Two-year outcomes with a fully repositionable and retrievable percutaneous aortic valve in 250 high surgical risk patients: Results from the REPRISE II trial extended cohort

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on behalf of the REPRISE II Investigators

19 September 2016 • London, UK

Disclosures

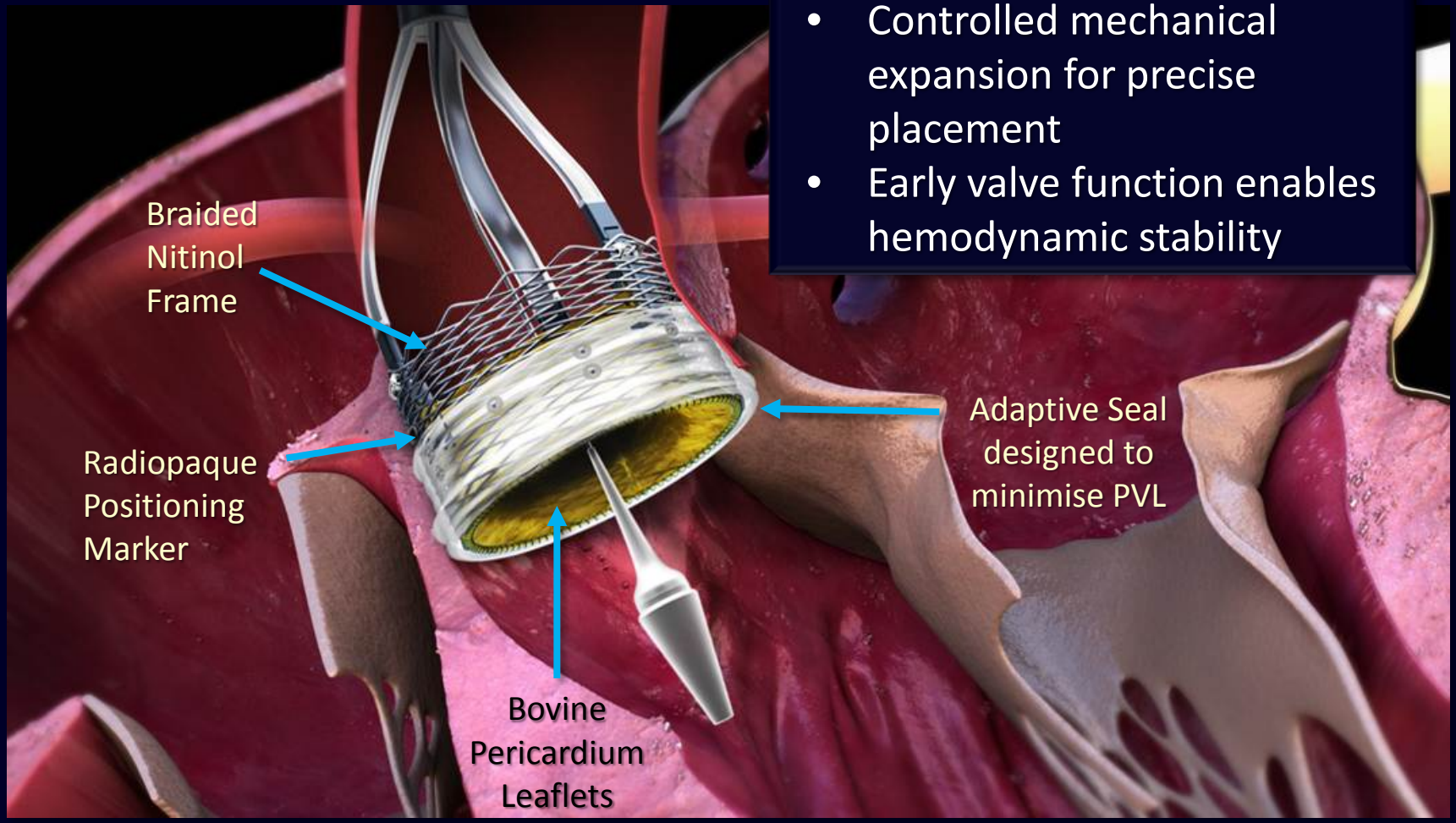
Ian T. Meredith AM

- Consultant Fee / Honoraria / Speaker's Bureau:
  - Boston Scientific (Significant)

The REPRISE studies are sponsored and funded by Boston Scientific Corporation.

Lotus Valve System

Fully repositionable & retrievable



- Controlled mechanical expansion for precise placement
- Early valve function enables hemodynamic stability

Information not intended for use in France. Lotus is an investigational device and not for sale or distribution in the US.
CE mark received 2013. Information for the Lotus Valve System is for use in countries with applicable product registrations.
Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

REPRISE II Study with Extended Cohort

OBJECTIVE

- Evaluate safety & performance of the Lotus Valve System for TAVI in symptomatic patients with severe calcific aortic stenosis considered high risk for surgical valve replacement

DESIGN

- Prospective; single-arm; multicentre
- Available valve sizes: 23mm & 27mm
- F/U at 7 days/discharge, 30 days, 3 & 6 months, annually 1–5 years

