THE 25TH ANNIVERSARY CRT22 CARDIOVASCULAR RESEARCH TECHNOLOGIES

Transcatheter Interatrial Shunt for Treatment of Heart Failure

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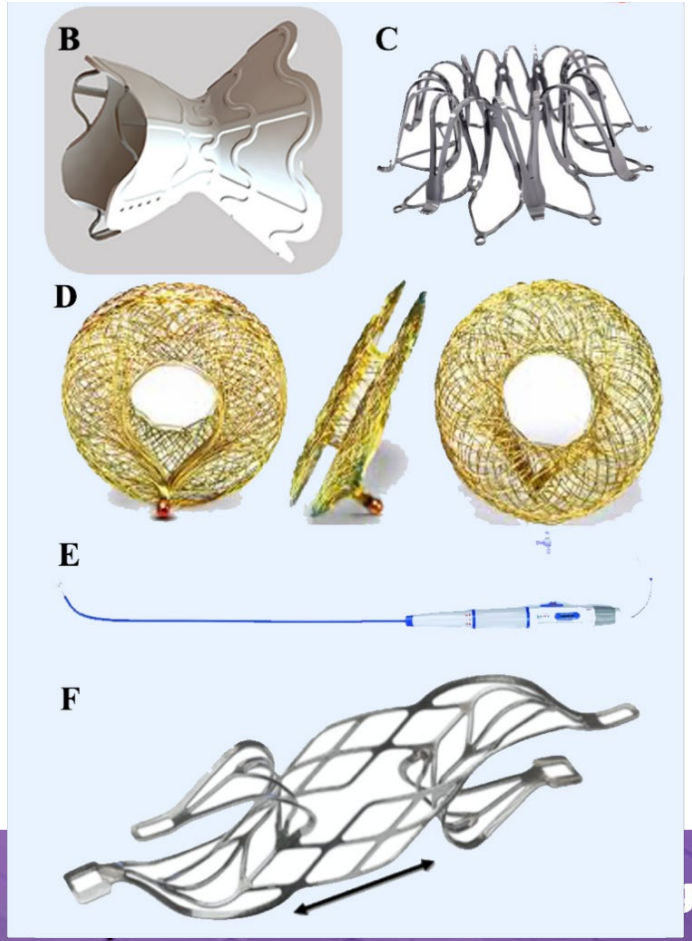
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Grant/Research Support	Abiomed, Ancora, Axon, Edwards,
Consulting Fees/Honoraria	Abbott, AquaPass, Axon, BackBeat Medical, BioMind, Corvia, Impulse Dynamics, Therox, Zoll
Ownership/Founder	PVLoops LLC

At least 7 Approaches to creating IASD

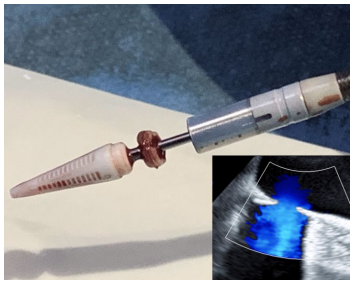
- Implantable devices:
  - Corvia Atrial Shunt System
  - V-Wave Ventura Shunt
  - Occlutech Atrial Flow Regulator (AFR)
  - Edwards Coronary Sinus Shunt



