Efficacy and Safety of Omecamtiv Mecarbil in Heart Failure with Reduced Ejection Fraction According to Age: the GALACTIC-HF Trial

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BACKGROUND

Older age is associated with a high prevalence of comorbidities and worse cardiovascular (CV) outcomes in patients with heart failure with reduced ejection fraction (HFrEF). Omecamtiv mecarbil (OM), a selective cardiac myosin activator, is relatively hemodynamically neutral with limited extra-cardiac effects, and thus may be well-tolerated in older individuals. The safety profile and clinical benefits of OM across the age spectrum remain uncertain.

AIMS

We aimed to assess the CV outcomes, treatment response and tolerability to OM according to age, in patients enrolled in the GALACTIC-HF trial.

METHODS

- Patients were categorized using predefined age groups (<65 or ≥65 years).
- Primary outcome: CV death or first HF event (hospitalization or urgent visit for HF).
- The association between age and outcomes was analyzed using Cox proportional hazards models.
- We examined the treatment effect of OM vs placebo for the primary endpoint as well as safety outcomes according to age groups.
- The treatment effect of OM vs. placebo was further analyzed in patients with severe HF (LVEF ≤30%, NYHA Class III/IV, HF hospitalization within 6 months), according to age groups.

RESULTS

GALACTIC-HF is a global, multicenter, randomized clinical trial testing OM against placebo in patients with symptomatic HF, an LVEF ≤35% and elevated natriuretic peptides. Patients aged <18 or >85 years were excluded.

Among 8,232 patients included (mean age 64.5±11.4 years, 21% women), 4,485 (54.5%) were aged ≥65 years.

Table 1. Patient's Baseline Characteristics According to Age Categories

	Age <65 years (n=3,747)	Age ≥65 years (n=4,485)
Age	54.6 ± 8.2	72.8 ± 5.4
Women	737 (19.7)	1,012 (22.6)
NYHA III/IV	1,650 (44.0)	2,214 (49.4)
BMI	29.6 ± 6.8	27.6 ± 5.4
SBP	115.3 ± 15.4	117.4 ± 15.2
eGFR	66.8 [53.4, 82.6]	51.8 [39.3, 65.9]
Ischemic HD	1,632 (43.6)	2,783 (62.1)
Type 2 DM	1,392 (37.1)	1,917 (42.7)
AFF	735 (19.6)	1,510 (33.7)
LVEF	25.8 ± 6.4	27.2 ± 6.1
NT-proBNP	1,604 [784, 3,282]	2,423 [1,238, 4,780]
OM arm	1,874 (50.0)	2,246 (50.1)
ACEi, ARB or ARNi	3,333 (89.0)	3,826 (85.3)
MRA	3,112 (83.1)	3,285 (73.2)
β-blocker	3,583 (95.6)	4,180 (93.2)
SGLT2i	118 (3.1)	100 (2.2)

Figure 1. Event Rates and Hazard ratios of CV Death or HF Event Across the Age Spectrum

	Events %	Event rate (95% CI)	Unadjusted HR (95% CI)	Adjusted* HR (95% CI)
Age <65 yrs	33.6	21.4 (20.3-22.6)	1 (reference)	1 (reference)
Age ≥65 yrs	41.6	28.8 (27.5-30.1)	1.31 (1.22-1.41)	1.10 (1.02-1.20)

*Adjusted for sex, BMI, race, AFF, type 2 DM, ischemic etiology, COPD, cerebrovascular disease, eGFR, LVEF, NYHA, SBP, heart rate, ACEi, ARB or ARNI, beta-blocker, MRA, SGLT2 inhibitor, CRT, ICD, treatment arm.

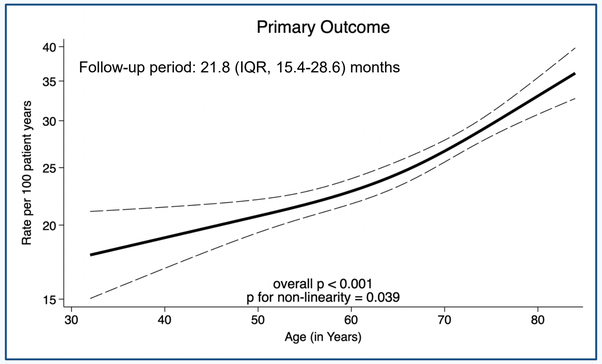
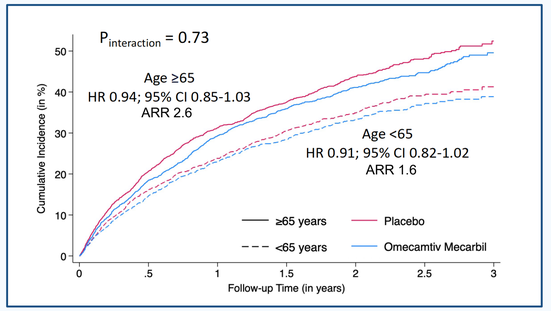


Figure 2. Efficacy of Omecamtiv Mecarbil According to Age Category, (A) in the Overall Population, (B) Among Patients with Severe HF

Overall Population



Patients with Severe HF

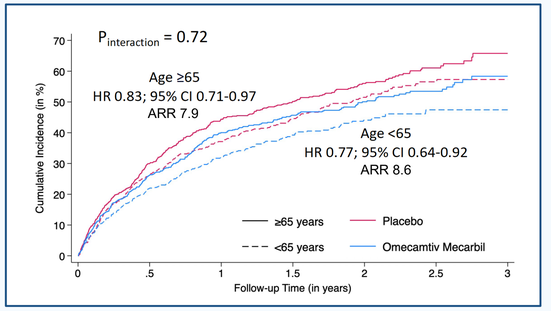


Table 2. Safety Outcomes According to Age Categories

	Age <65 years		Age ≥65 years		P interaction
	Placebo (N=1,873)	OM (N=1,874)	Placebo (N=2,239)	OM (N=2,246)	
Any Adverse Event Requiring Treatment Discontinuation					
%	10.2	10.3	11.6	11.0	0.67
OR (95% CI)	1.01 (0.81-1.24)		0.94 (0.79-1.14)		
Adverse Event: Ventricular Tachyarrhythmia					
%	9.0	8.3	7.7	7.6	0.66
OR (95% CI)	0.92 (0.72-1.17)		0.99 (0.79-1.25)		
Adjudicated Major Cardiac Ischemic Events					
%	4.2	4.6	4.9	5.1	0.76
OR (95% CI)	1.10 (0.81-1.51)		1.04 (0.79-1.36)		
Adjudicated Stroke					
%	2.6	1.6	2.9	2.1	0.65
OR (95% CI)	0.62 (0.39-0.98)		0.71 (0.48-1.04)		

LIMITATIONS

- *Post hoc* analysis of a clinical trial.
- Patients of advanced age (>85 years) were excluded, and the age categories, although predefined, were arbitrary.
- Severe HF was defined post hoc, patients with a clinically unstable condition were excluded.

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CONCLUSIONS

In this post hoc analysis of the GALACTIC-HF trial, older individuals faced higher risks of CV events. Treatment with OM was safe irrespective of age, and reduced the risk of CV death or first HF event across the age spectrum, especially in those with severe HF, suggesting the benefit/risk profile of OM is as favorable in older as in younger patients.

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