PCR 2015 london valves

RESPOND

Post-market evaluation of a fully repositionable and retrievable aortic valve in 500 patients treated in routine clinical practice: interim results from the RESPOND study

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on behalf of the RESPOND Investigators

Conflict of Interest 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.

Professor Volkmar Falk, MD

Affiliation/Financial Relationship	Company
• Institutional Grant/Research Support	• Boston Scientific • Phillips • Heartware • Berlin Heart • Biotronik

The RESPOND study is sponsored and funded by Boston Scientific Corporation.

The LOTUS™ Valve

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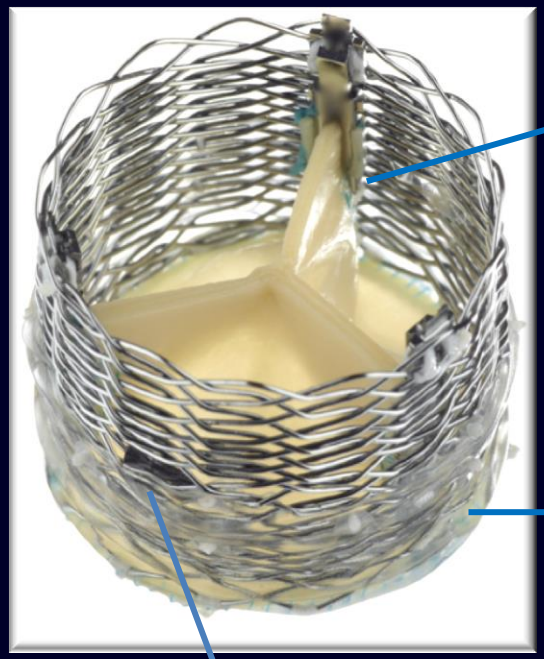

- Controlled mechanical expansion
- Valve functions early in deployment to provide hemodynamic stability
- Valve is fully repositionable & retrievable throughout the entire deployment process
- Adaptive seal conforms to irregular anatomic surfaces to minimise paravalvular leak

Study Design

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DESIGN

- Prospective, single arm, multicentre, observational post market study
- Up to 60 centres in Europe, Asia-Pacific, and South America
- Available valve sizes: 23mm, 25mm, & 27mm (for native annulus sizes ≥20mm to ≤27mm)
- Follow-up at discharge, 30 days, and annually 1–5 years

PATIENTS

- All TAVI patients at each site selected to receive a Lotus Valve were evaluated for enrolment
- No protocol-specific inclusion/exclusion criteria

INDEPENDENT DATA ASSESSMENTS

- Core Lab review of baseline, discharge, & 1-year echo data
- Death and stroke assessed by an Independent Medical Reviewer (IMR)
- 100% monitoring of all VARC-2 safety events

Endpoints

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Primary Endpoint

- All-cause mortality at 30 days and 1 year after the implant procedure
  - Mortality at 30 days will be compared to a performance goal

Secondary Endpoints

- Safety composite of all-cause mortality and disabling stroke at 30 days and 1 year
- In-hospital mortality
- Clinical efficacy composite at 30 days per VARC-2
- Time-related valve safety composite at 1 year per VARC-2
- Grade of paravalvular aortic valve regurgitation pre-discharge
  - Moderate and severe paravalvular aortic valve regurgitation (by echocardiography) will be compared to a performance goal

Enrollment

500 Patients Between May 2014 & June 2015

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	Patients
Sabine Bleiziffer Deutsches Herzzentrum Muenchen Munich, Germany	62
David Hildick-Smith Royal Sussex County Hospital Brighton, United Kingdom	52
Jochen Wöhrle Universitaetsklinikum Ulm Ulm, Germany	52
Nicolas Van Mieghem Erasmus Medical Center Rotterdam, the Netherlands	46
Daniel J. Blackman The General Infirmary Leeds, United Kingdom	38
Mohamed Abdel-Wahab Segeberger Kliniken GmbH Bad Segeberg, Germany	32
Axel Linke Herzzentrum Universitaet Leipzig Leipzig, Germany	30
Ulrich Gerckens Gemeinschaftskrankenhaus Bonn GmbH Bonn, Germany	24
Øyvind Bleie Haukeland University Hospital Bergen, Norway	21

