DukeHeart *On The Go*

METEORIC-HF: The Effect of Omecamtiv Mecarbil on Exercise Tolerance in Patients With Chronic Heart Failure and Reduced Ejection Fraction

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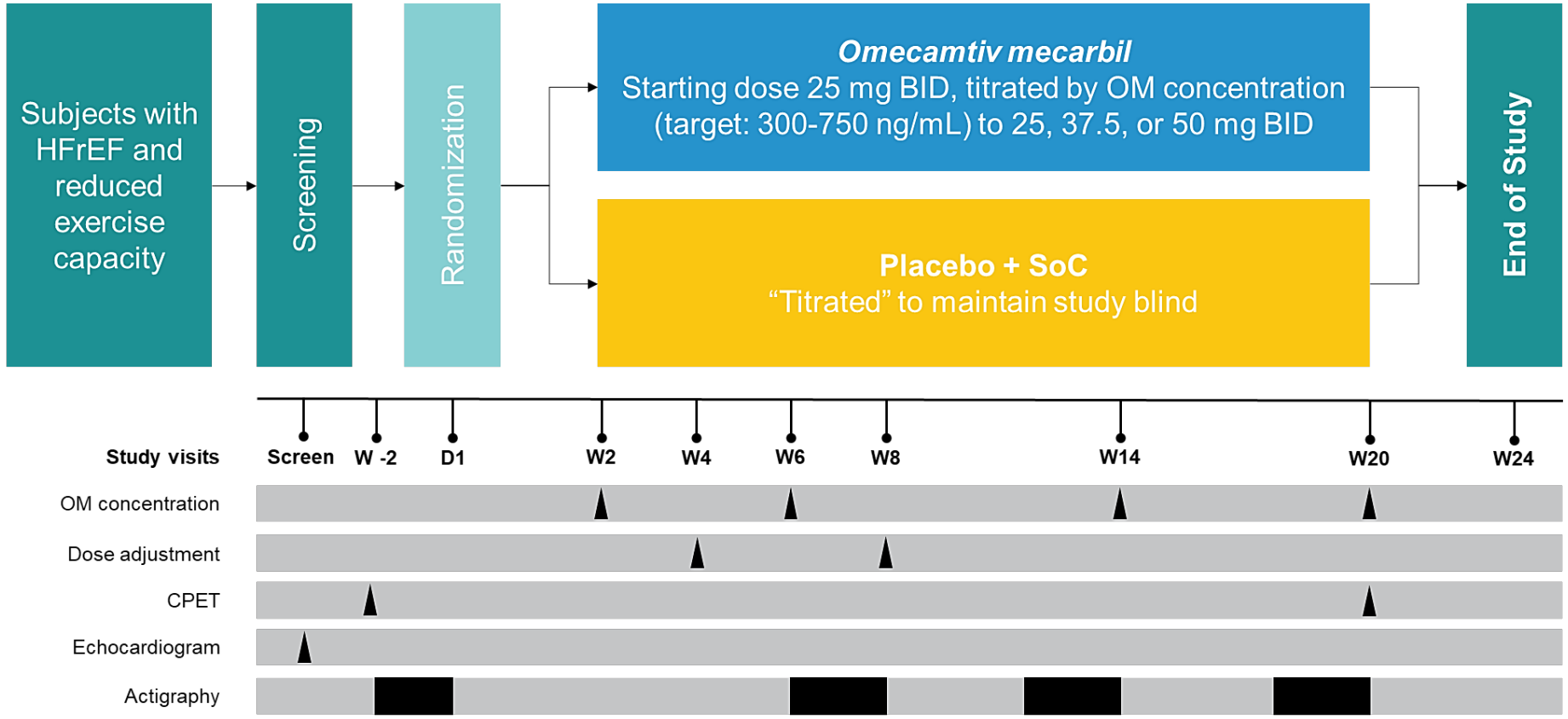
MedEd ON THE GO

Background

- Exercise intolerance is a cardinal manifestation of heart failure but is not improved by current medical therapies
- Omecamtiv mecarbil is a novel selective cardiac myosin activator that increases cardiac performance and improves outcomes in patients with heart failure and reduced ejection fraction (HFrEF)
- The METEORIC-HF study (NCT03759392) was designed to test the hypothesis that omecamtiv mecarbil can improve exercise capacity in patients with HFrEF

