Clinical and Echocardiographic Outcomes at 30 Days with the SAPIEN 3 TAVR System in Inoperable, High-Risk and Intermediate-Risk AS Patients

Susheel Kodali, MD
on behalf of The PARTNER Trial Investigators

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Disclosure Statement of Financial Interest

Susheel Kodali, MD

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	• Edwards Lifesciences, Medtronic, Boston Scientific, Claret Medical
• Steering Committee	• Edwards Lifesciences, Claret Medical, Meril
• SAB (Equity)	• Thubrikar Aortic Valve, Inc
• Honoraria	• St. Jude Medical, Claret Medical

Background

THE PARTNER II TRIAL

- Based on randomized trials with first generation devices, transcatheter aortic valve replacement (TAVR) has been incorporated into the treatment strategy for high-risk and inoperable patients with severe AS.
- Procedural complications remain a concern with TAVR, including stroke, vascular complications, paravalvular leak (PVL) and conduction disturbances.
- Addressing these limitations will support TAVR use in lower risk populations.

Evolution of the Edwards Balloon-Expandable Transcatheter Valves

THE PARTNER II TRIAL

Cribier-Edwards

2002

SAPIEN

2006

SAPIEN XT

2009

SAPIEN 3

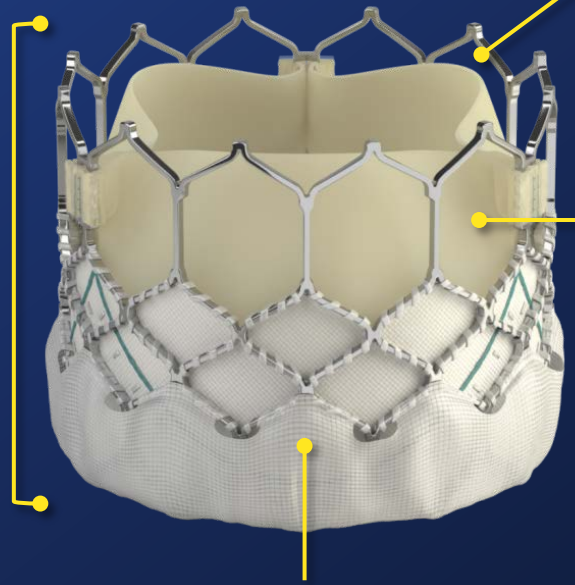
2013

** Sheath compatibility for a 23 mm valve*

SAPIEN 3 Transcatheter Heart Valve

Distinguishing Features

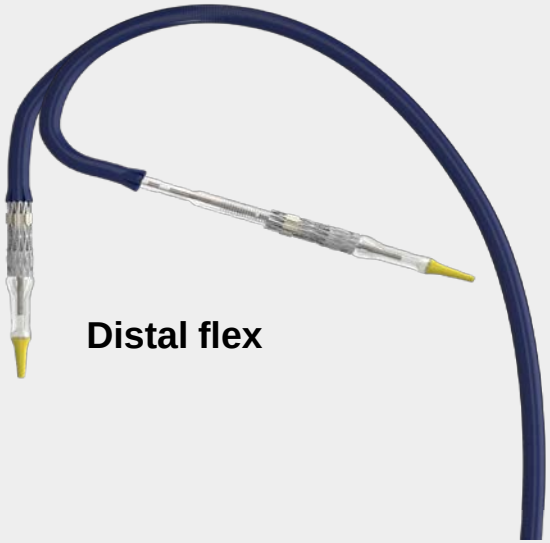
THE PARTNER II TRIAL



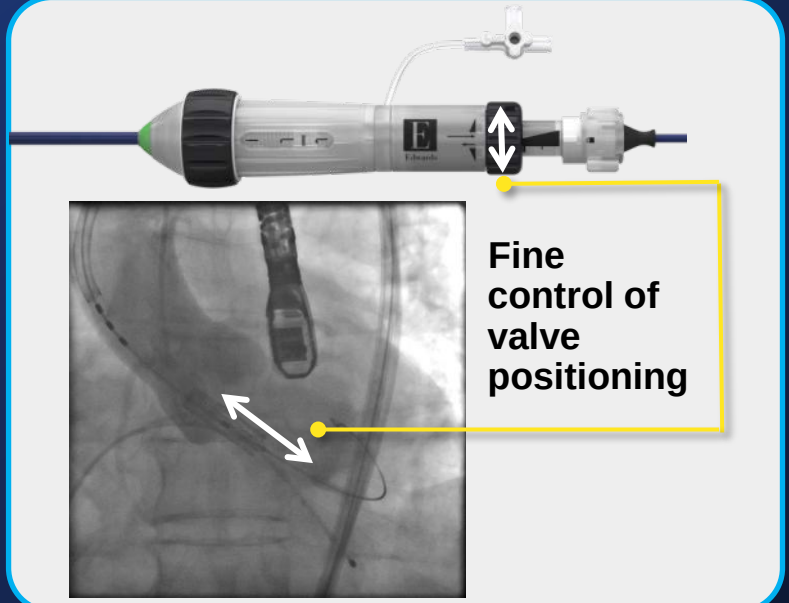
SAPIEN 3 Commander Delivery System
Distinguishing Features

THE PARTNER II TRIAL

- Improved coaxial alignment



- Accurate positioning



SAPIEN 3 Valve Size	20 mm	23 mm	26 mm	29 mm
Expandable Sheath	14F	14F	14F	16F
Minimum Access Vessel Diameter	5.5 mm	5.5 mm	5.5 mm	6.0 mm

The PARTNER II S3 Trial

Purpose

To evaluate the safety and efficacy of the SAPIEN 3 transcatheter heart valve system at 30 days in inoperable, high-risk, and intermediate-risk patients.

The PARTNER II S3 Trial

Study Design

THE PARTNER II TRIAL

Symptomatic Severe Aortic Stenosis

ASSESSMENT by Heart Valve Team

SAPIEN 3

2 Single Arm Non-Randomized Historical-Controlled Studies

- **PII A SAVR**
- **PI A SAPIEN**

Intermediate Risk Operable (PII S3i)

n = 1076 Patients

- **ASSESSMENT: Optimal Valve Delivery Access**
  - **Transfemoral (TF)** → **TF TAVR SAPIEN 3**
  - **Transapical / Transaortic (TA/TAo)** → **TAA TAVR SAPIEN 3**

High Risk Operable / Inoperable (PII S3HR)

n = 583 Patients

- **ASSESSMENT: Optimal Valve Delivery Access**
  - **Transfemoral (TF)** → **TF TAVR SAPIEN 3**
  - **Transapical / Transaortic (TA/TAo)** → **TAA TAVR SAPIEN**

Key Inclusion Criteria

THE PARTNER II TRIAL

- Risk determined by STS score and heart team:
  - **High Risk / Inoperable (S3HR):** STS score > 8 or heart team determination
  - **Intermediate Risk (S3i):** STS score between 4 and 8 or heart team determination
- Severe aortic stenosis determined by echocardiography:
  - Valve area < 0.8 cm^2 or Valve area index < 0.5 cm^2/m^2 ***and*** mean gradient > 40mmHg or peak velocity > 4 m/s

Key Exclusion Criteria

THE PARTNER II TRIAL

- MI within one month
- Bicuspid aortic valve
- Severe aortic regurgitation
- Prior prosthetic valve in any position
- Untreated significant CAD (S3HR only)
- LVEF < 20%
- Stroke or TIA within 6 months
- Upper GI bleed within 3 months
- Creatinine > 3.0 or dialysis
- Estimated life expectancy < 24 months

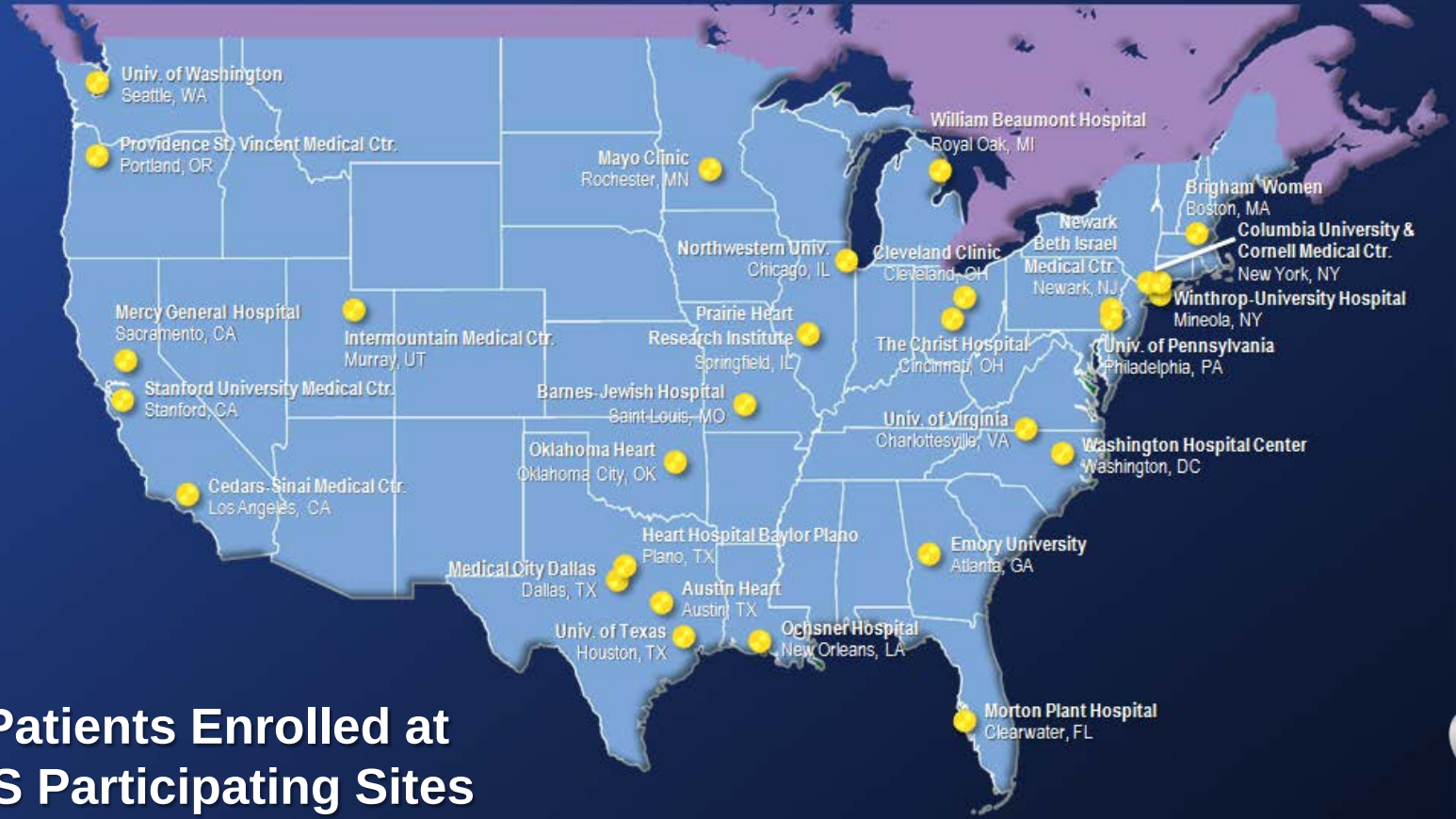
Study Methodology

THE PARTNER II TRIAL

- All patients presented on a screening call for approval prior to implant.
- 3D imaging of annulus (CT or 3D TEE) recommended for S3HR and required for majority of S3i with core lab analysis prior to implant.
- All patients evaluated by a neurologist at baseline and at follow-up time points.
- **Primary Analysis:** As treated patients
- S3HR and S3i combined for echocardiographic analyses (valve implant patients).

