Atrioventricular Interval Modulation Therapy

Device-based Therapy for Hypertension and Diastolic Heart Failure

David E. Kandzari, MD, FACC, MSCAI
Chief, Piedmont Heart Institute and Cardiovascular Services
Chief Scientific Officer
Director, Interventional Cardiology

CRF®
THT®
TECHNOLOGY AND HEART FAILURE THERAPEUTICS®

Disclosure

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below

Affiliation/Financial Relationship	Company
Grant/Research Support (Institutional)	Medtronic CardioVascular, Biotronik, Orbus Neich, Ablative Solutions, Teleflex, Orchestra BioMed, Supira Medical
Consulting Fees/Honoraria	Boston Scientific, Medtronic CardioVascular, DeepQure, Brattea
Major Stock Shareholder/Equity	BioStar Ventures (none related to ASI)
Royalty Income	None
Ownership/Founder	None
Intellectual Property Rights	None
Other Financial Benefit	None

Piedmont HEART

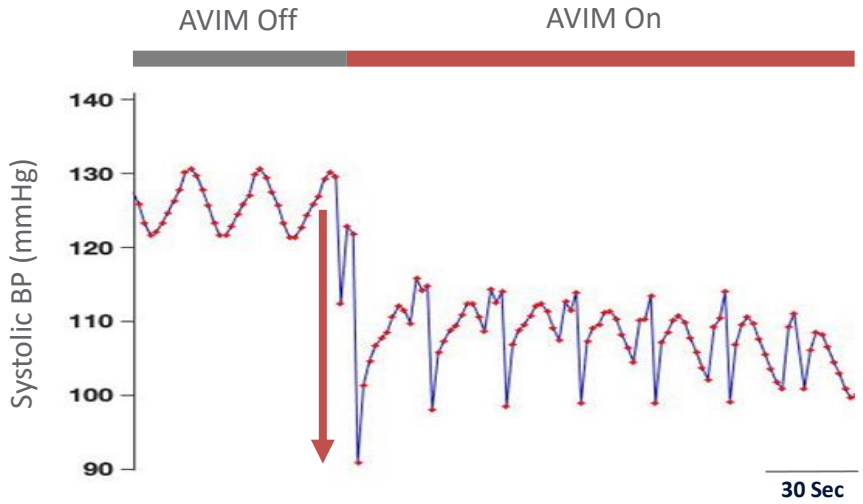
Atrioventricular Interval Modulation Therapy

Mechanisms of Action

Designed to Have an Immediate, Clinically Meaningful, and Sustained Effect[1]

- **Short AV intervals**: reduce cardiac preload, **immediately lowering BP**
- **Intermittent longer AV intervals**: modulate ANS response (baroreceptor reflex) and reduce afterload (TPR), **sustaining BP reduction**
- Delivered via Medtronic Astra™ or Azure™ dual-chamber pacemaker
- **No additional surgical procedure** and compatible with both RV pacing and conduction system pacing
- **Programmable, adjustable,** and not dependent on **patient adherence**

Novel & Potent Mechanism[1]



[1]Kalarus et al. JAHA 2021;10:e020492ahajournals.org/doi/10.1161/JAHA.120.020492

