Transcatheter or Surgical Aortic Valve Replacement in Intermediate Risk Patients with Aortic Stenosis:

Final Results from the PARTNER 2A Trial – Sapien S3

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Highlights From the SAPIEN 3 Experience in Intermediate-Risk Patients

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SAPIEN Platforms in PARTNER
Device Evolution

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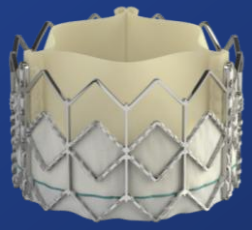
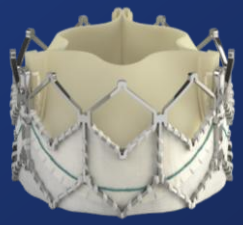
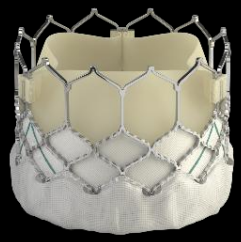
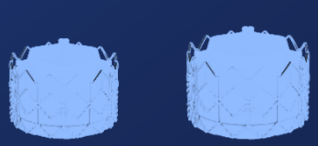
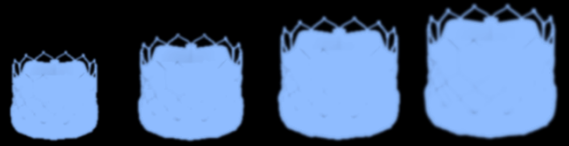
	SAPIEN	SAPIEN XT	SAPIEN 3
Valve Technology			
Sheath Compatibility	 22-24F	 16-20F	 14-16F
Available Valve Sizes	 23 mm, 26 mm	 23 mm, 26 mm, 29 mm	 20 mm, 23 mm, 26 mm, 29 mm

SAPIEN 3 Commander Delivery System
Distinguishing Features

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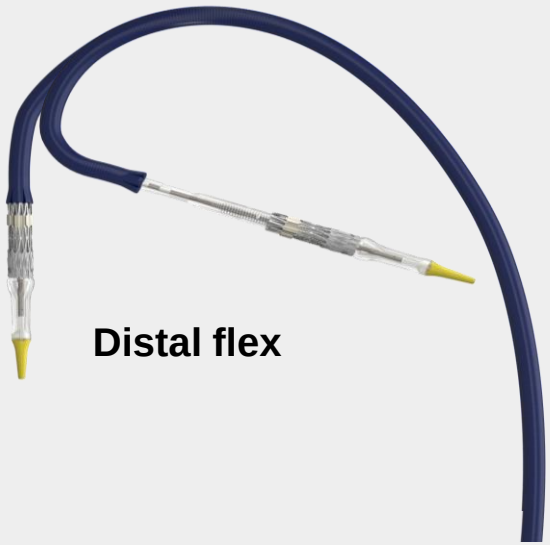
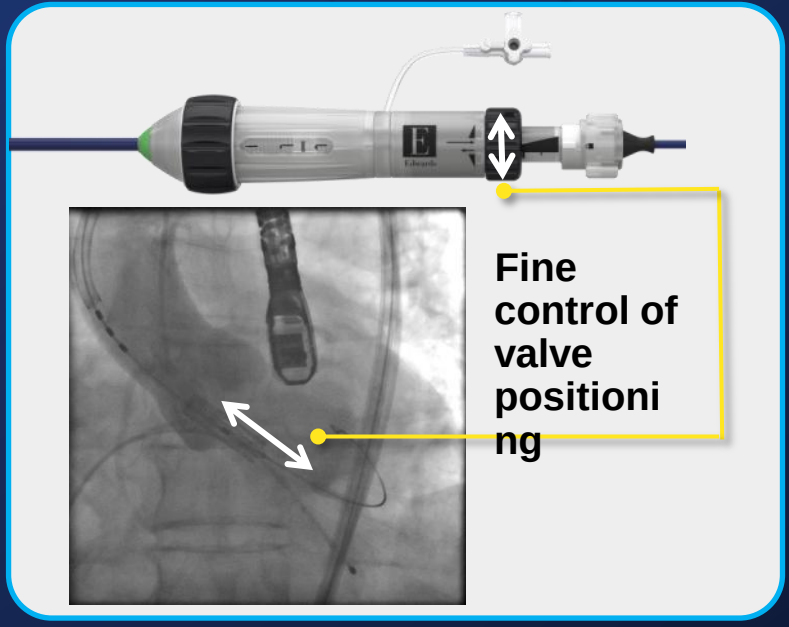
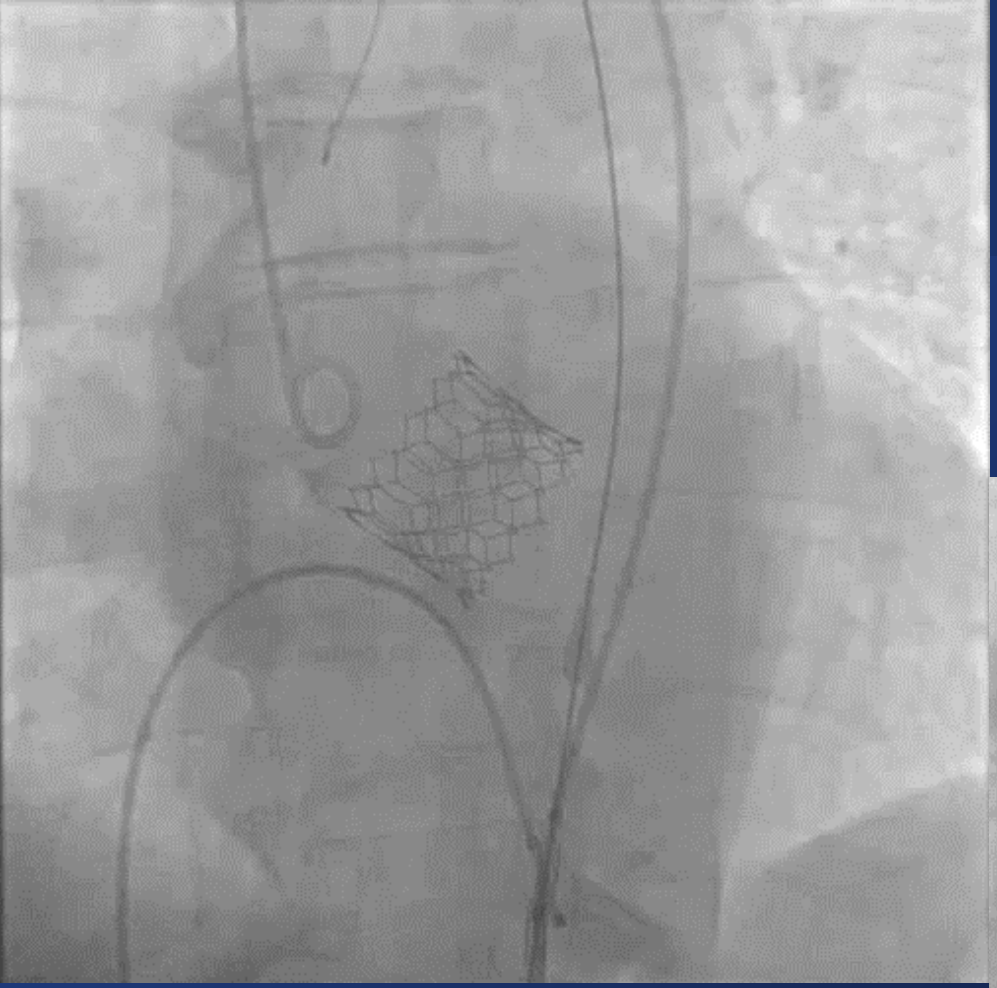
- Improved coaxial alignment



