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PROTECTED TAVR Study with SENTINEL™ CPS

PROTECTED TAVR Study Design

Study Chair
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Principal Investigators
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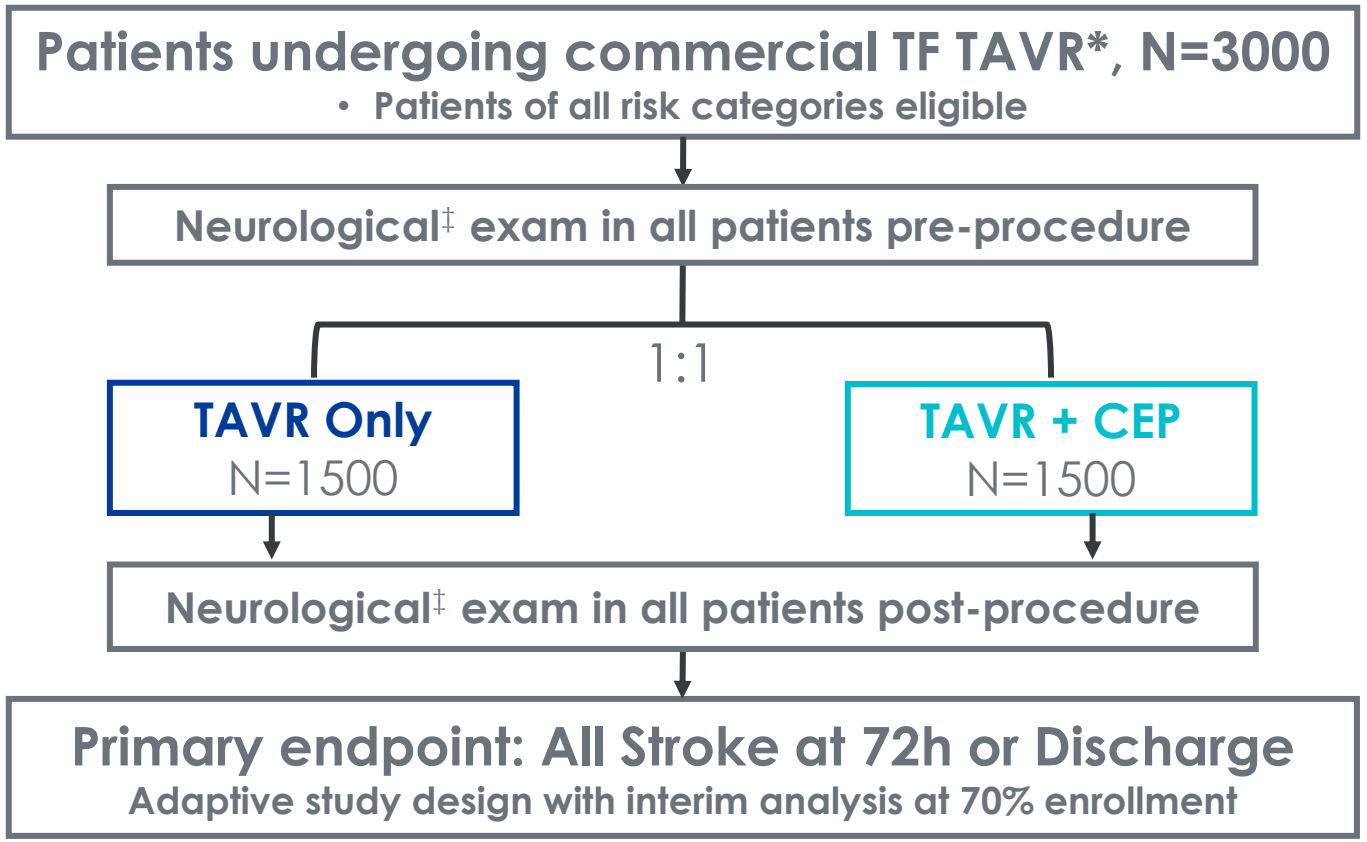
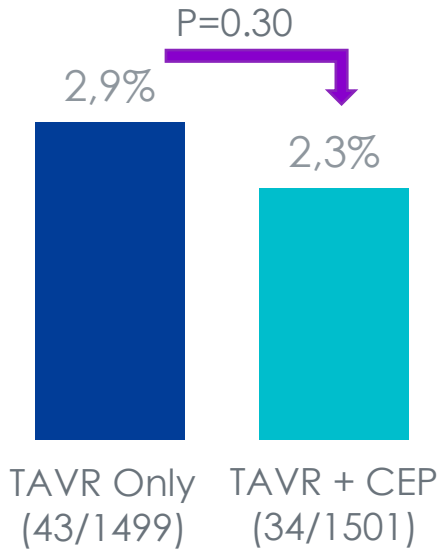
Co-PI: Axel Linke, MD



