Percutaneous Ventricular Restoration Therapy (PVRT) in patients with ischemic, dilated heart failure: 2-year clinical and echo outcomes of the first-in-human study of the Parachute left ventricle partitioning device

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Presenter Disclosure:

Advisory/Speaker Bureau: Boston Scientific, St Jude LightLab, Cordis, Abbott, Medtronic, Scitech, **CardioKinetix**

Institutional research support: St Jude LightLab, Cordis, Abbott, Medtronic
Problem Statement:

Congestive Heart Failure

A Global Healthcare Problem in Need of a Therapeutic Solution

Median LOS: 6 days; N = 38,702
Among Medicare beneficiaries, 27% of HF patients are re-hospitalized within 30 days

Aghababian RV. Rev Cardiovasc Med 2002; 3:S3
Jencks and Williams. NEJM 2009; 360:1418
Rationale:
LV Volume and Geometry Impact HF Outcomes

Increase in LV Volume to Compensate for Abnormal Wall Motion
High LV Filling Pressure due to Larger Volume and Stiffer Wall

LV Volume and Outcomes

Kraemer et al, J Am Coll Cardiol 2010
Konstam et al, JACC 2011
Percutaneous Ventricle Restoration Therapy (PVRT)

Goals of PVRT

1. Partition damaged myocardium
2. LV Volumes Reduction
3. Restore LV Conical Shape
4. Preserve Torsional Contraction
5. LVED Pressure Reduction
6. Increase LV Apical Ejection
7. Minimize procedural risk
8. Minimize risk of scar-related ventricular arrhythmias
Parachute Implant

- Nitinol struts with anchors
- ePTFE membrane
- Radiopaque polymer foot

The Parachute™ device is comprised of a fluoropolymer (ePTFE) membrane stretched over a nitinol frame

Nitinol frame supports torsional contraction and optimize LV outflow ejection

Shape was designed to restore conical/longitudinal geometry

The device is deployed into the apex of the left ventricle and partitions off non-contractile damaged myocardium to reduce LV volume and optimize performance of contractile, healthy myocardial

75, 75s, 85, 85s sizes currently have CE Mark
Guide Catheter (Sheath)

• 3D MSCT Modeling (Ao Arch, LVOT, LV Apex)
  – Images are 2D projections of the 3D curves
  – F/L/T views rotated 30° off true A-P for clarity

Ventricle axis

Aortic arch axis
The Parachute Delivery System

Delivery Guide
- 14 and 16 Fr. guides
- Multiple shapes
- Variable stiffness
- Kink resistant
- Dilator with 6 Fr. lumen

Delivery Catheter
- Shaped to match guides
- Flexible torque drive
- Threaded implant attachment
- Lockable handle
- Large balloon > 30mm
Parachute Pre-Clinical Data
Mechanism of Action

Mechanical Efficiency Improved by 22%

External Work
[External Work + Potential Energy]

Sheep Model

Treated
Non-Treated

Westerhof N Cardiovasc Res 2000;48:4-7
Copyright © 2000, European Society of Cardiology
PARACHUTE: First-in-Human Clinical Trials

FIH PARACHUTE (n=19)
October 2005-June 2007

PARACHUTE Feasibility (n=20)
March 2008-June 2009

Enrolled

<table>
<thead>
<tr>
<th></th>
<th>US</th>
<th>EU</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled</td>
<td>20</td>
<td>19</td>
<td>39</td>
</tr>
<tr>
<td>Implanted Per Protocol</td>
<td>18</td>
<td>16</td>
<td>34</td>
</tr>
<tr>
<td>Discharged with PARACHUTE*</td>
<td>17</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>6 mo follow-up</td>
<td>15</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>12 mo follow-up</td>
<td>14</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>24 mo follow-up</td>
<td>13</td>
<td>14</td>
<td>27</td>
</tr>
</tbody>
</table>

Population:

- NYHA Class II-IV
- EF ≥15% and ≤ 40%
- Post LAD MI, no revascularization option
- Dilated apical region with akinetic or dyskinetic wall motion abnormality
- Warfarin and ASA 1yr post implant

Independent Clinical Event Adjudication

Independent Echocardiographic and EKG Core Labs
PARACHUTE Cohort A + US Feasibility Enrollers