INDEPENDENT DATA ASSESSMENTS

- Clinical Events Committee
- Core Labs: Angiography, ECG, Echocardiography, Pathology

REPRISE II Study Organisation

PRINCIPAL INVESTIGATOR

Ian T. Meredith, MBBS, PhD, Monash Medical Centre, Clayton, Australia

CORE LABORATORIES

Angiography & CT/X-ray	Jeffrey J. Popma, MD (Director) Harvard Medical Faculty Physicians at Beth Israel Deaconess Medical Center, Boston, MA, USA
Echocardiography	Neil J. Weissman, MD (Director) MedStar Health Research Institute, Washington, DC, USA
Electrocardiography	Peter J. Zimetbaum, MD (Director) Harvard Clinical Research Institute, Boston, MA, USA
Pathology	Renu Virmani, MD (Director) CV Path Institute, Inc., Gaithersburg, MD, USA

CLINICAL EVENTS COMMITTEE

Sergio Waxman, MD (IC, Chair)

Carey Kimmelstiel, MD (IC)

Gregory Smaroff, MD (CT Surg)

Roberto Rodriguez, MD (CT Surg)

Viken Babikian, MD (Neurologist)

Enrollment – REPRISE II with Extended Cohort

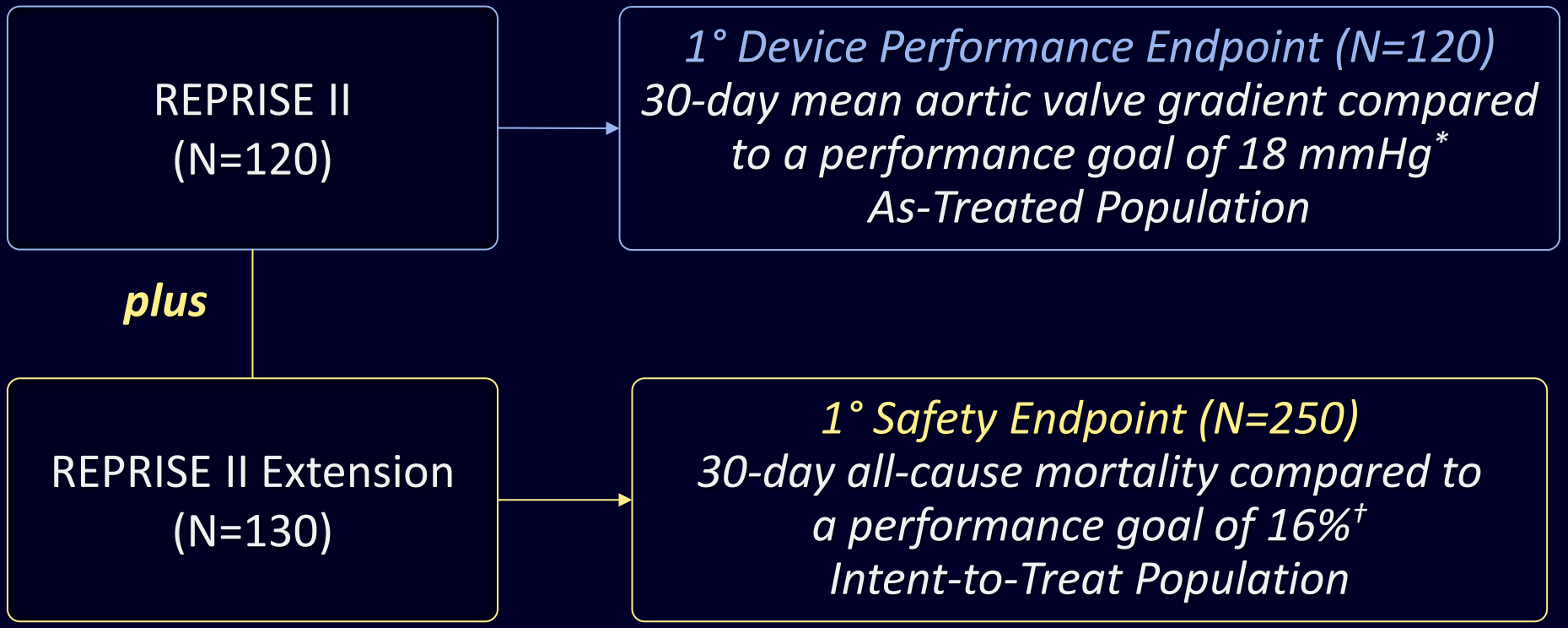
250 patients between Oct 2012 & Apr 2014 at 20 sites

	Patients
Ian Meredith Monash Medical Centre, Clayton, Australia	38
Nicolas Dumonteil Centre Hôpital Universitaire Rangueil , Toulouse, France	29
Daniel Blackman The General Infirmary, Leeds, UK	22
Didier Tchétché Clinique Pasteur, Toulouse, France	21
David Hildick-Smith Royal Sussex County Hospital, Brighton, UK	19
Ganesh Manoharan Royal Victoria Hospital, Belfast, UK	19
Darren Walters The Prince Charles Hospital, Brisbane, Australia	19
Jan Harnek University Hospital of Lund, Lund, Sweden	16
Stephen Worthley Royal Adelaide Hospital, Adelaide, Australia	13
Gilles Rioufol Hôpital Cardiologique de Lyon, Bron, France	10

