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

Patients with severe aortic stenosis requiring intervention

Heart team decision

Screening Log ← TF TAVI → SAVR

Randomized controlled trial (739 patients)

1:1 Randomization

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

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.
Baseline characteristics

Age

- **ACURATE neo**: 83
- **SAPIEN 3**: 83

Female sex

- **ACURATE neo**: 58.6%
- **SAPIEN 3**: 55%

STS-PROM

- **ACURATE neo**: 3.7
- **SAPIEN 3**: 3.4

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.

SH-1415703-AA
SCOPE I: Primary Endpoint At 30-Days

Key Components of the Primary Endpoint

<table>
<thead>
<tr>
<th></th>
<th>ACURATE neo (N=367)</th>
<th>SAPIEN 3 (N=364)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI, stage 2 or 3</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Valve-related Dysfunction (echo)*</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

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.

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.

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 cm² (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.
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

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.
739 patients with severe, symptomatic aortic stenosis selected for TF TAVI by the Heart Team

372 allocated to **ACURATE neo**
- 369 TF TAVI initiated
  - 363 received ACURATE neo
    - 11 multiple valve implantation
    - 2 conversion to SAVR
    - 6 received SAPIEN 3
  - 3 TF TAVI not initiated
    (2 deaths, 1 infection)
- 13 withdrawal of consent
- 13 lost-to-follow-up

367 allocated to **SAPIEN 3**
- 363 TF TAVI initiated
  - 362 received SAPIEN 3
    - 2 multiple valve implantation
    - 1 received ACURATE neo
  - 4 TF TAVI not initiated
    (2 deaths, 1 withdrawal, 1 planned TA TAVI)
- 18 withdrawal of consent
- 9 lost-to-follow-up

**Follow-up**
- 345 (93%) Follow-up complete
- 1 Follow-up incomplete, but alive
- 340 (93%) Follow-up complete

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

<table>
<thead>
<tr>
<th>Event Type</th>
<th>ACURATE neo</th>
<th>SAPIEN 3</th>
<th>Hazard ratio/Sub-hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All-cause death</strong></td>
<td>84/346 (24.3%)</td>
<td>85/340 (25.0%)</td>
<td>0.98 (0.73 to 1.33)</td>
</tr>
<tr>
<td><strong>Cardiovascular death</strong></td>
<td>58/346 (16.8%)</td>
<td>57/340 (16.8%)</td>
<td>1.01 (0.70 to 1.45)</td>
</tr>
<tr>
<td><strong>Non-cardiovascular death</strong></td>
<td>26/346 (7.5%)</td>
<td>28/340 (8.2%)</td>
<td>0.91 (0.53 to 1.56)</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>21/345 (6.1%)</td>
<td>20/343 (5.8%)</td>
<td>1.04 (0.56 to 1.92)</td>
</tr>
<tr>
<td><strong>Disabling stroke</strong></td>
<td>12/345 (3.5%)</td>
<td>8/343 (2.3%)</td>
<td>1.48 (0.60 to 3.65)</td>
</tr>
<tr>
<td><strong>Non-disabling stroke</strong></td>
<td>12/345 (3.5%)</td>
<td>13/343 (3.8%)</td>
<td>0.92 (0.42 to 2.00)</td>
</tr>
<tr>
<td><strong>Hospitalization for valve-related dysfunction/CHF</strong></td>
<td>48/345 (13.9%)</td>
<td>62/342 (18.1%)</td>
<td>0.74 (0.51 to 1.07)</td>
</tr>
<tr>
<td><strong>New onset atrial fibrillation/flutter</strong></td>
<td>23/343 (6.7%)</td>
<td>35/341 (10.3%)</td>
<td>0.64 (0.38 to 1.08)</td>
</tr>
<tr>
<td><strong>Myocardial infarction</strong></td>
<td>13/343 (3.8%)</td>
<td>7/341 (2.1%)</td>
<td>1.85 (0.74 to 4.67)</td>
</tr>
<tr>
<td><strong>New permanent pacemaker</strong></td>
<td>48/307 (15.6%)</td>
<td>51/311 (16.4%)</td>
<td>0.92 (0.62 to 1.37)</td>
</tr>
</tbody>
</table>

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.

SH-1415703-AA
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.
Echocardiography - Mean Gradient & EOA

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.

SH-1415703-AA
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.
Acquired Bioprosthetic Valve Dysfunction

Structural valve deterioration
(with at least moderate HVD)*

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

0.4% 2.9%
ACURATE neo 1/273 SAPIEN 3 8/258

Endocarditis

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

1.4% 2.1%
ACURATE neo 5/345 SAPIEN 3 7/340

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

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.

SH-1415703-AA
Bioprosthetic Valve Dysfunction and Failure

**Valve thrombosis**

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

  - ACURATE neo: 0.3% (1/343)
  - SAPIEN 3: 1.8% (6/341)

**Aortic valve re-intervention**

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

  - ACURATE neo: 1.2% (4/344)
  - SAPIEN 3: 0.9% (3/340)

**Valve-related death***

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

  - ACURATE neo: 0.6% (3/346)
  - SAPIEN 3: 0.9% (2/340)

*all due to infective endocarditis

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.

SH-1415703-AA
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.