*Any commercially available TAVR device; ‡ Neurological examination at baseline, and post-procedure and through 72 hours after TAVR or discharge (whichever comes first), performed by a neurology professional (board certified/board eligible neurologist, neurology fellow, neurology physician assistant, or neurology nurse practitioner)

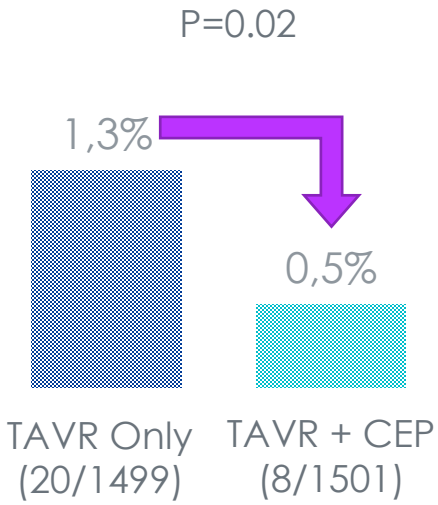
PROTECTED TAVR Results

Primary Endpoint: All Stroke



21%
relative risk reduction
in **All Stroke**
through 72 hours

Secondary Analysis: Disabling Stroke



60%
relative risk reduction
in **Disabling Stroke**
through 72 hours

- Largest randomized TAVR trial to date with 3,000 patients enrolled at more than 50 global sites
- Data demonstrated a non-significant but numerical trend toward a lower risk of stroke in patients treated with the SENTINEL device
- Secondary analysis of disabling stroke showed a statistically significant reduction with SENTINEL