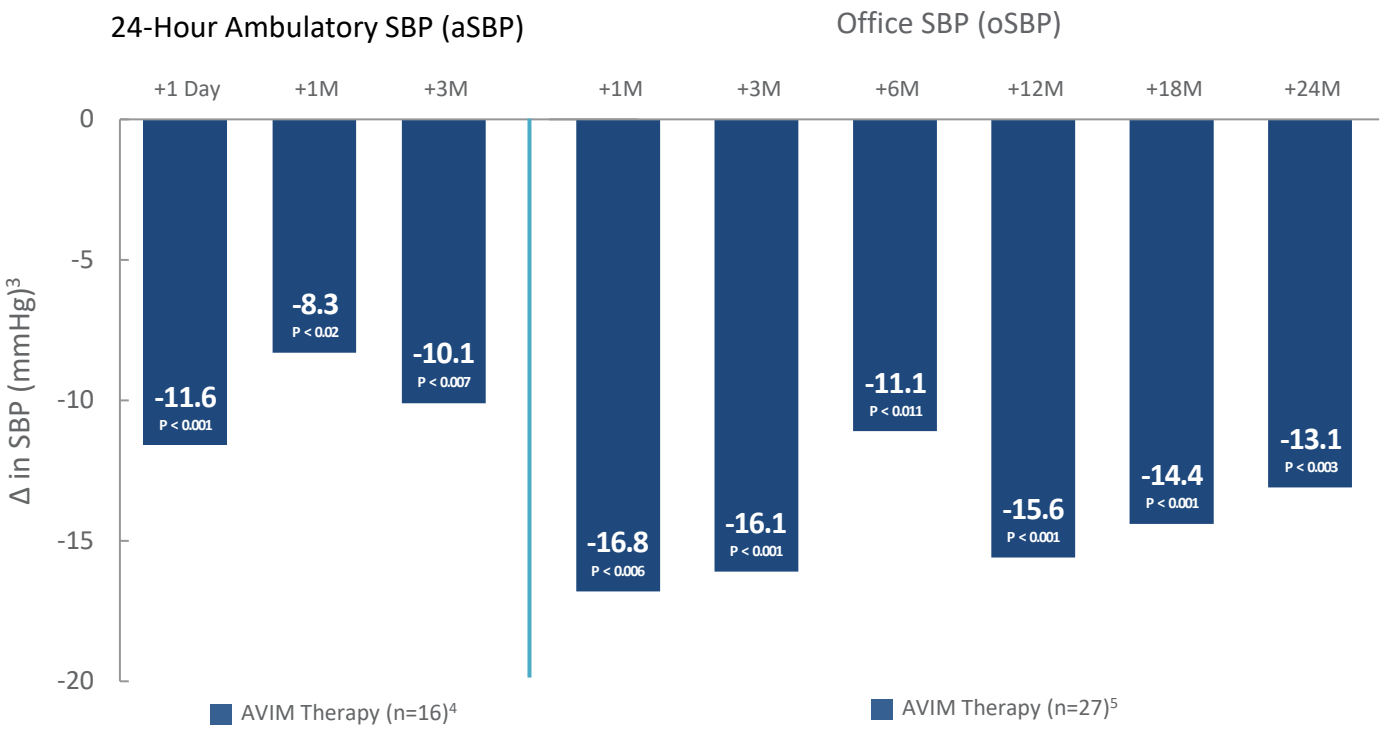
Piedmont HEART

AVIM Therapy and Blood Pressure Reduction

Moderato I Pilot Study

A prospective, single-arm study of 27 patients with persistent hypertension (oSBP >150 mmHg) despite 2 or more anti-hypertensive medications and an indication for pacemaker[1,2]

Reduction in Systolic Blood Pressure (SBP)[3]



