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Corporate Presentation

October 2026

Forward-Looking Statements

Disclaimers

Except for historical information, all of the statements, expectations and assumptions contained in this presentation are forward-looking statements. These forward-looking statements include, but are not limited to, statements regarding our expectations about the design, enrollment, conduct, timing, and potential outcomes of the LEVEL-2 clinical trial; interpretations of clinical data from the LEVEL trial, including subgroup and post-hoc analyses, and the applicability of those data to the design and expected performance of LEVEL-2; our beliefs about the potential efficacy, safety, and regulatory path for oral levosimendan; our estimates of the potential market opportunity for our product candidates; our intellectual property position; our projected cash runway and ability to fund operations. Actual results might differ materially from those explicit or implicit in the forward-looking statements. Important factors that could cause actual results to differ materially include: risks of our clinical trials, including, but not limited to, the timing, delays, costs, design, location, initiation, enrollment, and results of such trials, including that the Phase 3 LEVEL trial did not meet its primary endpoint of change in 6-minute walk distance (6MWD) in the overall enrolled population; the risk that the Company's interpretation and characterization of clinical trial data, may not be shared by regulatory authorities, the medical and scientific communities, or investors, and that data from the LEVEL trial that the Company views as supportive of its LEVEL-2 trial design might not be predictive of LEVEL-2 outcomes; any delays in regulatory review and approval of product candidates in development; risks related to our business strategy, including the prioritization and development of product candidates; reliance on third parties, including Orion Corporation, our manufacturers and CROs; risks regarding the formulation, production, marketing, customer acceptance and clinical utility of our product candidates; the potential advantages of our product candidates; our competitive position; intellectual property risks; our ability to maintain our culture and recruit, integrate and retain qualified personnel and advisors, including on our Board of Directors; volatility and uncertainty in the global economy and financial markets in light of unexpected changes in tariffs and the possibility of pandemics, global financial and geopolitical uncertainties, including in the Middle East and the Russian invasion of and war against the country of Ukraine; risks associated with our cash needs; changes in legal, regulatory and legislative environments in the markets in which we operate and the impact of these changes on our ability to obtain regulatory approval for our products; and other risks and uncertainties set forth from time to time in our SEC filings. All forward-looking statements in this presentation speak only as of the date of this presentation and are based on the Company's current expectations and assumptions. Tenax Therapeutics assumes no obligation and does not intend to update these forward-looking statements except as required by law. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities of the Company.

Evidence-Driven Phase 3 Program

LEVEL DATA ENHANCES HELP TRIAL PROOF OF CONCEPT TO DE-RISK ONGOING PHASE 3; WELL-ESTABLISHED SAFETY PROFILE

1. TNX-103, or Oral Levosimendan, is a potential first-in-class PH-HFpEF treatment
2. Levosimendan brings a well-established safety profile and MOA uniquely suited to treating PH-HFpEF
3. LEVEL data validates levosimendan MOA in PH-HFpEF and defines clear enrichment strategy for potential registration
4. Global Phase 3 LEVEL-2 clinical trial using predictive enrichment strategy driven by LEVEL findings
5. Company funded through Q2 2028

PH-HFpEF: pulmonary hypertension in heart failure with preserved ejection fraction; MOA: mechanism of action.

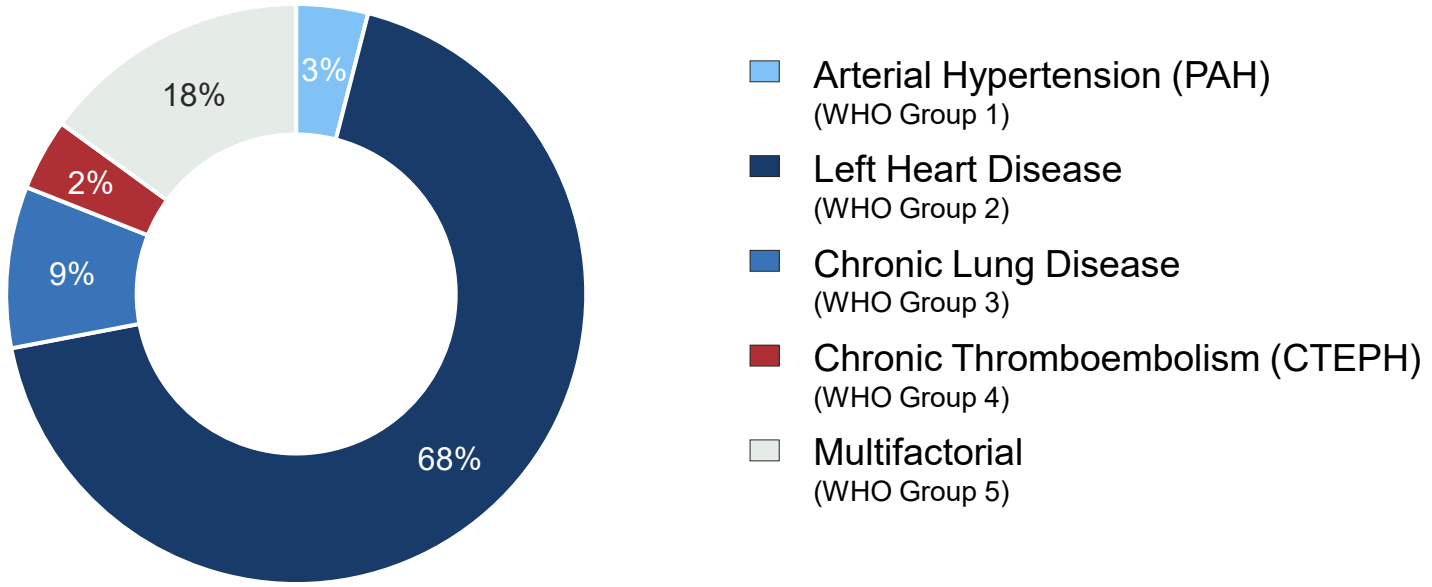
Pulmonary Hypertension in Heart Failure with Preserved Ejection Fraction (PH-HFpEF)

Group 2 Pulmonary Hypertension (Left Heart Disease)

PH-HFpEF is the most common form of PH

- Patients present with shortness of breath, leg edema, and poor exercise capacity
- A progressive, debilitating and often fatal disease
- No approved treatment is recommended by current guidelines

Pulmonary Hypertension Global Prevalence



~50% of Group 2 patients have PH-HFpEF, a large patient population with significant unmet need

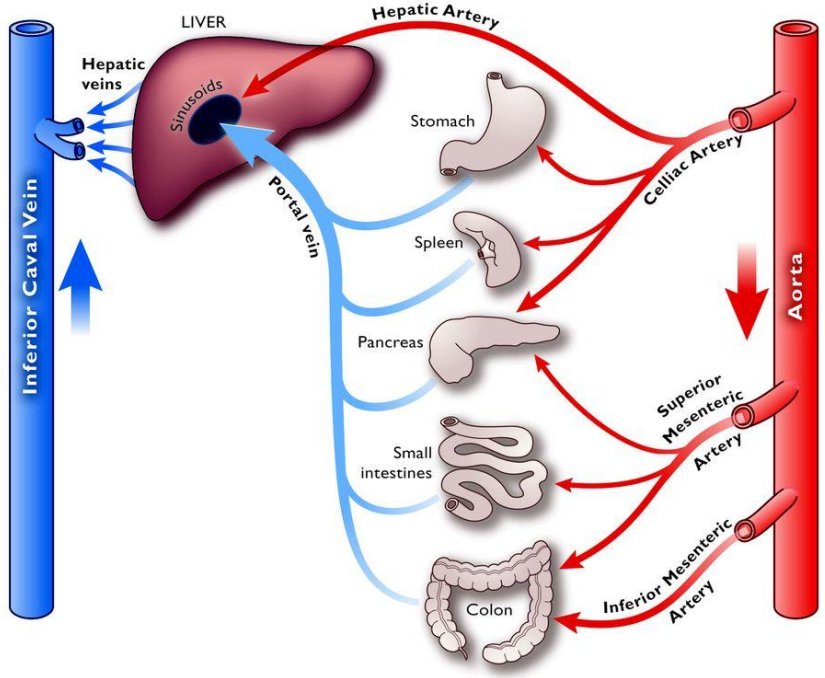
PH: pulmonary hypertension; PH-HFpEF: pulmonary hypertension in heart failure with preserved ejection fraction; WHO: World Health Organization.

Strange G, et al. *Heart (British Cardiac Society)* vol. 98,24 (2012): 1805-11.

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The Fundamental Role of the Splanchnic Reservoir

35% of circulating blood is in the systemic veins



35% of circulating blood is in the systemic arteries

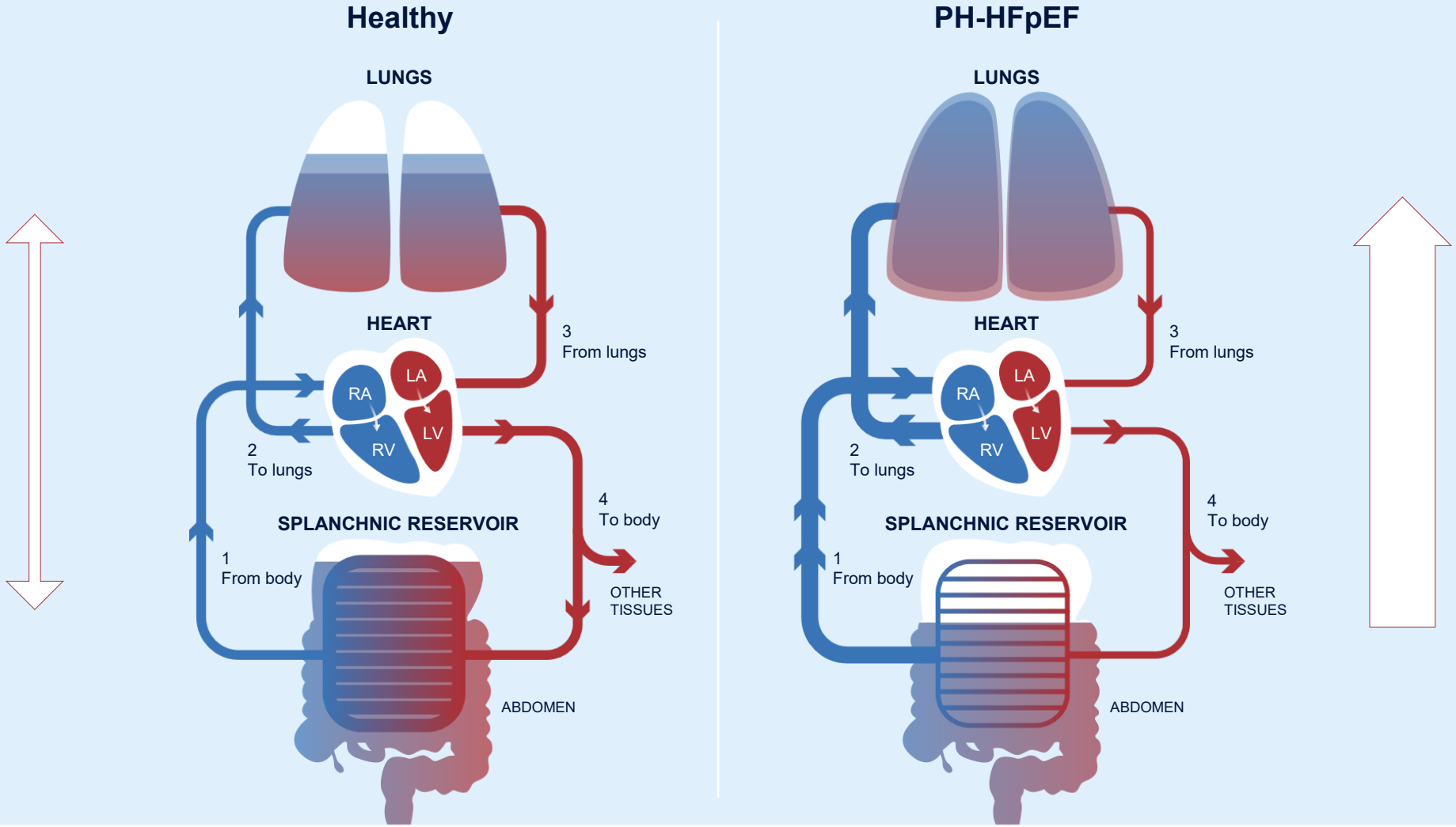
30% of circulating blood is in the splanchnic vascular reservoir

Gelman S and Mushlin PS. *Anesthesiology* vol. 100,2 (2004): 434-9.

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Blood Volume Distribution

REDUCING BLOOD VOLUME TO LOWER VENOUS AND PULMONARY PRESSURE



LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; PH-HFpEF, pulmonary hypertension in heart failure with preserved ejection fraction.

Gelman S, et al. *J Am Soc Anesthesiol*. 2004;100(2):434-439.; Fudim M, et al. *Eur J Heart Fail*. 2021;23:1076-1084.; Yaku H, et al. *J Cardiol*. 2024;83:330-337.

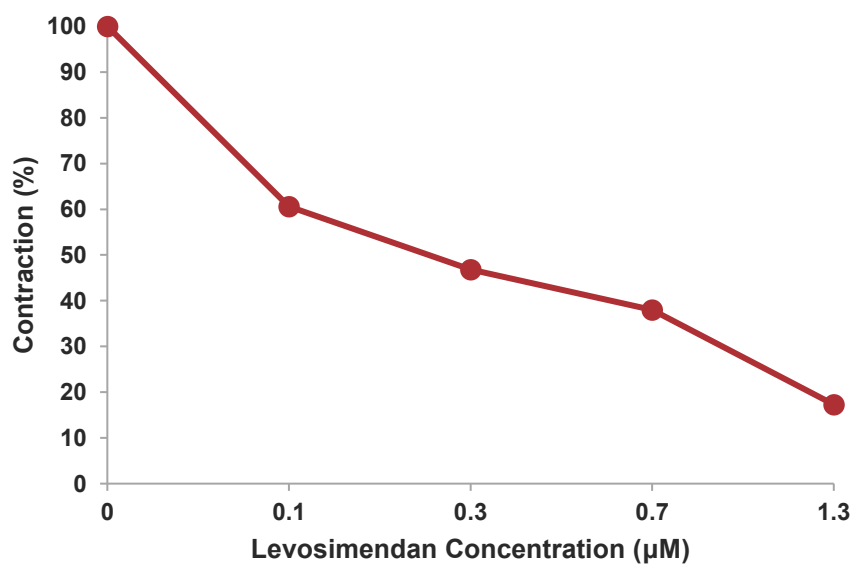
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Oral Levosimendan (TNX-103)

Levosimendan's MOA is Uniquely Suited to Treat PH-HFpEF

NOVEL, POTENTIAL FIRST-IN-CLASS K-ATP CHANNEL ACTIVATOR AND CALCIUM SENSITIZER

Dose-dependent dilation of human portal vein with levosimendan



Vein Becomes Less Contracted as Concentration of Levosimendan Increases

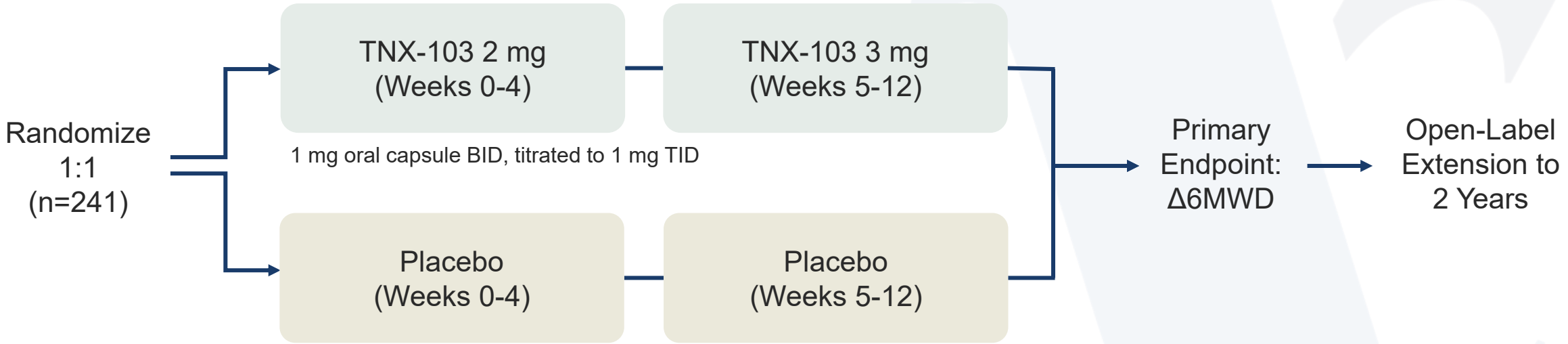
- Human portal vein placed in tissue bath
- Vein is contracted with norepinephrine to mimic human physiology
- Levosimendan is then progressively added to tissue bath

MOA: mechanism of action; K-ATP: potassium adenosine triphosphate-sensitive.
Patariczа J, et al. *The Journal of pharmacy and pharmacology* vol. 52,2 (2000): 213-7.

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Phase 3 LEVEL Trial Design

PHASE 3 REGISTRATIONAL TRIAL IN U.S. AND CANADA



Hemodynamic Inclusion Criteria

RHC with qualifying hemodynamics at rest:

- PCWP ≥ 18 mmHg, and
- mPAP ≥ 30 mmHg, and
- RAP ≥ 8 mmHg

OR

Hemodynamics with passive leg raise

- PCWP ≥ 20 mmHg, and
- mPAP ≥ 32 mmHg, and
- RAP ≥ 8 mmHg

OR

Hemodynamics with bicycle exercise

- PCWP ≥ 25 mmHg, and
- mPAP ≥ 35 mmHg, and
- RAP ≥ 10 mmHg

BID: twice a day; TID: three times a day; 6MWD: 6-minute walk distance; RHC: right heart catheterization; PCWP: pulmonary capillary wedge pressure; mPAP: mean pulmonary artery pressure; RAP: right atrial pressure.

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We Believe LEVEL Confirms the Biological Thesis

PRIMARY ENDPOINT MISSED ON PATIENT SELECTION, NOT ON DRUG EFFECT: LEVEL-2 IS DE-RISKED AS A RESULT

THE BIOLOGY IS CONFIRMED

Bi-ventricular disease, bi-ventricular effect
PH-HFpEF combines volume overload on both sides of the heart, with preload on the left ventricle and afterload and elevated PA pressure on the right. TNX-103 effect on both ventricles demonstrated across numerous echocardiographic parameters.

Preload down
Site-specific splanchnic venodilation cut cardiac wall stress 49% (NT-proBNP), by dramatically lowering filling pressures.

Pulmonary pressure down
RVSP fell 3.5 mmHg over 12 weeks in overall population, and 4.9 mmHg in the below-the-median population, in LEVEL (p-value 0.009).

THE MISS IS EXPLAINED

Design, not drug
The neutral primary result reflects a protocol design flaw, not an ineffective drug: too many patients walked too far at baseline to improve.

A clear gradient
Δ6MWD rises as baseline walk falls. The most limited patients gained more than 26 M in 12 weeks, tracking HELP ($p = 0.0112$).

Not a chance finding
Baseline 6MWD, NT-proBNP and RVSP analyses converge on the same responder population.

LEVEL-2 IS DE-RISKED

Selection now defined
Enrichment is set by observed data, not assumption. LEVEL-2 population's baseline disease severity predicts a significant, clinically meaningful primary endpoint benefit.

Safety supports it
Treatment-emergent AEs were similar in patients above and below the median baseline walk.

More to come
Protocol design paper, primary publication and further analyses through 1H 2027.

PH-HFpEF: pulmonary hypertension in heart failure with preserved ejection fraction; RVSP: right ventricular systolic pressure; LV: left ventricle; RV: right ventricle; 6MWD: 6-minute walk distance; NT-proBNP: N-terminal pro B-type natriuretic peptide; AE: adverse events.

Patient Demographics

BASELINE CHARACTERISTICS WERE BROADLY BALANCED ACROSS TREATMENT ARMS

Characteristic	TNX-103 (N=120)	Placebo (N=121)	Overall (N=241)
Age, years, mean (SD)	69.8 (9.7)	68.5 (10.1)	69.1 (9.9)
Female, n (%)	86 (71.7)	86 (71.1)	172 (71.4)
BMI, kg/m², mean (SD)	33.2 (5.8)	32.9 (6.6)	33.1 (6.2)
eGFR <60 mL/min/1.73 m², n (%)	33 (27.5)	44 (36.4)	77 (32.0)
SGLT2 inhibitor use, n (%)	80 (66.7)	93 (76.9)	173 (71.8)
GLP-1 receptor agonist use, n (%)	36 (30.0)	32 (26.4)	68 (28.2)
MRA use, n (%)	68 (56.7)	76 (62.8)	144 (59.8)
Diuretic use, n (%)	103 (85.8)	106 (87.6)	209 (86.7)
Baseline 6MWD, m, mean (SD)	316.5 (87.3)	322.5 (83.5)	319.5 (85.3)

Characteristic	TNX-103 (N=120)	Placebo (N=121)	Overall (N=241)
NYHA Functional Class II, n (%)	53 (44.2)	55 (45.5)	108 (44.8)
NYHA Functional Class III, n (%)	67 (55.8)	64 (52.9)	131 (54.4)
NYHA Functional Class IV, n (%)	0	2 (1.7)	2 (0.8)
Qualified at rest, n (%)	46 (38.3)	51 (42.1)	97 (40.2)
Qualified on provocation, n (%)	74 (61.7)	70 (57.9)	144 (59.8)
Slow acetylator, n (%)	66 (55.0)	54 (44.6)	120 (49.8)
Intermediate acetylator, n (%)	33 (27.5)	48 (39.7)	81 (33.6)
Rapid acetylator, n (%)	14 (11.7)	7 (5.8)	21 (8.7)
Acetylator status unknown, n (%)	7 (5.8)	12 (9.9)	19 (7.9)

BMI: body mass index; 6MWD: 6-minute walk distance; eGFR: estimated glomerular filtration rate; NYHA: New York Heart Association.

Safety

TOLERABILITY DIFFERENCE BETWEEN ARMS; SERIOUS EVENTS AND CLINICAL WORSENING BALANCED

Adverse event summary	TNX-103 (N=120)	Placebo (N=121)
Any adverse event, n (%)	104 (86.7)	87 (71.9)
Treatment-related adverse event, n (%)	46 (38.3)	21 (17.4)
Leading to treatment discontinuation, n (%)	10 (8.3)	2 (1.7)
Leading to dose reduction, n (%)	18 (15.0)	5 (4.1)
Serious adverse event, n (%)	13 (10.8)	13 (10.7)
Adverse event of special interest, n (%)	11 (9.2)	7 (5.8)
Associated with adjudicated CWE, n (%)	3 (2.5)	3 (2.5)
Unplanned 24-hr CV hospitalization	0 (0)	3 (2.5)
Outpatient visit for IV diuretics	1 (0.8)	0 (0)
Death	2 (1.7)	0 (0)

- Higher rates of treatment-related AEs, dose reductions and discontinuations on drug, driven by headache, palpitations and hypotension
- Serious AEs and adjudicated clinical worsening events were balanced across arms
- No new-onset atrial fibrillation or ventricular tachycardia in patients without pre-existing evidence

CWE: clinical worsening event; AE: adverse event; CV: cardiovascular; IV: intravenous.

Treatment Emergent Adverse Events

BALANCED BETWEEN TNX-103 AND PLACEBO IN THE ≥ AND < MEDIAN BASELINE 6MWD SUBGROUPS

	TNX-103			Placebo		
System Organ Class (SOC) Preferred Term (PT), n (%)	Overall (N=120)	BL 6MWD < Median (N=62)*	BL 6MWD ≥ Median (N=58)*	Overall (N=121)	BL 6MWD < Median (N=57)*	BL 6MWD ≥ Median (N=64)*
Subjects with at least one TEAE	104(86.7%)	54(87.1%)	50(86.2%)	87(71.9%)	45(78.9%)	42(65.6%)
Headache	25(20.8%)	13(21.0%)	12(20.7%)	17(14.0%)	6(10.5%)	11(17.2%)
Palpitations	16(13.3%)	8(12.9%)	8(13.8%)	9(7.4%)	6(10.5%)	3(4.7%)
Dizziness	14(11.7%)	7(11.3%)	7(12.1%)	9(7.4%)	7(12.3%)	2(3.1%)
Diarrhoea	15(12.5%)	10(16.1%)	5(8.6%)	5(4.1%)	4(7.0%)	1(1.6%)
Dyspnoea	9(7.5%)	5(8.1%)	4(6.9%)	9(7.4%)	5(8.8%)	4(6.3%)
Oedema peripheral	12(10.0%)	8(12.9%)	4(6.9%)	6(5.0%)	3(5.3%)	3(4.7%)
Nausea	6(5.0%)	5(8.1%)	1(1.7%)	11(9.1%)	5(8.8%)	6(9.4%)
Fatigue	5(4.2%)	2(3.2%)	3(5.2%)	8(6.6%)	6(10.5%)	2(3.1%)

- Treatment Emergent Adverse Events, defined as AEs that appeared, or worsened, after start of study drug
- TEAE types and rates are representative of a typical HFpEF population, and would not qualify as serious
- Trend observed: some events with higher frequency reported on levosimendan, none likely to impact benefit risk
- No concerning difference in frequency of events in participants with baseline 6MWD below vs. above the median

*Prespecified subgroup
BL: baseline; TEAE: treatment emergent adverse event; 6MWD: 6-minute walk distance.

