The Impact of Tricuspid Regurgitation on Clinical Outcomes in GALACTIC-HF

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Conflicts of interest

- Funded by Amgen, Inc., Cytokinetics, Inc., and Servier Laboratories.

- Speaker disclosures:

M. Adamo received speaker fees from Abbott Vascular and Medtronic

Background

GALACTIC-HF

- Tricuspid regurgitation (TR) is common in patients with heart failure (HF)[1,2]
- Recent studies reported a possible prognostic impact of TR in HF patients, but they are limited by a retrospective and observational design. [3-5]
- Data from selected and fully characterized patients with heart failure with reduced ejection fraction (HFrEF) are lacking
- Global Approach to Lowering Adverse Cardiac outcomes Through Improving Contractility in Heart Failure (GALACTIC-HF) is the largest contemporary trial of HFrEF patients with information on patients with TR[6]

[1]Chioncel et al. *Eur J Heart Fail.* 2017;19(12):1574-1585; [2]Chioncel et al. *Eur J Heart Fail.* 2019;21(11):1338-1352.
[3]Messika-Zeitoun at al. *Eur J Heart Fail*. 2020;22(10):1803-1813; [4]Chorin et al. *Eur Heart J Cardiovasc Imaging.* 2020;21(2):157-165
[5]Benfari et al. *Circulation.* 2019;140(3):196-206. ; [6]Teerlink et al. *N Engl J Med*. 2021 Jan 14;384(2):105-116.

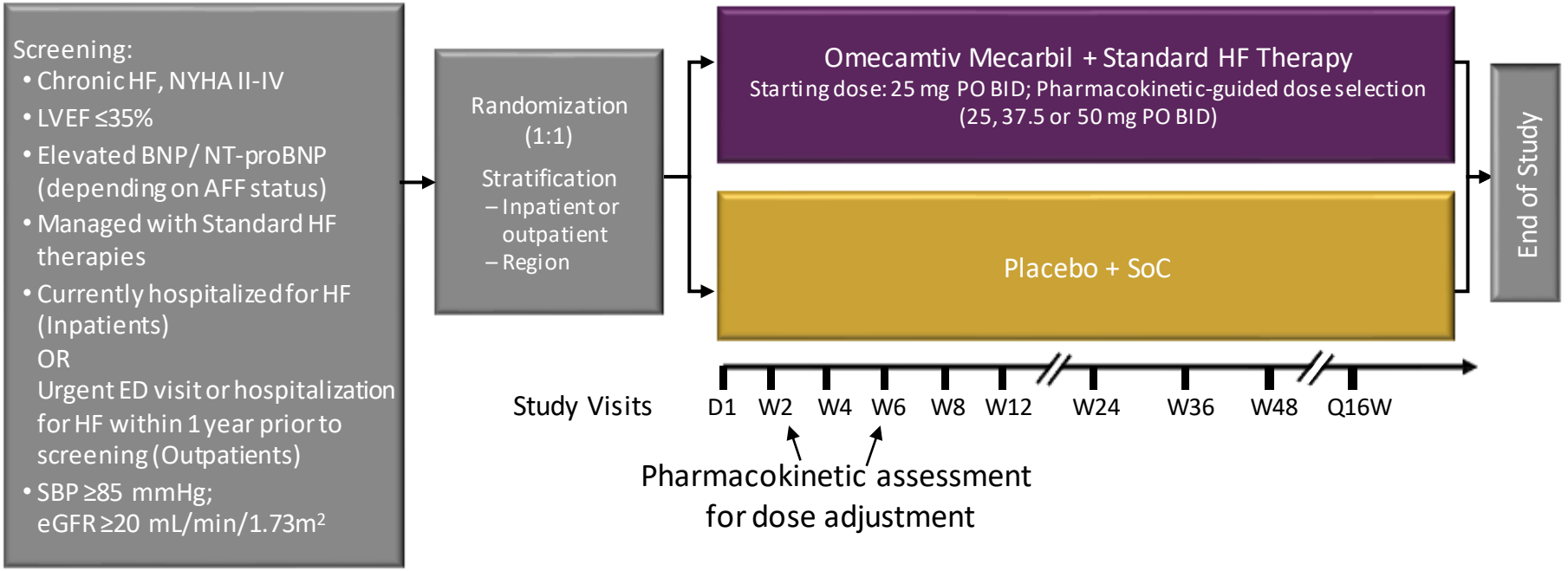
Objectives

- To evaluate whether **moderate/severe TR may have an impact on the effectiveness of omecamtiv mecarbil** versus placebo

