

Menopausal Status and Clinical Outcomes in Women with Heart Failure with Reduced Ejection Fraction: the GALACTIC-HF Trial

Maria A. Pabon, Muthiah Vaduganathan, Brian L. Claggett, Xiaowen Wang, G. Michael Felker, Marco Metra, Rafael Diaz, John J.V. McMurray, Fady I. Malik, John R. Teerlink, Scott D. Solomon
Cardiovascular Division, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

Background

- Mechanisms driving disease progression and potential responsiveness to investigational therapies may theoretically differ among women with heart failure (HF) based on menopausal status.
- Few data are available describing the clinical course of premenopausal and postmenopausal women with HF.

Study Aim

- To describe the differences in baseline characteristics, clinical outcomes, and response to omecamtiv mecarbil in premenopausal and postmenopausal women participants of the GALACTIC-HF trial.

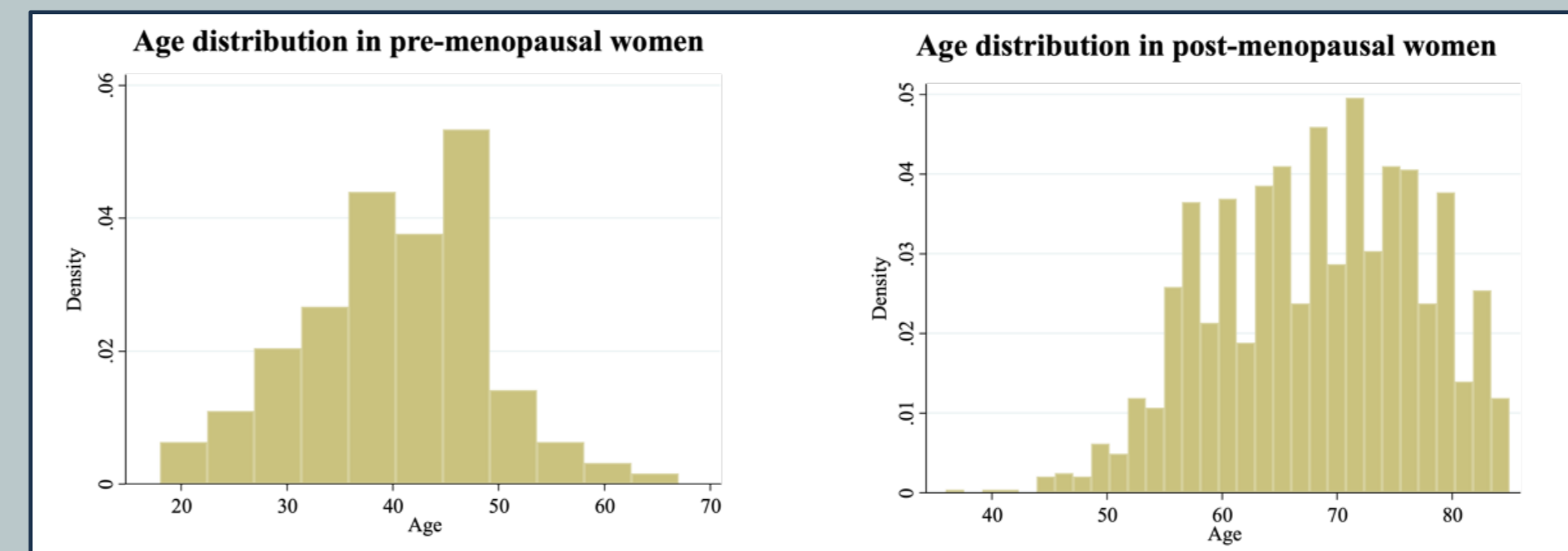
Methods

- The GALACTIC-HF trial randomized patients with HFrEF and LVEF of 35% or less to omecamtiv mecarbil or placebo.
- Menopausal status was collected at randomization. When menopausal status was unknown/unreported, menopausal status was inferred based on the expected distribution of age at menopause in the general population.
- Risk of primary endpoint (worsening HF event or CV death), was compared among women by menopausal status using Cox regression models adjusted for clinical covariates. Treatment effect heterogeneity was evaluated by menopausal status.