Primary and Key Secondary Endpoints

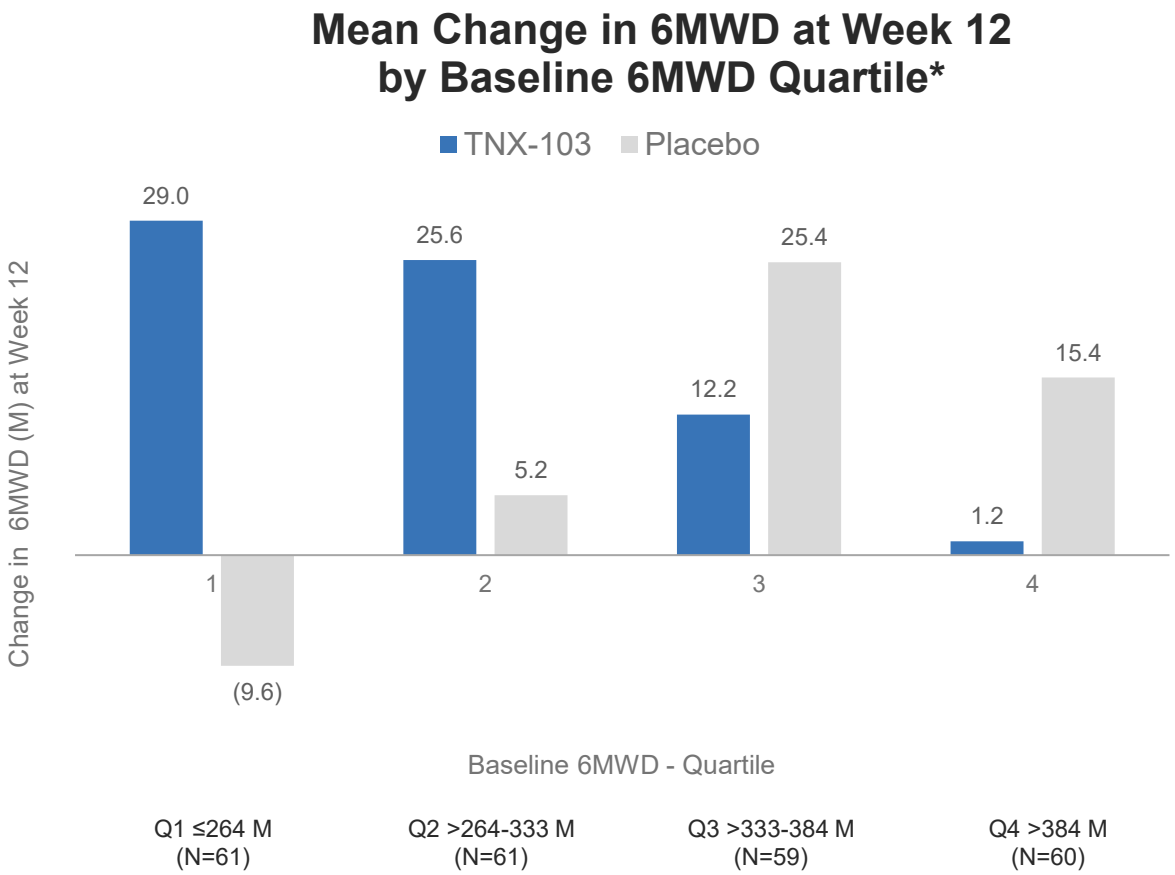
Primary Endpoint (Week 12)		TNX-103 (N=116)	Placebo (N=120)	Treatment difference
6MWD	LS mean	14.0 M (SE: 7.7 M)	10.4 M (SE: 7.6 M)	3.5 M (SE: 7.3; p = 0.63)
	Mean	17.7 M (SD: 40.2 M)	9.8 M (SD: 54.7 M)	8.0 M

Secondary Endpoints (Week 12)	TNX-103 (N=116)	Placebo (N=120)	Treatment difference
KCCQ-TSS, LS mean change	6.6 (SE: 2.4)	6.5 (SE: 2.3)	0.1 (SE: 2.2); NS
NYHA functional class improvement, n (%)	28 (24.1)	27 (22.5)	NS
Adjudicated clinical worsening, n (%)	3 (2.5)*	3 (2.5)*	NS

*N=120 and N=121 for TNX-103 and placebo arms, respectively.
6MWD: 6-minute walk distance; LS: least squares; SE: standard error; SD: standard deviation; KCCQ-TSS: Kansas City Cardiomyopathy Questionnaire-Total Symptom Score; NYHA: New York Heart Association; NS: not significant p-value.

Mean Change in 6MWD by Baseline 6MWD Quartile

INVERSE LINEAR RELATIONSHIP BETWEEN BASELINE 6MWD AND TREATMENT EFFECT



Levosimendan produced a large and clinically meaningful improvement in 6MWD in those patients who had a lower baseline walk distance (sicker) and room for improvement

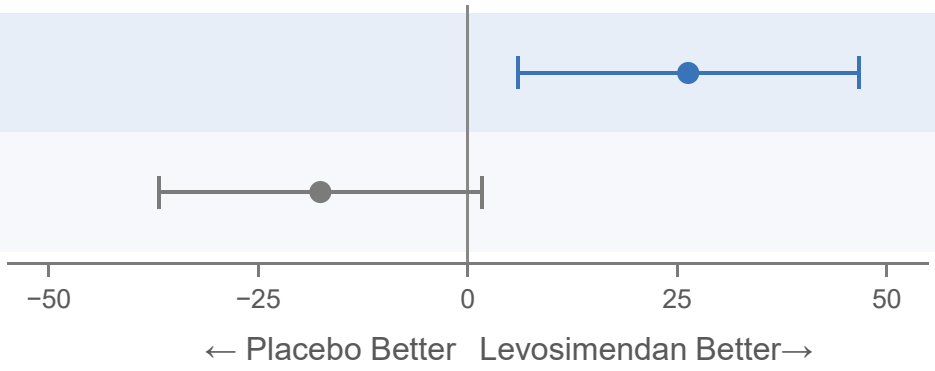
Subgroup and quartile analyses show very clear evidence of treatment effect modification by baseline 6MWD: the treatment × baseline 6MWD interaction term in the primary analysis was significant in all 100 imputed datasets, with an average p-value of 0.006.

*Post-hoc analysis
6MWD: 6-minute walk distance; LS: least squares.

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Drug Response Correlates with Baseline 6MWD

Baseline 6MWD	LS Mean Difference in Δ6MWD (95% CI)	Levosimendan N / LS Mean (95% CI)	Placebo N / LS Mean (95% CI)	LS Mean Difference (95% CI)
Below Median (<333 M)		61 / 21.1 (−0.5, 42.7)	56 / −5.2 (−27.3, 16.8)	**26.3 (6.0, 46.7)**
Above Median (≥ 333 M)		55 / 5.8 (−14.3, 25.9)	64 / 23.4 (4.2, 42.5)	−17.6 (−36.9, 1.7)



*Prespecified analysis
6MWD: 6-minute walk distance; LS: least squares; CI: confidence interval.

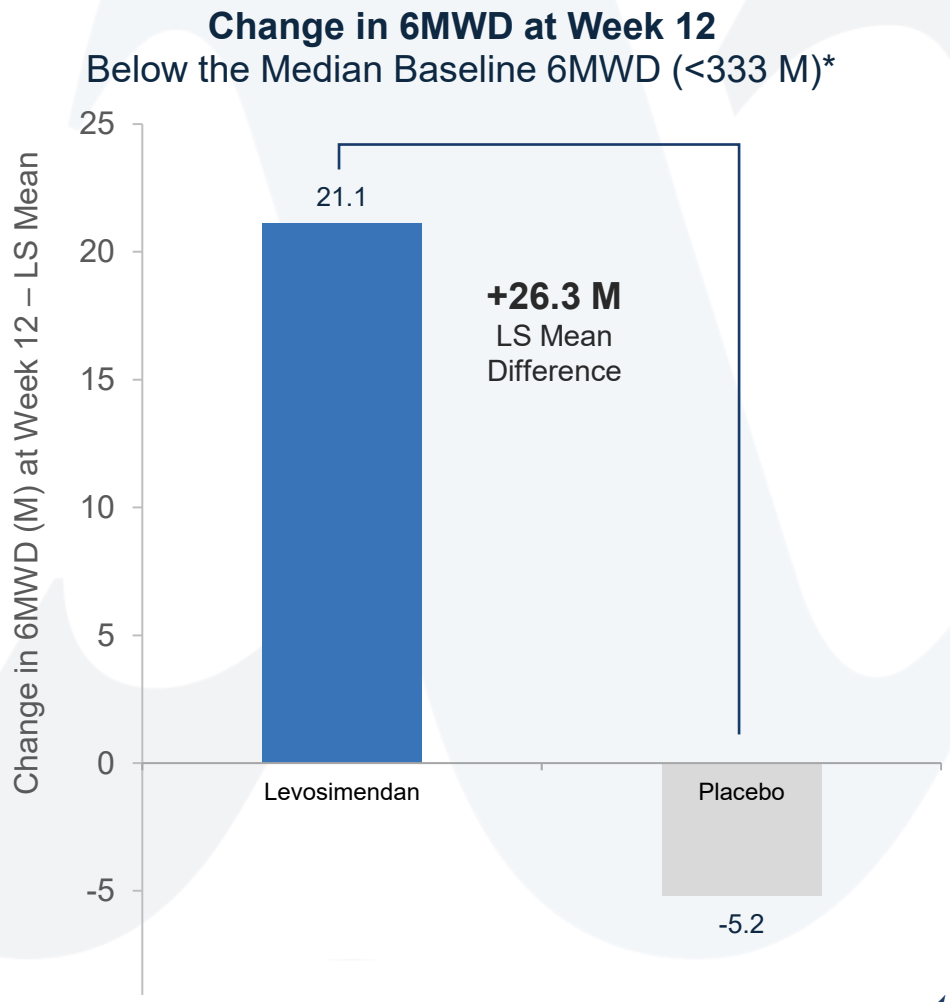
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Patients with Greater Exercise Limitation Demonstrated Large Treatment Effect

Multi-variable analyses identified baseline 6MWD as the strongest predictor of improvement in 6MWD

Treatment with TNX-103 resulted in a 26.3 M improvement compared to placebo in patients with a baseline 6MWD <333 M

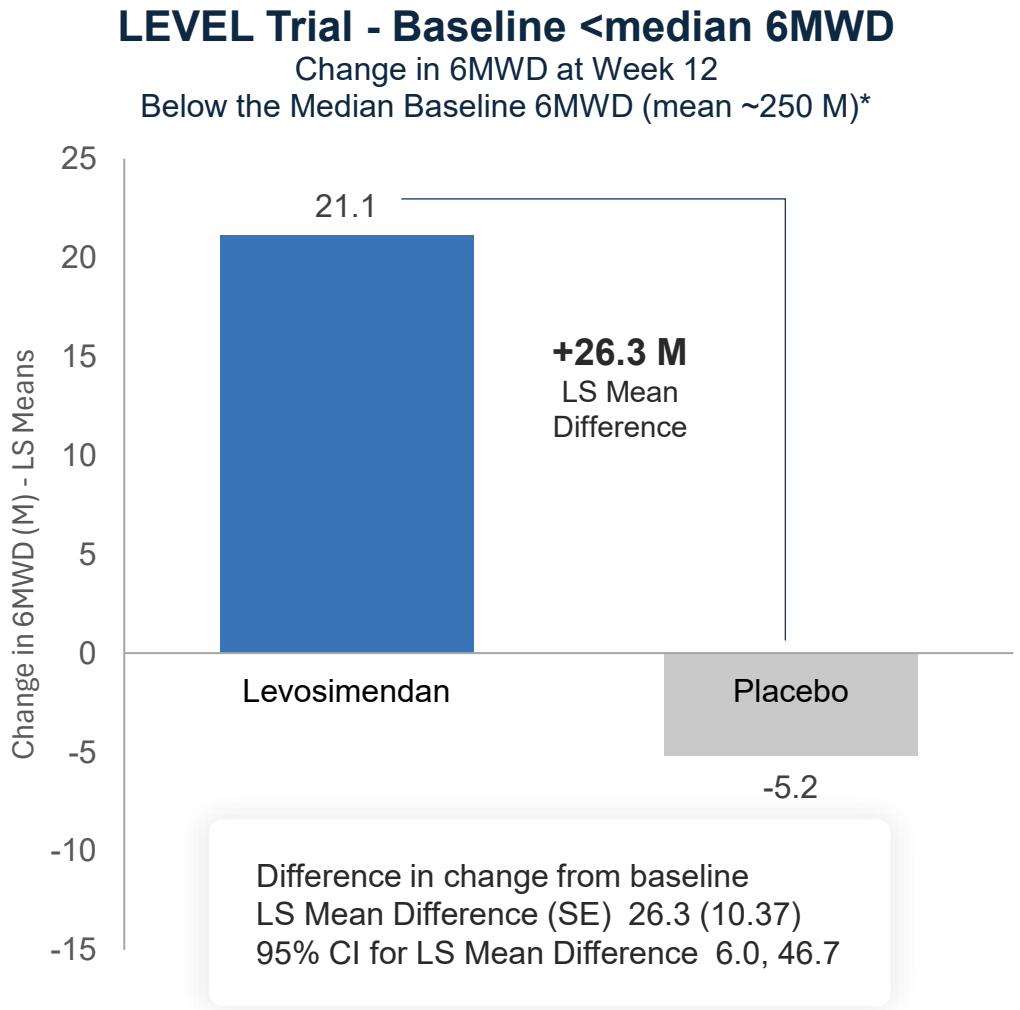
(95% CI: 6.0, 46.7; p = 0.0112#)

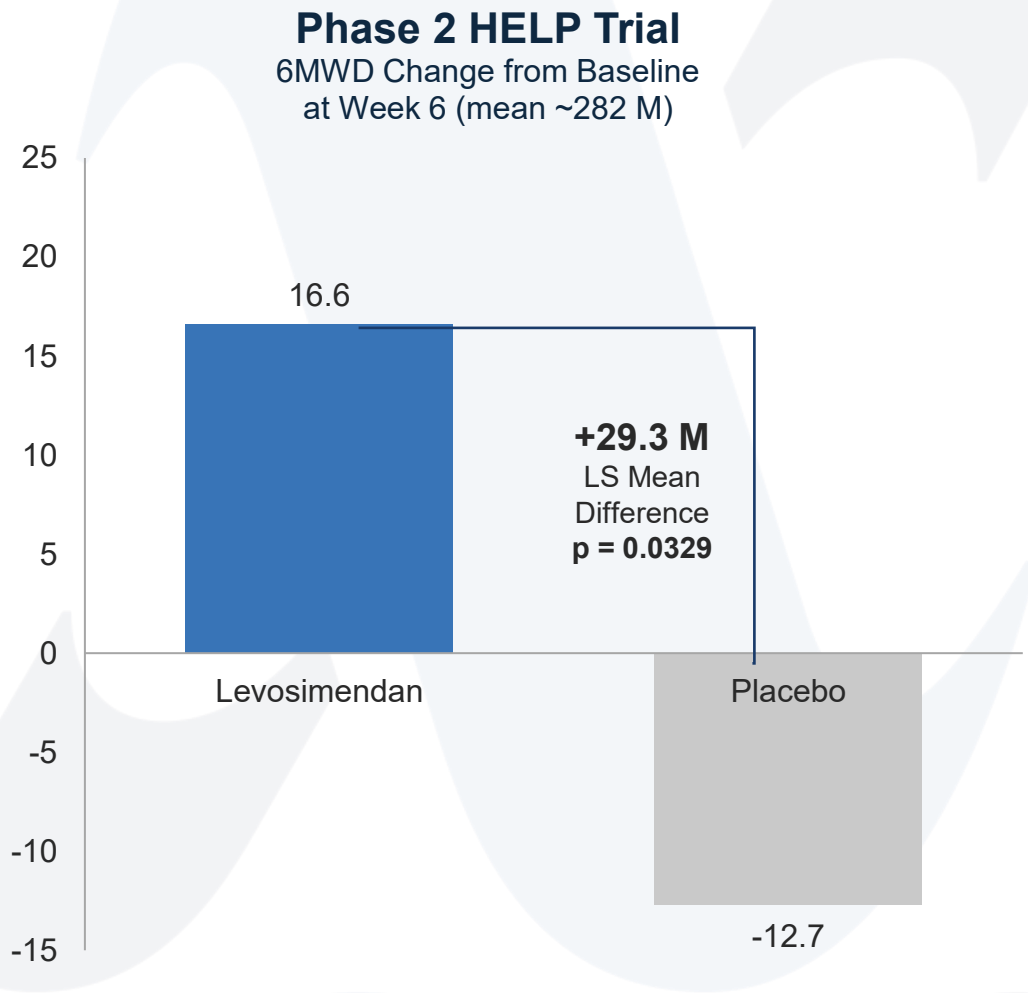


*Prespecified analysis. #For patients with a baseline 6MWD ≥333 M, the change in 6MWD was -17.6 M (95% CI -36.9, 1.7; nominal p-value 0.0744)
6MWD: 6-minute walk distance; LS: least squares; SE: standard error; CI: confidence interval.

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LEVEL Patients with Baseline 6MWD <Median: Improvement Similar to HELP

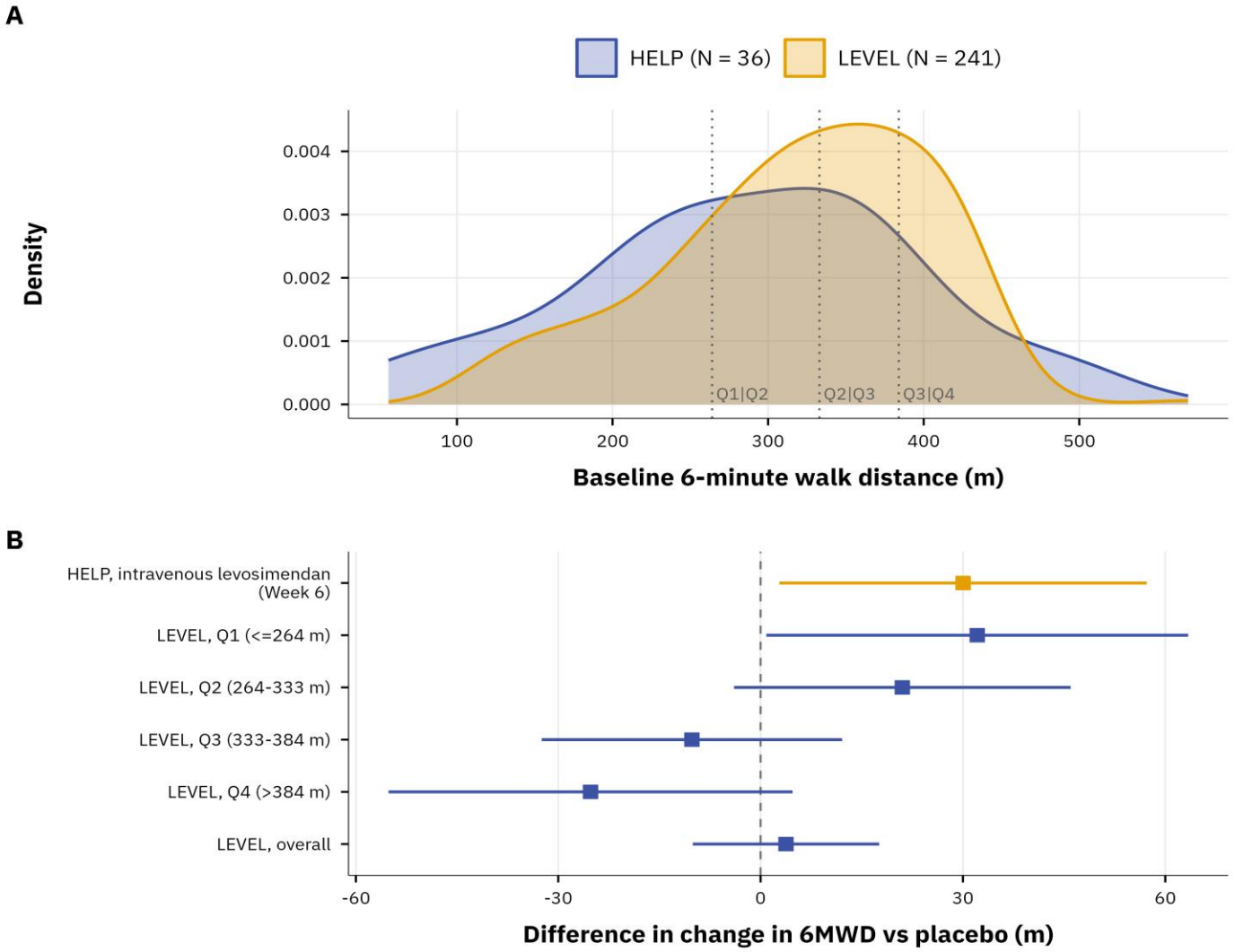




*Prespecified subgroup
6MWD: 6-minute walk distance; LS: least squares; SE: standard error; CI: confidence interval.

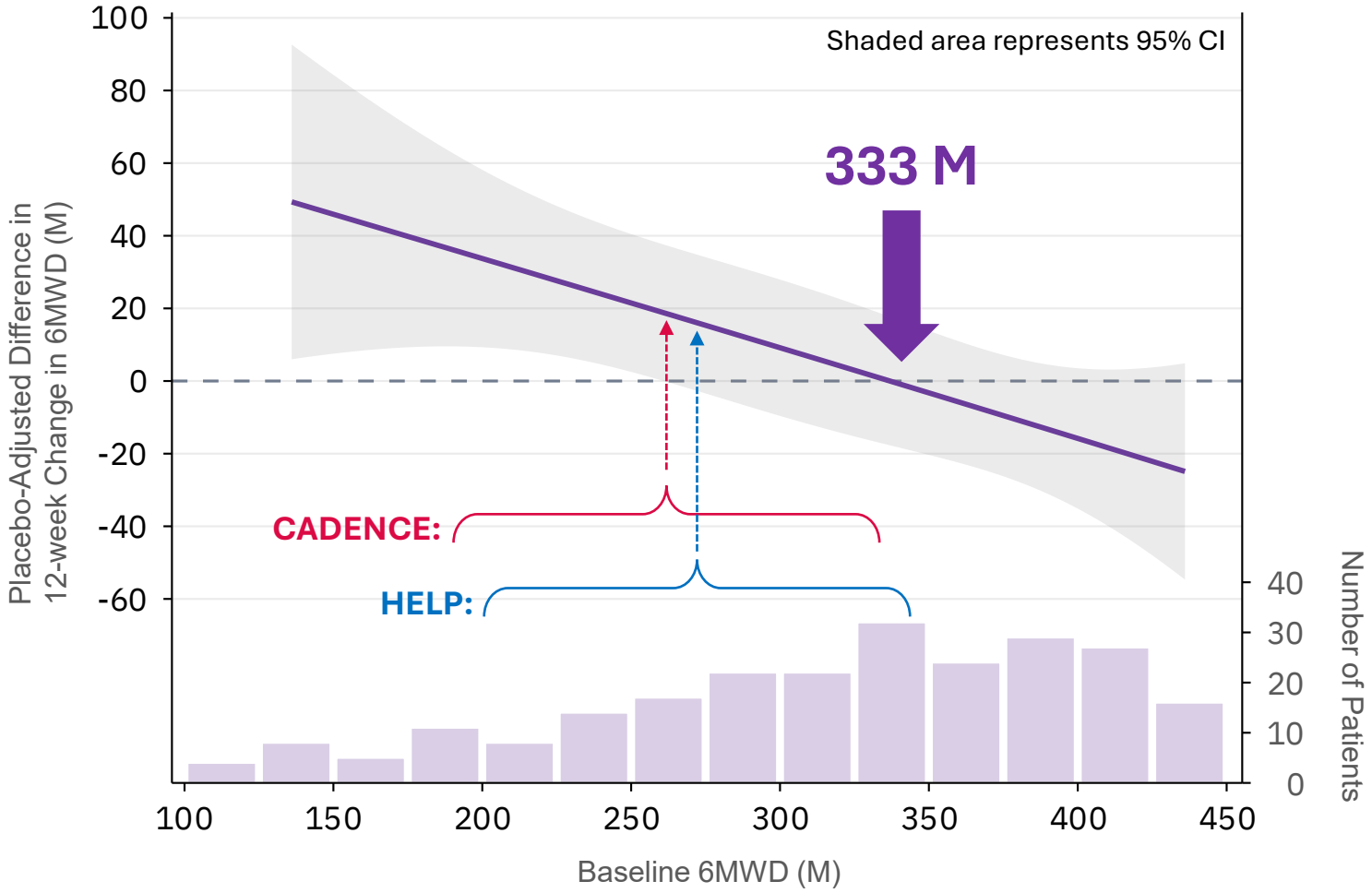
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6MWD Treatment Effect: Comparison of LEVEL (12 Weeks) & HELP (6 Weeks)



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Lower 6MWD, Greatest Benefit



- Inverse linear relationship between baseline 6MWD and treatment effect
- In LEVEL, levosimendan-treated patients whose baseline 6MWD matched HELP and CADENCE (274-285 M) had a ~20 M placebo-adjusted improvement in 6MWD

Data presented by Dr. Sanjiv Shah at ESC Congress 2026 on August 29, 2026.
6MWD: 6-minute walk distance.