	Patients
Peter Wenaweser University Hospital Bern Bern, Switzerland	18
Mika Laine University of Helsinki Meilahti Hospital Helsinki, Finland	14
Francesco Bedogni Istituto Clinico S, Ambrogio S.p.A. Milan , Italy	14
Karl Eugen Hauptmann Krankenhaus der Barmherzigen Brueder Trier, Germany	13
Nikos Werner University KH Bonn Bonn, Germany	12
Anna Sonia Petronio Azienda Ospedaliero Universitaria Pisana Pisa, Italy	9
Julinda Mehilli Klinkum Grosshadern Siegburg, Germany	8
Saib Khogali New Cross Hospital Wolverhampton, UK	8
Peter Boekstegers Helios Klinikum Siegburg, Germany	8

	Patients
Stephan Kische Vivantes Klinikum im Friedrichshain Berlin, Germany	8
Antonio Colombo Fondazione Centro San Raffaele Milan, Italy	6
Sanjeevan Pasupati Waikato Hospital Waikato, New Zealand	5
Raul Moreno Hospital La Paz Madrid, Spain	5
Jan Kovac Glenfield Hospital Leicester, UK	4
Stephen Brecker St. Georges Hospital London, UK	4
Christoph Nienaber University of Rostock Rostock, Germany	3
Mariano Larman Policlinica Guipuzcoa San Sebastian, Spain	2
Florian Krackhardt Charite Campus Virchow Klinikum Berlin, Germany	2

Study Flow

500-Patient Interim Analysis

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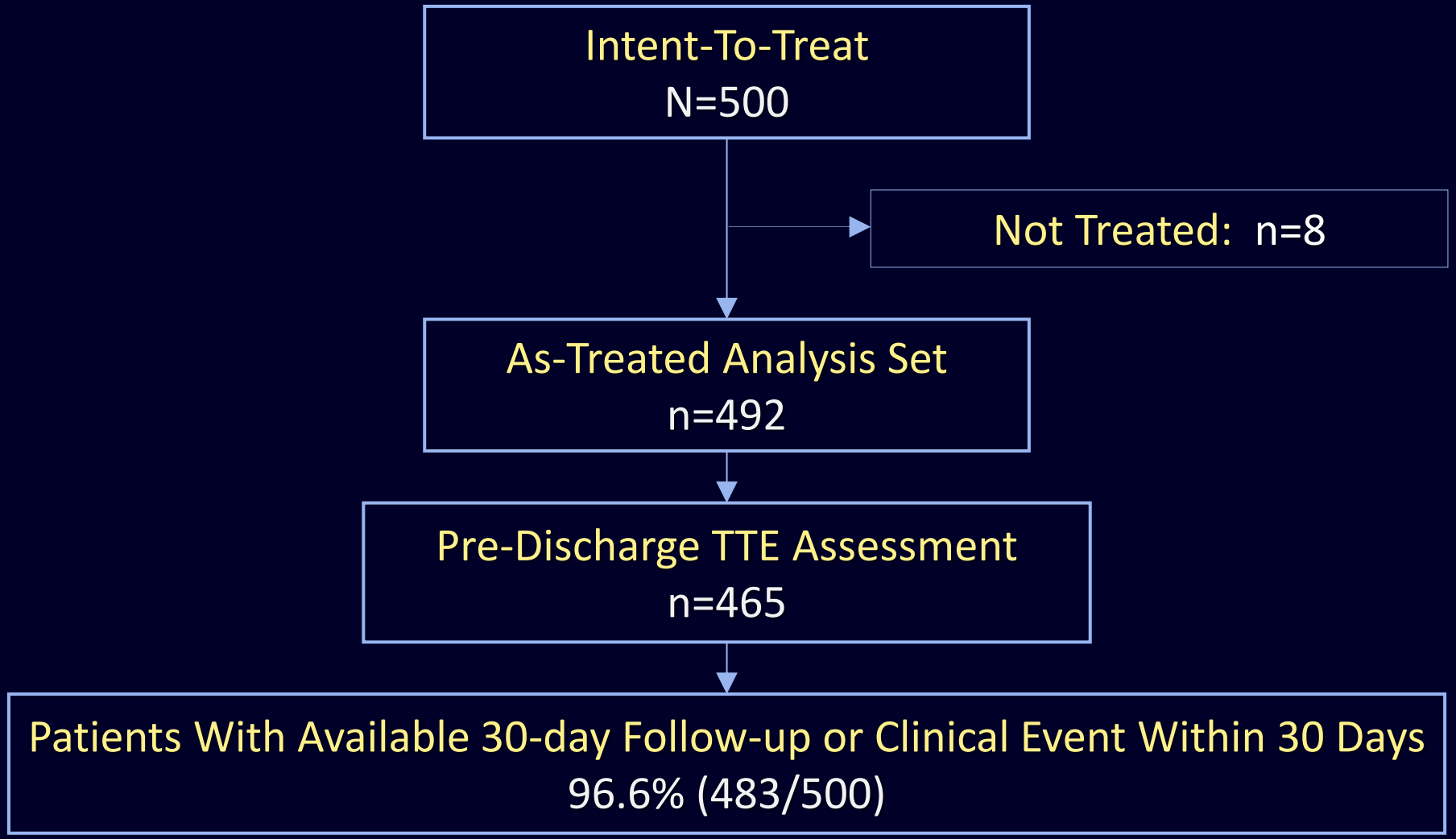