Baseline characteristics by menopausal status of women participants of GALACTIC-HF

Characteristic	Premenopausal n=143	Postmenopausal n=1544	p-value
Age — years.	40.3 ± 8.7	68.2 ± 8.9	< 0.001
Race or ethnic group — no.(%)			< 0.001
White	64 (44.8%)	1151 (74.5%)	
Asian	17 (11.9%)	109 (7.1%)	
Black	41 (28.7%)	133 (8.6%)	
Other	21 (14.7%)	151 (9.8%)	
Inpatient setting — no. (%)	33 (23.1%)	368 (23.8%)	0.84
Clinical features — no. (%)			
Atrial fibrillation or flutter	21 (14.7%)	616 (39.9%)	< 0.001
Type 2 diabetes mellitus	36 (25.2%)	635 (41.1%)	< 0.001
Ischemic heart failure	21 (14.7%)	689 (44.6%)	< 0.001
Body mass index	31.1 ± 9.6	28.3 ± 6.7	< 0.001
LVEF — %	25.9 ± 6.2	27.3 ± 6.2	0.009
NYHA classification— no. (%)			0.11
II	82 (57.3%)	760 (49.2%)	
III/IV	61 (42.7%)	7384 (50.7%)	
Median NT-proBNP (IQR)	1190 [579, 2699]	2196 [1068, 4532]	<0.001
Median troponin I (IQR)	10.0 [10.0, 27.0]	20.0 [10.0, 44.0]	< 0.001
Median eGFR	77.1 ± 25.0	53.9 ± 20.1	< 0.001
Heart Failure Therapies			
ACEi/ARB/ARNI+BB+MRA	93 (65.0%)	962 (62.3%)	0.52
ACE inhibitor	66 (46.2%)	694 (44.9%)	0.78
ARB	19 (13.3%)	375 (24.3%)	0.003
ARNI	36 (25.2%)	262 (17.0%)	0.014
Beta-blocker	138 (96.5%)	1443 (93.5%)	0.15
MRA	116 (81.1%)	1172 (75.9%)	0.16
ICD	34 (23.8%)	373 (24.2%)	0.92

