Corvia Medical InterAtrial Shunt Device (IASD®) for Heart Failure with Preserved Ejection Fraction

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Disclosure Statement of Financial Interest

I, Scott Lilly 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.
**Heart Failure**

**Preserved Ejection Fraction**

**DIAGNOSIS:** Exercise Hemodynamics

- Elevated left atrial pressure at rest or with activity, is a near-universal finding in patients with HFpEF
- Greater increase in PCW pressure than RA pressure

<table>
<thead>
<tr>
<th></th>
<th>Resting</th>
<th>Exercise</th>
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</thead>
<tbody>
<tr>
<td>RA</td>
<td>5 ± 2</td>
<td>14 ± 4</td>
</tr>
<tr>
<td>PCW</td>
<td>11 ± 2</td>
<td>32 ± 6</td>
</tr>
<tr>
<td>PASP</td>
<td>31 ± 7</td>
<td>59 ± 11</td>
</tr>
<tr>
<td>PVR</td>
<td>3.2 ± 1.5</td>
<td>2.4 ± 1.2</td>
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<tr>
<td>RA</td>
<td>4 ± 2</td>
<td>6 ± 3</td>
</tr>
<tr>
<td>PCW</td>
<td>9 ± 3</td>
<td>13 ± 5</td>
</tr>
<tr>
<td>PASP</td>
<td>24 ± 6</td>
<td>35 ± 7</td>
</tr>
<tr>
<td>PVR</td>
<td>2.1 ± 1</td>
<td>1.9 ± 0.9</td>
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</tbody>
</table>

**Borlaug et al. Circ Heart Fail. 2010; 3:588-595.**
**PROGNOSIS:** Related to LAP

*Left atrial pressure is related to exercise capacity, heart failure hospitalizations, and survival*

*Exercise-associated pressures can better discriminate*
Heart Failure
Preserved Ejection Fraction

Can an Interatrial Shunt be Therapeutic?

Elevated LV filling pressures (Elevated LAP)
Pulmonary Venous hypertension
Pulmonary Congestion Dyspnea

RA → LA Flow
Sustained Patency

Heart Failure
Preserved Ejection Fraction

Observational Basis for Interatrial Shunt Therapy


Mask HFpEF
Closure precipitates HF
Relieves Congestion
?Benefit in Left Heart Disease

Atrial Septostomy for Left Atrial Decompression During Extracorporeal Membrane Oxygenation by Inoue Balloon Catheter

Yen-Nien Lin, MD, Yin-Huei Chen, MD, Huang-Joe Wang, MD; Jui-Sung Hung, PhD, Kuan-Cheng Chung, PhD, Ping-Han Lo, MD

Background: Refractory pulmonary edema is an infrequent but serious complication in patients receiving veno-venous extracorporeal membrane oxygenation (VV-ECMO) for myocardial failure. Left atrial (LA) decompression in this setting is important. Although a few methods have been reported, the experience is mostly limited to children. We aimed to evaluate the feasibility of inoue balloon catheter in percutaneous trans-apical LA decompression in adult cardiogenic patients.
Heart Failure
Preserved (& Mid-Range Ejection) Fraction

Corvia IASD® Device, Clinical Studies

- Pilot study (N=11): non-randomized, single-arm
  - Completed (Søndergaard L, et al. Eur J Heart Fail 2014)
- REDUCE LAP-HF (CE Mark) Study (N=64): non-randomized, single-arm
  - Completed (Hasenfuß Lancet 2016; Kaye Circ. HF 2016)
  - 2Y follow-up complete (Kaye, ESC 2018)
- REDUCE LAP-HF I (N=44): RCT mechanistic study
  - FDA IDE 30 Day Complete (Feldman T, Shah SJ. Circulation. 2018;137:364–375)
  - 1Y follow-up complete (Shah SJ, Feldman T, JAMA 2018)
- REDUCE LAP-HF II (N=608): RCT pivotal study
  - FDA approved IDE; recruiting
- HFrEF Feasibility study
  - FDA approved IDE; recruiting
- REDUCE LAP-HF III (N=100): Post-market Registry
  - Germany
  - Recruiting
Heart Failure
Preserved (& Mid-Range Ejection) Fraction

**REDUCE LAP HF I**

**Design**
Randomized, sham-controlled trial
1:1 randomization
- Sedation, femoral venous access, ICE/TEE
- + transseptal IASD implantation

**Inclusion**
NYHA III-IV, LVEF > 40%,
1-yr HF Hosp or
↑BNP/NT-Pro BNP
ePCW ≥ 25 mm Hg
PCW - RA ≥ 5 mm Hg

**Exclusion**
Cardiac index < 2.0
Sig valve disease
Sig RV dysfunction
PVR > 4 Wood units
Heart Failure
Preserved & Mid-Range Ejection Fraction

Randomized, controlled trial (1:1)
NYHA III-IV, LVEF > 40%, HF Hosp or ↑BNP
PCW ≥ 25 mm Hg (Exercise); PCW - RA ≥ 5 mm Hg

REDUCE LAP-HF I (n=44)