The PARTNER II S3 Trial: S3HR

Participating Sites



583 Patients Enrolled at
29 US Participating Sites

The PARTNER II S3 Trial: S3i
Participating Sites

1076 Patients Enrolled at
51 US Participating Sites

The PARTNER II S3 Trial: S3HR & S3i

Top 10 Enrollment Sites

THE PARTNER II TRIAL

S3HR

Cedars-Sinai Medical Ctr. Los Angeles, CA	73
Columbia University Medical Ctr. New York, NY	65
Emory University Atlanta, GA	63
University of Pennsylvania Philadelphia, PA	43
Heart Hospital Baylor Plano Plano, TX	30
Ochsner Hospital New Orleans, LA	26
University of Texas, Houston Houston, TX	25
Stanford University Medical Ctr. Stanford, CA	24
Newark Beth Israel Medical Ctr. Newark, NJ	21
Washington Hospital Ctr. Washington, DC	19

S3i

Cedars-Sinai Medical Ctr. Los Angeles, CA	106
University of Pennsylvania Philadelphia, PA	66
Emory University Atlanta, GA	62
University of Texas, Houston Houston, TX	52
Columbia University Medical Ctr. New York, NY	48
Heart Hospital Baylor Plano Plano, TX	46
Cleveland Clinic Foundation Cleveland, OH	41
Newark Beth Israel Medical Ctr. Newark, NJ	38
The Christ Hospital Cincinnati, OH	38
Mayo Clinic Rochester, MN	35

Study Administration

THE PARTNER II TRIAL

Co-Principal Investigators

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S. Chris Malaisrie
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Study Flow: S3HR & S3i

30 Day Patient Status

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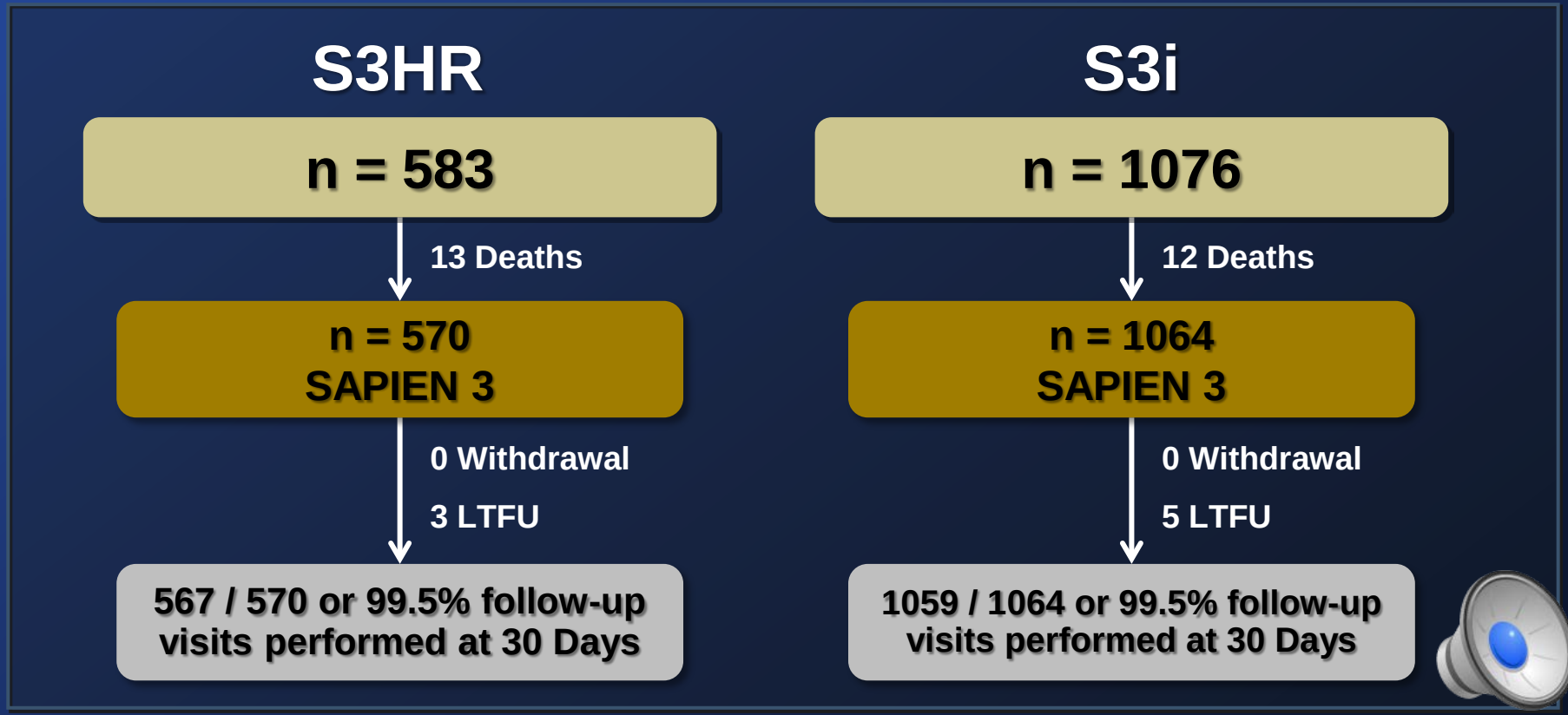

Baseline Patient Characteristics

S3HR Patients

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N = 583

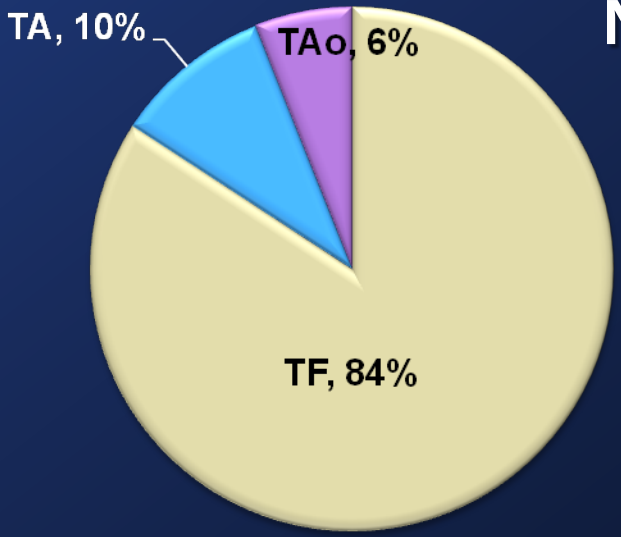
Average STS =

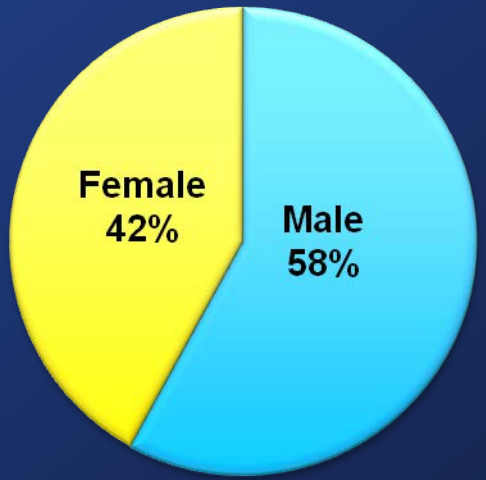
8.6%

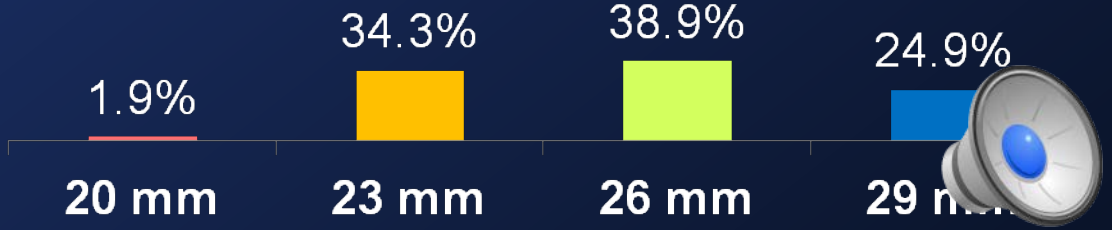
(Median 8.4%)

