Inter-atrial Shunt Device

Corvia Medical

Ted Feldman, M.D., MSCAI FACC FESC
Evanston Hospital

29th Annual Scientific Symposium
Transcatheter Cardiovascular Therapeutics
October 29th-November 2nd, 2017
Denver, CO
Disclosure Information

The following relationships exist:

Grant support: Abbott, BSC, Corvia, Edwards, WL Gore
Consultant: Abbott, BSC, Edwards, WL Gore
Stock Options: Mitralign, Cardiac Dimensions

Off label use of products and investigational devices will be discussed in this presentation
Pulmonary capillary wedge pressure at rest and during exercise and long-term mortality in patients with dyspnea & suspected heart failure with preserved ejection fraction
Mortality and modest 6M ePAD changes

18% had PAD decrease with decreased mortality

29% had PAD increase with increased mortality

18% had PAD decrease with decreased mortality

29% had PAD increase with increased mortality
Corvia Medical Investigational Device

- Catheter
- Handle
- Implant
  - 19mm OD
  - 8 mm ASD

16F introducer compatible
Fluoroscopic Images

LA legs deployed

Post deployment
Left Atrial Decompression:
Computer simulation: 8mm interatrial shunt device (IASD) provides acute LA decompression at rest & during exercise

Kaye et al J Cardiac Fail 2014;20:212e221
A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial

Gund-Hanfjügg, Chris Haywood, Dan Burkhoff, Frank E Silvency, Scott McGann, Fintz Gestadsson, Filip Molko, Jan Van der Heyden, Irene Long, Mark C Perin, John G G Cockman, Martin Leun, David M Kaye, on behalf of the REDUCE LAP-HF study investigators

Summary
Background Heart failure with preserved ejection fraction (HFP EF) is a common, globally recognised, form of heart failure for which no treatment has yet been shown to improve symptoms or prognosis. The pathophysiology of HFP EF is complex but characterised by increased left atrial pressure, especially during exertion, which might be a key therapeutic target. The rationale for the present study was that a mechanical approach to reducing left atrial pressure might be effective in HFP EF.

Methods The REDUCE Elevated Left Atrial Pressure in Patients with Heart Failure (REDUCE LAP-HF) study was an open-label, single-arm, phase 1 study designed to assess the performance and safety of a transcatheter intracardiac shunt device (IASS, Corvia Medical, Tewksbury, MA, USA) in patients other than 40 years of age with symptoms of HFP EF despite pharmacological therapy, left ventricular ejection fraction higher than 40%, and a raised pulmonary capillary wedge pressure at rest (≥15 mm Hg) or during exercise (≥25 mm Hg). The study was done at 21 centres (all departments of cardiology in the UK, Netherlands, Belgium, France, Germany, Austria, Denmark, Australia, and New Zealand). The coprimary endpoints were the safety and performance of the IASS at 6 months, together with measures of clinical efficacy, including functional capacity and clinical status, assessed per protocol. This study is registered in ClinicalTrials.gov, number NCT01919363.

Findings Between Feb 8, 2014, and June 19, 2015, 68 eligible patients were entered into the study. IASS placement was successful in 64 patients and seemed to be safe and well tolerated; no patient had a peri-procedural or major adverse cardiac or cerebrovascular event or need for cardiac surgical intervention for device-related complications during 6 months of follow-up. At 6 months, 31 (52%) of 60 patients had a reduction in pulmonary capillary wedge pressure at rest. 34 (58%) of 59 had a lower pulmonary capillary wedge pressure during exercise, and 23 (39%) of 59 fulfilled both those criteria. Mean exercise pulmonary capillary wedge pressure was lower at 6 months than at baseline, both at 20 watts workload (mean 32 mm Hg [SD 9] at baseline vs 29 mm Hg [7] at 6 months, p<0·0124) and at peak exercise (34 mm Hg [9] in 32 [8], p=0·0255), despite increased mean exercise duration (baseline vs 6·7 min [SD 3·1] vs 8·2 min [4·9], p=0·048). Sustained device patency at 6 months was confirmed by left-right shunting (pulmonary/systemic flow ratio: 1·06 [SD 0·32] at baseline vs 1·27 [0·28] at 6 months, p=0·004).

Interpretation Implementation of an intracardiac shunt device is feasible, seems to be safe, reduces left atrial pressure during exertion, and could be a new strategy for the management of HFP EF. The effectiveness of IASS compared with existing treatment for patients with HFP EF requires validation in a randomised controlled trial.
Intracardiac shunt device for HFpEF
(REDUCE LAP-HF): multicentre, open-label, single-arm, phase 1 trial

<table>
<thead>
<tr>
<th>Age, years</th>
<th>69 (8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>22</td>
</tr>
<tr>
<td>Women</td>
<td>42</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>18</td>
</tr>
<tr>
<td>III</td>
<td>46</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
</tr>
<tr>
<td>Body-mass index, kg/m²</td>
<td>33 (6)</td>
</tr>
<tr>
<td>eGFR, ml/min per 1.73 m²</td>
<td>62 (21)</td>
</tr>
<tr>
<td>Haemoglobin, g/L</td>
<td>133 (5)</td>
</tr>
</tbody>
</table>