	Patients
Thierry Lefèvre Institut Cardiovasculaire - Paris Sud, Massy, France	9
Thomas Modine CHRU Lille - Hôpital Cardiologique, Lille, France	9
Nicolas Van Mieghem Erasmus Medical Center, Rotterdam, The Netherlands	8
Rüdiger Lange Deutsches Herzzentrum Muenchen, Muenchen, Germany	4
Robert Whitbourn St. Vincent's Hospital (Melbourne), Fitzroy, Australia	4
Simon Redwood Guys and St. Thomas' NHS Foundation Trust, London, UK	3
Corrado Tamburino Ospedale Ferrarotto, Catania, Italy	3
Ralf Müller HELIOS Klinikum Siegburg, Siegburg, Germany	2
Eulogio Garcia Hospital Clinico San Carlos, Madrid, Spain	1
Stephan Windecker Universitätsspital Bern, Bern, Switzerland	1

REPRISE II Study with Extended Cohort

Preplanned Analysis of Pooled Data

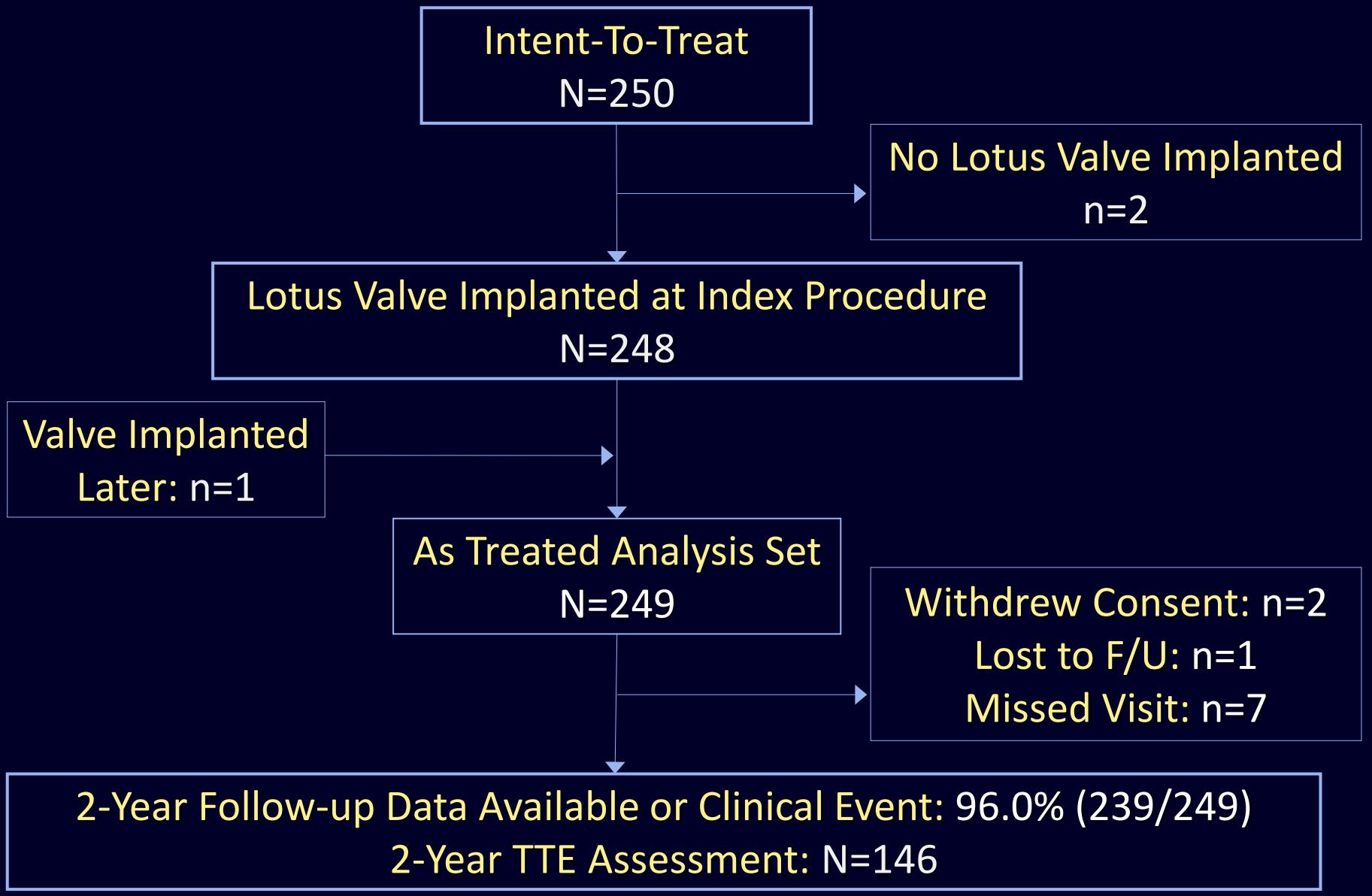


Additional endpoints according to the VARC-2 metrics

* Meredith, et al. JACC 2014;64:1339

† Meredith, et al. PCR London Valves 2014

Study Flow – REPRISE II with Extended Cohort



Intent ion-to-treat population.