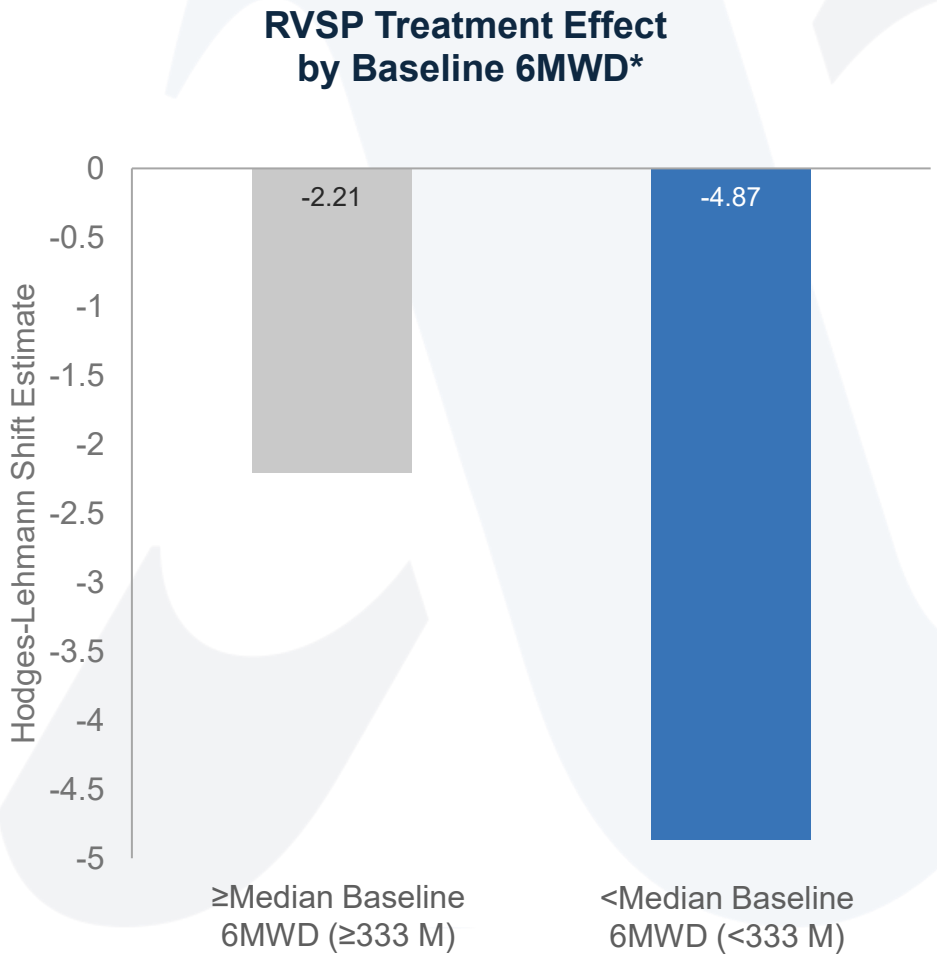
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RVSP Reduction Greatest in Patients with Baseline 6MWD <Median (<333 M)

LEVOSIMENDAN EFFECTIVELY LOWERS RVSP ACROSS THIS PULMONARY HYPERTENSION POPULATION

Physiologic improvement in RVSP aligns with 6MWD improvement in this cohort (Baseline 6MWD <333 M*)

	≥Median Baseline	<Median Baseline
	-2.210 (1.5817)	-4.873 (1.8776)
95% CI	-5.370, 0.830	-8.410, -1.050
p-value	0.1322	0.0090

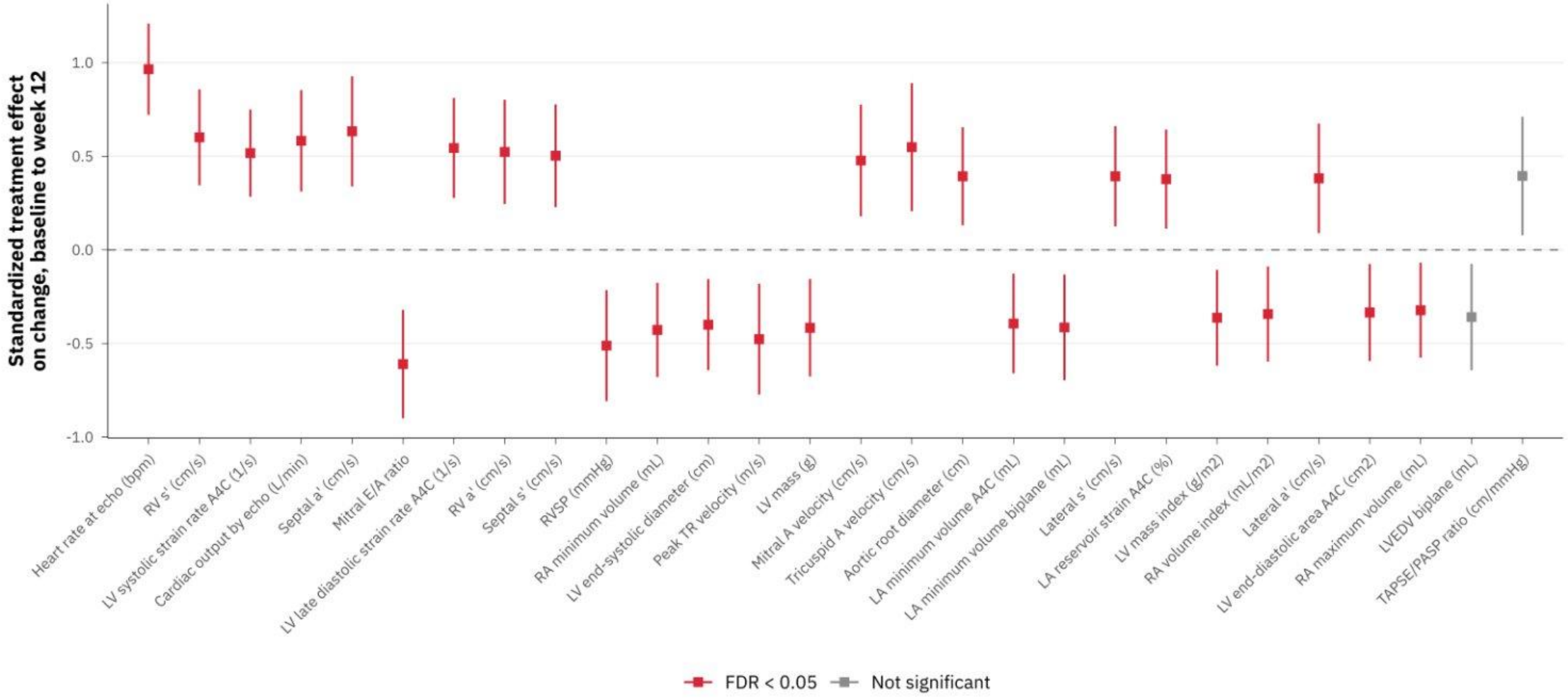


*Prespecified subgroup
6MWD: 6-minute walk distance; CI: confidence interval.

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Echocardiographic Measures Point to RV & LV Functional Enhancement

ECHOCARDIOGRAPHY CONDUCTED AT BASELINE AND WEEK 12



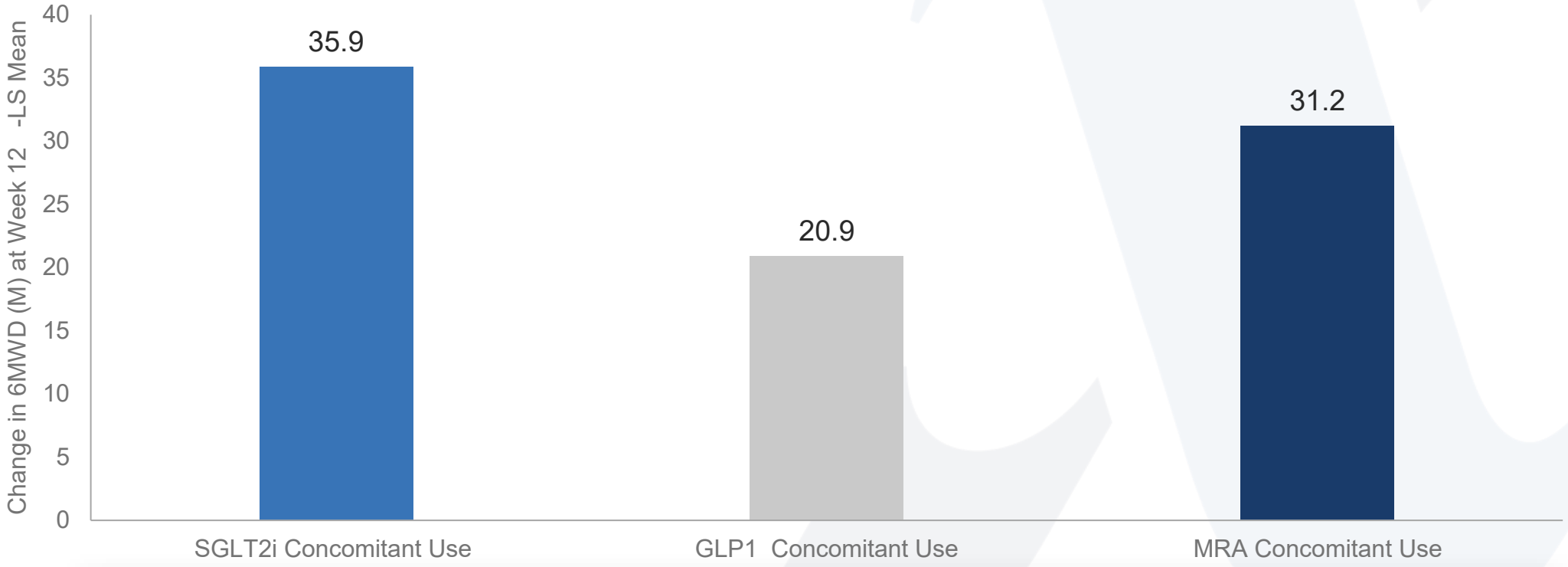
Echocardiographic summary provided by Northwestern University core lab

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TNX-103 Benefited Patients on State-of-the-Art Therapy

PATIENTS WITH BASELINE 6MWD <MEDIAN (333 M) AND ON GLP-1s & GUIDELINE-DIRECTED MEDICAL THERAPY BENEFIT MOST

LS Mean Difference in 6MWD at Week 12
By Background Medication Use at Baseline in Patients
Below the Median Baseline 6MWD (<333 M)*



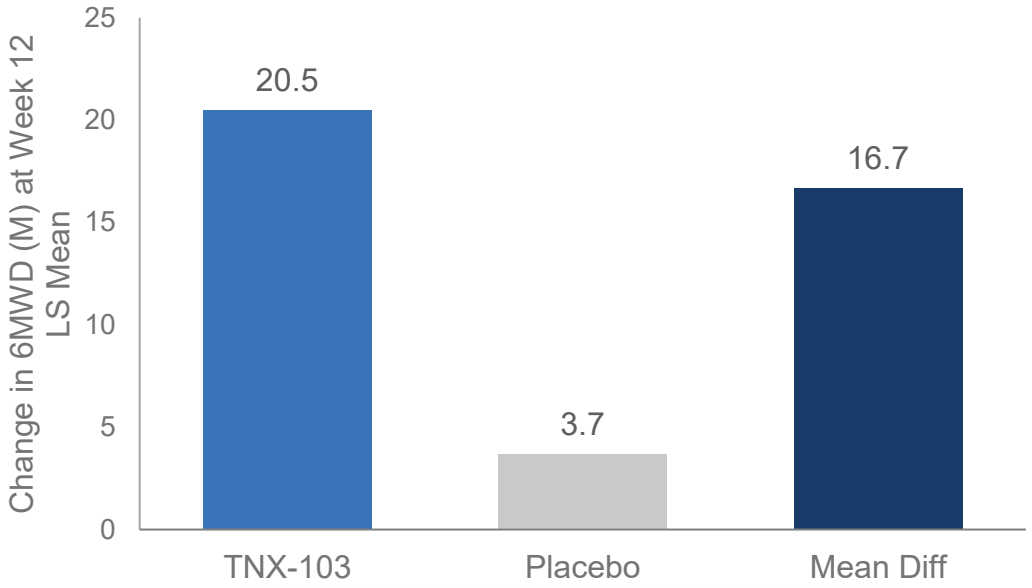
SGLT2i Concomitant Use	GLP1 Concomitant Use	MRA Concomitant Use
Difference in change from baseline LS Mean Difference (SE) 35.9 (12.17) 95% CI for LS Mean Difference 12.1, 59.8	Difference in change from baseline LS Mean Difference (SE) 20.9 (14.59) 95% CI for LS Mean Difference -7.7, 49.4	Difference in change from baseline LS Mean Difference (SE) 31.2 (11.78) 95% CI for LS Mean Difference 8.1, 54.3

*Prespecified subgroup
6MWD: 6-minute walk distance; LS: least squares; SE: standard error; CI: confidence interval.

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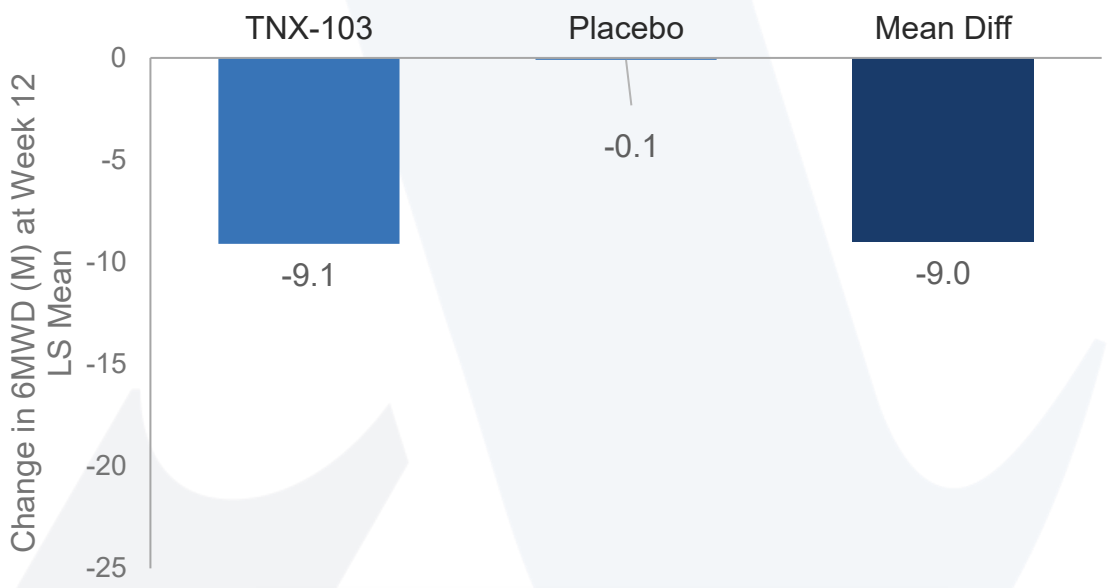
LEVEL Study 6MWD Change by Baseline NT-proBNP

LS Mean Difference in 6MWD at Week 12
Baseline NT-proBNP ≥Median (≥225 pg/mL)*



Difference in change from baseline	
LS Mean Difference (SE)	16.7 (9.72)
95% CI for LS Mean Difference	-2.3, 35.8

LS Mean Difference in 6MWD at Week 12
Baseline NT-proBNP <Median (<225 pg/mL)*



Difference in change from baseline	
LS Mean Difference (SE)	-9.0 (10.83)
95% CI for LS Mean Difference	-30.2, 12.3

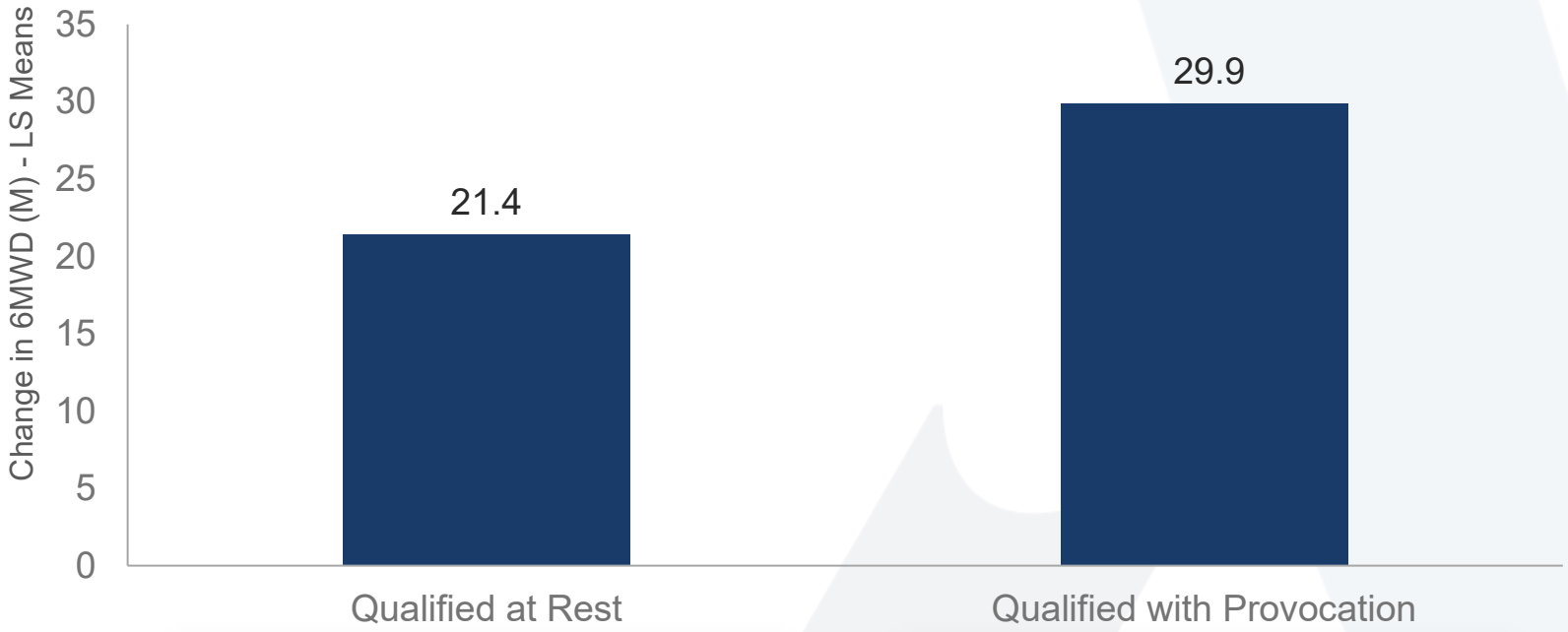
*Post-hoc analysis
6MWD: 6-minute walk distance; NT-proBNP: N-terminal pro B-type natriuretic peptide; LS: least squares; SE: standard error; CI: confidence interval.

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Δ6MWD by Type of Qualifying RHC Hemodynamic Assessment

BY SUBGROUP WITH BASELINE 6MWD < MEDIAN (<333 M)

LS Mean Treatment Difference in 6MWD at Week 12
Based on Qualifying Hemodynamic Assessment for Patients Below the Median Baseline 6MWD (<333 M)*



Difference in change from baseline
LS Mean Difference (SE) 21.4 (15.15)
95% CI for LS Mean Difference -8.3, 51.1

Difference in change from baseline
LS Mean Difference (SE) 29.9 (14.12)
95% CI for LS Mean Difference 2.2, 57.6

*Post-hoc analysis
6MWD: 6-minute walk distance; NT-proBNP: N-terminal pro B-type natriuretic peptide; LS: least squares; SE: standard error; CI: confidence interval.

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Strongest Δ6MWD has been Observed in Lowest Baseline 6MWD Cohort

PAH STUDIES WITH BEST RESULTS IN LOWEST 6MWD COHORT

- **SERAPHIN Trial** (1) (macitentan) <300 M baseline cohort
- **SUPER-1 Trial** (2) (sildenafil) <325 M baseline cohort
- **PHIRST Trial** (3) (tadalafil) <325 M baseline cohort
- **TRIUMPH-1** trial (4) (treprostinil) <350 M baseline cohort

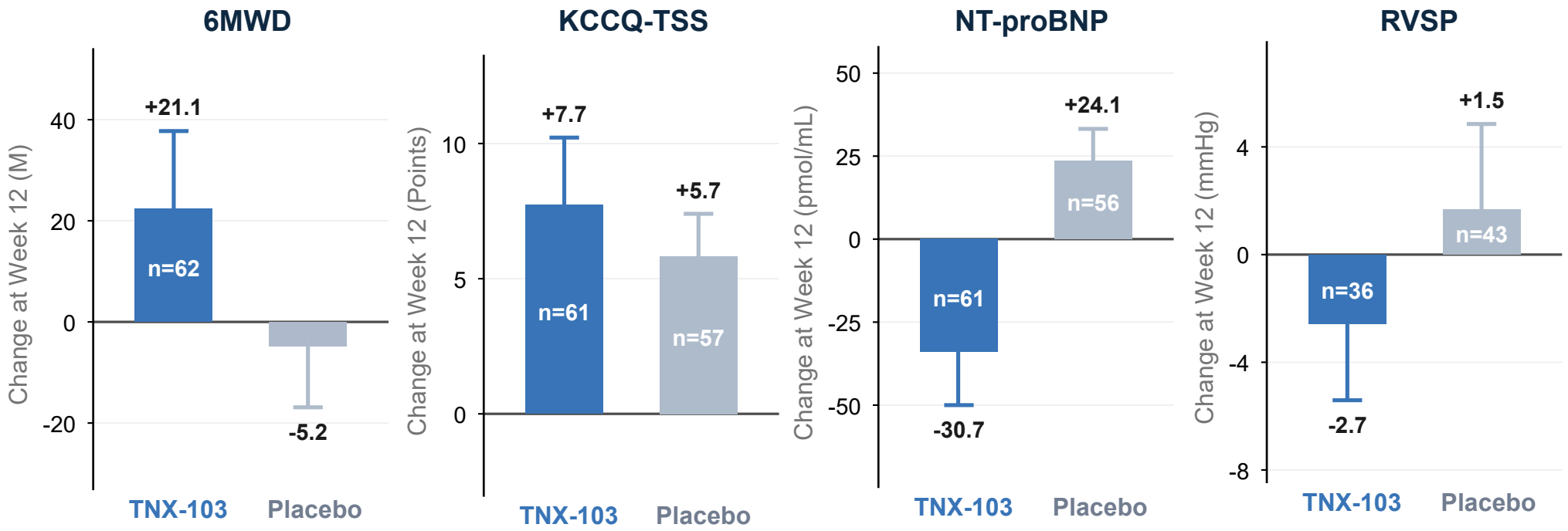
PH/HFPEF STUDIES REPORTING POSITIVE 6MWD RESULTS

- **PRESERVED-HF** (5) (dapagliflozin) mean 244 M baseline
- **CADENCE** (6) (low dose sotatercept) median 259 M
- **HELP** (IV levosimendan) median 282 M

1. Souza, Rogério, et al. Association between six-minute walk distance and long-term outcomes in patients with pulmonary arterial hypertension: data from the randomized SERAPHIN trial. PLoS One 2018; 13.3: e0193226.
2. Galiè N, Ghofrani HA, Torbicki A, et al. Sildenafil citrate therapy for pulmonary arterial hypertension. N Engl J Med 2005; 353(20):2148–2157
3. Galiè N, Brundage BH, Ghofrani HA, et al. Tadalafil therapy for pulmonary arterial hypertension. Circulation 2009; 120(12):1068–1076
4. McLaughlin VV, Benza RL, Rubin LJ, et al. Addition of inhaled treprostinil to oral therapy for pulmonary arterial hypertension: a randomized controlled clinical trial. Journal of the American College of Cardiology 2010; 55(18):1915–1922
5. Nassif, Michael E., et al. The SGLT2 inhibitor dapagliflozin in heart failure with preserved ejection fraction: a multicenter randomized trial. Nature medicine 2021; 27.11: 1954-1960.
6. Gomberg-Maitland, Mardi, et al. Sotatercept for combined post-and precapillary pulmonary hypertension associated with heart failure: results from the phase 2, randomized, placebo-controlled CADENCE study. Circulation 2026: 153.19: 1446-1459.

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Baseline 6MWD Below Median (<333 M) Subgroup



	6MWD	KCCQ-TSS	NT-proBNP	RVSP
Difference or Treatment Effect	+26.3 M	+2.0 points	0.53 ratio	-4.9 mmHg
95% CI	6.0, 46.7	-4.8, 8.7	0.42, 0.65	-8.4, -1.1
Nominal p-value	0.0112	0.5676	<0.0001	0.0090

6MWD: 6-minute walk distance; KCCQ-TSS: Kansas City Cardiomyopathy Questionnaire-Total Symptom Score;
NT-proBNP: N-terminal pro B-type natriuretic peptide;
RVSP: right ventricular systolic pressure; CI: confidence interval

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We Believe Learnings from LEVEL will De-risk LEVEL-2

Strong treatment effect in patients with baseline 6MWD below the median (<333 M) is real:

- Prespecified subgroup finding supported by multivariable analysis
- No evidence that regression to the mean explains the finding
- RVSP reduction aligns with the improvement in 6MWD improvement
- Magnitude of improvement in 6MWD is consistent with Phase 2 HELP trial
- Treatment effect is additive to GLP-1s and guideline-directed medical therapy for HFpEF
- Other PAH and PH-HFpEF studies have observed the strongest responses in patients with lower baseline 6MWD

6MWD: 6-minute walk distance; RVSP: right ventricular systolic pressure; HFpEF: heart failure with preserved ejection fraction; PAH: pulmonary arterial hypertension; PH: pulmonary hypertension.