Average Age =

82.6yrs







Baseline Patient Characteristics

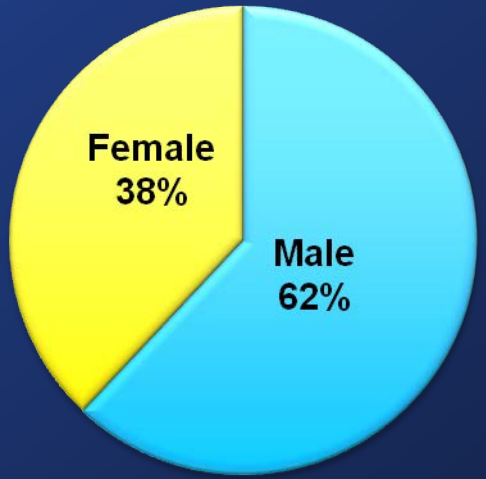
S3i Patients

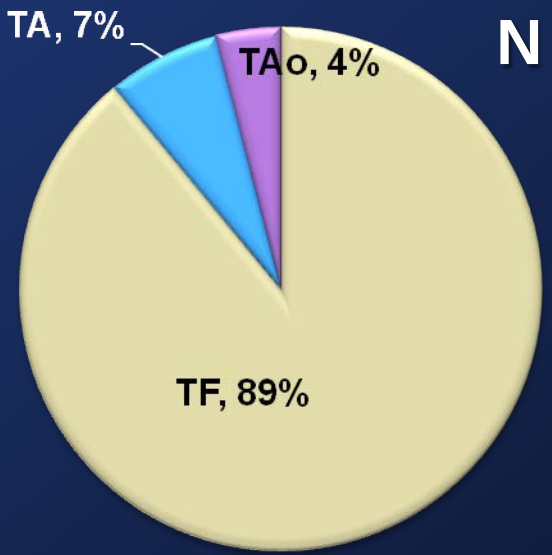
THE PARTNER II TRIAL

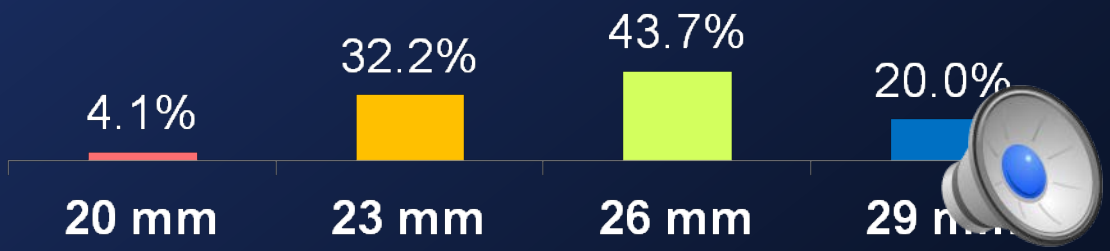
Average STS = **5.3%** (Median 5.2%)

Average Age = **81.9yrs**

N = 1076







Baseline Patient Characteristics
Demographics

THE PARTNER II TRIAL

Characteristic (%)	S3HR (n=583)	S3i (n=1076)
NYHA Class III or IV	90.1	72.6
Previous CABG	33.1	28.0
Previous CVA	11.0	8.9
Peripheral Vascular Disease	35.2	28.3
Diabetes	34.5	34.1
COPD - O_2 Dependent	11.7	5.0
CKD - Creat. ≥ 2mg/dL	12.0	7.5
Atrial Fibrillation	43.7	36.0
Permanent Pacemaker	16.3	13.2
Frailty	30.9	8.6

Baseline Echocardiography

THE PARTNER II TRIAL

Characteristic	S3HR (n=583)	S3i (n=1076)
AV Area - cm^2 (mean ± SD)	0.67 ± 0.18	0.70 ± 0.17
Annulus Diam. - cm (mean ± SD)	2.2 ± 0.2	2.2 ± 0.2
AV Gradient - mmHg (mean ± SD)	45.5 ± 14.3	46.3 ± 12.7
LV Ejection Fraction (%)	56.4 ± 14.8	58.6 ± 13.3
Mod-Severe MR (%)	3.0	2.3

Procedural Factors

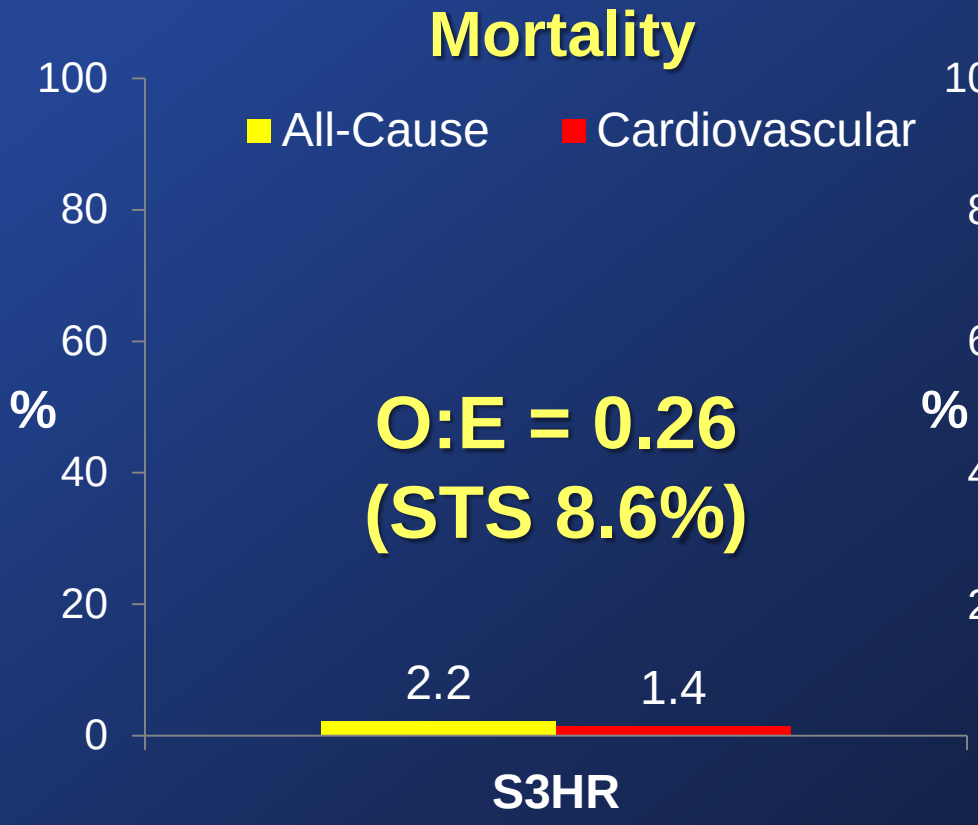
THE PARTNER II TRIAL

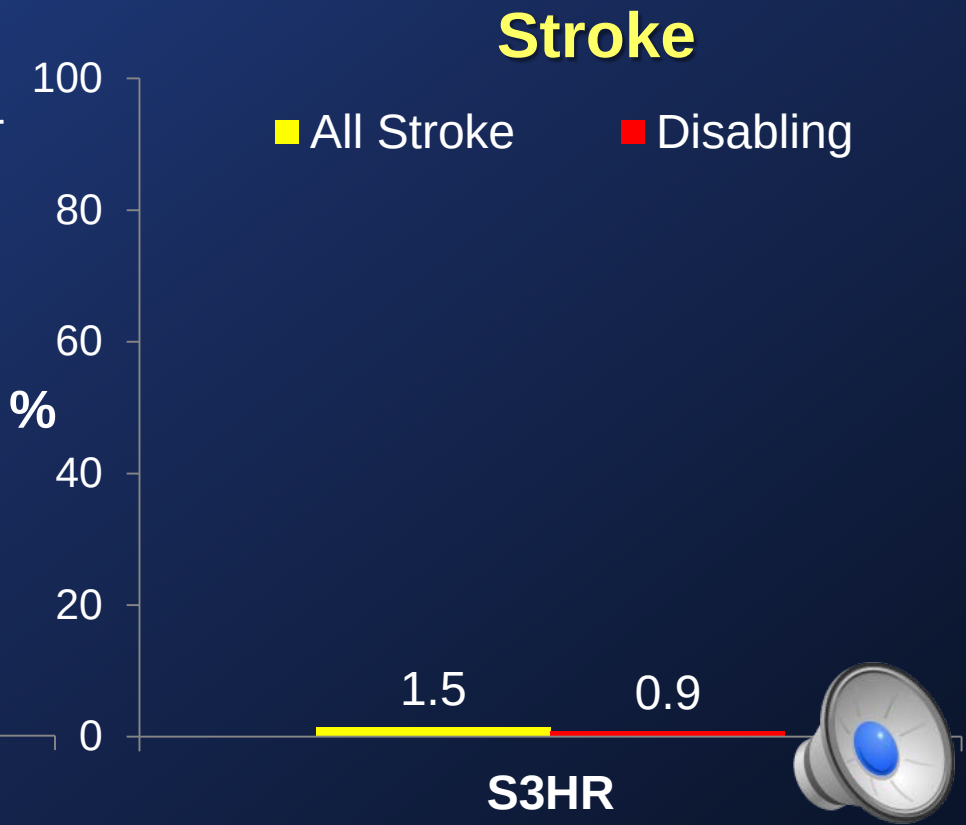
	S3HR (n=583)	S3i (n=1076)
Post-Dilatation (%)	14.8	11.3
>1 Valve Implanted (%)	0.9	0.4
Valve Embolization (%)	0.2	0.1
IABP During Procedure (%)	0.5	0.4
Cardiopulmonary Bypass (%)	1.2	0.6
Conscious Sedation (%)	13	17
Median LOS – Days (Min, Max)	5 (1, 33)	4 (1, 64)

Mortality and Stroke: S3HR

At 30 Days (As Treated Patients)