10.1 mmHg Reduction
in 24-Hour aSBP
at 3 months

Sustained 13.1 mmHg Reduction
in oSBP
at 2 years

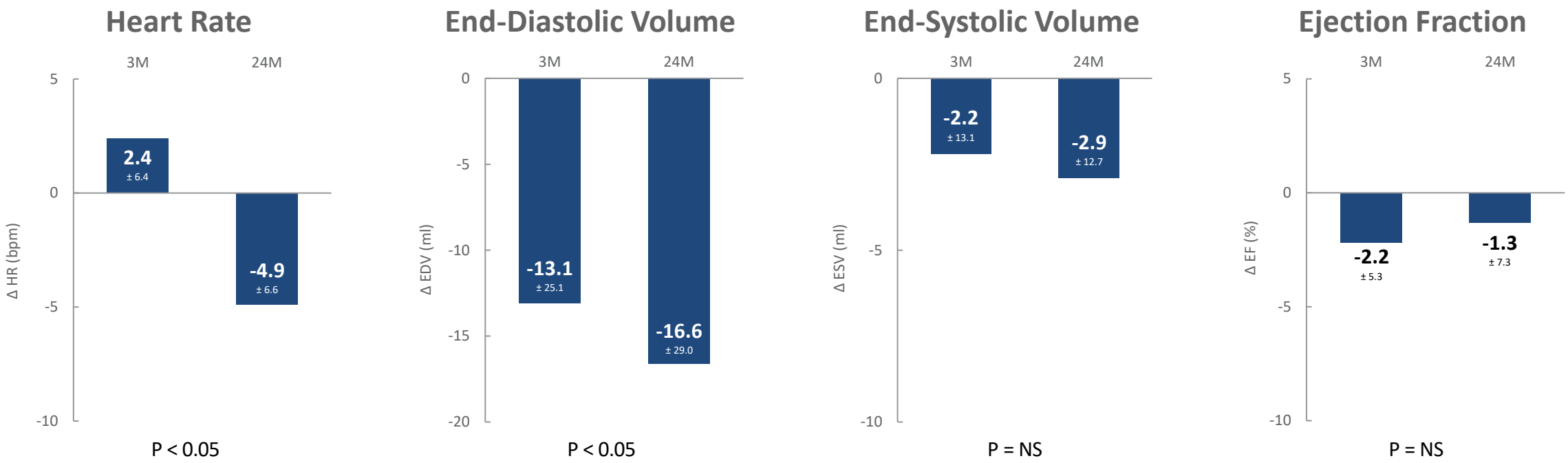
[1]Neuzil et al. *JAHA* 2017. [2]Burkhoff MODERATO I Study 2-Year Results TCT 2018. [3]Compared to pre-activation. [4]aSBP (n=16) at pre-activation. [5]AVIM (n=21) continued after completion of study at 3 months to be followed for 2 years.

Piedmont HEART

AVIM Therapy and Hemodynamic Effects

Moderato I Pilot Study

Significant Reduction in Heart Rate & End-Diastolic Volume at 24 Months[1]