Confirming Biological Activity Using NT-proBNP

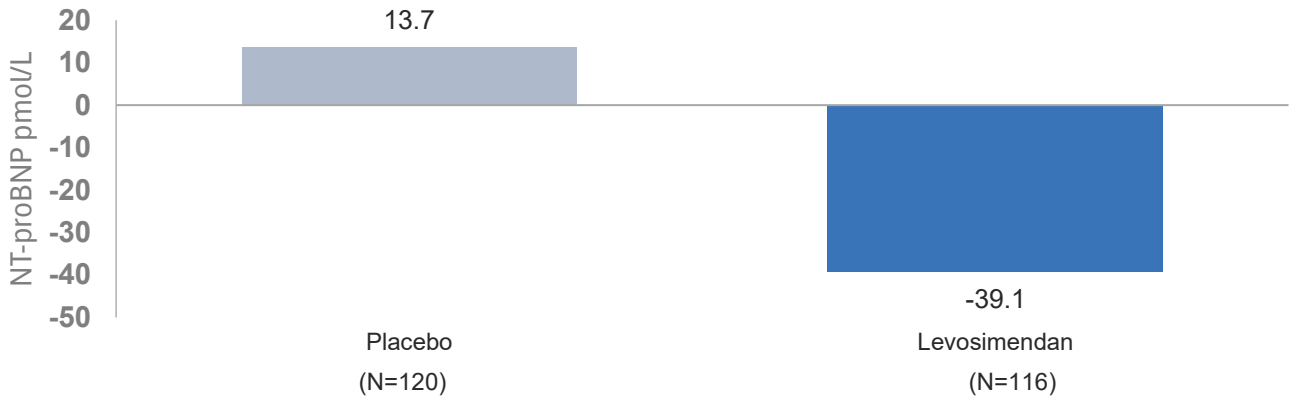
NT-proBNP FELL IN OVERALL POPULATION WITH SUBSTANTIAL REDUCTION OBSERVED IN FIRST VISIT AFTER RANDOMIZATION

All Patients

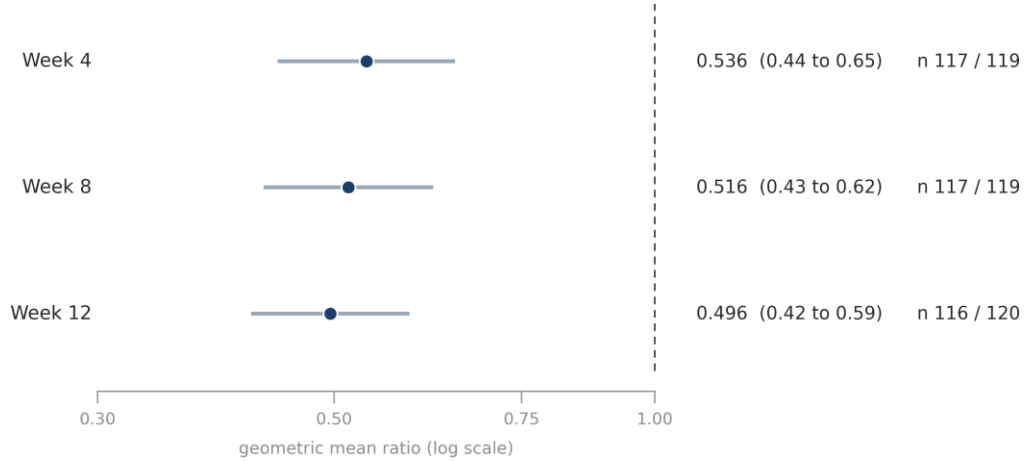
– 49%

NT-proBNP vs. placebo at Week 12
Geometric LS mean ratio 0.51
(95% CI: 0.43, 0.60; p < 0.0001*)

NT-proBNP Mean Change from Baseline at Week 12



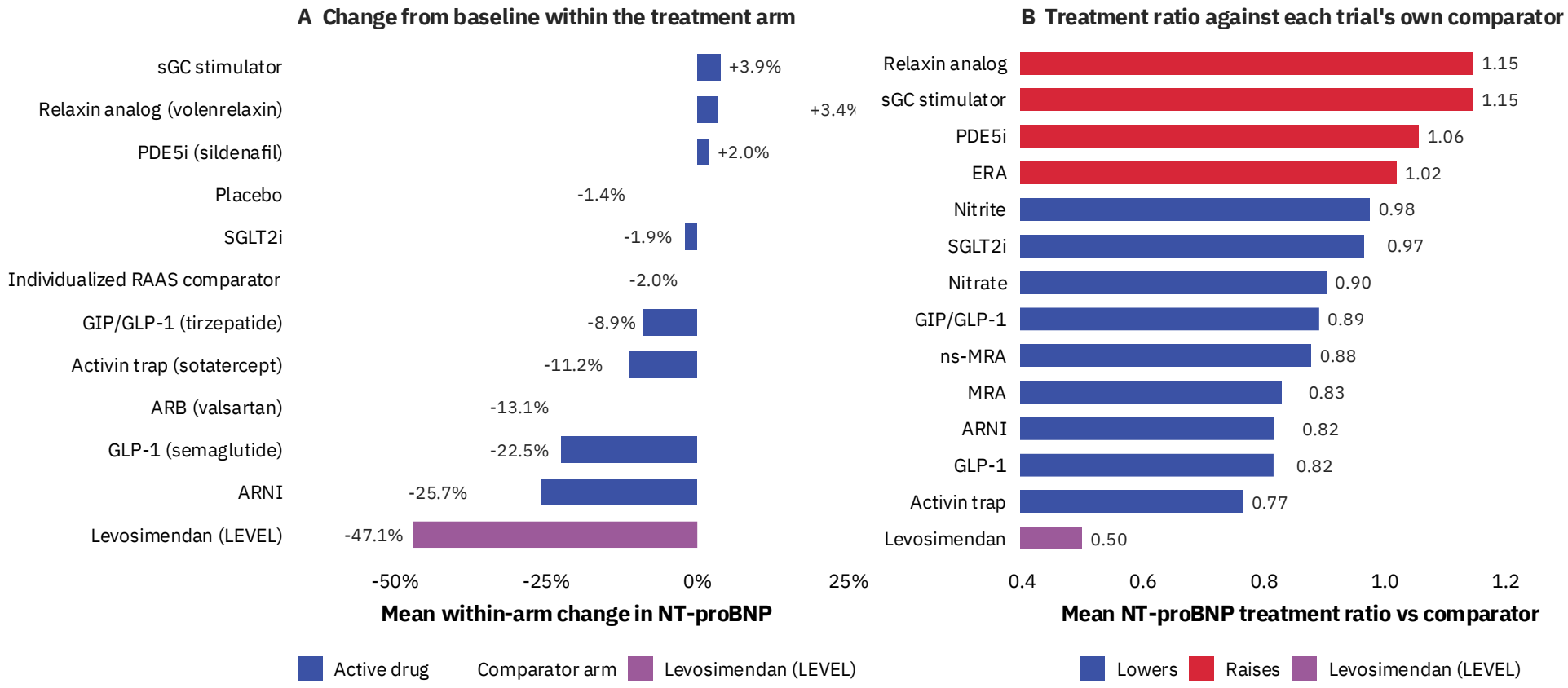
Substantial NT-proBNP reduction noted in first four weeks of TNX-103 treatment



*nominal p-value.
NT-proBNP: N-terminal pro B-type natriuretic peptide; LS: least squares; CI: confidence interval.

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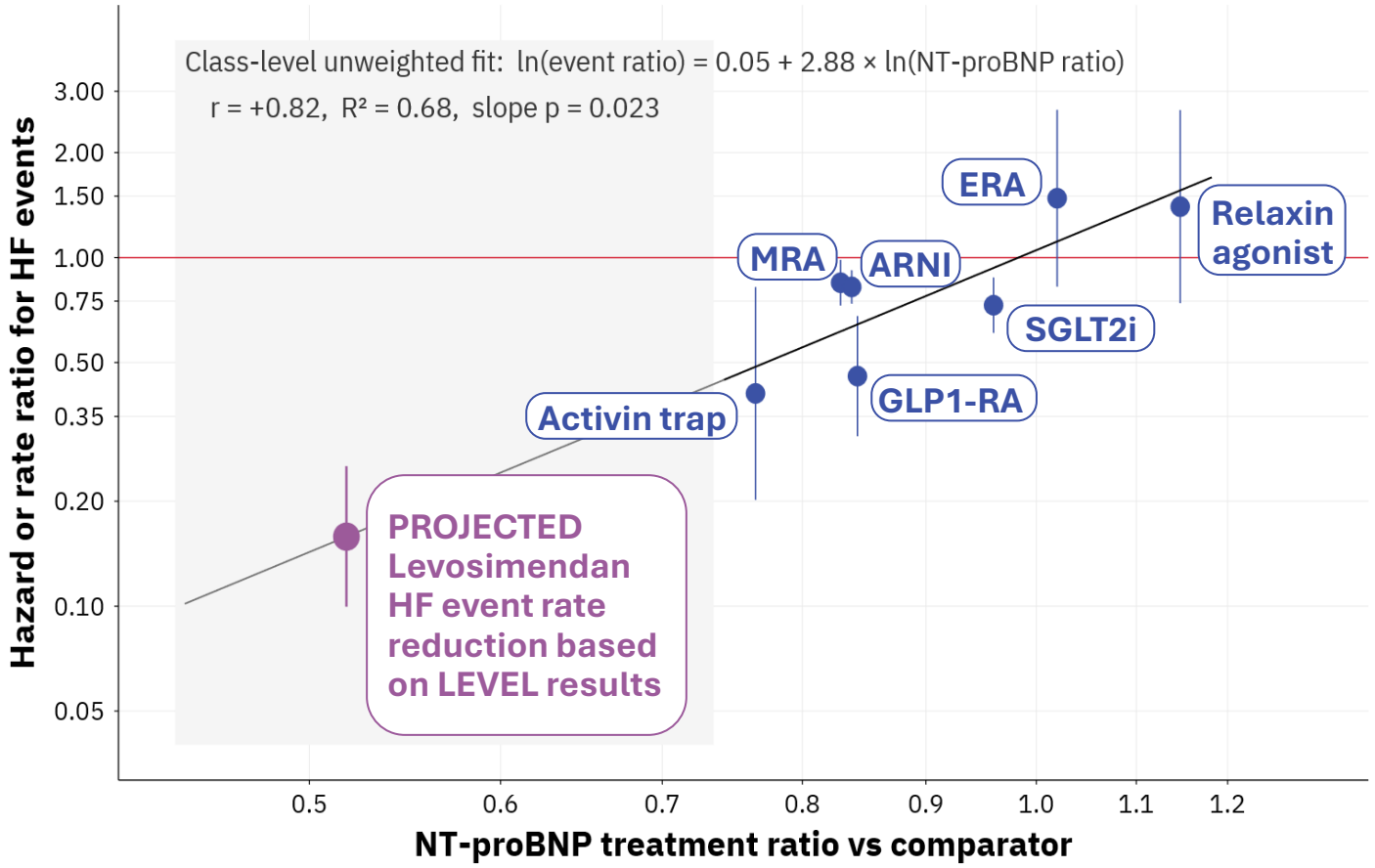
LEVEL: Largest Reduction in NT-proBNP To Date in HFpEF



Data presented by Dr. Sanjiv Shah at ESC Congress 2026 on August 29, 2026

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↓ NT-proBNP: Predicted Effect on ↓ HF Events



Data presented by Dr. Sanjiv Shah at ESC Congress 2026 on August 29, 2026

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What LEVEL Tells Us

KEY LEARNINGS FROM THE FIRST PHASE 3 TRIAL

LEVEL did not meet its primary endpoint, but a strong treatment effect was seen across patients with higher disease burden

What we confirmed

- Oral levosimendan is safe and well-tolerated, with 1 mg BID/TID providing PK concentrations expected
- Targeting volume overload with K-ATP channel activation has direct effects on NT-proBNP and RVSP, two prespecified endpoints
- Treatment effect seen in HELP study validated
- Successful trial execution by sites and clinical development team

What we learned

- Drug effect is evident in patients with higher disease burden
- Study entry criteria allowed patients with moderate disease and little room to improve in 6MWD
- In patients with baseline 6MWD* < 333 m, treatment effect was **+26.3 m vs placebo** (95% CI: 6.0, 46.7; nominal p = 0.0112)
- In patients with baseline 6MWD* ≤ 300 m, or 300 m ≤ 6MWD ≤ 400 m & RAVI ≥ 25 mL/m^2, treatment effect was **+34 m vs placebo** (95% CI: 15, 53; nominal p = 0.001)
- In the overall population, NT-proBNP was reduced by 49% vs placebo (nominal p < 0.0001)

WHAT WE ARE DOING NOW

Amending LEVEL-2 to enrich on baseline 6MWD and RAVI

*Prespecified analysis; nominal p-values are not adjusted for multiplicity.
PK: pharmacokinetics; NT-proBNP: N-terminal pro B-type natriuretic peptide; RVSP: right ventricular systolic pressure; HELP: Hemodynamic Evaluation of Levosimendan in Patients with PH-HFpEF; 6MWD: 6-minute walk distance; CI: confidence interval; RAVI: right atrial volume index.

Building on LEVEL

A DATA-DRIVEN ENRICHMENT STRATEGY FOR LEVEL-2

- **Multivariable analyses** were used to identify a sub-population with strong treatment effects. 6MWD at baseline and Right Atrial Volume Index (RAVI) were the most robust and consistent predictors of treatment response
- **RAVI** reflects the size of the right atrium in relation to body surface area, and identifies those LEVEL patients with higher exercise capacity (walking 300m to 400m at baseline) most likely to benefit from treatment with levosimendan
- **Baseline 6MWD and RAVI requirements for LEVEL-2** are drawn from the LEVEL population with the strongest treatment effect
- **Tenax intends to Amend the LEVEL-2 protocol** to enrich the population for patients with high likelihood of demonstrating greater treatment effects resulting from their volume overload and demonstrated by more pronounced exercise impairment at baseline

Enriched LEVEL-2 entry criterion: [100m ≤ 6MWD ≤ 300m] OR [300m < 6MWD ≤ 400m AND RAVI ≥ 25 mL/m^2]

In LEVEL patients meeting these criteria:

- > **34 meters vs placebo at Week 12** (95% CI: +15 M, +53 M; nominal p = 0.001)
- > 50% of LEVEL patients meet these criteria

6MWD: 6-minute walk distance; RAVI: right atrial volume index; CI: confidence interval; PH: pulmonary hypertension; HF: heart failure.

Right Atrial Volume Index (RAVI) Identifies Patients with Strong Response to a Volume-Reduction Strategy

The primary driver of PH-HFpEF is excessive blood volume filling the heart and lungs

The established MOA of levosimendan in patients with PH-HFpEF is dilation of the veins of the splanchnic circulation, thereby reducing this excessive volume

- The excess blood entering the heart initially enters the right atrium, where the effect of this excess can be measured during a right heart catheterization (RHC) as right atrial pressure (RAP)
- LEVEL and LEVEL-2 participation requires an RAP of at least 8 mmHg on entry. Normal resting RA pressure is 5 mmHg, and the upper limit of normal is 8 mmHg

- Right atrial volume index (RAVI) is an echo measure of RA size. Normal RAVI is 25 for men and 21 for women, with an upper limit of normal of 30 for both
- Analysis of LEVEL data demonstrates:
  - a baseline 6MWD ≤ 300m predicts a strong response to levosimendan
  - a baseline 6MWD of >300 – 400m **and** a RAVI ≥25 mL/m^2 predict a strong response to levosimendan

LEVEL results enable the identification of patients most likely to have a robust response to levosimendan as those with qualifying hemodynamics, and a baseline 6MWD ≤300 meters, or a 6MWD of >300 – ≤400 meters with a RAVI ≥25 mL/m^2

RAVI: right atrial volume index; PH-HFpEF: pulmonary hypertension in heart failure with preserved ejection fraction; MOA: mechanism of action; 6MWD: 6-minute walk distance.

LEVEL-2 Update: Protocol Amendment Implementation

TEMPORARY ENROLLMENT PAUSE; FDA INTERACTIONS

Effective execution of the Amended LEVEL-2 protocol requires a temporary pause in enrollment

- **Timely:** pause in screening and randomization instituted upon confirmation of enrichment strategy, to maximize enrollment of patients with these enrichment factors. LEVEL analyses demonstrate these patients stand to benefit most from treatment with levosimendan: those who demonstrated higher disease burden at baseline according to the most robust factors predicting improvement in exercise tolerance. Echocardiography collected at screening will be centrally reviewed to confirm eligibility
- **Temporary:** pause in enrollment will be limited to the time required to institute this Amendment. It is estimated less than 5% of LEVEL-2 patients to be included in the primary efficacy analysis will have been enrolled without meeting the stricter criteria in the Amended protocol
- **Not safety-related:** temporary pause in enrollment does not affect the ongoing treatment of patients enrolled in Q1-Q3 2026, who remain blinded for one year, and then can continue in LEVEL-SET. The enrollment pause is not related to a concern about safety, nor was it made in response to any request from a regulatory authority

FDA interactions

- Topline LEVEL results were shared with FDA in mid-August
- Tenax has since requested a Type C meeting to discuss the overall development of levosimendan in PH-HFpEF
- Publication of the LEVEL-2 protocol design paper is expected in Q1 2027
- **Further updates on levosimendan development are expected in Q1 2027**

FDA: U.S. Food and Drug Administration; PH-HFpEF: pulmonary hypertension in heart failure with preserved ejection fraction.

IP Portfolio Protects Global Rights to Levosimendan Use in PH-HFpEF

- US patents for oral (TNX-103), IV, expanded dose and combination use through 2040
- Global protection pending across potential markets
- All patents have continuation applications pending

United States:

US 11,213,524, issued January 4, 2022, **expires November 14, 2039** (SC Formulation/Use)
US 11,607,412, issued March 21, 2023, **expires December 15, 2040** (IV Use)
US 11,701,355, issued July 18, 2023, **expires December 15, 2040** (Oral Use)
US 11,969,424, issued April 30, 2024, **expires December 15, 2040** (Expanded dose & CV drug combo use)
US 12,616,694, issued May 5, 2026, **expires October 15, 2041** (SC Use)

All patents have continuation applications pending

Europe

EP 4076398 B1 issued February 18, 2026, **expires December 15, 2040**

Japan/Canada/New Zealand/Australia/Thailand/ Malaysia/Singapore:

Regional stage applications filed (PCT/US2020/065166)
Canadian Patent Application No. 3,161,960 – Allowed

Other PCT Applications:

PCT/US2022/080708, filed November 30, 2022 (Combination use of levosimendan and SGLT-2 in HF)
PCT/US2022/082561, filed December 29, 2022 (Oral Levosimendan use in PH-HFpEF)

EPO: European Patent Office; USPTO: U.S. Patent and Trademark Office; SC: subcutaneous; CV: cardiovascular.

Evidence-Driven Phase 3 Program

LEVEL DATA ENHANCES HELP TRIAL PROOF OF CONCEPT TO DE-RISK ONGOING PHASE 3; WELL-ESTABLISHED SAFETY PROFILE

1. TNX-103, or Oral Levosimendan, is a potential first-in-class PH-HFpEF treatment
2. Levosimendan brings a well-established safety profile and MOA uniquely suited to treating PH-HFpEF
3. LEVEL data validates levosimendan MOA in PH-HFpEF and defines clear enrichment strategy for potential registration
4. Global Phase 3 LEVEL-2 clinical trial using predictive enrichment strategy driven by LEVEL findings
5. Company funded through Q2 2028

PH-HFpEF: pulmonary hypertension in heart failure with preserved ejection fraction; MOA: mechanism of action.

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Developing a therapy uniquely suited for PH-HFpEF

Appendix

Drug Development Veterans Joined By Preeminent PH Experts



Chris Giordano
President & CEO

IQVIA



Stuart Rich, MD
CMO

Northwestern Medicine®
Feinberg School of Medicine



Doug Randall
CBO

The Medicines Company

SANOFI



Tom Staab
CFO

bioCryst® LENSAR



Tim Healey
CCO

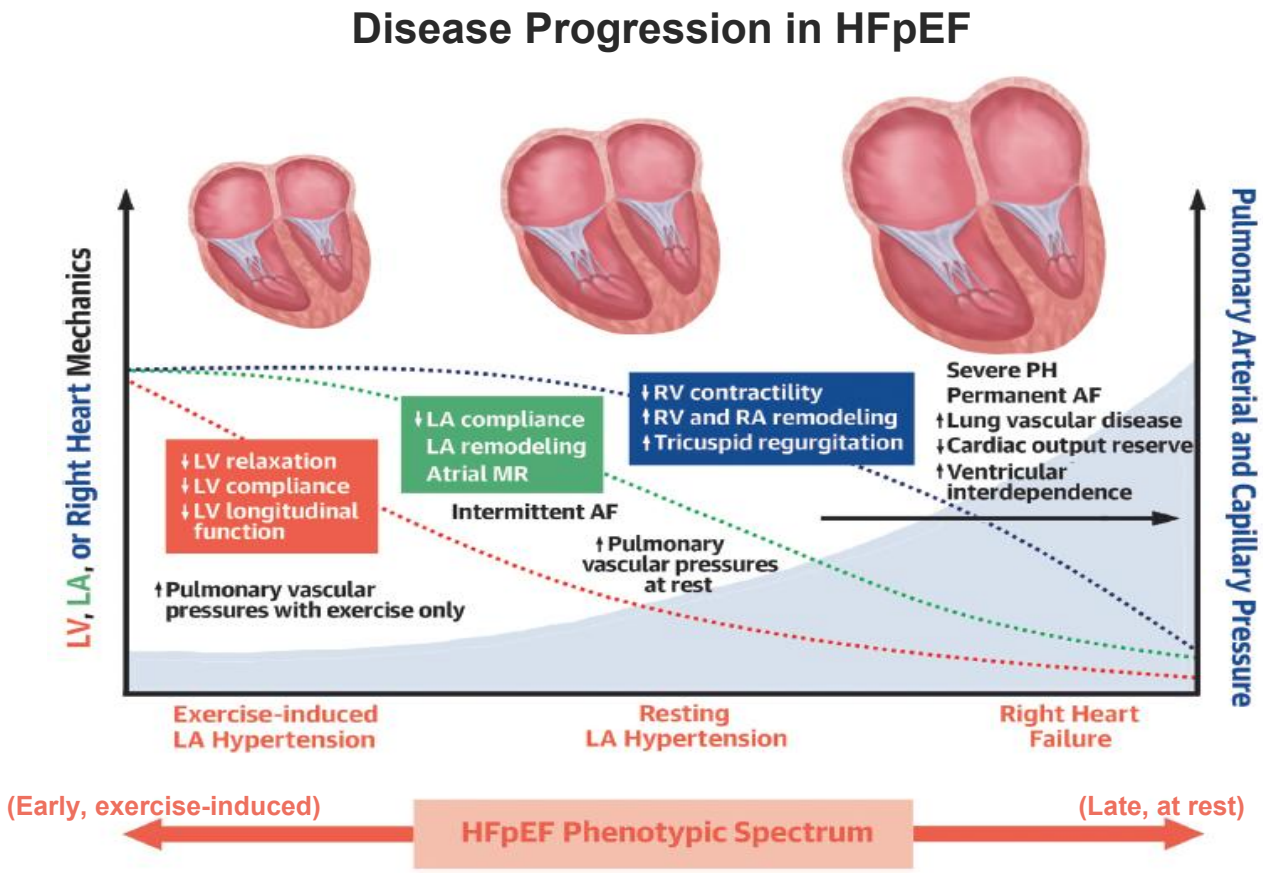
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Pulmonary Hypertension Can Present Across HFpEF Phenotypic Spectrum



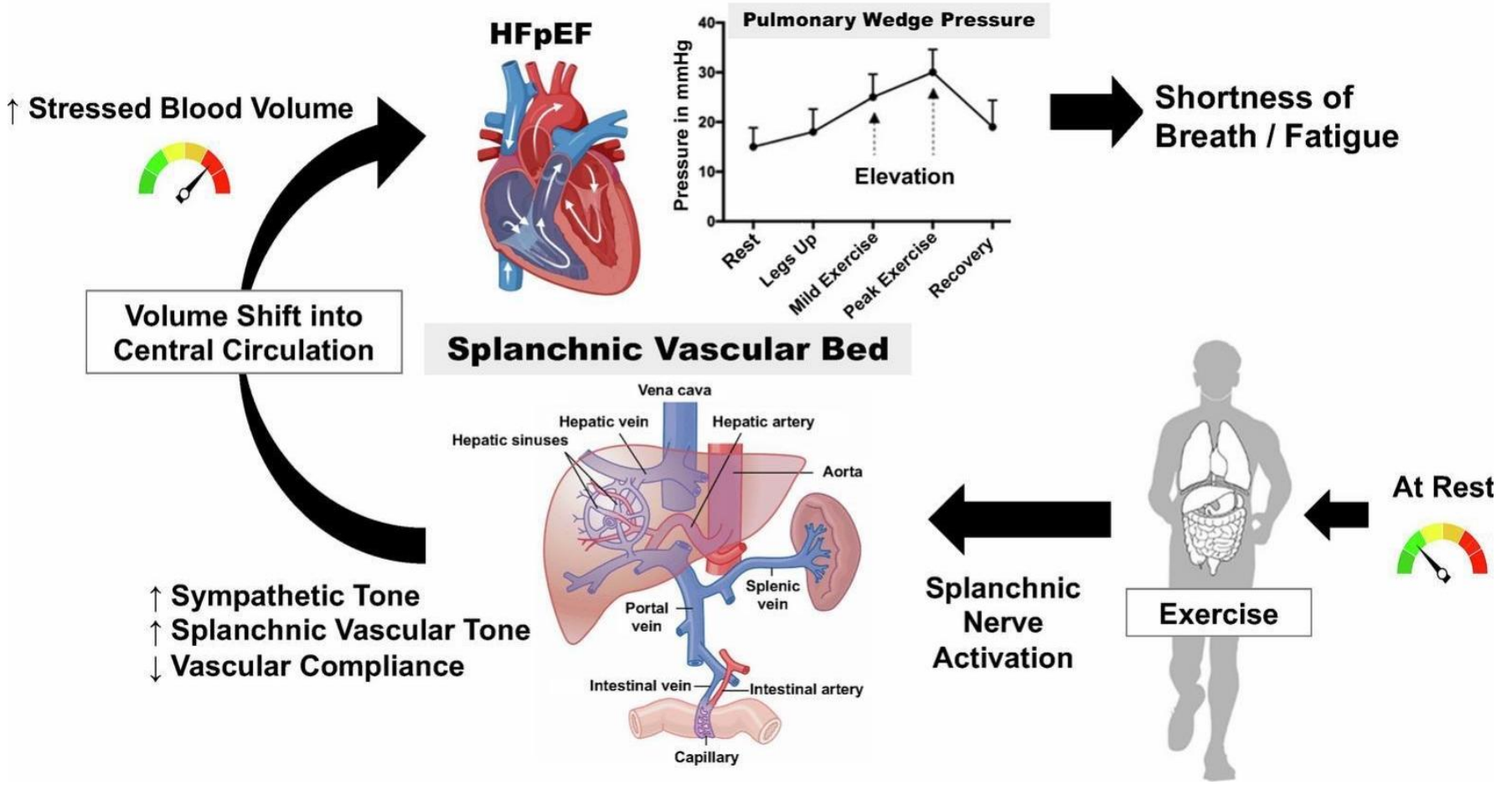
>80% of patients with HFpEF are estimated to have pulmonary hypertension

HFpEF: heart failure with preserved ejection fraction; LA: left atrial; LV: left ventricular; RA: right atrial; RV: right ventricular; MR: mitral regurgitation; PH: pulmonary hypertension.

Borlaug BA, et al. *Journal of the American College of Cardiology* vol. 81,18 (2023): 1810-1834.; Guazzi M, et al. *The Journal of heart and lung transplantation* vol. 34,3 (2015): 273-81.

Splanchnic Circulation

VOLUME REDISTRIBUTION

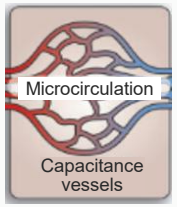


HFpEF: heart failure with preserved ejection fraction.

Yaku H, et al. *Journal of cardiology* vol. 83,5 (2024): 330-337.