Baseline Characteristics

500-Patient Interim Analysis

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Comorbidities & Baseline Scores

Age (Years)	80.7 ± 6.6 (492)	NYHA Class III or IV	65.2% (321/492)
Gender (Female)	51.2% (252/492)	EuroSCORE 2011 (%)	8.9 ± 9.1 (457)
Diabetes, treated	23.1% (113/490)	STS Score (%)	6.7 ± 8.2 (414)
Baseline PPM	13.0% (64/492)	Katz Index (frail if <6)	5.7 ± 0.8 (256)

Echocardiographic Measurements (Core Lab Assessment)

AVA (cm^2)	0.7 ± 0.2 (446)	LVEF (%)	50.2 ± 10.4 (373)
MR (mod/severe)	11.2% (53/473)	Mean gradient (mmHg)	38.2 ± 16.1 (463)
AR (mod/severe)	7.8% (37/473)	Peak gradient (mmHg)	62.0 ± 24.9 (463)

Indications for TAVI (Site-Reported)

Native valve aortic stenosis	99.0% (487/492)
Tricuspid aortic valve stenosis	95.5% (470/492)
Bicuspid aortic valve stenosis	3.5% (17/492)
Low flow/low gradient	3.5% (17/492)
Lotus in failing prosthetic valve	0.8% (4/492)

Procedural Characteristics

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	As-Treated (N=492)
Valve size implanted	
23mm	26.2% (129/492)
25mm	40.0% (197/492)
27mm	33.5% (165/492)
Vascular Access Site	
Transfemoral	97.4% (479/492)
Subclavian	1.2% (6/492)
Transaortic	1.4% (7/492)
No balloon valvuloplasty performed	41.4% (197/476)
Conversion to open heart surgery	0% (0/492)
Unplanned use of cardiopulmonary bypass	0% (0/492)

Device Success – VARC 2 Metrics

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	As-Treated (N=492)
No procedural mortality	100% (492/492)
Correct positioning of one valve in proper location	99.6% (490/492)
Mean aortic valve gradient <20 mmHg	97.2% (446/459)
Peak velocity <3 m/s	96.9% (445/459)
No moderate/severe prosthetic valve regurgitation	99.6% (463/465)

