SCOPE I: One-year outcomes of a randomized trial comparing a self-expanding to a balloon-expandable transcatheter aortic valve

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on behalf of the SCOPE I investigators

Disclosure Statement of Financial Interest

- I, Thomas Walther, have no personal financial conflicts do disclose in relation to this presentation

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 TAVR.
- **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 TAVR devices were ***driven by moderate or severe paravalvular regurgitation*** and stage 2 or 3 ***acute kidney injury*** in favor of the SAPIEN 3 device.

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

Statistical Methods

- Sample size: ***739 patients*** (based on pre-specified primary composite endpoint and non-inferiority margin at 30 days)
- ***Randomization stratified*** by STS-PROM category and site
- ***Cumulative incidence curves*** of clinical events generated by **Kaplan Meier method**, groups compared by **Cox proportional hazards regression** adjusted for STS-PROM strata
- ***Clinical outcomes*** assessed in **intention-to-treat cohort**
- ***Echocardiographic data*** reported for **valve-implant cohort**

Trial Organization

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

Study Sites

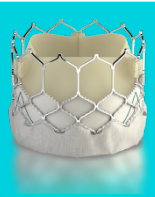
20 European sites, 4 Nations: *Switzerland (3), Germany (15), Netherlands (1), UK (1)*

Study Site	Local Principal Investigator
Klinikum Augsburg	Christian Thilo, 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 Thomas Walther, MD
Cardio-vascular Center Bad Neustadt,	Sebastian Kerber, MD
St.-Johannes-Hospital, Dortmund	Helge Möllmann, MD
Heart Center, Dresden	Axel Linke, MD
Helios Klinik, Karlsruhe	Lars Conzelmann, MD
St. Vincentius-Kliniken, Karlsruhe	Alexander Würth, MD
Städtisches Klinikum, Karlsruhe	Gerhard Schymik, 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	Pieter Stella, MD
St Thomas` Hospital, London	Simon Redwood, MD
Bern University Hospital, Bern	Thomas Pilgrim, MD
Lucerne Cantonal Hospital, Lucerne	Stefan Toggweiler, MD
University Hospital Zurich, Zurich	Maurizio Taramasso, MD

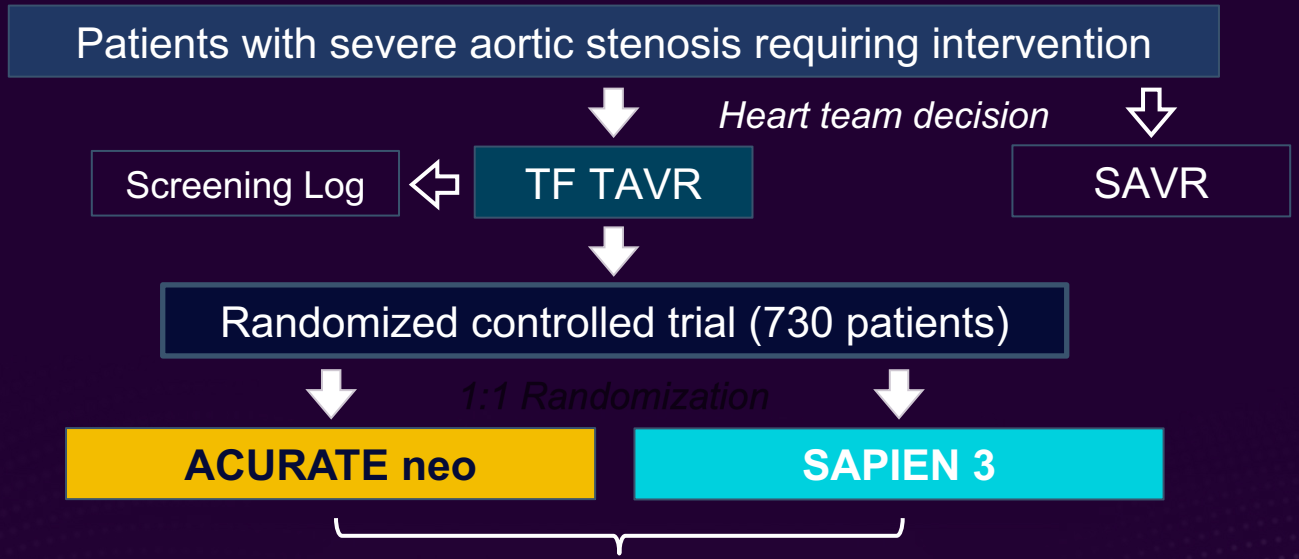
Objectives

To compare the ***self-expanding ACURATE neo*** to the ***balloon-expandable SAPIEN 3*** transcatheter heart valve system with respect to pre-specified **clinical, functional** and **echocardiographic outcomes at 1 year**

