SCOPE I

Final 3-Year Outcomes of a Randomized Trial Comparing a Self-expanding to a Balloon-expandable Transcatheter Aortic Valve

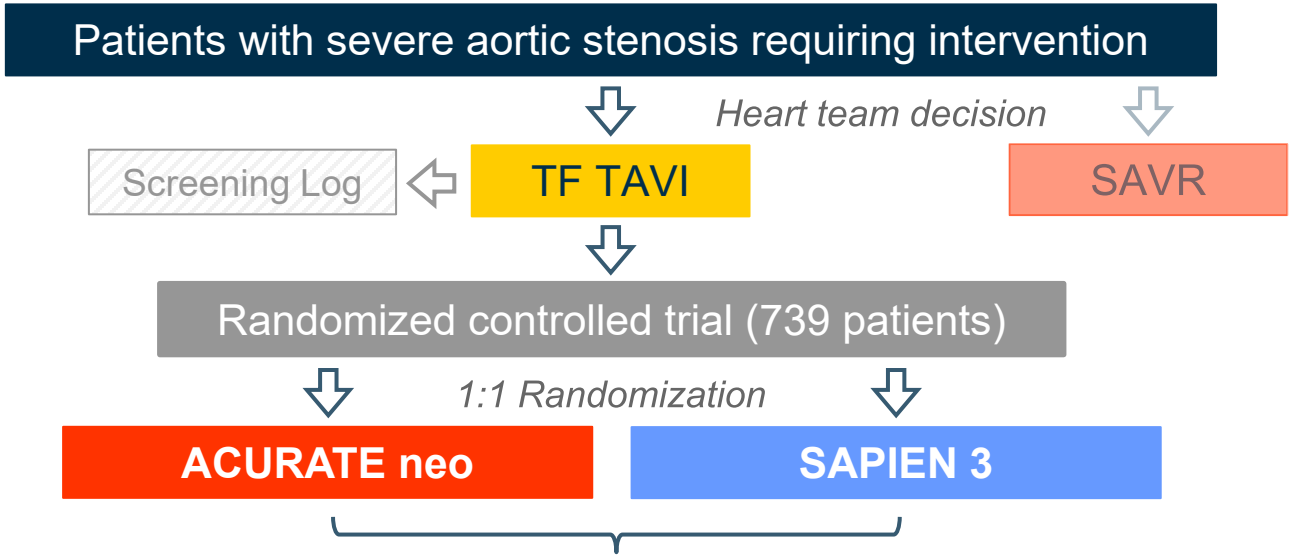
Jonas Lanz
on behalf of the SCOPE I investigators

Disclosure Statement of Financial Interest

I, Jonas Lanz, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Faculty disclosure information can be found on the app

Study Design



Primary endpoint:
Combined early safety & clinical efficacy at 30 days
(VARC-2)

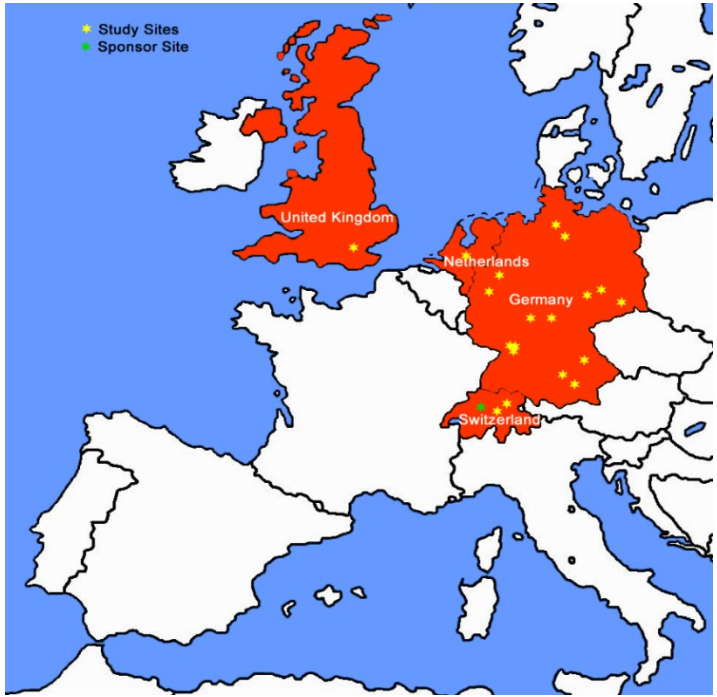
Clinical and echocardiographic follow-up:
at 30-days, 1 year and 3 years

Study Devices

	ACURATE neo Aortic Valve System	SAPIEN 3 Transcatheter Heart Valve System
Frame	Nitinol	Cobalt-chromium
Leaflets	Porcine pericardium, supra-annular	Bovine pericardium, intra-annular
Expansion	Self-expanding (top-down)	Balloon-expandable
Recapturable	No	No
Valve sizes	S (23 mm), M (25 mm), L (27 mm)	23 mm, 26 mm and 29 mm
Sheath inner diameter	18-French	14- and 16-French expandable
Paravalvular leakage reduction	Outer & inner skirt	Outer cuff & inner skirt
CE mark / FDA approval	Sep 2014 / No	Jan 2014 / Jun 2015