- To explore the **impact of mild and moderate/severe TR on clinical outcomes** of patients with HFrEF enrolled in the GALACTIC-HF trial

GALACTIC-HF design

Multicenter, international, randomized, double-blind, placebo-controlled, event-driven Phase 3 study

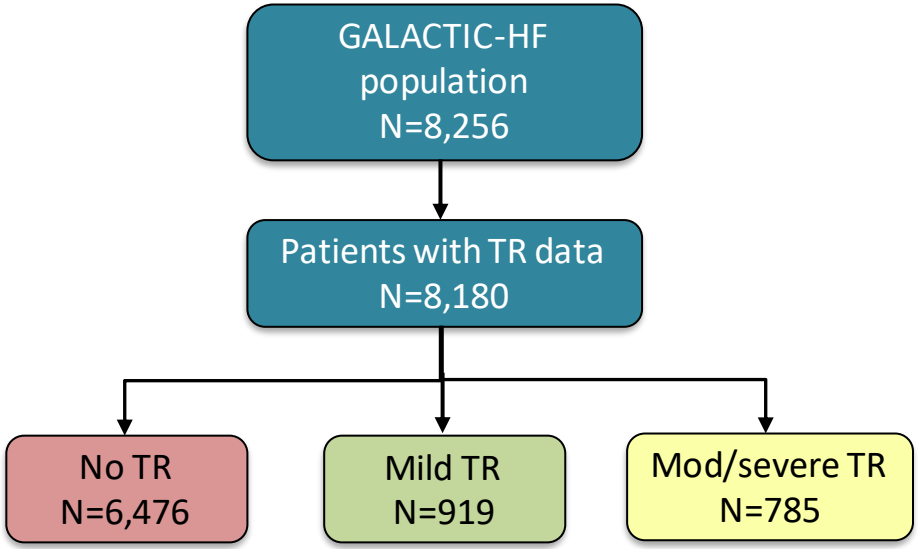


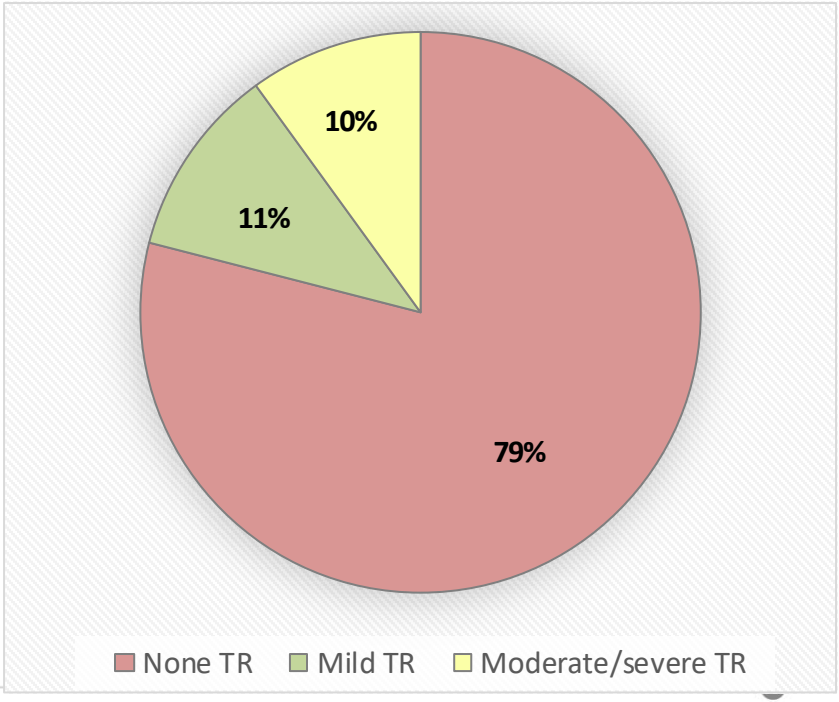
- **Primary outcome:** Time to composite of CV death or HF events
- **Secondary outcomes:** CV death, HF events, all-cause death, changes in QoL from baseline to week 24

Teerlink JR, et al. *JACC Heart Fail* 2020;8:329–40.