Comorbidities
- Diabetes: 21 (33%)
- Hypertension: 52 (81%)
- Atrial fibrillation: 23 (36%)
- Coronary artery disease: 23 (36%)

Echocardiography
- Left ventricular end diastolic volume index, ml/m²: 68 (13)
- Left ventricular ejection fraction, %: 47 (7)
- Left ventricular mass index, g/m²: 119 (36)
- Left arterial diastolic volume index, ml/m²: 34 (17)
- Right ventricle diastolic volume index, ml/m²: 22 (9)
- Right artery volume index, ml/m²: 35 (17)
- E/A ratio: 1.3 (0.8)
- E/e' ratio: 13.9 (5.9)
- TAPSE, mm: 20 (4)
- NT-proBNP, pg/mL: 377 (222–925)

Resting hemodynamics
- Mean right arterial pressure, mm Hg: 9 (4)
- Mean pulmonary arterial pressure, mm Hg: 25 (7)
- Mean pulmonary capillary wedge pressure, mm Hg: 17 (5)
- Cardiac output, L/min: 5.5 (1.6)

n=64
Hasenfuß G. Lancet 2016; 387: 1298–304
Intracardiac shunt device for HFP EF (REDUCE LAP-HF): multicentre, open-label, single-arm, phase 1 trial

Baseline 6 Months

Exercise PCWP-20W

PCWP mmHg

p=0.012

Hasenfuß G: Lancet 2016; 387: 1298–304
1-Year Outcomes After InterAtrial Shunt Device for HFpEF

Qp:Qs

Baseline 6 Months 12 Months

Qp:Qs

REDUCE LAP-HF Kaye Circ Heart Fail. 2016 Dec;9(12). pii: e003662
1-Year Outcomes After InterAtrial Shunt Device for HFpEF

Workload indexed peak exertion wedge pressure

REDUCE LAP-HF Kaye Circ Heart Fail. 2016 Dec;9(12). pii: e003662
Sustained Clinical Efficacy

At one year IASD therapy was associated with sustained improvements in NYHA class, quality of life score and six minute walk distance.

**NYHA Class**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6M</th>
<th>12M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>50%</td>
<td><strong>66%</strong></td>
<td>*<strong>77%</strong></td>
</tr>
<tr>
<td>II</td>
<td>20%</td>
<td><strong>20%</strong></td>
<td><strong>20%</strong></td>
</tr>
<tr>
<td>III</td>
<td>10%</td>
<td><strong>5%</strong></td>
<td><strong>10%</strong></td>
</tr>
<tr>
<td>IV</td>
<td>5%</td>
<td><strong>3%</strong></td>
<td><strong>2%</strong></td>
</tr>
</tbody>
</table>

**MLWHF Score**

Mean Δ at 1 year: 15 points

**6MWD**

Mean Δ at 1 year: 33m

RM-Friedman's test:

**p<0.01, ***p<0.001

REDUCE LAP-HF Kaye Circ Heart Fail. 2016 Dec;9(12). pii: e003662
Freedom from HF Re-Hospitalization
Comparison to CARDIOMEMS Preserved EF Cohort

CHAMPION Treated Arm
n=62
CHAMPION Control Arm
n=57
REDUCE LAP IASD
n=16

% Free from Re-Hospitalization ≈ 18 months
71
44
81

Cardiomems data: FDA panel pack
Circ Heart Fail. 2016 Dec;9(12)
Transcatheter InterAtrial Shunt Device for the Treatment of Heart Failure: Rationale and Design of the Randomized Trial to REDUCE Elevated Left Atrial Pressure in Heart Failure (REDUCE LAP-HF I)

- HF patients with an LV ejection fraction >40% and elevated left sided filling pressures who remain symptomatic despite optimal guideline directed medical therapy
- multicenter, prospective, randomized, controlled, single blinded trial
- **40 subjects** at 20 investigational sites in the U.S. and 5 sites OUS
- Non-implant control group and **1:1 randomization**
- qualification with supine bicycle **exercise testing during right heart catheterization**
  - elevated PCWP and gradient between PCWP and RA pressure
- all patients will be sedated and both arms will undergo femoral venous access
  - blinding will include sedation, earphones with music, and blindfolding, or the use of opaque screens to prevent viewing imaging screens
  - each site will assign blinded and un-blinded staff to facilitate unbiased patient assessments through 12 months of follow-up
- control patients who still meet inclusion criteria allowed to crossover to treatment at ≥12 months after the baseline procedure
- **30 day results presented as LBCT at AHA**

Corvia Medical Clinical Study Pipeline

- Pilot study (n=11): non-randomized, single-arm
  - Completed (Søndergaard L, et al. Eur J Heart Fail 2014); extended follow-up ongoing

- CE Mark Study (n=64): non-randomized, single-arm
  - Completed (Hasenfuß Lancet 2016; Kaye Circ. HF 2016 ); 2Y follow-up complete Q3 2017

- REDUCE LAP-HF I (n=44): RCT mechanistic study
  - FDA approved IDE; (enrollment complete); 1Y follow-up complete Dec 2017

- REDUCE LAP-HF II (n=380): 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