

# Effects of AtrioVentricular Interval Modulation (AVIM) Therapy in Subjects with Hypertension and Diastolic Dysfunction

Marat Fudim, MD, MHS

Advanced Heart Failure Specialist, Cardiologist  
Duke University Health System



**THT**

TECHNOLOGY  
AND HEART FAILURE  
THERAPEUTICS



# Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

## Nature of Financial Relationship

Grant/Research Support

Consultant Fees/Honoraria

Individual Stock(s)/Stock Options

Royalties/Patent Beneficiary

Executive Role/Ownership Interest

Other Financial Benefit

## Ineligible Company

No relevant disclosures

Orchestra BioMed

No relevant disclosures

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No relevant disclosures

No relevant disclosures

# Atrioventricular Interval Modulation (AVIM) Therapy

**AVIM Therapy Uses a Dual-chamber Pacemaker to Deliver Repeated Sequences of Short and Longer AV Intervals to Reduce Blood Pressure<sup>1</sup>**



**Short AV intervals:** Reduce cardiac preload, **immediately lowering blood pressure**

Utilizes well characterized physiologic mechanisms (Frank-Starling) to **favorably impact circulatory hemodynamics<sup>2</sup>**:

- Reduces intra-cardiac volumes and pressures
- Improves cardiovascular efficiency
- No adverse impact on contractility

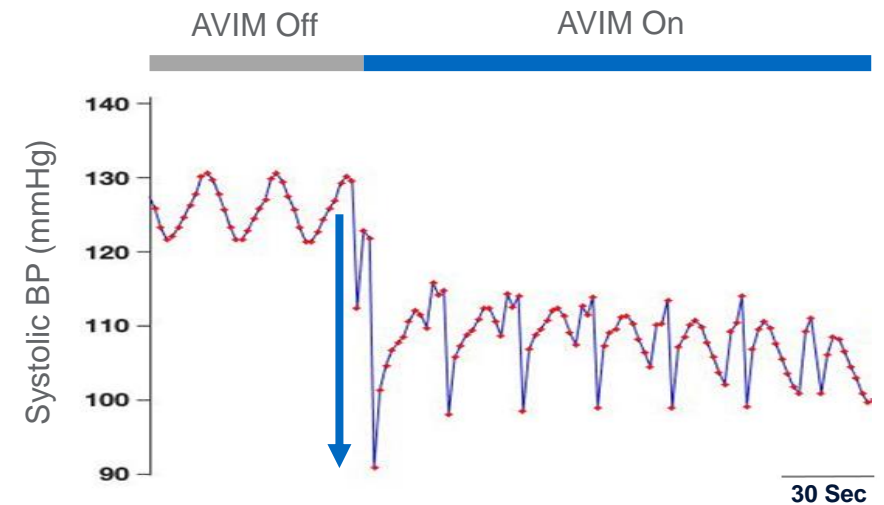


**Intermittent longer AV intervals:** modulate autonomic nervous system response (baroreceptor reflex) and reduce afterload (total peripheral resistance), **sustaining blood pressure reduction**