Methods

- TR assessment was made from data entered into the CRFs by the investigator at each centre and not through evaluation of echo images





Baseline Demographic Characteristics

GALACTIC-HF

	No TR	Mild TR	Moderate/Severe TR	P-value
Age	64.3 ± 11.4	65.1 ± 11.1	65.4 ± 11.5	0.003
Sex, female	1359 (21.0%)	188 (20.5%)	184 (23.4%)	0.21
Geographic Region				<0.001
Asia	542 (8.4 %)	82 (8.9 %)	37 (4.7 %)	
Eastern Europe/Russia	1801 (27.8%)	414 (45.0%)	451 (57.5%)	
Latin America	1435 (22.2%)	85 (9.2 %)	52 (6.6 %)	
US And Canada	1094 (16.9%)	173 (18.8%)	109 (13.9%)	
Western Europe/South Africa/Australasia	1604 (24.8%)	165 (18.0%)	136 (17.3%)	
Inpatient	1580 (24.4%)	239 (26.0%)	252 (32.1%)	<0.001

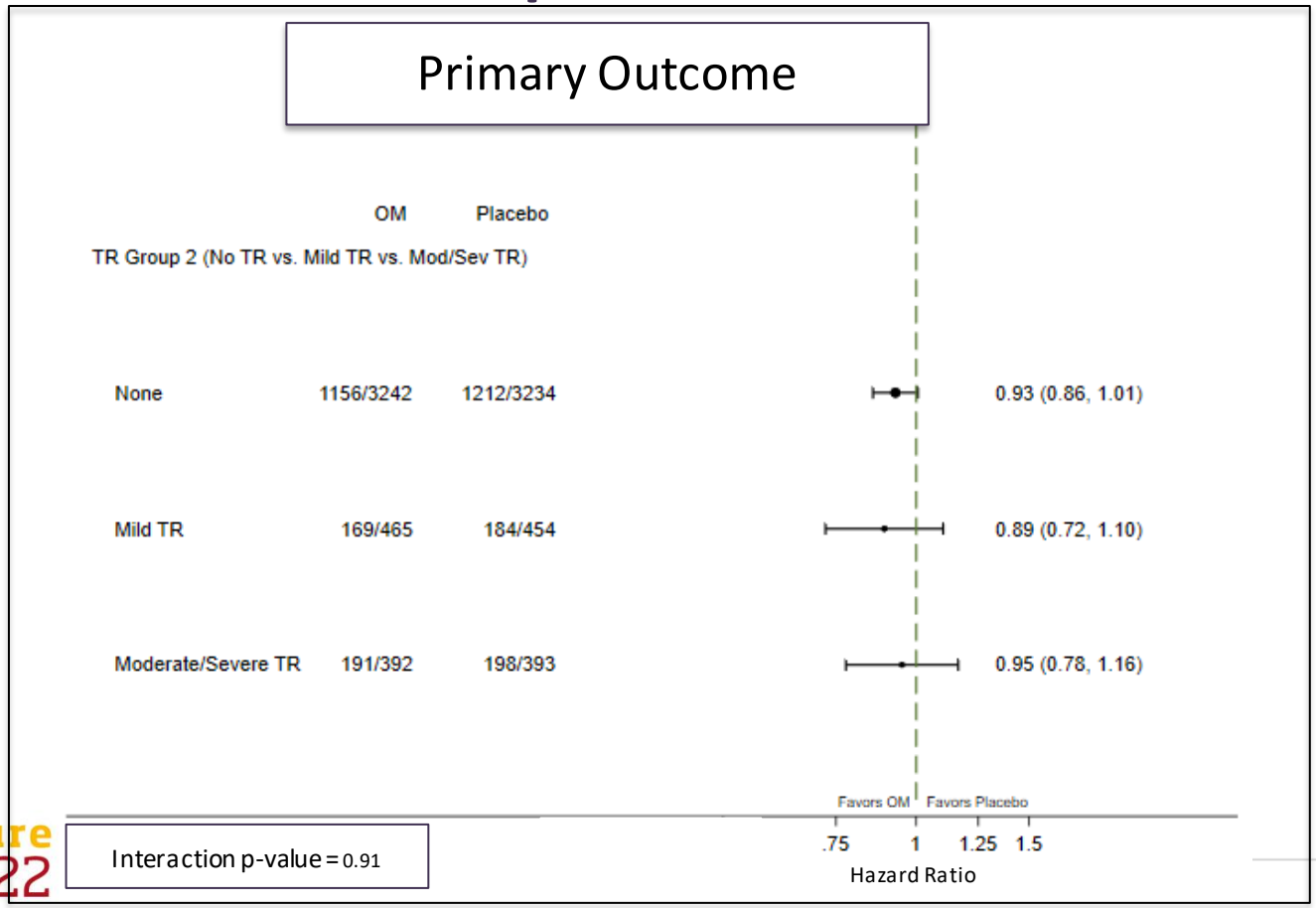
Baseline Clinical Characteristics