Study Devices

	 **ACURATE neo™** Aortic Valve System *© 2019 Boston Scientific Corporation*	 **SAPIEN 3™** Transcatheter Heart Valve System *© 2019 Edwards Lifesciences Corporation*
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

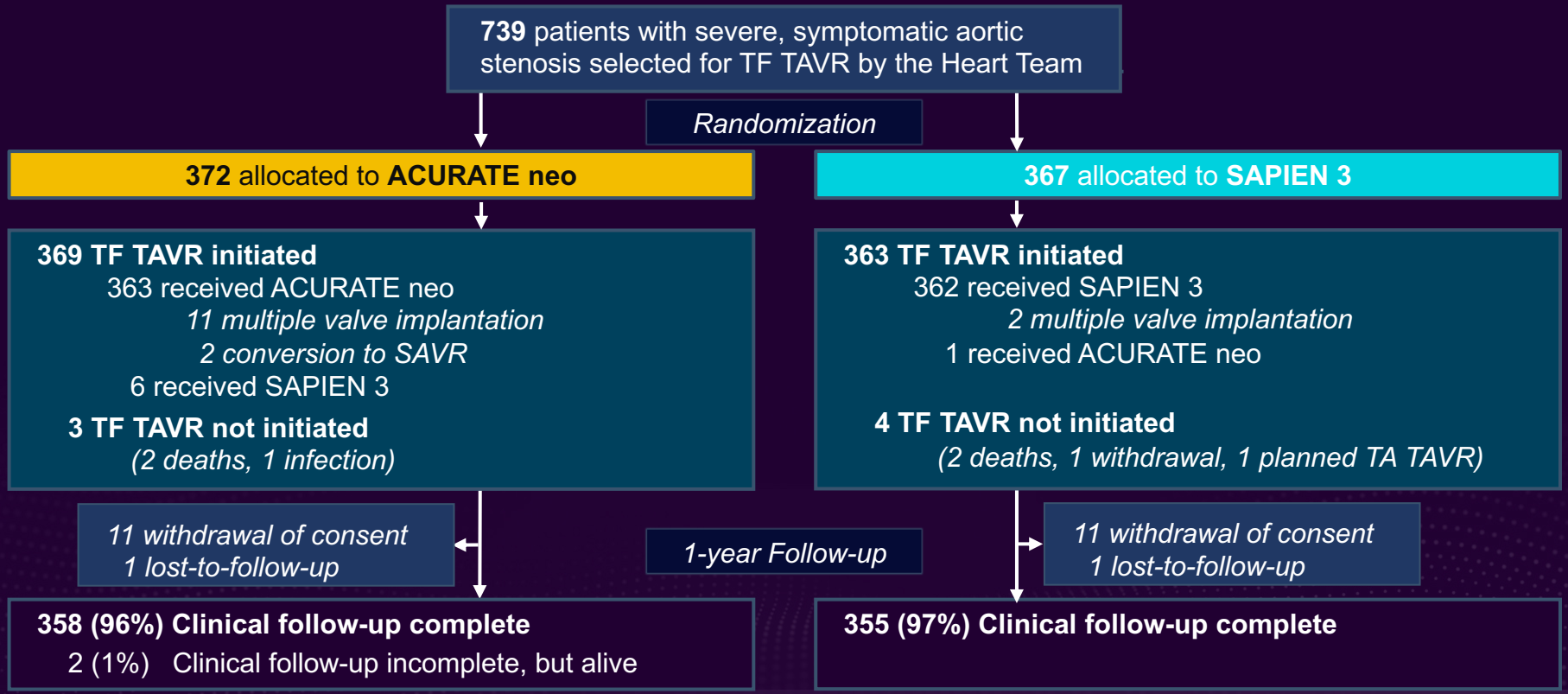
Study Design



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

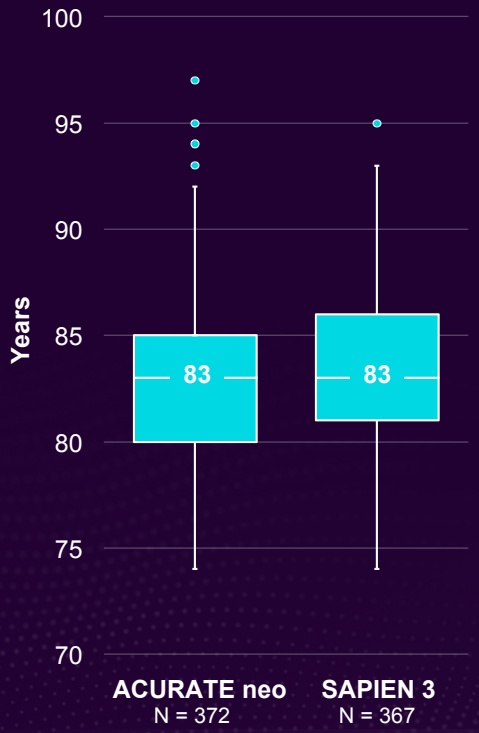
Follow-up: at 30-days, ***1 year*** and 3 years