Stroke is Unpredictable

Subgroup Analysis comparing CEP + TAVR vs. TAVR alone

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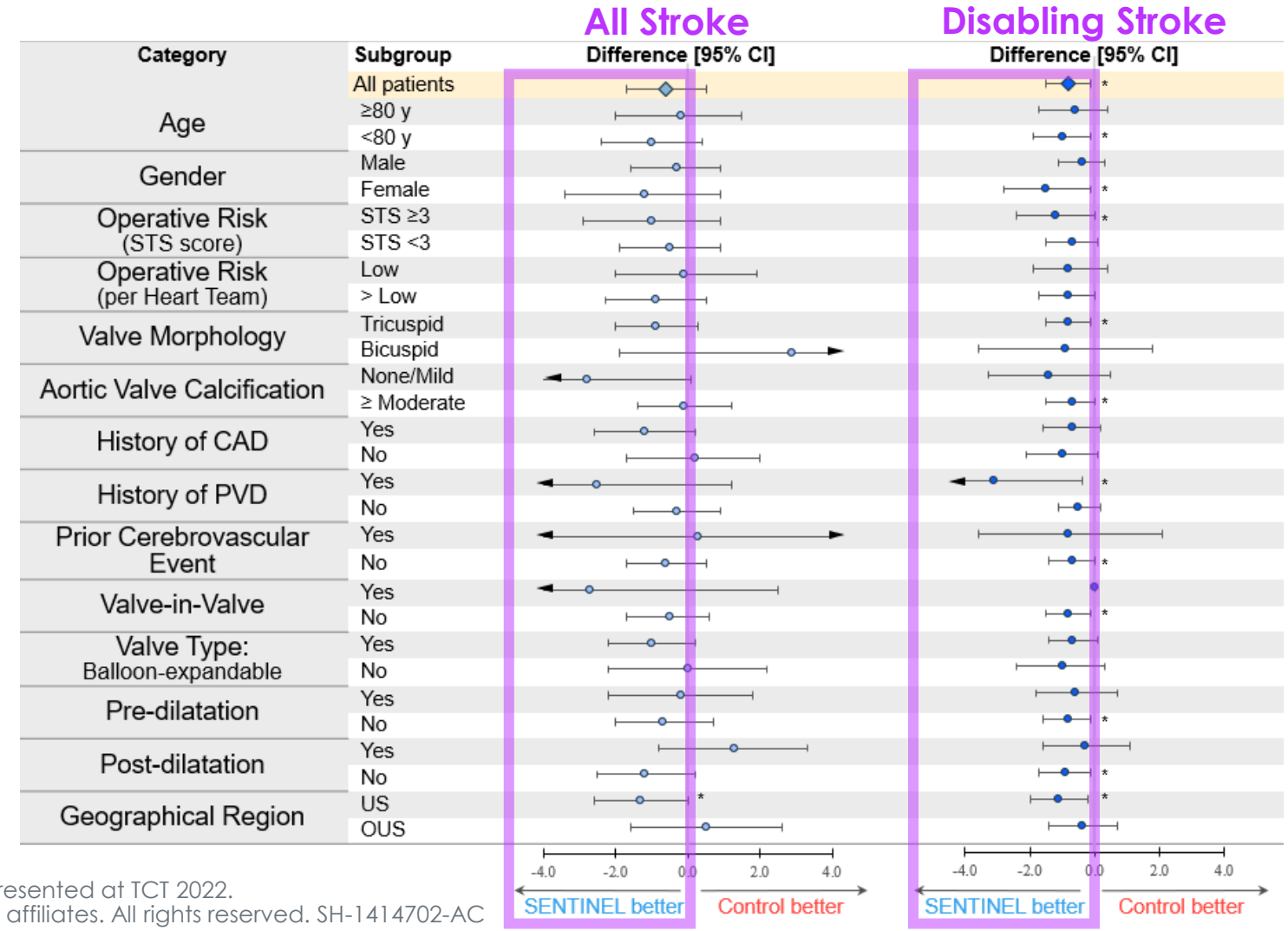
Demonstrates CEP reduces disabling strokes consistently across all patient subgroups



*p≤0.05

Kapadia, S. PROTECTED TAVR trial data presented at TCT 2022.

Disabling Stroke Costs

Significant Increase in Acute and Long-Term Disabling Stroke Costs

Acute

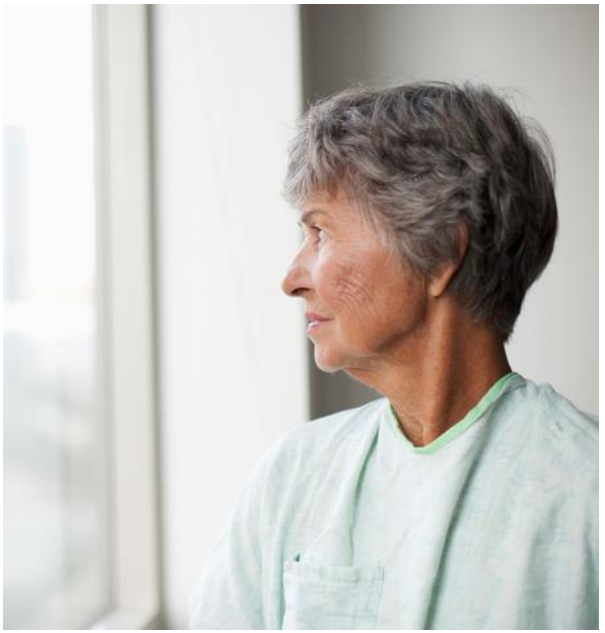
Cost of an Acute Severe Ischemic Stroke is estimated to be **$59,010**[1]

One Year

One-year cumulative severely disabling stroke costs are roughly **$132,590**[1]

Long Term

The cumulative costs of disabling stroke are estimated to be **$206,170**[1] after two years post-stroke



1. Reddy et al. Time to Cost-Effectiveness Following Stroke Reduction Strategies in AF Warfarin Versus NOACs Versus LAA Closure. JACC Vol. 66, No. 24, December 22, 2015
2. Alkhouli, M, et al. "Cost of procedural stroke in TAVR in a US Medicare population" Valve20A-POS01; PCR London Valves 2020

Stroke Happens. Protection Works.