GALACTIC-HF

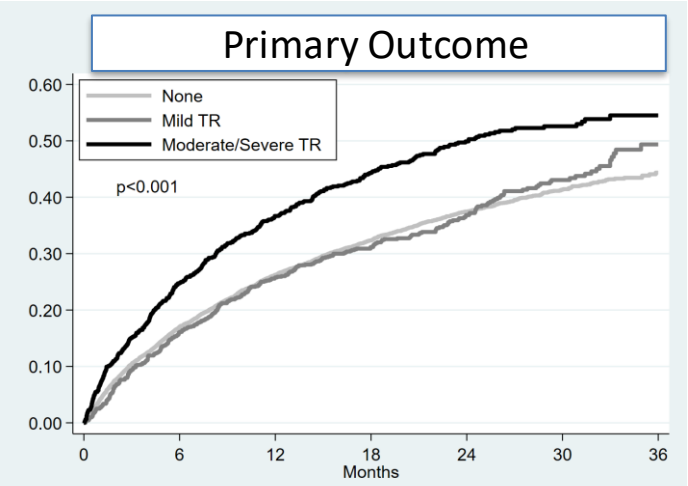
	No TR	Mild TR	Moderate/Severe TR	P-value
AF or flutter	1615 (24.9%)	278 (30.3%)	329 (41.9%)	<0.001
Ischaemic HF	3483 (53.8%)	488 (53.1%)	424 (54.0%)	0.96
NYHA III-IV	2906 (44.9%)	440 (47.8%)	490 (62.4%)	<0.001
SBP (mmHg)	116.7 ± 15.4	116.2 ± 15.7	114.7 ± 14.5	<0.001
HR (bpm)	72.1 ± 12.1	72.3 ± 12.2	74.3 ± 12.4	<0.001
LVEF (%)	26.6 ± 6.2	26.6 ± 6.3	26.1 ± 6.6	0.08
NT-proBNP (pg/mL)	1881 [925 - 3895]	2137 [1114 - 3939]	2974 [1538 - 5720]	<0.001
Cardiac Tn I (ng/L)	26 [14 - 50]	27 [14 - 53]	30 [17 - 59]	<0.001
eGFR (mL/min/1.73m2)	59.4 [44.7 - 74.6]	58.2 [43.1 - 71.9]	54.7 [41.5 - 71.9]	<0.001

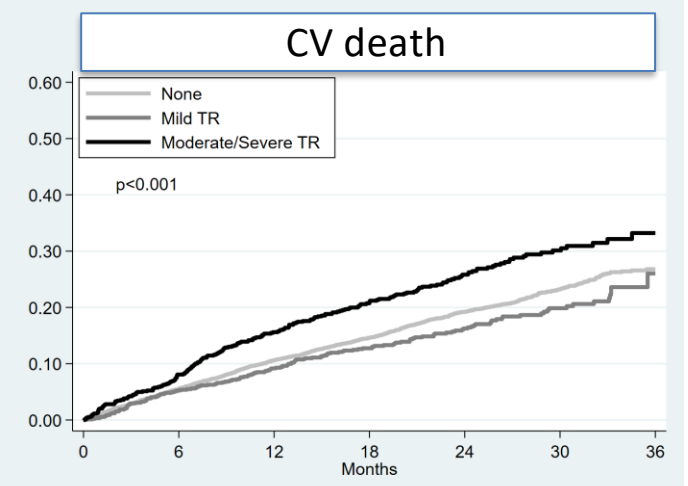
Omecamtiv Mecarbil Treatment Benefit Consistent Across TR Groups

