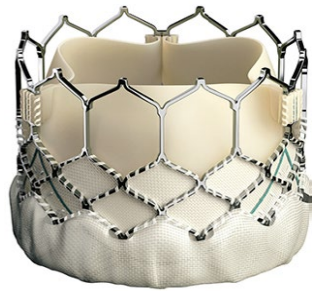
Three-Year Outcomes of the Randomized SCOPE I Trial Comparing the ACURATE *Neo* vs the SAPIEN 3 Transcatheter Heart Valve System in Patients With Symptomatic Severe Aortic Stenosis

Presented by Jonas Lanz at TCT 2022

SCOPE I THV Device Overview

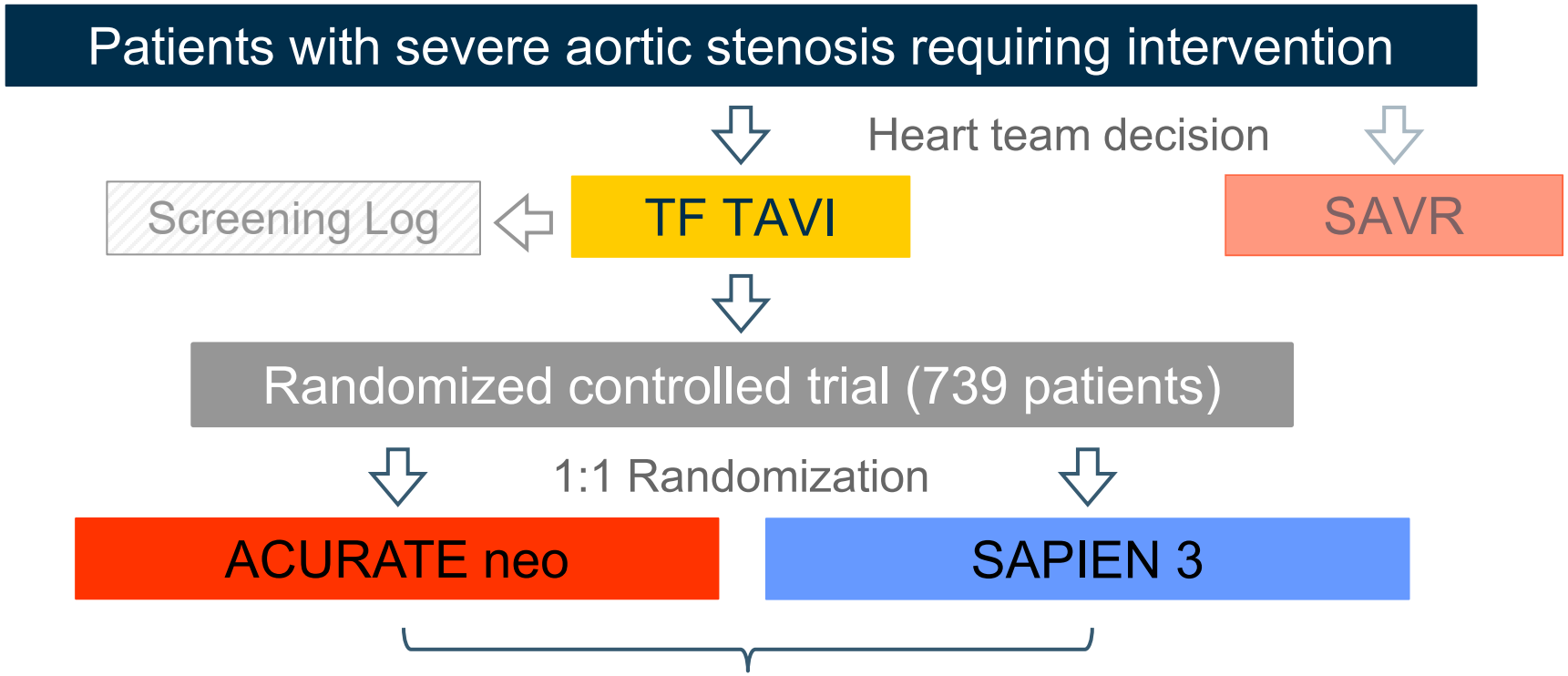
1st Generation* ACURATE *neo*™
Supra Annular Leaflets, Porcine Pericardium
Self-Expanding (Top-down) Nitinol frame



3rd Generation SAPIEN 3 THV
Intra-annular Leaflets, Bovine Pericardium
Balloon-Expanding Cobalt-Chromium Frame

*The 2nd Generation ACURATE *neo2* was not studied in SCOPE 1

Study Design

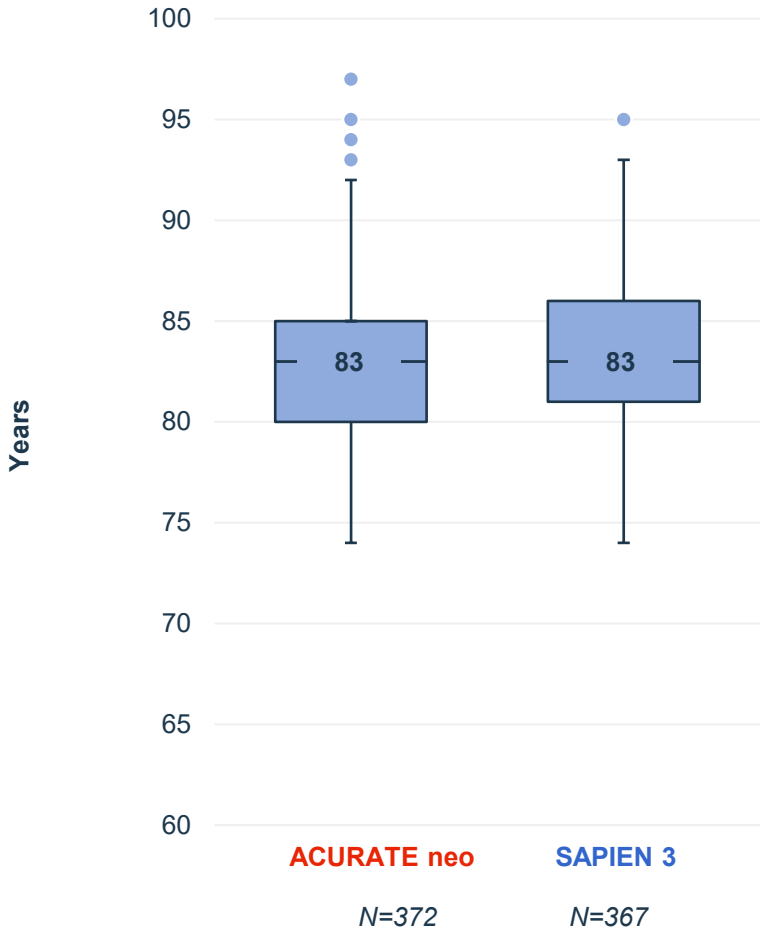


Primary endpoint:
Combined early safety & clinical efficacy at 30 days
(VARC-2)