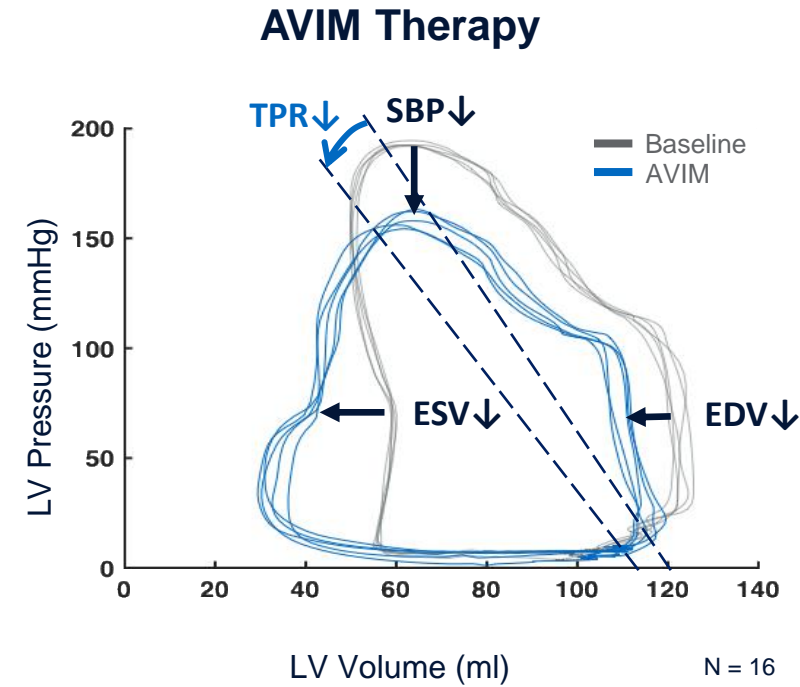
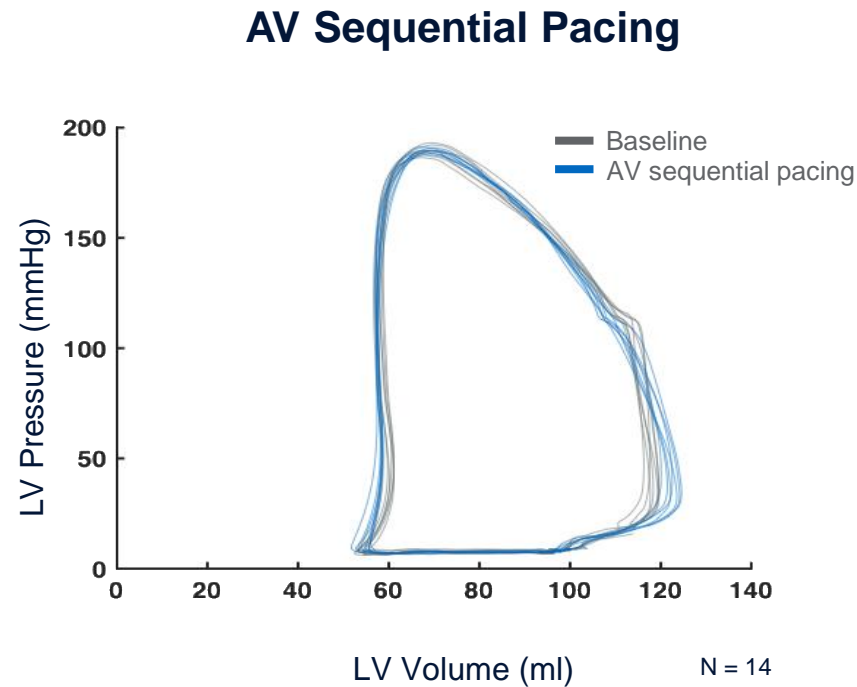
**Independent of lead position:** compatible with traditional RV pacing or conduction system pacing

**Designed to Immediately, Substantially and Persistently Lower Blood Pressure**



# AVIM Therapy Shows Favorable Acute Hemodynamics

## AVIM Therapy Reduces Blood Pressure, Intra-Cardiac Volumes and Total Peripheral Resistance



Single center study of patients indicated for a pacemaker with hypertension  $140 < \text{oSBP} < 180$  despite medical therapy. Baseline utilized atrial pacing with intrinsic conduction. Paired Data (baseline vs. AV sequential pacing or baseline vs. AVIM therapy)<sup>1</sup>