Baseline Characteristics

REPRISE II with Extended Cohort (N=250; Intent-To-Treat)

Comorbidities & Baseline Scores

Age (Years)	84.0 ± 5.2 (250)	NYHA Class III or IV	77.2% (193)
Gender (Female)	52.4% (131)	euroSCORE 2011 (%)	6.4 ± 6.2 (250)
Diabetes, treated	24.0% (60)	STS Score (v 2.73; %)	6.5 ± 4.2 (250)
Atrial fibrillation	37.2% (93)	STS Plus Score (%)	10.6 ± 7.7 (250)

Echocardiographic Measurements*

AVA (cm^2)	0.7 ± 0.2 (197)	LVEF (%)	53.1 ± 10.5 (126)
MR (mod/severe)	10.6% (24)	Mean gradient (mmHg)	45.2 ± 13.6 (212)
AR (mod/severe)	13.3% (29)	Peak gradient (mmHg)	74.7 ± 21.1 (212)

Frailty Indices

		Threshold
5 Meter gait speed (sec)	8.6 ± 5.2 (236)	> 6
Max grip strength average (kg)	21.1 ± 11.5 (246)	≤ 18
Katz Index	5.7 ± 0.8 (247)	< 6
Mini-Cognitive Assessment for Dementia	3.5 ± 1.4 (244)	< 4

* Independent Core Lab assessment

Device Performance

REPRISE II with Extended Cohort (N=250; Intent-To-Treat)

Successful access, delivery, deployment & system retrieval	98.8%
Successful valve repositioning, if attempted (n=85)	100.0%
Partial valve resheathing (n)	71
Full valve resheathing (n)	14
Successful valve retrieval, if attempted (n=13)	92.3%
Aortic valve malpositioning	0.0%
Valve migration	0.0%
Valve embolisation	0.0%
Ectopic valve deployment	0.0%
TAV-in-TAV deployment	0.0%

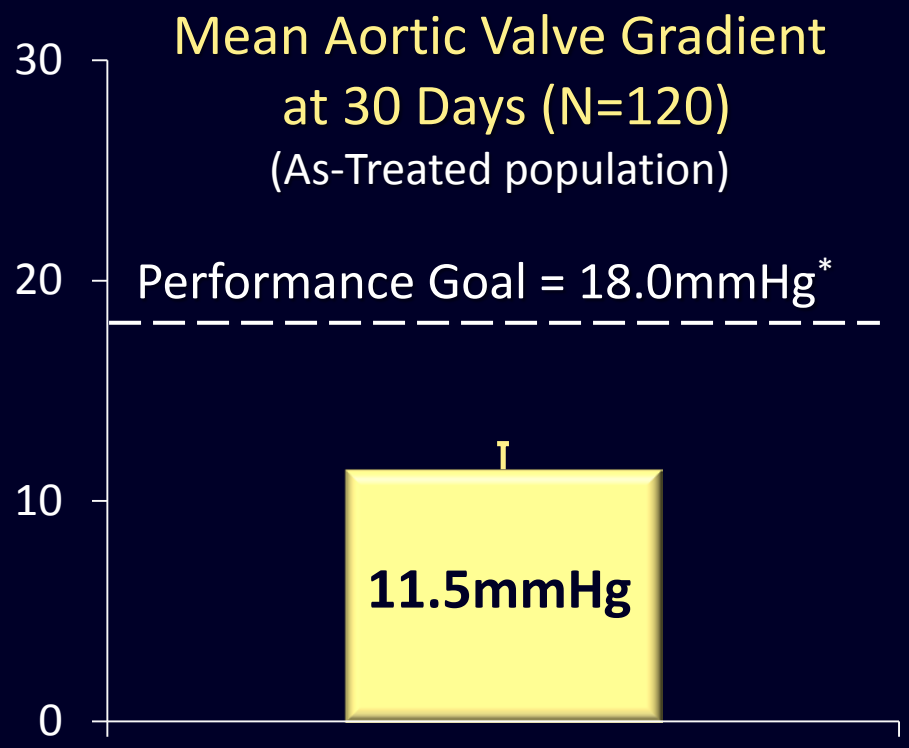
Procedural Device Success – VARC 2 Metrics