Patient Flow Chart

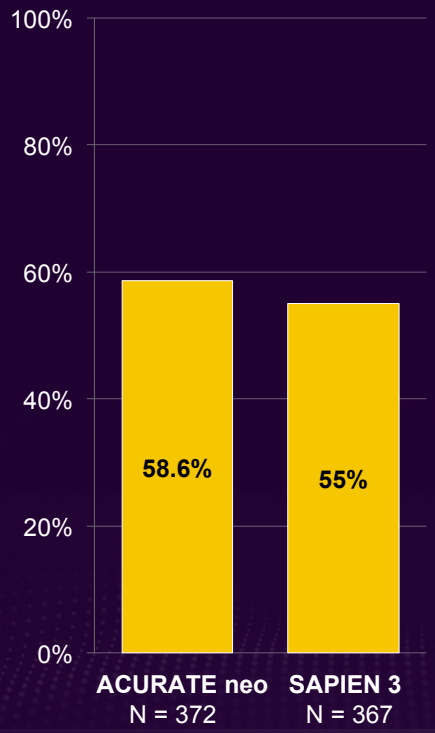


Baseline Characteristics

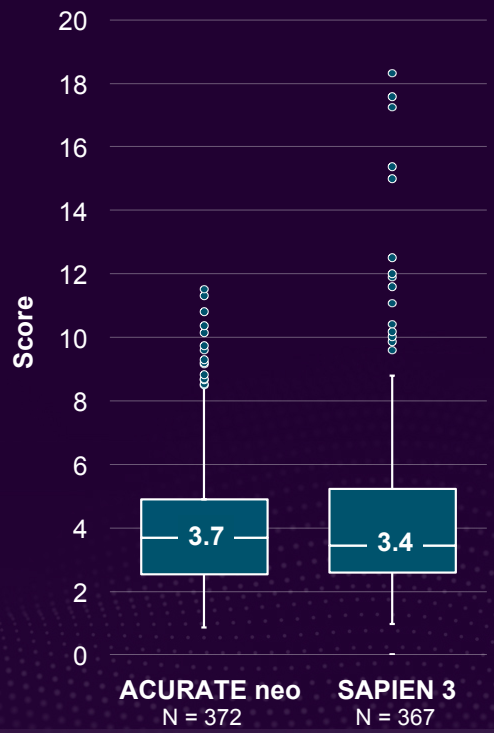
Age



Female sex



STS-PROM



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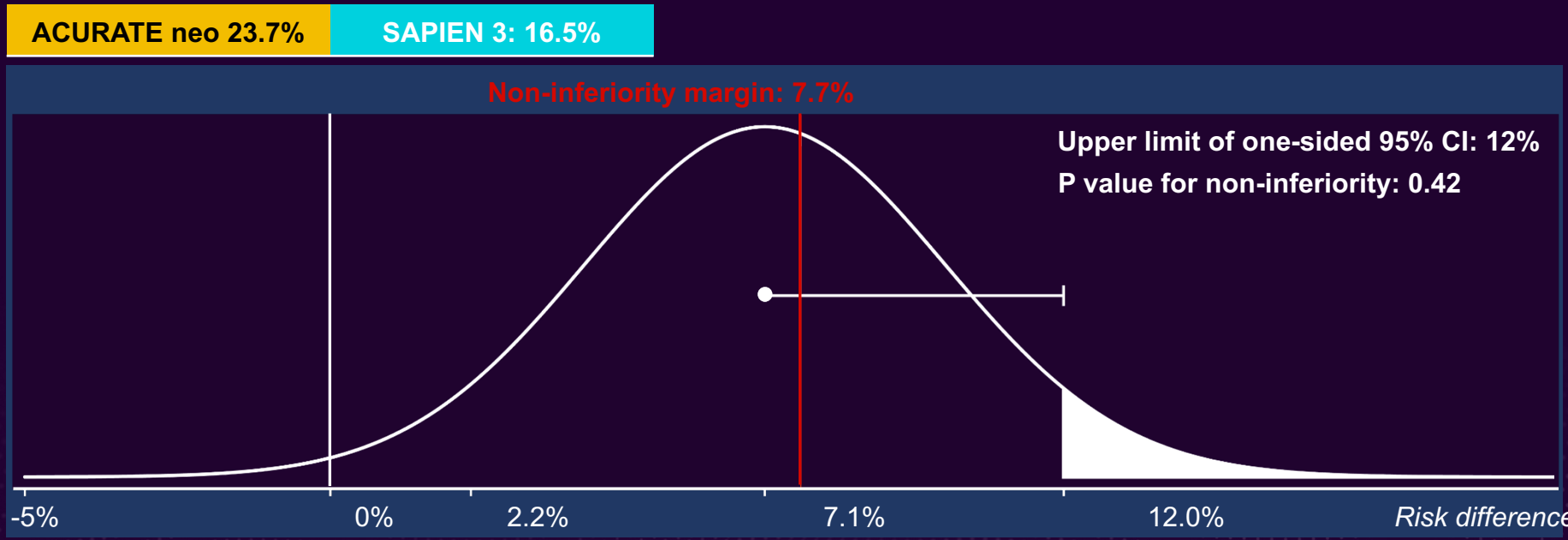
Primary Endpoint at 30 days