- 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



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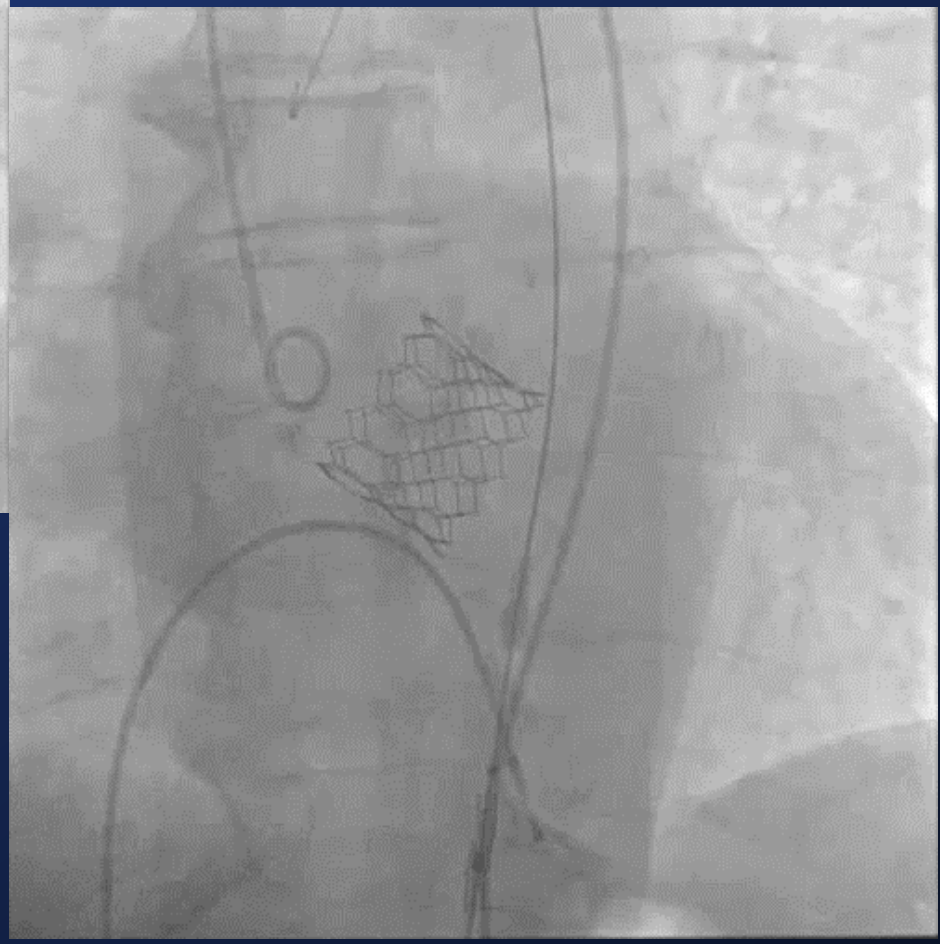
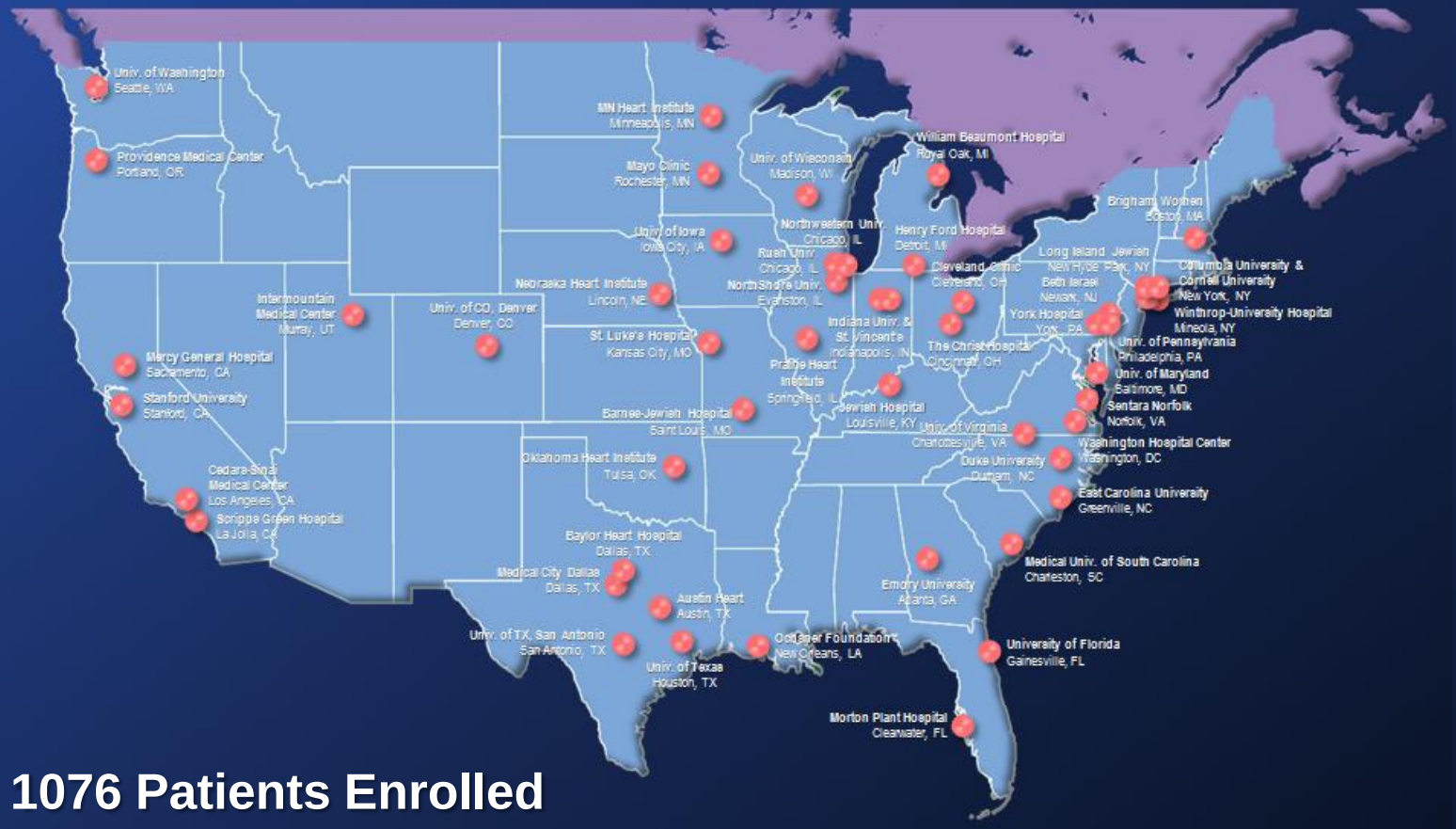