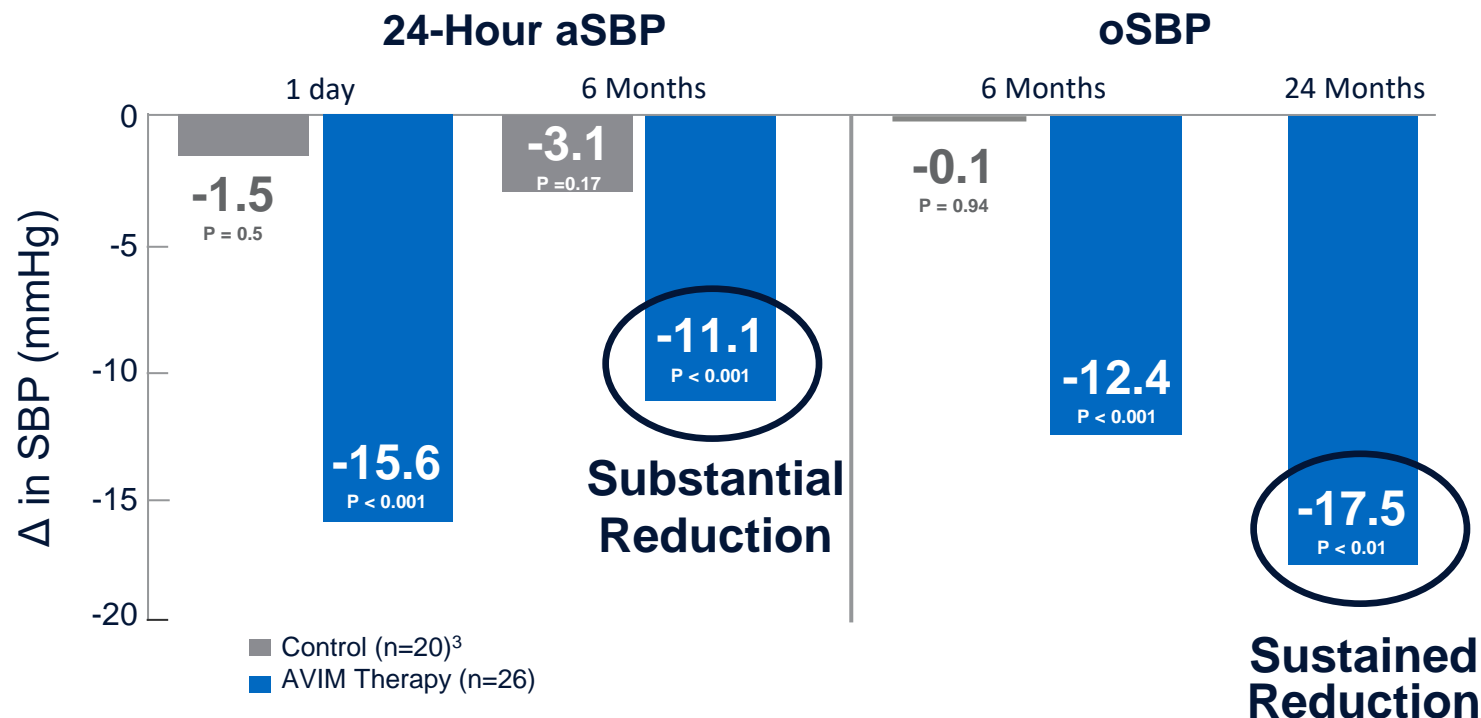
# MODERATO II Prospective, Randomized, Double-Blind Pilot Study