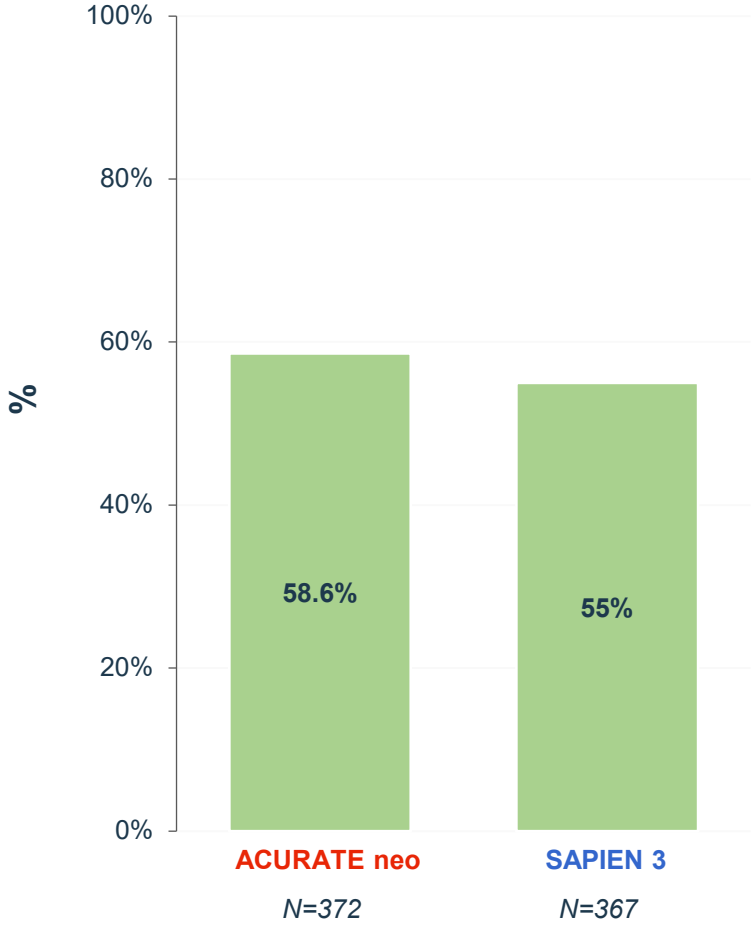
Clinical and echocardiographic follow-up:
at 30-days, 1 year and 3 years