The PARTNER II S3 Trial: S3i
Participating Sites



1076 Patients Enrolled at 51 US Participating Sites

The PARTNER 2A and S3i Trials
Study Design

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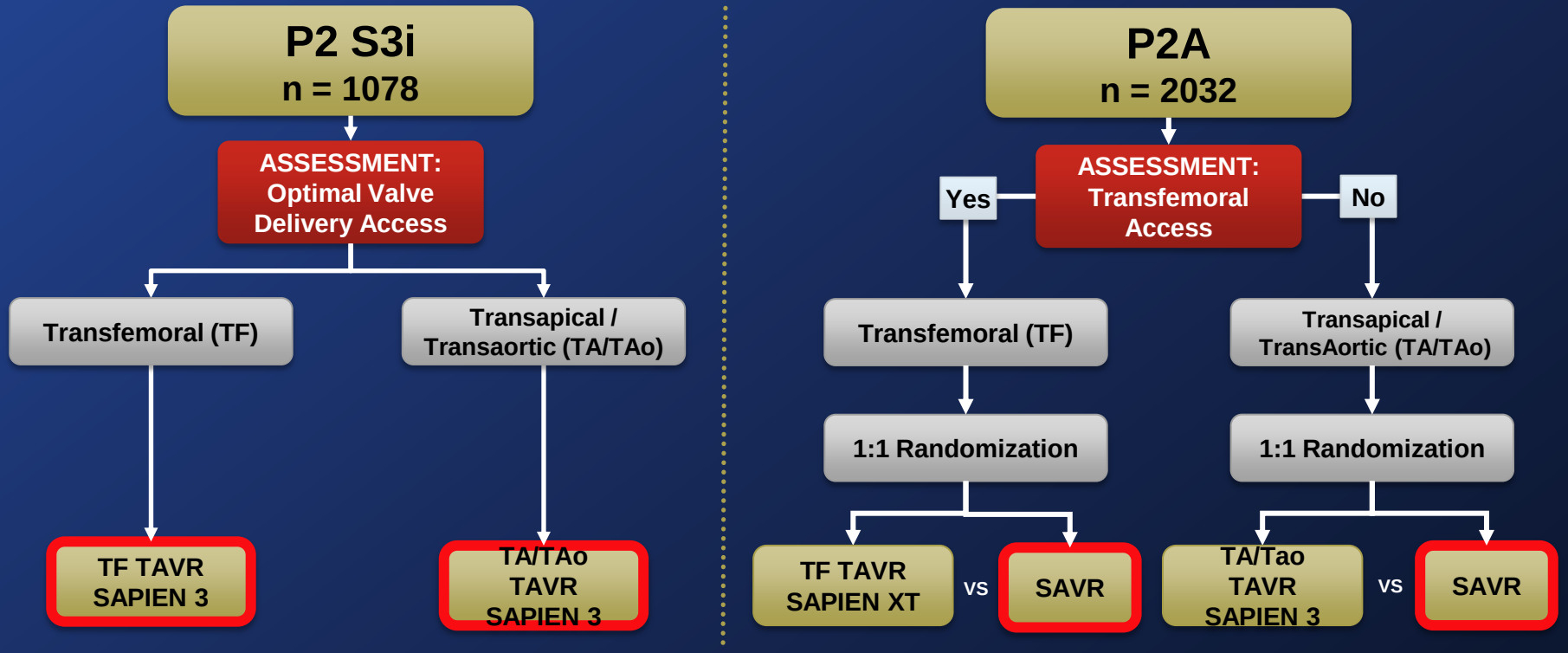
Intermediate Risk Symptomatic Severe Aortic Stenosis

Intermediate Risk ASSESSMENT by Heart Valve Team



Primary Endpoint: All-Cause Mortality, All Stroke, or Mod/Sev AR at One Year
(Non-inferiority Propensity Score Analysis)

The PARTNER 2A and S3i Trials
Inclusion Criteria

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- *Severe AS:* Echo-derived AVA ≤ 0.8 cm^2 (*or* AVA index < 0.5 cm^2/m^2) and mean AVG > 40 mmHg *or* peak jet velocity > 4.0 m/s

- *Cardiac Symptoms:* NYHA Functional Class ≥ II

- *Intermediate Risk:*
  1. Determined by a multi-disciplinary Heart Team
  2. Using a guideline STS between 4-8%*, and
  3. Adjudicated by case review committee

* PARTNER 2A used guideline STS ≥ 4%

The PARTNER 2A and S3i Trials
Primary Endpoint and Methodology

- Primary Endpoint
  - Non-hierarchical composite of *all-cause mortality, all stroke, or ≥ moderate AR at 1 year*
  - Propensity score analysis of the VI populations from S3i compared to the surgical arm of the PARTNER 2A trial
  - All patients followed for at least 1 year, event rates by Kaplan-Meier estimates
  - Non-inferiority trial design followed by superiority testing for the primary endpoint and components was performed
- Methodology
  - Systematic assessment by neurologists before and after index procedures for ascertainment of neurologic events
  - MDCT evaluation of annulus dimensions for all TAVR S3i patients (with core laboratory analyses)
  - CEC adjudication of major clinical events (VARC 2 definitions whenever possible)

Baseline Patient Characteristics
Demographics (AT)

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Characteristic	TAVR (n = 1077)	Surgery (n = 944)	p-value
Age - yrs	81.9 ± 6.6	81.6 ± 6.8	0.23
Male - %	61.7	55.0	0.002
BMI - kg/m^2	28.7 ± 6.1	28.4 ± 6.2	0.32
Median STS Score - %	5.2 [4.3, 6.3]	5.4 [4.4, 6.7]	0.0002
NYHA Class III or IV - %	72.5	76.1	0.07

mean ± SD, median [IQR]

Baseline Patient Characteristics
Other Co-morbidities (AT)

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Characteristic (%)	TAVR (n = 1077)	Surgery (n = 944)	p-value
CAD	69.6	66.5	0.14
Previous CABG	27.9	25.7	0.27
Cerebrovascular Disease	9.0	10.3	0.36
PVD	28.2	32.2	0.05
COPD	30.0	30.2	0.92
Cr level > 2 mg/dL	7.5	5.4	0.06
Atrial Fibrillation	36.0	34.9	0.61
Permanent Pacemaker	13.2	12.0	0.42
15 ft Walk Test > 7s	41.3	45.7	0.06

Primary Endpoint - Non-inferiority

Death, Stroke, or AR ≥ Mod at 1 Year (VI)

