30-Day Outcomes Following Implantation of a Repositionable Self-Expanding Aortic Bioprosthesis: First Report From the FORWARD Study

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On behalf of the FORWARD Study Investigators
Disclosures

- Stephan Windecker receives research grants to the institution from Abbott, Biotronik, Boston Scientific, Edwards, Medtronic, and St. Jude
Evolut R Clinical Program

CE Mark Study (Safety and performance)
- N=60; single arm, 26 mm and 29 mm valves
- Primary Safety EP = Death & any stroke at 30 days

US IDE Study (Safety and efficacy)
- N=241; single arm, 23 mm, 26 mm and 29 mm valves
- Primary Safety EP = Death & disabling stroke at 30 days
- Follow-up through 5 years

All-Comers Trial (Safety)
- N=1000; single arm, 23 mm, 26 mm and 29 mm valves
- Primary EP = Death at 30 days
- Follow-up through 3 years

US IDE Addendum (Safety and efficacy)
- N=60; single arm, 34 mm valve
- Primary Safety EP = Death & disabling stroke at 30 days
- Follow-up through 5 years

Forward TCT 2016

Initial Results

1-Year Follow-up TCT.16

Interim Results TCT.16

Final 2-Year Follow-up TCT.16
Evolut R System

Transcatheter Valve
Supra-annular design, optimized sealing

Catheter Delivery System
14Fr-equivalent profile

Inline Sheath

Loading System
Evolut R FORWARD Study

- FORWARD is a multicenter, prospective, single-arm, observational post-market study to evaluate safety and performance of the Evolut R system in a routine hospital setting.
  - **Objective:** To document the clinical and device performance outcomes of the Evolut R system used in routine hospital practice
  - **Primary Endpoint:** The all-cause mortality rate at 30 days
  - **Sample Size:** 1000 patients
  - **Present Analysis:** Interim 30-day results in first 300 patients
Secondary Endpoints

Efficacy

- Absence of procedural mortality
- Correct positioning of a single prosthetic heart valve into the proper anatomical location
- Absence of patient-prosthesis mismatch, mean gradient < 20 mmHg (or peak velocity < 3 m/sec), and no moderate or severe prosthetic valve regurgitation.
- Hemodynamic performance at 24 hours to 7 days (discharge) and 1 year

Safety

- VARC-II Safety Composite Endpoint and Components at 30 days post procedure
  - All-cause mortality, All stroke, Life-threatening bleeding, Acute kidney injury: stage 2 or 3, Coronary artery obstruction requiring intervention, Major vascular complication, and valve-related dysfunction requiring repeat procedure (BAV, TAVI, or SAVR)
- Rate of new permanent pacemaker implant at 30 days post procedure
Inclusion and Exclusion Criteria

**INCLUSION**

- Symptomatic native aortic valve stenosis or surgical bioprosthetic valve failure
- Acceptable candidate for elective treatment with the Evolut R System in conformity with the local regulatory context
- Age ≥80 years OR considered to be at high or greater risk for surgical aortic valve replacement (AVR) where high risk is defined as:
  - STS predicted risk of mortality ≥8%
  - OR
  - Heart team agreement of risk for AVR due to frailty or comorbidities.

**EXCLUSION**

- Contraindication to aspirin, heparin, bivalirudin, ticlopidine, clopidogrel, Nitinol, contrast media
- Mechanical heart valve in aortic position
- Sepsis, including active endocarditis
- Anatomically not suitable for the Evolut R system
- Estimated life expectancy <1 year
- Participating in another trial that may influence the outcome of this trial
- Need for emergency surgery for any reason
Study Oversight and Participation

Steering Committee Members
*Eberhard Grube, University of Bonn
*Stephan Windecker, Inselspital/Universitätsspital Bern
Sabine Bleiziffer, Deutsches Herzzentrum München
Johan Bosmans, UZ Antwerp
Ganesh Manoharan, Royal Victoria Hospital Belfast
Thomas Modine, CHRU de Lille
Nicolas Van Mieghem, Erasmus MC Rotterdam

Echocardiographic Core Lab
Jae Oh, Mayo Clinic, Rochester, MN

Clinical Events Committee
Harvard Clinical Research Institute

Sponsor
Medtronic

*Co-principal Investigators

60 sites in 23 countries
Enrollment to date: 805
## Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EVOLUT R N=300</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>82.0 ± 5.7</td>
</tr>
<tr>
<td>Female</td>
<td>67.3</td>
</tr>
<tr>
<td>STS Score (%)</td>
<td>5.6 ± 3.8</td>
</tr>
<tr>
<td>&lt;4%</td>
<td>43.3</td>
</tr>
<tr>
<td>4-8%</td>
<td>40.0</td>
</tr>
<tr>
<td>&gt;8%</td>
<td>16.7</td>
</tr>
<tr>
<td>EuroSCORE II (%)</td>
<td>5.6 ± 4.8</td>
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<tr>
<td>NYHA III/IV</td>
<td>72.6</td>
</tr>
<tr>
<td>Diabetes</td>
<td>30.0</td>
</tr>
<tr>
<td>Serum Creatinine &gt;2 mg/dl</td>
<td>7.4</td>
</tr>
<tr>
<td>Chronic Lung Disease (COPD)</td>
<td>24.5</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>14.7</td>
</tr>
<tr>
<td>Frailty</td>
<td>34.1</td>
</tr>
<tr>
<td>Assisted Living</td>
<td>13.2</td>
</tr>
</tbody>
</table>
## Procedural Data