Baseline characteristics

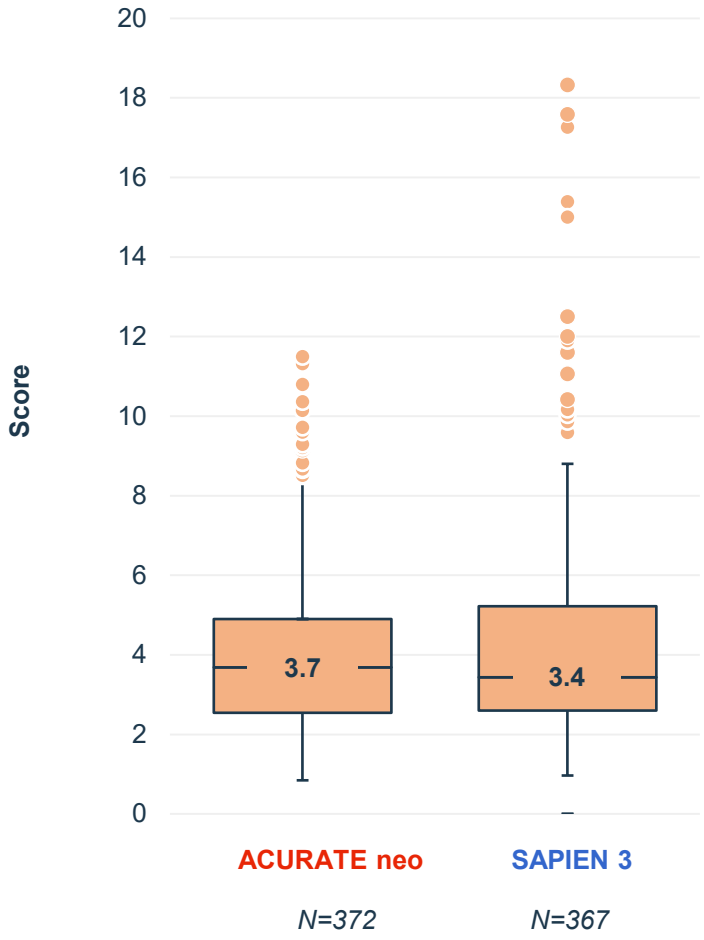
Age



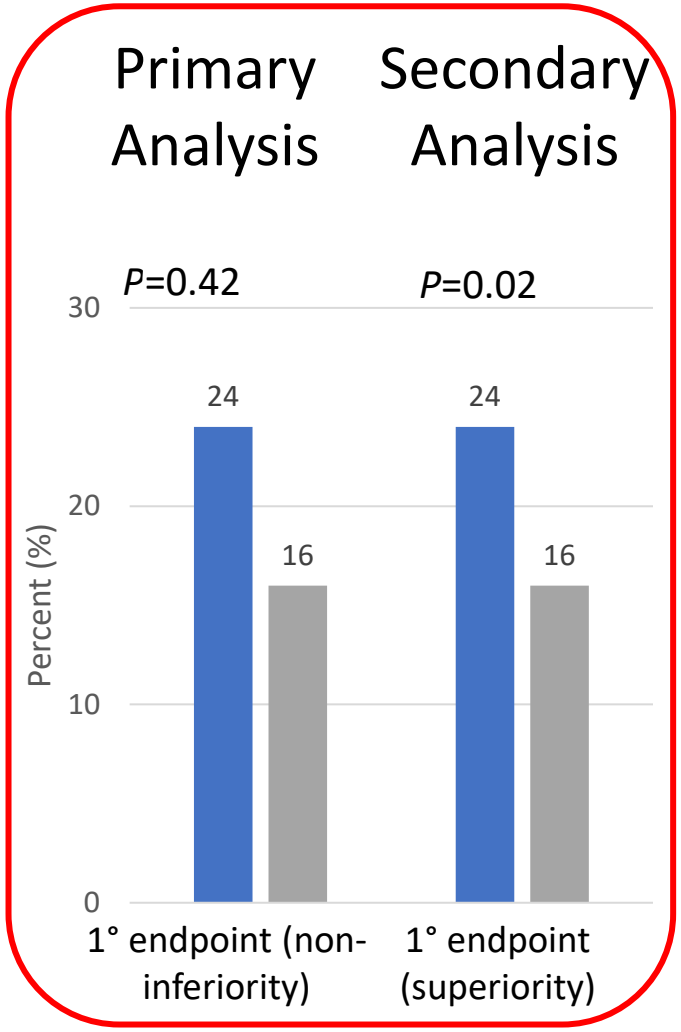
Female sex



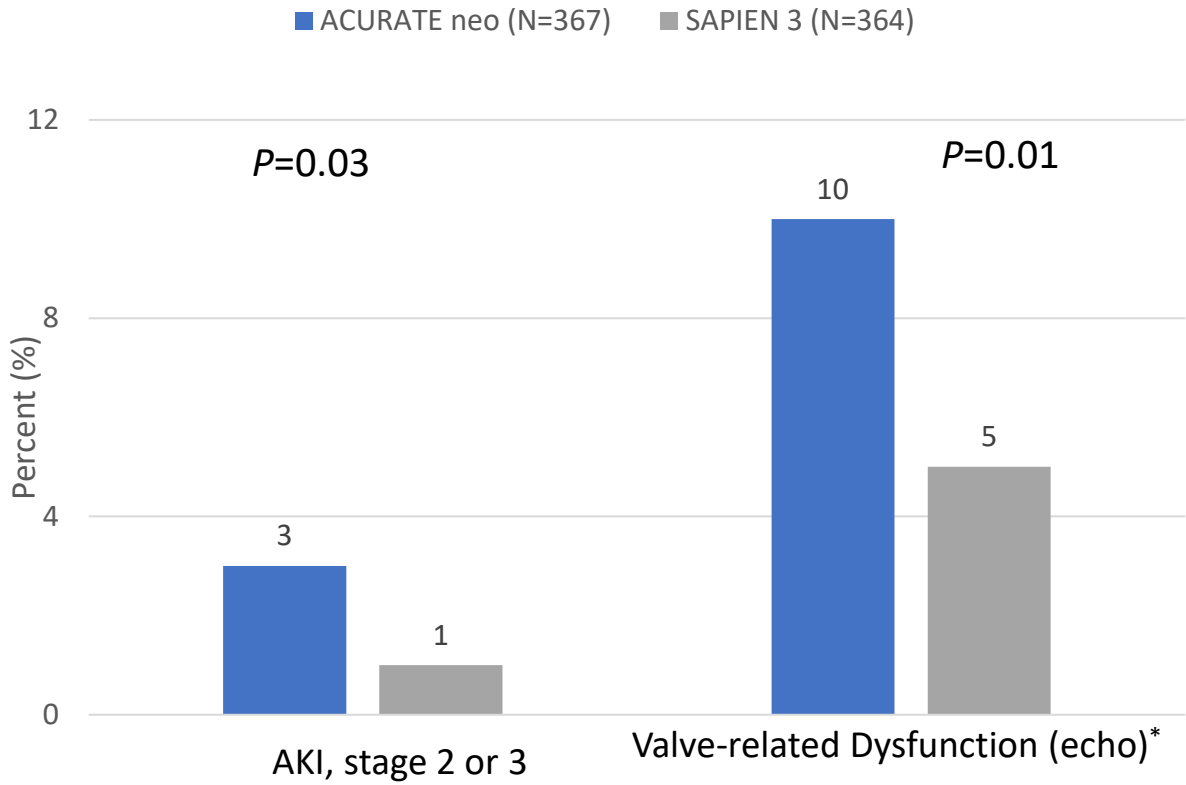
STS-PROM



SCOPE I: Primary Endpoint At 30-Days



ACURATE *neo* failed to meet pre-specified criteria for non-inferiority compared to S3 regarding the primary composite efficacy and safety endpoint due to **higher rates of paravalvular regurgitation and acute kidney injury**.



Pre-specified non-inferiority margin: 7.7%. Absolute risk difference for primary endpoint: 7.1% with a 1-sided upper 95% CI of 12.0%.
Thus, non-inferiority of ACURATE *neo™* was not established for the primary endpoint.

Remaining components of the primary endpoint were not statistically different between valves. *Valve-related dysfunction (ACURATE *neo™,* n=361; SAPIEN™ 3 n=363) comprises mean aortic valve gradient ≥20 mm Hg and either effective orifice area ≤0.9–1.1 cm^2 (depending on body surface area) or Doppler velocity index <0.35; or moderate or severe prosthetic valve regurgitation as defined by VARC-2; patients for whom follow-up echocardiography was not available (owing to a primary endpoint-related clinical event) were included in the primary endpoint analyses, but not in the individual echocardiographic component. All measures were assessed at an independent echocardiographic core laboratory. Lanz, J. et al. *Lancet* 2019 In Press; doi: 10.1016/S0140-6736(19)32219-6.

The ACURATE *neo* and *neo2™* Valve System are CE-marked. The ACURATE *neo2™* Valve System is an investigational device in the US and restricted under federal law to investigational use only.