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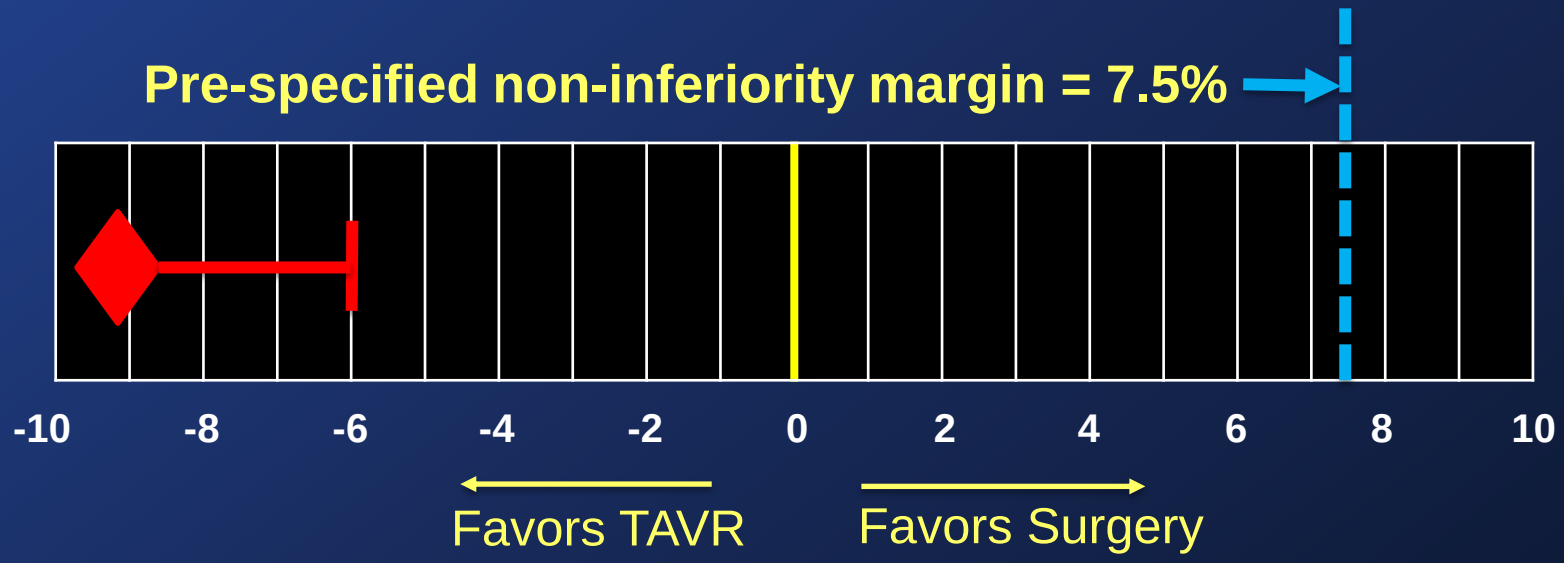
Weighted Difference	**-9.2%**
Upper 1-sided 95% CI	**-6.0%**

Non-Inferiority p-value < 0.001



Primary Non-Inferiority Endpoint Met

Primary Endpoint - Superiority

Death, Stroke, or AR ≥ Mod at 1 Year (VI)

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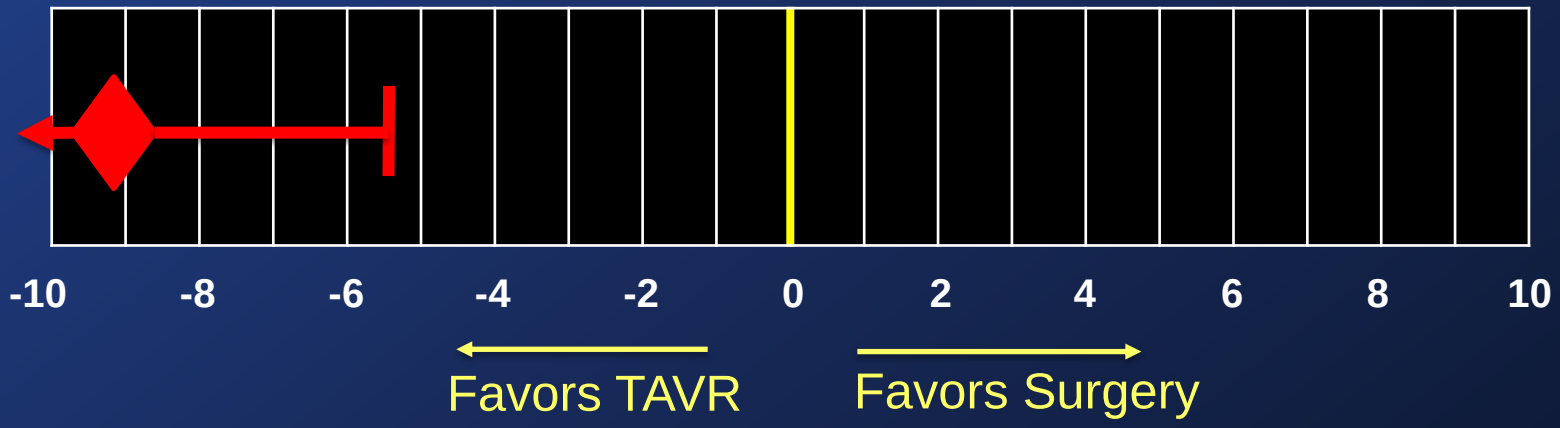
Weighted Difference	**-9.2%**
Upper 2-sided 95.0% CI	**-5.4%**

Superiority Testing p-value < 0.001



Superiority Achieved

Superiority Analysis
Components of Primary Endpoint (VI)