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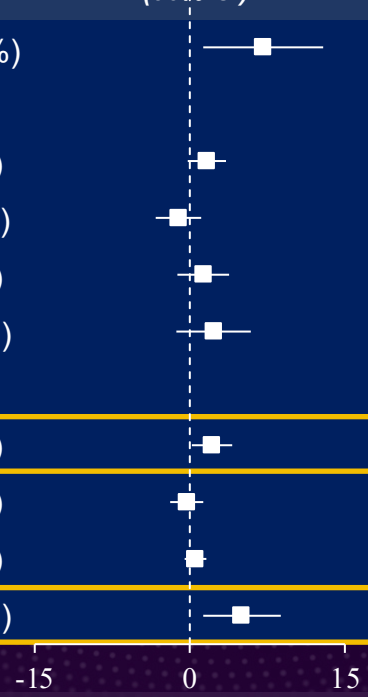
Primary Endpoint Components at 30 days

	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



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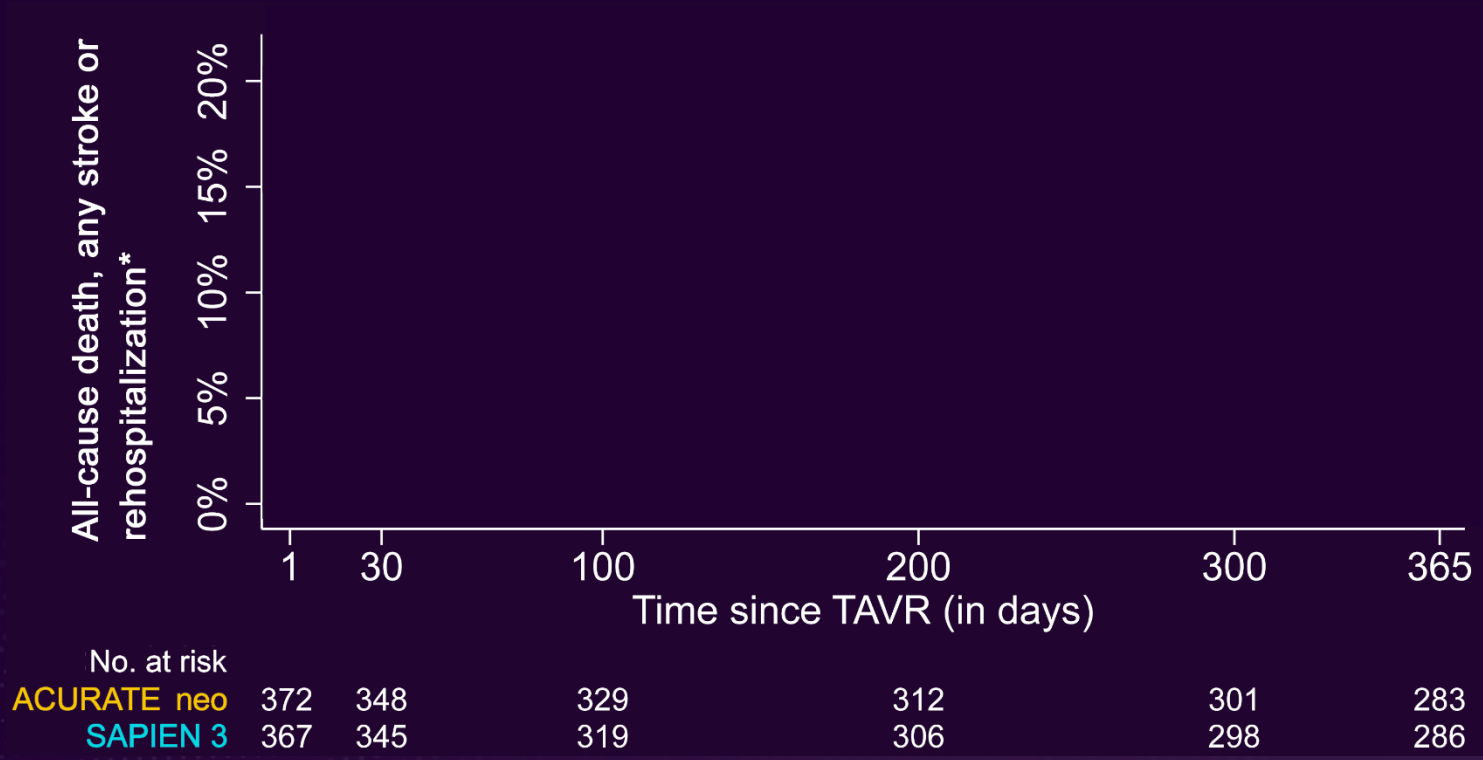
All-cause Death at 1 Year