REPRISE II with Extended Cohort (N=250; Intent-To-Treat)
Core-lab adjudicated

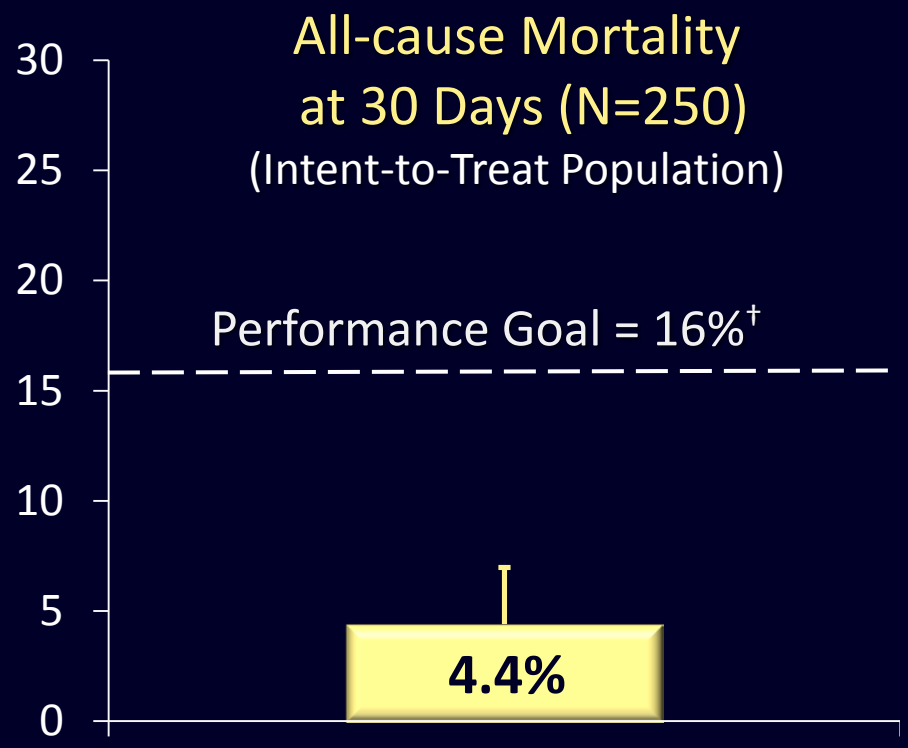
No procedural mortality	98.4% (246/250)
Correct positioning of one valve in proper location	99.2% (248/250)
Mean aortic valve gradient <20 mmHg	95.0% (210/221)
Peak velocity <3 m/s	94.6% (210/222)
No moderate/severe prosthetic valve regurgitation	98.2% (217/221)

Primary Endpoints

REPRISE II with Extended Cohort



11.5mmHg ± UCB (12.6mmHg) is significantly below the performance goal (P<0.001)‡



4.4% ± UCB (6.97%) is significantly below the performance goal (P<0.001)§

* Based on an expected mean of ≤15mmHg (literature review) plus a test margin of 3mmHg

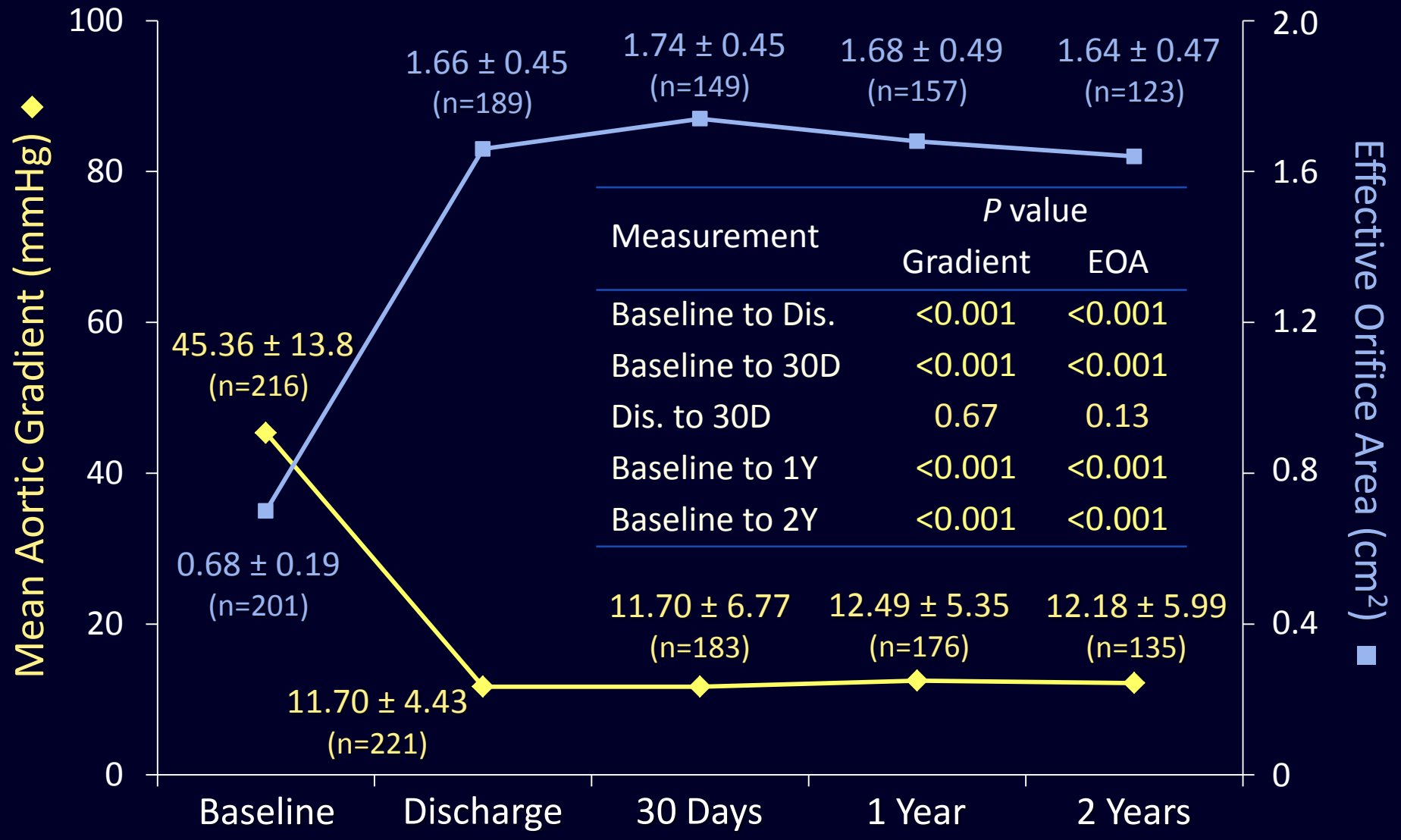
† Based on an expected rate of 9.8% (literature review) plus a test margin of 6.2%