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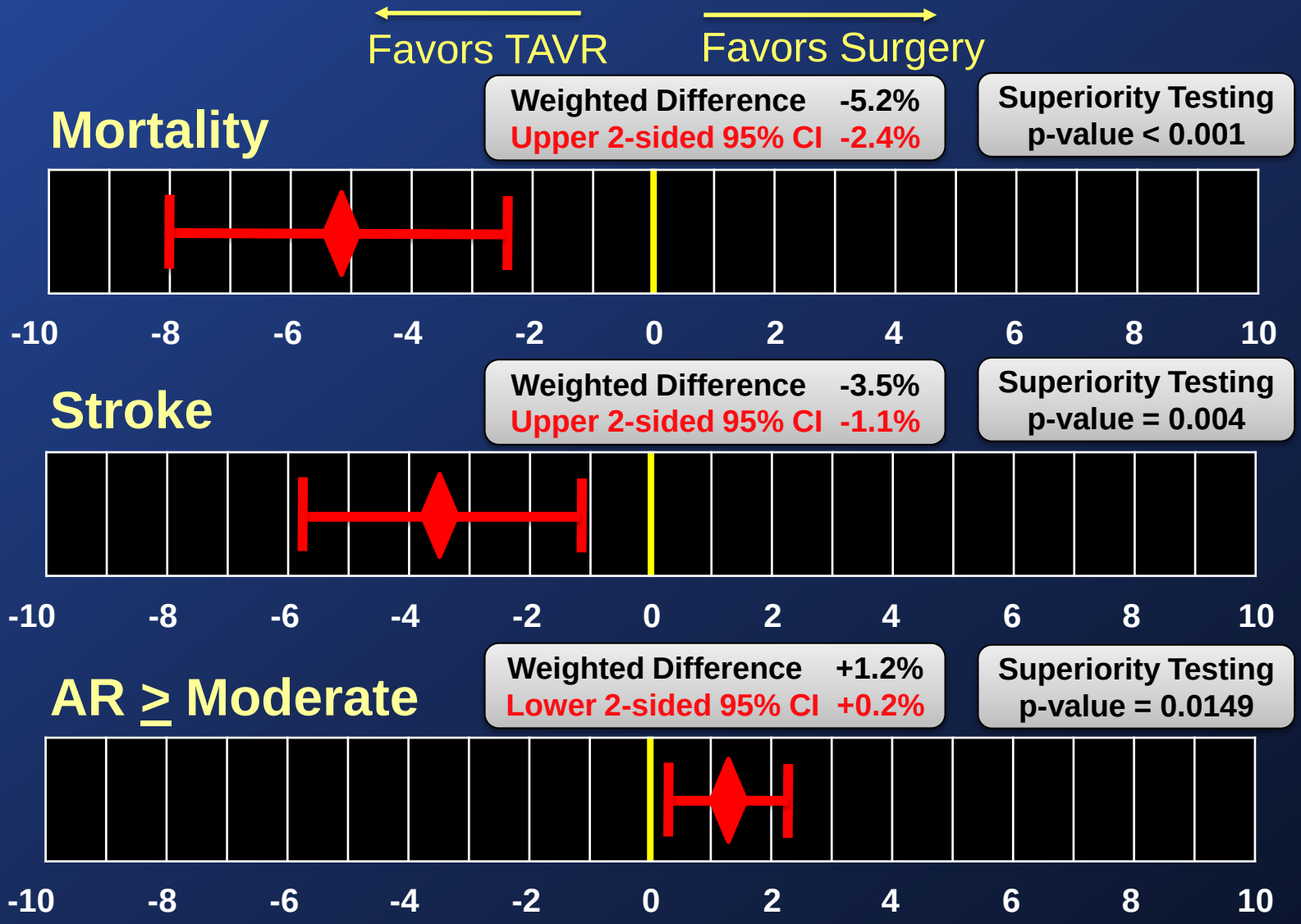

Unadjusted Time-to-Event Analysis
All-Cause Mortality and All Stroke (AT)

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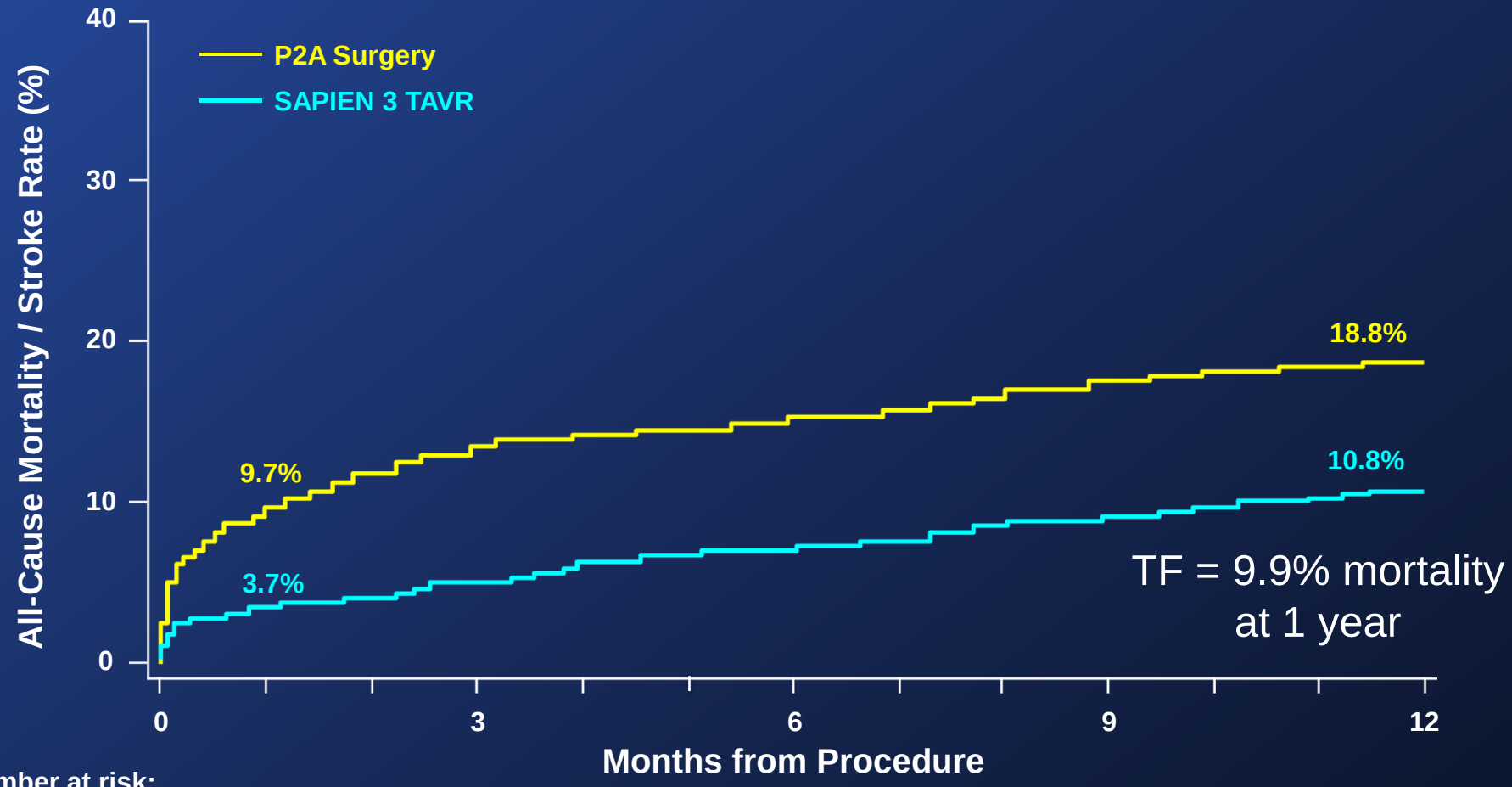
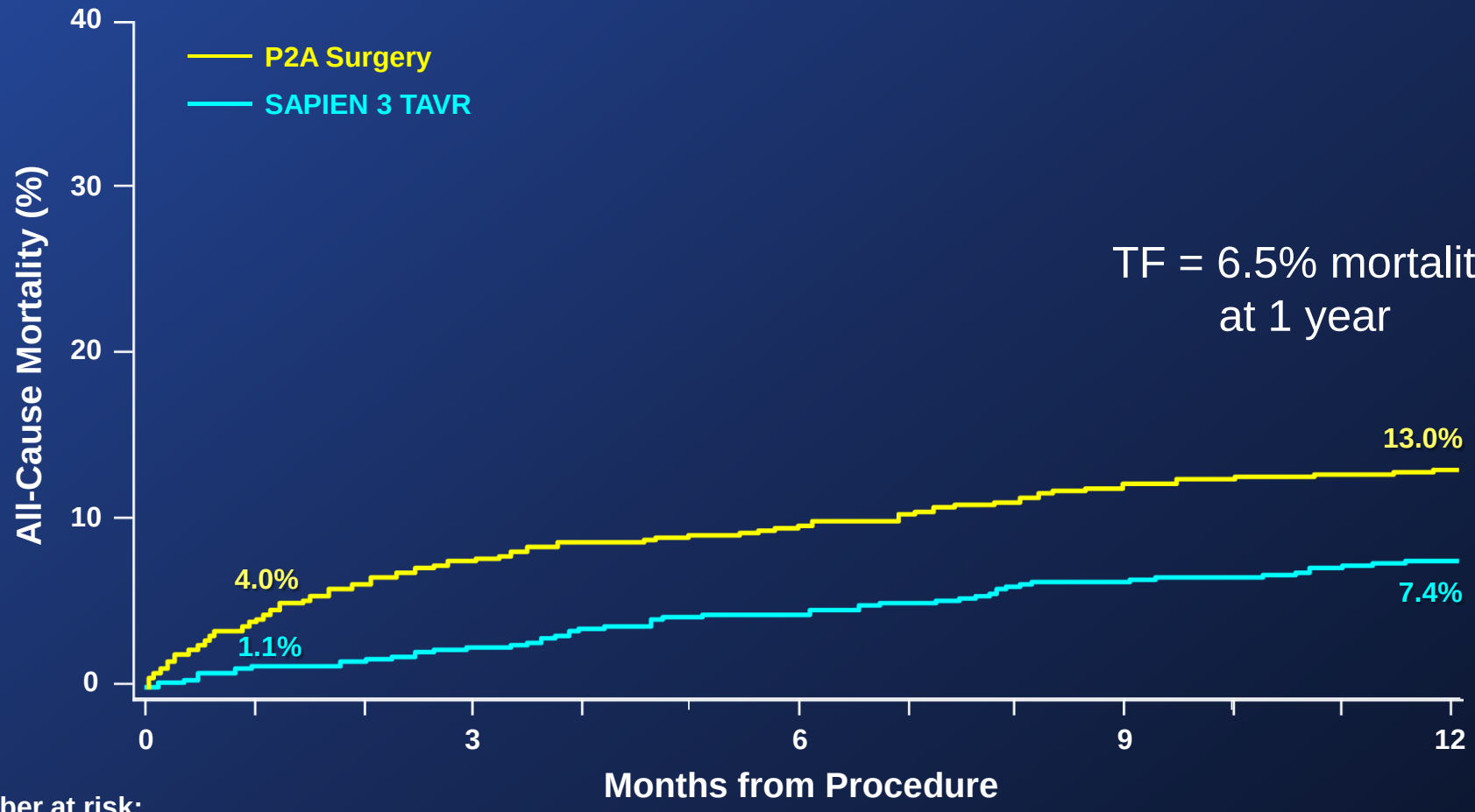