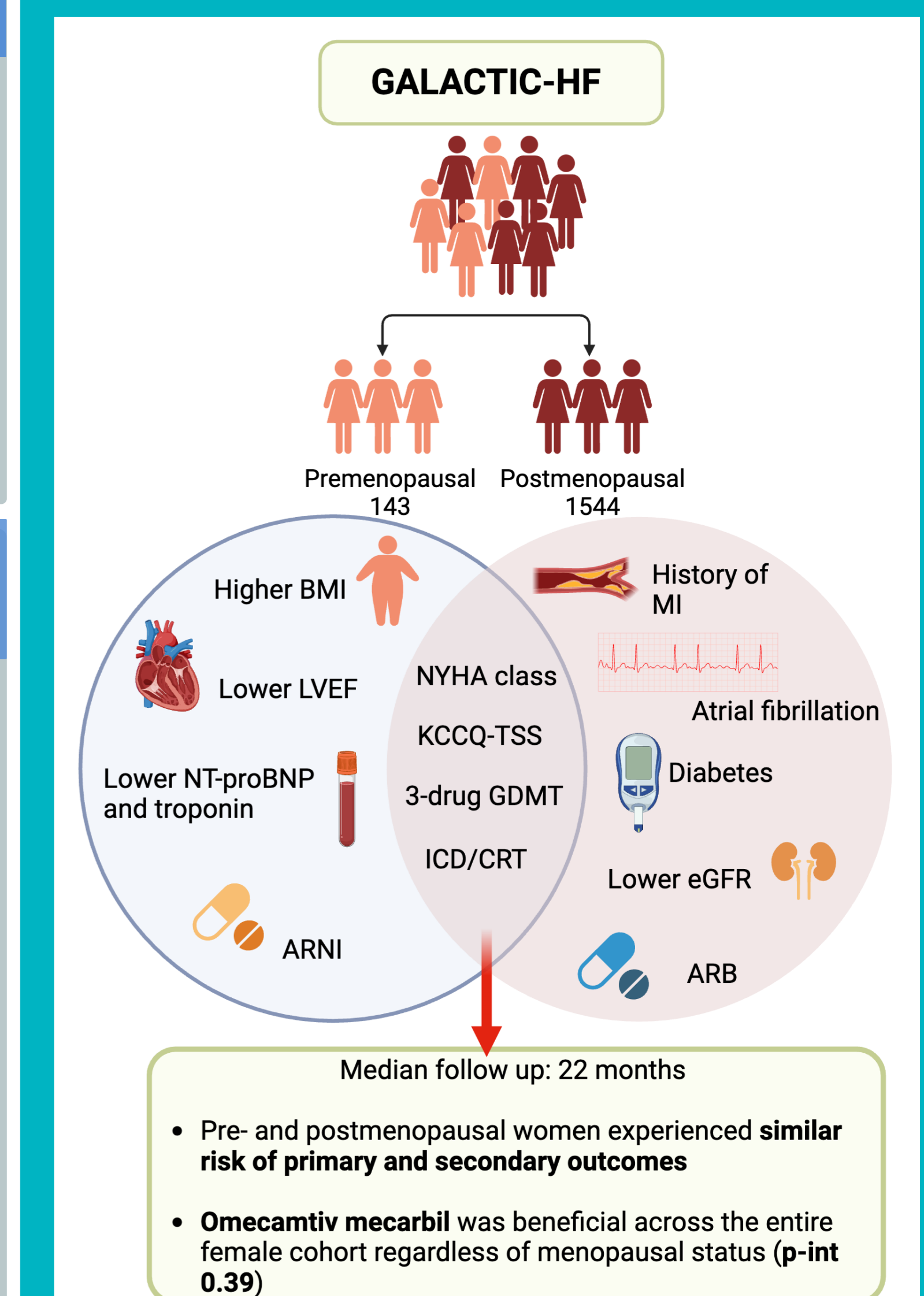
Age distribution in premenopausal and postmenopausal women at baseline



Primary and secondary outcomes by menopausal status

Outcome	Premenopausal n=143	Postmenopausal n=1544	p-value
Primary outcome	45 events (21.8 per 100 patient yrs.) (REF)	538 events (22.6 per 100 patient yrs.) HR= 0.83 (0.55-1.26)	0.38
Cardiovascular death	15 events (8.6 per 100 patient yrs.) (REF)	293 events (10.2 per 100 patient yrs.) HR= 0.75 (0.39, 1.41)	0.37
First HF hospitalization	14 events (8.9 per 100 patient yrs.) (REF)	403 events (16.3 per 100 patient yrs.) HR= 0.99 (0.60, 1.62)	0.96
Death from any cause	17 events (9.7 per 100 patient yrs.) (REF)	381 events (13.2 per 100 patient yrs.) HR= 0.69 (0.39, 1.19)	0.18
Heart failure event	16 events (10.2 per 100 patient yrs.) (REF)	421 events (17.2 per 100 patient yrs.) HR= 0.97 (0.60, 1.57)	0.90

Conclusion:



Disclosure information: The GALACTIC-HF study was sponsored by Cytokinetics.

In this high-risk HFrEF cohort, premenopausal women experienced similar rates of adverse cardiovascular outcomes as postmenopausal women despite younger age, fewer comorbidities, and lower cardiac biomarkers. The treatment benefits of omecamtiv mecarbil in reducing the risk of HF event or CV death did not appear to differ by menopausal status.