PARACHUTE Cohort A (19 subjects)

- Belgrade, Serbia | PI: Dr. Sinisa Gradinac | 12 subjects
- Frankfurt, Germany | PI: Dr. Horst Sievert | 5 subjects
- Bad Nauheim, Germany | PI: Dr. Albrecht Elsasser | 2 subjects

PARACHUTE US Feasibility (20 subjects)

- Geisinger Clinic | PI: Dr. Peter Berger | 2 subjects
- The Ohio State University | PI: Dr. Ernest Mazzaferri | 7 subjects
- Texas Heart Institute | PI: Dr. Igor Gregoric | 4 subjects
- Washington Hospital | PI: Dr. Ron Waksman | 1 subject
- Northwestern Hospital | PI: Dr. Charlie Davidson | 2 subjects
- Mission Hospitals – Asheville | PI: Dr. William Abernethy | 1 subject
- Morristown Memorial Hospital | PI: Dr. Frank Smart | 1 subject
- Belgrade, Serbia | PI: Dr. Sinisa Gradinac | 2 subjects
Parachute PVRT Procedure

Case Example (Courtesy from Dr. Ince)

- 66 year old man
- Anteroseptal MI 5/97, CABG 6/97, ICD-Implantation 8/97
- Ischemic Heart Failure with NYHA III
- LVEF 27%, LVEDV 184 ml, LVESV 133 ml
- Anteroapical regional wall motion abnormalities
Parachute pre-implantation echo assessment
Parachute implantation
Parachute implantation
Parachute implantation
Post-Parachute implantation echo assessment
Post-Parachute implantation (3D Cardiac CT)

Device Positioning, Preserved LV Systolic Torsion
## Device Related Major Events

<table>
<thead>
<tr>
<th>MACE Category</th>
<th>Prior to Discharge</th>
<th>Discharge to 6 Mo.</th>
<th>6 Mo. to 12 Mo.</th>
<th>Total (events)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization for heart failure</td>
<td></td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Inadequate Attachment</td>
<td></td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Total (events)</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>
Histology: 5-month Post Parachute

The luminal surface is completely endothelialized by smooth, glistening tan-white tissue. The foot is centered at the LV apex.

Foot is well apposed to the endocardial surface at the LV apex, with good healing response characterized by endothelialization on both sides of the ePTFE membrane.

Cause of Death: STEMI

R. Virmani (CV Path)
Left Ventricle Hemodynamic Assessment (LVEDP)

Normal Range 5-12 mmHg

Baseline: 20 mmHg
Post-Procedure: 18 mmHg
6-month: 14 mmHg

Paired data, n=8. Mean ± SEM
p=0.02, Baseline-6 month

p=0.02
Serial Echo Case Example

Diastole  
BASELINE  
Systole

Diastole  
TWO YEARS  
Systole

LV
LA
### Summary: Echocardiographic Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6M</th>
<th>12M</th>
<th>24M</th>
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</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>N=27</td>
<td>N=28</td>
<td>N=27</td>
<td>N=26</td>
</tr>
<tr>
<td><strong>Left Ventricle End Diastolic Volume Index (LVEDVI), ml/M²</strong></td>
<td>127.5 ± 19.6</td>
<td>106.7 ± 17.4</td>
<td>109.7 ± 24.8</td>
<td>114.7 ± 20.5</td>
</tr>
<tr>
<td><strong>Left Ventricle End Systolic Volume Index (LVESVI), ml/M²</strong></td>
<td>93.8 ± 19.4</td>
<td>75.3 ± 15.6</td>
<td>78.0 ± 20.5</td>
<td>83.5 ± 17.1</td>
</tr>
<tr>
<td><strong>Cardiac Output, L/min</strong></td>
<td>4.4 ± 1.1</td>
<td>4.3 ± 1.4</td>
<td>4.2 ± 1.5</td>
<td>4.5 ± 1.5</td>
</tr>
<tr>
<td><strong>Longitudinal Length (cm)</strong></td>
<td>10.1 ± 0.6</td>
<td>8.9 ± 0.9</td>
<td>8.6 ± 0.8</td>
<td>8.7 ± 0.7</td>
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<tr>
<td><strong>EF (%)</strong></td>
<td>26.9 ± 6.9</td>
<td>29.6 ± 7.6</td>
<td>29.3 ± 8.31</td>
<td>27.3 ± 5.9</td>
</tr>
<tr>
<td><strong>Stroke Volume (ml)</strong></td>
<td>68.8 ± 16.5</td>
<td>64.2 ± 17.3</td>
<td>65.3 ± 20.7</td>
<td>64.5 ± 17.6</td>
</tr>
<tr>
<td><strong>Heart Rate (beats/min)</strong></td>
<td>63.2 ± 8.8</td>
<td>66.9 ± 11.4</td>
<td>64.6 ± 9.2</td>
<td>70.1 ± 11.8</td>
</tr>
<tr>
<td><strong>LV Mass (g)</strong></td>
<td>292.2 ± 57.9</td>
<td>272.3 ± 57.2</td>
<td>289.4 ± 72.9</td>
<td>278.2 ± 59.3</td>
</tr>
</tbody>
</table>
Sustained Left Ventricle Volume Reduction

