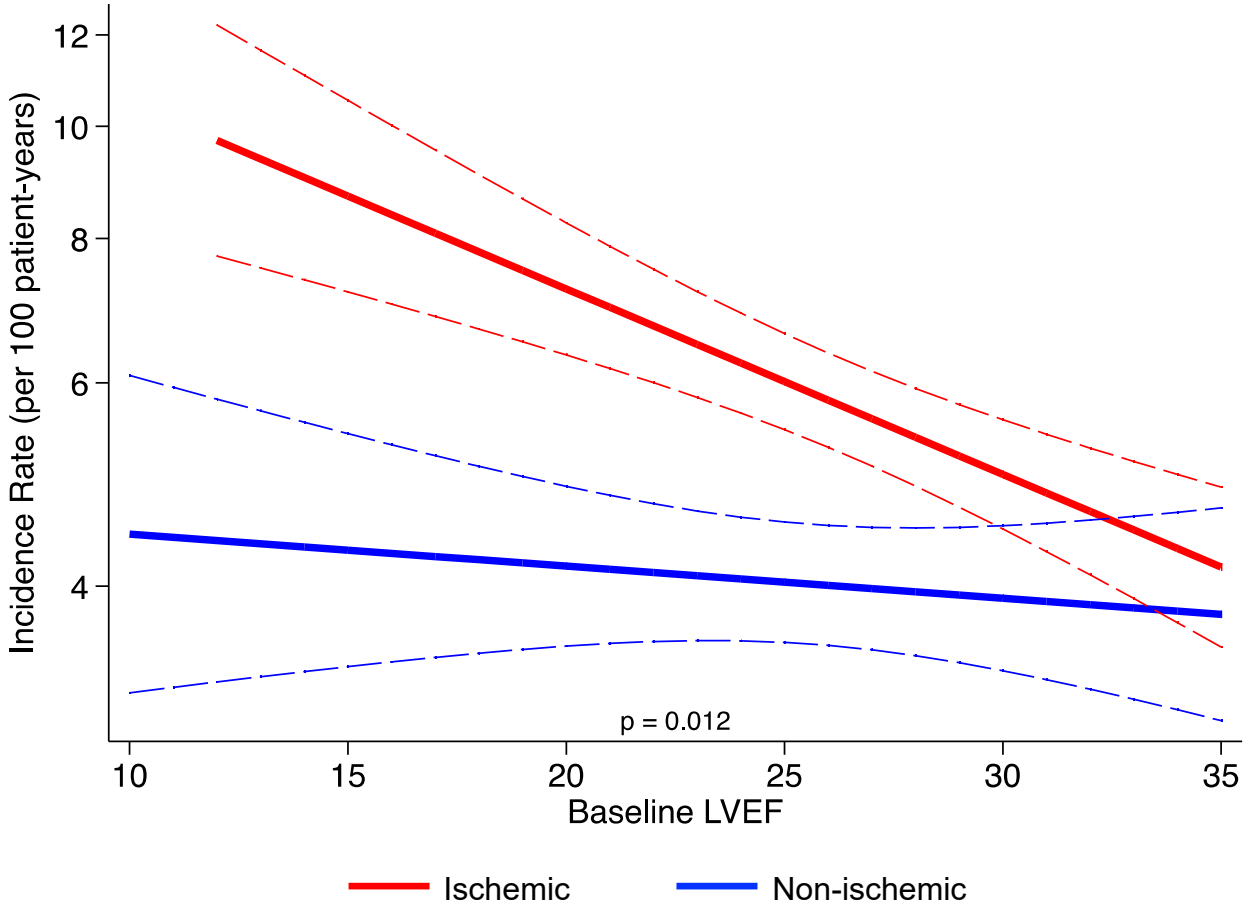
BASELINE CHARACTERISTICS	No VA / cardiac arrest / SD (N=7526)	VA / cardiac arrest / SD (N=706)	P value
Age	64.5 ± 11.4	64.9 ± 10.9	0.35
Male	5880 (78.1%)	603 (85.4%)	<0.001
In-patient setting	1908 (25.4%)	176 (24.9%)	0.80
Ischemic etiology	3979 (52.9%)	436 (61.8%)	<0.001
Previous ventricular arrhythmia	1703 (22.6%)	251 (35.6%)	<0.001
LVEF	26.6 ± 6.3	26.0 ± 6.4	0.019
NYHA class			
II	4032 (53.6%)	336 (47.6%)	0.008
III	3272 (43.5%)	344 (48.7%)	
IV	222 (2.9 %)	26 (3.7 %)	
eGFR - ml/min/1.73m2	60.6 ± 21.9	57.3 ± 21.3	<0.001
NT-proBNP	1947 [962-3929]	2697 [1396-5240]	<0.001
Troponin	26 [13-50]	35 [20-64]	<0.001
Systolic blood pressure - mmHg	116.7 ± 15.4	114.0 ± 14.5	<0.001
ACEi/ARB/ARNI	6568 (87.3%)	591 (83.7%)	0.007
CRT	1009 (13.4%)	149 (21.1%)	<0.001
ICD	2323 (30.9%)	291 (41.2%)	<0.001

RESULTS

Independent predictors of VA /cardiac arrest / SD in the overall GALACTIC-HF population