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SCOPE I Study

Objective: To evaluate whether early differences in device performance between the 1st generation ACURATE *neo* and 3rd generation SAPIEN 3 translate into differences in patient clinical outcomes 3 years after TAVR

Randomized parallel-group assessor-blinded trial

n = 739 Patients | 20 European Centers | Enrollment: Feb 2017 – Feb 2019

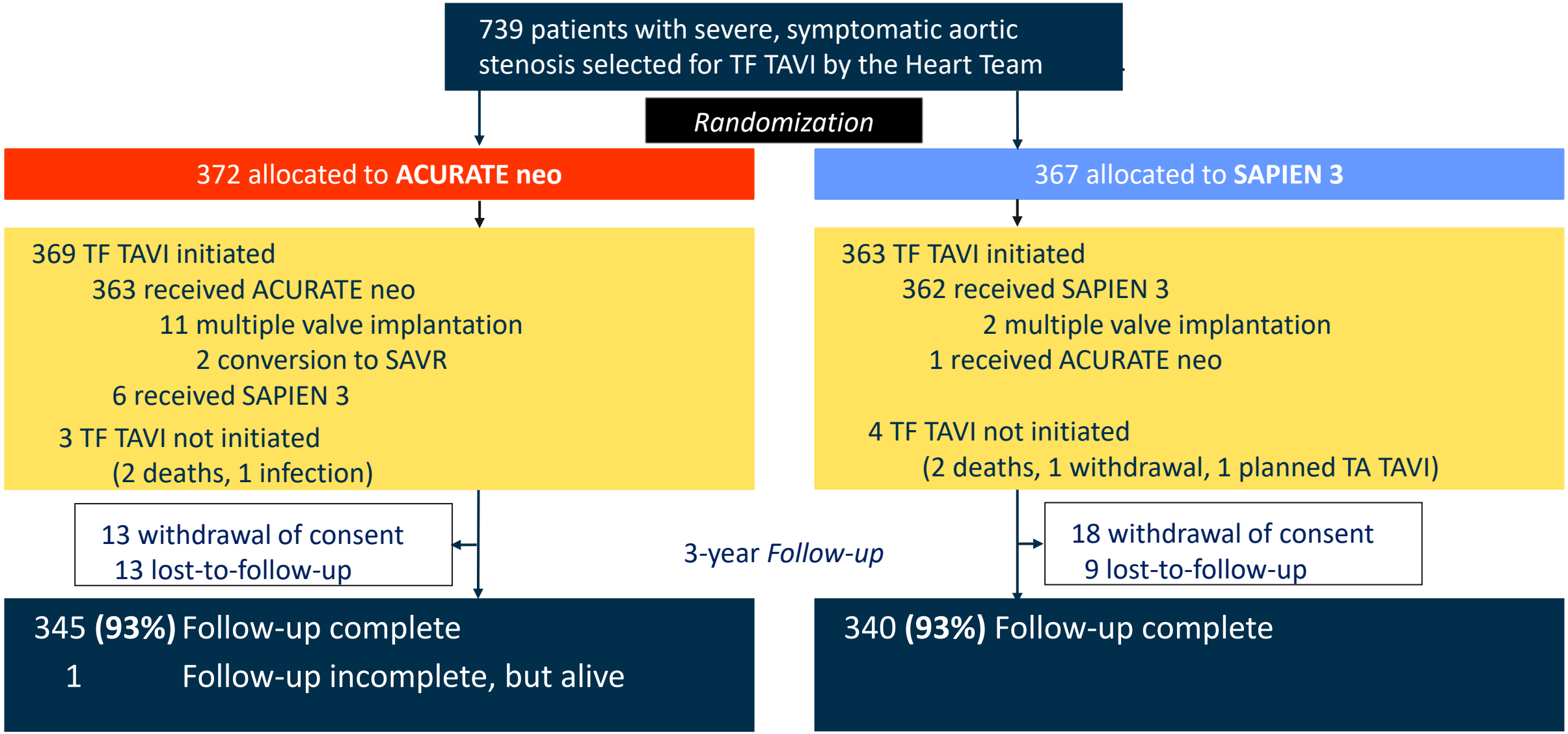
3-year follow-up analysis 26 June 2022 – 4 August 2022

Key Endpoints at 3-years presented at TCT*:

- Death, stroke, hospitalization for valve-related dysfunction or congestive heart failure, new onset atrial fibrillation and myocardial infarction as defined by VARC-2.
- Bioprosthetic valve dysfunction (BVD) and bioprosthetic valve failure (BVF) based on VARC-3.

*Clinical endpoints were adjudicated by an independent clinical events committee blinded to treatment allocation