EDVi post vs. 24M Volume (p = 0.74)
3D MSCT Assessment: Volume Reduction, Geometric Restoration Segmental Functional Assessment

PRE Percentage Wall Thickening

Segmental Ejection Fraction

Improvement of contractility in basal segments

Data to be presented at ESC 2012
PARACHUTE Outcomes in Perspective

Therapies that reduce ESV have higher probability to decrease mortality

* Kramer et al, J Am Coll Cardiol 2010
Functional Outcomes

NYHA

<table>
<thead>
<tr>
<th>Baseline</th>
<th>6M</th>
<th>12M</th>
<th>24M</th>
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</thead>
<tbody>
<tr>
<td>2.6</td>
<td>1.7</td>
<td>1.6</td>
<td>1.9</td>
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p < 0.01

MLWHF

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<th>Baseline</th>
<th>6M</th>
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<td>39</td>
<td>29</td>
<td>27</td>
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</table>

p < 0.05

6min Walk

<table>
<thead>
<tr>
<th>Baseline</th>
<th>6M</th>
<th>12M</th>
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<tbody>
<tr>
<td>351.6</td>
<td>377.9</td>
<td>389</td>
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</table>

p < 0.20
2-Year Cardiac Death
1-Year Worsening HF + Death

- Worsening HF:
  - 16.1%
2-Year Worsening HF + Death

Rates @ 2-year follow-up

Per Protocol (34)  32.9%
Treated pts (n=31) 32.2%
PARACHUTE Outcomes in Perspective

12M Mortality + Hosp. for WHF

Data from CHAMPION, MIRACLE, COMPANION, MIRACLE ICD, RETHINQ, CRT-HF, FIX, CARE, and PARACHUTE

12M estimates were made if only 6M data was published (6M x 1.5 = 12M)
PARACHUTE Current Clinical Trials

European Cohort B Feasibility Trial
- 40 Patients Enrolled to date
CE Mark PMS Trial
- Enrollment to start May 22, 2012

PARACHUTE IV (Pivotal, FDA IDE Trial)
N=478

1:1

Treated
N~239

Control
N~239

6M, 1-5Y FU

- Open Label, Randomized
- IDE Approved, start enrollment Summer ’12
- 50 US, 15 European sites
- Key Inclusion Criteria:
  - NYHA Class III-IV
  - EF >15% and < 35%
  - Post LAD MI, disfunctional apex
- CT imaging at baseline for sizing and anatomy
- Echo at Baseline, 6mo, and annually
- Treated patients on Warfarin and ASA 1yr
Conclusions

- Percutaneous Ventricular Restoration (PVR) therapy using the Parachute™ device in patients with ischemic heart failure and LV anterior-apical wall dilatation was shown to be safe, associated with sustained reduction in LV volumes by echocardiography and relatively low clinical events and up to 2 years.

- These promising results led to the design and conduct of a large multicenter, multinational randomized pivotal trial to evaluate the efficacy of PVR utilizing the Parachute™ LV partitioning device compared with optimal medical therapy (OMT) in patients with ischemic HF and dilated anterior-apical wall.