## AVIM Therapy Significantly Reduces Systolic Blood Pressure



Pacemaker Patients  
with Uncontrolled  
Hypertension Despite  
Medical Therapy

LVEF  $\geq$  50% and  
absence of HF  
symptoms



**0% MACE** vs.  
14.3% in control  
group at 6 months<sup>4</sup>

# Retrospective Analysis of MODERATO II Patients with Diastolic Dysfunction

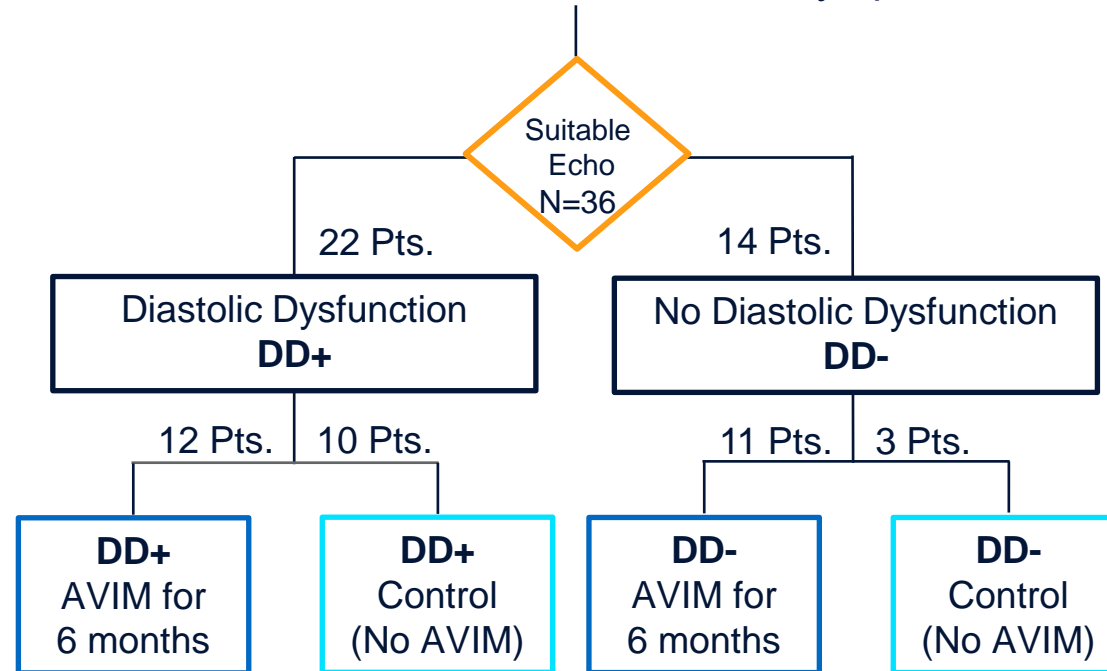
- **Hypertension is the leading cause of diastolic dysfunction (DD).** Both conditions are common in the elderly and contribute to the development of Heart Failure<sup>1</sup>
- Conducted a retrospective, treatment-blinded analysis of MODERATO II core lab echocardiograms with **independent blinded adjudication**
  - Classified patients as with or without DD
  - Assessed impact of 6 months of AVIM therapy on SBP and echocardiographic markers of DD
- DD identified using the American Society of Echocardiography Guidelines, requiring  $\geq 2$  of the following criteria:
  - Average  $E/e' > 14$  or septal  $e' < 7\text{cm/sec}$  or lateral  $e' < 10\text{cm/sec}$  or  $\text{TR} > 2.8\text{m/sec}$
  - LA volume index  $> 34\text{ml/m}^2$
  - LVH  $> 1.1\text{ cm}$