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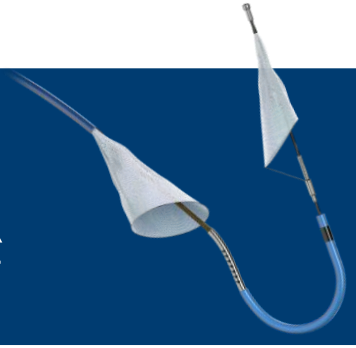
Stroke is devastating for patients and the healthcare system.

SENTINEL is safe, captures debris and significantly reduces the risk of disabling stroke.

PROTECTED TAVR

CEREBRAL EMBOLIC PROTECTION DURING TRANSCATHETER AORTIC VALVE REPLACEMENT



TOPLINE RESULTS

PRIMARY ENDPOINT
ALL STROKE
21%
Relative Risk Reduction
through 72-hours[4]

SECONDARY ANALYSIS
DISABLING STROKE
60%
Relative Risk Reduction
through 72-hours[4]

STROKE IS UNPREDICTABLE

#1 PATIENT FEAR
Stroke is the top concern of TAVR patients, even more than death[1]

78%
of patients say **maintaining independence** is their top goal post-TAVR[2]

THE TRUE COST OF STROKE

$59K
1-Year Acute Cost for Disabling Stroke[3]

$132K
1-Year Cumulative Cost for Disabling Stroke[3]

A LANDMARK STUDY

#1
Largest Randomized TAVR Trial

3,000
Patients Enrolled

50+
Global Sites

1:1
Randomized Double-Arm Design

SENTINEL SAFETY PROFILE

94%
Safe & Effective Device **Delivery & Retrieval**[4]

0.1%
Low Complication Rates at Vascular Access Site[4]

SUB-GROUP ANALYSIS

ALL
Patient Populations
Favored SENTNEL use to reduce disabling stroke risk[4]

1. Audience survey, Hawkey M, presented at ACC 2016.
2. Leon M. Future considerations: The role of shared decision making and adoption of CEP in practice. TCT 2018, San Diego, CA.
3. Reddy et al. Time to Cost-Effectiveness Following Stroke Reduction Strategies in AF Warfarin Versus NOACs Versus LAA Closure. JACC Vol. 66, No. 24, December 22, 2015.
4. Kapadia, S. PROTECTED TAVR trial data presented at TCT 2022.

Key Takeaways

Stroke is the #1 fear of patients undergoing TAVI – greater even than death. It is **unpredictable** and, in addition to the impact on the patient, **an economic burden** on the healthcare system, family & caregivers

PROTECTED TAVR, the largest randomized TAVI trial to-date, despite **missing primary endpoint** showed that SENTINEL is **safe** and **significantly reduces the risk of disabling stroke by 60%**

The reduction in disabling stroke with SENTINEL was **consistent across all subgroups**

A therapy that is safe and reduces the risk of disabling stroke by 60% **should be attractive to patients and physicians**