Study Sites

20 European sites, 4 Nations: Switzerland (3), Germany (15), Netherlands (1), UK (1)

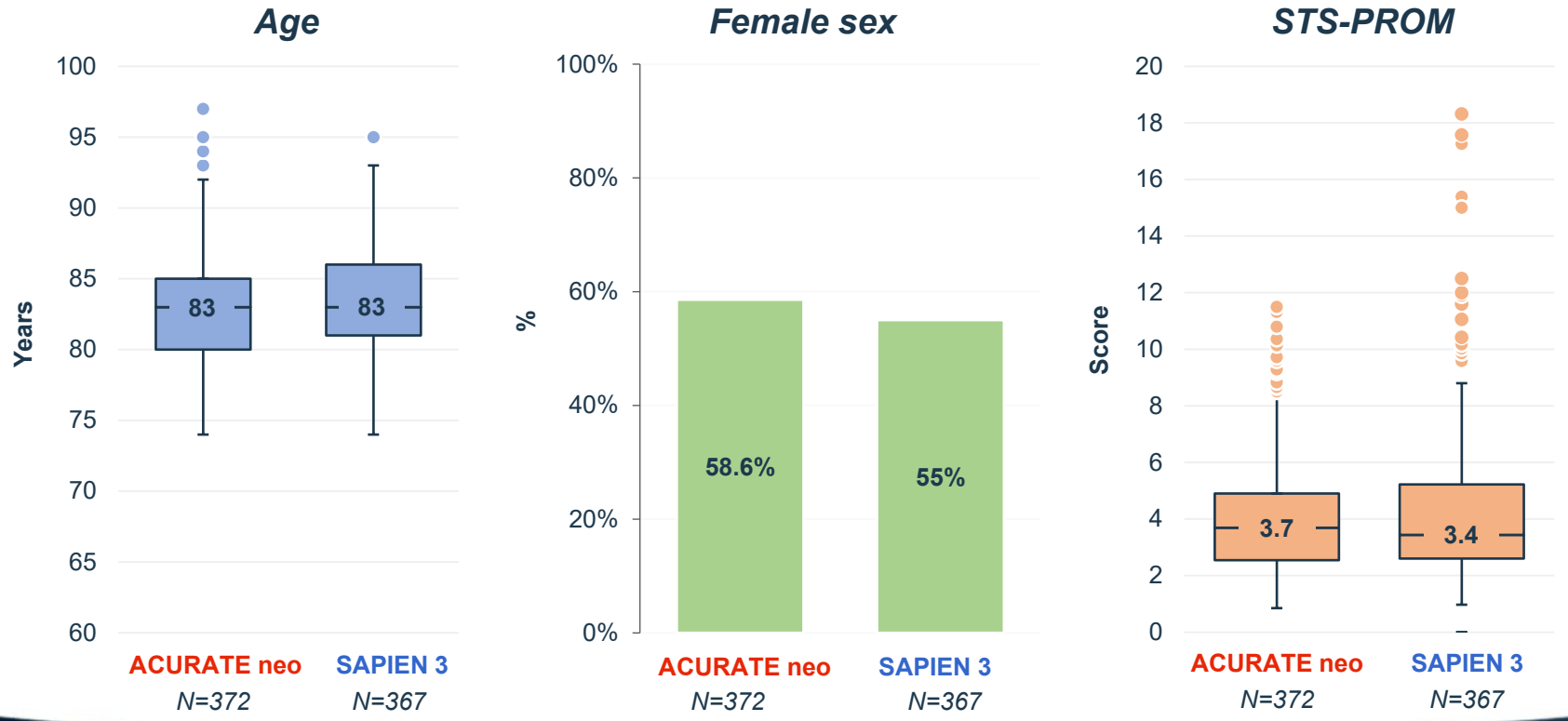


Study sites with 3 year follow-up	Current investigators
Klinikum Augsburg	Eva Hammel, MD
Zentralklinik, Bad Berka	Stefan Richter, MD
Heart and Vascular Center, Bad Bevensen	Christof Burgdorf, MD
Kerckhoff Heart and Thorax Center, Bad Nauheim	Won-Keun Kim, MD (former: Thomas Walther, MD)
Cardio-vascular Center Bad Neustadt,	Sebastian Kerber, MD
St.-Johannes-Hospital, Dortmund	Helge Möllmann, MD
University Heart and Vascular Center, Hamburg	Lenard, Conradi, MD
Heart Center, Dresden	Axel Linke, MD
Helios Klinik, Karlsruhe	Lars Conzelmann, MD
Städtisches Klinikum, Karslruhe	Grotherr Philipp, MD
University Heart Center, Cologne	Stephan Baldus, MD
Heart Center, Leipzig	Holger Thiele, MD
German Heart Centre, Munich	Michael Joner, MD
University Medical Center, Regensburg	Michael Hilker, MD
University Medical Center, Utrecht	Michiel Voskuil, MD
St Thomas` Hospital, London	Simon Redwood, MD
Bern University Hospital, Bern	Thomas Pilgrim, MD
Lucerne Cantonal Hospital, Lucerne	Stefan Toggweiler, MD