Study Design

Double-blind, placebo-controlled, multi-center, randomized clinical trial



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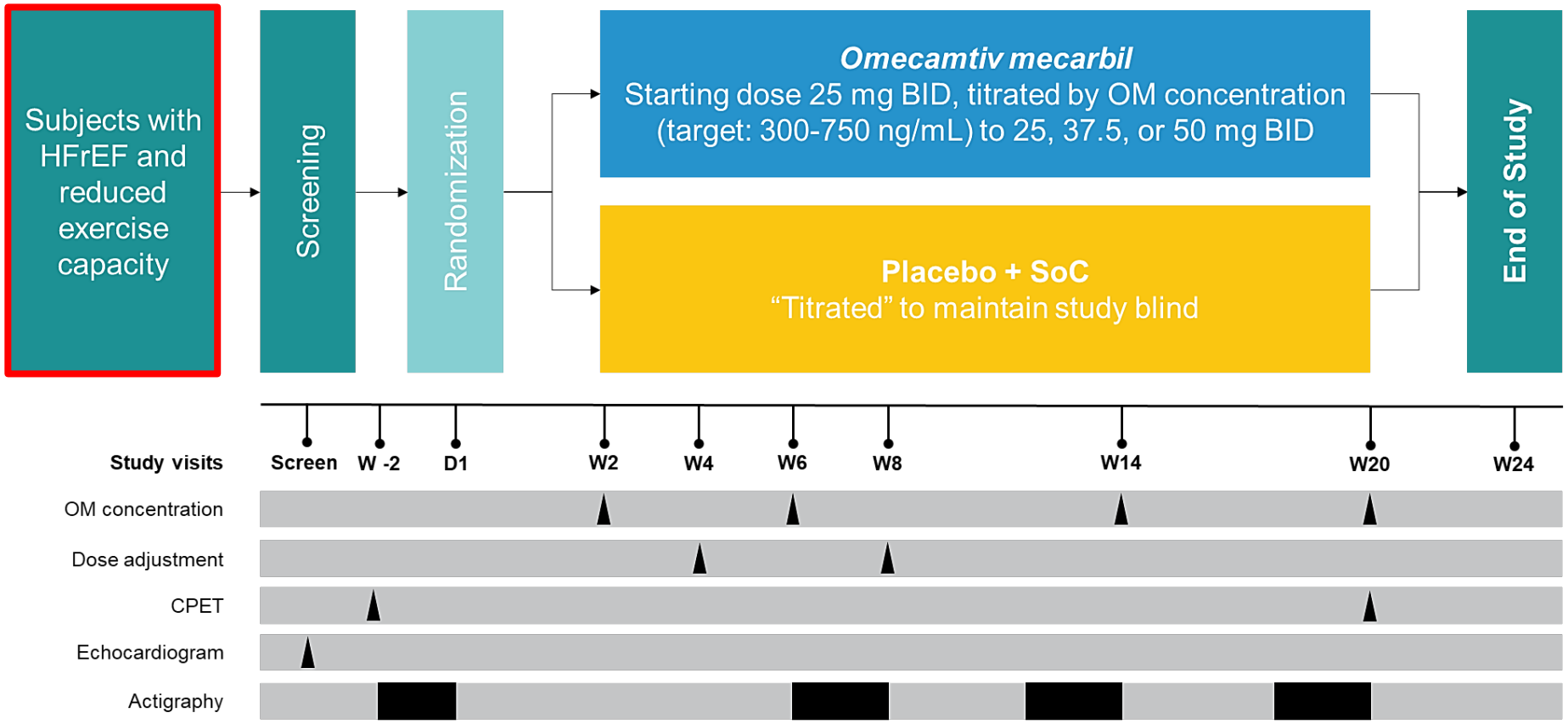