ACURATE neo	372	358	345	335	327	320
SAPIEN 3	367	361	346	336	332	326

All-cause Death or Disabling Stroke at 1 Year

No. at risk						
ACURATE neo	372	354	342	332	323	316
SAPIEN 3	367	357	341	332	328	322

All-cause Death or Stroke or Rehospitalization* at 1 Year



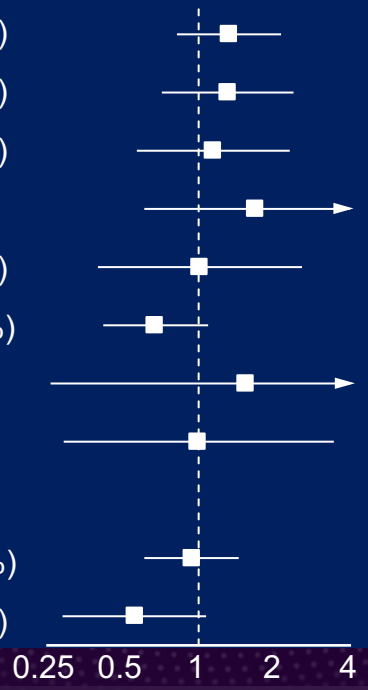
Death by Prosthetic Aortic Regurgitation

	All-cause Death *No. of events/total no. (%)*	Hazard ratio *(95%-CI)*	P value
Moderate/severe** vs. **no AR	3/44 (6.8%) vs. 32/375 (8.5%)	0.84 (0.26 - 2.74)	0.77
Mild** vs. **no AR	22/285 (7.7%) vs. 32/375 (8.5%)	0.96 (0.56 - 1.66)	0.88