# Retrospective Analysis of MODERATO II Patients with Diastolic Dysfunction



47 Pacemaker Patients with Uncontrolled Hypertension Despite Medical Therapy

LVEF  $\geq$  50% and Absence of HF Symptoms



# Demographics

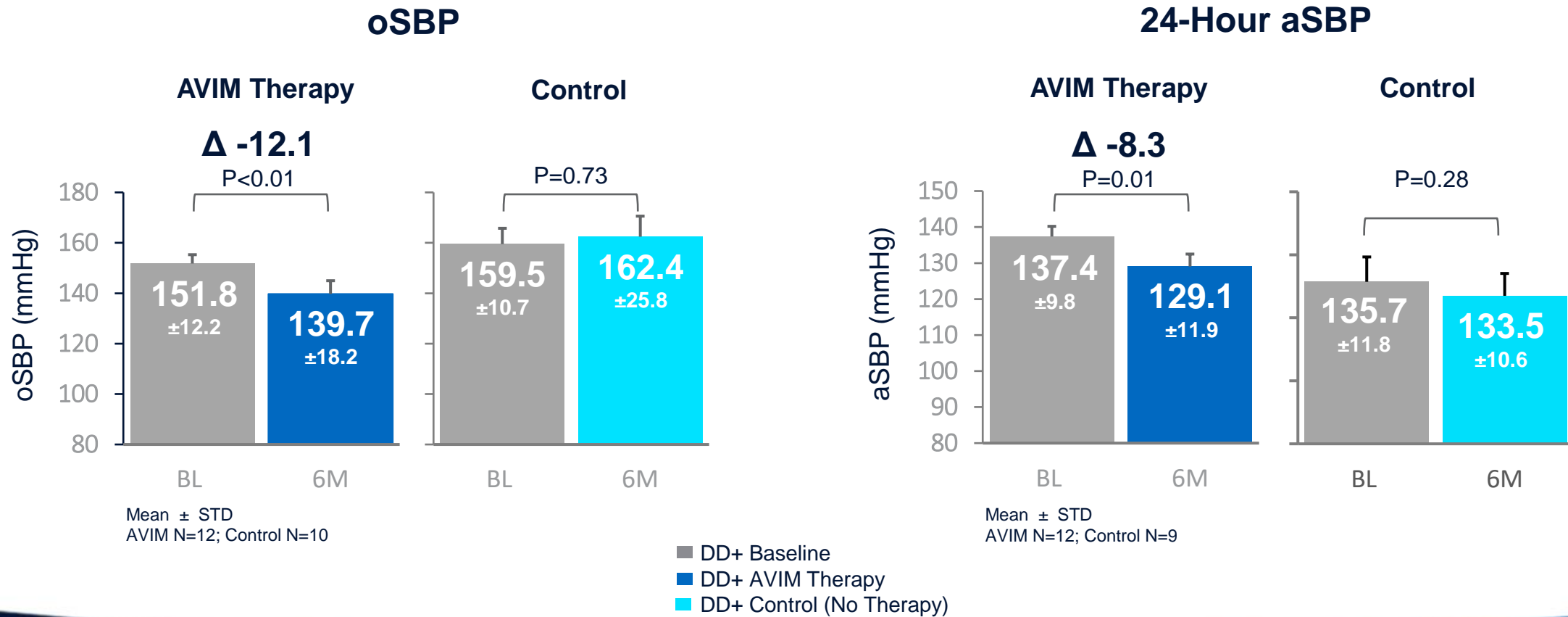
	All (n=36)	DD+ (n=22)	DD- (n=14)
Age (yrs)	73.2± 8.8	74.0 ± 8.7	72.0 ± 9.2
Gender	23 M / 13F	13M / 9 F	10M / 4F
Comorbidities			
AF	(8) 22%	(3) 14%	(5) 36%
Diabetes	(16) 44%	(9) 41%	(7) 50%
CAD	(16) 44%	(12) 55%	(4) 29%
Stroke	(1) 3%	(1) 5%	(0) 0%
ISH	81%	77%	86%
# HTN Meds	3.2 ± 1.4	3.3 ± 1.5	2.9 ± 1.4

	All (n=36)	DD+ (n=22)	DD- (n=14)
oSBP	154.8±19.4	156.6±19.8	152.0±19.2
aSBP	136.2±9.3	136.3±10.0	136.0±8.5
LV EF (%)	62.8±5.7	62.9±6.2	62.6±5.2
LA size (mL/m <sup>2</sup> )	40.6±4.6	42.1±4.8	38.3±3.3 <sup>*</sup>
E (cm/sec)	64.7±18.2	63.1±18.8	67.1±17.6
e' (cm/sec)	6.6±2.3	6.2±2.0	7.3±2.8
E/A	0.79±.35	0.80±0.35	0.79±0.30
E/e'	10.6±3.6	11.6±3.9	9.5±3.1