No significant change in end-systolic volume or ejection fraction

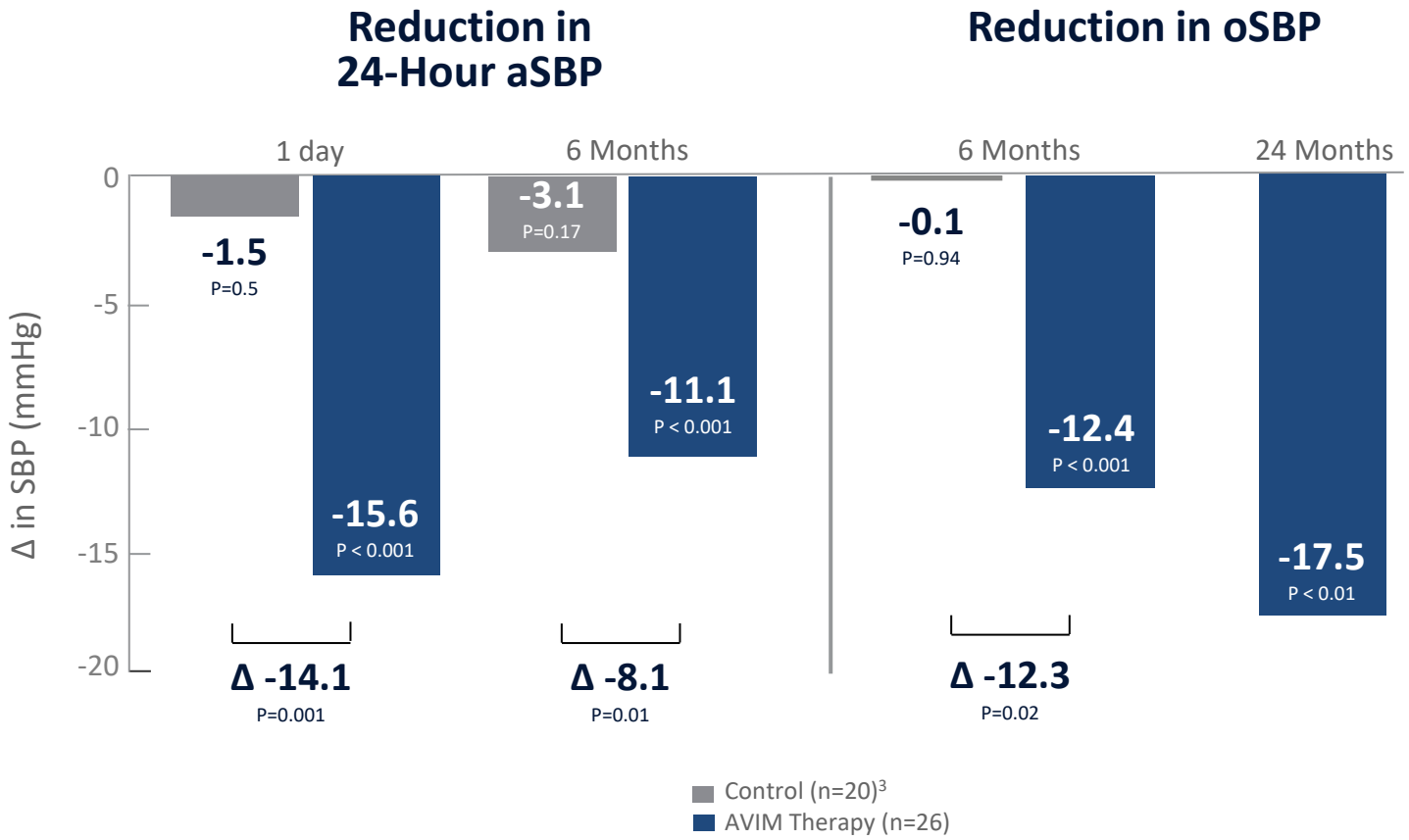
[1]Burkhoff MODERATO I Study 2-Year Results TCT 2018

Piedmont HEART

AVIM Therapy and Blood Pressure Reduction

Moderato II Randomized, Double-Blind Pilot Study

- Pacemaker patients with hypertension despite medical therapy
- LVEF ≥ 50%
- **0% MACE** at 6 months[4]



[1]Kalarus et al. *JAHA*. 2021; [2]Burkhoff MODERATO II Study 2-Year Results TCT 2021; [3]24-Hr aSBP Control (n=19); [4]A blinded evaluation Data Safety Monitoring Board report for MODERATO II included a revised MACE rate, from 9.5% to 14.3%, in the control group to reflect a HF event after study result publication.

Piedmont HEART

AVIM Therapy and Hemodynamic Effects

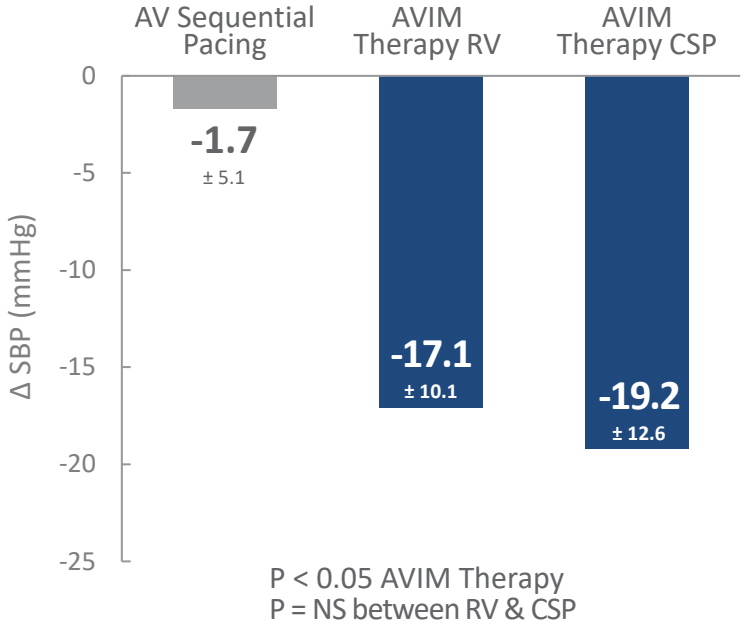
Acute Pressure Volume Relationship with AVIM