THE PARTNER II TRIAL

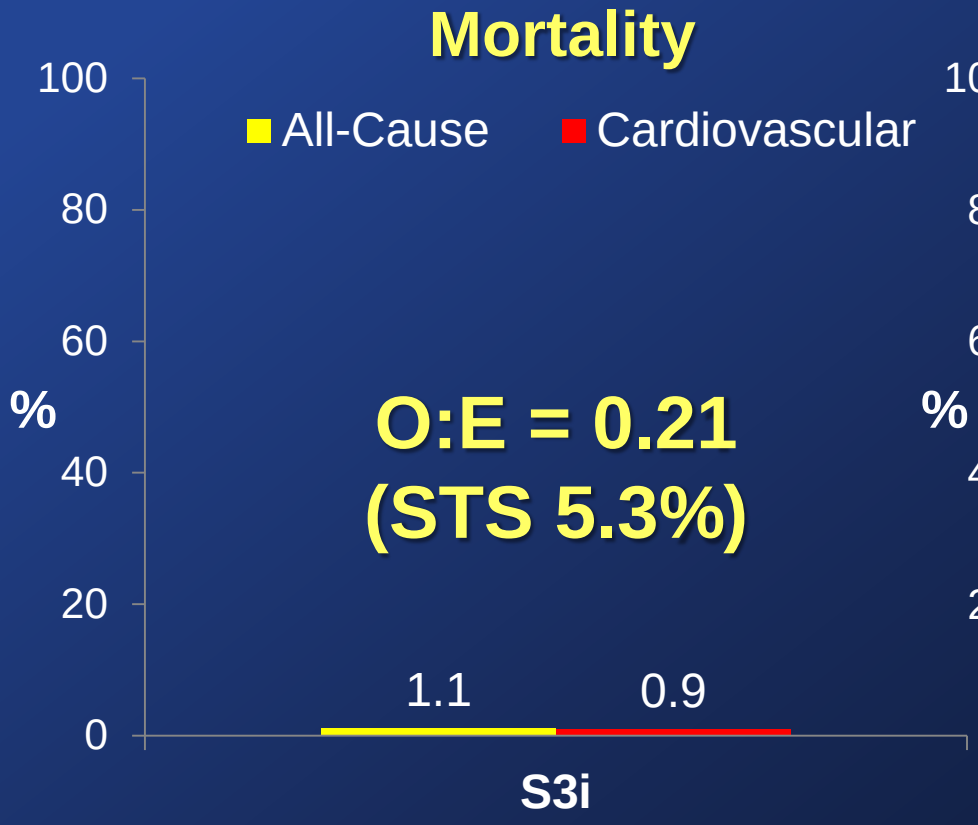




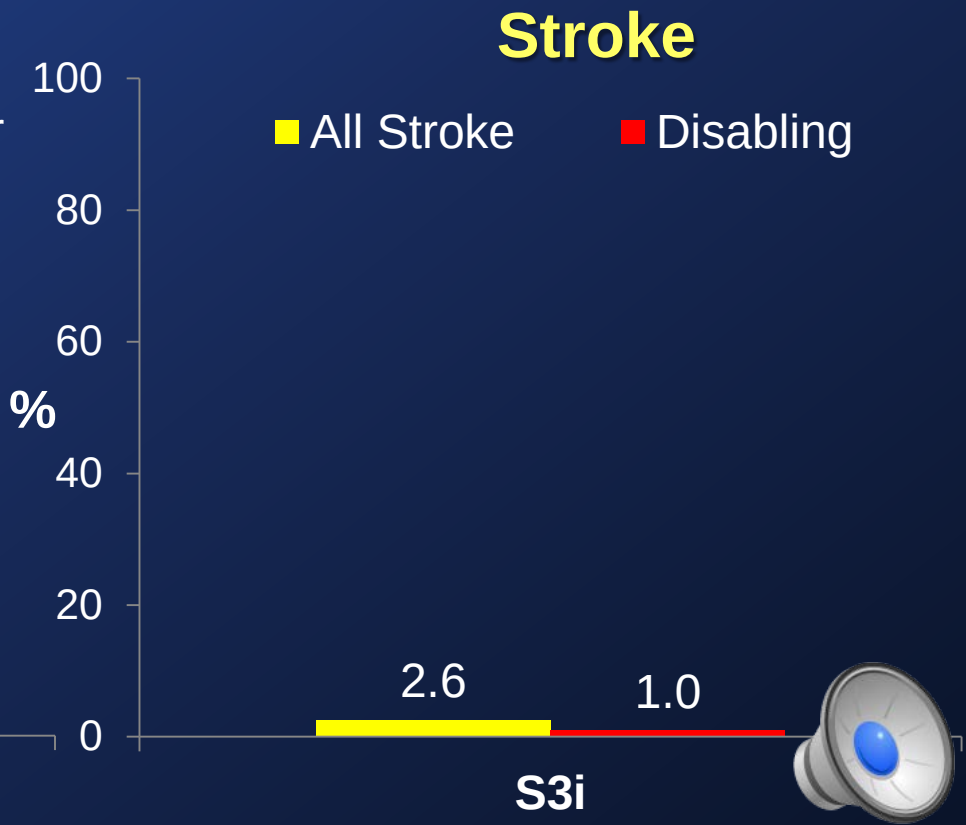
Mortality and Stroke: S3i

At 30 Days (As Treated Patients)

THE PARTNER II TRIAL



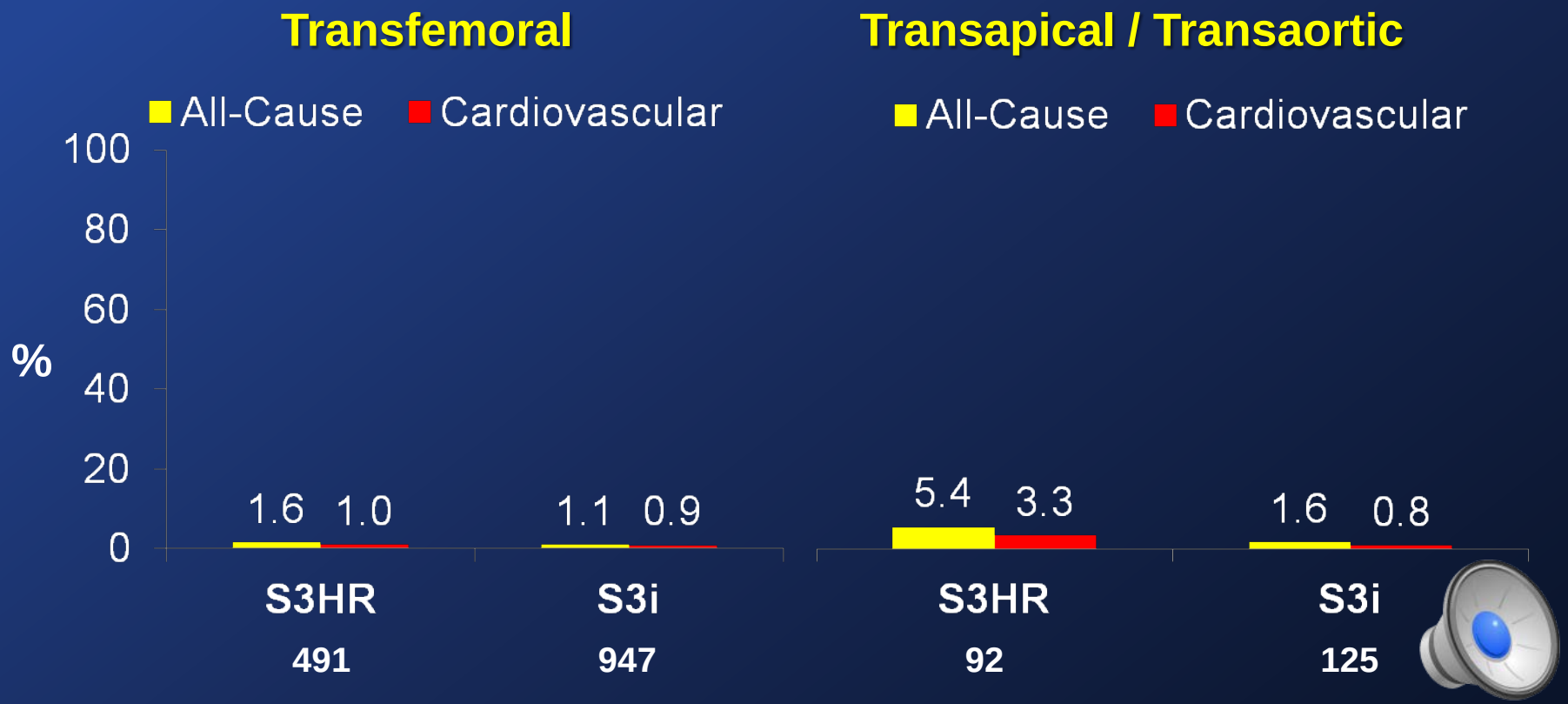
O:E = 0.21
(STS 5.3%)



Mortality: S3HR & S3i

At 30 Days (As Treated Patients)

THE PARTNER II TRIAL



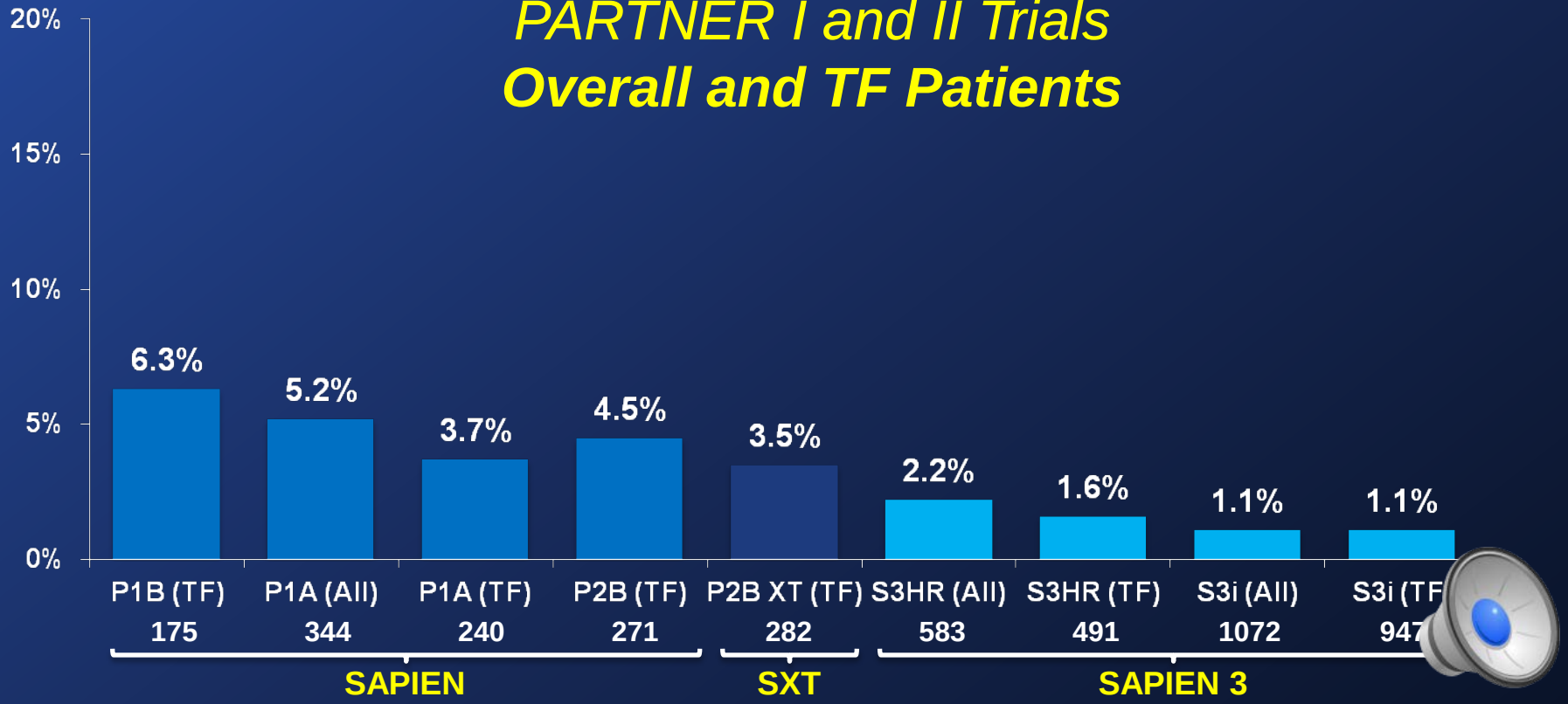
All-Cause Mortality at 30 Days

Edwards SAPIEN Valves (As Treated Patients)