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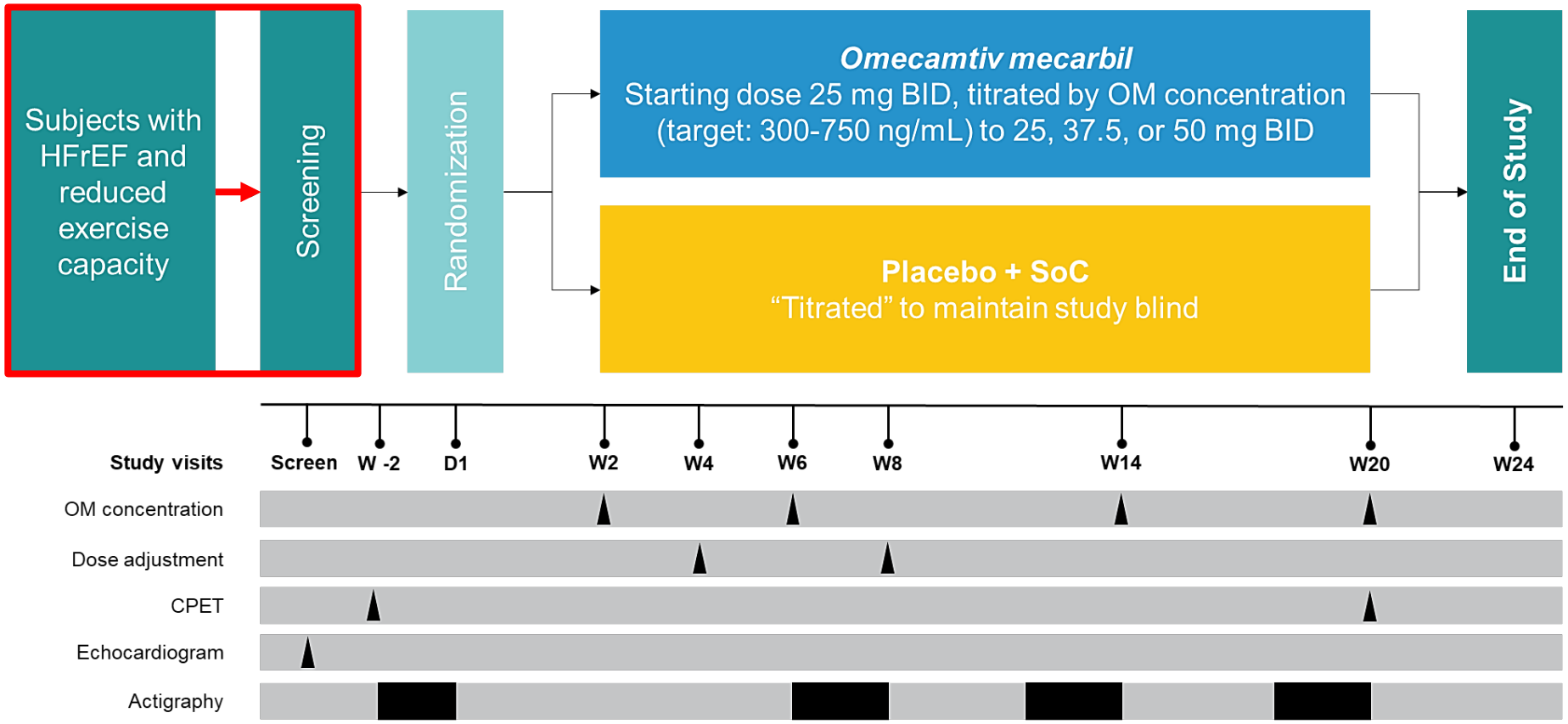