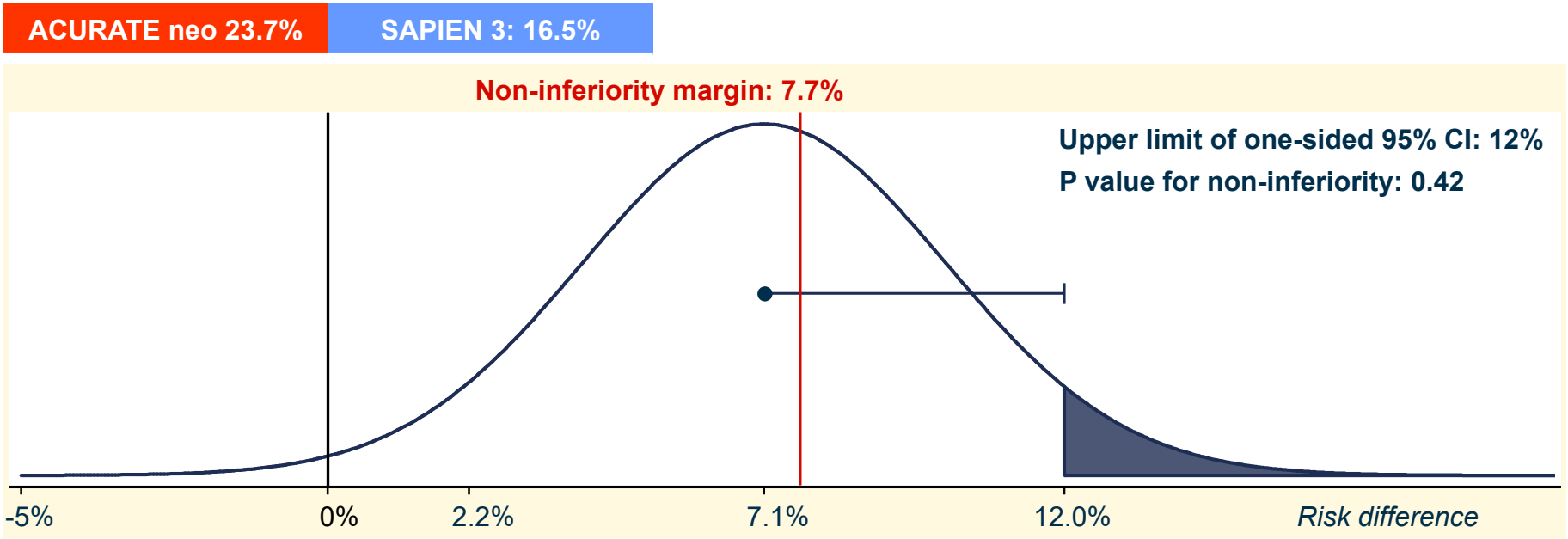
Trial Organization

- **Sponsor:** Department of Cardiology, Bern University Hospital, CH
- **Data management & Monitoring:** University Hospital & Clinical Trials Unit, University of Bern, CH
- **Statistics:** Clinical Trials Unit, University of Bern, CH
- **Clinical Events Committee:** Cardiovascular European Research Center (CERC), Massy, FR
- **Echocardiography Core Laboratory:** Medical Research Development, Hospital La Zarzuela, Madrid, ES
- **Funder:** Boston Scientific, Marlborough, Massachusetts, US

Baseline Characteristics

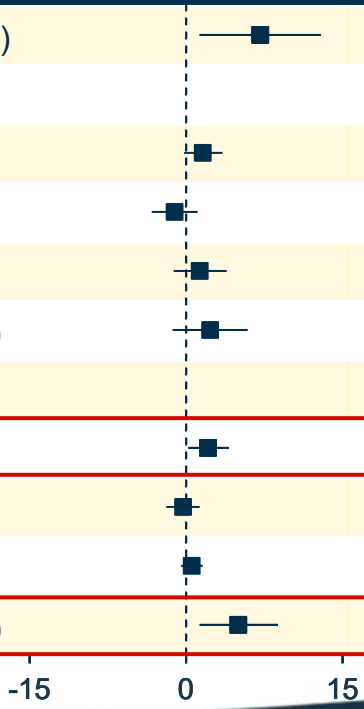


Primary Composite Endpoint at 30 Days



Primary Composite Endpoint at 30 Days

	ACURATE neo	SAPIEN 3	Risk difference % (95%-CI)	P value
	No. of events/total no. (%)			
Primary endpoint *(superiority analysis)*	87/367 (23.7%)	60/364 (16.5%)		0.0156
Single components of primary endpoint				
All-cause death	9/367 (2.5%)	3/364 (0.8%)		0.09
Stroke (any)	7/367 (1.9%)	11/364 (3.0%)		0.33
Life-threatening or disabling bleeding	14/367 (3.8%)	9/364 (2.5%)		0.30
Major vascular complications	29/367 (7.9%)	20/364 (5.5%)		0.21
Coronary artery obstruction requiring intervention	0/367 (0%)	0/364 (0%)		n/a
Acute kidney injury, stage 2 or 3	11/367 (3.0%)	3/364 (0.8%)		0.0340
Re-hospitalization for valve-related dysfunction or CHF	4/367 (1.1%)	5/364 (1.4%)		0.72
Valve-related dysfunction requiring repeat procedure	3/367 (0.8%)	1/364 (0.3%)		0.32
Valve-related dysfunction *(echocardiography)*	35/361 (9.7%)	17/363 (4.7%)		0.0084



Lanz et al. Lancet. 2019;394:1619-1628.

Summary of Background

- **SCOPE I** is a randomized trial comparing the **self-expanding ACURATE neo** to the **balloon-expandable SAPIEN 3** in patients with symptomatic, severe aortic stenosis undergoing **transfemoral TAVI**
- **ACURATE neo did not meet non-inferiority** compared to the SAPIEN 3 device regarding the **primary** composite safety and efficacy **endpoint at 30 days**
- **Differences** between the two TAVI devices were **driven by moderate or severe paravalvular regurgitation** and stage 2 or 3 **acute kidney injury in favor of** the **SAPIEN 3** device