Patient Flow Chart



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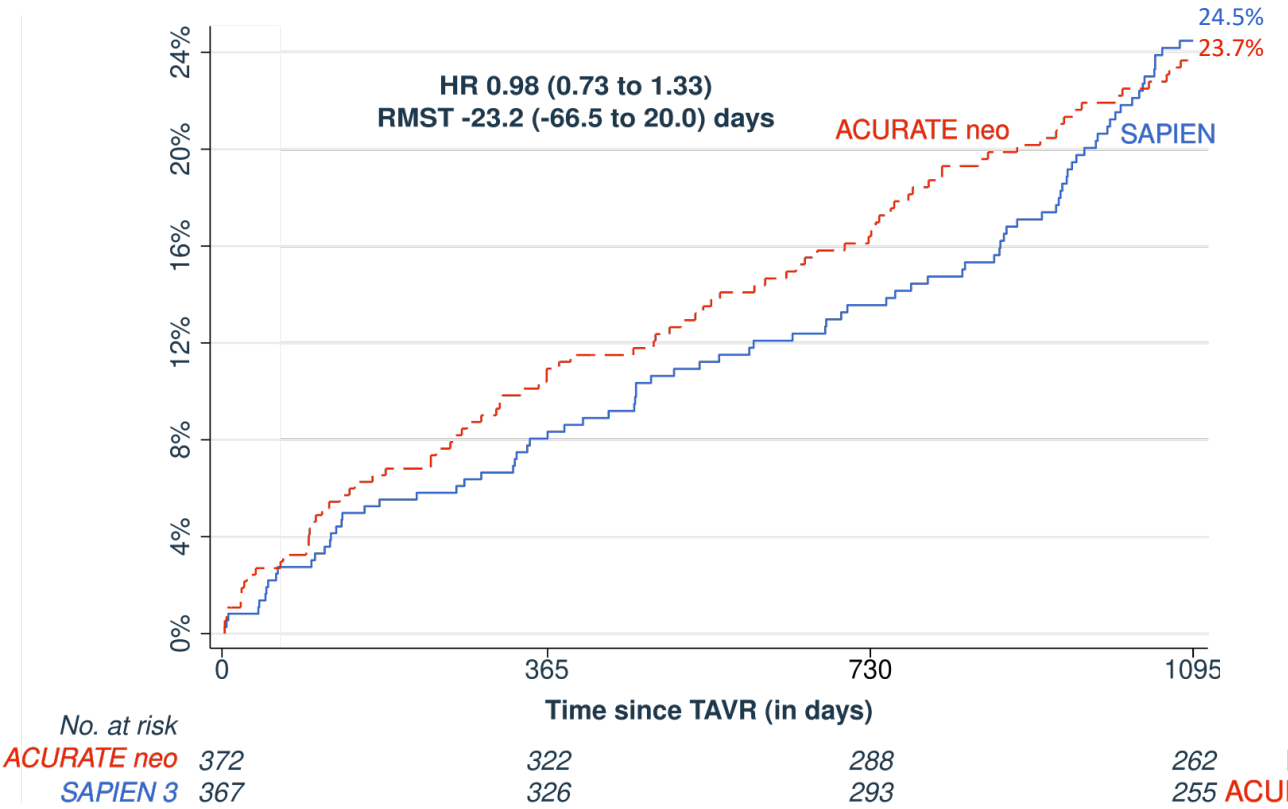
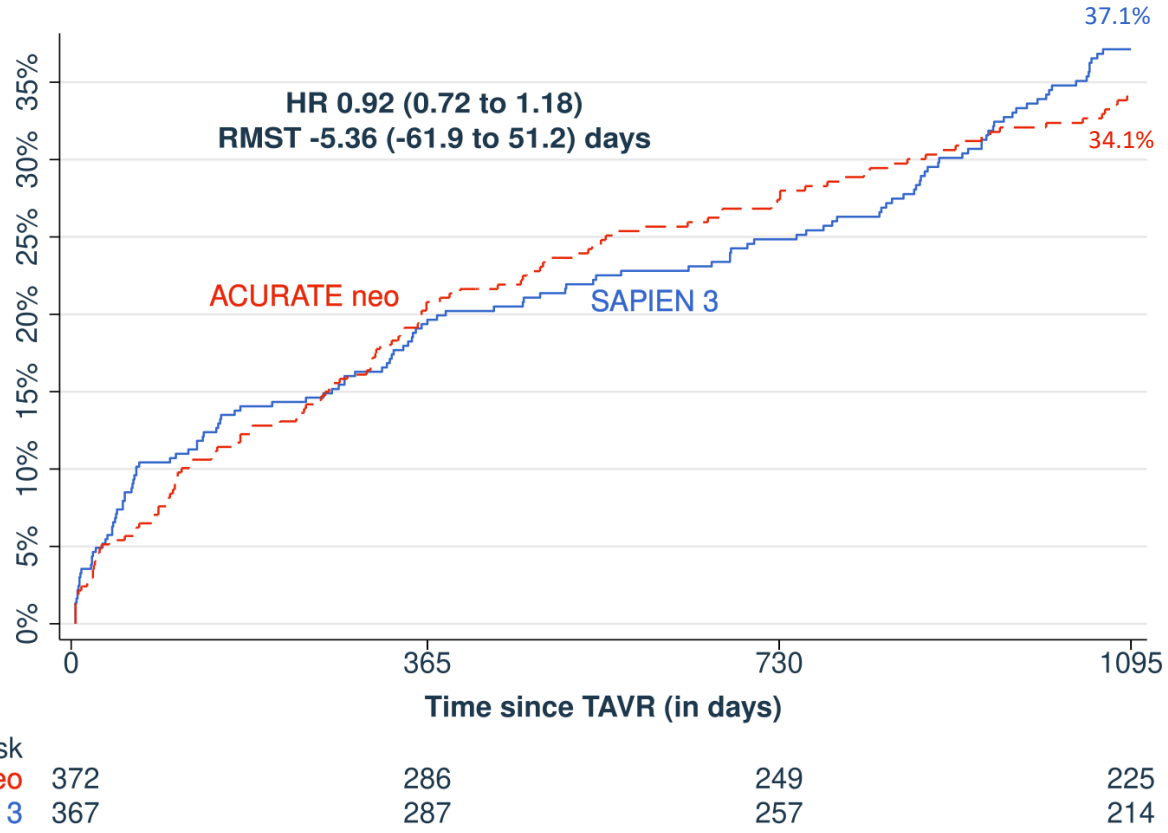
SCOPE I 3-years– Kaplan Meier Cumulative Event Curves

- 30-day differences in device performance between *neo* and S3 did not translate into differences in clinical outcomes at 3 years

All-cause death

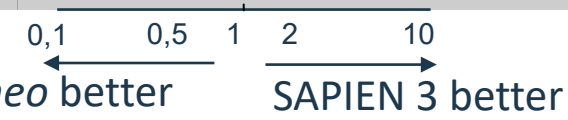


All-cause death, or stroke or heart failure re-hospitalization



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)



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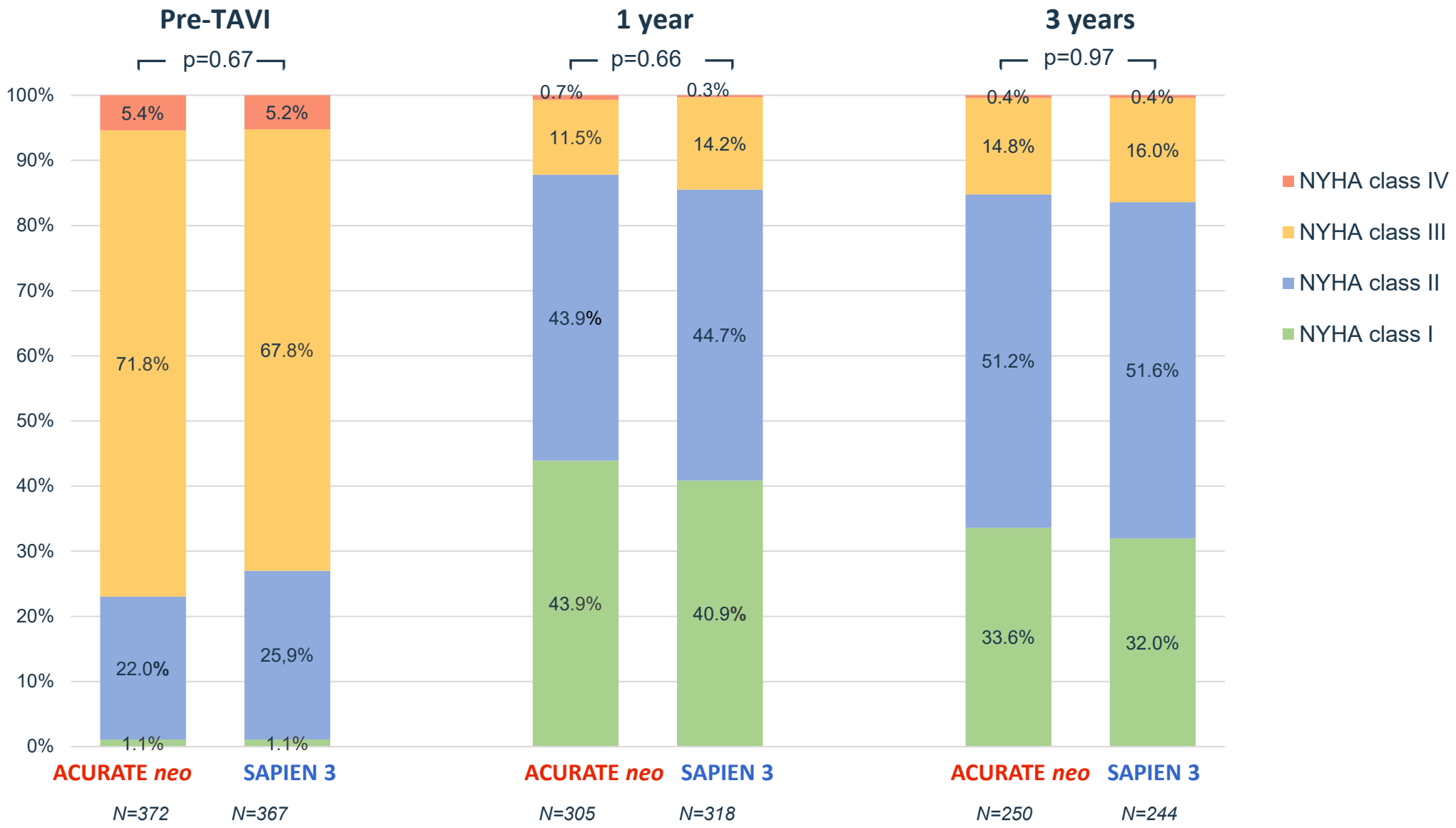
Functional Outcomes - NYHA Class