Number at risk:

P2A Surgery	944	805	786	757	743
S3 TAVR	1077	1012	987	962	930

Unadjusted Time-to-Event Analysis
All-Cause Mortality (AT)

THE PARTNER II TRIAL



TF = 6.5% mortality at 1 year

Number at risk:

P2A Surgery	944	859	836	808	795
S3 TAVR	1077	1043	1017	991	963

Unadjusted Time-to-Event Analysis
All Stroke (AT)

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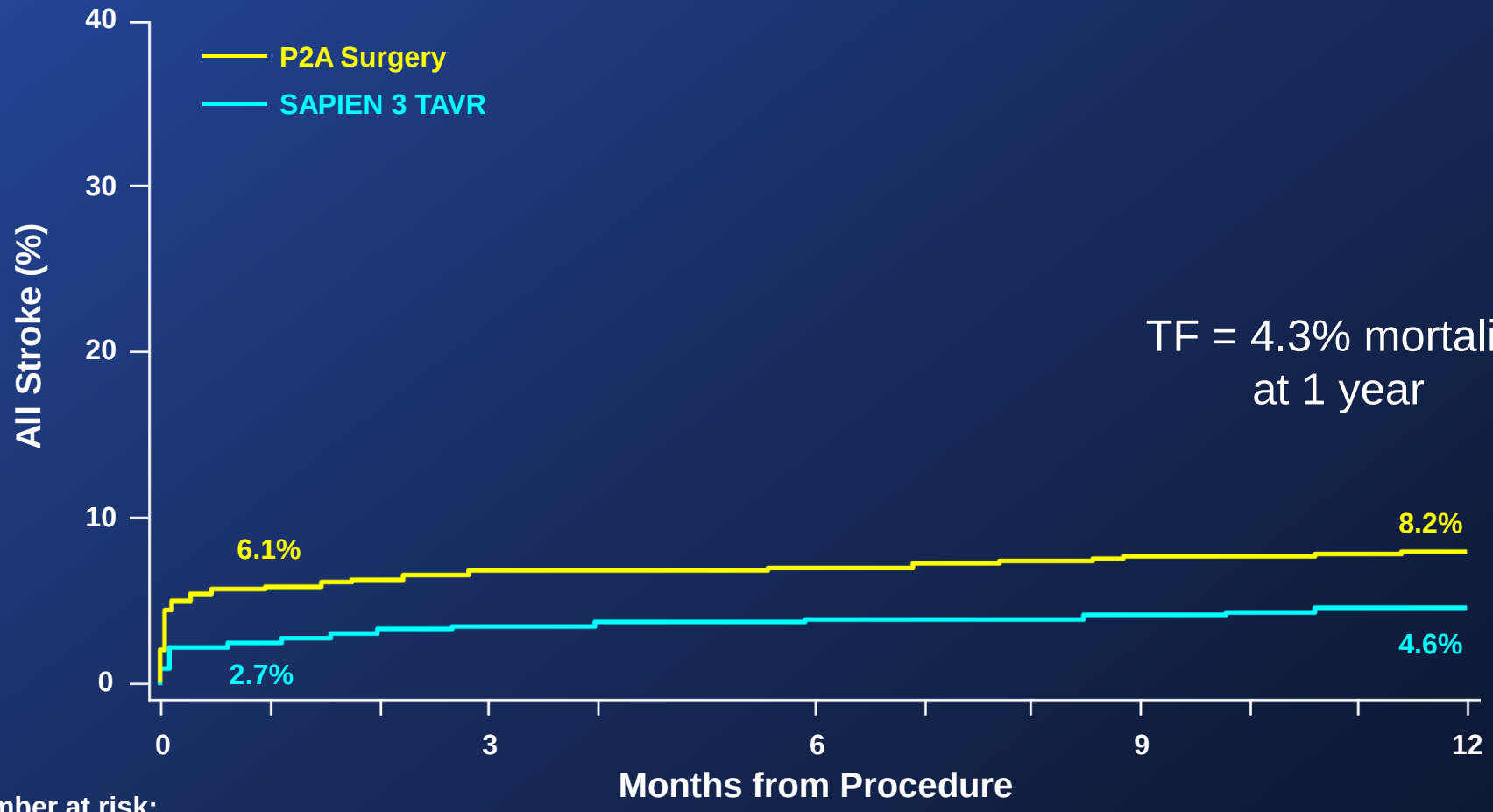