<table>
<thead>
<tr>
<th>Characteristic - %</th>
<th>EVOLUT R</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Anesthesia</td>
<td>37.0</td>
</tr>
<tr>
<td>Iliofemoral Access Route</td>
<td>98.3</td>
</tr>
<tr>
<td>Implant Size</td>
<td></td>
</tr>
<tr>
<td>23mm</td>
<td>7.0</td>
</tr>
<tr>
<td>26mm</td>
<td>40.5</td>
</tr>
<tr>
<td>29mm</td>
<td>52.5</td>
</tr>
<tr>
<td>Pre-TAVR Balloon Dilation Performed</td>
<td>49.0</td>
</tr>
<tr>
<td>Post-Implant Dilatation Performed</td>
<td>33.4</td>
</tr>
<tr>
<td>EnVeo InLine Sheath used</td>
<td>92.6</td>
</tr>
<tr>
<td>Multiple Valve (≥ 2 Implanted)</td>
<td>1.3</td>
</tr>
</tbody>
</table>
30-Day All-Cause Mortality

Days Post-Procedure

No. at risk: 300

Estimated STS 30-Day Mortality: 5.6%

Observed 30-Day Mortality: 2.0%

TCT 2016
Implant depth as assessed by aortography and reported by the sites:
NCS: 4.8 ± 2.7mm
LCS: 6.0 ± 2.8mm

Patient Prosthesis Mismatch: Defined as AVA <0.85cm²/m² for subjects with BMI <30kg/cm², or <0.7cm²/m² for subjects with BMI ≥ 30kg/cm²
VARC-II Safety Endpoints at 30 Days

VARC-II Combined Safety Endpoint = 10.1%

1Valve-related dysfunction requiring repeat procedure
### Additional 30-Day Safety Endpoints

<table>
<thead>
<tr>
<th>Event, Kaplan-Meier Rate (%)</th>
<th>Evolut R N=300</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial Infarction</td>
<td>0.3</td>
</tr>
<tr>
<td>New Pacemaker&lt;sup&gt;1&lt;/sup&gt;</td>
<td>15.4</td>
</tr>
<tr>
<td>Prosthetic Valve Thrombosis</td>
<td>0.0</td>
</tr>
<tr>
<td>Prosthetic Valve Endocarditis</td>
<td>0.0</td>
</tr>
<tr>
<td>Valve Embolization&lt;sup&gt;*&lt;/sup&gt;</td>
<td>1.0</td>
</tr>
<tr>
<td>Valve Migration</td>
<td>0.0</td>
</tr>
<tr>
<td>Mitral Valve Apparatus Damage</td>
<td>0.0</td>
</tr>
</tbody>
</table>

<sup>1</sup>Subjects with pacemaker or ICD at baseline are included in the denominator.

*per VARC II; all 3 were pop-outs
Resheath and Recapture

Resheath (19.7% of patients)
- 67.8% did not undergo resheath
- 16.9% underwent 1 resheath
- 13.6% underwent 2 resheath
- 1.7% underwent >3 resheath

Recapture (9.0% of patients)
- 74.1% did not undergo recapture
- 18.5% underwent 1 recapture
- 7.4% underwent 2 recapture

Resheath or Recapture = 25.1% of Patients

Patients who underwent resheath/recapture had a similar mortality rate (1.3% vs. 2.3%) and pacemaker implantation rate (13.3% vs. 16.2%) as those who did not undergo resheath/recapture.
Hemodynamic Outcomes*

Valve Performance

<table>
<thead>
<tr>
<th>Effective Orifice Area (cm²)</th>
<th>N= 190</th>
<th>42.5 ± 17.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Gradient (mmHg)</td>
<td>N= 270</td>
<td>0.8 ± 0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.7 ± 6.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.9 ± 0.6</td>
</tr>
</tbody>
</table>

Paravalvular Regurgitation

<table>
<thead>
<tr>
<th>Percent of Patients</th>
<th>1-7 Days (N=254)</th>
</tr>
</thead>
</table>
|                     | Severe 0.4% 
|                     | Moderate 25.6% 
|                     | Mild 71.6% 
|                     | None/Trace 2.4% 

*Echocardiographic Core Lab*

TCT 2016
New York Heart Association Functional Class

<table>
<thead>
<tr>
<th>NYHA Class</th>
<th>Baseline (N=299)</th>
<th>30 Days (N=257)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA I</td>
<td>26.4%</td>
<td>40.9%</td>
</tr>
<tr>
<td>NYHA II</td>
<td>64.9%</td>
<td>48.2%</td>
</tr>
<tr>
<td>NYHA III</td>
<td>7.7%</td>
<td>0.8%</td>
</tr>
<tr>
<td>NYHA IV</td>
<td>0.0%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

NYHA Change from Baseline to 30 Days
- Improved: 78.9%
- No Change: 19.5%
- Worsened: 1.6%
Conclusions

• Interim results at 30 days in this real-world, global experience with Evolut R demonstrate:
  – Low incidence of all-cause mortality, stroke and major vascular complications
  – Reduced pacemaker rate post TAVR
  – Excellent hemodynamic results and low rate of moderate/severe PVR
  – Resheath/recapture was used safely in 25% of cases

• Primary endpoint for 1000 patients at EuroPCR 2017