Primary & Key Secondary Endpoints

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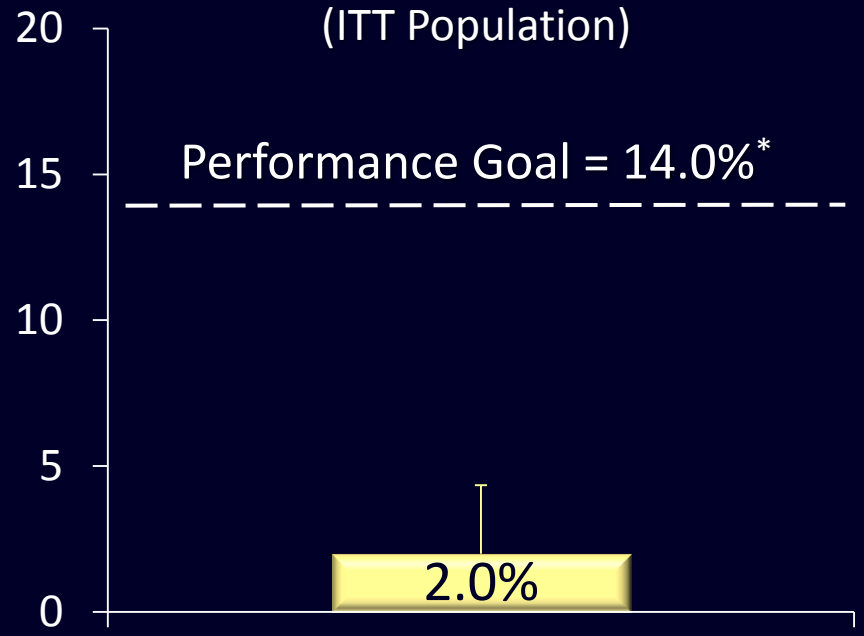
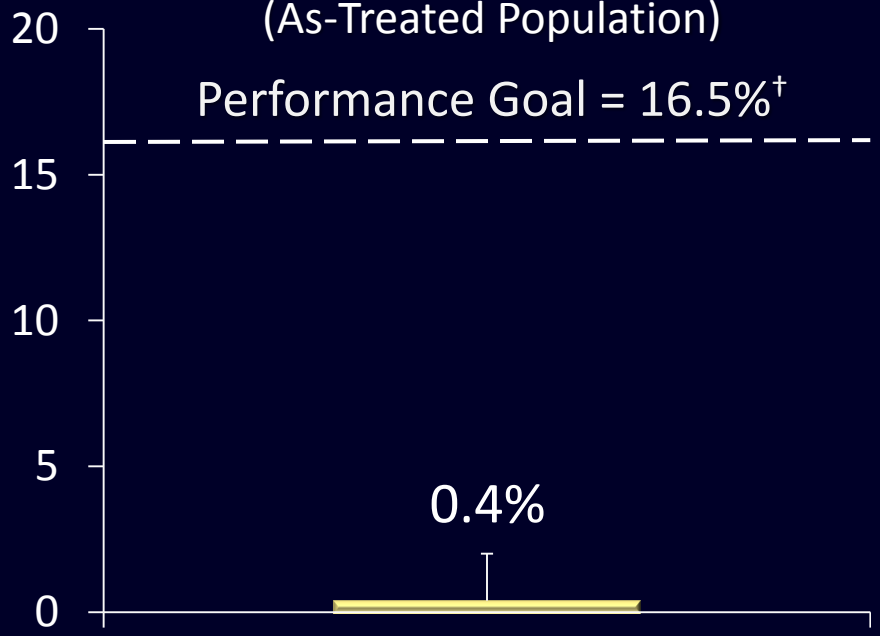
500-Patient Interim Analysis

All-Cause Mortality at 30 Days (ITT Population)



2.0% ± UCB (4.36%) is significantly below the performance goal (P<0.001)

Moderate/Severe Paravalvular Regurgitation at Hospital Discharge (As-Treated Population)



0.4% ± UCB (2.01%) is significantly below the performance goal (P<0.001)

* Based on an expected rate of 10% (based on literature review) plus a test margin of 4%. Intent-to-treat population.

† Based on an expected rate of 16.5% from the FRANCE 2 registry

P values are from the one-sample z test.

Safety Endpoints – Periprocedural

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Major vascular complications	1.6% (8/492)
Periprocedural myocardial infarction	0.2% (1/492)
Coronary obstruction	0.2% (1/492)
Cardiac tamponade	0.4% (2/492)
Valve migration	0% (0/492)
Valve embolisation	0.2% (1/492)
Ectopic valve deployment	0.2% (1/492)
TAV-in-TAV deployment	0.2% (1/492)
Mitral apparatus damage	0.2% (1/492)
Ventricular septal perforation	0% (0/492)

As-treated population.

Safety Endpoints at 30 Days

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All-cause mortality	1.9% (9/483)
Cardiovascular mortality	1.7% (8/483)
All stroke	3.9% (19/483)
Disabling stroke	2.7% (13/483)
Life-threatening or disabling bleeding	1.7% (8/483)
Myocardial infarction (>72h post-procedure)	0.2% (1/483)
Acute kidney injury (Stage 2 or 3)	1.7% (8/483)
Repeat procedure for valve-related dysfunction	0% (0/483)
Valve- or CHF-related repeat hospitalisation	0.8% (4/483)
Newly implanted permanent pacemaker	30.6% (148/483)
Pacemaker dependent at 30 days (site-reported)	36.5% (54/148)

As-treated population.