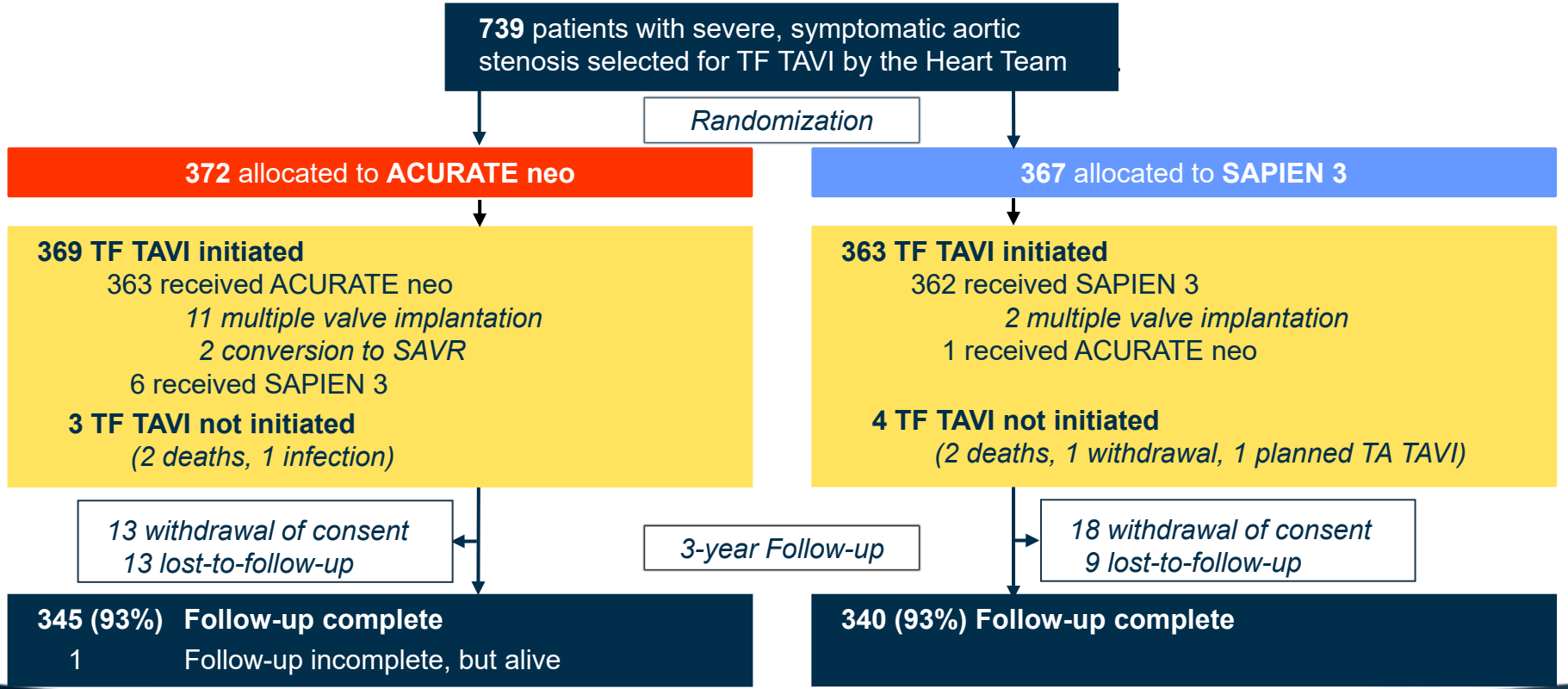
Objective

to evaluate
whether **early** differences in device performance between
a self-expanding and a balloon-expandable device translate into
differences in **clinical outcomes 3 years** after TAVI

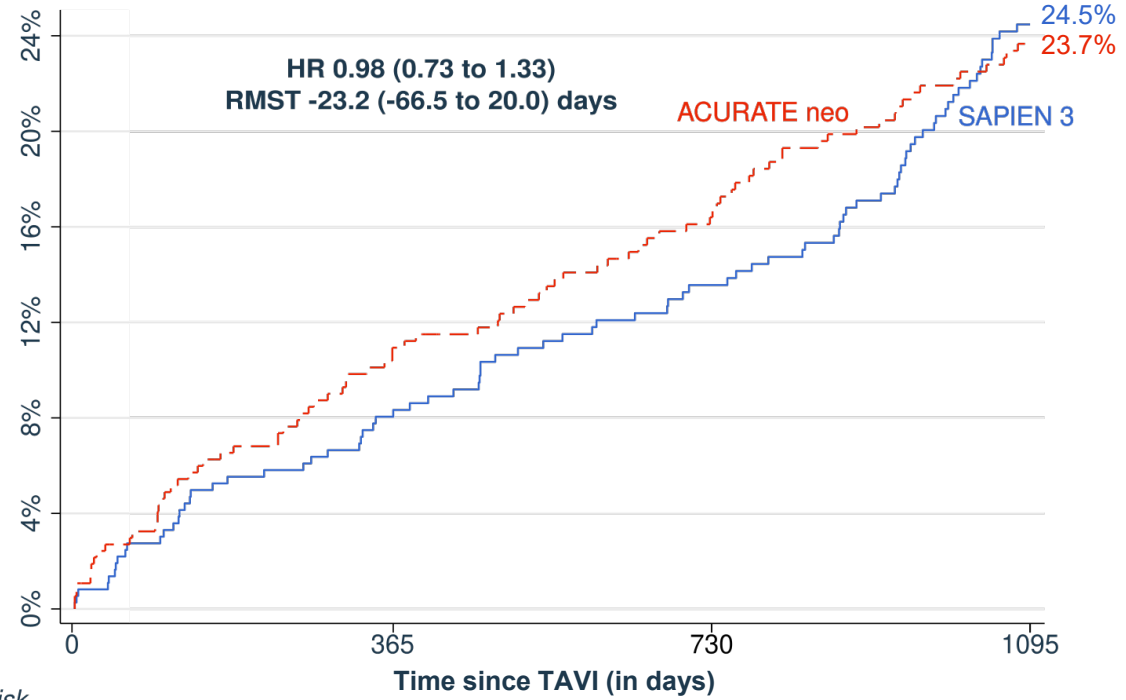
Statistical Methods

- Cumulative incidence curves generated by **Kaplan Meier** method
- Groups compared by **Cox proportional** or **Fine-Gray sub-distribution hazard models**
- **Restricted mean survival time** to assess difference in average survival time
- Clinical outcomes assessed in **intention-to-treat** cohort
- Echocardiographic measures, bioprosthetic valve dysfunction and failure reported for **valve-implant** cohort