TF = 4.3% mortality at 1 year

Number at risk:

P2A Surgery	944	805	786	757	743
S3 TAVR	1077	1012	987	962	930

Paravalvular Regurgitation
3-Class Grading Scheme (VI)

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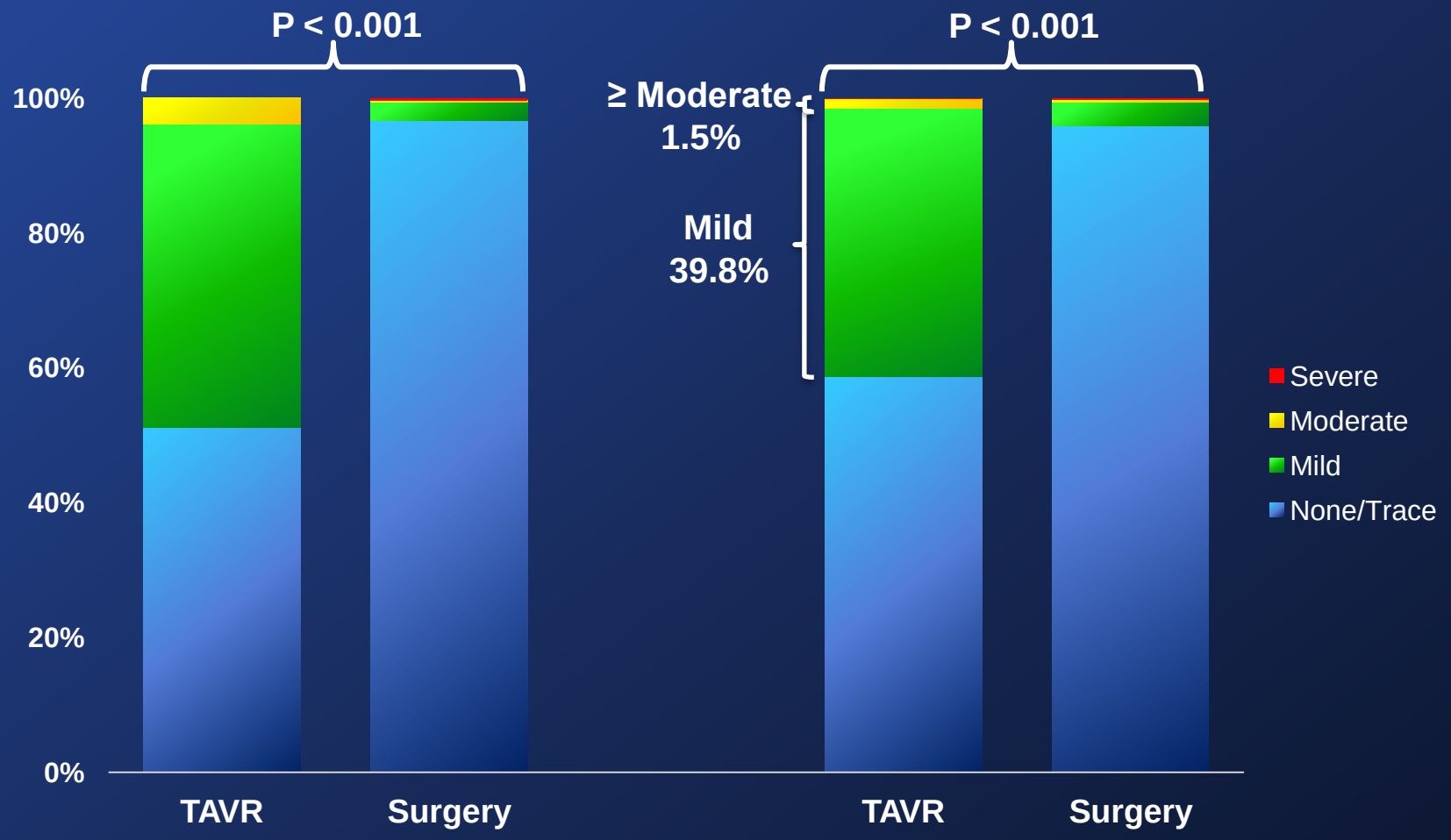

No. of echos	30 Days	1 Year
P2A Surgery	755	610
S3i TAVR	992	875

Mortality by PVR Severity

S3i (VI)

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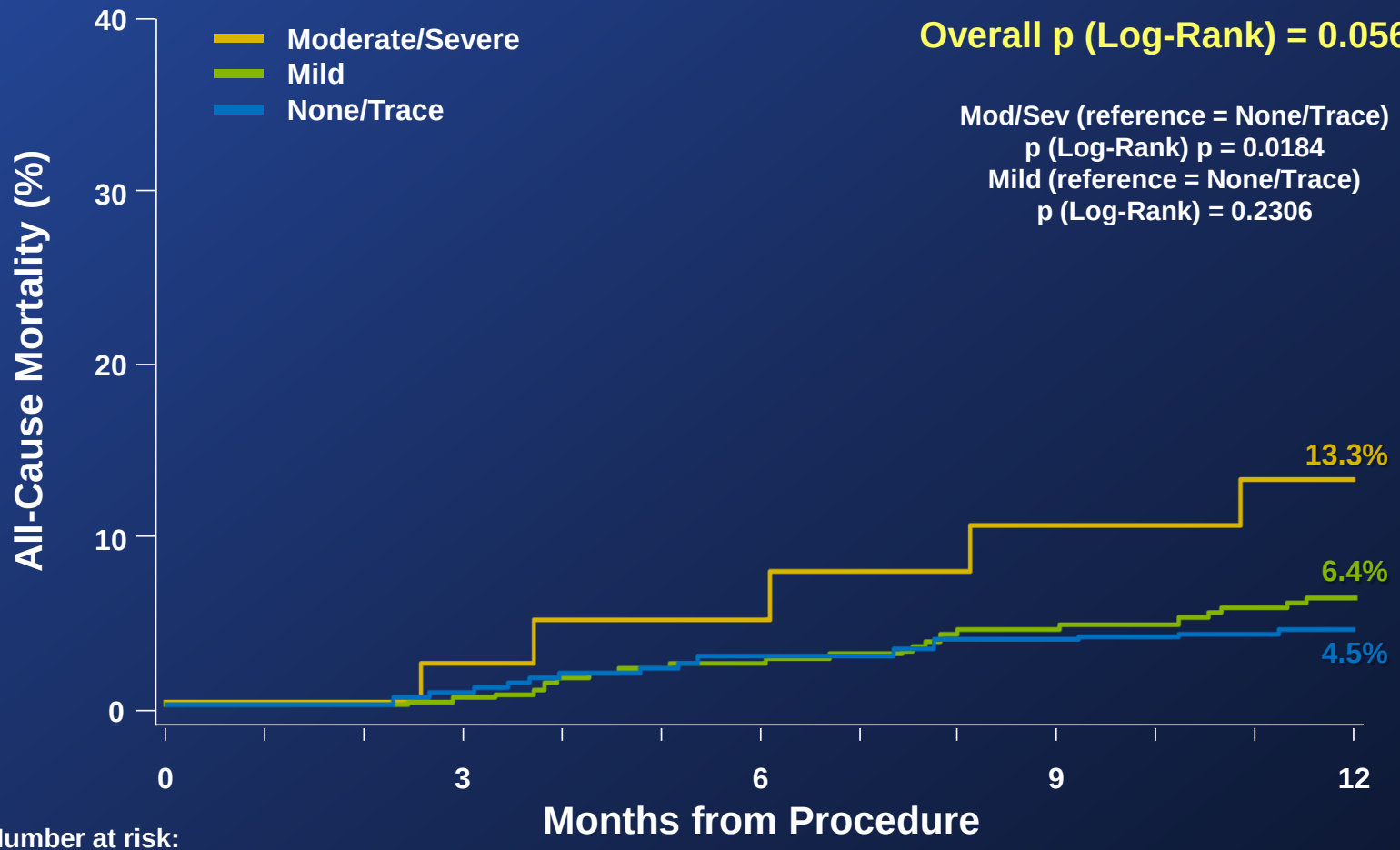