SBP Reduction (Independent of Lead Position) & Favorable Impact on Hemodynamics[1]

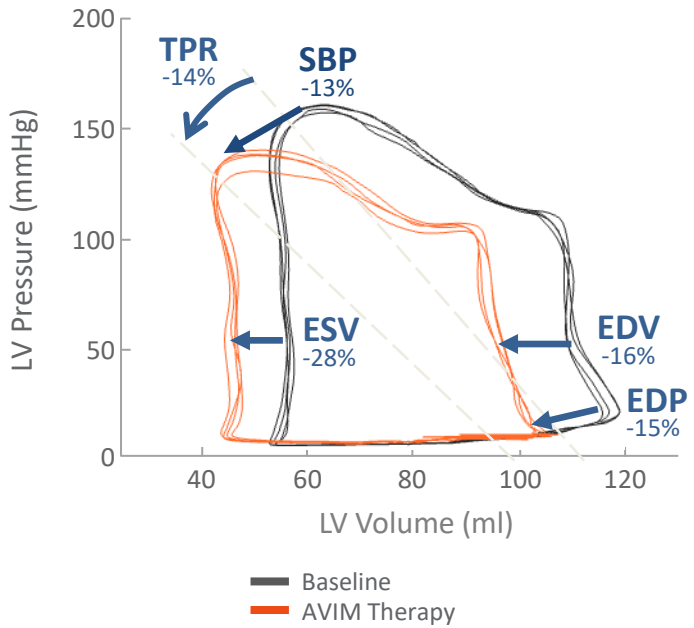
Significant reduction in pre-load and afterload without change in contractility (± 1%)

Significant 21% reduction in stroke work without significant reduction in stroke volume

SBP Reduction, N=16



PV Loops



[1]Chovanec M, et al. *JACC Clin Electrophysiol*. 2025

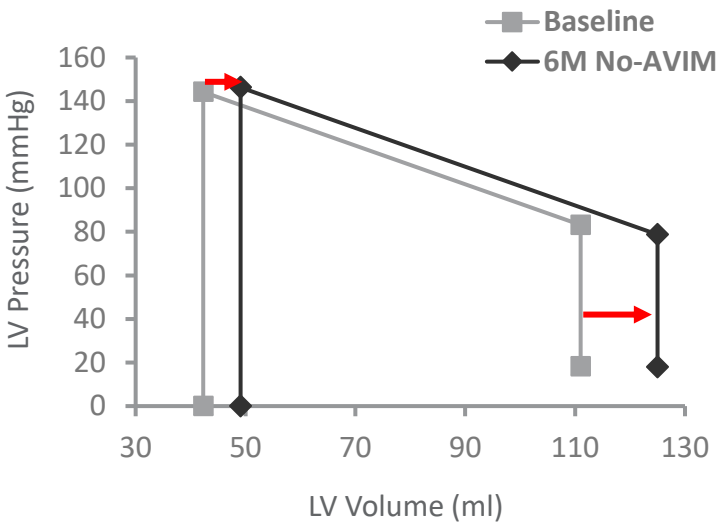
n=16 for AVIM therapy in both lead positions. n=14 for AV sequential pacing. Baseline is atrial pacing with intrinsic conduction. CSP type is LBBA.