SENTINEL™ Cerebral Protection System

- **INDICATIONS FOR USE**: The SENTINEL System is indicated for use as an embolic protection device to capture and remove embolic material (thrombus/debris) that may enter the cerebral vascular system during endovascular procedures. The SENTINEL Cerebral Protection System is indicated for use as an embolic protection device to capture and remove thrombus/debris while performing transcatheter aortic valve replacement procedures. The diameters of the arteries at the site of filter placement should be between 9.0 mm – 15.0 mm for the brachiocephalic and 6.5 mm – 10.0 mm in the left common carotid. **CONTRAINDICATIONS**: Do not use in patients for whom anticoagulant and antiplatelet therapy is contraindicated. Do not use in patients with a known hypersensitivity to nickel-titanium. Do not use in vessels with excessive tortuosity. Do not use in patients with uncorrected bleeding disorders. Do not use in patients with compromised blood flow to the right upper extremity. Do not use in patients who have arterial stenosis >70% in either the left common carotid artery or the brachiocephalic artery. Do not use in patients whose brachiocephalic or left carotid artery reveals significant stenosis, ectasia, dissection, or aneurysm at the aortic ostium or within 3 cm of the aortic ostium**. WARNINGS**: The SENTINEL System should only be used by physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects, and hazards commonly associated with endovascular procedures. Carefully read all instructions and labeling prior to use. Observe all warnings, cautions, and precautions noted throughout these instructions. Failure to do so may result in complications. Refer to the instructions for use supplied with any interventional device to be used in conjunction with the SENTINEL System for their intended uses, sizing, warnings, and precautions. The appropriate antiplatelet/anticoagulation therapy should be administered pre- and post-procedure in accordance with standard medical practice. Prior to use, the packaging and product should be inspected for signs of damage. Never use damaged product or product from a damaged package. Never advance or withdraw the SENTINEL System without proper fluoroscopic guidance or against resistance until the cause is determined. Advancing with such resistance may lead to embolization of debris, and vessel and/or device damage. It is recommended that the patency of the right radial or brachial artery be assessed prior to the introduction of the SENTINEL System. **PRECAUTIONS:** Do not forcefully bend or reshape the Articulating Sheath of the SENTINEL System. This may cause device damage. Do not use the product if the packaging sterile barrier has been damaged or compromised. Improper bending of the SENTINEL System may damage the catheter. Do not re-sterilize or reuse on another vessel or patient. . **ADVERSE EVENTS:** Possible adverse events associated with SENTINEL System use and application procedure include, but are not limited to, the following: Access Site Complication/Injury, Angina, Bleeding, Death, Dissection, Embolism, Emergent Surgery, Hematoma, Ischemia, Infection, Myocardial Infarction, Renal Insufficiency, Stroke, and Vessel Injury **CAUTION**: Prior to use, please see the complete “Directions for Use” for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator’s Instructions.

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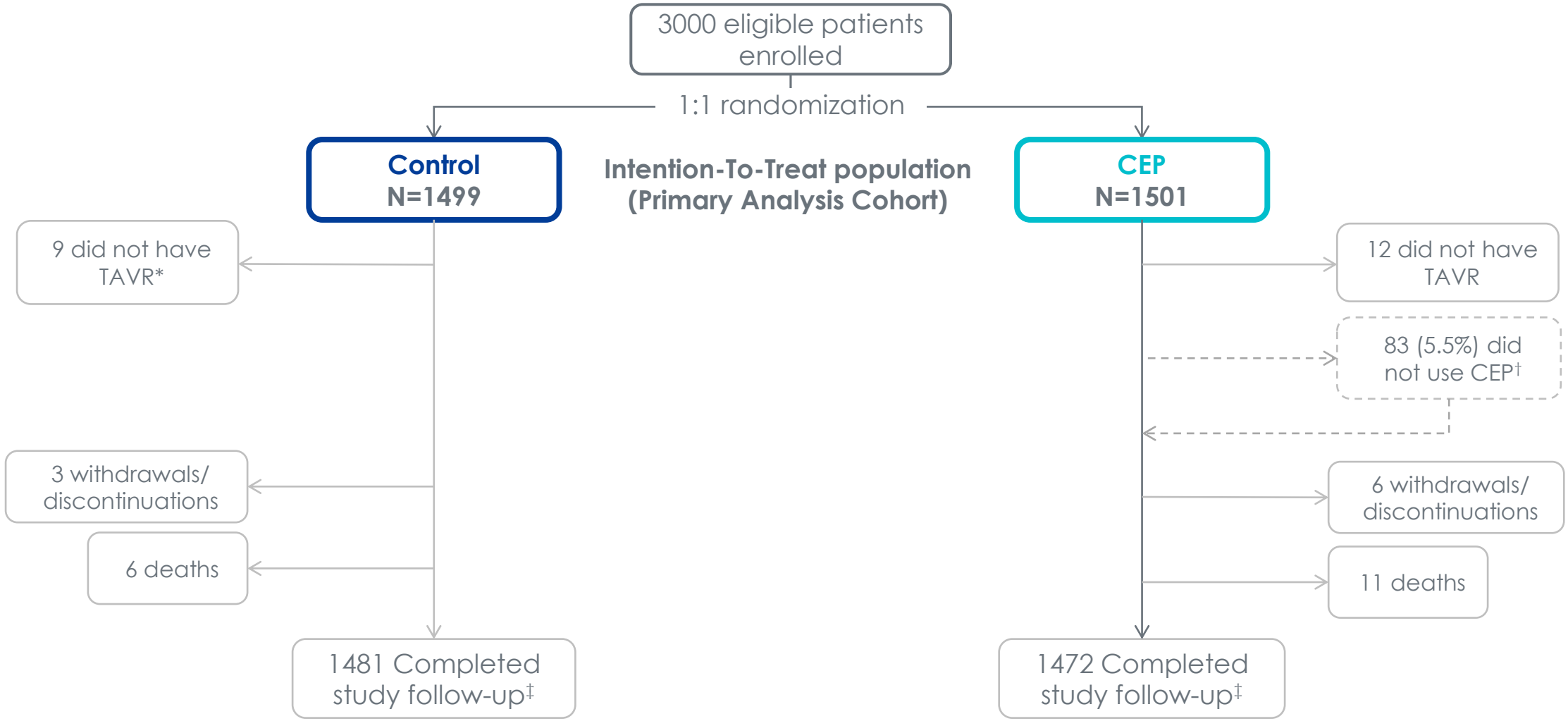
Back-Up