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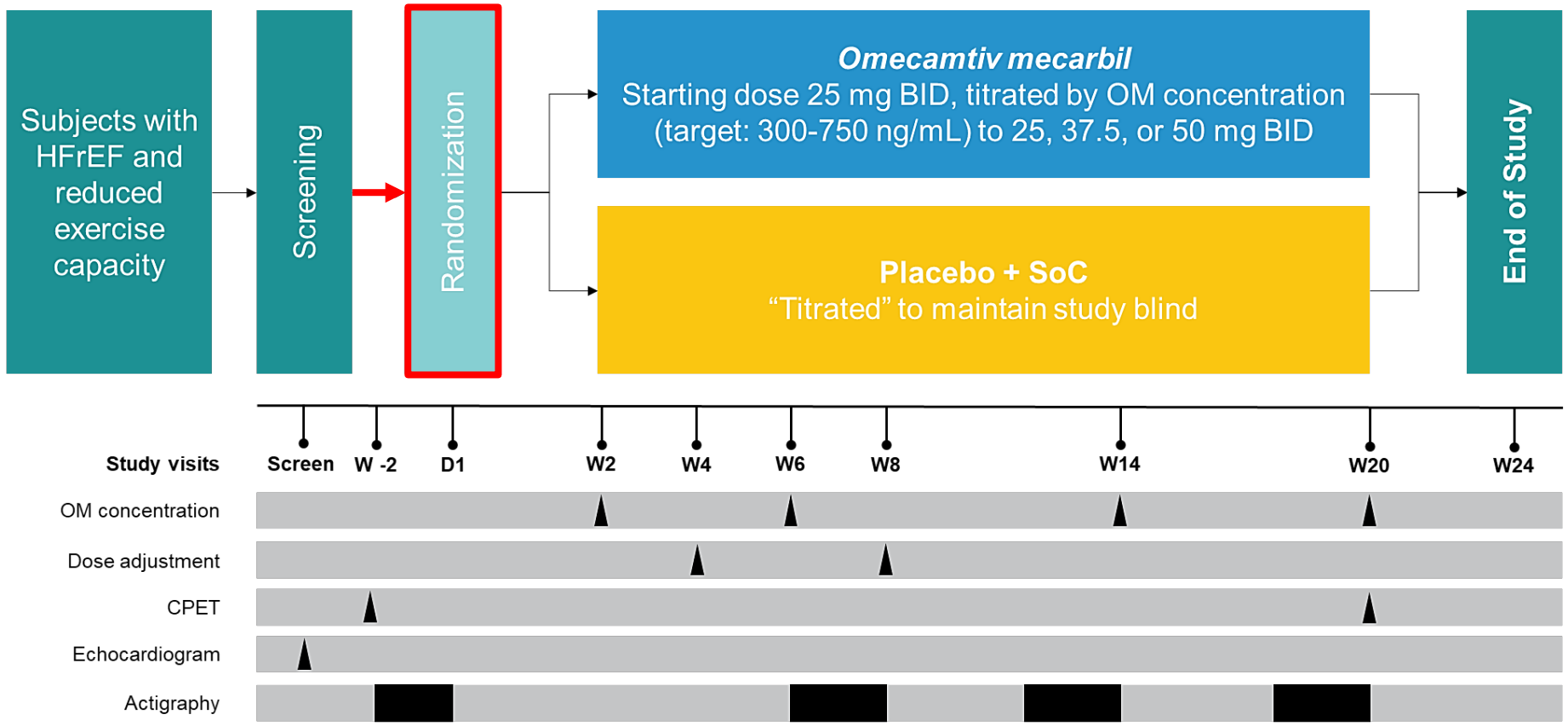

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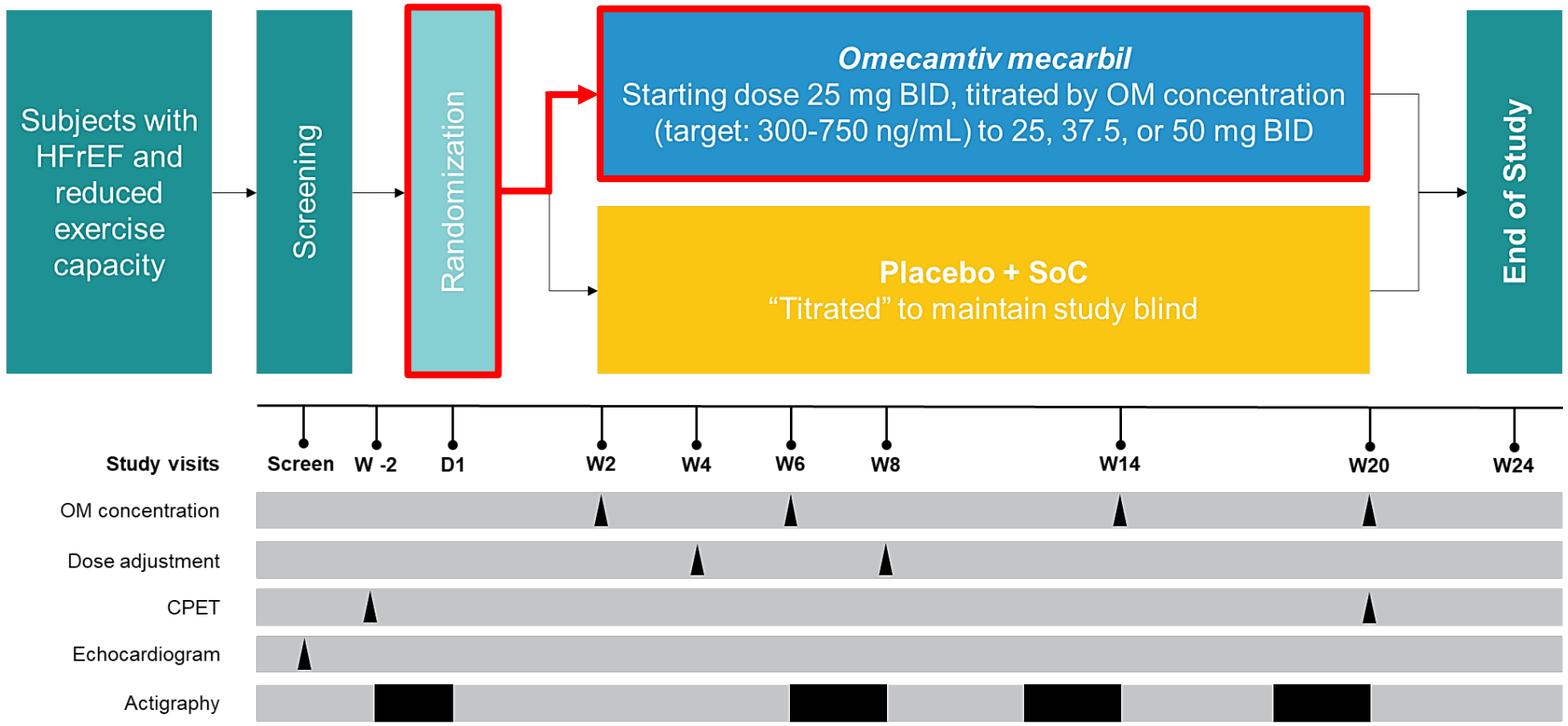