CONTROL

IASD

Heart Failure
Preserved & Mid-Range Ejection Fraction

REDUCE LAP-HF I One Year Results

**IASD Change in NYHA**

- **Baseline**
- **1 Month**
- **6 Months**
- **12 Months**

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<th>Improved I Class</th>
<th>Improved II Classes</th>
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**Control Change in NYHA**

- **Baseline**
- **1 Month**
- **6 Months**
- **12 Months**

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**Shunt Fraction**

- **Baseline**
- **6 Mo**
- **12 Mo**

- **1.27**
- **1.25**

At 12 months, even with a small sample size there was a trend toward greater improvement in NYHA class compared to control. Shunt patency has been 100%, and the QpQs has been stable over the observed study period.
## Heart Failure
Preserved & Mid-Range Ejection Fraction

### REDUCE LAP-HF | One Year Results

<table>
<thead>
<tr>
<th></th>
<th>IASD</th>
<th>Control</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in NYHA class (12M – baseline)</td>
<td>-1 (-1,0) [n=20]</td>
<td>0 (-1,0) [n=19]</td>
<td>0.083</td>
</tr>
<tr>
<td>Change in 6MWT distance (12M – baseline)</td>
<td>16 (-57,30) [n=20]</td>
<td>13.6 (-10,72) [n=19]</td>
<td>0.308</td>
</tr>
<tr>
<td>Change in QOL (12M – baseline)</td>
<td>[KCCQ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Summary score</td>
<td>+10.5 (0.7,18.8) [n=20]</td>
<td>+8.1 (-5.7,20.6) [n=19]</td>
<td>0.570</td>
</tr>
<tr>
<td>Clinical Summary score</td>
<td>+10.4 (-6.5,26.0)</td>
<td>+3.1 (-4.2,18.8)</td>
<td>0.827</td>
</tr>
</tbody>
</table>
Heart Failure
Preserved & Mid-Range Ejection Fraction

REDUCE LAP-HF I One Year Results

P = 0.20

P = 0.08

MACCRE: Major adverse cardiac, cerebrovascular and renal events
Heart Failure
Preserved & Mid-Range Ejection Fraction

<table>
<thead>
<tr>
<th>325 Patient Years of follow-up</th>
<th>Pilot study (N=11)</th>
<th>REDUCE LAP-HF (N=64)</th>
<th>REDUCE LAP-HF I (N=22)</th>
<th>Combined (N=97)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1Y % NYHA I/II vs. baseline</td>
<td>55% vs. 0%</td>
<td>82% vs. 29%</td>
<td>63% vs. 0%</td>
<td>74% (vs.19%)</td>
</tr>
<tr>
<td>2Y % NYHA I/II vs. baseline</td>
<td>NA</td>
<td>69% vs. 29%</td>
<td>TBD</td>
<td></td>
</tr>
<tr>
<td>3Y % NYHA I/II vs. baseline</td>
<td>NA</td>
<td>65% vs. 27%</td>
<td>TBD</td>
<td></td>
</tr>
<tr>
<td>1Y Freedom from IV HFH</td>
<td>82%</td>
<td>80%¹</td>
<td>81%</td>
<td>80%</td>
</tr>
<tr>
<td>1Y Freedom from IV HFH in</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>patients with prior year HFH</td>
<td>67%</td>
<td>88%</td>
<td>75%</td>
<td>79%</td>
</tr>
<tr>
<td>1 Y Patency with L→R flow</td>
<td>100%²</td>
<td>100%²</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>
Heart Failure
Preserved & Mid-Range Ejection Fraction

Aggregate Safety Profile

<table>
<thead>
<tr>
<th>325 Patient Years of follow-up</th>
<th>Pilot study (N=11)</th>
<th>REDUCE LAP-HF (N=64)</th>
<th>REDUCE LAP-HF I (N=22)</th>
<th>Combined (N=97)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Year Survival</td>
<td>100%</td>
<td>95.4%</td>
<td>95.2%</td>
<td>96%</td>
</tr>
<tr>
<td>2 Year Survival</td>
<td>91%</td>
<td>92%</td>
<td>91%</td>
<td>91%</td>
</tr>
<tr>
<td>3 Year Survival</td>
<td>82%</td>
<td>89%</td>
<td>TBD</td>
<td></td>
</tr>
<tr>
<td>4 Year Survival</td>
<td>73%</td>
<td>84%</td>
<td>TBD</td>
<td></td>
</tr>
<tr>
<td>1 Year Freedom from CVA</td>
<td>100%</td>
<td>98.5%</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>2 Year Freedom from CVA</td>
<td>100%</td>
<td>98.5%</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>3 Year Freedom from CVA</td>
<td>100%</td>
<td>98.5%</td>
<td>TBD</td>
<td></td>
</tr>
<tr>
<td>4 Year Freedom from CVA</td>
<td>100%</td>
<td>NA</td>
<td>TBD</td>
<td></td>
</tr>
<tr>
<td>IASD thrombosis/removal</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Conclusions

• Interatrial shunt therapies can reduce activity-related elevations in left atrial pressure (eRHC)
• Mid-term safety and efficacy profiles are favorable
• Patient-selection is important (eRHC)
• Shunt diameter is important, may relate to patency and efficacy
Thank You

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