



Omeamtiv mecarbil and red cell distribution width in patients with heart failure and reduced ejection fraction: Results from the GALACTIC-HF trial

Mingming Yang on behalf of the GALACTIC-HF investigators

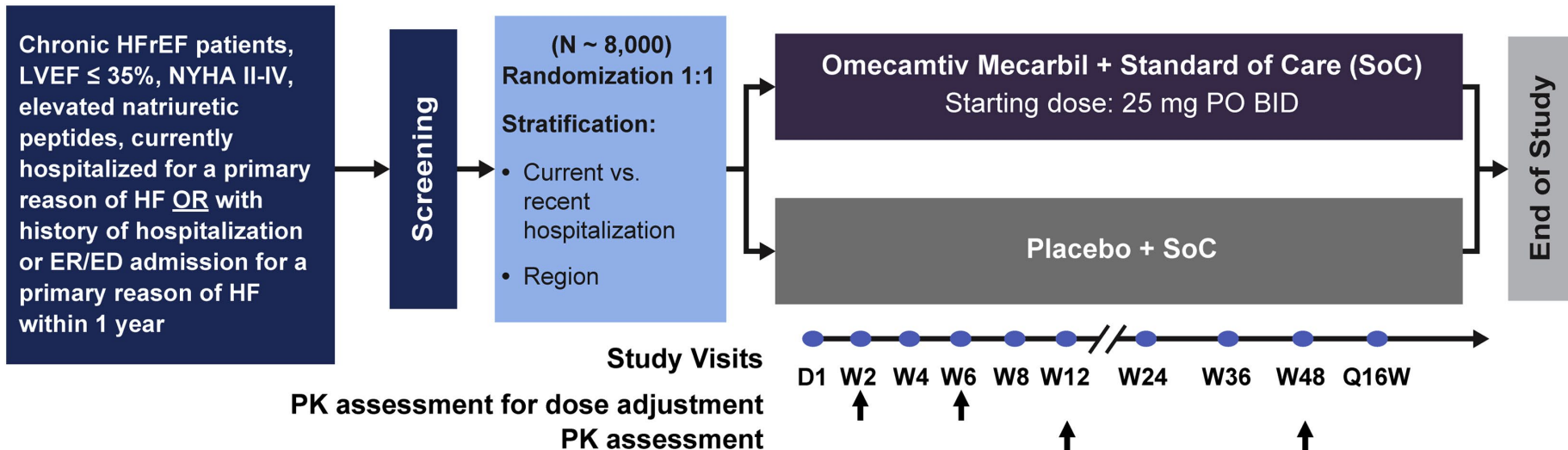
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Background and aims: Red cell distribution width (RDW) in heart failure with reduced ejection fraction (HFrEF)

- RDW is a routinely measured hematological biomarker, that provides a measure of the variability in the size of erythrocytes (anisocytosis).
- Since first reported in 2007, RDW has consistently been shown to provide prognostic information in patients with HFrEF (and other diseases).
- It is uncertain whether RDW remains valuable when added to other prognostic variables in a contemporary population with HFrEF.
- We sought to assess the relationship between RDW and clinical characteristics and outcomes in patients with HFrEF. To quantify the effect of omecamtiv mecarbil according to baseline RDW in GALACTIC-HF.

GALACTIC-HF study design

Randomized, double-blind, placebo-controlled trial testing the hypothesis that omecamtiv mecarbil can safely improve symptoms, prevent clinical HF events, and delay CV death in patients with chronic HFrEF.



Primary outcome:

A composite of a first heart-failure event (hospitalization or urgent visit for heart failure) or death from cardiovascular causes

Selected baseline characteristics according to baseline RDW (quartiles)

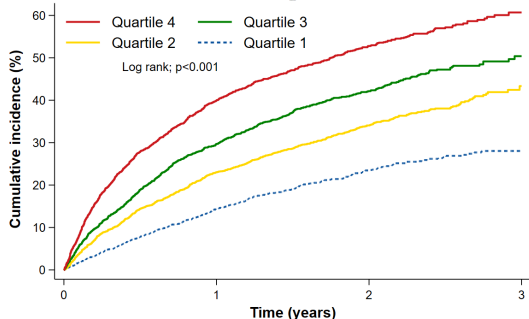
	Q1: 11.9-14.5	Q2: 14.6-15.8	Q3: 15.9-17.4	Q4: 17.5-34.7	<i>P for trend</i>
Atrial fibrillation, %	18.9	26.7	29.6	33.5	<0.001
Myocardial infarction, %	38.3	41.5	42.5	44.3	<0.001
Peripheral artery disease, %	7.8	10.2	10.3	12.6	<0.001
Type 2 diabetes, %	35.3	39.2	41.7	43.8	<0.001
COPD, %	12.2	16.0	17.8	19.2	<0.001
Anemia, %	15.5	20.9	29.3	45.7	<0.001
KCCQ-TSS, mean	77.1	70.8	68.8	61.5	<0.001
NYHA III/IV, %	38.9	43.8	48.1	55.8	<0.001
LVEF, % mean	27.3	27.0	26.3	25.8	<0.001
NT-proBNP (pg/ml), median	1209	1745	2294	3318	<0.001
Troponin I (ng/L), median	20	25	28	35	<0.001
eGFR (ml/min/1.73m ²), mean	66.4	60.5	58.7	56.5	<0.001