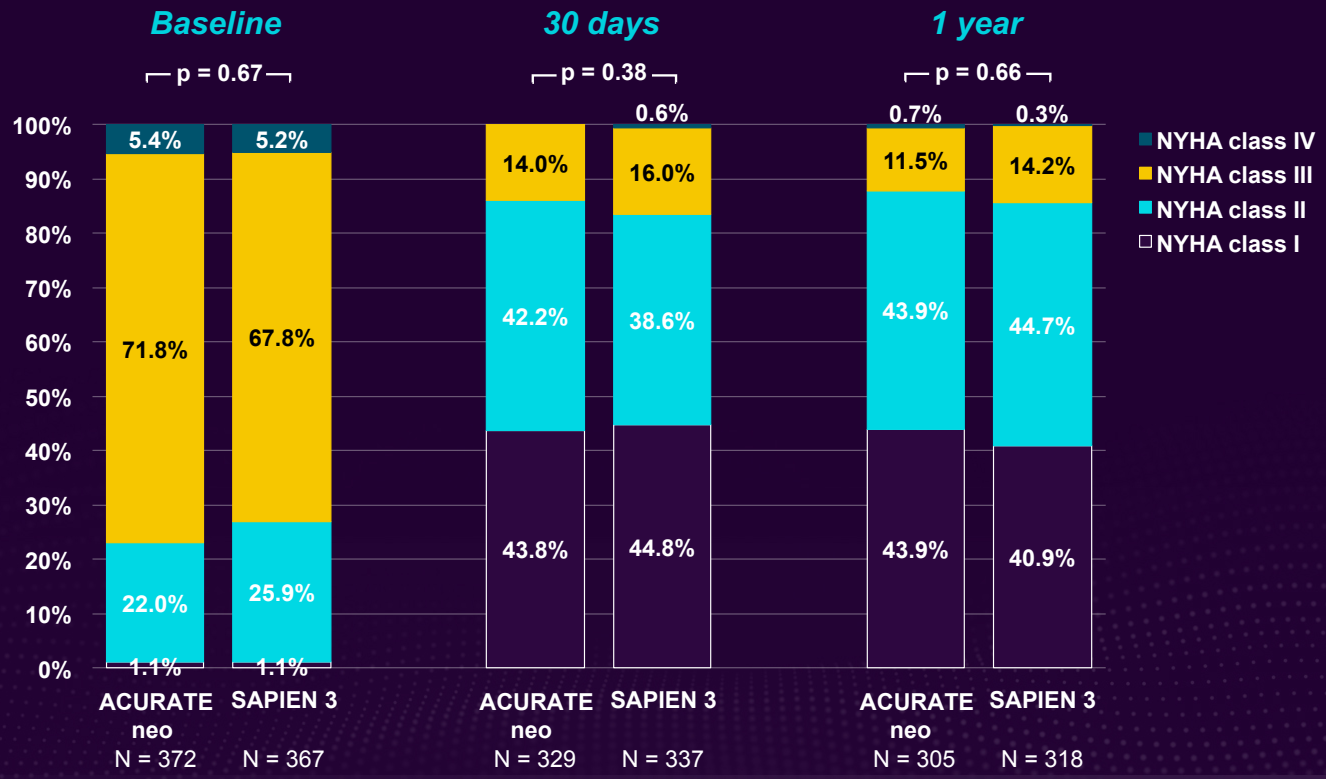
	Cardiovascular Death *No. of events/total no. (%)*	Hazard ratio *(95%-CI)*	P value
Moderate/severe** vs. **no AR	3/44 (6.8%) vs. 17/375 (4.5%)	1.54 (0.45 - 5.28)	0.49
Mild** vs. **no AR	13/285 (4.6%) vs. 17/375 (4.5%)	1.09 (0.53 - 2.26)	0.81