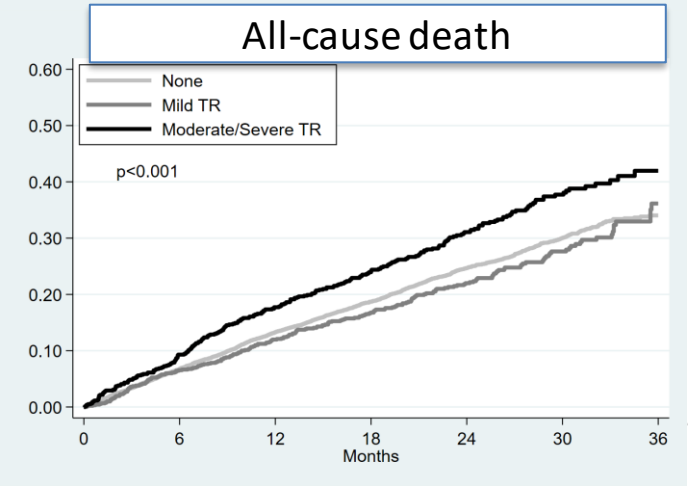
GALACTIC-HF

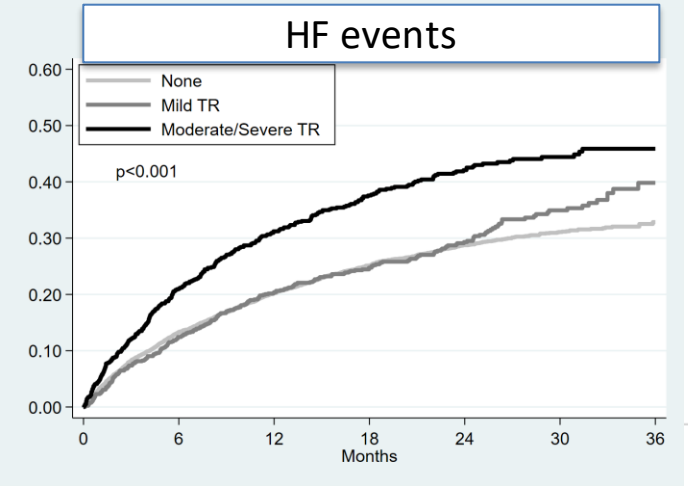


Association between TR and clinical outcomes









Impact of TR on the RR* of clinical outcomes

GALACTIC-HF

	No/Mild TR	Moderate/Severe TR
Outcome	N = 7395	N = 785
Primary Outcome	2721 events	389 events
	[24.3 / 100py]	[35.3 / 100py]
	Reference group	HR=1.14 (1.02,1.27)
Overall p=0.025		p = 0.025
CV Death	1392 events	209 events
	[10.5 / 100py]	[14.8 / 100py]
	Reference group	HR=1.09 (0.94,1.27)
Overall p=0.258		p = 0.258
Heart Failure Events	1991 events	313 events
	[17.6 / 100py]	[28.0 / 100py]
	Reference group	HR=1.20 (1.06,1.36)
Overall p=0.005		p = 0.005
All-cause Death	1860 events	264 events
	[14.0 / 100py]	[18.7 / 100py]
	Reference group	HR=1.06 (0.93,1.22)
Overall p=0.384		p = 0.384

**Adjusted for: Age, Female Sex, Race, Region, Inpatient Setting, Myocardial Infarction, Coronary Artery Bypass Graft, Percutaneous Coronary Revascularization, Stroke, Atrial Fibrillation or Flutter, Diabetes Mellitus, LVEF, NYHA Class, Ischemic HF Etiology, KCCQ, Heart Rate, NT-proBNP (log-transformed), Troponin (Log Transformed), eGFR.*