‡ Meredith, et al. *JACC* 2014; 64:1339.

§ Meredith, et al. PCR London Valves 2014.

Mean Aortic Gradient & EOA at 2 Years

REPRISE II With Extended Cohort (N=249; As Treated)

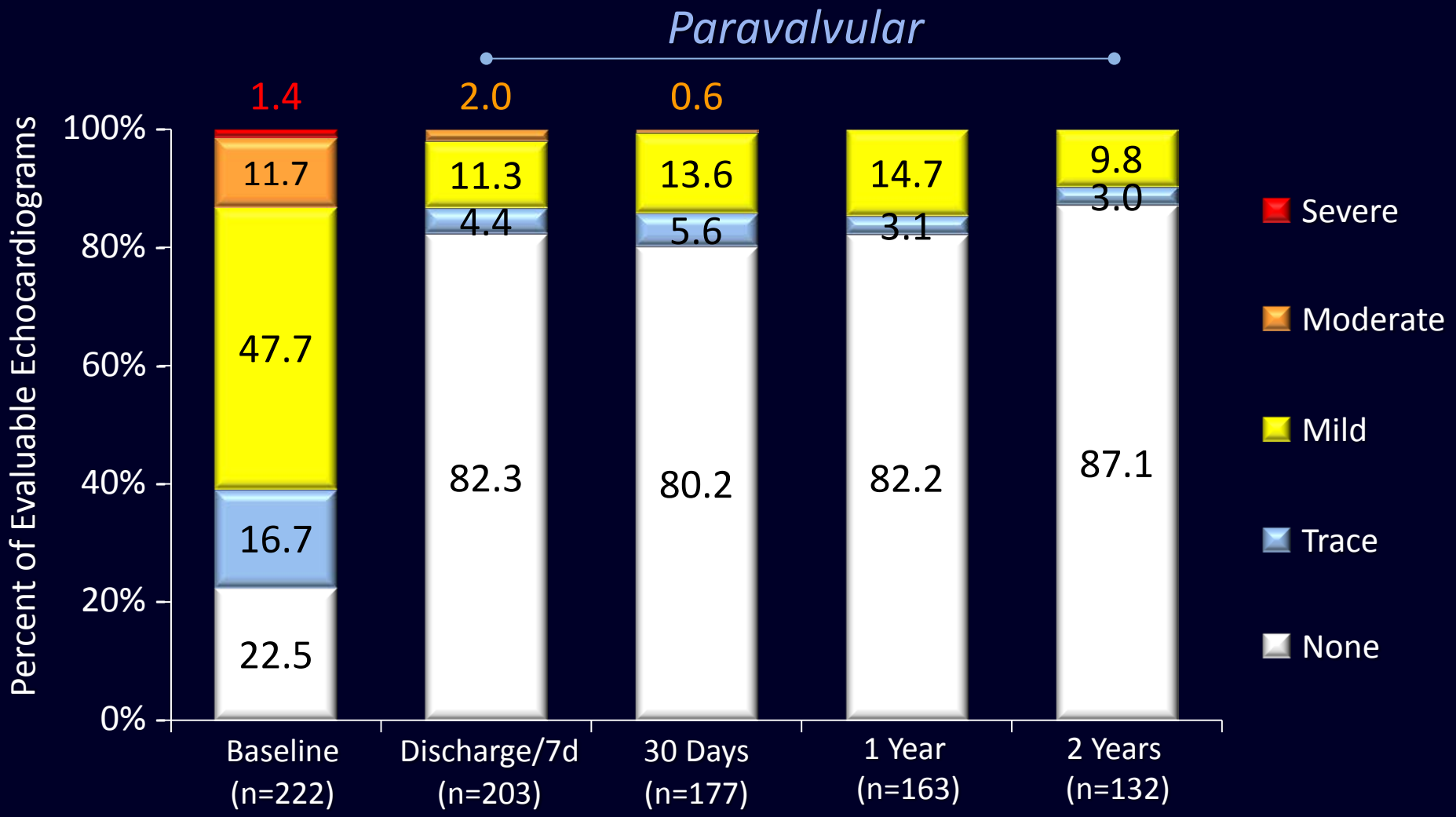


Measurement	*P* value	
	Gradient	EOA
Baseline to Dis.	<0.001	<0.001
Baseline to 30D	<0.001	<0.001
Dis. to 30D	0.67	0.13
Baseline to 1Y	<0.001	<0.001
Baseline to 2Y	<0.001	<0.001

Values are mean ± standard deviations. As-treated population.