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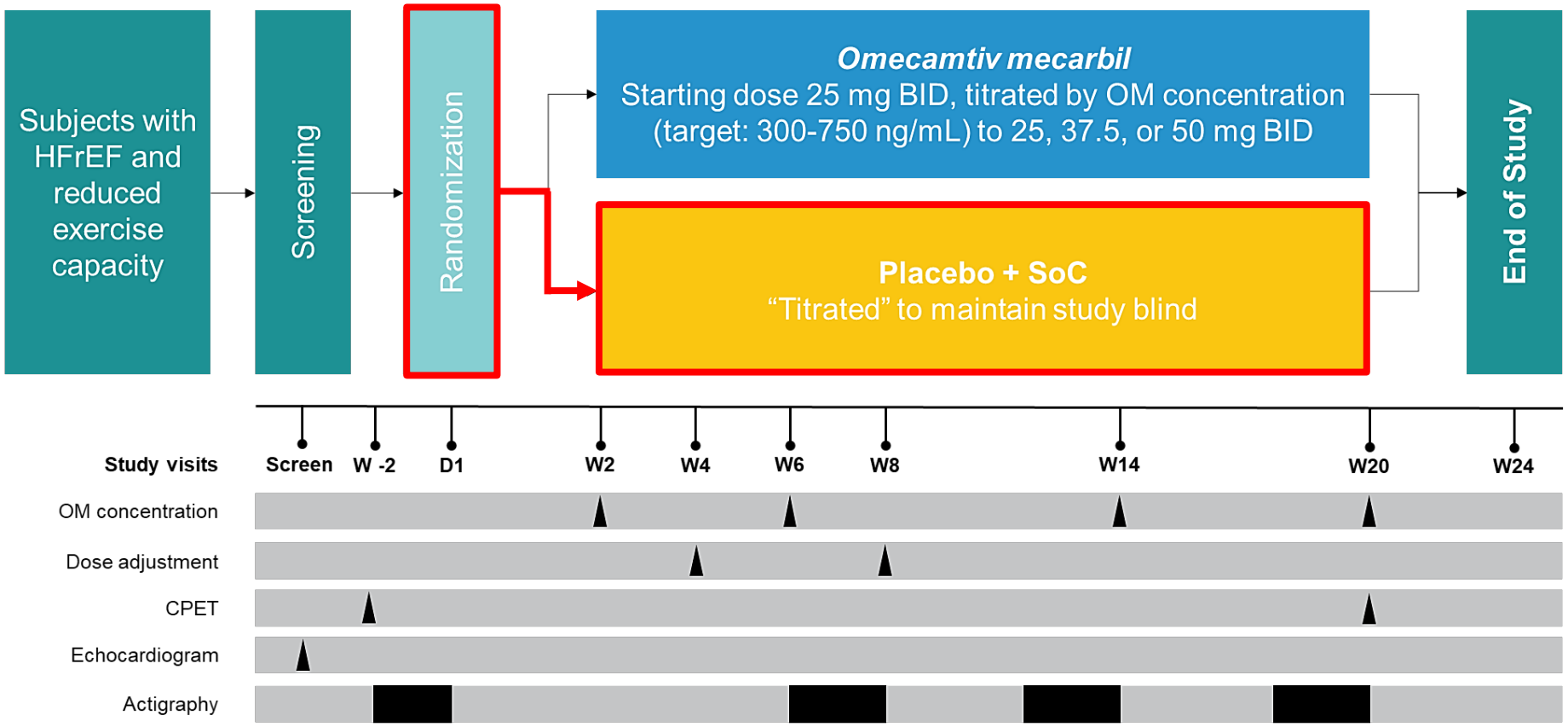