THE PARTNER II TRIAL

PARTNER I and II Trials

Overall and TF Patients



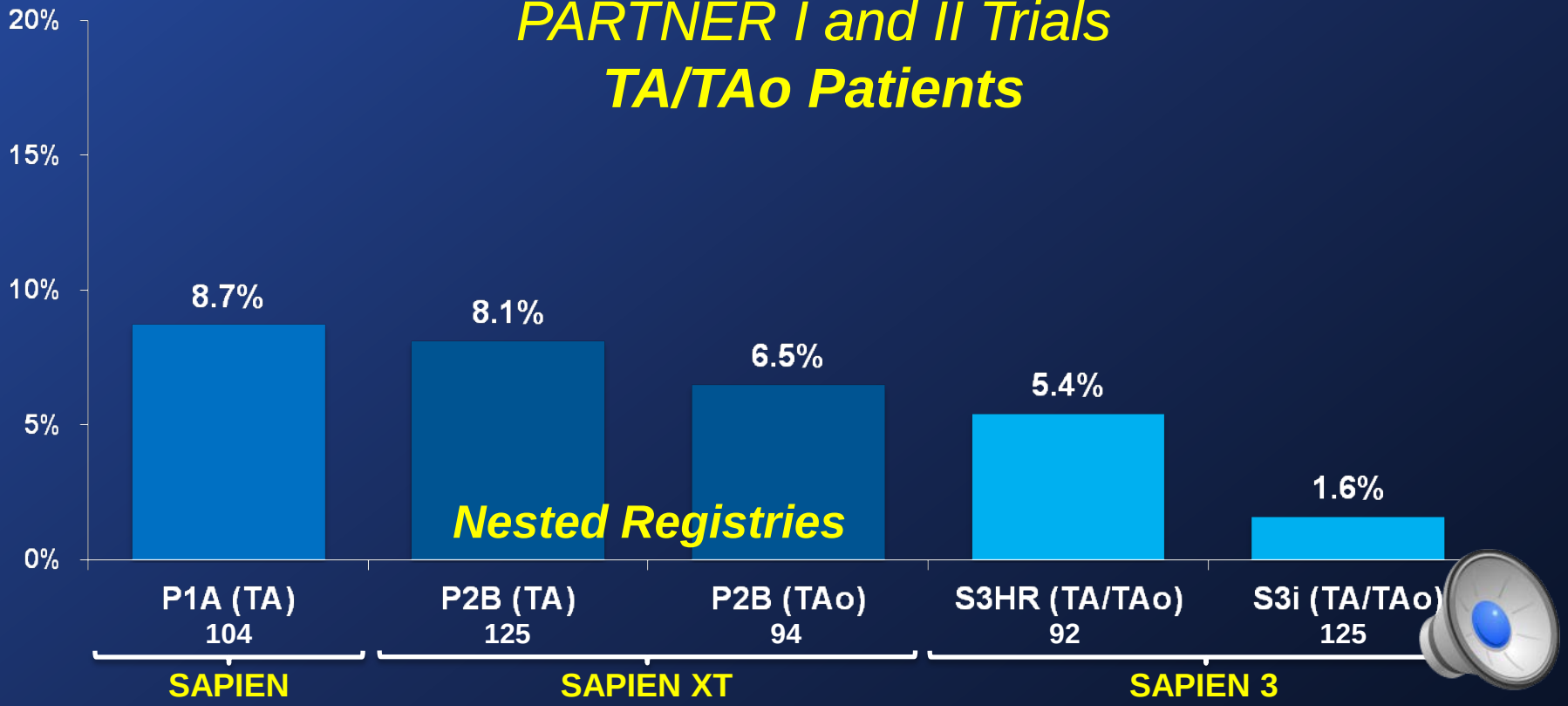
All-Cause Mortality at 30 Days

Edwards SAPIEN Valves (As Treated Patients)

THE PARTNER II TRIAL

PARTNER I and II Trials

TA/TAo Patients



Strokes

At 30 Days (As Treated Patients)

THE PARTNER II TRIAL

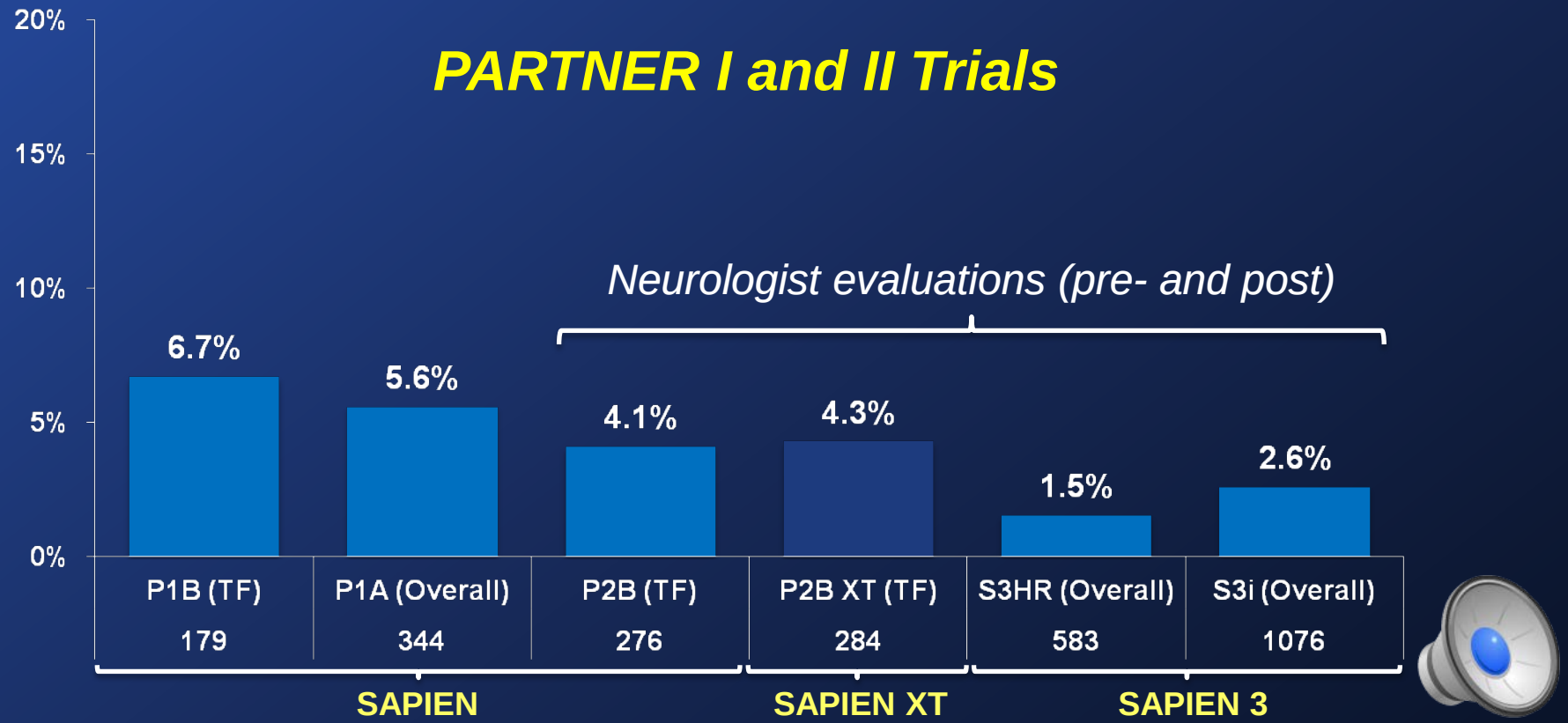
Events (%)	S3HR Overall (n=583)	S3HR TF (n=491)	S3HR TA/TAo (n=92)	S3i Overall (n=1076)	S3i TF (n=951)	S3i TA/TAo (n=125)
All	1.54	1.63	1.09	2.60	2.42	4.00
Disabling*	0.86	0.81	1.09	1.02	0.95	1.60
Non-Disabling	0.69	0.81	0	1.58	1.47	2.40
TIA	0.69	0.61	1.09	0.37	0.42	0

**CEC adjudicated or Modified Rankin Score ≥ 2 at 30 days*

All Strokes at 30 Days

Edwards SAPIEN Valves

THE PARTNER II TRIAL



Other Clinical Events

At 30 Days (As Treated Patients)