Principal Safety Results by 1st or 2nd 250 Pts

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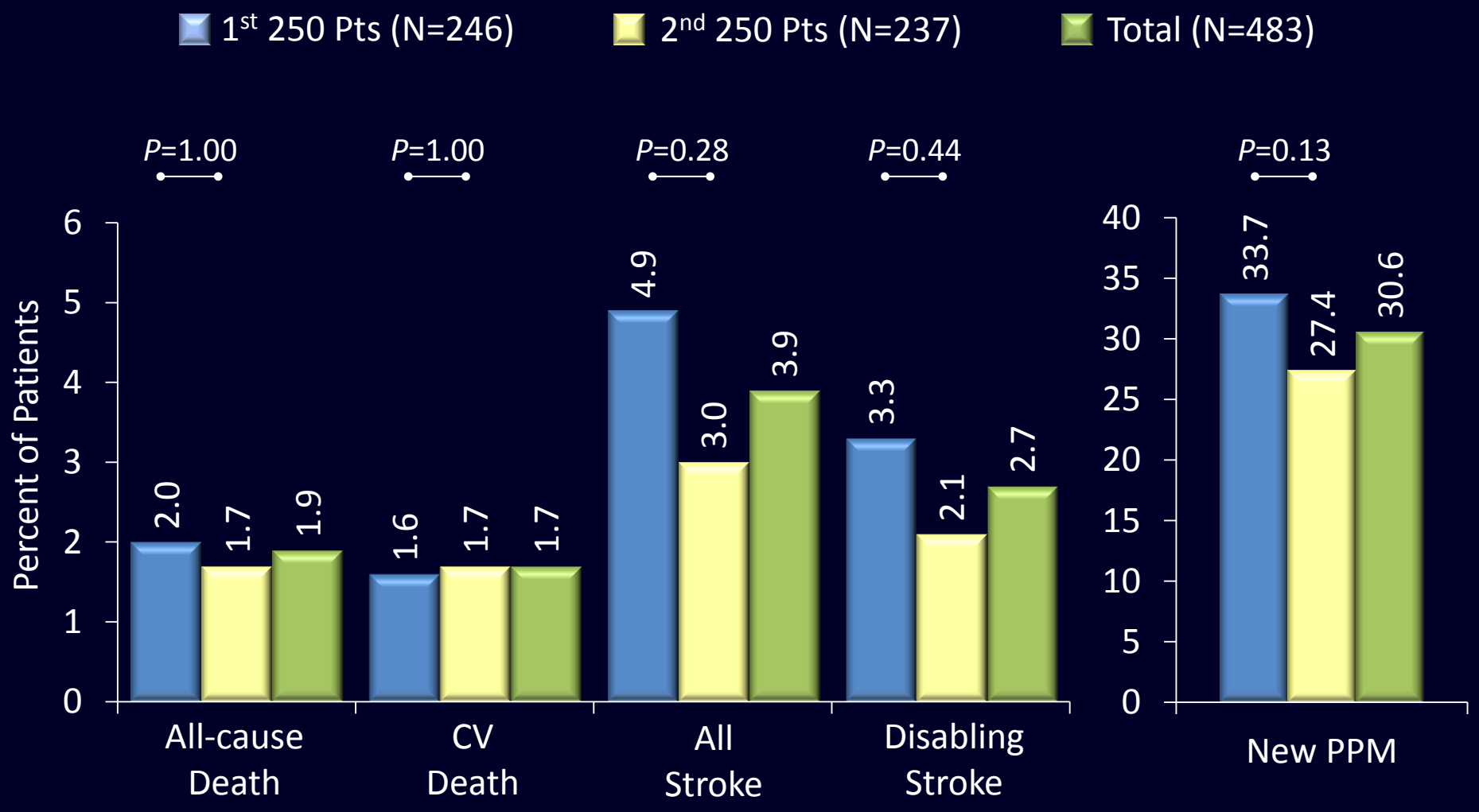