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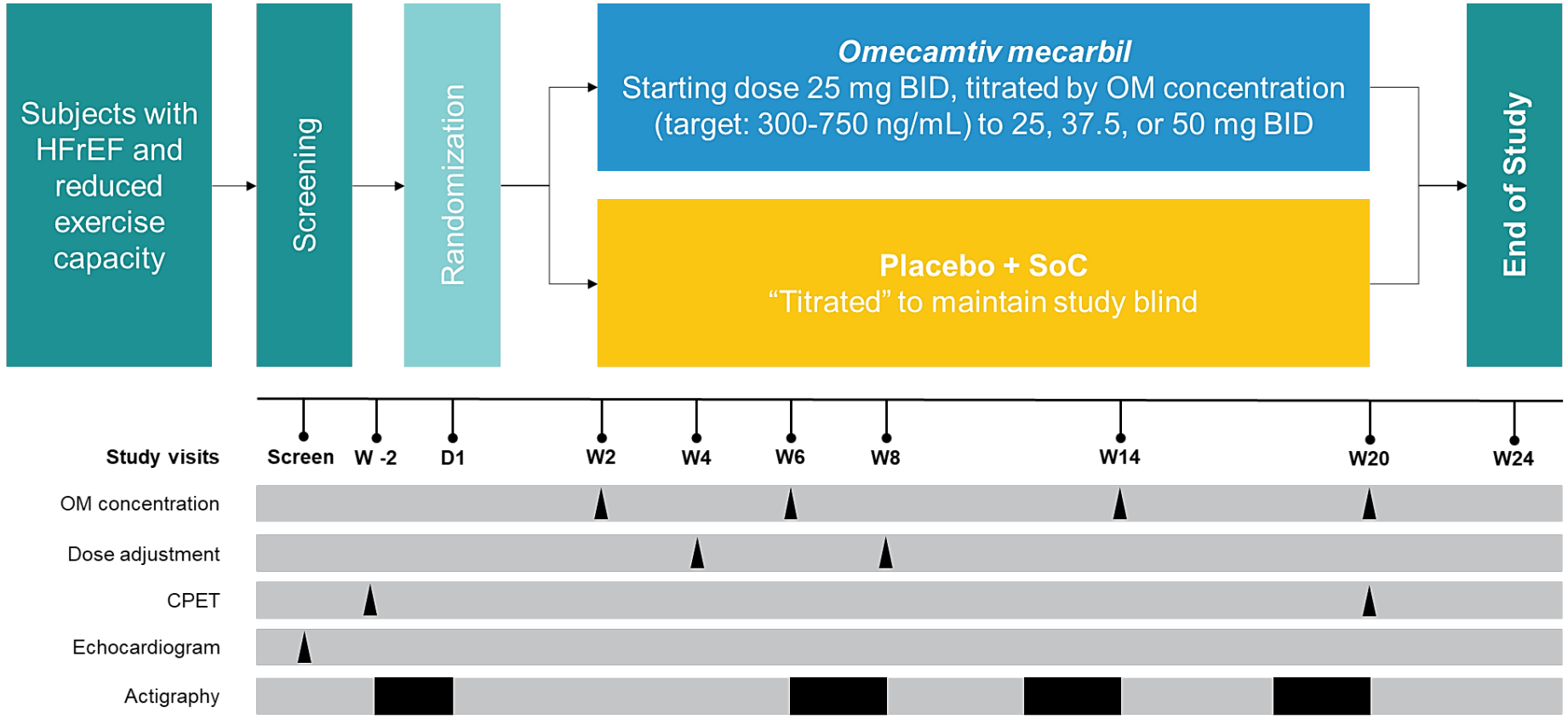


Inclusion and Exclusion Criteria

Key inclusion criteria

- Age ≥18 to ≤85 years
- Chronic NYHA class II–III heart failure
- LVEF ≤35% within 12 months
- On maximally tolerated HF therapies if not contraindicated
- NT-proBNP ≥200 pg/mL
- pVO_2 ≤75% of the age-predicted normal value on screening CPET
- RER ≥1.05 on screening CPET