Chronic Constriction of the Splanchnic Circulation in PH-HFpEF

ALTERS BLOOD VOLUME AND CARDIOPULMONARY FUNCTION



A maladaptive shift of blood from the splanchnic reservoir to the central circulation

- ↑ Sympathetic tone
- ↑ Splanchnic venoconstriction
- ↑ Blood volume



An excessive venous return to the right and left sides of the heart

- ↑ Right atrial pressure
- ↑ Left atrial pressures



Pulmonary congestion in the lungs

- ↑ Reactive increase in pulmonary pressure
- ↑ Pulmonary vascular remodeling
- ↓ Alveolar-capillary O_2 exchange

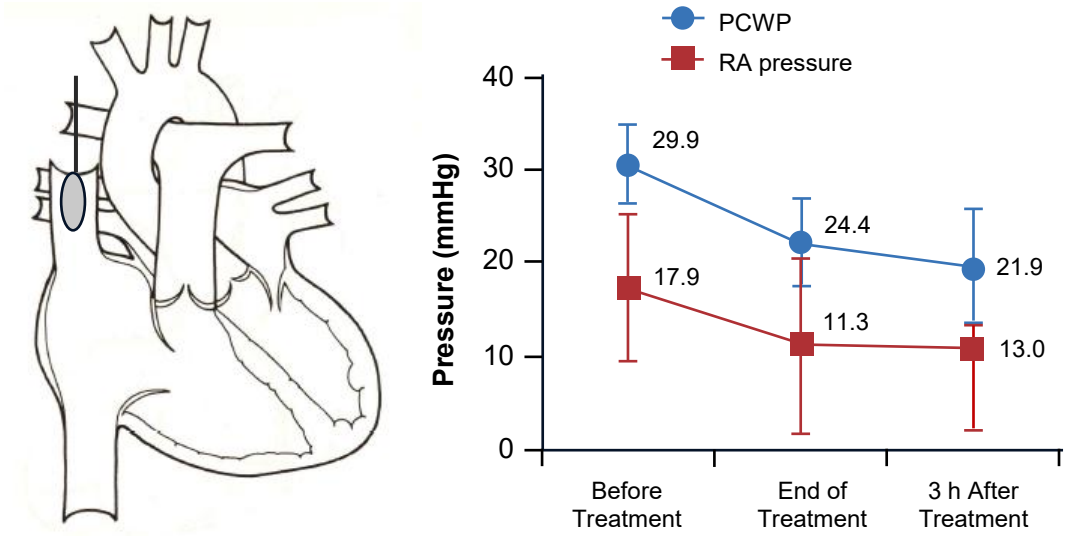
BV: blood volume; O_2: oxygen; PH-HFpEF: pulmonary hypertension in heart failure with preserved ejection fraction; SNS: sympathetic nervous system.

Yaku H, et al. *Journal of cardiology* vol. 83,5 (2024): 330-337.; Gelman S and Mushlin PS. *Anesthesiology* vol. 100,2 (2004): 434-9.; Lai YC, et al. *The Journal of physiology* vol. 597,4 (2019): 1143-1156.

Mechanical Preload Reducing Device

PROOF-OF-CONCEPT FOR VENOUS MODULATING THERAPIES

SVC Balloon Occlusion



Acute decompensated HF with LVEF <40%

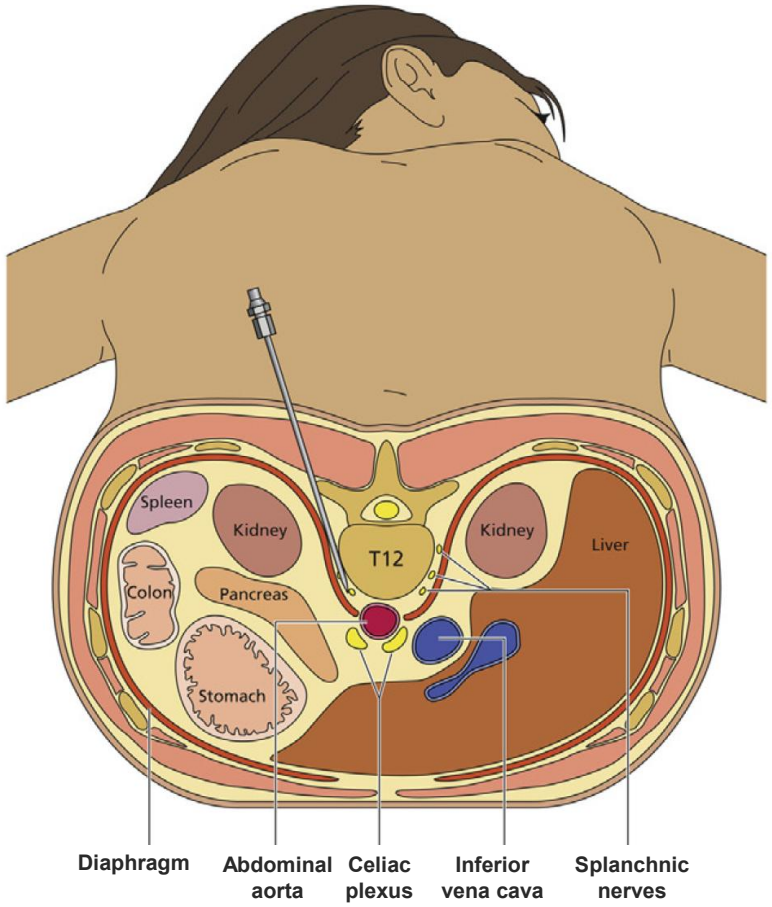
- Mean PAP 40.8 to 33.3 mmHg; p<0.0001
- PVR had no change; p=0.472
- Cardiac Index had no change; p>0.99
- Urine output increased 3.1L; p<0.001

SVC: superior vena cava; HF: heart failure; LVEF: left ventricular ejection fraction; PAP: pulmonary artery pressure; PVR: pulmonary vascular resistance.
Yousefzai R, et al. *JACC. Heart failure*, 102841. 11 Dec. 2025.

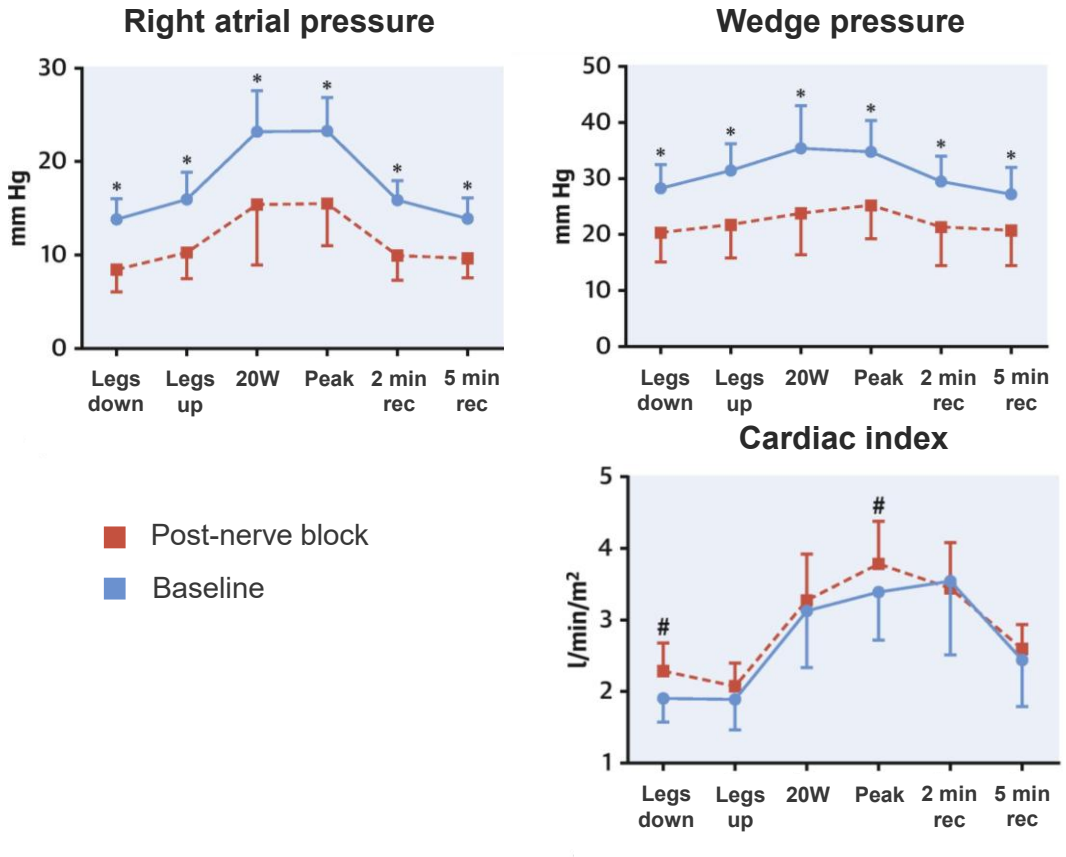
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Splanchnic Nerve Block

PROOF-OF-CONCEPT FOR VENOUS MODULATING THERAPIES



Splanchnic nerve block provides proof of concept for benefit of volume modulating therapies



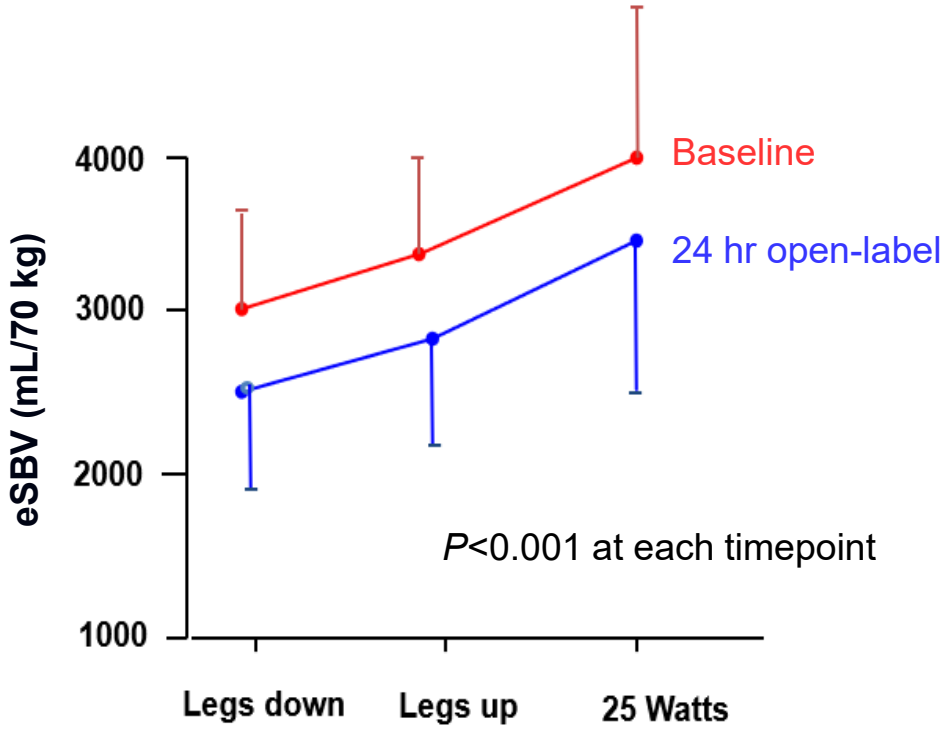
*Adjusted P<0.01 for a pairwise comparison with the pre-SNB value; #Unadjusted P<0.05, adjusted P>0.05.
rec: recovery after peak exercise; SNB: splanchnic nerve block; W: watt.
Fudim M, et al. *JACC. Heart failure* vol. 8,9 (2020): 742-752.

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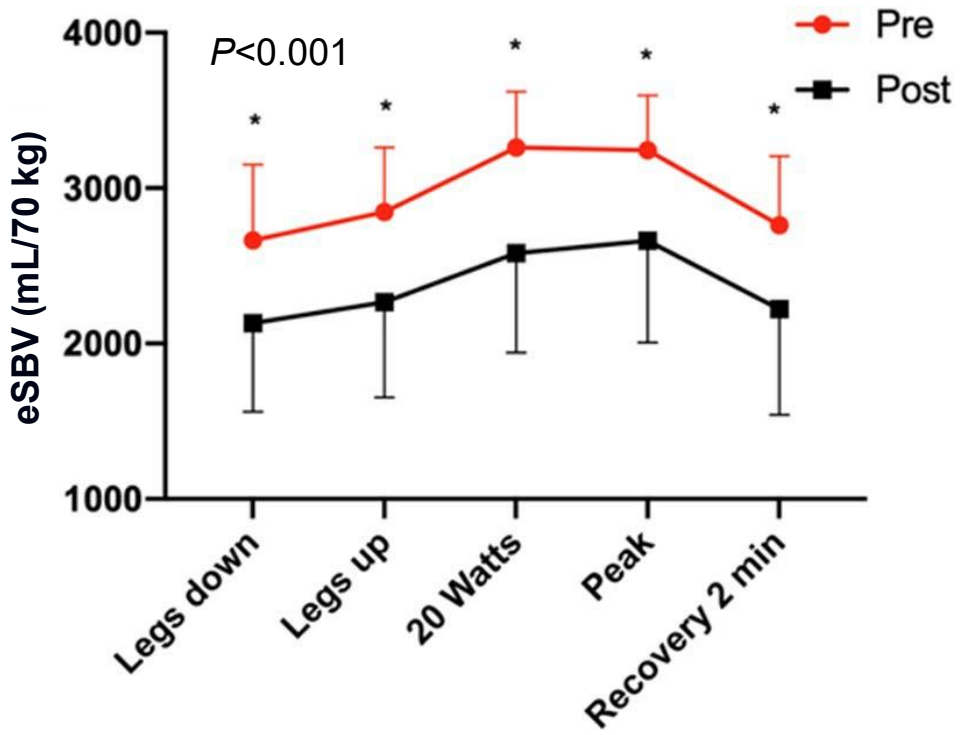
Levosimendan vs Splanchnic Nerve Block

EFFECT ON REDUCING BLOOD VOLUME PROVIDES PROOF-OF-CONCEPT

Levosimendan (from HELP Trial)



Splanchnic Nerve Block

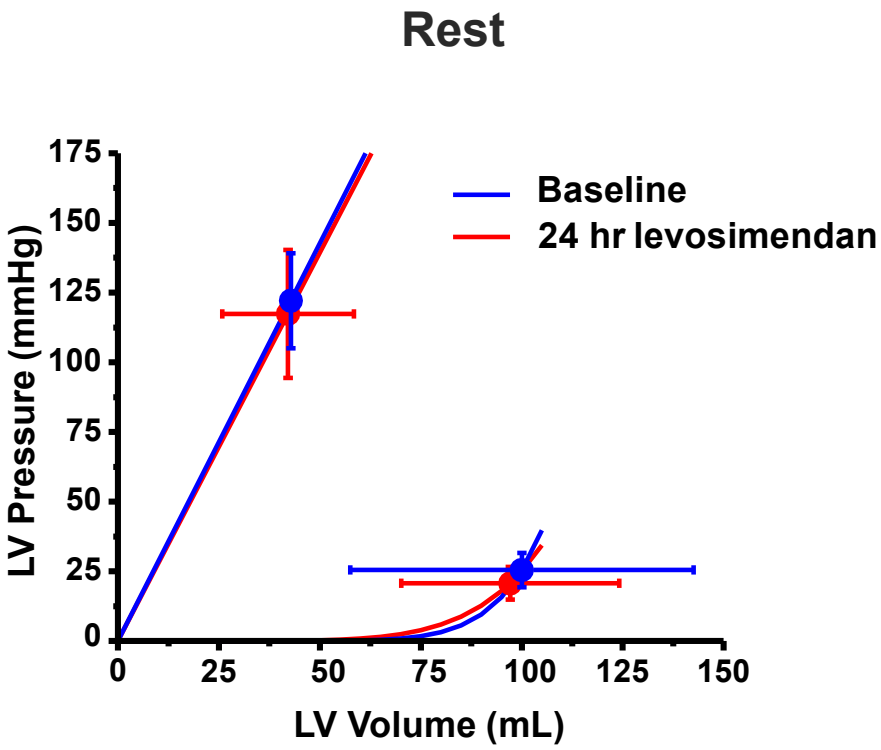


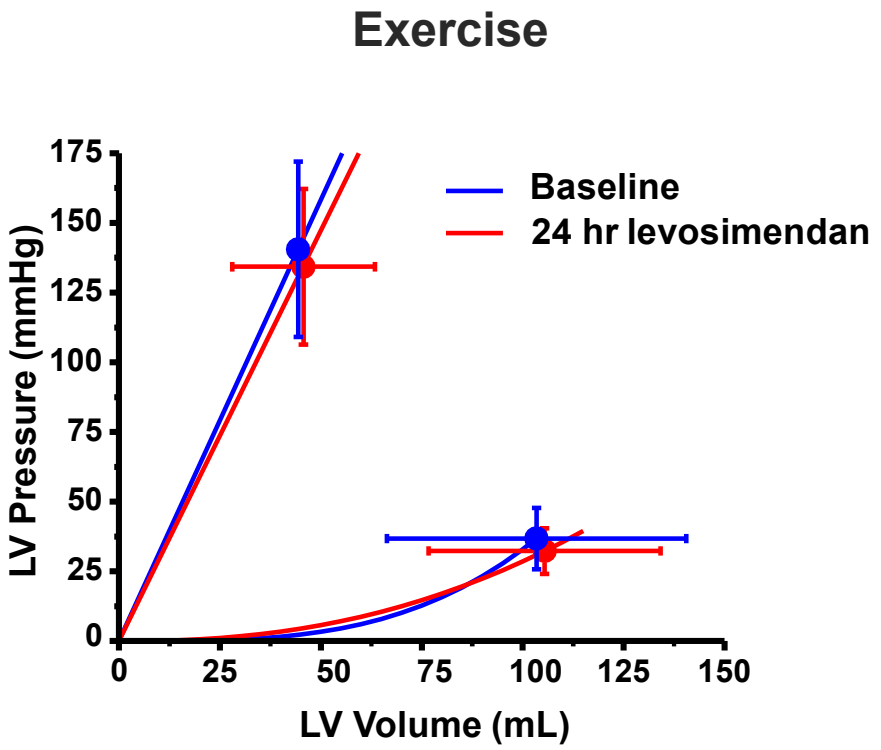
eSBV: estimated stressed blood volume.

Data on file, Tenax 2025.; Fudim M, et al. *J Am Coll Cardiol HF*. Vol. 9 (2021): 293-300.

Baseline vs 24-Hour Levosimendan Infusion on LV Contractility (HELP Trial)

NO EVIDENCE OF INCREASED CONTRACTILITY AT REST OR WITH EXERCISE

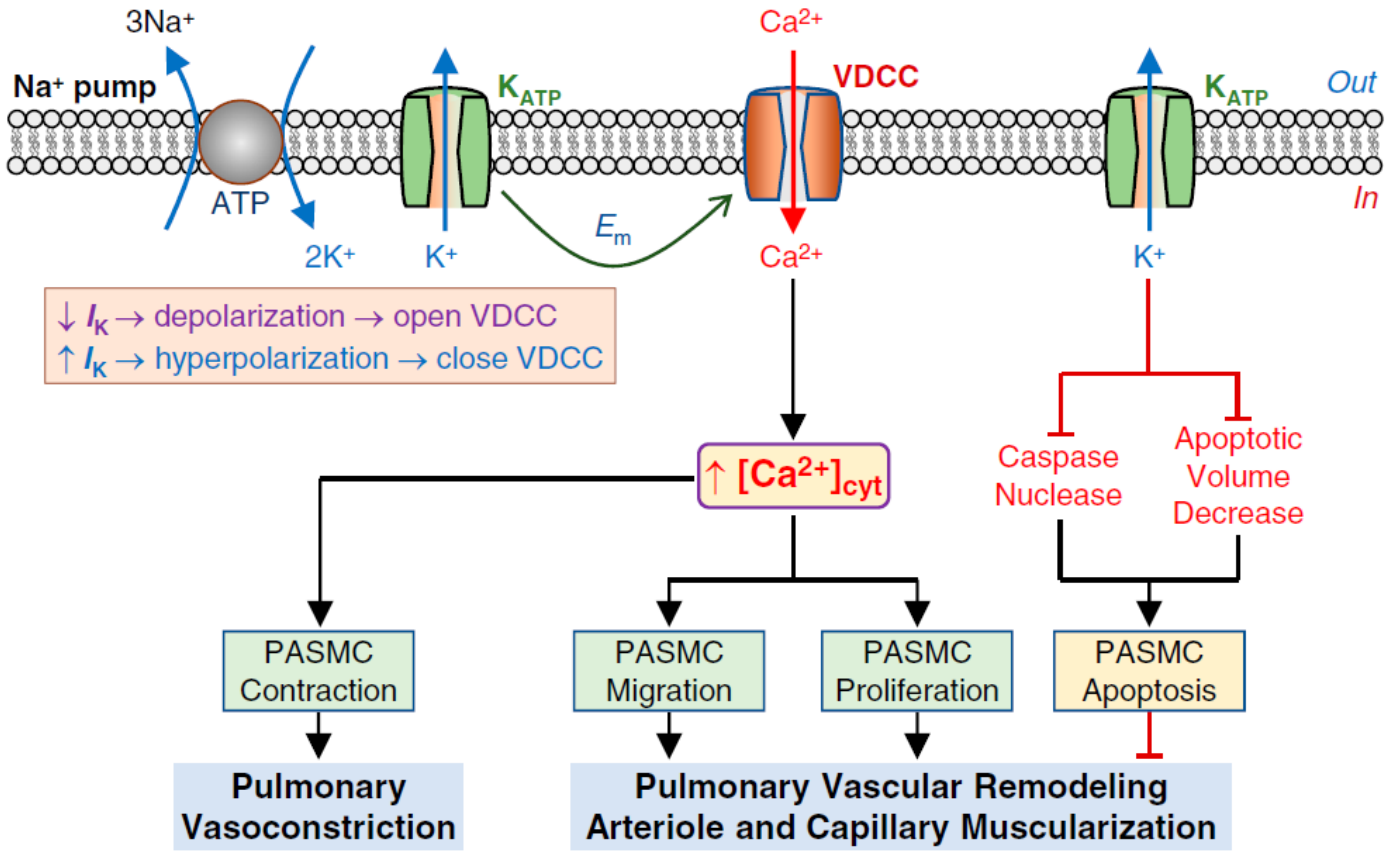




LV: left ventricle
Data on file, Tenax 2025.

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Pulmonary Vascular Remodeling in PH is Associated with Downregulation of K-ATP Channels

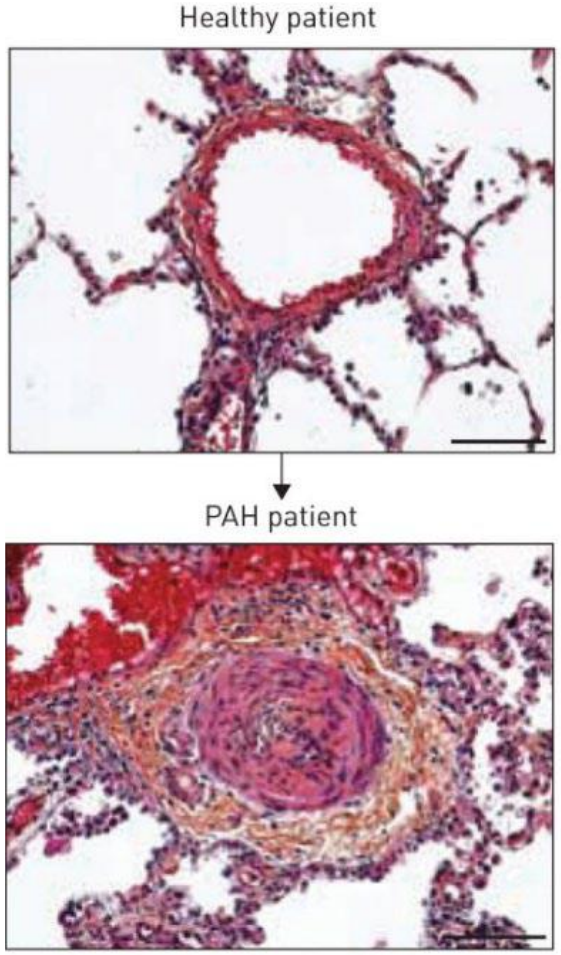


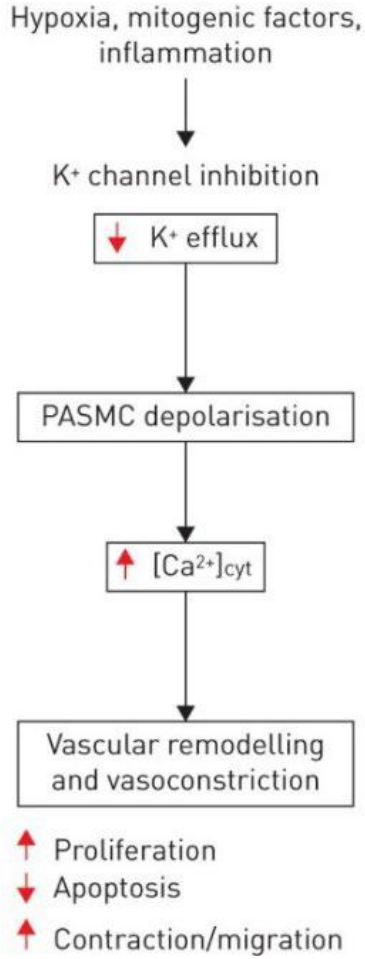
Ca^{2+}: calcium; Cyt: cytosolic; I_K: K+ currents; K^+: potassium; K^+ ATP: potassium adenosine triphosphate-sensitive; Na+: sodium; PASMC: pulmonary artery smooth muscle cell; PH: pulmonary hypertension; VDCC: voltage-dependent Ca^{2+} channels.

Breen E, and Jason XJ Y. *American journal of respiratory cell and molecular biology* vol. 66,5 (2022): 476-478.