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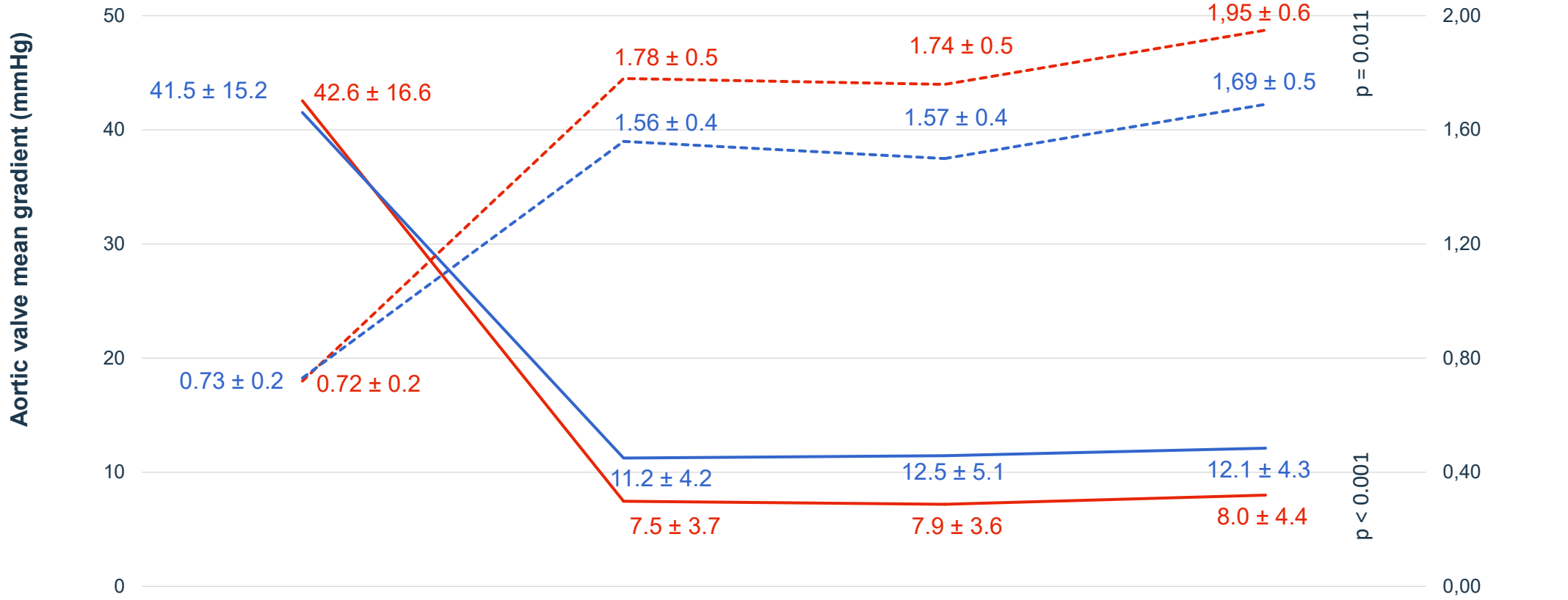
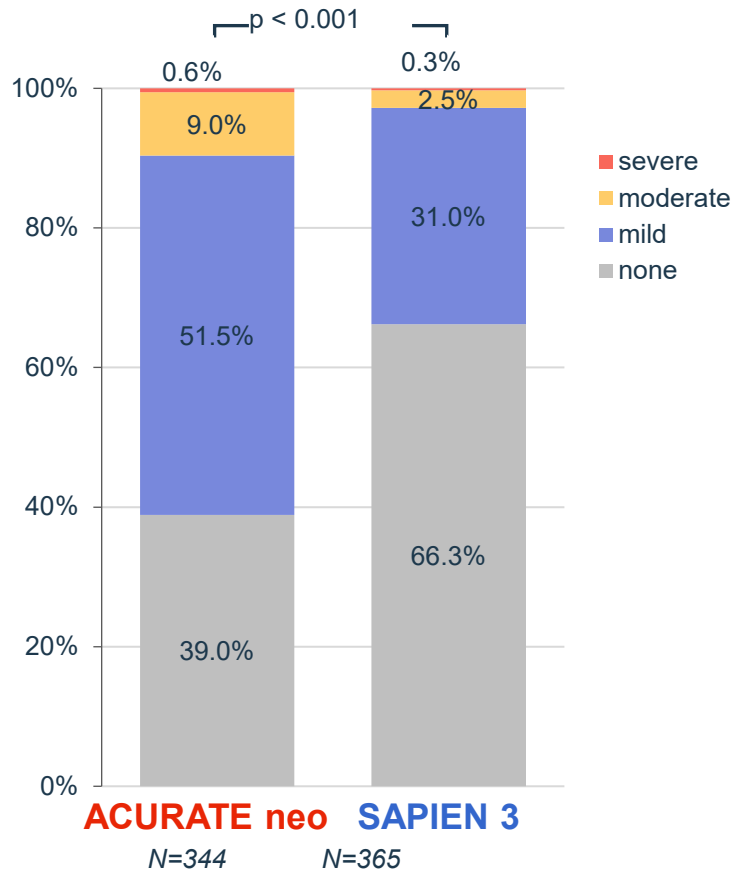
Echocardiography - Mean Gradient & EOA



