A Randomized Comparison of the ACURATE neo versus the SAPIEN 3 Transcatheter Heart Valve Systems in Patients with Symptomatic Severe Aortic Stenosis


on behalf of the SCOPE I investigators
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.
Background

• TAVR has become an indispensable treatment option for patients with symptomatic severe aortic stenosis across all risk categories.

• The generalizability of outcomes observed in landmark trials comparing TAVR with SAVR to other commercial TAVR systems is limited by differences in device properties and lack of head-to-head device comparisons.

• Iterations of the SAPIEN balloon-expandable TAVR system have been extensively investigated in several large-scale, high-quality randomized trials and registries setting the current benchmark in terms of safety and efficacy.

• The ACURATE neo is a novel, self-expanding TAVR system associated with favorable outcomes in non-randomized studies.
Study Design

Patients (≥ 75 yo) with symptomatic severe aortic stenosis

Heart team decision

Randomized controlled trial

1:1 Randomization

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

Primary endpoint:
Combined early safety & clinical efficacy (VARC-2) at 30 days
(non-inferiority analysis)
Patient Flow Chart

739 patients
mean age: 82.3 years, 57% female,
median STS Risk Score: 3.5, mean transvalvular aortic gradient: 42.2 mmHg

1:1 Randomization

372 allocated to ACURATE neo

- 369 TF TAVR initiated
  - 363 received ACURATE neo
  - 11 multiple valve implantation
  - 2 conversion to surgical valve replacement
  - 6 received SAPIEN 3
- 3 TF TAVR not initiated (2 deaths, 1 infection)
- 5 withdrawal of consent
- 0 lost-to-follow-up

367 (99%) Clinical endpoints assessed
361 (97%) Echocardiography performed and analyzed

367 allocated to SAPIEN 3

- 363 TF TAVR initiated
  - 362 received SAPIEN 3
  - 2 multiple valve implantation
  - 1 received ACURATE neo
- 4 TF TAVR not initiated
  - (2 deaths, 1 consent withdrawal, 1 transapical TAVR)
- 3 withdrawal of consent
- 0 lost-to-follow-up

30-day Follow-up

739 patients
mean age: 82.3 years, 57% female,
median STS Risk Score: 3.5, mean transvalvular aortic gradient: 42.2 mmHg
Primary Endpoint

Primary analysis at 30 days (intention-to-treat)

Primary endpoint rates: ACURATE neo 23.7% SAPIEN 3: 16.5%

Pre-specified non-inferiority margin: 7.7%

Risk difference: 7.1%
Upper limit of one-sided 95% CI: 12%
P value for non-inferiority: 0.42

Non-inferiority not met
Primary Endpoint - Secondary Analyses

<table>
<thead>
<tr>
<th>Intention-to-treat cohort at 30 days</th>
<th>ACURATE neo</th>
<th>SAPIEN 3</th>
<th>Risk difference % (95%-CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint (superiority analysis)</strong></td>
<td>87/367 (23.7%)</td>
<td>60/364 (16.5%)</td>
<td></td>
<td>0.0156</td>
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<tr>
<td><strong>Single components of primary endpoint</strong></td>
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<td>All-cause death</td>
<td>9/367 (2.5%)</td>
<td>3/364 (0.8%)</td>
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<td>0.09</td>
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<td>Stroke (any)</td>
<td>7/367 (1.9%)</td>
<td>11/364 (3.0%)</td>
<td></td>
<td>0.33</td>
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<td>Life-threatening or disabling bleeding</td>
<td>14/367 (3.8%)</td>
<td>9/364 (2.5%)</td>
<td></td>
<td>0.30</td>
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<tr>
<td>Major vascular complications</td>
<td>29/367 (7.9%)</td>
<td>20/364 (5.5%)</td>
<td></td>
<td>0.21</td>
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<tr>
<td>Coronary artery obstruction requiring intervention</td>
<td>0/367 (0%)</td>
<td>0/364 (0%)</td>
<td></td>
<td>n/a</td>
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<td>Acute kidney injury, stage 2 or 3</td>
<td>11/367 (3.0%)</td>
<td>3/364 (0.8%)</td>
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<td>0.0340</td>
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<tr>
<td>Re-hospitalization for valve-related dysfunction or CHF</td>
<td>4/367 (1.1%)</td>
<td>5/364 (1.4%)</td>
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<td>0.72</td>
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<td>Valve-related dysfunction requiring repeat procedure</td>
<td>3/367 (0.8%)</td>
<td>1/364 (0.3%)</td>
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<td>0.32</td>
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<tr>
<td>Valve-related dysfunction (echocardiography)</td>
<td>35/361 (9.7%)</td>
<td>17/363 (4.7%)</td>
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<td>0.0084</td>
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</tbody>
</table>
Echocardiographic Valve Performance (at 30 days)

- **Paravalvular Aortic Regurgitation**
  - ACURATE neo: 9.4% ≥ moderate, 50.1% mild, 40.4% none
  - SAPIEN 3: 2.6% ≥ moderate, 31.1% mild, 66.1% none

- **Mean Gradient ≥20 mmHg AND EOA ≤ 0.9-1.1 cm² and/or DVI < 0.35**
  - ACURATE neo: 0.6% yes, 99.4% no
  - SAPIEN 3: 2.2% yes, 97.8% no

- **Effective Orifice Area**
  - ACURATE neo: 1.73 cm²
  - SAPIEN 3: 1.47 cm²

*P < 0.0001 for all comparisons*
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.

An early composite safety and efficacy endpoint proved useful in discriminating the performance of different TAVR systems.