\* P < 0.05

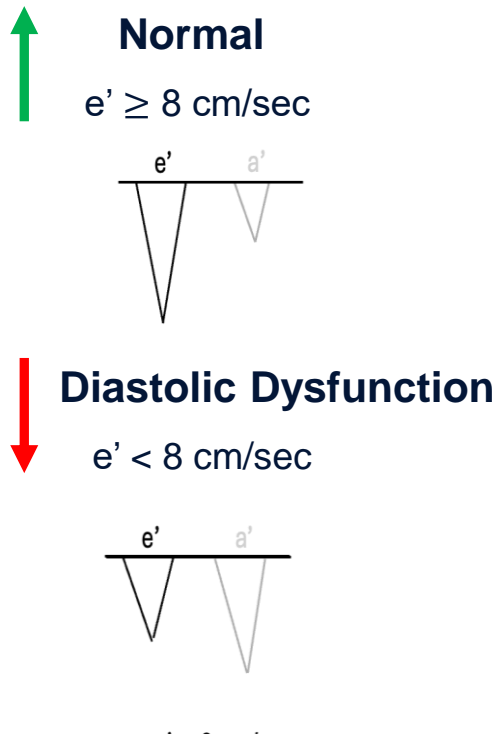
# AVIM Therapy Significantly Reduces SBP in Patients with Diastolic Dysfunction

*AVIM Therapy Significantly Reduces Office & Ambulatory Systolic BP Through 6 Months*