Primary outcome according to baseline RDW category and in combination with other recognized prognostic variables

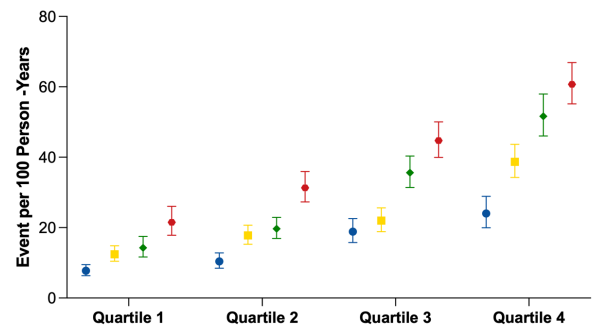
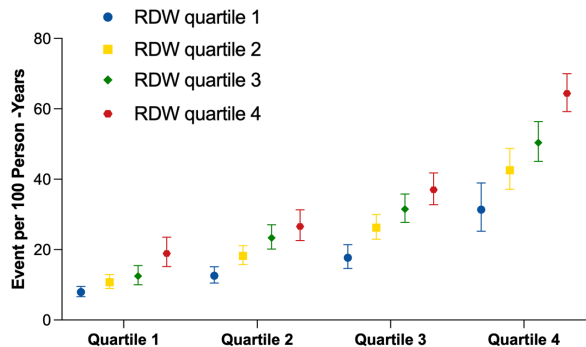
RDW combined with other prognostic biomarkers

RDW category

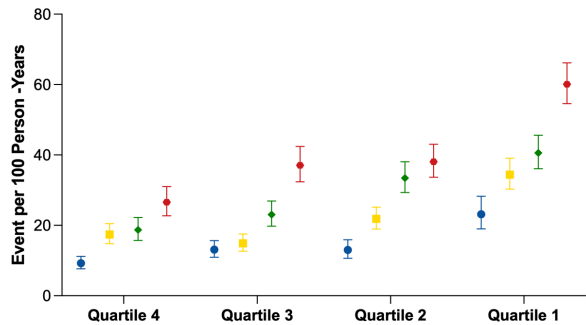
HF event or CV death



No. at risk	Time (years)	0	1	2	3
Quartile 1	1802	1515	787	72	
Quartile 2	2111	1593	741	55	
Quartile 3	1920	1306	554	60	
Quartile 4	2031	1160	497	46	