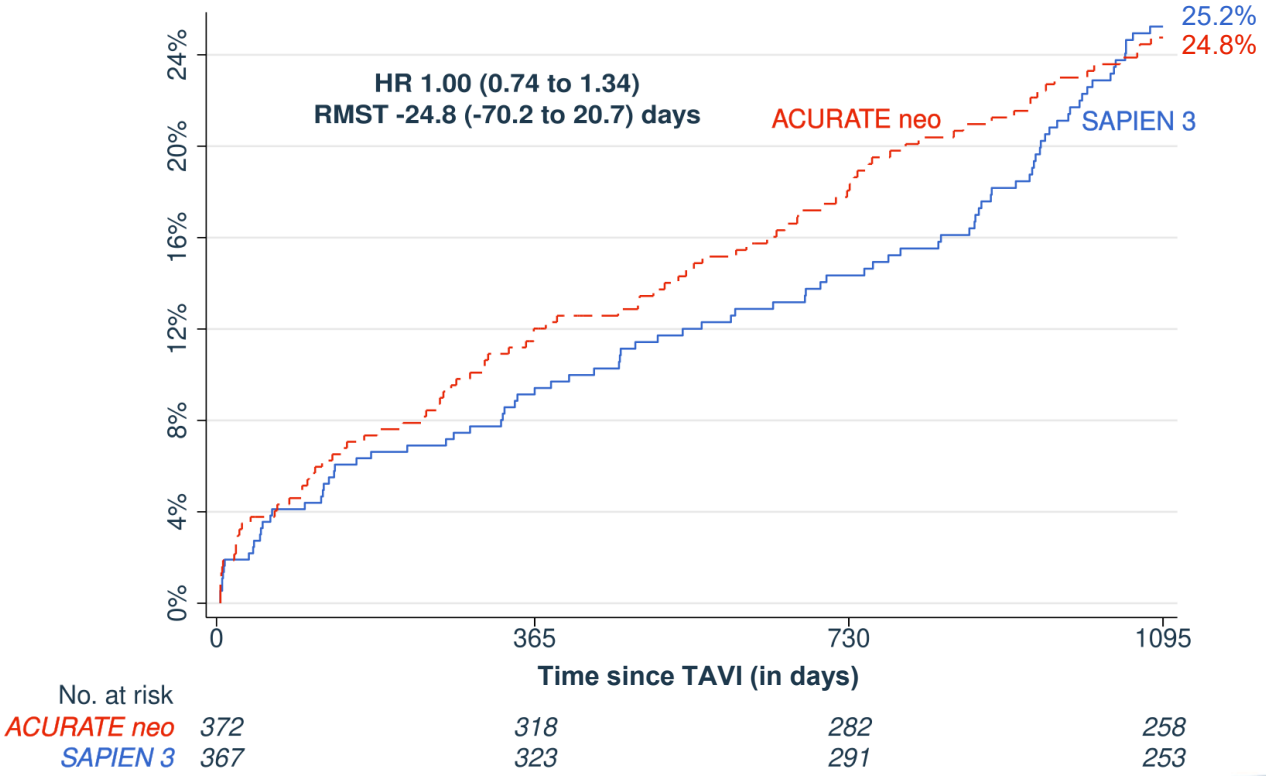
Patient Flow Chart



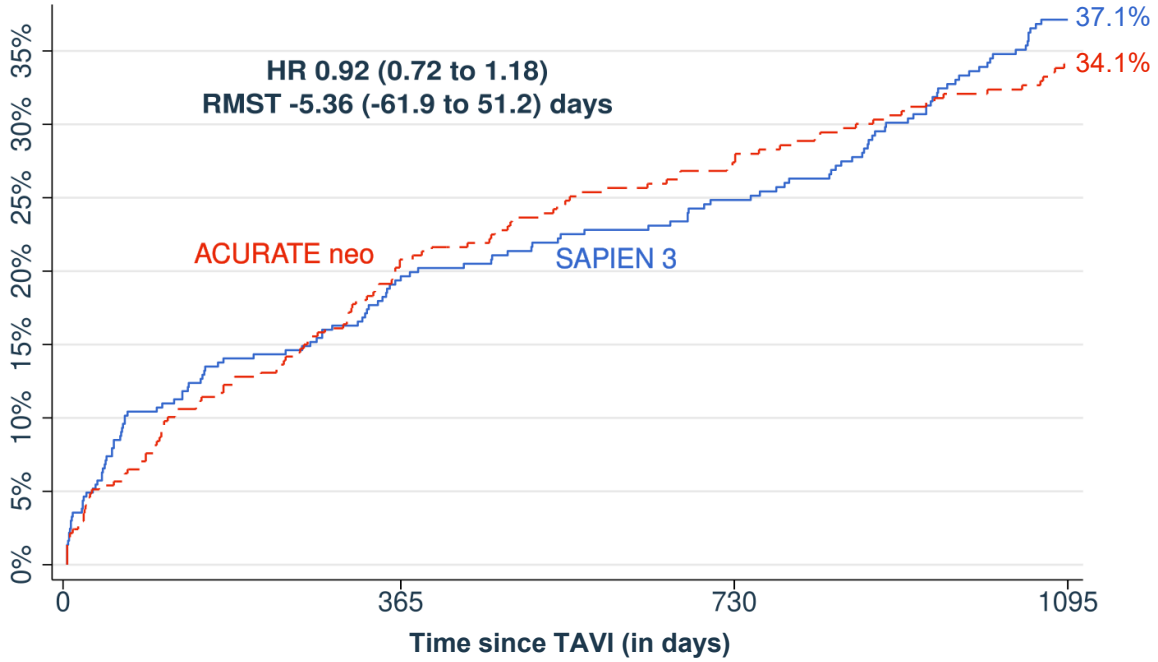
All-cause Death at 3 Years



All-cause Death or Disabling Stroke at 3 Years



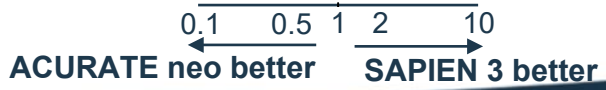
All-cause Death or Stroke or Heart Failure Hospitalization