Paravalvular Aortic Regurgitation at 2 Years

REPRISE II With Extended Cohort (N=249; As Treated)



No moderate or severe paravalvular aortic regurgitation at 2 years

Core-lab adjudicated data. Values may not add to 100% due to rounding. As-treated population.

Safety: Death & Stroke at 2 Years

REPRISE II with Extended Cohort (N=249; As Treated)

Event	*30 Days*	*1 Year*	*2 Years*
All-cause death	4.0% (10)	11.8% (29)	19.1% (47)
Cardiovascular death	3.6% (9)	7.8% (19)	9.5% (23)
Disabling stroke	2.9% (7)	3.7% (9)	4.7% (11)
Non-disabling stroke	4.1% (10)	4.9% (12)	4.9% (12)

All REPRISE II patients (n=120) were assessed by a neurologist before and after TAVI. KM rates.

Pacemaker Implantation at 2 Years

REPRISE II with Extended Cohort (N=249; As Treated)

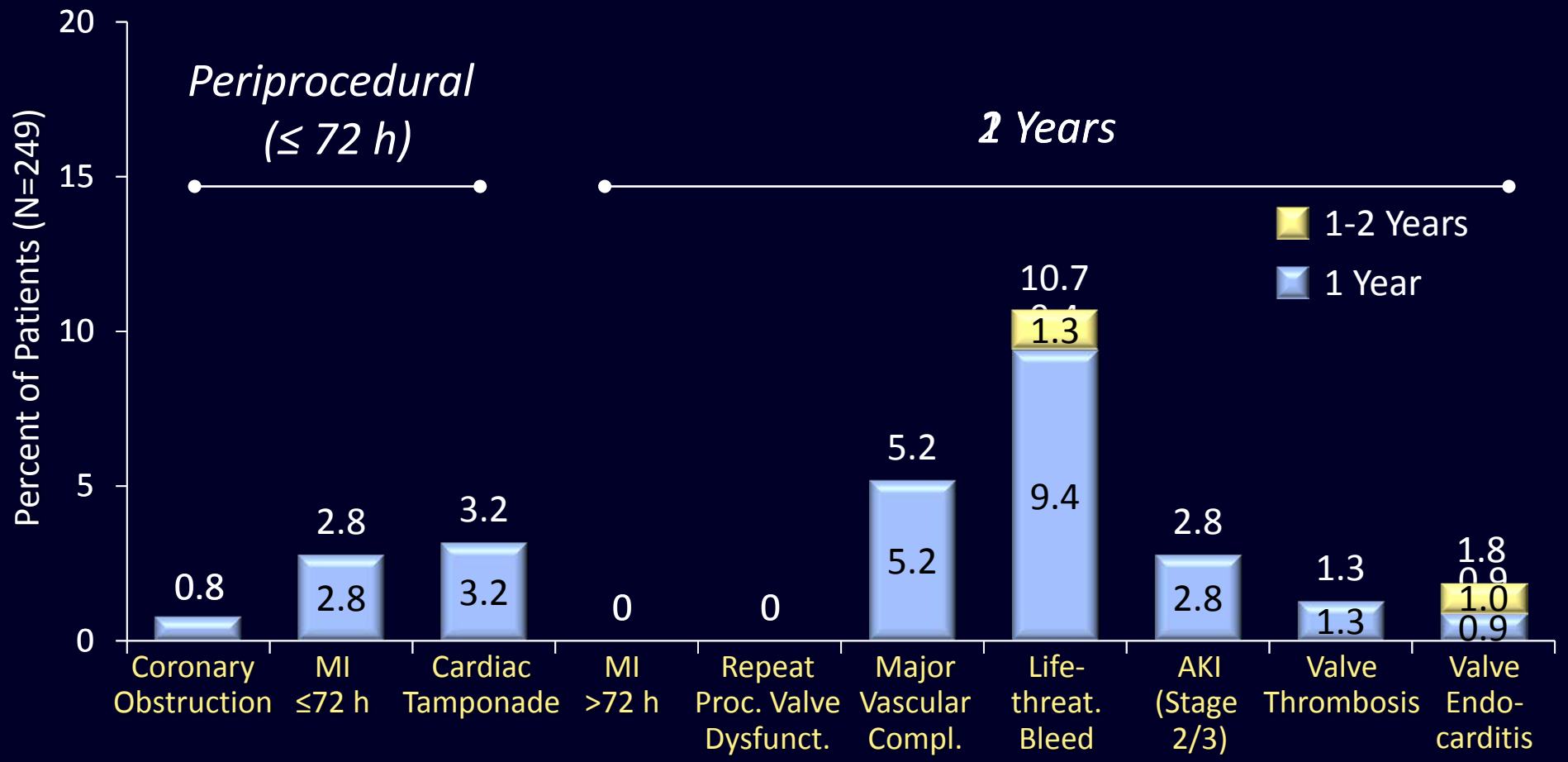
New Permanent Pacemaker (N=249)

0 days to 1 Year	81 (33.1%)
1 Year to 2 Years	4 (1.9%)
3rd degree AV block on day 432	1
Symptomatic bradycardia (days 527, 663, and 673)	3
0 Days to 2 Years	85 (35.1%)

Kaplan-Meier rates. Events may not add over time due to censoring.