Piedmont HEART

AVIM Therapy and Hemodynamic Effects

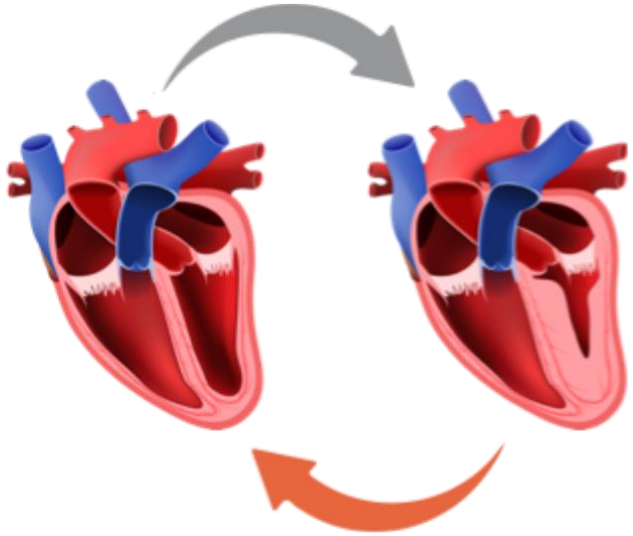
Moderato II Substudy Noninvasive PV Loop Analysis

Control Group Showed Progressive Ventricular Remodeling at 6 Months[1]



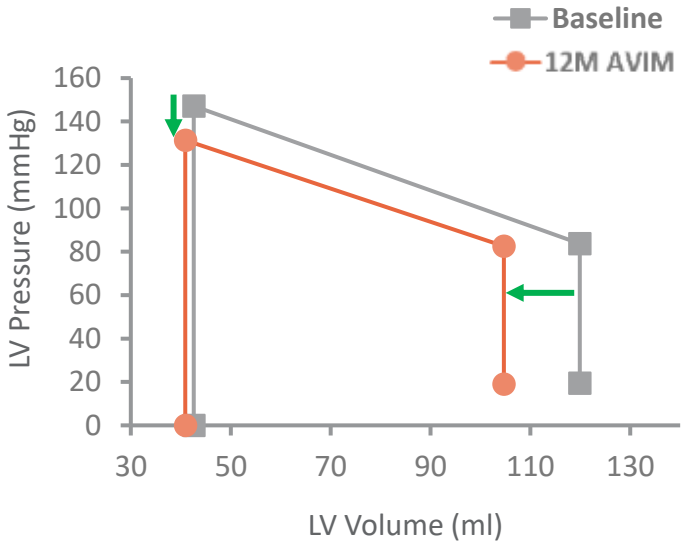
n=11

Control Group Developed Ventricular Remodeling



AVIM Therapy Induced Reverse Remodeling

AVIM Therapy Showed Reverse Remodeling at 12 months[1]