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Altered K-ATP/K Channel Signaling Associated with Pulmonary Vasculopathies



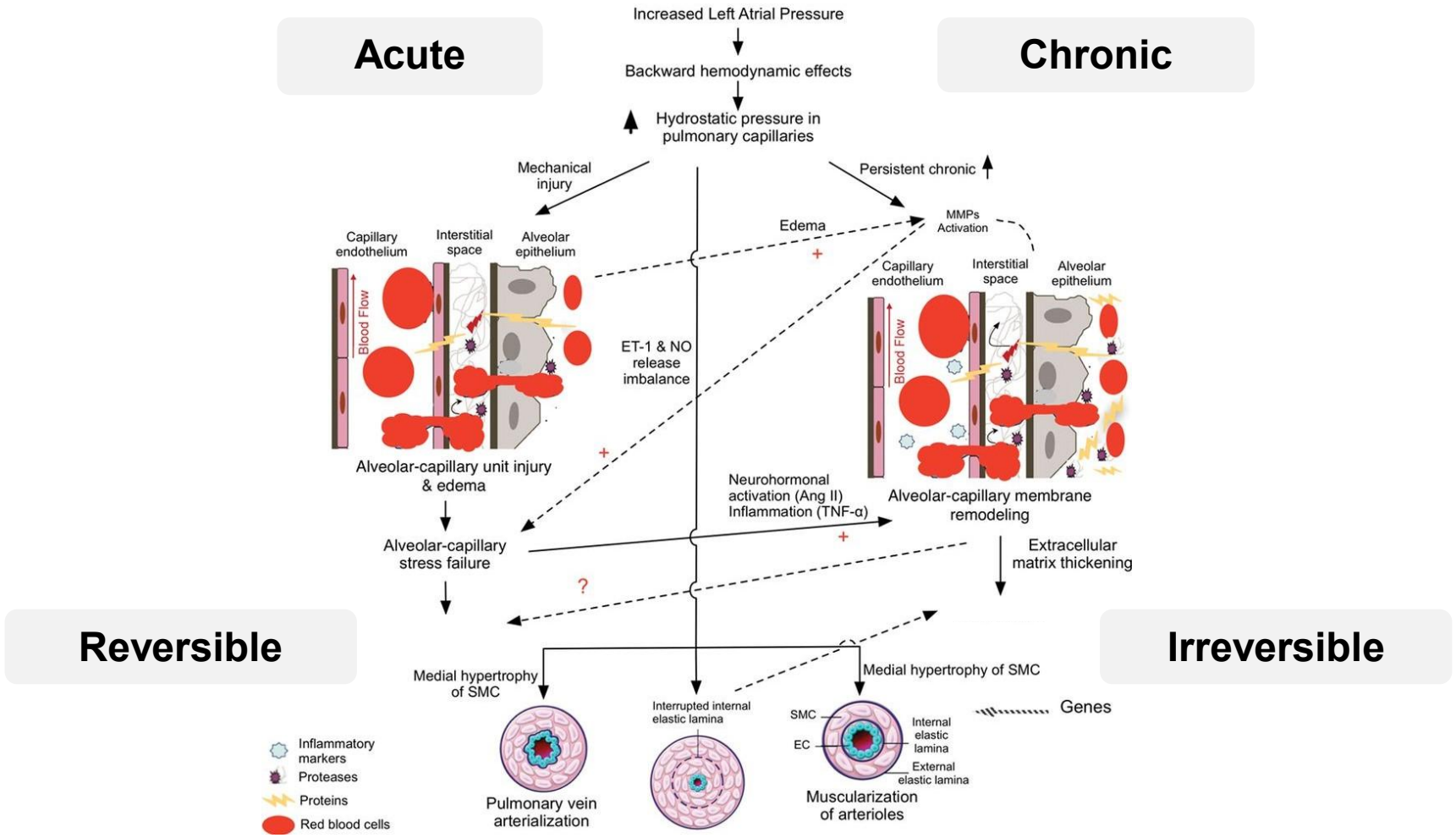


K^+: potassium; K-ATP: potassium adenosine triphosphate-sensitive; Ca^{2+}: calcium.
Mandegar M, and Jason XJ Y. *Vascular pharmacology* vol. 38,1 (2002): 25-33.

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Pulmonary Vascular Component

PATHWAYS FROM INCREASED PCWP TO PULMONARY HYPERTENSION



Ang II: angiotensin II; EC: endothelial cell; ET-1: endothelin-1; MMP: matrix metalloproteinase; NO: nitric oxide; SMC: smooth muscle cell; TNF-α: tumor necrosis factor-α; PCWP: pulmonary capillary wedge pressure.

Georgiopoulou VV, et al. *Circulation. Heart failure* vol. 6,2 (2013): 344-54.

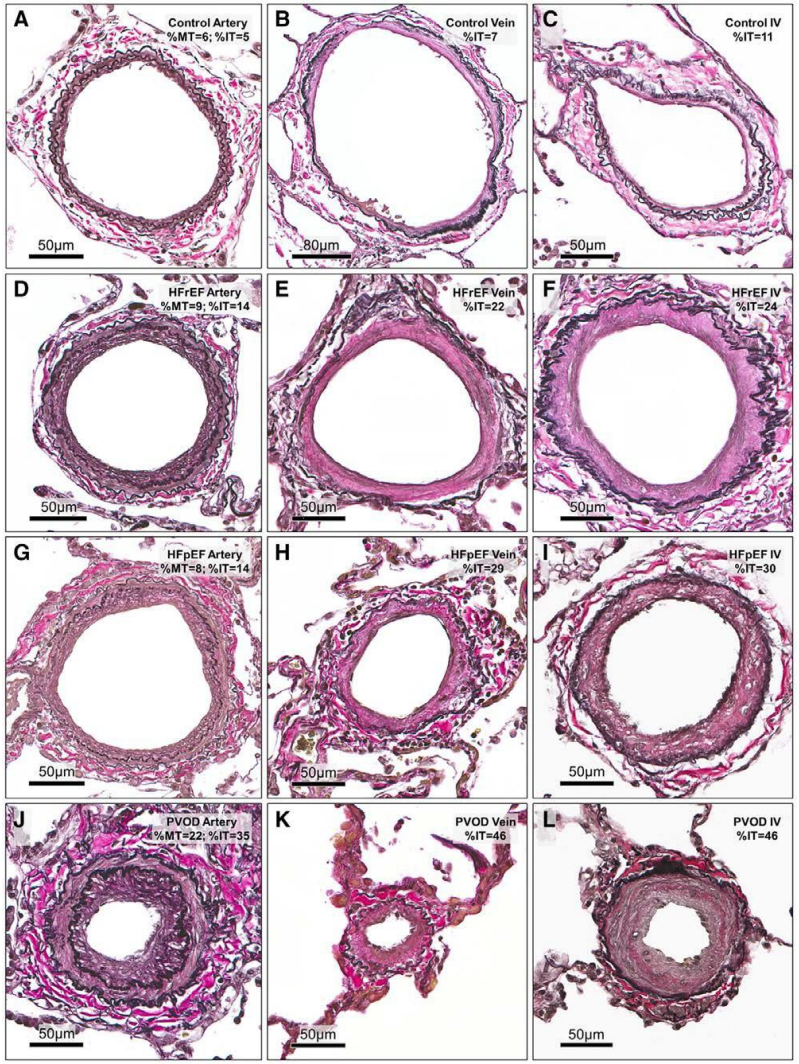
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PH-HFpEF Has Distinct Pathology

ORIGINAL RESEARCH ARTICLE

Global Pulmonary Vascular Remodeling in Pulmonary Hypertension Associated With Heart Failure and Preserved or Reduced Ejection Fraction

- Involvement of the pulmonary arteries, pulmonary veins, and arteriole/venule interface.
- Triggered via the increased pressure within the left atrium and/or pulmonary veins.
- The signaling pathway is uncertain.



Fayyaz AU, et al. *Circulation* vol. 137,17 (2018): 1796-1810.

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Levosimendan: Potential Ideal Treatment for PH-HFpEF

PROBLEM	PROPERTY
Excessive venous return (increased venous blood volume) causing marked elevations in PCWP and RA pressure	K^+ATP channel activation with direct vasodilation of splanchnic circulation reducing venous blood volume and lowering the PCWP (HELP) and RA pressure (HELP numerically at 6 weeks, LEVEL stat sig at 12 weeks)
Remodeling of the pulmonary arteries resulting in elevations in PA pressure	K^+ATP channel activation with antiproliferative effects on the pulmonary vasculature to lower PA pressure
Right ventricular failure from the chronic pulmonary hypertension	Ca^{2+} sensitization of cardiac myocytes to improve right ventricular function

Ca^{2+}: calcium; K^+: potassium; K^+ ATP: potassium adenosine triphosphate-sensitive; PA: pulmonary artery; PCWP: pulmonary capillary wedge pressure; RA: right atrial; PH-HFpEF: pulmonary hypertension in heart failure with preserved ejection fraction.

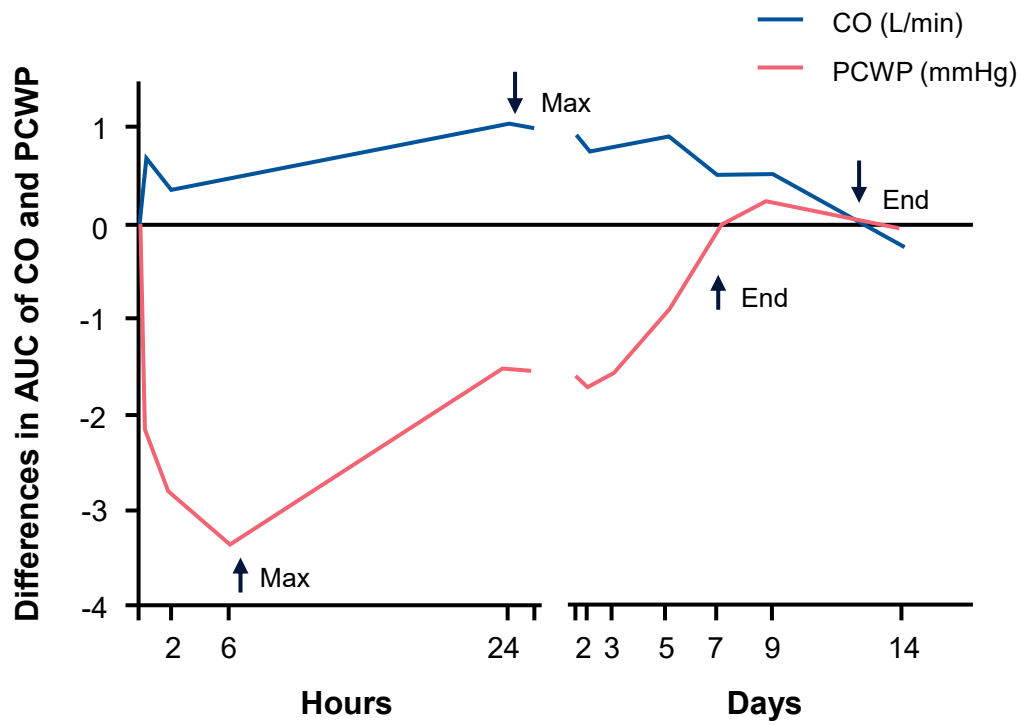
Lai YC, et al. *The Journal of physiology* vol. 597,4 (2019): 1143-1156.; Brener MI, et al. *Journal of cardiac failure* vol. 27,9 (2021): 1023-1026.; Breen E and Yuan JX. *Am J Respir Cell Mol Biol*. vol 66,5 (2002):476-478.; Hansen MS, et al. *Pulmonary circulation* vol. 8,3 (2018): 2045894018790905.

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Changes in Cardiac Output and PCWP Over Time From Levosimendan in Patients With HFrEF

- Levosimendan produced a marked, rapid fall in the PCWP that preceded the increase in cardiac output
  - Attributed to a reduction in venous blood volume

Differences in the PCWP and CO in levosimendan- treated patients



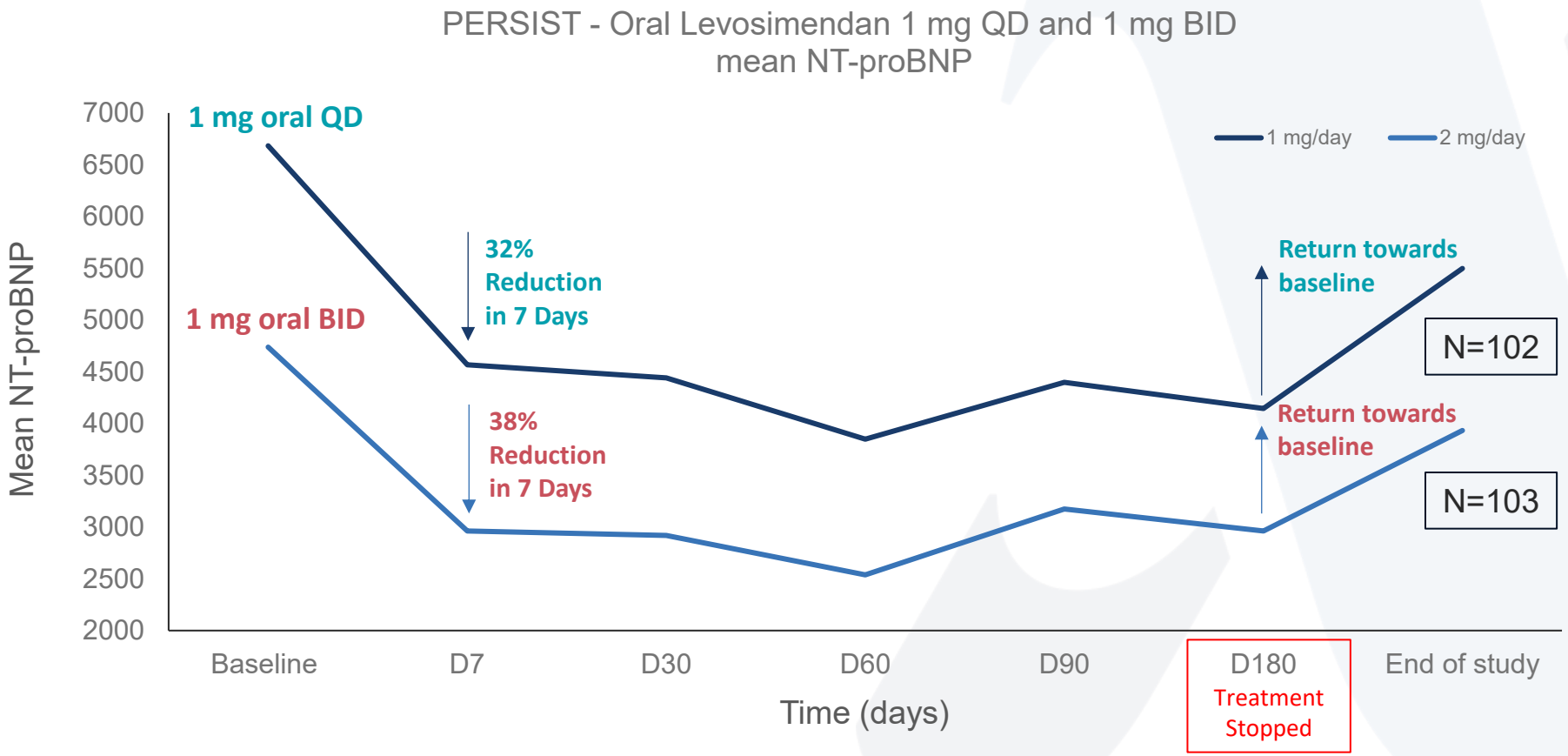
AUC: area under the curve; CO: cardiac output; PCWP: pulmonary capillary wedge pressure; HFrEF: heart failure with reduced ejection fraction.

Lilleberg J, et al. *Eur J Heart Fail*. 2007;9(1):75-82.

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Oral Levosimendan Causes Rapid, Sustained Reduction in NT-proBNP

DATA FROM PERSIST TRIAL: 1mg & 2mg DAILY ORAL LEVOSIMENDAN REDUCE WALL STRESS < 3mg TESTED IN LEVEL TRIAL



QD: once a day; BID: twice a day; BNP: brain natriuretic peptide; NT-proBNP: N-terminal pro B-type natriuretic peptide.

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Oral Levosimendan Drives Sustained Reduction in PCWP in CHF

DATA FROM PERSIST TRIAL

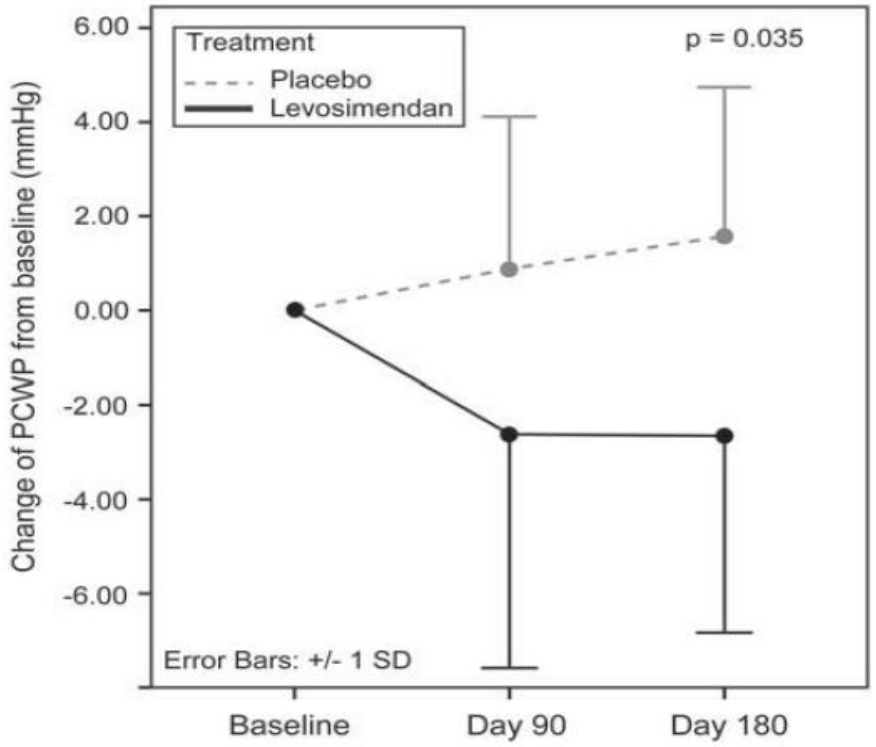


Figure 2. Change of echocardiographic PCWP from baseline to day 180 in placebo and levosimendan treated patients analysed by repeated measures ANOVA (p = 0.035).

PCWP: pulmonary capillary wedge pressure; CHF: congestive heart failure.

Jalanko M, et al. *Scandinavian Cardiovascular Journal: SCJ* vol. 45,2 (2011): 91-7.

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Targeting PVR in PH-HFpEF Has Not Proven Successful

Multicenter Trials of Pulmonary Vasodilators in PH-HFpEF Patients

Drug	Multicenter Trial	PCWP/PAWP Change vs Placebo	PVR Change vs Placebo	6MWD or CPET Change vs Placebo	Safety	Conclusion
Bosentan	BADDHY	Not Reported	Not Reported	No Difference (6MWD)	Questionable, study stopped early	**Ineffective**
Macitentan	MELODY	No Difference	No difference	No Difference (6MWD)	Questionable, fluid retention	**Ineffective**
Riociguat	DYNAMIC	No Difference	Decreased	No Difference (6MWD)	Questionable, increased dropouts for AEs in drug arm	**Ineffective**
Tadalafil	PASSION	Not Reported	Not Reported	No Difference (6MWD)	Questionable, all-cause death was higher (HR, 5.10 [95% CI, 1.10–23.69]; *P*=0.04)	**Ineffective**
Sildenafil	Hoendermis *et al*	Reduction in favor of placebo	No Difference	No Difference (CPET)	No concerns	**Ineffective**

PVR: pulmonary vascular resistance; PCWP: pulmonary capillary wedge pressure; PAWP: pulmonary artery wedge pressure; 6MWD: 6-minute walk distance; CPET: cardiopulmonary exercise test.

Koller B, et al. *Heart, lung & circulation* vol. 26,5 (2017): 433-441.; Mascherbauer J, et al. *Wien Klin Wochenschr* vol. 128 (2016): 882-889.; Vachiéry JL, et al. *The European respiratory journal* vol. 51,2 (2018): 1701886.; Hoeper MM, et al. *Circulation* vol. 150,8 (2024): 600-610.; Hoendermis ES, et al. *European heart journal* vol. 36,38 (2015): 2565-73.

Phase 2 HELP Study

Proof-of-Concept Established in Phase 2 HELP Study

STUDY DEMONSTRATED SAFETY AND EFFICACY OF LEVOSIMENDAN IN PH-HFpEF

Phase 2 HELP Study

- Open-label study to evaluate IV levosimendan (TNX-101), specifically the effects on hemodynamics at rest and exercise after 24 hours
- 37 PH-HFpEF patients with initial responses were then enrolled into randomized, double-blinded treatment with once weekly IV infusions for 6 weeks
- Final assessment after 6 weeks of 6-minute walk distance and hemodynamics study

Summary of Results

- Confirmed academic-oriented hypothesis of levosimendan's effectiveness in treating PH-HFpEF
- First study in any HFpEF population to show improvement in 6MWD
- Follow-up OLE established PoC for oral levosimendan

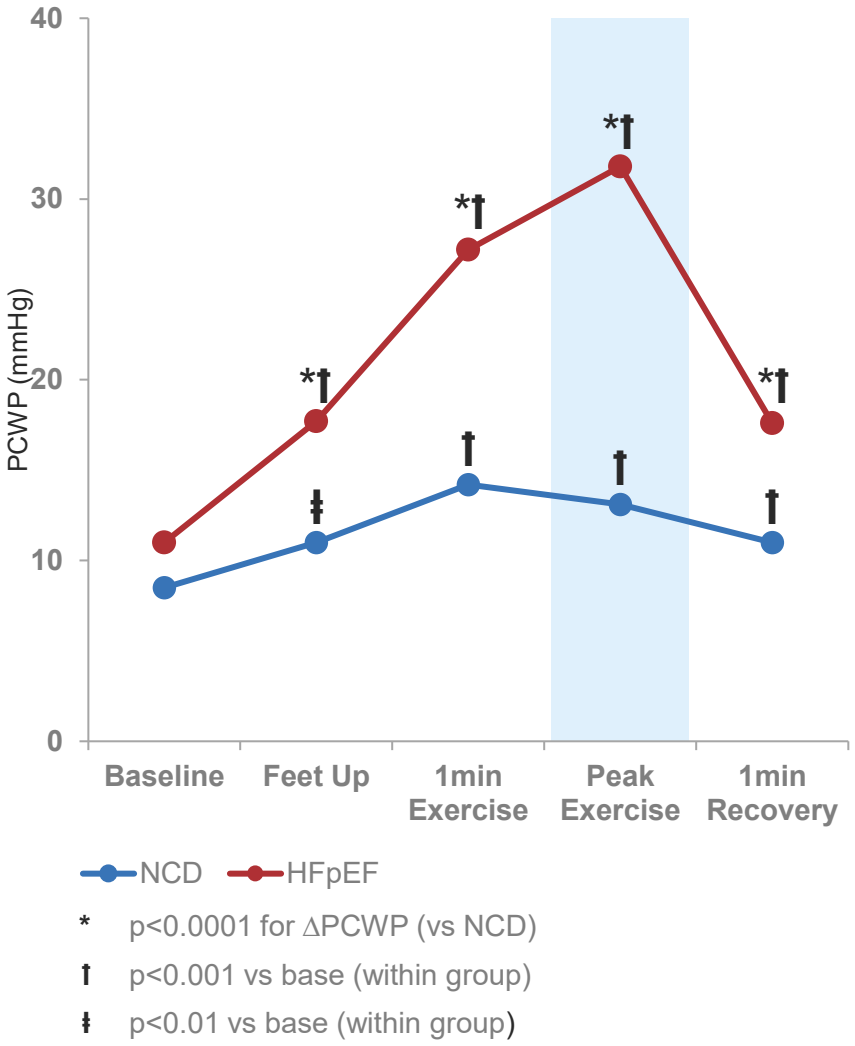
6MWD: 6-minute walk distance; OLE: open-label extension; PoC: proof-of-concept.
Burkhoff D, et al. *JACC. Heart failure* vol. 9,5 (2021): 360-370.

Overview of PH-HFpEF Hemodynamics

Exercise hemodynamics data from HELP study confirm diagnosis

- Increase in PCWP during exercise is the defining impairment in PH-HFpEF
- No known treatment has been able to prevent increase in PCWP during exercise

ΔPCWP at Rest and Exercise

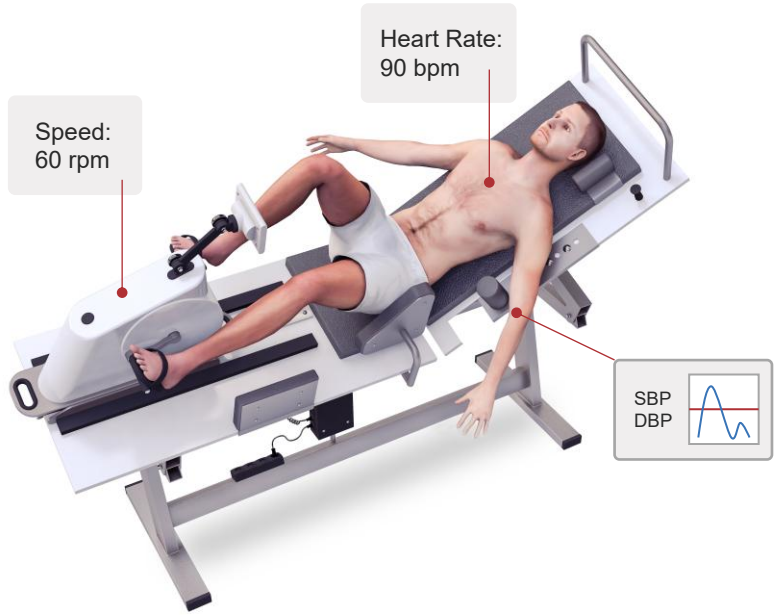


* p<0.0001 for ΔPCWP (vs NCD)

† p<0.001 vs base (within group)

‡ p<0.01 vs base (within group)

Experimental Set Up During Isometric Leg Exercise



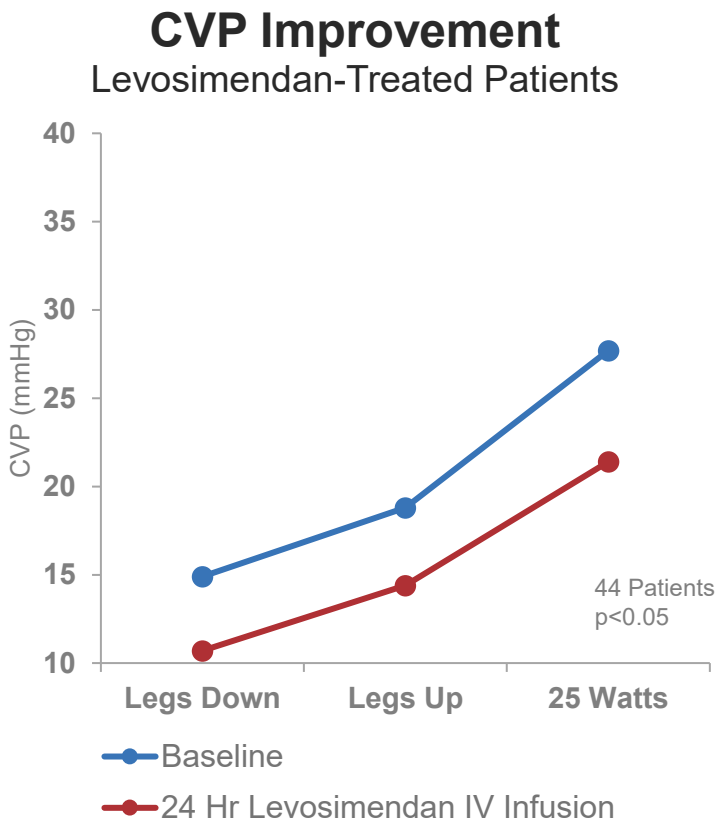
DBP: diastolic blood pressure; NCD: noncardiac dyspnea; PCWP: pulmonary capillary wedge pressure; SBP: systolic blood pressure.