As-treated population

Mean Aortic Gradient & EOA

500-Patient Interim Analysis
Core-Lab Adjudicated Data

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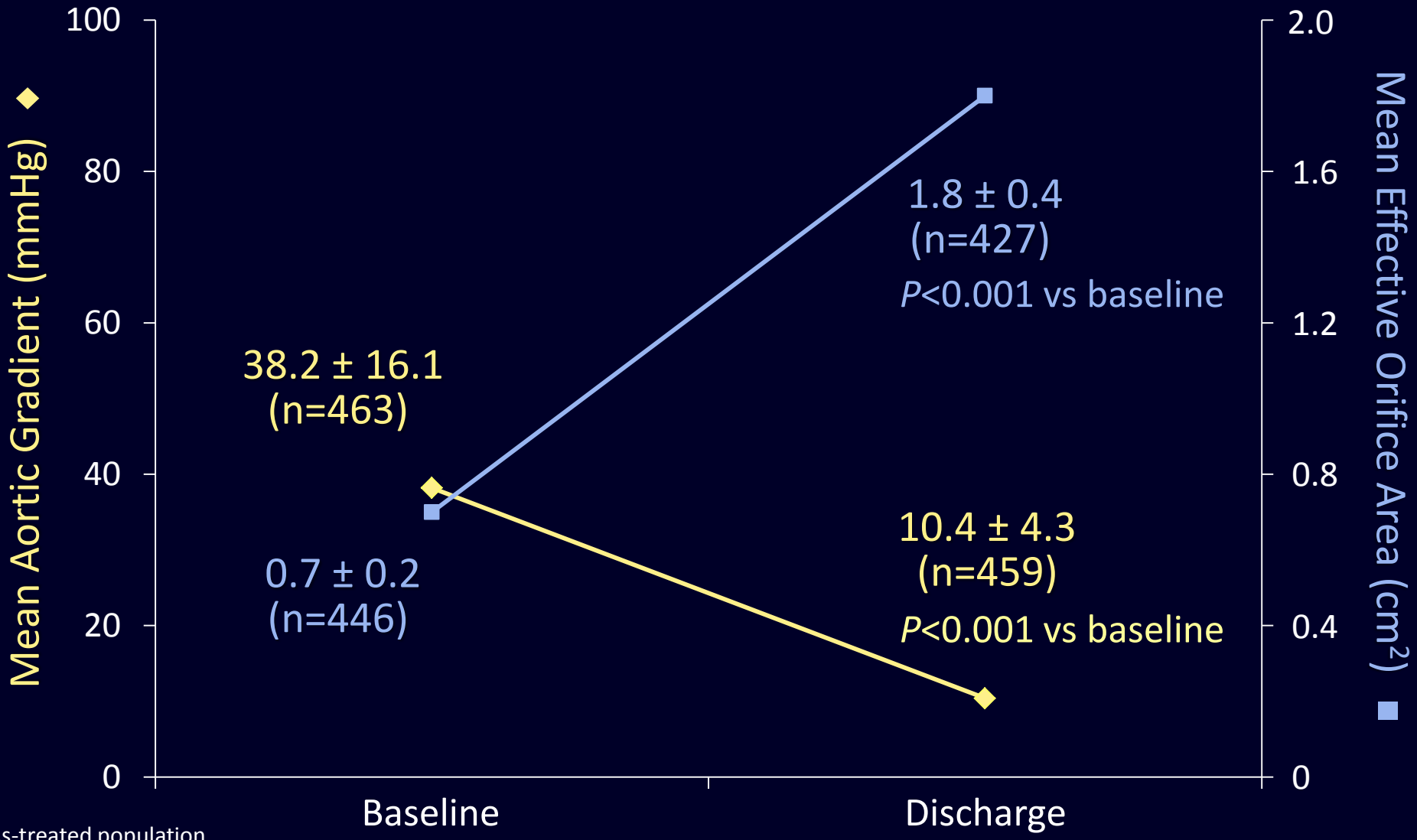