n=14

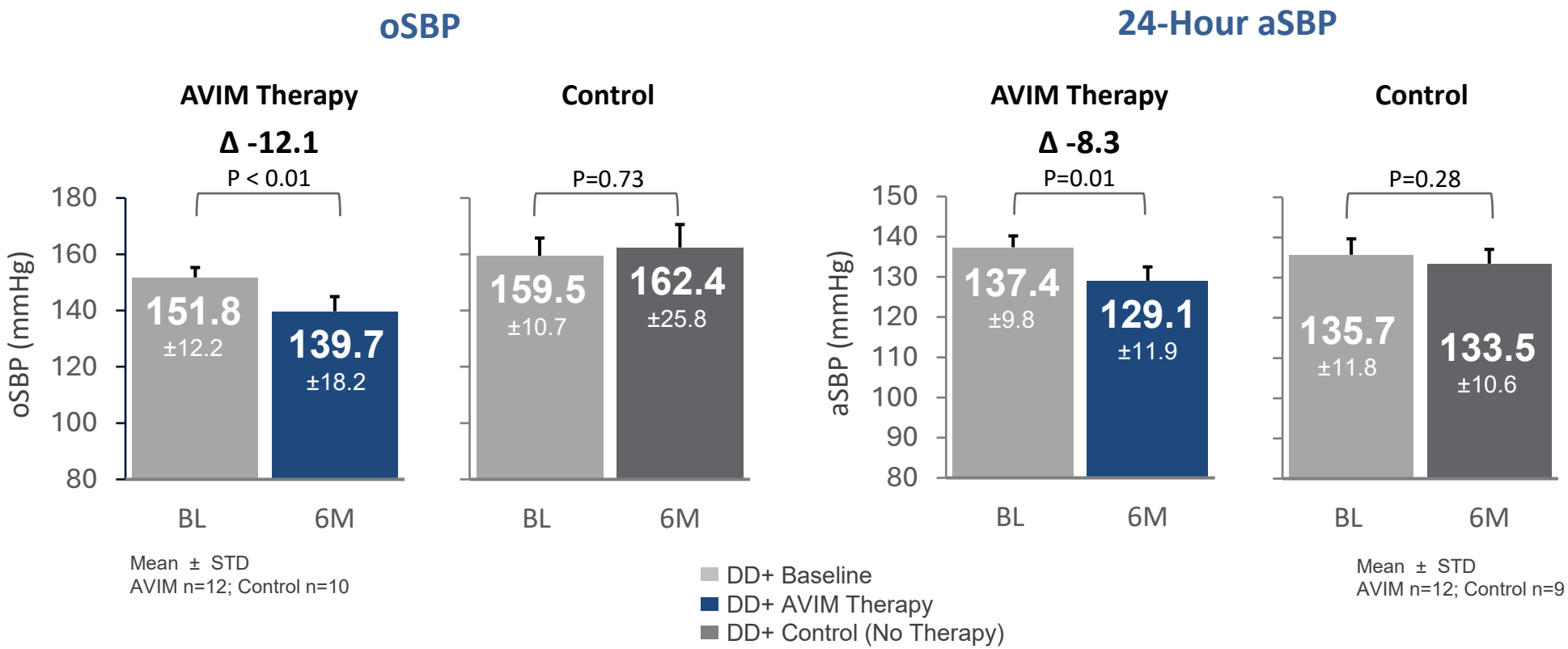
[1]Chovanec M, et al. *JACC Clin Electrophysiol*. 2025

Piedmont HEART

AVIM Therapy and Diastolic Dysfunction

Moderato II Substudy

61% of AVIM Therapy Patients in MODERATO II had Diastolic Dysfunction[1,2]



Core lab echoes were assessed with independent blinded adjudication

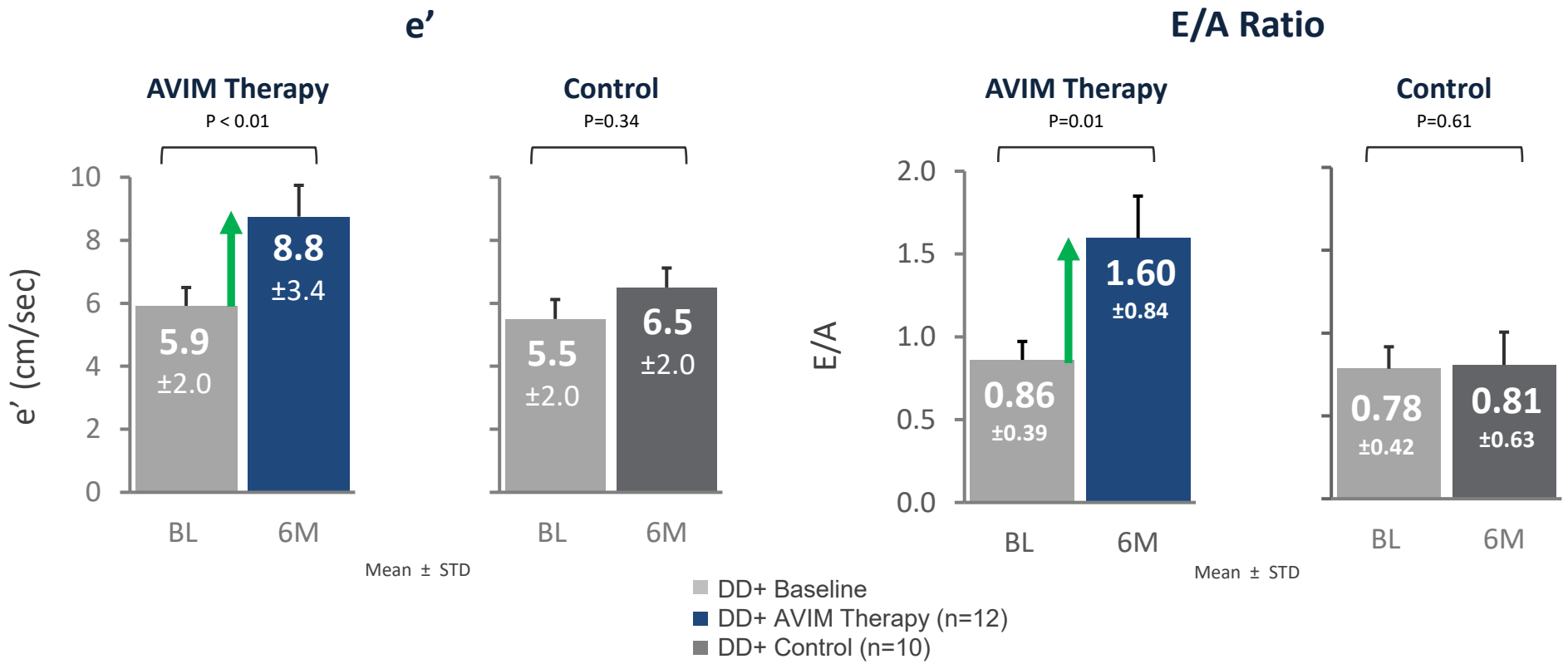
[1]Fudim M et al. *JACC: Advances 2025;* [2]DD assessed via American Society of Echocardiography guidelines.