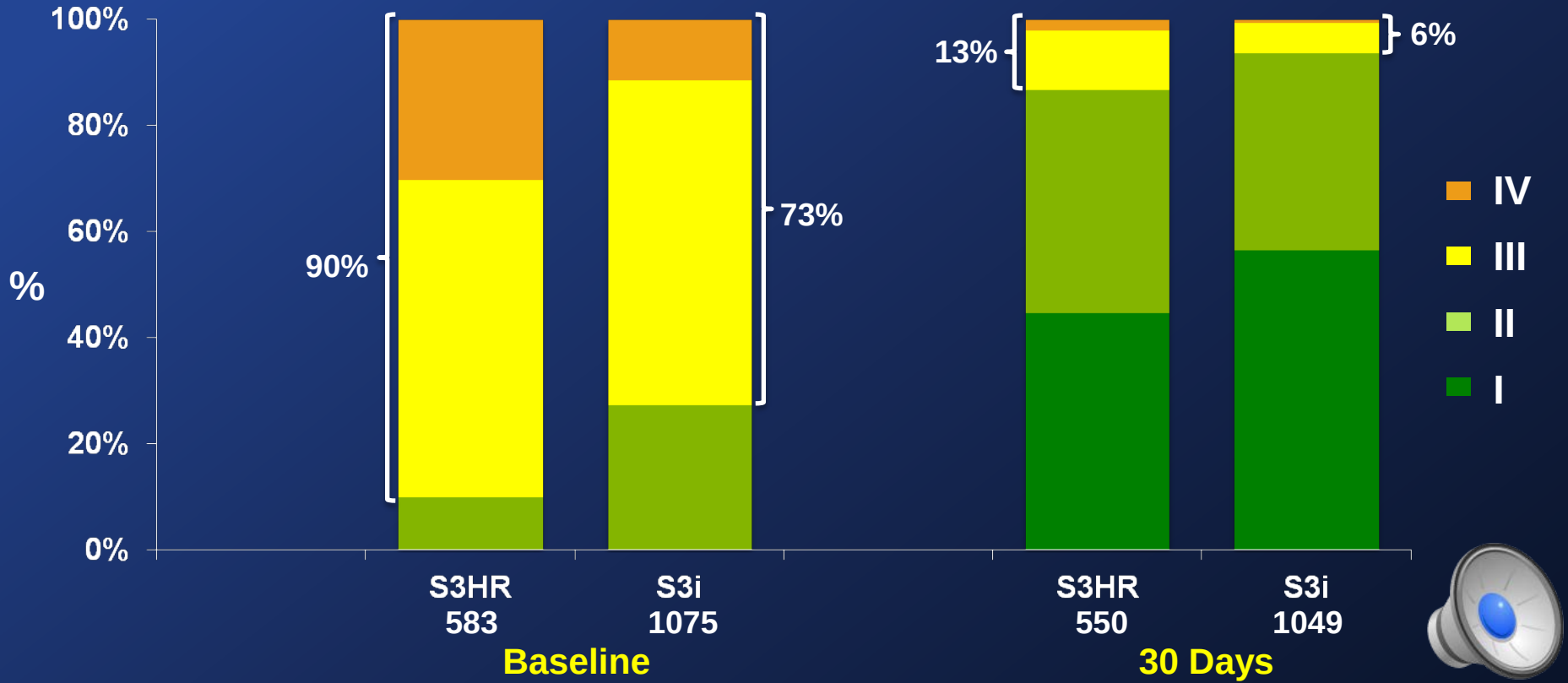
THE PARTNER II TRIAL

Events (%)	S3HR Overall (n=583)	S3HR TF (n=491)	S3HR TA/TAo (n=92)	S3i Overall (n=1076)	S3i TF (n=951)	S3i TA/TAo (n=125)
Major Vascular Comps.	5.0	5.3	3.3	5.6	5.9	3.2
Bleeding - Life Threatening	6.3	5.5	10.9	5.4	4.4	12.9
Annular Rupture	0.3	0.2	1.1	0.2	0.2	0
Myocardial Infarctions	0.5	0.4	1.1	0.3	0.3	0
Coronary Obstruction	0.2	0	1.1	0.4	0.4	0
Acute Kidney Injury	1.0	0.8	2.2	0.5	0.3	1.6
New Permanent Pacemaker	13.0	13.2	12.0	10.1	10.4	7.2
Aortic Valve Re-intervention	1.0	0.8	2.2	0.7	0.8	
Endocarditis	0.2	0.2	0	0.1	0.1	

NYHA Functional Class

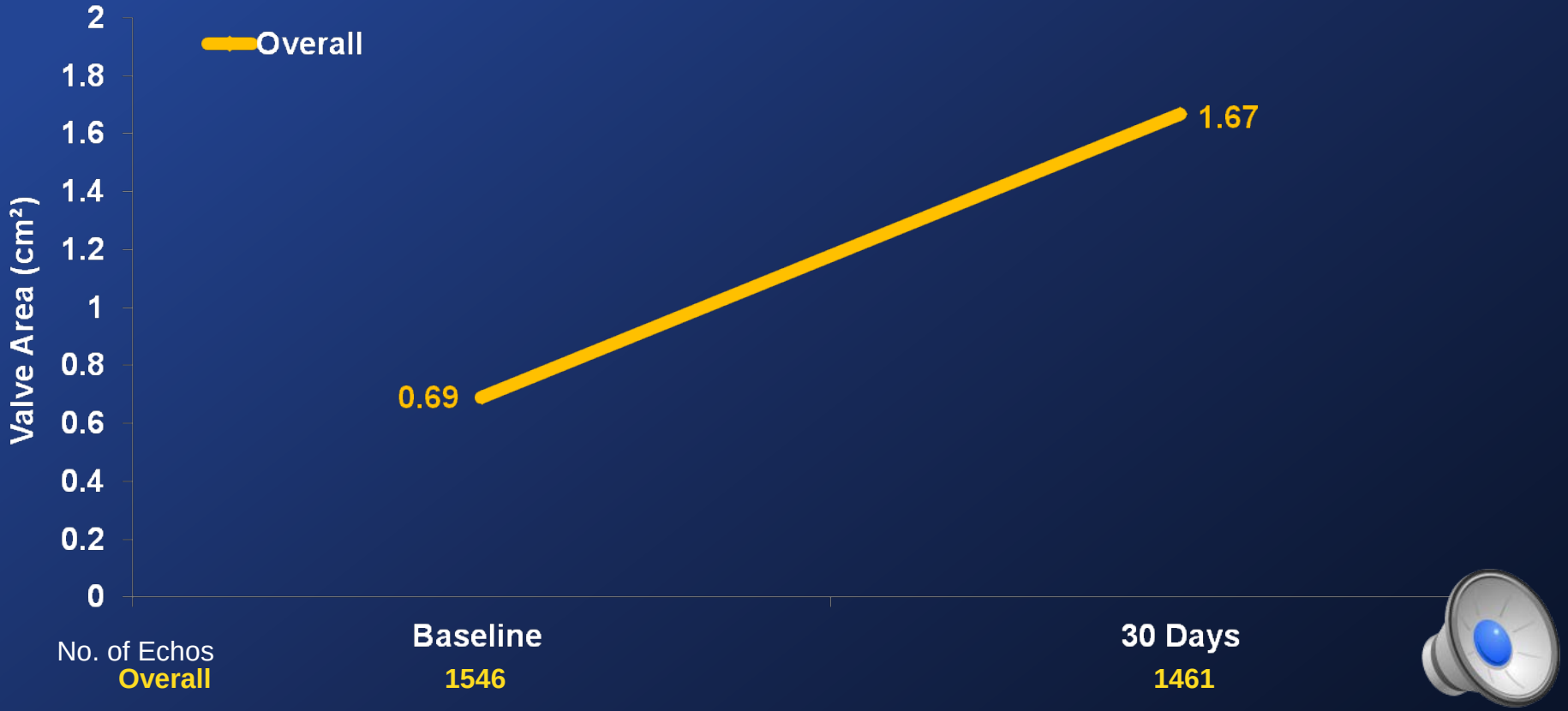
At 30 Days (As Treated Patients)

THE PARTNER II TRIAL



Echo Findings: S3HR & S3i

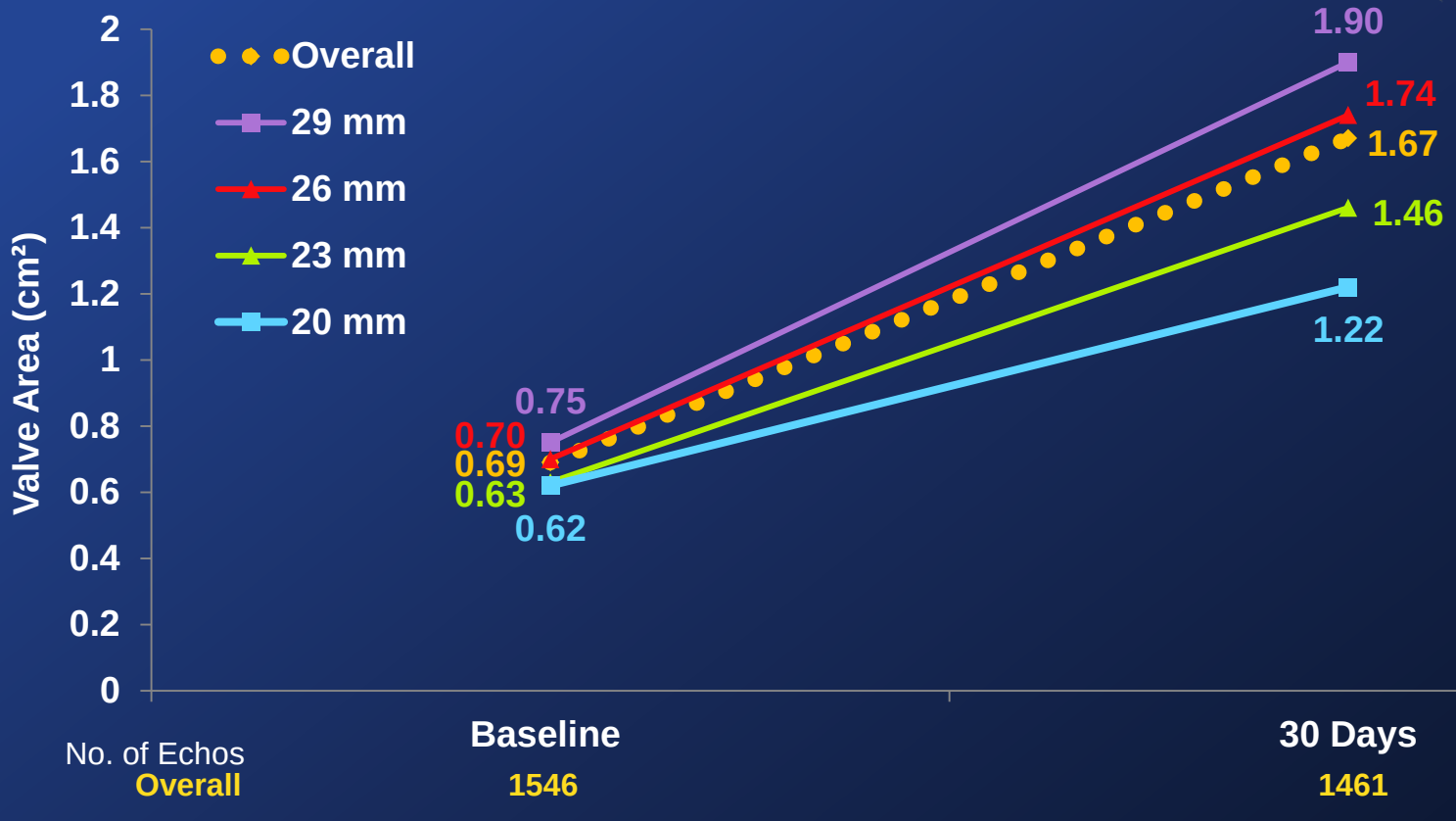
Aortic Valve Area (Valve Implant Patients)