As-treated population

Paravalvular Aortic Regurgitation

500-Patient Interim Analysis

Core-Lab Adjudicated Data

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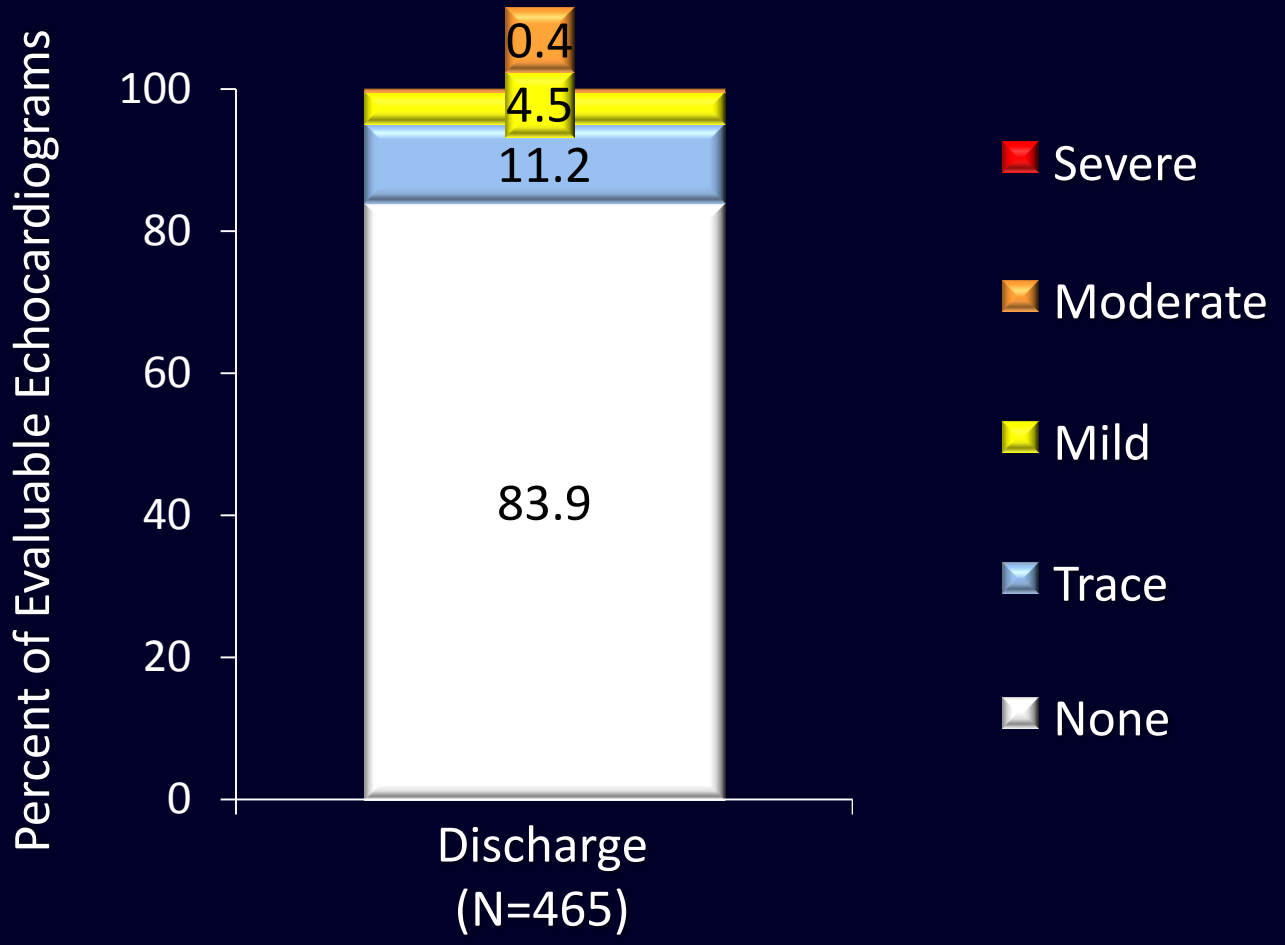