Key exclusion criteria

- Decompensated HF within prior 3 months
- SBP >140 or <85 mmHg
- Resting HR >90 or <50 bpm
- Hemoglobin <10.0 g/dL
- eGFR <30 mL/min per 1.73 m2
- Severe uncorrected valvular heart disease
- Paroxysmal atrial fibrillation or flutter requiring treatment within prior 6 months
- Untreated severe ventricular arrhythmias
- Symptomatic bradycardia, second-degree Mobitz type II, or third-degree heart block

Baseline Characteristics

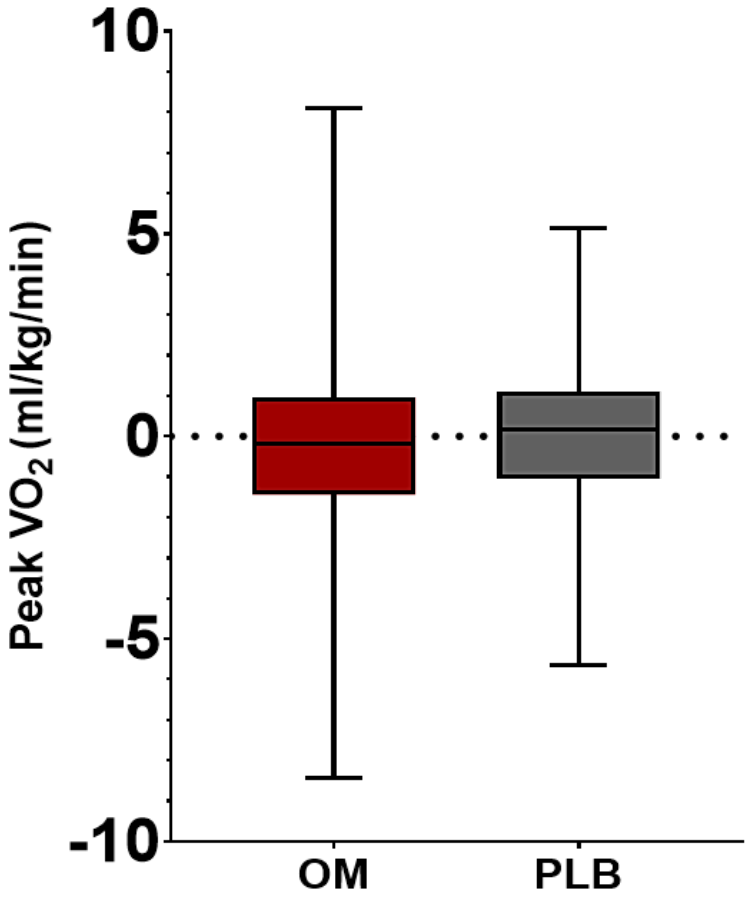
	Omecamtiv Mecarbil (N=185)	Placebo (N=91)	All (N=276)
Demographics and Medical History			
Age, years	63 (10)	64 (11)	64 (10)
White, n (%)	163 (88%)	82 (90%)	245 (89%)
Women, n (%)	27 (15%)	15 (16%)	42 (15%)
SBP (mmHg)	115 (18)	113 (17)	114 (17)
Heart Rate (bpm)	69 (10)	67 (11)	69 (10)
Ischemic HF, n (%)	117 (63%)	48 (53%)	165 (60%)
Atrial Fibrillation, n (%)	26 (14%)	12 (13%)	38 (14%)
LVEF (%)	27 (7)	27 (6)	27 (6)
NYHA Class II, n (%)	143 (77%)	74 (81%)	217 (79%)
eGFR (mL/min/1.73m^2)	66 (21)	68 (22)	67 (21)
NT-proBNP (pg/mL)	1343 (1854)	1271 (1490)	1320 (1740)

*Values are mean (SD) or N (%)

	Omecamtiv Mecarbil (N=185)	Placebo (N=91)	All (N=276)
Medical and Device Therapy			
Beta-Blocker, n (%)	175 (95%)	90 (99%)	265 (96%)
MRA, n (%)	131 (71%)	67 (74%)	198 (72%)
ACEi/ARB/ARNi, n (%)	176 (96%)	85 (93%)	261 (95%)
ARNi, n (%)	124 (67%)	58 (64%)	182 (66%)
SGLT2i, n (%)	31 (17%)	19 (21%)	50 (18%)
Digoxin, n (%)	27 (15%)	8 (9%)	35 (13%)
CRT-D, n (%)	39 (21%)	27 (30%)	66 (24%)
ICD only, n(%)	107 (58%)	42 (46%)	149 (54%)