Association between TR and KCCQ-TSS

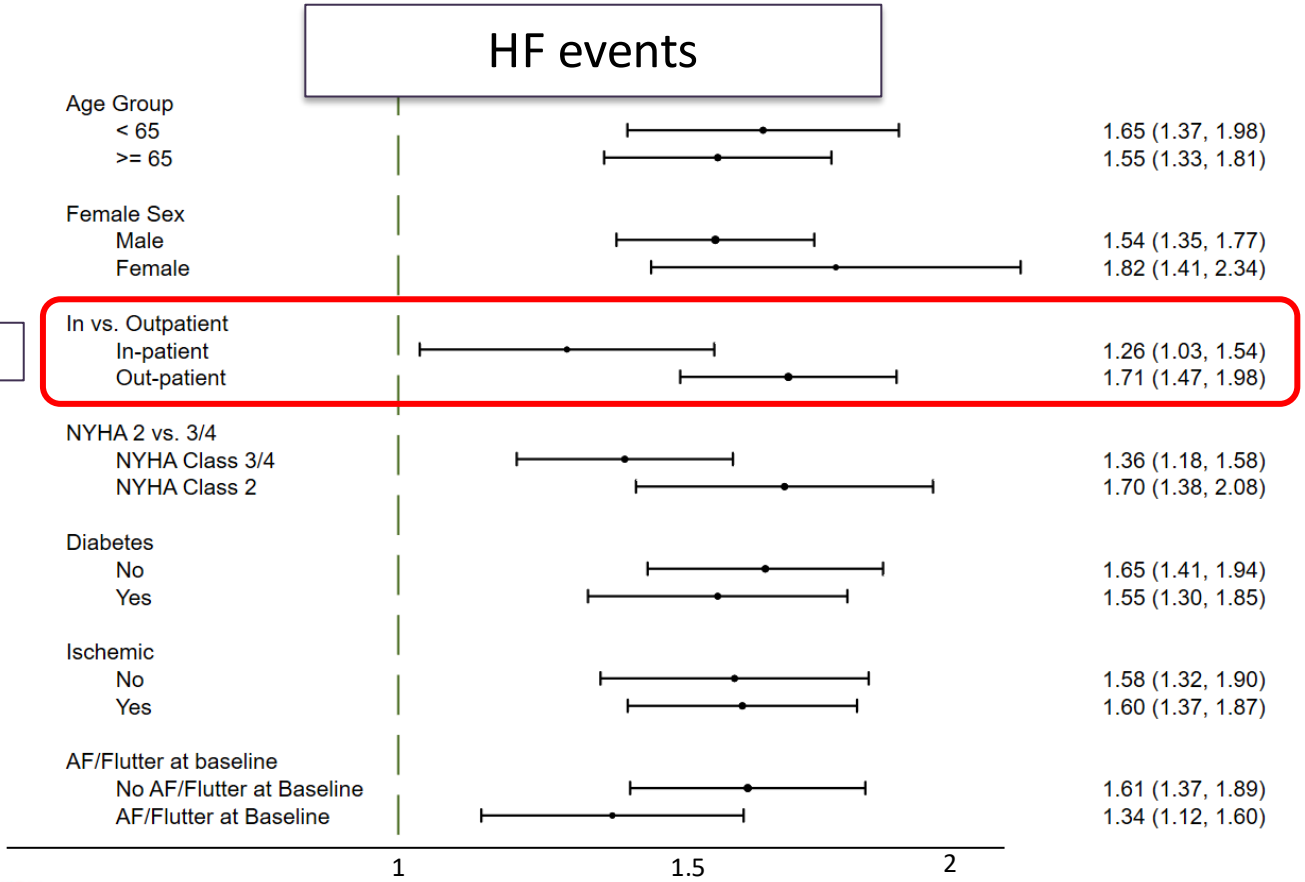
All Patients				
	No TR	Mild TR	Moderate/Severe TR	
	n=6476	n=919	n=785	
KCCQ Total Symptom Score	66.7 ± 25.2	68.3 ± 23.8	61.3 ± 25.9	p<0.001
KCCQ 5: Total Symptom Score Week 24	77.9 ± 21.4	78.0 ± 20.3	74.2 ± 21.9	p<0.001
Change from Baseline	9.7 ± 24.1	8.8 ± 21.6	11.3 ± 26.9	p=0.15

In-patients				
	No TR	Mild TR	Moderate/Severe TR	
	n=1580	n=239	n=252	
KCCQ Total Symptom Score	52.6 ± 25.4	57.5 ± 24.8	48.2 ± 25.5	p<0.001
KCCQ 5: Total Symptom Score Week 24	76.4 ± 21.9	74.7 ± 20.5	73.9 ± 22.6	p=0.22
Change from Baseline	22.8 ± 29.0	16.7 ± 26.9	24.1 ± 29.5	p=0.010