Study Flow



* One patient experienced a stroke post-randomization, leading to cancellation of planned TAVR procedure; patient died within 30 days.
† CEP was not used due to radial/brachial access issues (spasm/tortuosity) in 42 patients, due to brachiocephalic / subclavian tortuosity in 31 patients, and due to other reasons (eg, other use for radial access, PI discretion, etc.) in 10 patients.
‡ Data collection continued through hospital discharge/72h post-TAVR (whichever came first) in all subjects; subjects diagnosed with post-procedural stroke were followed for 30±7 days post stroke.

Baseline Demographics & Risk Scores

	Control (N=1499)	CEP (N=1501)	P-value
Age; yr	78.9±7.8	78.9±8.0	0.9543
Female Sex	37.8% (566)	42.0% (631)	0.0167
EuroSCORE II; %	4.3±5.2	4.6±5.1	0.2665
Society of Thoracic Surgeons score, %	3.4±2.8	3.3±2.7	0.7056
Society of Thoracic Surgeons score <3	58.2% (862)	55.6% (823)	0.1540
Surgical Risk (per Heart Team)			
Extreme/High Risk	30.4% (456)	30.4% (457)	0.6989
Intermediate Risk	34.2% (512)	33.2% (499)	0.5974
Low risk	35.4% (531)	36.3% (545)	0.6131
Native Valve Calcification Severity (site-reported)			0.3429
None/Mild	15.2% (215/1417)	16.2% (227/1398)	
Moderate	29.5% (418/1417)	29.3% (385/1398)	
Severe/Extreme	55.3% (784/1417)	54.4% (760/1398)	
CHA_2DS_2-VASC score	4.2±1.3	4.2±1.3	0.6740