Echo Findings: S3HR & S3i

Aortic Valve Area (Valve Implant Patients)

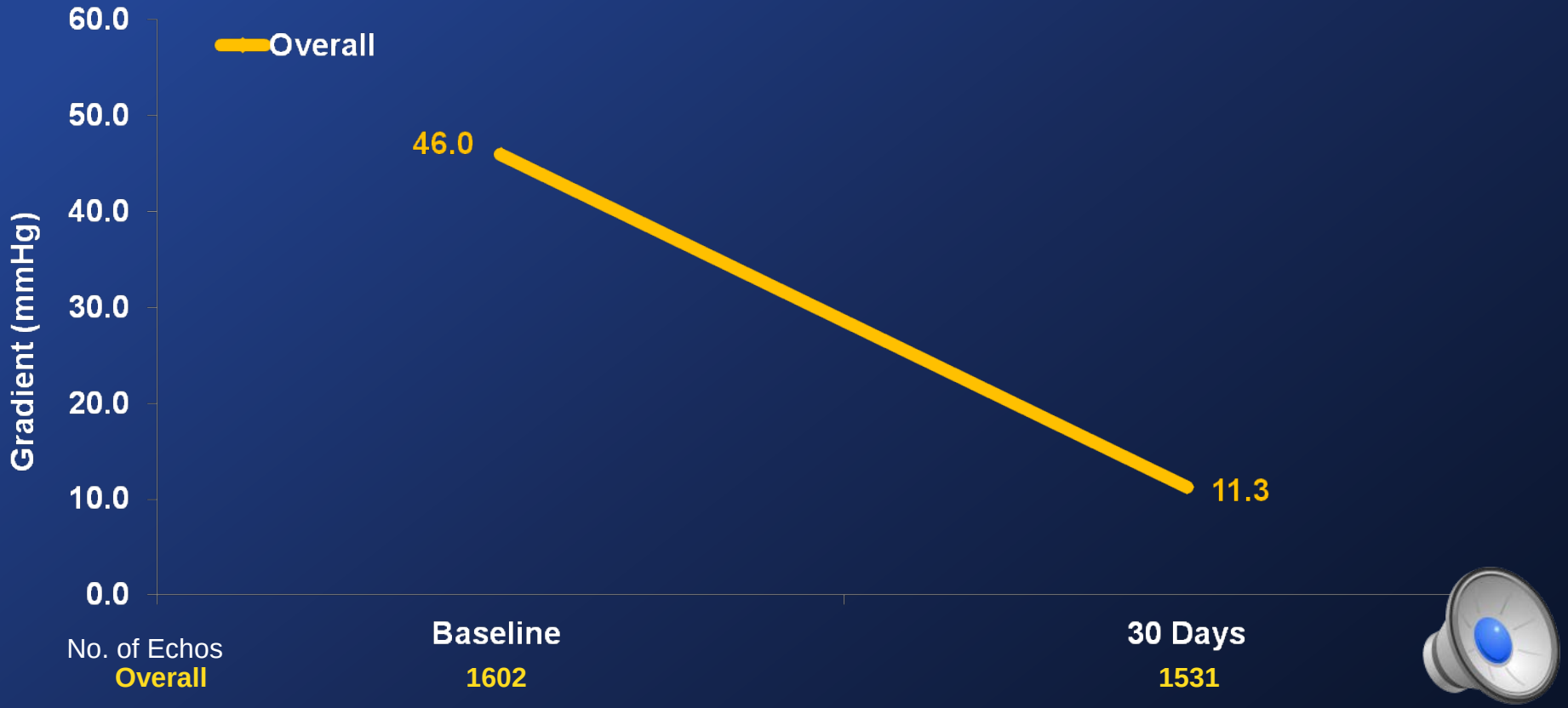
THE PARTNER II TRIAL



Echo Findings: S3HR & S3i

Mean Gradients (Valve Implant Patients)