Additional VARC 2 Safety Endpoints at 2 Years

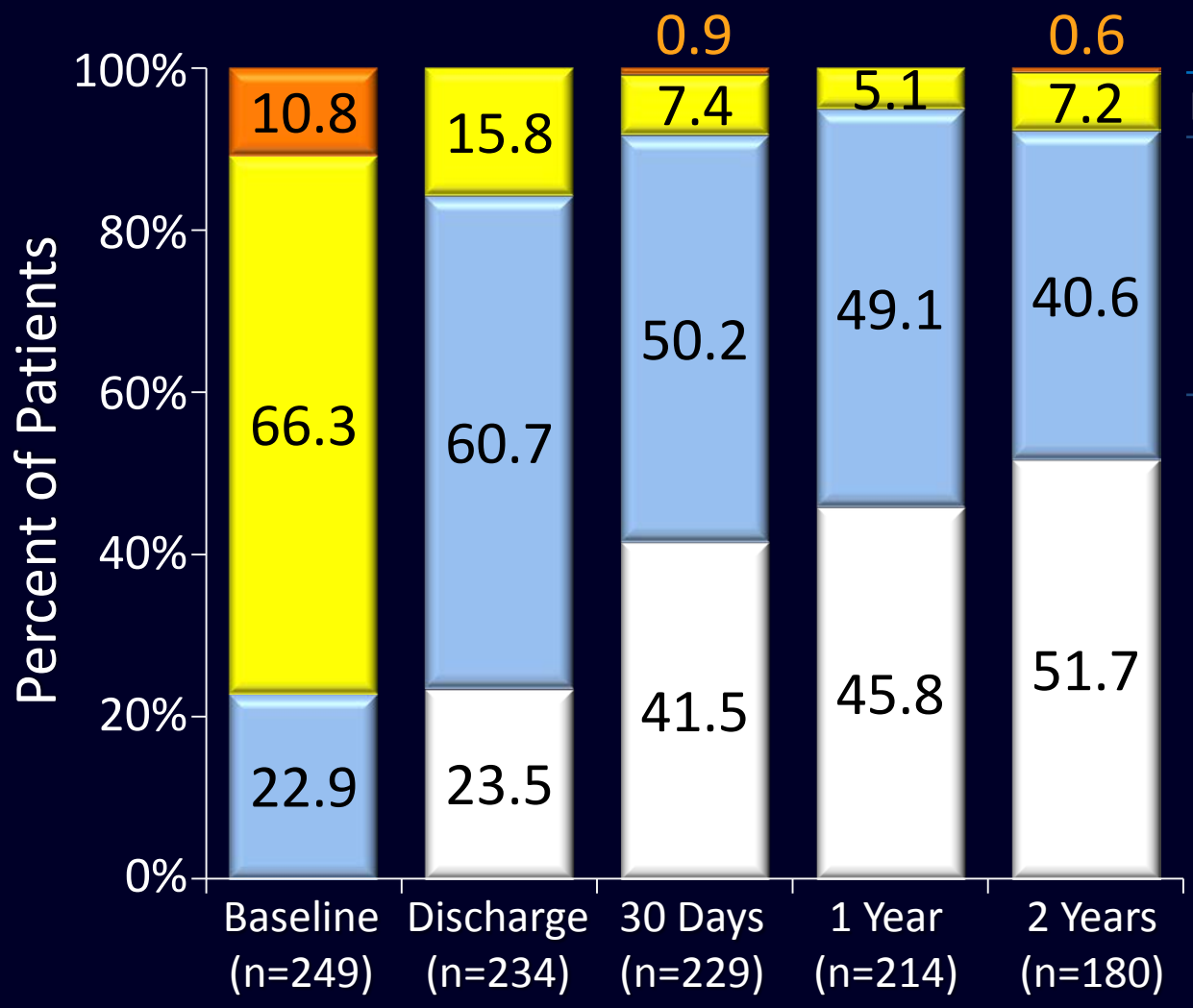
REPRISE II With Extended Cohort (N=249; As Treated)



Kaplan-Meier rates. Individual values may not sum to cumulative values due to rounding.

NYHA Class Changes at 2 Years

REPRISE II with Extended Cohort (N=249; As Treated)



Measurement	*P* value
Baseline to Discharge	<0.001
Baseline to 2 Years	<0.001
Discharge to 30 Days	<0.001
1 Year to 2 Years	0.80

P values calculated from paired Wilcoxon signed-rank test.

Conclusions

REPRISE II with Extended Cohort (N=250)

- At 2 years
  - Continued excellent safety and efficacy
  - Conserved valve haemodynamics
  - No moderate or severe PVL
    - >90% of patients had no/trace PVL
  - Significant and sustained improvement in NYHA functional class
    - >92% of patients NYHA Class I or Class II
  - Adverse event rates consistent with those reported for other valves
- These findings are consistent with those reported for the REPRISE II main cohort at 2 years, and support the use of the Lotus Valve for the treatment of aortic stenosis in high-risk surgical patients.