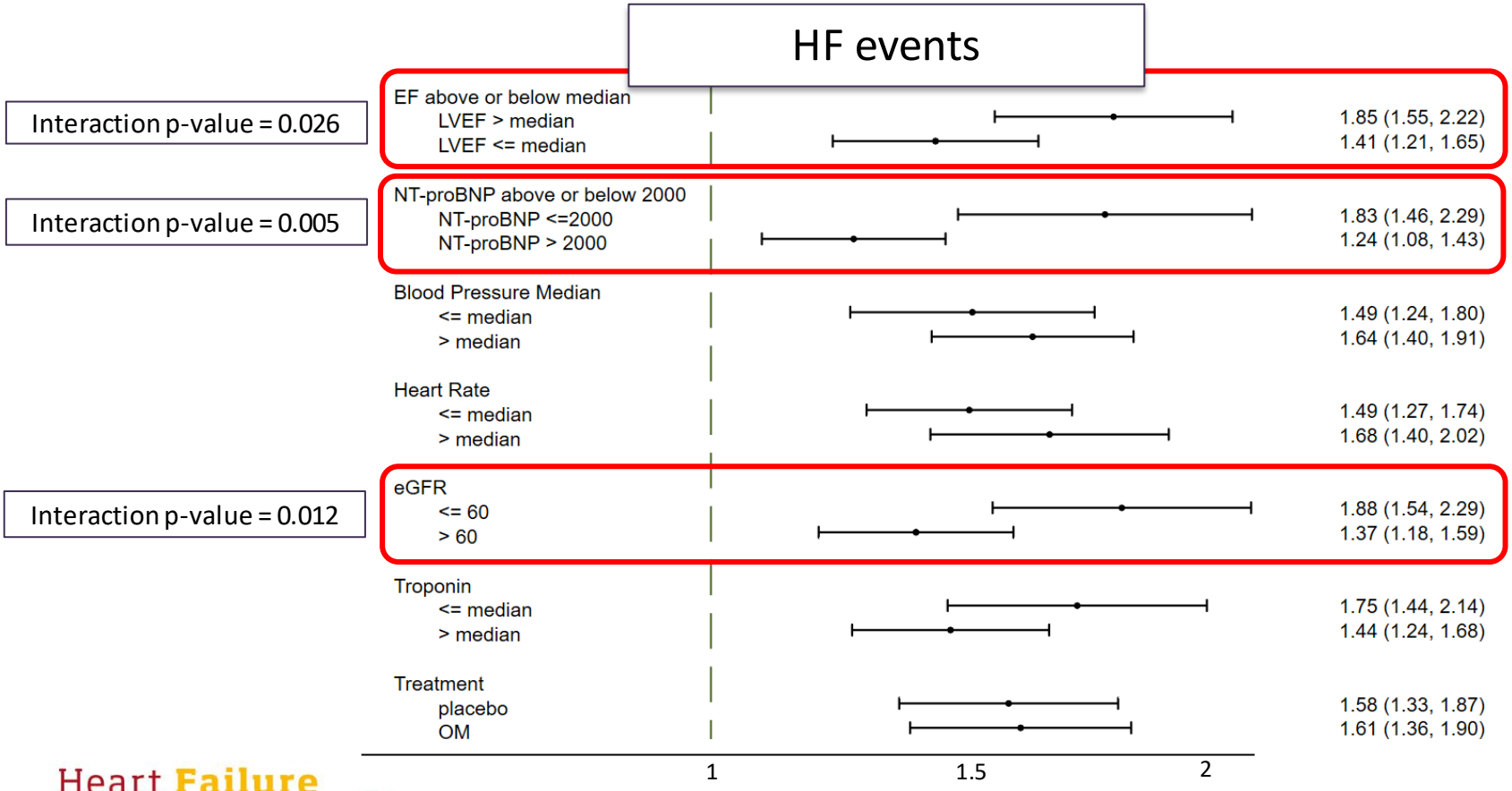
Out-patients				
	No TR	Mild TR	Moderate/Severe TR	
	n=4896	n=680	n=533	
KCCQ Total Symptom Score	71.3 ± 23.3	72.2 ± 22.3	67.5 ± 23.7	p<0.001
KCCQ 5: Total Symptom Score Week 24	78.3 ± 21.2	79.3 ± 20.1	74.4 ± 21.6	p<0.001
Change from Baseline	5.9 ± 21.1	5.9 ± 18.4	5.6 ± 23.5	p=0.96

Impact of moderate/severe TR by subgroups

Interaction p-value = 0.018



Impact of moderate/severe TR by subgroups



Conclusions

- The beneficial treatment effect of Omecamtiv Mecarbil on the primary outcome was not modified by baseline TR
- Baseline moderate/severe TR was independently associated with cardiovascular death or HF events in patients with HFrEF enrolled in the GALACTIC-HF study
- Baseline moderate/severe TR was associated with a worse quality of life
- The impact of moderate/severe TR on HF events is more pronounced in outpatients and patients with higher LVEF, lower NT-proBNP and lower eGFR