Background HF therapy in METEORIC-HF was better than in any prior global HF trial

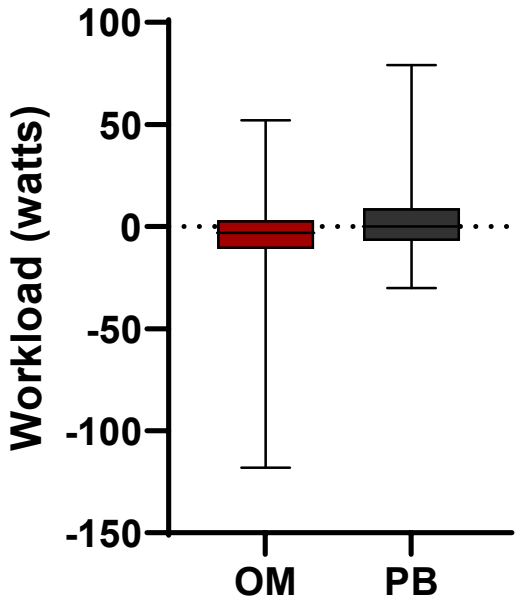
Primary Endpoint: Change in Peak VO_2



	Omecamtiv Mecarbil	Placebo
LSM (SE)	−0.24 (0.17)	0.21 (0.24)
LSM Diff (95% CI)	**−0.45 (−1.0, 0.13)**	
p-value	**0.13**	

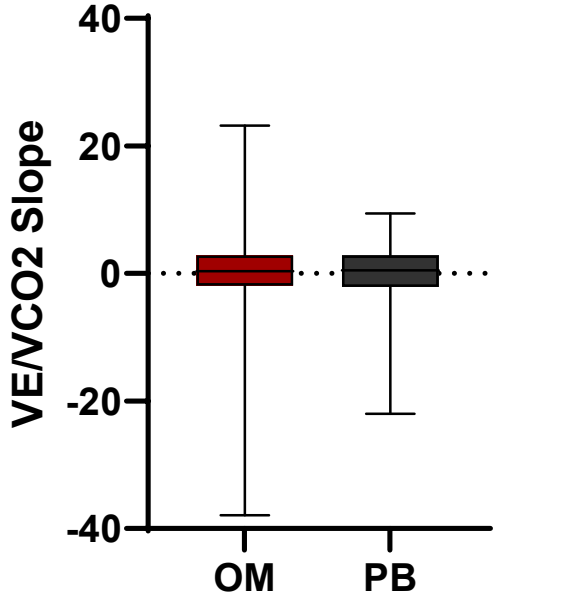
Secondary Endpoints

Change in Workload



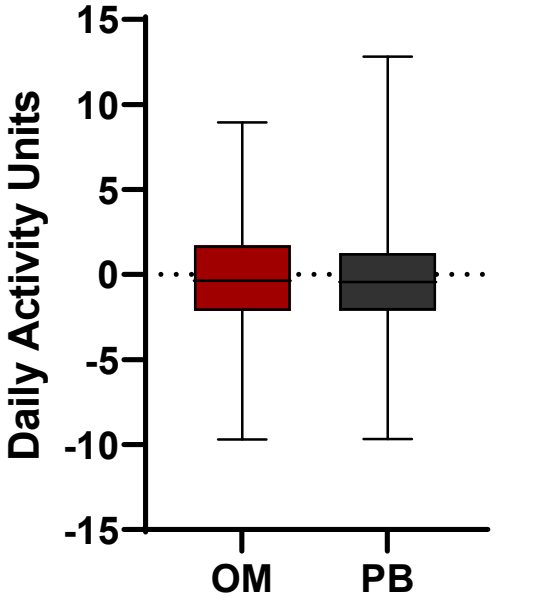
Mean difference: -5.4
p-value: 0.025

Change in Ventilatory Efficiency



Mean difference: 0.41
p-value: 0.51

Change in Actigraphy



Mean difference: 0.30
p-value: 0.54

Conclusions

- In well-treated patients with chronic HFrEF, omecamtiv mecarbil did not improve measures of exercise capacity over 20 weeks compared to placebo
- Consistent with prior studies of omecamtiv mecarbil, overall safety was comparable to placebo, without safety signals related to peak exercise
- Identifying medical therapies that safely improve exercise capacity in HFrEF remains an unmet challenge