More women were in the CEP arm

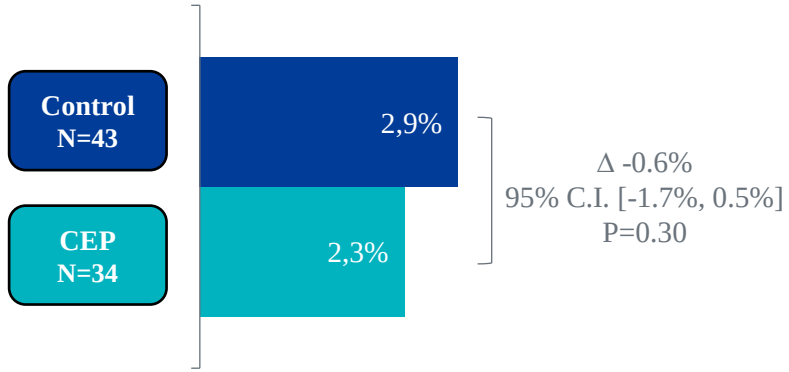
Operative risk was well-balanced

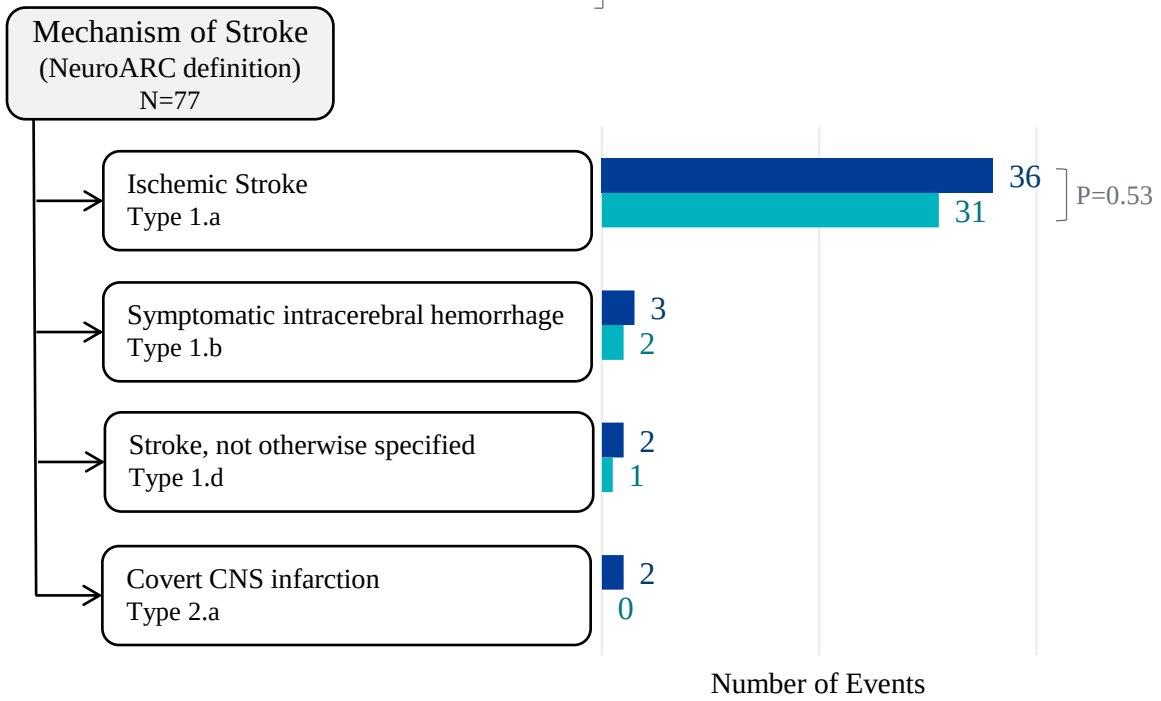
High degree of valvular calcification

All values are % (n) or mean [±SD] (n), unless otherwise indicated.

