Safety and Efficacy of a Leadless Pacemaker: Results from the LEADLESS II clinical trial

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• COI: St Jude Medical Inc – Grant support & Consultant
• I will be discussing the use of non-FDA approved devices
DECLARATION OF INTEREST

- Research contracts
- Consulting/Royalties/Owner/ Stockholder of a healthcare company
Today’s Leadless Pacemaker System
The Nanostim Device

• Percutaneous femoral vein delivery
  - 18F introducer /steerable catheter
  - <30 minute skin-to-skin procedure

• Self-contained device in ventricle
  - No lead or surgical pocket
  - Inherently MRI compatible

• Conventional Features
  - Temperature-Based Rate Response
  - >10-yr battery life
  - Hysteresis
  - Magnet Mode

• Flexible replacement options
  - Catheter-based retrieval
  - Deliver additional leadless pacemakers
  - Revert to conventional pacing lead
Leadless II Clinical Trial Overview

- Prospective, multicenter, non-randomized, FDA IDE study
- Objective:
  - To evaluate the clinical safety and efficacy of non-surgical implantation of the leadless cardiac pacemaker in patients indicated for a VVI(R) pacemaker.
- Primary Cohort: 1st 300 patients followed for 6mo (June 2015)
- Total Cohort: All patients enrolled by June 2015 (n=526)
- Primary Endpoints (by ITT):
  - Safety: Freedom from Serious Adverse Device Effects at 6 months
  - Efficacy: Acceptable pacing capture threshold (d2.0 V at 0.4 msec) and a therapeutically acceptable sensing amplitude (R wave e5.0 mV, or a value equal to or greater than the value at implantation) through 6 mo.
- 56 Centers in the U.S., Canada and Australia
  - 100 Operators (only one had prior experience with leadless pacing)
• Device was successfully implanted in ~96% of patients

• **Primary Safety Endpoint (Intent-to-Treat Analysis)**
  - 280 of the 300 patients achieved endpoint (93.3%; 95% CI = 89.9 to 95.9)
  - This exceeded the performance goal of 86% (P < 0.001)

• **Primary Efficacy Endpoint (Intent-to-Treat Analysis)**
  - 270 of the 300 patients achieved endpoint (90.0%; 95% CI = 86.0 to 93.2)
  - This exceeded the performance goal of 85% (P = 0.007)

• **Efficacy (Successful implants)**
  - 289 patients with successful device implant
  - 270 of the 289 patients achieved endpoint (93.4%; 95% CI = 89.9 to 96.0)
  - This exceeded the performance goal of 85% (P < 0.001)

• Based on device-use characteristics, the battery longevity is estimated to be **15.0 ± 6.7 yrs** (95% CI, 14.2 to 15.8 yrs)
## Leadless II Clinical Trial

### Device-Related SAEs

<table>
<thead>
<tr>
<th>Event</th>
<th>Primary Cohort (N=300)</th>
<th>Total Cohort (N=526)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Events</td>
<td>No. of Patients</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>Cardiac perforation</td>
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<td>4</td>
</tr>
<tr>
<td>Cardiac tamponade with intervention</td>
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<td>1</td>
</tr>
<tr>
<td>Cardiac perforation requiring intervention</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pericardial effusion with no intervention</td>
<td>2</td>
<td>2</td>
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<tr>
<td>Vascular complication</td>
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<td>4</td>
</tr>
<tr>
<td>Arrhythmia during device implantation</td>
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<td>2</td>
</tr>
<tr>
<td>Cardiopulmonary arrest during implantation procedure</td>
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<td>0</td>
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<tr>
<td>Device dislodgement</td>
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<td>5</td>
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<tr>
<td>Device migration during implantation owing to inadequate fixation</td>
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<td>0</td>
</tr>
<tr>
<td>Pacing threshold elevation with retrieval and implantation of new device</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Other*</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

* Includes: ischemic stroke, angina pectoris, pericarditis, acute confusion & expressive aphasia, dysarthria & lethargy post implant, contrast induced nephropathy, orthostatic hypotension with weakness, left leg weakness during implant, probable pulmonary embolism, ischemic stroke
The Leadless Pacemaker was successfully implanted in ~96% of attempted patients.

The trial met the pre-specified Safety and Efficacy endpoints
- Complication rate similar to that seen with conventional pacemakers
- Complication rate likely to improve with operator experience (Rem: in this study, 99 of 100 operators had never implanted a leadless device)

The device was shown to be retrievable in a subgroup of patients (n=7) who needed a replacement (Time from implant = 160±180 days; Range = 1 to 413 days)

The estimated device longevity based on the 6-month follow-up duration is encouraging
Limitations

- An Observational study (not Randomized)
- Mean Follow-Up of only 6 months
- How to manage device after battery depletion?
  - Possible to retrieve after ~1 year, but what about 5, 10, 15 yrs?
  - Retrieval vs Abandonment
- Limited device diagnostics (eg, no electrogram data)
- Large venous sheath (18Fr)
  - Now increasingly common used for cardiology procedures
  - Low observed rate of hematomas
- Single-chamber (RV) pacing only
  - Device-to-device communication is in development
  - Would lead to dual-chamber, CRT, etc