As-treated population

NYHA Functional Class & Quality of Life

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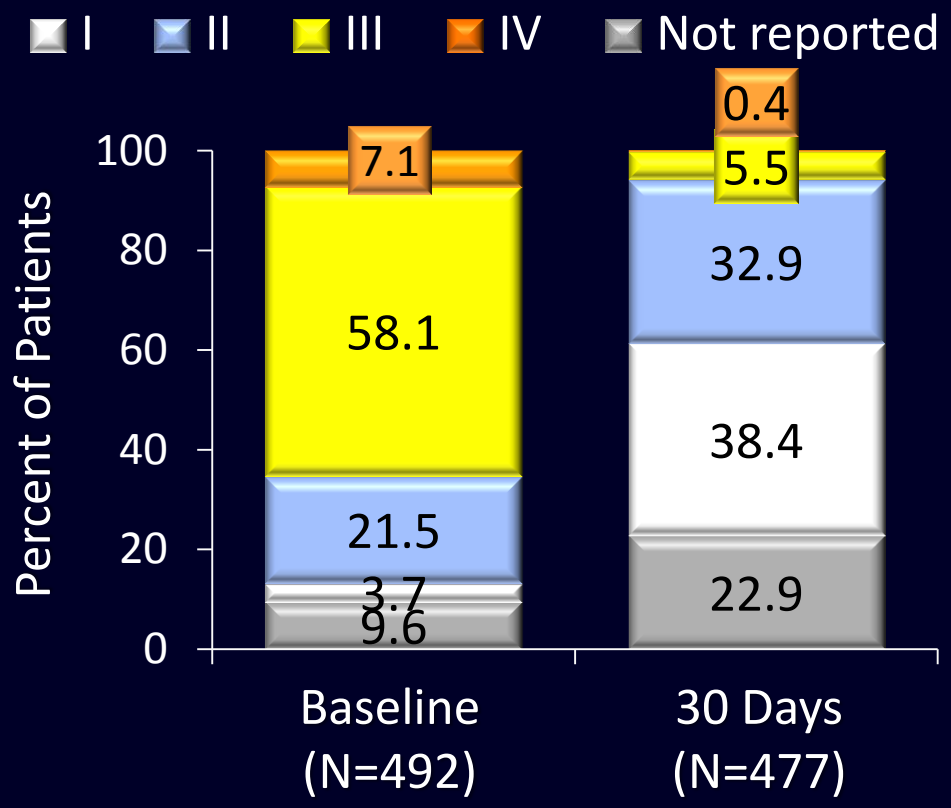
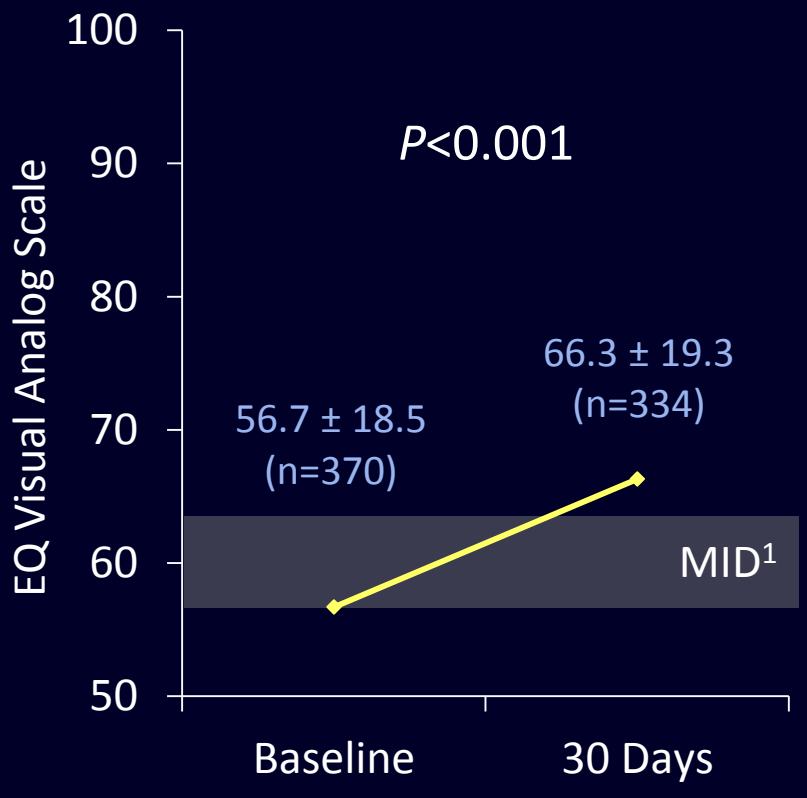
NYHA Class



P value vs baseline	<0.001
Improved at least 1 class	80.2%
Improved at least 2 classes	34.4%

EQ-5D Visual Analog Scale



MID = Minimally Important Difference (clinically meaningful change)

[1]Pickard AS, Neary MP, Cella D. *Health Qual Life Outcomes.* 2007, 5:70

As-treated population

Conclusions

500-Patient Interim Analysis

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- Outcomes at 30 days with the Lotus Valve as reported in prior clinical studies of selected patients are reproducible in routine clinical practice
  - 30-day mortality in patients who received a Lotus Valve was 1.9% in a real-world, elderly population with baseline STS Score of 6.7
  - 30-day disabling stroke was 2.7%
  - Minimal paravalvular regurgitation at hospital discharge by independent core lab adjudication
    - No patients with severe PVL and 0.4% moderate PVL
  - New permanent pacemaker rate in the second 250 cohort of enrolled patients was 27.4%, for an overall rate of 30.6% at 30 days
- Primary endpoint data from the full population of 1,000 patients anticipated to be available in 2016