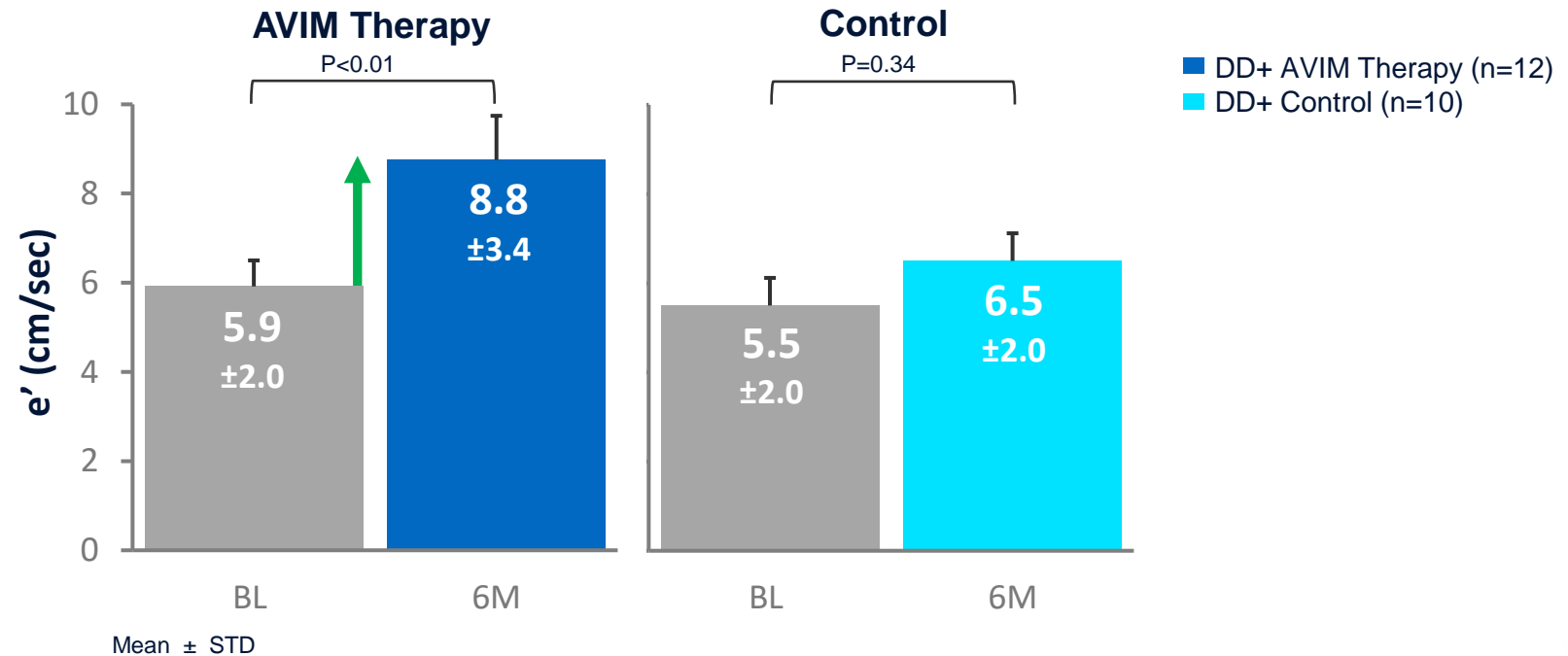


# AVIM Therapy Improved Diastolic Dysfunction

**AVIM Therapy Significantly Increased  $e'$  from 5.9 to 8.8 cm/sec  
% of Patients with Normal  $e'$  Increased from 16% to 58%**



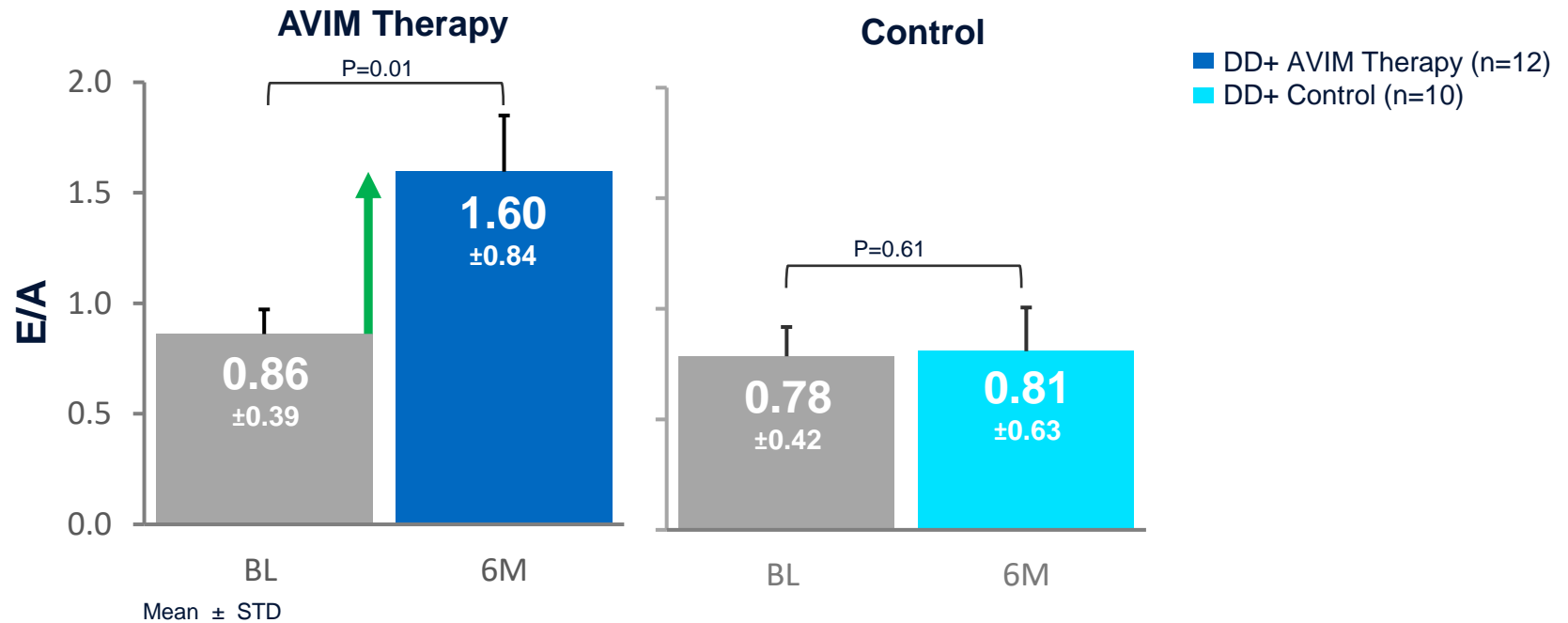
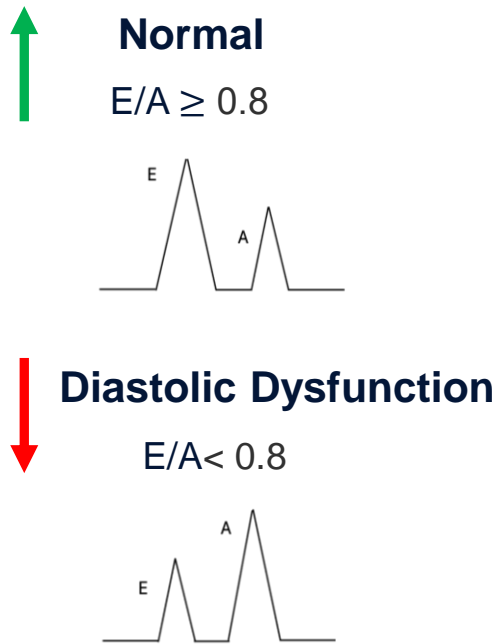
**AVIM Therapy Increased  $e'$  Indicating Improved Myocardial Relaxation**