Echocardiographic Findings:
Mean Gradients (VI)

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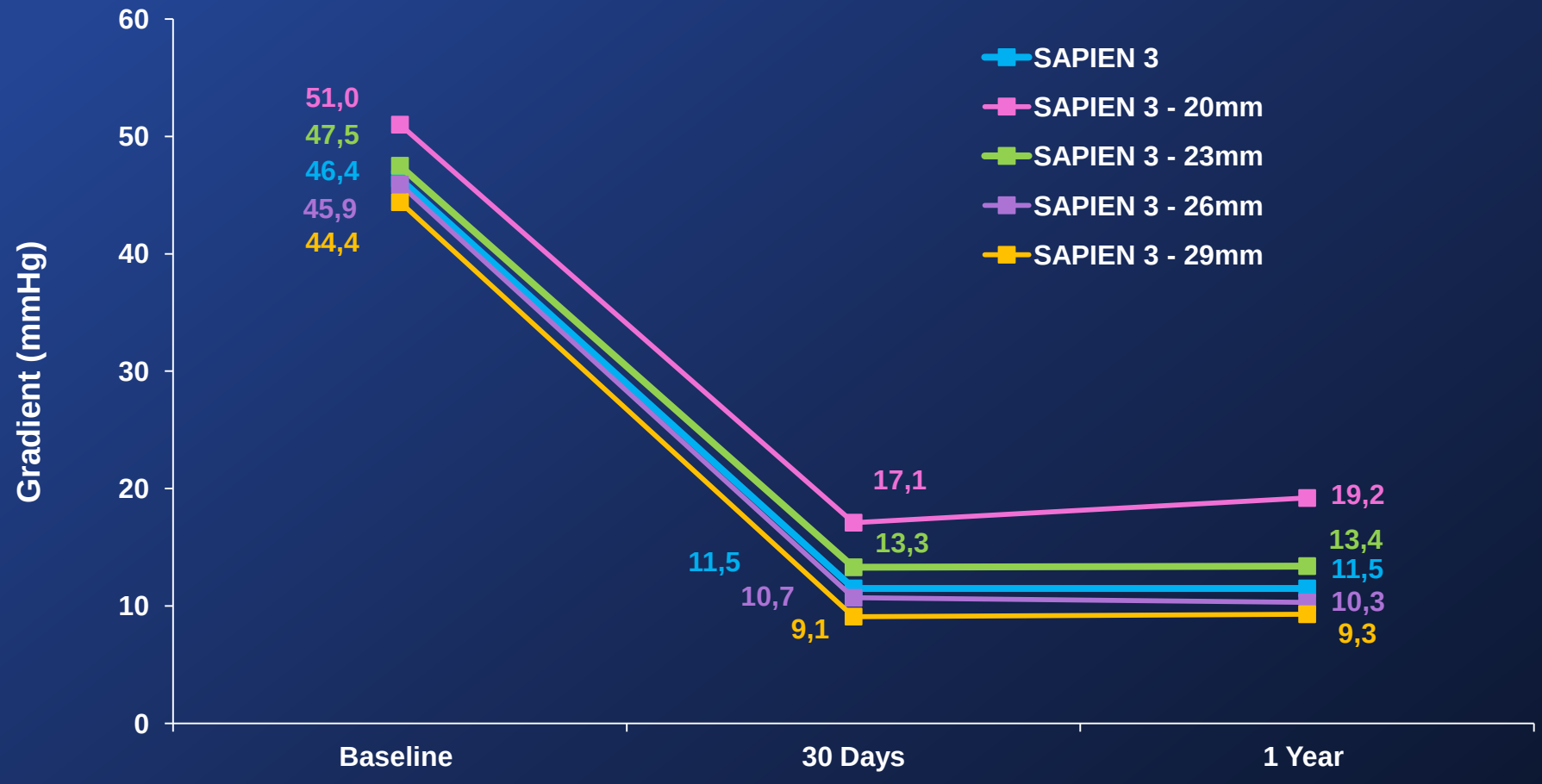

No. of Echos

SAPIEN 3	SAPIEN 3 - 20mm	SAPIEN 3 - 23mm	SAPIEN 3 - 26mm	SAPIEN 3 - 29mm
840	35	276	372	157

The PARTNER 2A and S3i Trials
Conclusions - 1

- In IR patients, SAPIEN 3 TAVR resulted in low 1-year rates of:
  - all-cause mortality = 7.4% (TF is 6.5%)
  - all stroke = 4.6% (TF is 4.3%) and
  - moderate or severe aortic regurgitation (1.5%)

The PARTNER 2A and S3i Trials
Conclusions - 2

- The rigorous propensity score analysis comparing SAPIEN 3 with SAVR in IR patients at 1 year demonstrated:
  - Non-inferiority for the primary endpoint (composite of all-cause mortality, all stroke, or AR ≥ moderate)
  - Superiority of SAPIEN 3 TAVR for the primary endpoint, all-cause mortality, and all stroke
  - Superiority of surgery for AR ≥ moderate
- Time-to-event analyses indicated that the benefits of SAPIEN 3 TAVR occurred in the first few months, suggesting procedure-related effects

The PARTNER 2A and S3i Trial
Clinical Implications

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- The conclusions from the PARTNER 2A randomized trial and this propensity score analysis provide strong evidence that in intermediate-risk patients with severe aortic stenosis, SAPIEN 3 TAVR when compared with surgery improves clinical outcomes and is the preferred therapy.

The PARTNER 2A and S3i Trial
The Lancet On-line

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Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

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Děkuji za pozornost