Clinical Outcomes at 1 year

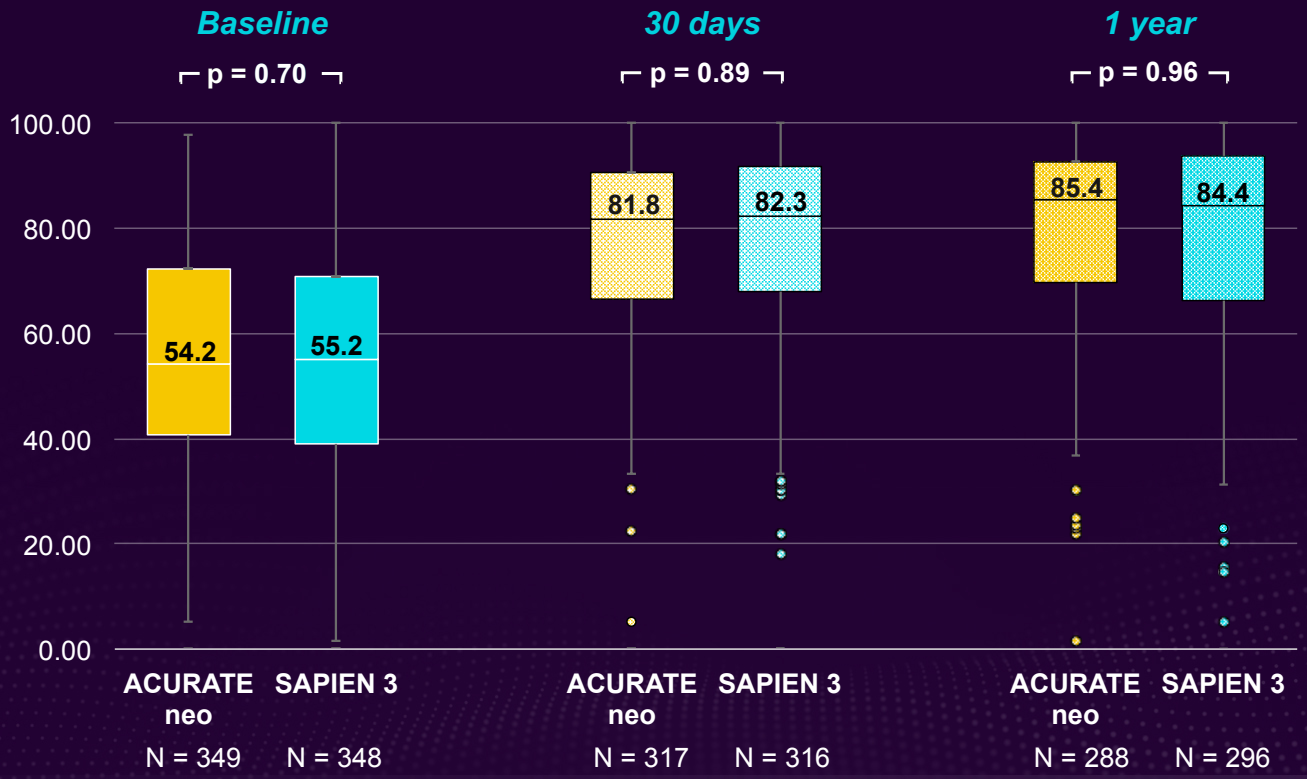
	ACURATE neo	SAPIEN 3	Hazard ratio (95%-CI)	P value
	No. of events/total no. (%)			
All-cause death	40/360 (11.1%)	30/355 (8.5%)		0.25
Cardiovascular death	25/360 (6.9%)	19/355 (5.4%)		0.39
Stroke	17/358 (4.7%)	15/356 (4.2%)		0.71
Disabling stroke	10/358 (2.8%)	6/356 (1.7%)		0.32
Non-disabling stroke	9/358 (2.5%)	30/356 (2.5%)		0.98
Hospitalization for valve-related dysfunction or CHF	28/359 (7.8%)	41/355 (11.5%)		0.10
Valve-related dysfunction requiring repeat procedure	3/358 (0.8%)	2/355 (0.6%)		0.64
Endocarditis	5/360 (1.4%)	5/355 (1.4%)		0.99
Valve thrombosis	0/358 (0.0%)	3/355 (0.8%)		NA
Permanent pacemaker implantation	41/361 (11.4%)	43/357 (12.0%)		0.76
New onset atrial fibrillation/flutter	14/358 (3.9%)	25/355 (7.0%)		0.08