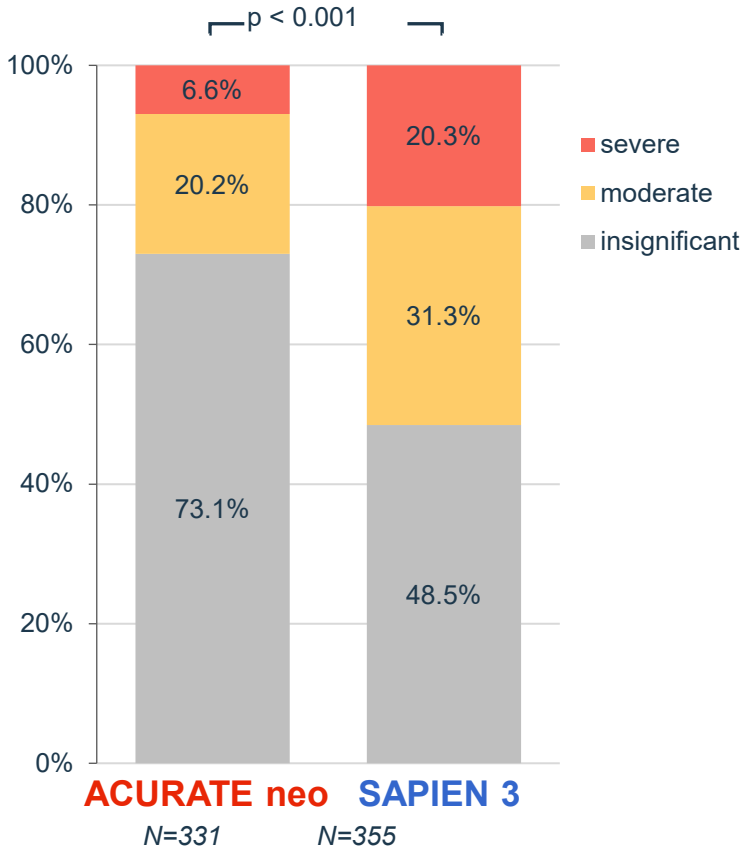
	Baseline*	30 days	1 year*	3 years*	(* site-reported)
ACURATE neo	*353/350*	*347/335*	*226/175*	*117/61*	*N (MG/EOA)*
SAPIEN 3	*366/363*	*365/353*	*257/187*	*134/63*	*N (MG/EOA)*

Non-Structural Bioprosthetic Valve Dysfunction

Prosthetic Aortic Valve Regurgitation
(at 30 days)



Prosthesis-patient mismatch
(at 30 days)



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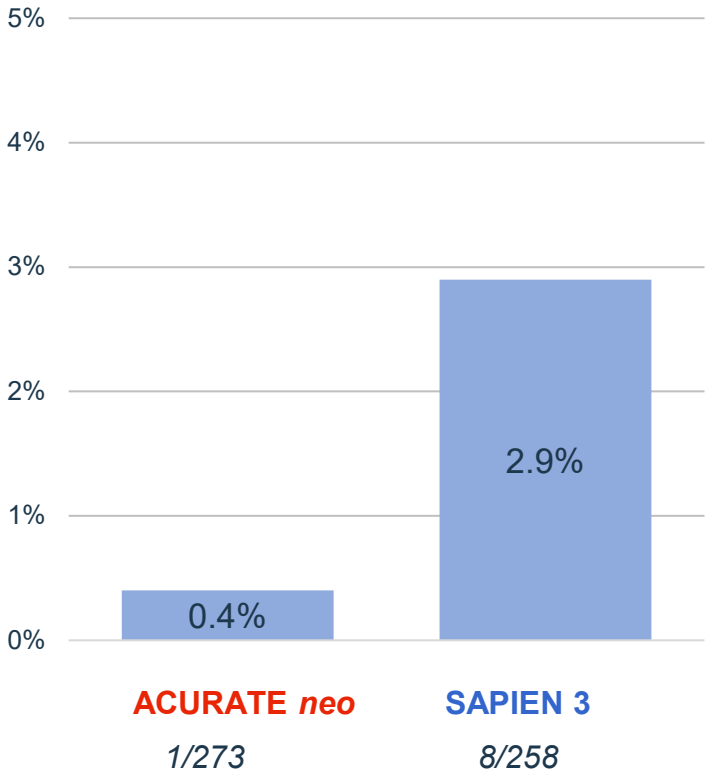
Acquired Bioprosthetic Valve Dysfunction

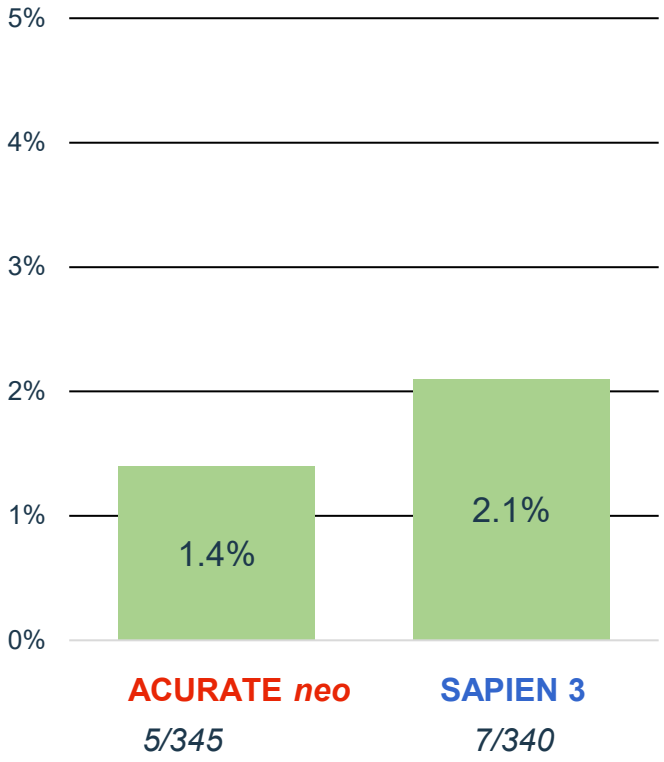
Structural valve deterioration
(with at least moderate HVD)*