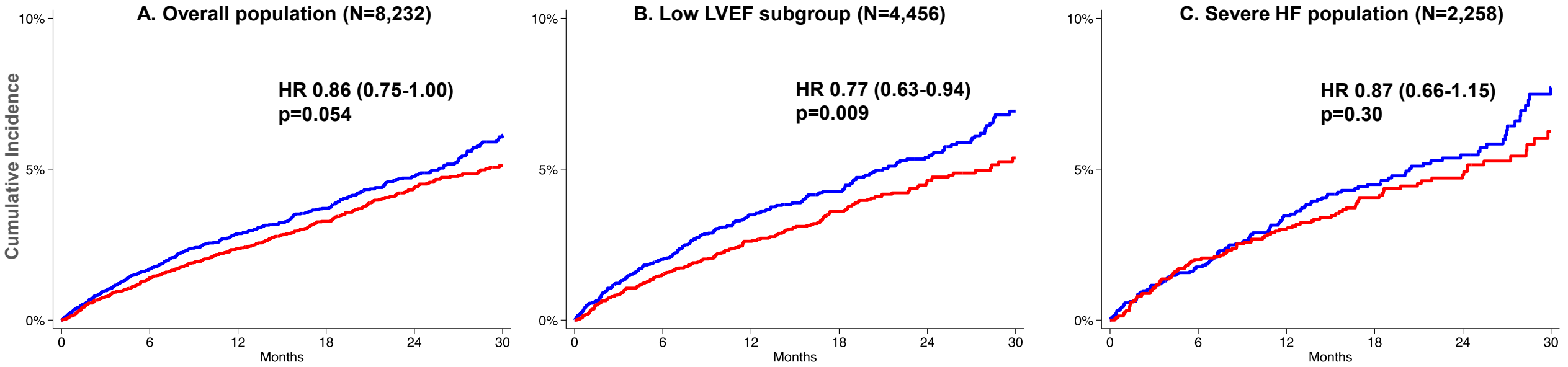
VARIABLE	HR (95% CI)	|z|	P value
NT-proBNP (doubling)	1.23 (1.17-1.30)	7.55	<0.001
Troponin (doubling)	1.21 (1.15-1.27)	7.10	<0.001
History of VA	1.53 (1.30-1.80)	5.10	<0.001
SBP (per 10 mmHg decrease)	1.13 (1.07-1.19)	4.69	<0.001
BMI (per 5 Kg/m2 increase)	1.14 (1.07-1.21)	4.16	<0.001
Ischemic etiology	1.35 (1.16-1.57)	3.80	<0.001
Amiodarone	1.36 (1.13-1.64)	3.25	0.001
Male sex	1.39 (1.12-1.72)	3.04	0.002
CRT	1.26 (1.04-1.52)	2.36	0.018
Omecamtiv mecarbil	0.85 (0.73-0.99)	2.12	0.034

Incident rates according to etiology

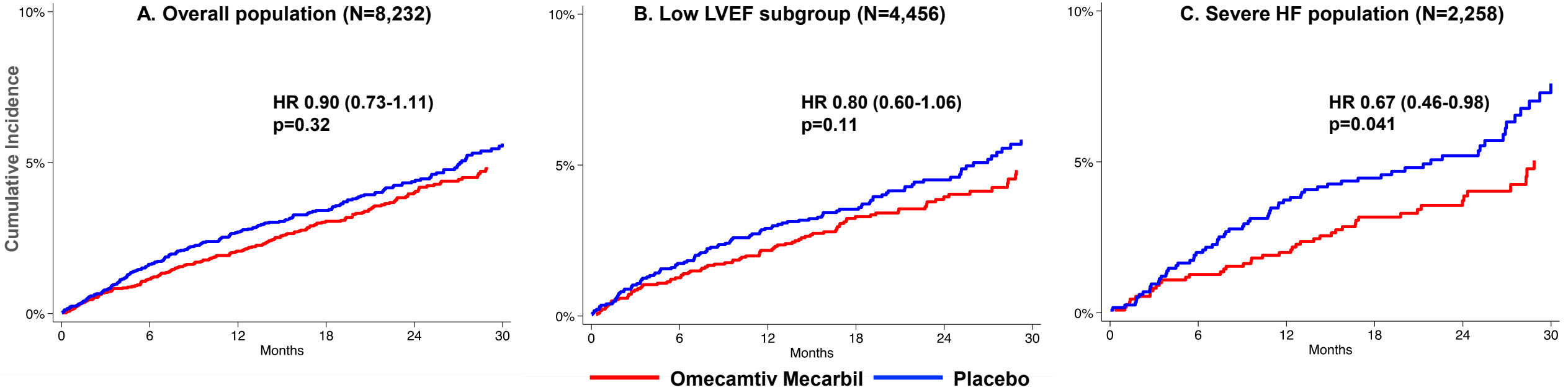


GALACTIC-HF

SERIOUS VENTRICULAR ARRHYTHMIA / CARDIAC ARREST / SUDDEN DEATH



SUDDEN DEATH



CONCLUSIONS

- In the GALACTIC-HF trial, randomization to OM was associated with a borderline reduced risk **of the composite outcome** of serious VA, cardiac arrest or SD
- Among participants with an LVEF ≤ the median, OM was associated with a reduced risk of the composite outcome
- In patients with severe HF according to the ESC-HFA criteria, OM was associated with a reduced risk of SD

Overall, these findings reinforce the clinical benefits and safety of OM in patients with HFrEF, especially in those with more advanced conditions