5-year Results with Balloon Expandable Stent Grafts [Advanta V12LD] in the Treatment of Aortic Coarctations [From the OUS – CoArc Trial]

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Potential conflicts of interest
Speaker’s name: Elchanan Bruckheimer

✓ I have the following potential conflicts of interest to report:

☐ Research contracts
✓ Consulting (Atrium Medical Corp)
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

CoArc: Objective

• To evaluate the safety and efficacy of the Large Diameter Advanta™ V12 Covered Stent for treatment of native and recurrent coarctation of the aorta in selected children, adolescents, and adults.

CoArc: Trial Design

Design: Prospective, Multicenter, Non-Randomized, Single Arm
Population: Eligible patients, children and adults, with a diagnosis of native or recurrent coarctation of the aorta
Sample Size: 70 subjects
Investigational Sites: 9 sites in 7 Countries (Australia, Brazil, Canada, Germany, Israel, Italy, & UK)
Enrollment: First patient enrolled: 30-Sep-09
Last patient enrolled: 23-Mar-12
Clinical F/U Visits: 30-day, 6, 12 (Primary Endpoint), 24, 36, 48, & 60 mo

CoArc: Primary Endpoints

Primary Efficacy Endpoint:
• A significant reduction in the gradient across the coarctation
  – Pre stent vs. immediately post stent & pre stent vs. 12 month follow-up
  – DV (diastolic velocity in cm/sec) and DV/SV (diastolic velocity /systolic velocity ratio) measured

Primary Safety Endpoint:
• The safety endpoint will include the evaluation of adverse events and complications occurring within 30 days of the procedure:
  – Major adverse vascular events (MAVE)
  – Major adverse events (MAE)
CoArc: Secondary Endpoints

Secondary Endpoint:
- The secondary efficacy endpoint: An increase in the diameter of the (CoA) after stent placement such that the diameter of the coarctation will be ≥80% of diameter of the transverse arch immediately distal to the left subclavian artery [isthmus] (CoA:DAo≥0.8) after the stenting procedure and maintain this increased diameter over a 12 month period.

Outcome Assessments:
- Device success, defined as the successful delivery and deployment of the study stent and intact retrieval of the delivery system
- No post procedural (12 month) stent migration
- MAE and MAVE at 12 months

CoArc: Site Information

<table>
<thead>
<tr>
<th>Site Ranking</th>
<th>Investigated Country</th>
<th>Institution</th>
<th>Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Brazil</td>
<td>Instituto Dante Pazzanese de Cardiologia Sao Paulo, Brazil</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>Italy</td>
<td>San Donato Hospital Milan, Italy</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>Israel</td>
<td>Schneider Children's Medical Center - Pediatric Institute Tel Hashomer, Israel</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>Canada</td>
<td>Hospital for Sick Children Toronto, Canada</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>Germany</td>
<td>Dept. of Congenital Heart Diseases - Heart Institute Berlin, Germany</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>UK</td>
<td>Bristol Royal Hospital for Children Bristol, UK</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>Australia</td>
<td>The Children's Hospital at Westmead Sydney, Australia</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>Germany</td>
<td>Asklepios Klinik - Sankt Augustin Sankt Augustin, Germany</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>Germany</td>
<td>CardioVascular Center - Schloßpark Klinik Hamburg, Germany</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Total Subjects Enrolled</strong></td>
<td>70</td>
</tr>
</tbody>
</table>

CoArc Advanta V12LD Trial

Doppler Echocardiographic Profile and Indexes in the Evaluation of Aortic Coarctation in Patients Before and After Stenting

10 yr old male – severe native coarctation treated with Advanta V12LD dilated to 14mm

CoArc Schedule of Events

<table>
<thead>
<tr>
<th>TESTING</th>
<th>PRE-PROCEDURE</th>
<th>POST-PROCEDURE</th>
<th>3 MONTH</th>
<th>6 MONTH</th>
<th>12 MONTH</th>
<th>24 MONTH</th>
<th>YEARLY FOLLOW-UP</th>
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<tbody>
<tr>
<td>Medical History</td>
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<tr>
<td>Physical Exam/Health Status</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Echocardiogram/Doppler</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Chest X-ray</td>
<td>X</td>
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<tr>
<td>CT Angiogram</td>
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<tr>
<td>Anus</td>
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<td>X</td>
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<tr>
<td>Anti-platelet/anticoagulation medication</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Adverse Events</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
CoArc Subject Visits Status

There is a significant reduction in gradient across the coarctation demonstrated by change in DV pre vs. post procedure and is maintained at 12 months.

There is also a significant reduction in gradient across the coarctation as assessed pre stent vs. immediately post stent and pre stent vs. 12 months post procedure.

Observed DV/SV differences at both time points are similar to what was observed by Tan:

The primary safety hypothesis is that the 30 day morbidity rate must be less than 17.6%.

In 70 subjects, there are 5 MAVES that occurred within 30 days (per Investigator), which is a rate of 7.1%.

Per CEC adjudication, only 1 MAVE remains (other 4 were determined not to be a MAVE per CEC), resulting in a morbidity rate of 1.4%.

Primary Efficacy: SPARTAN efficacy endpoint

SPARTAN endpoint requires that overall mean of the upper limb-lower limb peak systolic gradient at 12 months is less than 20mmHg.

Based on preliminary results below, the efficacy endpoint defined in SPARTAN would have been met in the COARC study.

<table>
<thead>
<tr>
<th>12 month measurement</th>
<th>N</th>
<th>Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right arm systolic</td>
<td>66</td>
<td>126.1</td>
</tr>
<tr>
<td>Left arm systolic</td>
<td>63</td>
<td>120.8</td>
</tr>
<tr>
<td>Lower limb systolic</td>
<td>63</td>
<td>119.6</td>
</tr>
</tbody>
</table>
Treated with Advanta V12LD dilated to 12mm - post dilated to 16mm 3 months later

CoArc: Aortic wall damage

- 62 follow up CT scans [88% of patients] at 1 year
- 1 patient had a hematoma at implantation which resolved
- 1 patient had a small aneurysm at distal edge of the stent at implantation treated with a second stent 2 months later
- 1 patient had an unrelated dissection treated endovascularly

CoArc: Infolding

CoArc: Infolding
CoArc: Advantages, Limitations and Precautions

- Advantages:
  - stent: covered, premounted - low profile, open cell
  - study: prospective trial with hemodynamic and imaging follow up
  - appears to be safe and effective in treatment of CoA

- Limitations and Precautions:
  - not randomized to surgery
  - late complications – particularly aneurysm, hypertension, effect on aortic compliance
  - infolding of stent edge