Corvia Medical IASD Clinical Results

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Standing in for: Mark Petrie, University of Glasgow
Conflict of interest

M Petrie:  
Unpaid member of the Corvia Medical Inc. Scientific Advisory Group

D Burkhoff:  
Hemodynamic Core Lab for/Consultant for Corvia
The Premise:
PCWP Increases Rapidly during Exercise

Circ Heart Failure 2010 Sep;3(5):588-95
Elevated left atrial pressure - pulmonary congestion and symptoms

Transcatheter implant to create a small permanent interatrial shunt

Reduce left atrial pressure
Studies and trials with Corvia IASD device

- Pilot study (n=11)  
- **Observational study REDUCE-LAP HF (n=64)**
- Pilot RCT (REDUCE LAP RCT I) in HEF-PEF (n=44)
- Pivotal RCT (REDUCE LAP RCT II) now recruiting (n=608)
- Pilot study in HF-REF
REDUCE LAP-HF
observational data (n=64)

1. Chronic HF documented by one or more of the following:
   - NYHA III/IV
   - One hospital admission for HF within the last 12 months

2. LVEF ≥ 40% as determined by echocardiography.

3. Hemodynamic inclusion criteria
   - PCWP at rest ≥15 mmHg and greater than CVP, OR
   - PCWP during supine bike exercise ≥25mm Hg

Lancet 2016;387:1298-304
REDUCE LAP-HF - data at 6 months

- Improved NYHA class
- Improved quality of life
- Improved 6 minute walk
- Improved exercise time
- Improved cardiac output (rest and exercise)
- Reduced PCWP (20W and peak exercise)
Inclusion criteria:
• Open label
• LVEF ≥ 40%,
• NYHA class II-IV
• Elevated PCWP
  – ≥ 15 mmHg (rest) or
  – ≥ 25 mmHg (supine bicycle exercise)

Acceptable safety profile at 12, 24 months
REDUCE LAP-HF – echocardiographic data at 1 year

**LVEF**

- Baseline
- 6M
- 12M

**RVEF**

- Baseline
- 6M
- 12M

**LVEDVI**

- Baseline
- 6M
- 12M

**RVEDVI**

- Baseline
- 6M
- 12M

*p*<0.05, **p**<0.01, ***p***<0.001
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2014

2019
Implantation of the IASD System II in patients with HF and EF ≥ 40% compared to sham control will result in:
- Reduction in exercise PCWP
REDUCE LAP-HF I RCT – inclusion criteria

- NYHA III or IV AND recent HF hospitalisation or NT-BNP>425 SR, >1265 AF
- EF≥40%
- End-expiratory PCWP during supine ergometer exercise ≥ 25mm Hg and greater than RAP by ≥ 5 mm Hg.
- Site determined echocardiographic evidence of “diastolic dysfunction”
REDUCE LAP-HF I RCT – exclusion criteria

- Significant RV dysfunction
  - TAPSE < 1.4 cm, RV > LV size

- PVR > 4 Wood units
**REDUCE LAP-HF I RCT (n=44)**

**Randomised:** 1:1 randomization to IASD vs. sham control
i) IASD: Sedation, femoral venous access with ICE/TEE + trans-septal IASD implantation
ii) Sham control: Sedation, femoral venous access with examination of interatrial septum and LA with ICE/TEE

**Blinded:** patient, HF physician, and research staff

**Primary end point:** Change in supine exercise PCWP at 1 month

Independent DSMB, CEC, hemodynamic, and echocardiographic core lab
Change in PCWP: Baseline to 1 month

0/22 MACCRE events in IASD group
1/22 MACCRE events in control group

Feldman T Circulation. 2018;137:364–375
What next?
The pivotal trial – REDUCE-LAP RCT II

608 patients

- IASD implantation
- No IASD implantation

BLINDED, SHAM-CONTROLLED
REDUCE LAP RCT II – patient population

- Chronic symptomatic HF documented by the following:
  - Symptoms of HF on diuretics for $\geq 30$ days
  - NYHA II (history of III)-IV HF
  - $\geq 1$ HF hospital admission OR elevated NT-BNP

- Ongoing stable HF management according to the 2017 ACC/AHA Guidelines for the Management of Heart Failure

- Site determined echocardiographic evidence of diastolic dysfunction

- PCWP during supine ergometer exercise $\geq 25$mm Hg and greater than RAP by $\geq 5$ mm Hg
**Randomised:** 1:1 randomization to IASD vs. sham control
- IASD: Sedation, femoral venous access with ICE/TEE + trans-septal IASD implantation
- Sham control: Sedation, femoral venous access with examination of interatrial septum and LA with ICE/TEE

**Blinded:** patient, HF physician, and research staff

Independent DSMB, CEC, hemodynamic, and echocardiographic core lab
Primary end point

- Cardiovascular mortality or non-fatal, ischemic stroke through 12 months
- Rate of total HF admissions or healthcare facility visits for IV diuresis for HF through 12 months
- Change in KCCQ score between baseline and 12 months
Primary end point

Hierarchy of end points

- CV death or CVA
- HF hospitalisation (recurrent)
- Change in KCCQ
Safety-related measures

- Device and or procedure related SAEs through 12 months
- All serious adverse events (SAEs) through 12 months
- Systemic embolic events through 12 months
- Increase in RV size/decrease in RV function through 12 months
Conclusion

Corvia

- Observational 64 patient study promising

- Pilot, feasibility, randomised, sham-controlled trial proved proof of concept

- Large RCT with hard end points is well underway
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