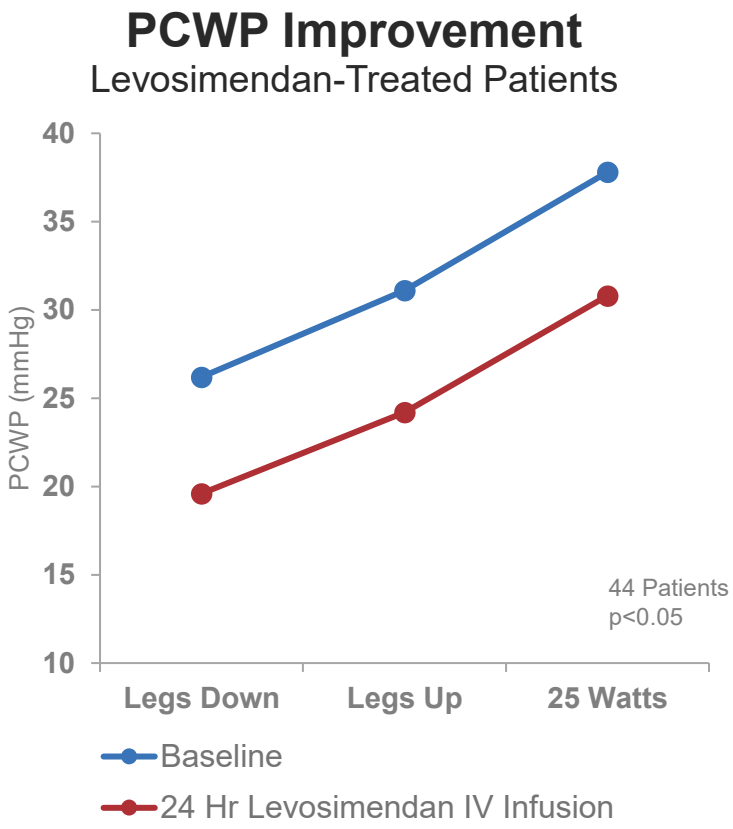
Borlaug BA, et al. *Circulation. Heart failure* vol. 3,5 (2010): 588-95.

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IV Levosimendan Improves CVP and PCWP After 24 Hour Infusion

- Improvements seen at rest and with exercise
- 85% of patients enrolled responded with robust decrease (>4 mmHg) in exercise PCWP



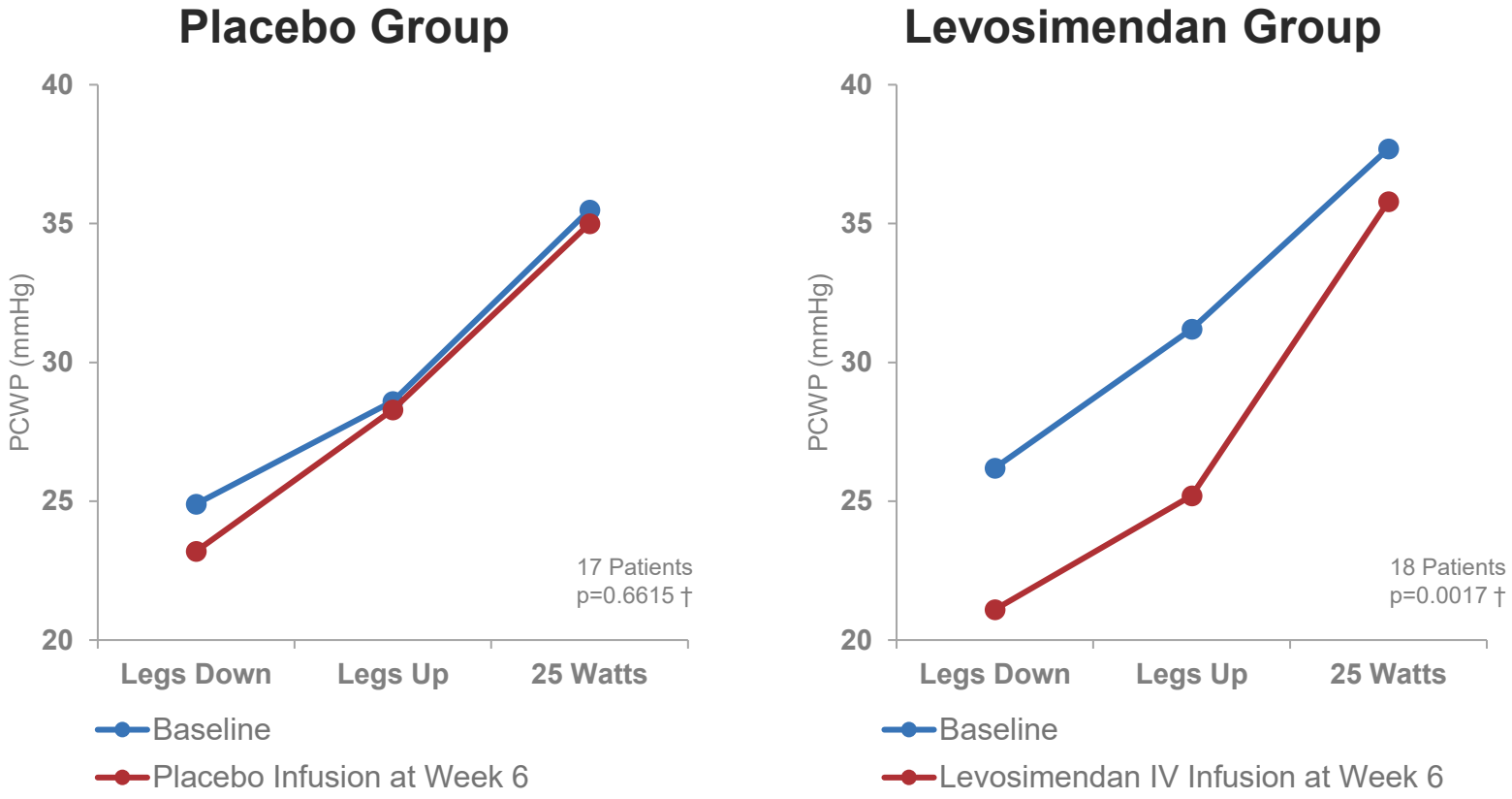


CVP: central venous pressure; PCWP: pulmonary capillary wedge pressure.
Burkhoff D, et al. *JACC. Heart failure* vol. 9,5 (2021): 360-370.

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IV Levosimendan Significantly Improves PCWP After 6 Weeks

- Following randomization for 6 weeks at trough, placebo patients experienced no change
- Meanwhile, pressure in patients treated with IV levosimendan markedly improved in 3 positions (as assessed by right heart catheterization)

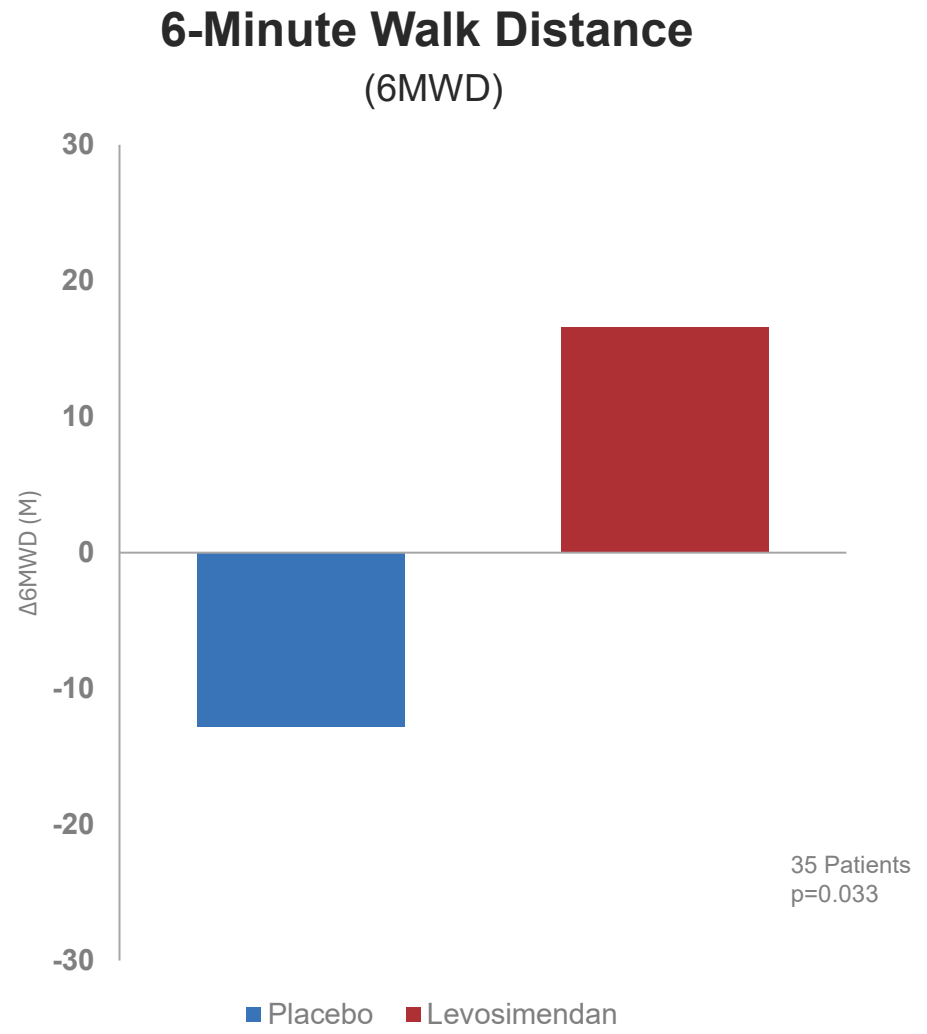


† Tested in a mixed effect model using treatments as factors and position as a random effect.
PCWP: pulmonary capillary wedge pressure.
Burkhoff D, et al. *JACC. Heart failure* vol. 9,5 (2021): 360-370.

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IV Levosimendan Improves Exercise Capacity After 6 Weeks at Trough

- 29m improvement in 6MWD
- Levosimendan is the first drug to improve 6MWD in any HFpEF patient population



37 patients met hemodynamic criteria and were randomized, of these, 2 patients dropped out due to palpitations and COVID-19 infection, both were in the placebo arm.
Burkhoff D, et al. *JACC. Heart failure* vol. 9,5 (2021): 360-370.

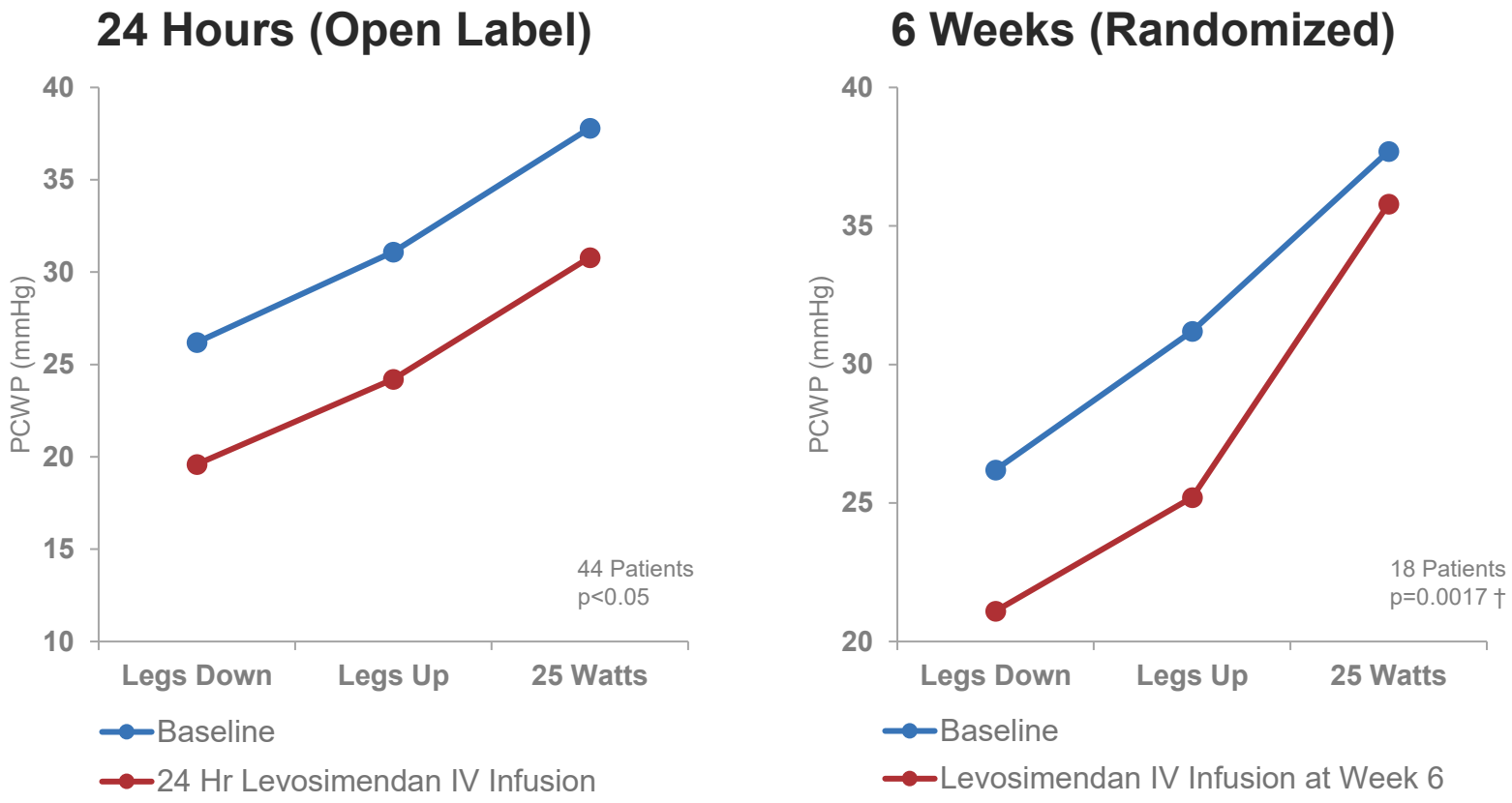
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Effect of IV Levosimendan on PCWP

After 24 Hours vs. After 6 Weeks

- After 24 hour infusion, PCWP was measured at rest, with legs up, and with exercise when concentration of OR-1896 was high
- Following randomization for 6 weeks, right heart catheterization was performed *at end of week following infusion*, with concentration of OR-1896 at trough

PCWP Improvement in Levosimendan-Treated Patients

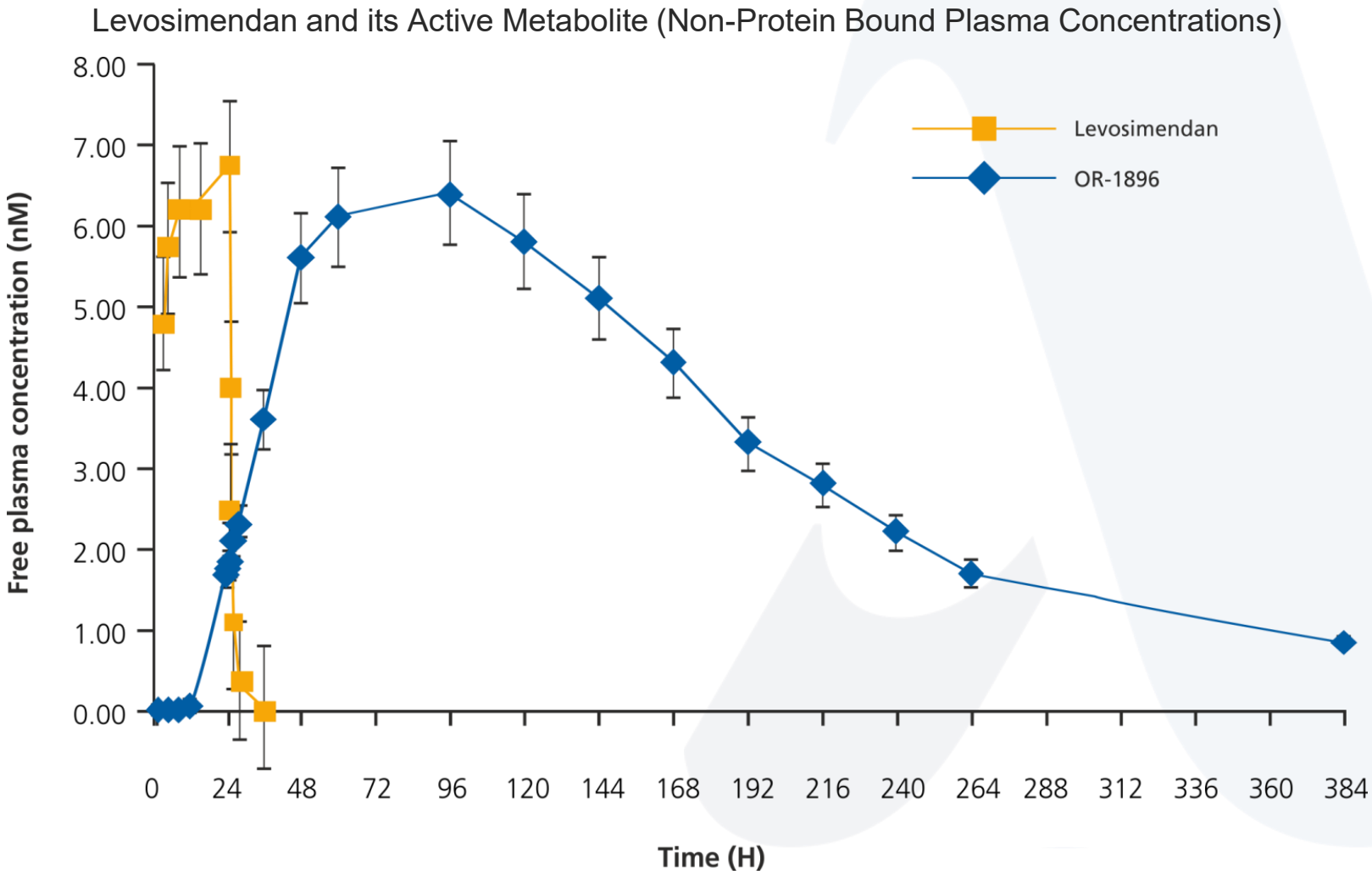


† Tested in a mixed effect model using treatments as factors and position as a random effect.
PCWP: pulmonary capillary wedge pressure.
Burkhoff D, et al. *JACC. Heart failure* vol. 9,5 (2021): 360-370.

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Rationale for Oral Dose Selection

24-HOUR IV INFUSION OF 0.2 µG/KG/MIN (AS COMPARED TO 0.1 µG/KG/MIN USED IN HELP)



Kivikko M, et al. *International journal of clinical pharmacology and therapeutics* vol. 40,10 (2002): 465-71.

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OLE Established Safety, Efficacy and Dosing for Oral Levosimendan

PATIENTS IN OLE WERE TRANSITIONED FROM IV TO ORAL LEVOSIMENDAN (TNX-103)

Study Objectives

- Safely transition patients from weekly IV to daily oral levosimendan over 6-8 week period to continue providing open-label treatment with TNX-103
- Confirm safety and tolerability of oral levosimendan (TNX-103)
- Determine effective dose to maintain safety and efficacy of IV levosimendan

Previous IV Infusion	Week 0* (Office)	Week 2 (Home)	Week 4 (Home)	Week 6 (Office)
0.10 µg/kg/min	1 mg QD (1 mg total daily dose) Morning	1 mg BID (2 mg total daily dose) Every 12 hr	1 mg TID (3 mg total daily dose) Every 8 hr	Patient evaluated for further titration†

*5-7 days after the last IV levosimendan infusion.; †The oral dose was increased every 2 weeks by 1 mg/day to a maximum of 4 mg/day over an 8-week period. The highest daily dose was determined by the investigator based on clinical assessments of symptoms and side effects.
BID: twice daily; IV: intravenous; OLE: open-label extension; TID: 3 times daily; QD: every day.
Thenappan T, et al. *J Card Fail*. Vol. 29,4 (2023): 714-715.

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Oral Levosimendan (TNX-103): Safe and Effective as IV Formulation

RESULTS FROM HELP OLE IV-TO-ORAL TRANSITION SUBSTUDY

Exercise capacity

+ 7 meters

6MWD was improved by 7 meters

Cardiac function

↓ 23% over IV

BNP/NT-proBNP improved by 23%

Patient-reported outcomes

↑ in 6 of 7 domains

KCCQ improved further in 6 of 7 different domains

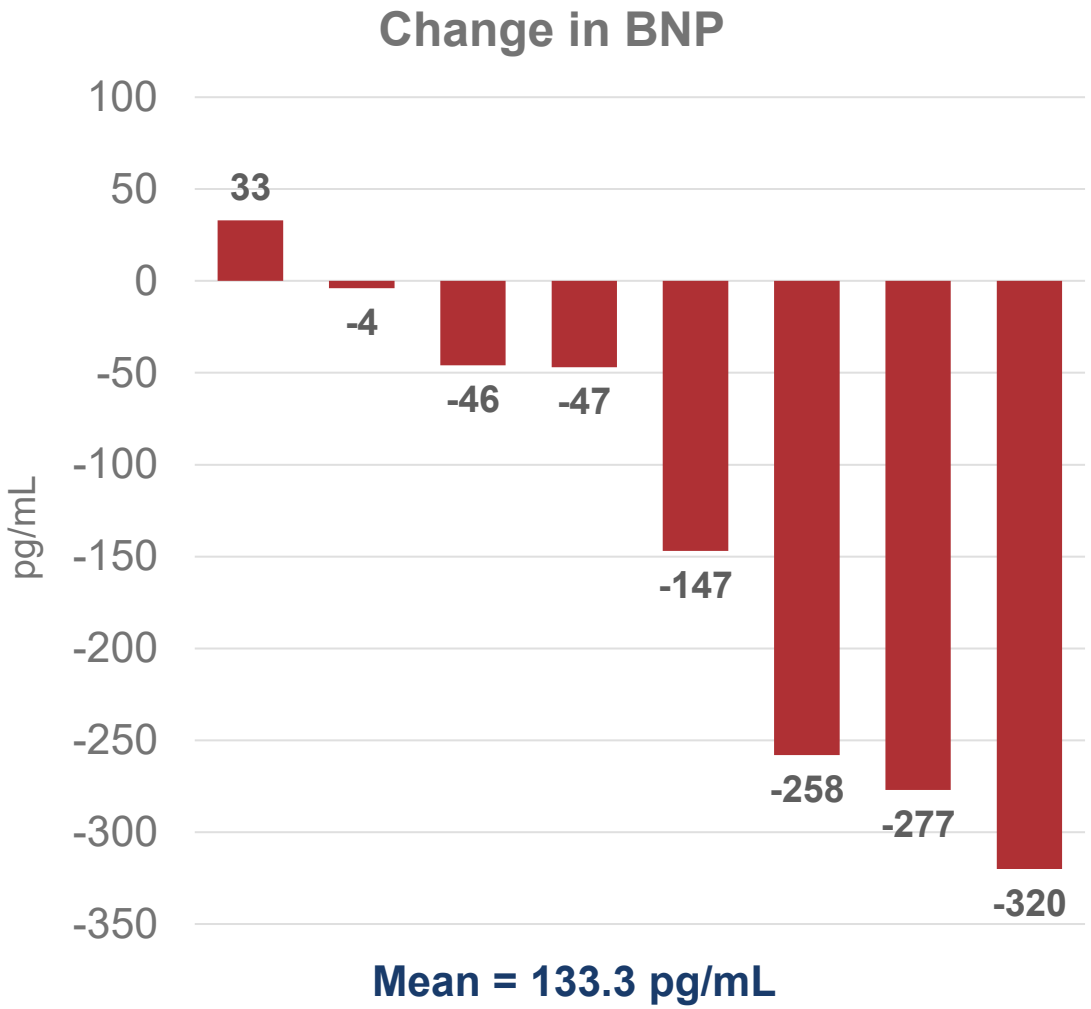
6MWD: 6-minute walk distance; BNP: brain natriuretic peptide; NT-proBNP: N-terminal pro B-type natriuretic peptide; KCCQ: Kansas City cardiomyopathy questionnaire; OLE: open-label extension.

Thenappan T, et al. *J Card Fail*. Vol. 29,4 (2023): 714-715.