Sub-hazard ratio:
0.19 (95% CI: 0.02 to 1.76)



Endocarditis

Sub-hazard ratio:
0.71 (95% CI: 0.22 to 2.27)

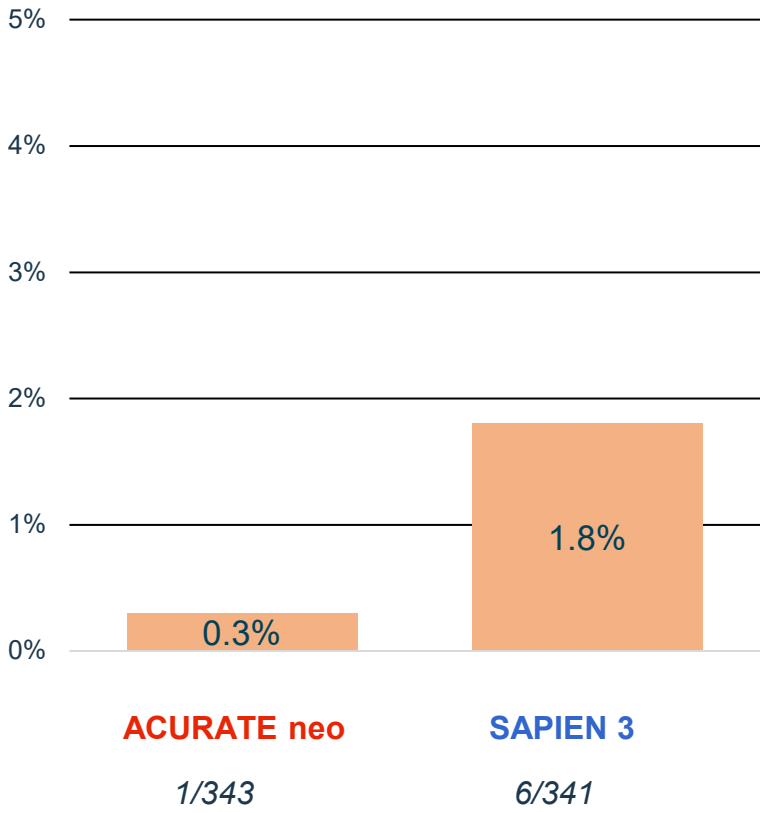


** increase in mean transvalvular gradient ≥ 10 mmHg resulting in a mean gradient ≥ 20 mmHg not due to valve thrombosis or endocarditis*

Bioprosthetic Valve Dysfunction and Failure

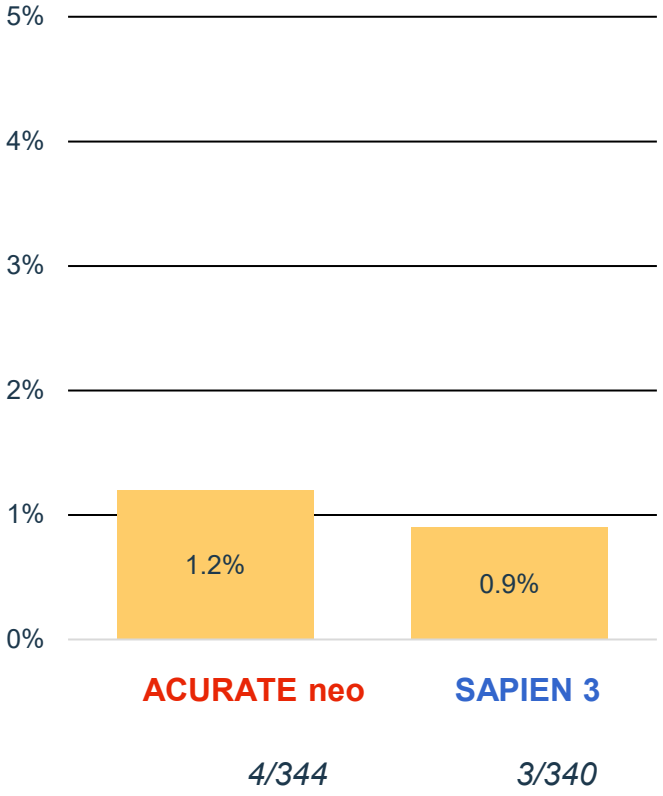
Valve thrombosis

Sub-hazard ratio:
0.16 (95% CI: 0.02 to 1.35)



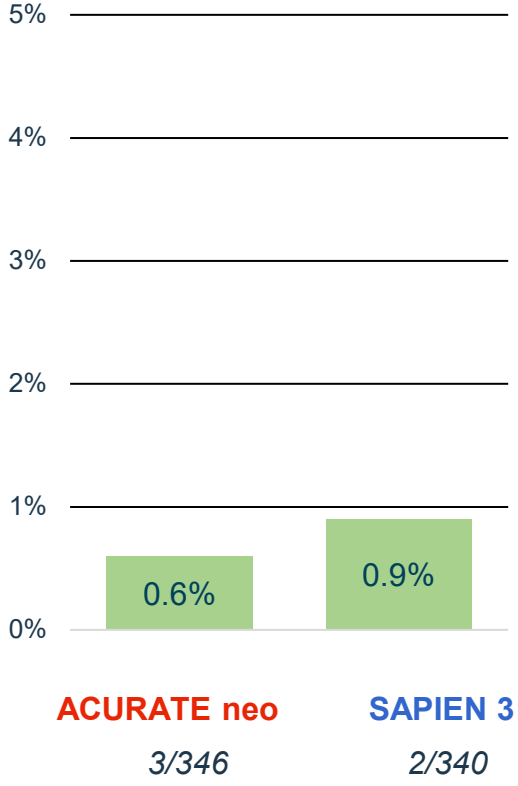
Aortic valve re-intervention

Sub-hazard ratio:
1.32 (95% CI: 0.30 to 5.85)



Valve-related death*

Sub-hazard ratio:
1.52 (95% CI: 0.25 to 9.28)



* 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
- Echocardiographic data 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

- 30-day differences in device performance between *neo* and S3 did not translate into significant differences in clinical outcomes or bioprosthetic valve failure (BVF) at 3 years.

- There is no evidence of compromised valve durability in *neo* in comparison to S3 over the course of the 3 years.