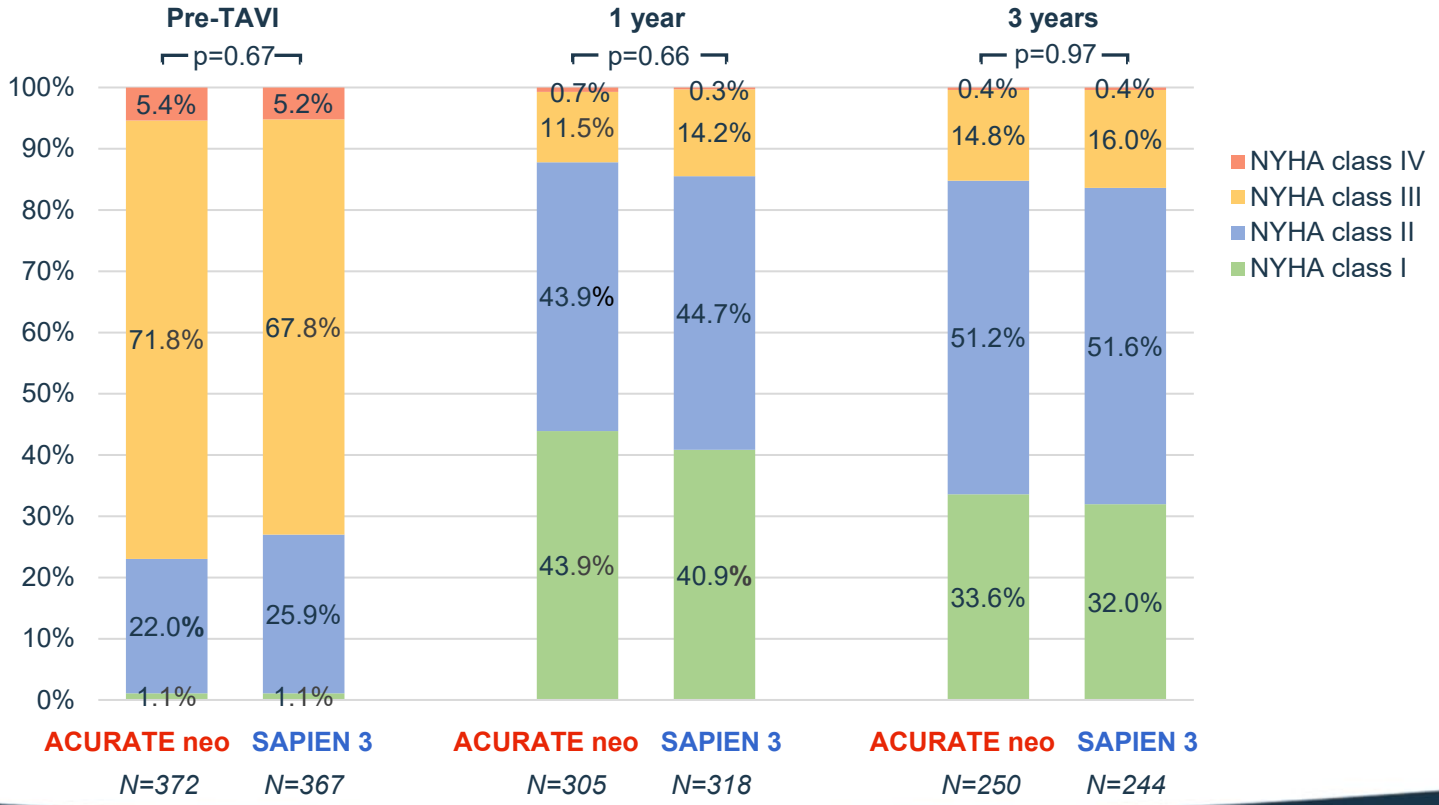
No. at risk				
ACURATE neo	372	286	249	225
SAPIEN 3	367	287	257	214

Clinical Outcomes at 3 Years

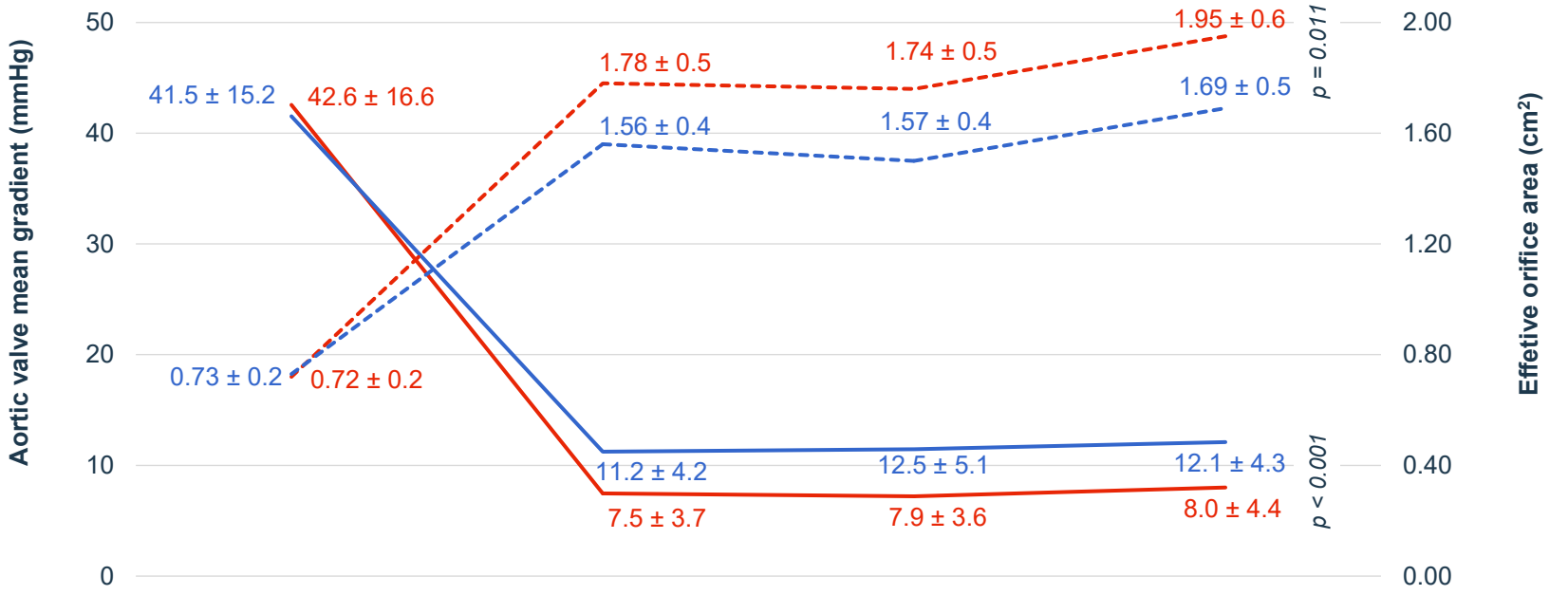
	ACURATE neo	SAPIEN 3	Hazard ratio/Sub-hazard ratio (95% CI)
	no. of events/total no. (%)		
All-cause death	84/346 (24.3%)	85/340 (25.0%)	0.98 (0.73 to 1.33)
Cardiovascular death	58/346 (16.8%)	57/340 (16.8%)	1.01 (0.70 to 1.45)
Non-cardiovascular death	26/346 (7.5%)	28/340 (8.2%)	0.91 (0.53 to 1.56)
Stroke	21/345 (6.1%)	20/343 (5.8%)	1.04 (0.56 to 1.92)
Disabling stroke	12/345 (3.5%)	8/343 (2.3%)	1.48 (0.60 to 3.65)
Non-disabling stroke	12/345 (3.5%)	13/343 (3.8%)	0.92 (0.42 to 2.00)
Hospitalization for valve-related dysfunction/CHF	48/345 (13.9%)	62/342 (18.1%)	0.74 (0.51 to 1.07)
New onset atrial fibrillation/flutter	23/343 (6.7%)	35/341 (10.3%)	0.64 (0.38 to 1.08)
Myocardial infarction	13/343 (3.8%)	7/341 (2.1%)	1.85 (0.74 to 4.67)
New permanent pacemaker	48/307 (15.6%)	51/311 (16.4%)	0.92 (0.62 to 1.37)