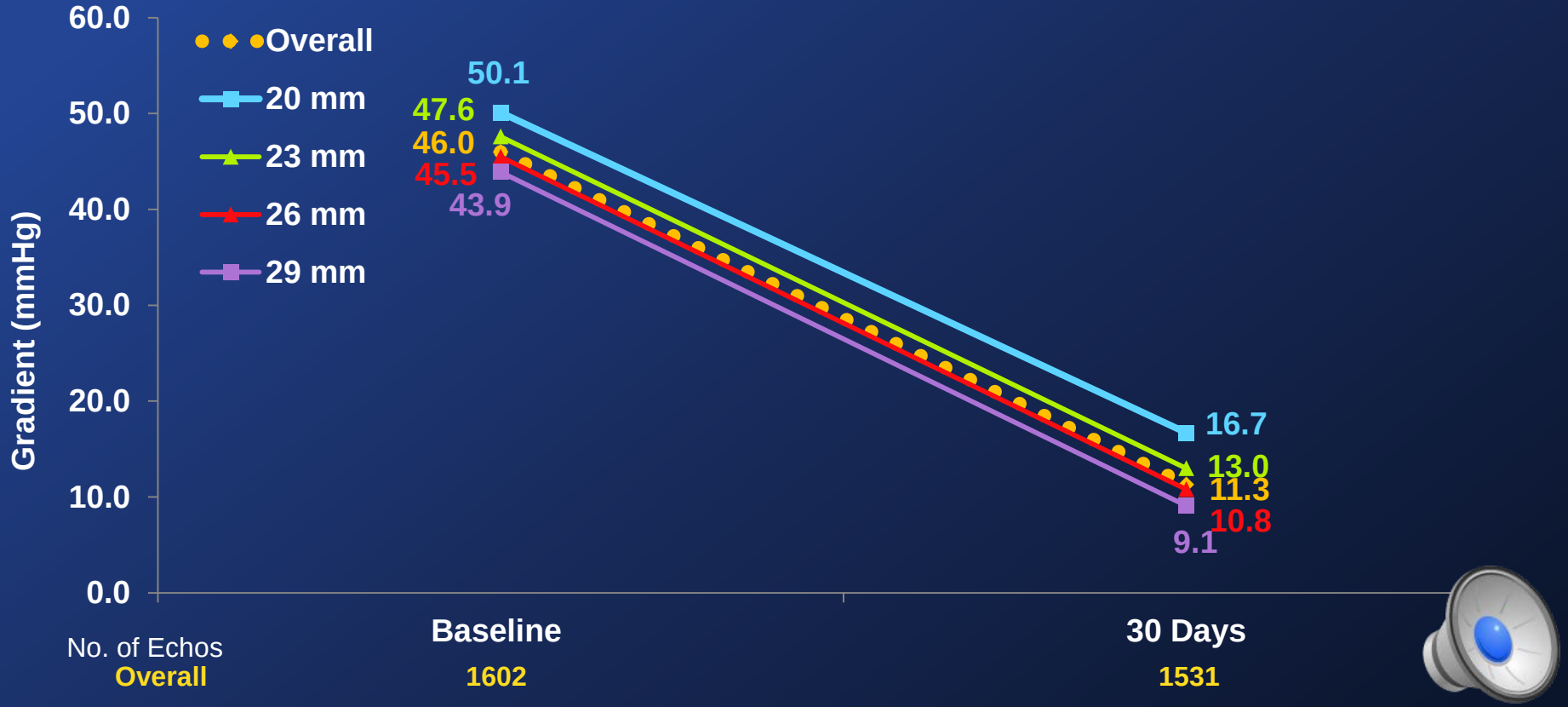
THE PARTNER II TRIAL



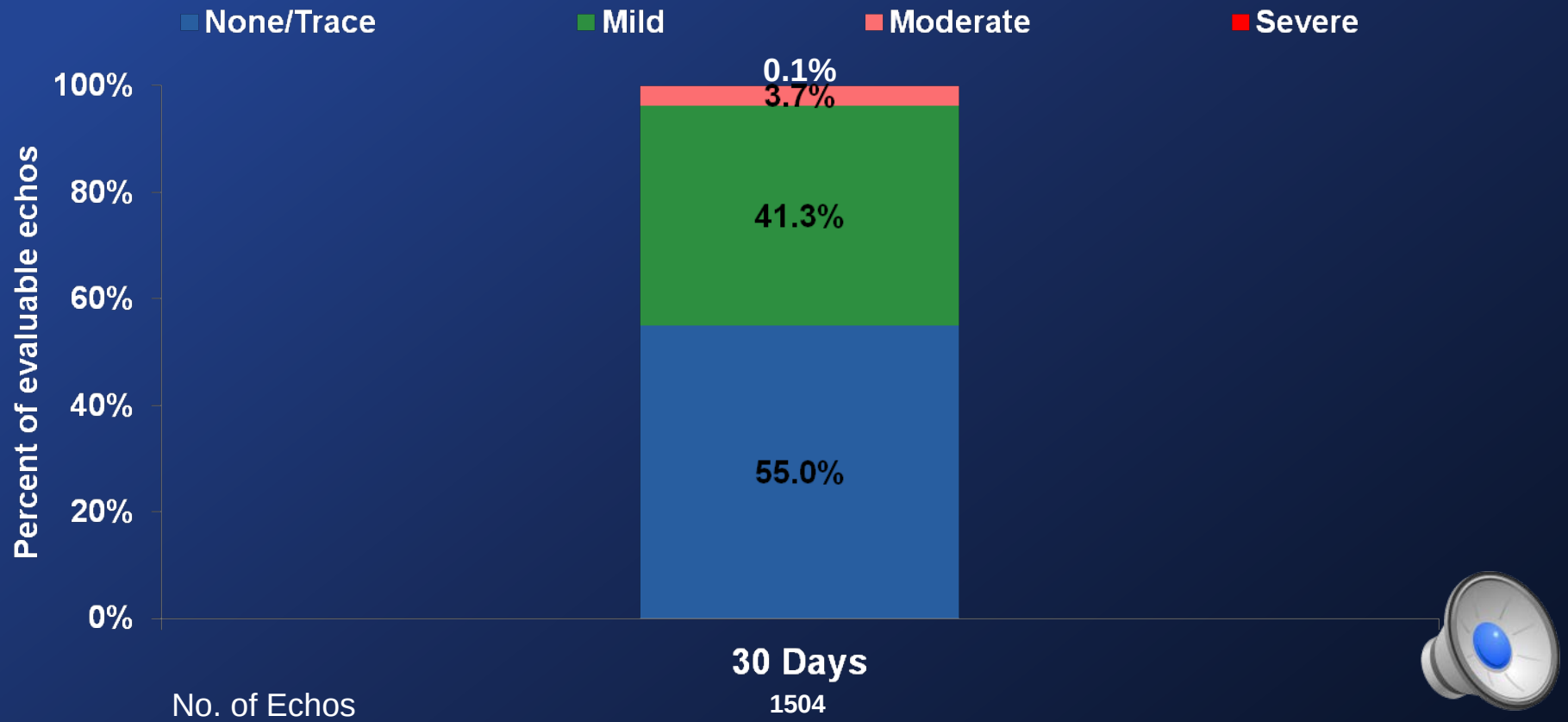
Echo Findings: S3HR & S3i

Mean Gradients (Valve Implant Patients)

THE PARTNER II TRIAL



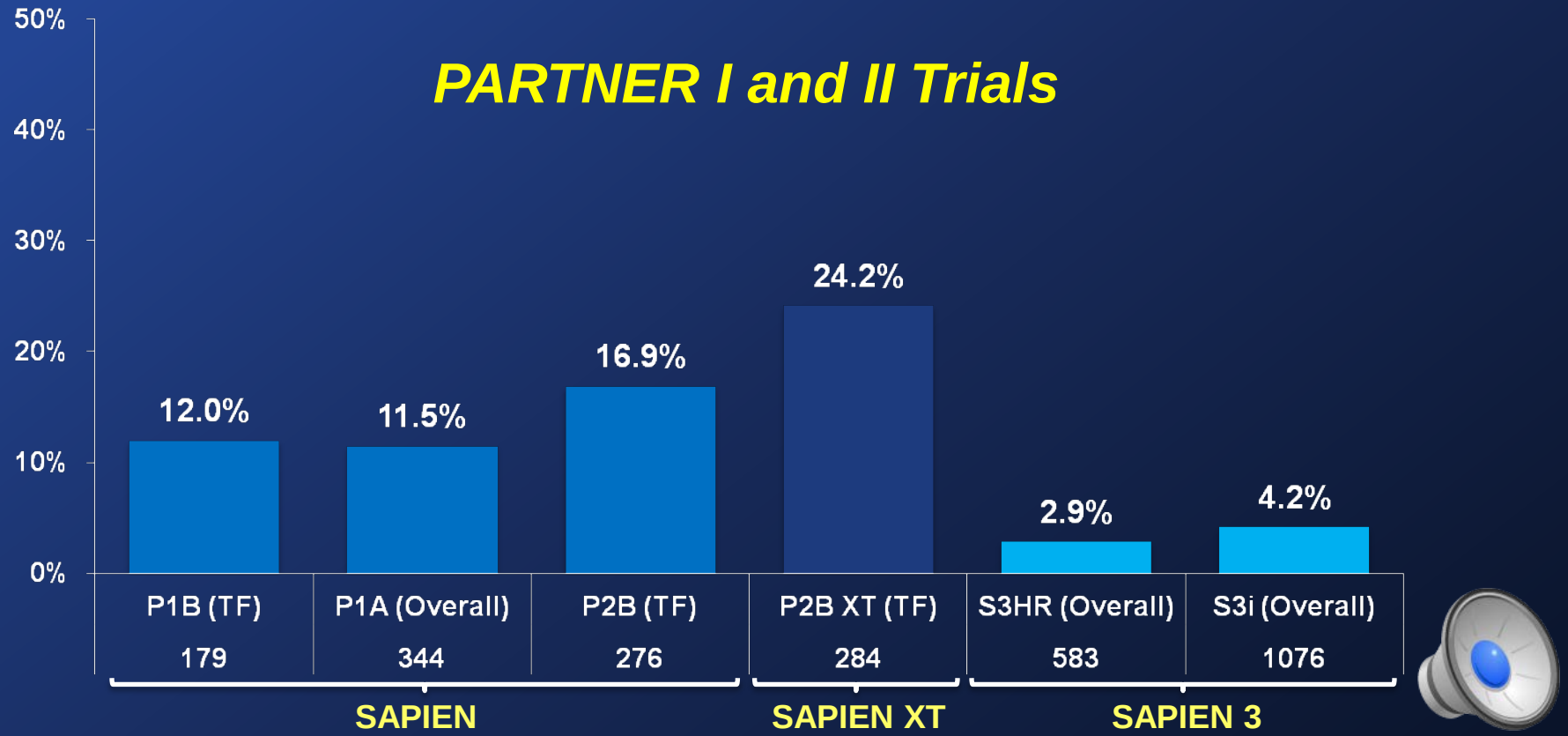
Paravalvular Leak: S3HR & S3i
(Valve Implant Patients)



Moderate/Severe PVL at 30 Days

Edwards SAPIEN Valves

THE PARTNER II TRIAL



Conclusions (1)

THE PARTNER II TRIAL

- In high-risk and inoperable patients (S3HR), the SAPIEN 3 TAVR system demonstrated low mortality and stroke and excellent clinical outcomes at 30 days:
  - **Mortality:** 2.2% (TF 1.6%, TA/TAo 5.4%)
  - **Disabling Stroke:** 0.9%
- In intermediate-risk patients (S3i), SAPIEN 3 was associated with strikingly low mortality and strokes at 30 days:
  - **Mortality:** 1.1% (TF 1.1%, TA/TAo 1.6%)
  - **Disabling Stroke:** 1.0%

Conclusions (2)

THE PARTNER II TRIAL

- Other important clinical findings with SAPIEN 3 (both S3HR & S3i) include:
  - **Major vascular complications:** ~5%
  - **Annular rupture:** ~0.2%
  - **Coronary obstruction:** ~0.3%
  - **New pacemakers:** ~10%
- Significant paravalvular regurgitation with SAPIEN 3 (both S3HR & S3i) was rare:
  - **Severe:** 0.1%
  - **Moderate:** 3.7%

Implications

THE PARTNER II TRIAL

- The rapid evolution of balloon-expandable TAVR, both procedural developments and technical enhancements, represented in the SAPIEN 3 clinical and echo results, indicates at least parity with the best surgical outcomes in comparable patients.
- *SAPIEN 3 TAVR should now be considered as an alternative to surgery, even in lower risk patients with aortic stenosis.*

Dedicated to the Memory of Mike Davidson, a Cherished Member of Our PARTNER Team

THE PARTNER II TRIAL

Backup Slides

Primary Endpoint: S3HR

THE PARTNER II TRIAL

- ***Primary Endpoint:*** *Non-Hierarchical composite of Death + All Stroke + Total AR ≥ Moderate*
- Patients in S3HR cohort are confirmed to be comparable to patients in P1A SAPIEN group via propensity modeling on baseline characteristics.
- Overall treatment effect is adjusted for propensity quintiles defined by propensity scores.
- Patients that received SAPIEN 3 have 9% lower event ra than patients that received SAPIEN.

Primary Endpoint: S3HR

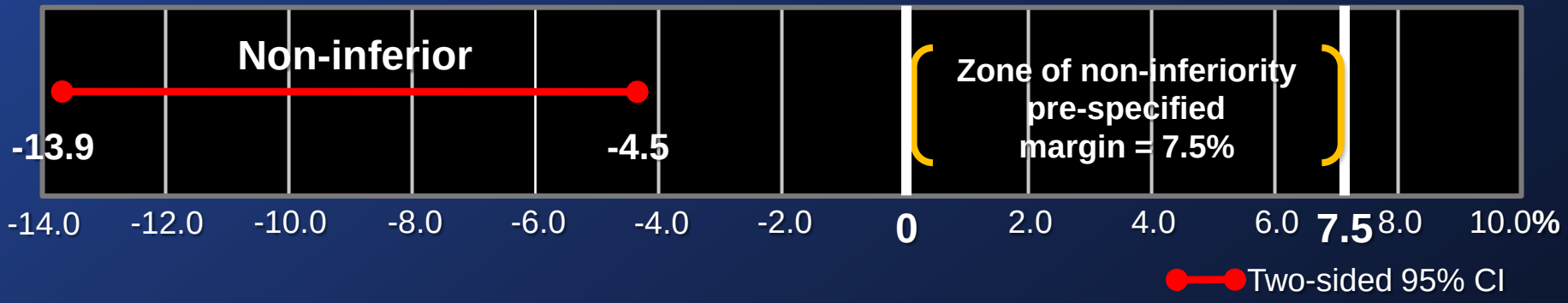
THE PARTNER II TRIAL

Primary Endpoint: *Non-Hierarchical Composite of Death + All Stroke + Total AR ≥ Moderate*

**Weighted*

Proportion Difference between SAPIEN 3 and SAPIEN: -9.0%*

Two-sided 95% Stratified Newcombe CI: [-13.9%, -4.5%]



Primary Non-Inferiority Endpoint Met: p < 0.001
Sequential Superiority Endpoint Met: p < 0.01