# AVIM Therapy Improved Diastolic Dysfunction

**AVIM Therapy Significantly Increased the E/A Ratio from 0.8 to 1.6, % of Patients with Normal E/A Increased from 42% to 73%**

**AVIM Therapy Increased E/A Ratio Suggesting Improved Myocardial Relaxation and Improved Diastolic Compliance**



# AVIM Therapy Effects in Diastolic Dysfunction Patients

**AVIM Therapy Significantly Increased  $e'$ ,  $E$ , and  $E/A$  with No Significant Changes in EF and LA Size**

Echocardiographic Markers of Diastolic Dysfunction						
	AVIM Therapy (N=12)			Control (N=10)		
	Baseline	6M	6M - BL	Baseline	6M	6M-BL
LV EF (%)	64.8 ± 6.8	61.8 ± 5.3	-3.0 ± 7.2	60.4 ± 4.1	59.7 ± 3.2	-0.57 ± 5.6
LA size (mL/m <sup>2</sup> )	41.1 ± 5.3	42.7 ± 5.6	1.6 ± 3.1	41.5 ± 4.9	43.3 ± 4.1	1.8 ± 2.2*
$E$ (cm/sec)	61.3 ± 15.9	89.3 ± 17.5	28.0 ± 18.6*	63.6 ± 20.6	65.3 ± 22.4	1.7 ± 14.3
$e'$ (cm/sec)	5.9 ± 2.0	8.8 ± 3.4	2.8 ± 2.9*	5.5 ± 2.0	6.5 ± 2.0	1.0 ± 3.1
$E/e'$	11.2 ± 4.1	11.1 ± 3.1	-0.08 ± 3.9	12.1 ± 3.9	10.9 ± 4.4	-1.2 ± 5.9
$E/A$	0.86 ± 0.39	1.60 ± 0.84	0.73 ± 0.77*	0.78 ± 0.42	0.81 ± 0.63	0.02 ± 0.31

\* P<0.05

# Conclusions

- In MODERATO II, a study of hypertensive pacemaker patients with LVEF  $\geq$  50% and NYHA  $<$  II, 61% of subjects had echocardiographic evidence of Diastolic Dysfunction
- AVIM therapy significantly **reduced SBP** in patients with Diastolic Dysfunction
- AVIM therapy **improved myocardial relaxation and improved diastolic compliance** as assessed by echocardiography
- Further studies warranted to confirm these findings and explore the potential clinical impact of AVIM therapy on Diastolic Dysfunction and HFpEF
- **BACKBEAT Pivotal Trial (NCT06059638)** currently enrolling patients indicated for a dual-chamber pacemaker with uncontrolled hypertension despite medical therapy