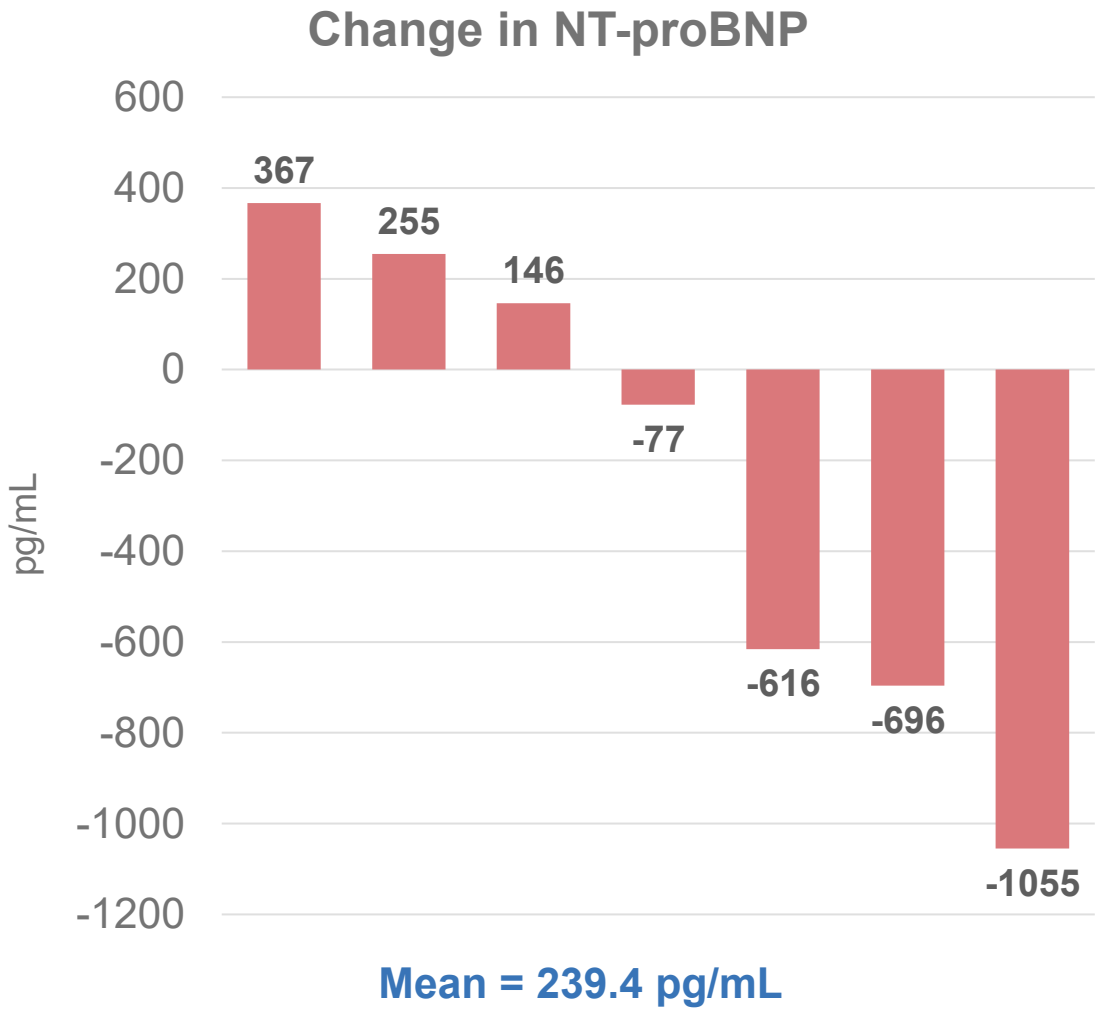
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BNP or NT-proBNP (Collected per Institutional Standard)

DATA FROM HELP OLE



Mean = 133.3 pg/mL



Mean = 239.4 pg/mL

BNP: brain natriuretic peptide; NT-proBNP: N-terminal pro B-type natriuretic peptide.

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Additional Findings from LEVEL Readout

Oral 2mg & 3mg Dose: Levosimendan & OR-1896 Pharmacokinetics

LEVOSIMENDAN

- Dose; 1 mg BID Weeks 1-4; titrated to 1 mg TID Weeks 5-12
- Represents 2 or 3 pulses of levosimendan per day; each dose cleared in ~4.5-5 hours
- Week 12 plasma levels ranged from 0.12 to 37.7 ng/mL, dependent on time of last dose

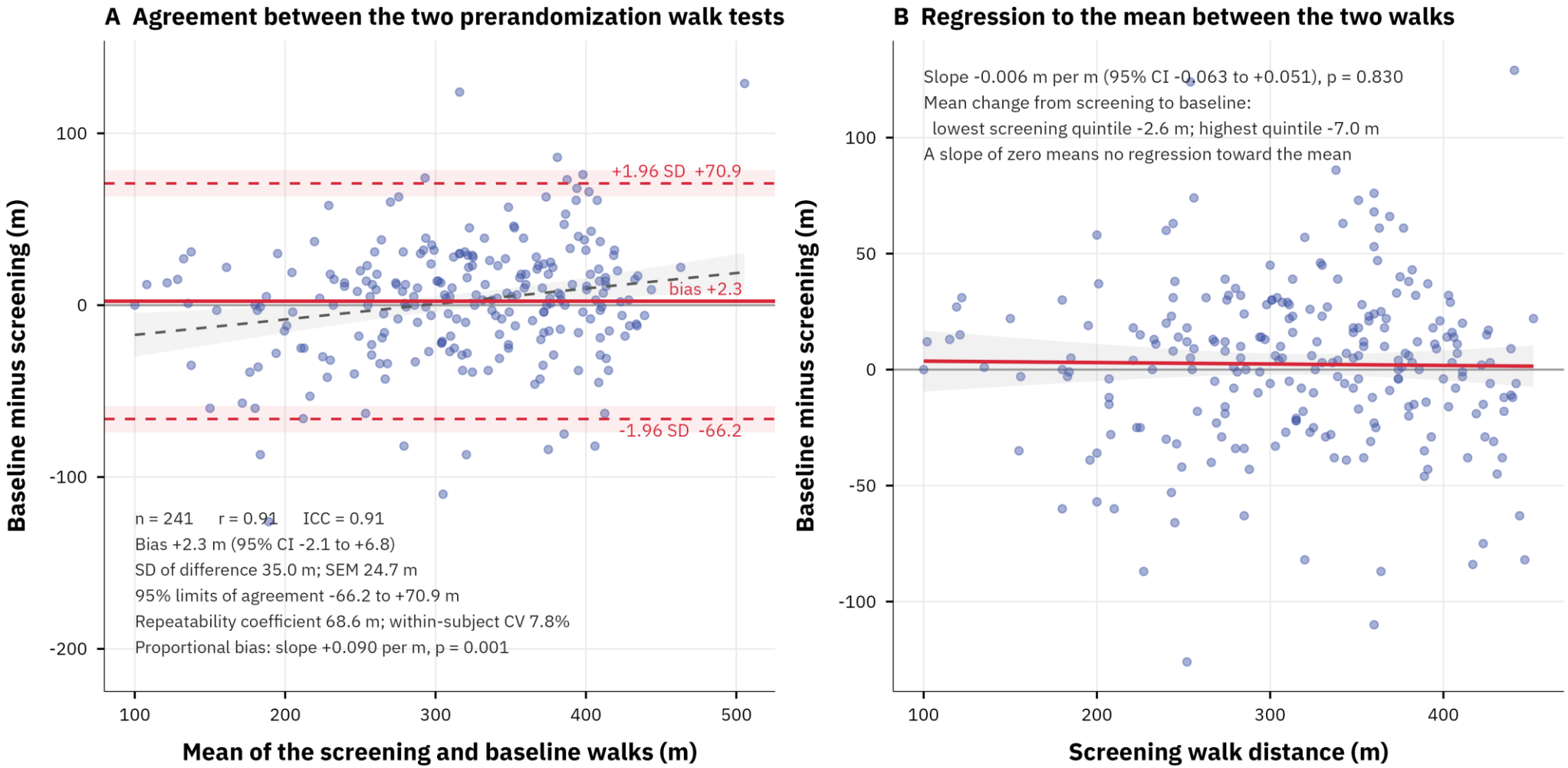
OR-1896 ACTIVE METABOLITE

- Plasma levels increased proportionally with dose to steady-state
- Week 4; mean (SD) = 7.1 (6.2) ng/mL
- Week 12; mean (SD) = 9.7 (8.1) ng/mL
- Comparable to levels observed in the IV-to-Oral Transition Substudy in HELP patients
- Patient acetylation status revealed OR-1896 levels consistent with previous studies. Slow / intermediate / rapid status did not determine a significant difference in safety or treatment effect

BID: twice a day; TID: three times a day; 6MWD: 6-minute walk distance; SD: standard deviation.

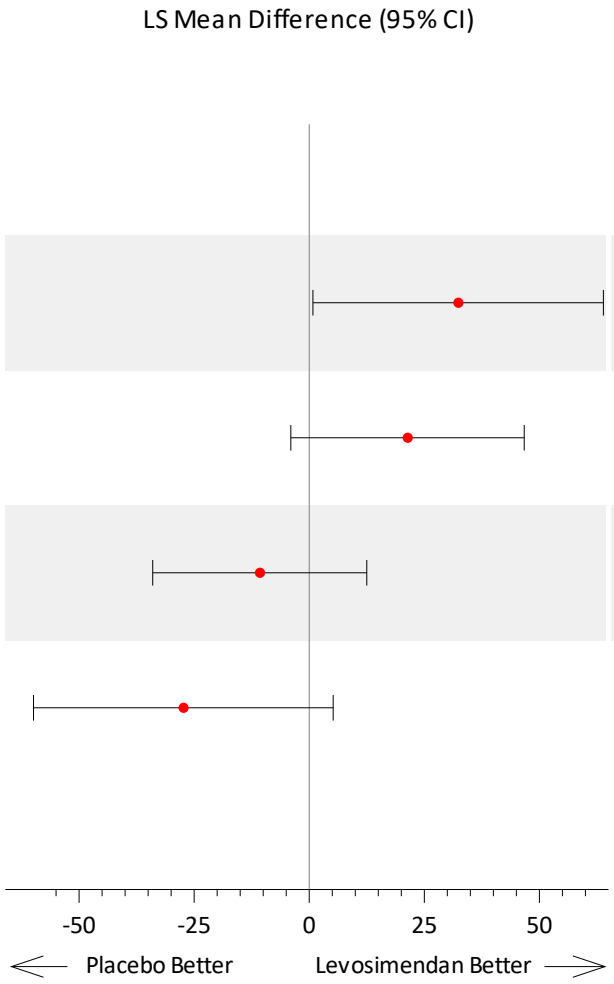
Is the Baseline-6MWD Interaction Regression to the Mean?

AGREEMENT BETWEEN THE SCREENING & BASELINE WALK TEST IN ALL 241 PATIENTS; ICC 0.91, BIAS +2.3M, 95% LIMITS OF AGREEMENT -66.2M to +70.9M



ICC: intraclass correlation coefficient; CV: covariate; SD: standard deviation; CI: confidence interval.

LS Mean Change in 6MWD by Baseline 6MWD Quartile*



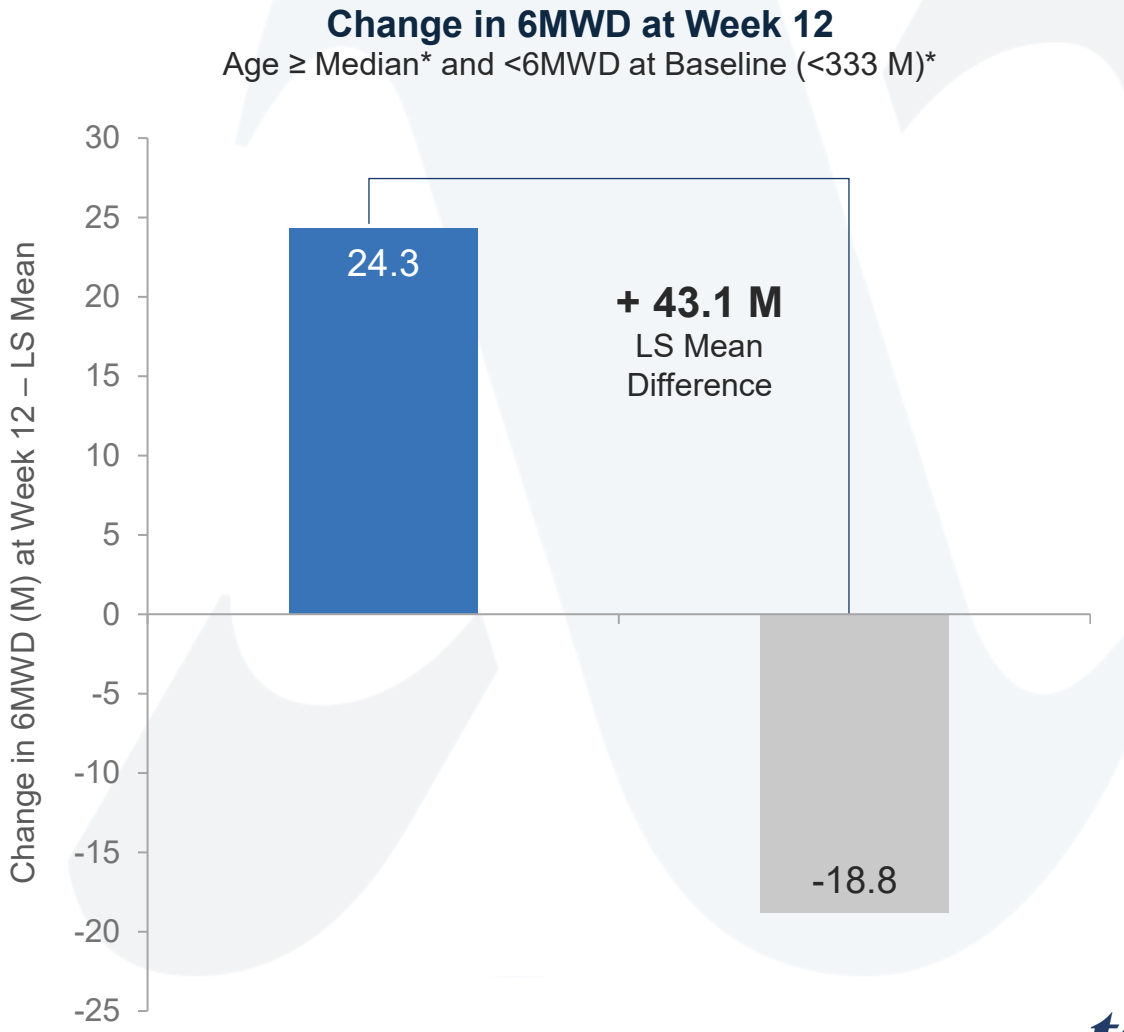
Baseline 6MWD Quartile	Levosimendan: n / LS Mean (95% CI)	Placebo: n / LS Mean (95% CI)	LS Means Difference (95% CI)
1st Quartile (Baseline <= 264 meters)	31 / 11.6 (-26.2, 49.5)	28 / -20.7 (-59.3, 17.9)	32.4 (0.8, 63.9)
2nd Quartile (Baseline > 264 meters and <= 333 meters)	32 / 31.9 (4.9, 58.8)	29 / 10.5 (-16.6, 37.6)	21.4 (-4.0, 46.7)
3rd Quartile (Baseline > 333 meters and <= 384 meters)	25 / 18.2 (-10.0, 46.5)	32 / 29.0 (1.8, 56.1)	-10.7 (-34.0, 12.5)
4th Quartile (Baseline > 384 meters)	28 / -10.8 (-41.4, 19.8)	31 / 16.5 (-12.2, 45.3)	-27.3 (-59.9, 5.2)

*Post-hoc analysis
6MWD: 6-minute walk distance; LS: least squares; CI: confidence interval.

LEVEL Treatment Effect Appears Magnified in Older Patients (<333 M Baseline)

THE PATIENTS WHO NEED THE DRUG THE MOST BENEFIT THE MOST

Difference in change from baseline
LS Mean Difference (SE) 43.1 (13.03)
95% CI for LS Mean Difference 17.5, 68.6



*Post-hoc analysis
6MWD: 6-minute walk distance; LS: least squares; SE: standard error; CI: confidence interval.

Impressive Reductions in Exploratory Endpoints

BIOMARKER AND HEMODYNAMIC REDUCTIONS EVEN MORE PRONOUNCED IN PATIENTS WITH HIGHER DISEASE BURDEN

All Patients Enrolled in LEVEL

Exploratory endpoint	TNX-103	Placebo	Treatment Difference
NT-proBNP, mean change	− 39.1 pmol/L	+ 13.7 pmol/L	49% (p < 0.0001*)
RVSP (PASP), median	− 3.6 mmHg	+ 0.5 mmHg	− 3.5 mmHg#H (p = 0.0045*)

LEVEL Patients with Lower Exercise Tolerance at Baseline

Below Median (Baseline < 333 M)

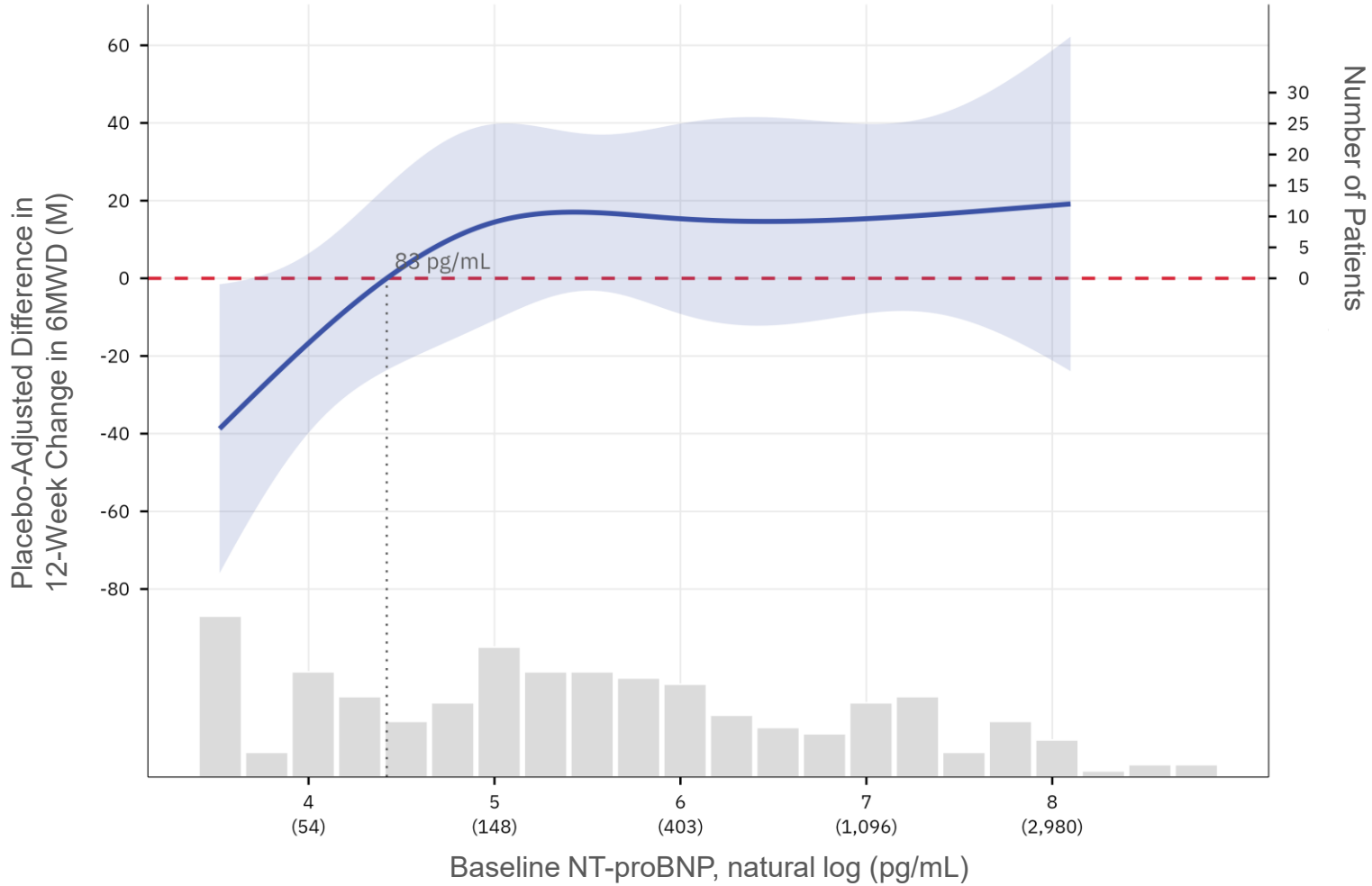
– 4.9 mmHg

RVSP Δ vs. placebo at Week 12
Echocardiography (p = 0.009*)

*nominal p-value; #95% confidence interval is -6.010, -1.100; HHodges-Lehmann shift estimate.
NT-proBNP: N-terminal pro B-type natriuretic peptide; RVSP: right ventricular systolic pressure; PASP: pulmonary artery systolic pressure; 6MWD: 6-minute walk distance.

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Treatment Effect by Baseline NT-proBNP



*Post-hoc analysis

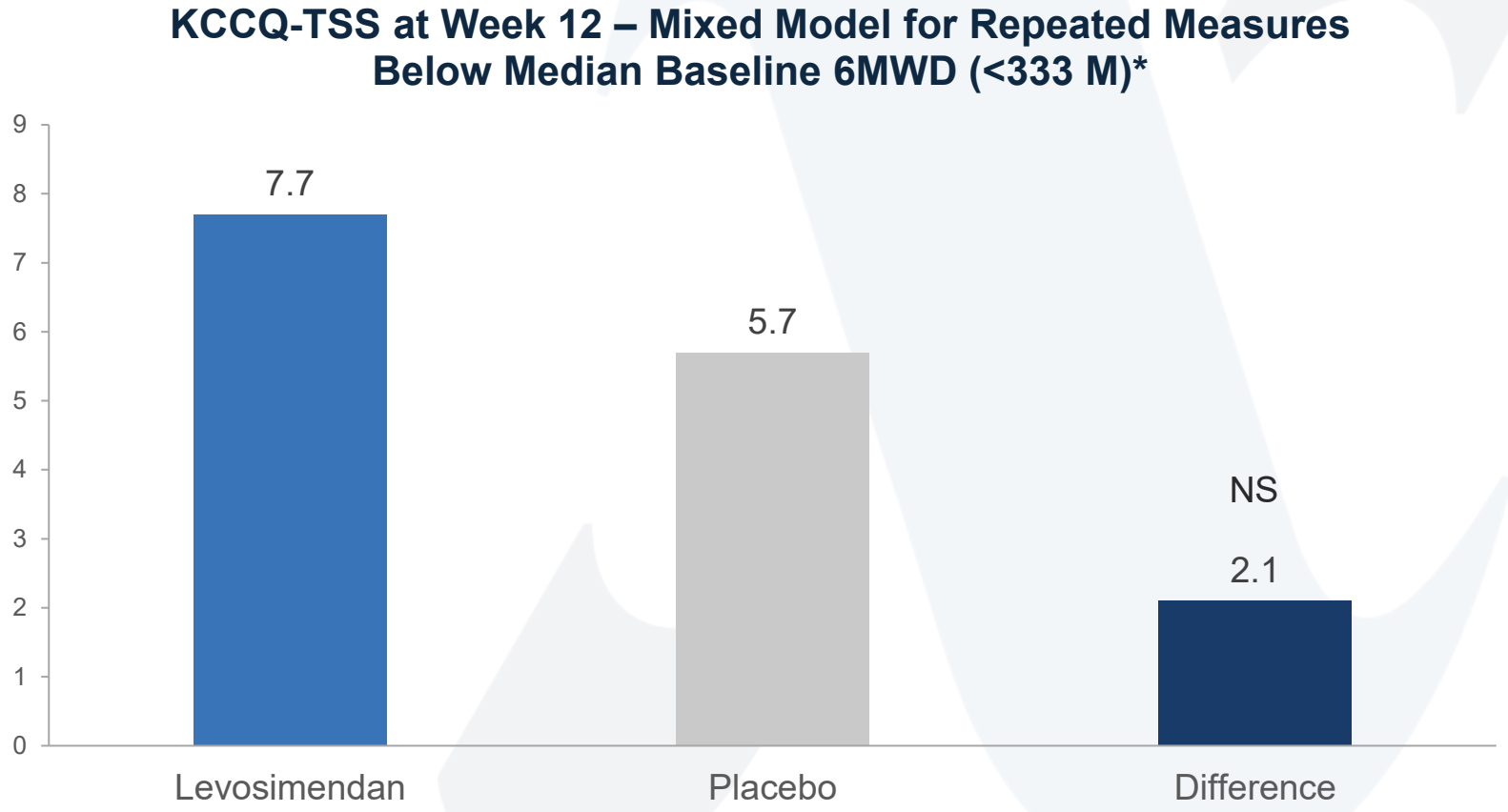
NT-proBNP: N-terminal pro B-type natriuretic peptide; 6MWD: 6-minute walk distance; LS: least squares; SE: standard error; CI: confidence interval.

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Change in KCCQ-TSS in LEVEL Patients <Median (333 M) 6MWD

MAGNITUDE OF EFFECT IS COMPARABLE TO CHANGES SHOWN BY SGLT-2i & MRAs IN MANY HFpEF TRIALS

Difference in change from baseline
LS Mean Difference (SE) 2.1 (3.41)
95% CI for LS Mean Difference -4.6, 8.7



*Post-hoc analysis
6MWD: 6-minute walk distance; KCCQ-TSS: Kansas City Cardiomyopathy Questionnaire-Total Symptom Score; LS: least squares; SE: standard error; CI: confidence interval; NS: not significant.

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Three Disease Burden Markers Correlate with Treatment Effect

KEY BASELINE CHARACTERISTICS PREDICT RESPONSE

By age	Δ 6MWD vs placebo	95% CI	Nominal p-value
Top tertile (> 74 years), N=77	+ 37.6 M	14.7, 60.5	0.0013
Above median (≥ 71 years), N=124	+ 27.1 M	9.9, 44.4	0.0021
Below median (< 71 years), N=117	- 19.2 M	- 42.0, 3.5	0.0972

By baseline NT-proBNP#	Δ 6MWD vs placebo*	95% CI	Nominal p-value
Above median (≥ 225 pg/mL), N=122	+ 16.7 M	- 2.3, 35.8	0.0850
Below median (< 225 pg/mL), N=119	- 9.0 M	- 30.2, 12.3	0.4074

By baseline 6MWD	Δ 6MWD vs placebo*	95% CI	Nominal p-value
Below median (< 333 M), N=119	+ 26.3 M	6.0, 46.7	0.0112
Above median (≥ 333 M), N=122	- 17.6 M	- 36.9, 1.7	0.0744

*Least squares mean difference; #post-hoc analysis.
6MWD: 6-minute walk distance; NT-proBNP: N-terminal pro B-type natriuretic peptide; CI: confidence interval.