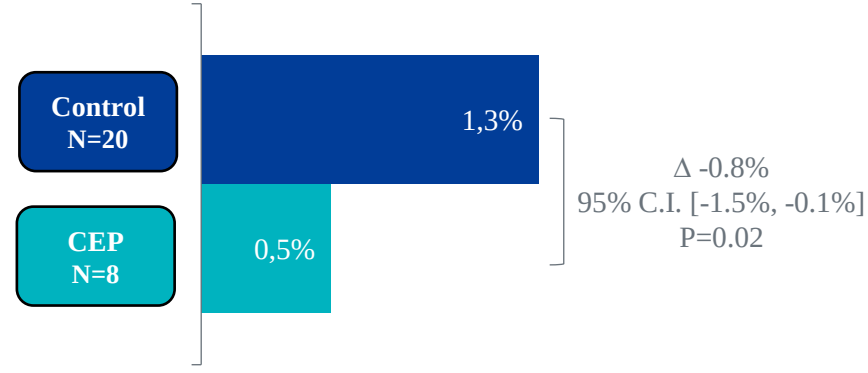
Stroke Rate and Mechanism of Stroke

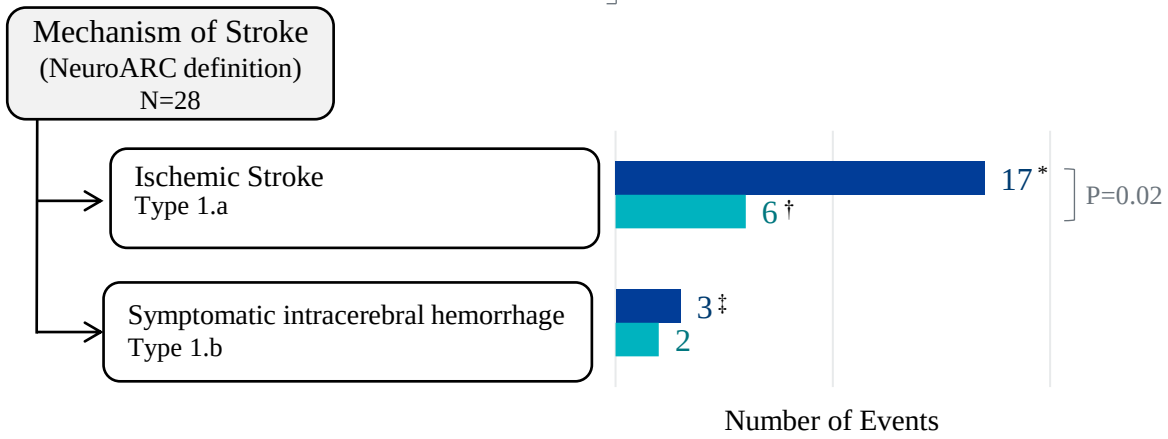
A. All Stroke





B. Disabling Stroke





*1 patient experienced an aortic dissection
†1 patient did not have CEP used; valve embolization occurred in 1 patient; 1 patient experienced clinical symptoms consistent with stroke, but unable to perform MRI; 2 patients experienced a stroke in the vertebral territory (unprotected vessel); 1 patient experienced a stroke in the left MCA territory (protected vessel);
‡1 patient did not undergo TAVR

Data on File.

Clinical Outcomes at Discharge

ITT population

Event ≤72 h / Discharge	Control (N=1499)	CEP (N=1501)	P-value
All Stroke (Primary Endpoint)	**2.9% (43)**	**2.3% (34)**	**0.30**
Disabling	1.3% (20)	0.5% (8)	0.02
Non-Disabling	1.5% (23)	1.7% (26)	0.67
All-cause Mortality	0.3% (4)	0.5% (8)	0.25
Cardiovascular Mortality	0.3% (4)	0.5% (8)	0.25
Safety composite (all-cause mortality and all stroke)	3.0% (45)	2.7% (41)	0.66
CEP Access Site-rel. Vasc. Compl. (Major or Minor)	N/A	0.1% (1)	1.00
Acute Kidney Injury (stage 2 or 3)	0.5% (7)	0.5% (8)	0.80

All values are % (n), unless otherwise indicated.

Data on File.

Neurologic Outcomes at Discharge

ITT population

Event ≤72 h / Discharge	Control (N=1499)	CEP (N=1501)	P-value
Neurological complications (composite of all stroke, TIA, and delirium)	3.7% (55)	3.1% (46)	0.36
Stroke	2.9% (43)	2.3% (34)	0.30
TIA	0.1% (2)	0.1% (1)	0.62
Delirium	0.7% (11)	0.8% (12)	0.83
Neurocognitive protection			
MoCA Total Score	24.5±4.5 (1440)	24.5±4.6 (1445)	0.97

All values are % (n) or mean [±SD] (n), unless otherwise indicated.

Data on File.

Continuing to Invest in Clinical Evidence

British Heart Foundation Randomised Clinical Trial of Cerebral Embolic Protection in Transcatheter Aortic Valve Implantation (BHF PROTECT-TAVI)

Patients undergoing transfemoral TAVI (n=7730)*

1:1 Randomisation

TAVI with CEP (n=3865)

TAVI without CEP (n=3865)

(Standardised questionnaire to assess stroke free status with mandated stroke physician review)

Primary outcome: Discharge or Stroke at 72hrs

Planned interim analysis for efficacy/futility at 50% and 70%

* Powered for control event rate of 3% and effect size of 33%

CAUTION: The law restricts these devices to sale by or on the order of a physician.
Indications, contraindications, warnings, and instructions for use can be found in the product labelling supplied with each device or at www.IFU-BSCI.com. Products shown for INFORMATION purposes only and may not be approved or for sale in certain countries. This material not intended for use in France.