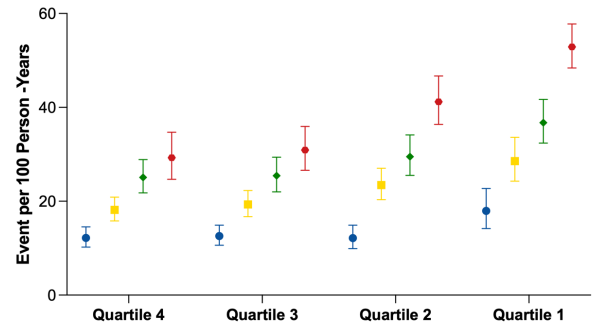


NT-proBNP



eGFR

Troponin I



Hemoglobin

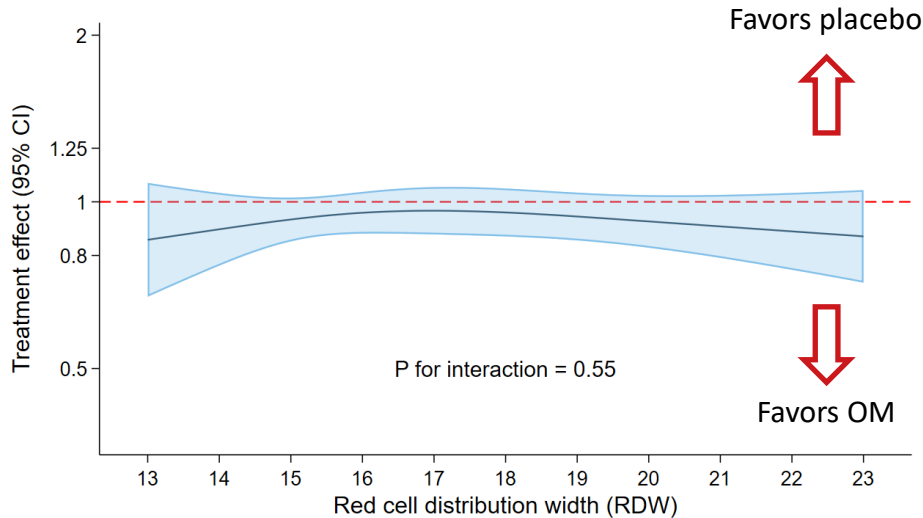
Harrell's C statistic for PREDICT-HF scores alone and PREDICT-HF scores with inclusion of RDW (outpatients)

	PREDICT-HF (C-statistic)	PREDICT-HF + RDW (C-statistic)	P value for difference	Integrated Discrimination Index (IDI)	Net Reclassification Index (NRI)
First HF hospitalization or CV death					
Overall	0.685 (0.673-0.696)	0.690 (0.679-0.702)	<0.001		
1 year	0.700 (0.687-0.713)	0.706 (0.693-0.719)	<0.001	0.008 (0.005-0.013) P <0.001	0.093 (0.057-0.124) P <0.001
2 year	0.686 (0.674-0.697)	0.691 (0.680-0.703)	<0.001	0.009 (0.005-0.014) P <0.001	0.108 (0.068-0.133) P <0.001
All-cause death					
Overall	0.712 (0.699-0.724)	0.717 (0.704-0.731)	<0.001		
1 year	0.728 (0.710-0.746)	0.736 (0.718-0.754)	<0.001	0.008 (0.004-0.014) P <0.001	0.124 (0.075-0.171) P <0.001
2 year	0.714 (0.700-0.728)	0.719 (0.705-0.733)	<0.001	0.009 (0.004-0.016) P <0.001	0.116 (0.074-0.155) P <0.001

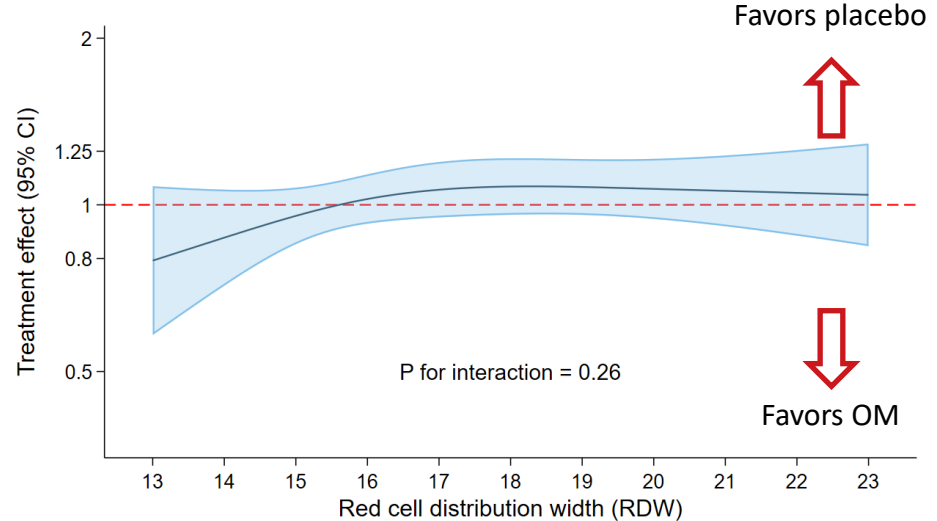
*PREDICT-HF is the most recent, comprehensive and validated prognostic model in HFrEF.

Effect of omecamtiv mecarbil on clinical outcomes across the range of RDW at baseline

Primary outcome



All-cause death



Conclusions: omecamtiv mecarbil and RDW in HFrEF

- RDW is an “independent” predictor of adverse outcomes in patients with HFrEF, providing incremental prognostic information beyond traditional risk factors and established biomarkers.
- Our findings support the use of this routinely measured and inexpensive laboratory test as a prognostic biomarker in ordinary clinical practice.
- In GALACTIC-HF, the benefit of omecamtiv mecarbil was consistent across the range of RDW examined.