Piedmont HEART

AVIM Therapy and Diastolic Dysfunction

Moderato II Substudy

Significantly Increased e' & E/A, Indicating Improved Myocardial Relaxation & Diastolic Compliance



AVIM therapy increased the percentage of patients with normal values for e' (16% → 58%) & E/A (42% → 73%)

Fudim M et al. *JACC Advances* 2025

Piedmont HEART

Backbeat Global Pivotal Trial

BACKBEAT
GLOBAL PIVOTAL STUDY

- Randomized, prospective, multi-center, double-blind, controlled trial
- Sponsored by Orchestra BioMed, conducted in partnership with Medtronic
- Actively enrolling up to 500 patients across 130 sites in US, Europe, & APAC
- NYHA I or II HF with LVEF ≥ 50% eligible
- Echocardiography and KCCQ at baseline, 3 months, & 12 months

Patients who **have or are scheduled to receive** a Medtronic Astra™ or Azure™ dual-chamber pacemaker and have **hypertension despite medication**

AVIM Therapy download & set-up

R

1:1

AVIM Therapy + Medical Therapy

Medical Therapy

Primary Efficacy Endpoint
Between group difference in the change in mean 24-hour aSBP at 3-months

Primary Safety Endpoint
Freedom from unanticipated serious device events at 3 months

Secondary Endpoints
Efficacy and safety endpoints after 12-month follow-up

Piedmont HEART

AVIM for Uncontrolled Hypertension and Heart Failure with Preserved Ejection Fraction

- AVIM therapy is a novel investigational, pacemaker-delivered treatment designed to have an immediate, substantial, and sustained effect in reducing BP, independent of lead position
  - Efficacy in both isolated systolic and combined hypertension
  - 'Always on' effect with sustained BP lowering through 3 years
- AVIM associated with improved hemodynamics in parallel with BP reductions
  - Significant reductions in both preload and afterload without decrease in contractility
  - Ventricular remodeling at 6 months with decreases in left ventricular pressure and volume
- In patients with diastolic dysfunction, AVIM therapy significantly reduced BP and improved measures of myocardial relaxation and diastolic compliance
- Ongoing BACKBEAT Global Pivotal Trial (NCT06059638) is intended to demonstrate the safety and effectiveness of AVIM in patients with uncontrolled HTN but will also offer insight to potential benefits in HFpEF