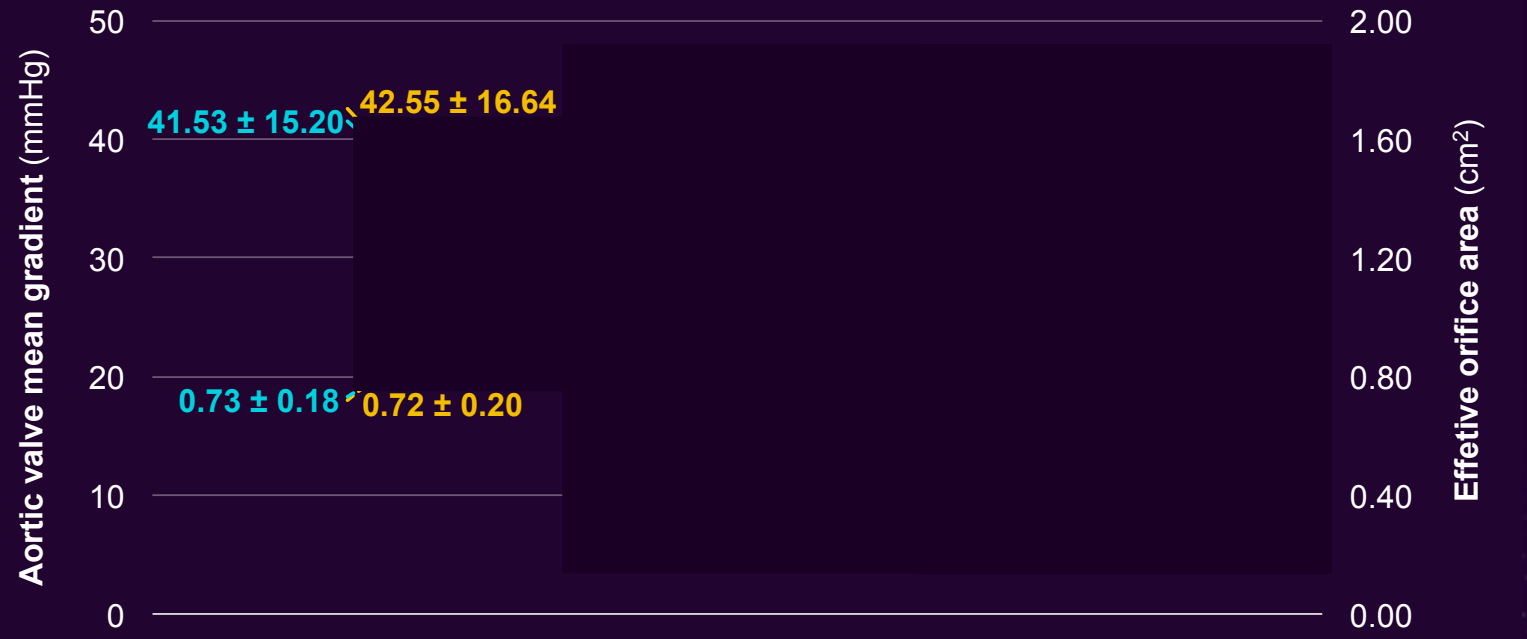
Functional Outcomes – NYHA Class



Functional Outcomes – KCCQ-12

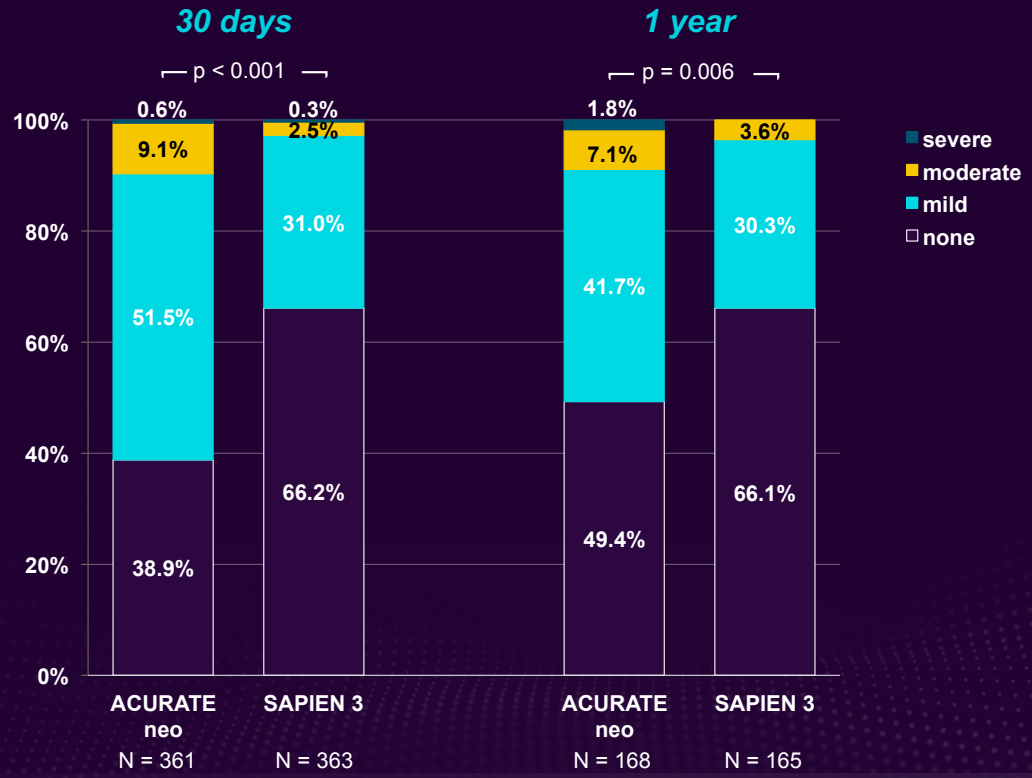


Echocardiography – mean Gradient & EOA



	Baseline*	30 days	1 year	
ACURATE neo	*353/350*	*347/335*	*162/152*	*N (MG/EOA)*
SAPIEN 3	*366/363*	*365/353*	*161/149*	*N (MG/EOA)*

Echocardiography – Aortic Regurgitation



Limitations

- Study not powered for clinical endpoints at 1 year
- Low rate of core laboratory adjudicated echocardiographic data at 1 year
- Lack of patient screening using central core laboratory assessment of baseline multi-slice computed tomographies

Conclusions

- **One-year clinical and functional outcomes** did ***not differ significantly*** between the ACURATE neo and the SAPIEN 3 platform in patients undergoing transfemoral TAVR.
- In terms of **valve performance**, the rate of ***PVR remained higher*** but the hemodynamic profile better with ***lower transprosthetic mean gradients*** and ***higher EOA*** at 1 year in patients treated with ACURATE neo.
- ***Extended follow up data*** will be crucial to determine the impact of the differential valve performance on long-term outcomes.