Functional Outcomes - NYHA Class



Echocardiography - Mean Gradient & EOA

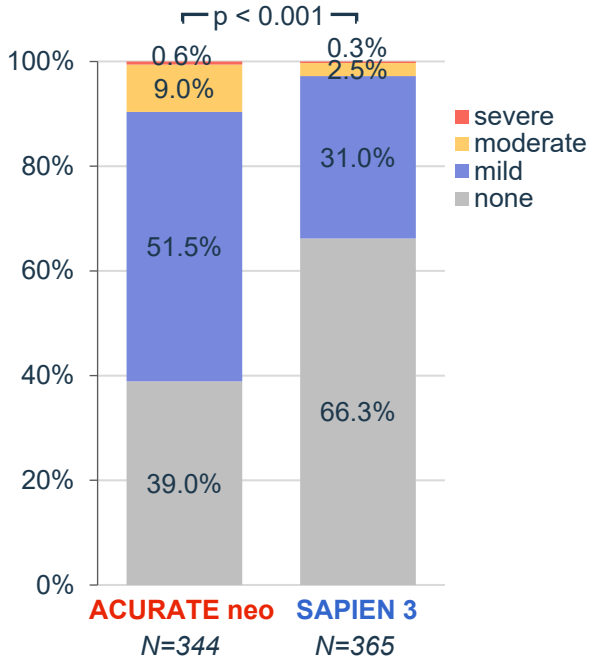


	Baseline*	30 days	1 year*	3 years*	(* site-reported)
ACURATE neo	353/350	347/335	226/175	117/61	N (MG/EOA)
SAPIEN 3	366/363	365/353	257/187	134/63	N (MG/EOA)

Non-Structural Bioprosthetic Valve Dysfunction

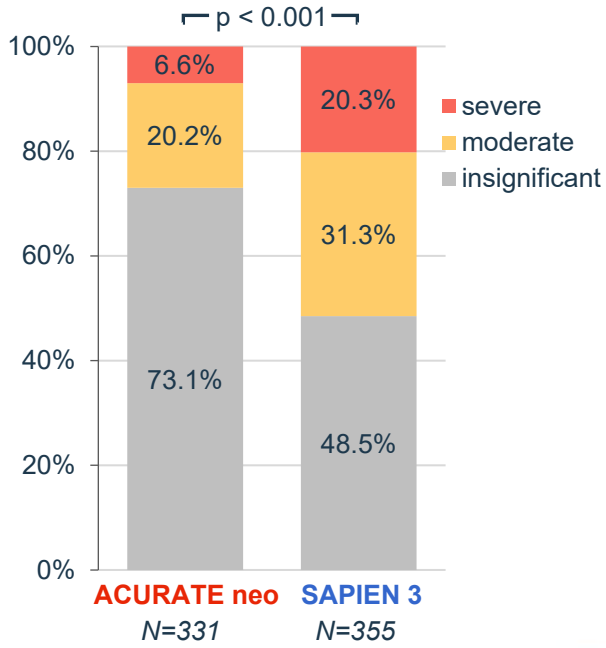
Prosthetic Aortic Valve Regurgitation

(at 30 days)



Prosthesis-patient mismatch

(at 30 days)



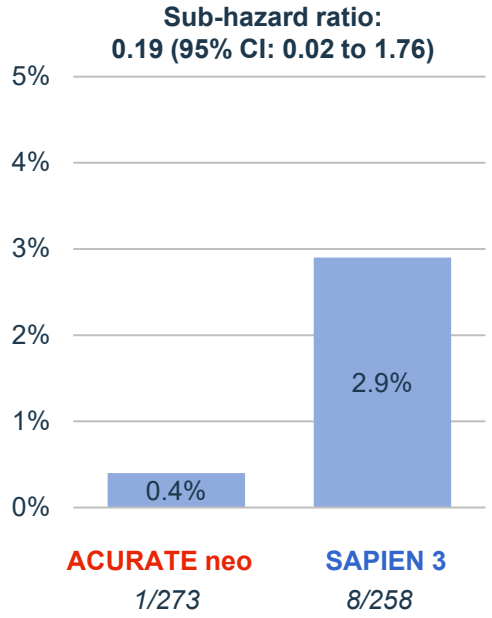
Echocardiographic Predictors of All-cause Death at 3 Years

	Baseline *(pre-TAVI)*	***30-day***
Multivariabel models*	***Hazard ratio (95% CI)***	***Hazard ratio (95% CI)***
LVEF, %	1.00 (0.98 to 1.01)	0.99 (0.97 to 1.00)
Mitral stenosis, moderate or severe	**2.87 (1.43 to 5.8)**	**2.62 (1.25 to 5.51)**
Mitral regurgitation, moderate or severe	0.91 (0.59 to 1.41)	**1.72 (1.08 to 2.74)**
Tricuspid regurgitation, moderate or severe	1.20 (0.76 to 1.89)	0.95 (0.58 to 1.55)
Aortic valve mean gradient, mmHg	0.99 (0.98 to 1.00)	NA
Right ventricular function, impaired	1.35 (0.86-2.12)	NA
Patient-prosthesis mismatch, severe	NA	0.93 (0.65 to 1.31)
Prosthetic aortic regurgitation, moderate or severe	NA	1.07 (0.53 to 2.13)

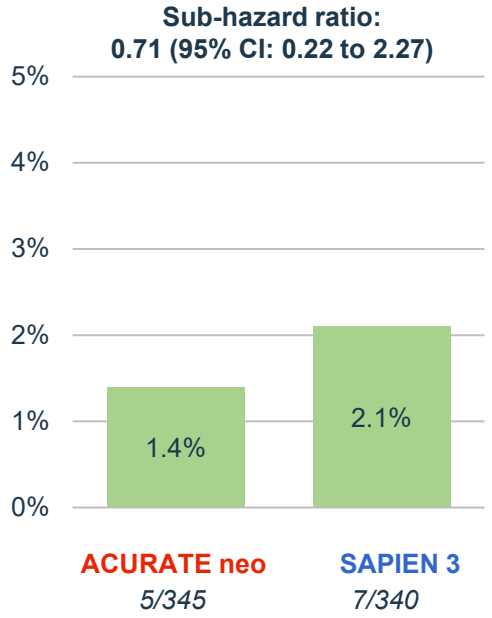
** Adjusted for age, sex, diabetes mellitus, chronic obstructive pulmonary disease, history of atrial fibrillation or flutter, creatinine, STS-PROM score, NYHA class III or IV*

Acquired Bioprosthetic Valve Dysfunction

Structural valve deterioration
*(with at least moderate HVD)**

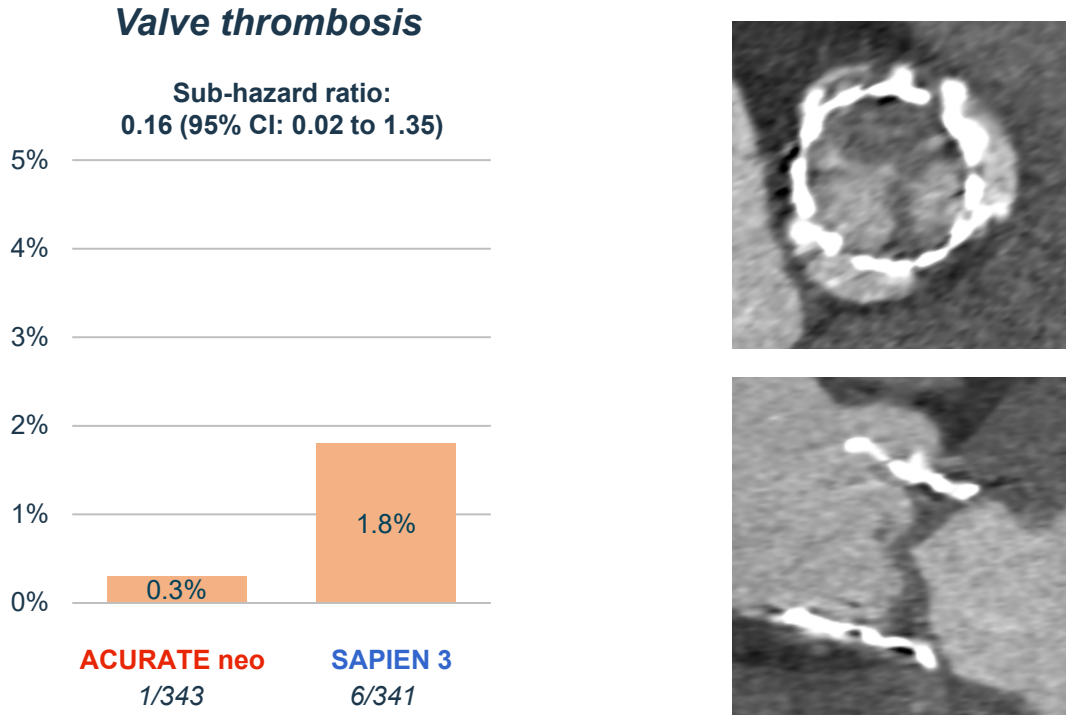


Endocarditis



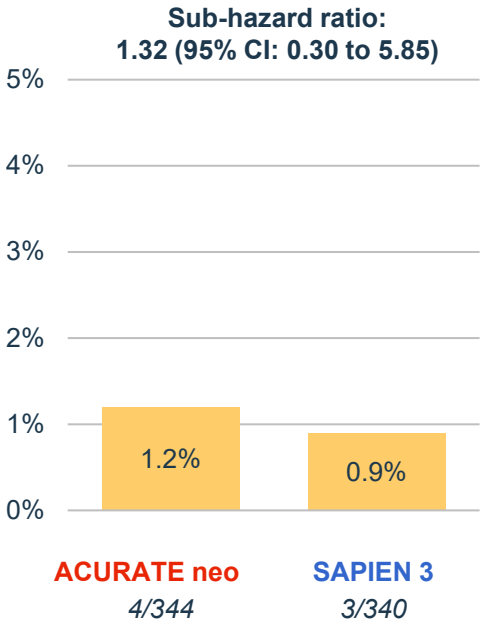
** increase in mean transvalvular gradient ≥10 mmHg resulting in a mean gradient ≥20 mmHg not due to valve thrombosis or endocarditis*

Acquired Bioprosthetic Valve Dysfunction

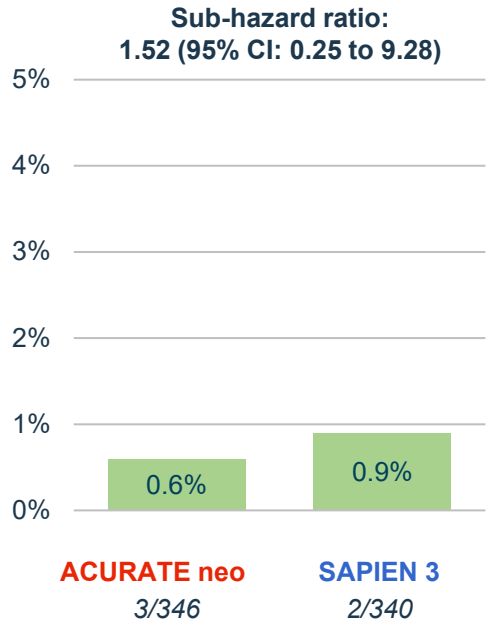


Bioprosthetic Valve Failure

Aortic valve re-intervention



*Valve-related death**



** all due to infective endocarditis*

Limitations

- Study not powered for clinical endpoints at 3 years
- Findings may not apply to low-risk populations with higher life-expectancy
- Echocardiograms at 3 years not core lab adjudicated and structural valve deterioration based on evolution of mean gradients only without morphological criteria
- New device iterations in clinical use or under randomized trial evaluation

Conclusion

Early differences in procedural outcomes and valve performance between the ACURATE neo and SAPIEN 3 devices **did not translate into significant differences in clinical outcomes or bio-prosthetic valve failure at 3 years** in an elderly population at intermediate surgical risk undergoing TAVI