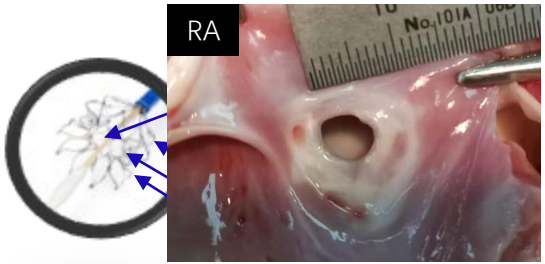
At least 7 Approaches to creating IASD

- 4 Implantable devices
- 3 that leave no device behind

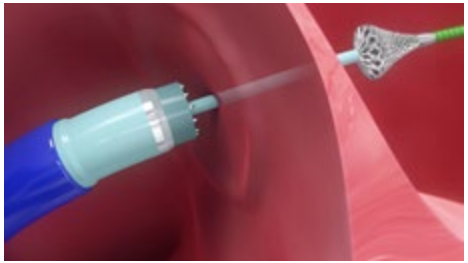
Alleviant



NoYa

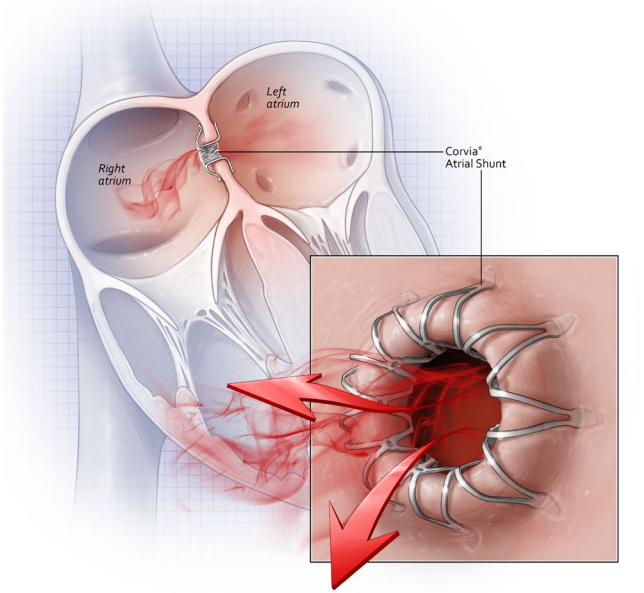


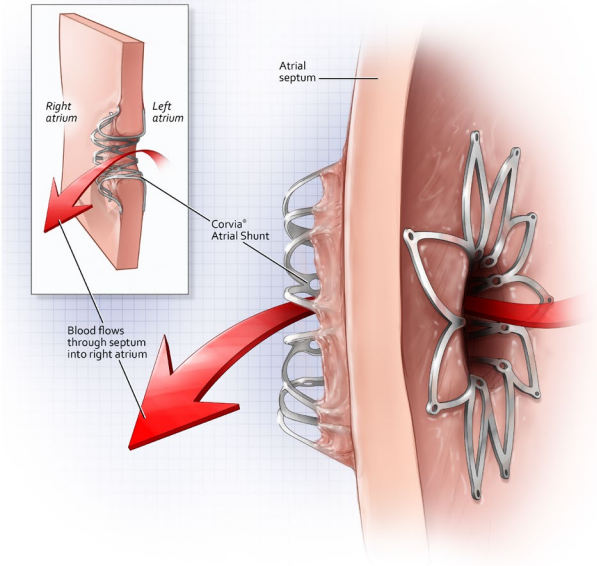
InterShunt



Corvia Atrial Shunt

MODE OF ACTION: Decompression of the left atrium by on-demand shunting from LA → RA (Qp:Qs 1.2-1.3)





Corvia Atrial Shunt Clinical Evidence Development

Patient Profile: Symptomatic HF, EF≥40%, hemodynamically confirmed elevated LAP

Pilot Study
*Observational study, 2013**
(n=11)

OBJECTIVE
Evaluate device safety & potential benefit at 30 days.

RESULTS
Evidence of significant PCWP drop and procedural safety at 30 days.[1] NYHA & QoL improvements at 1 year.[2]

REDUCE LAP-HF
*Observational study, 2015**
(n=64)

OBJECTIVE
Understand device safety & therapy performance in larger patient cohort.

RESULTS
Evidence of sustained PCWP drop and device patency at 6m & 12m. Sustained symptom, 6MWT, QoL improvement through 3 years.[3-5]

REDUCE LAP-HF I
*Randomized, blinded, sham-controlled trial, 2016**
(n=44)

OBJECTIVE
Evaluate peri-procedural safety & device effectiveness against control arm.

RESULTS
Demonstrated mechanistic effect. Improvement in HF events, QoL, and symptoms vs. control at 1 year. 100% shunt patency at 1 year.[6,7]

REDUCE LAP-HF II
*Randomized, blinded, sham-controlled trial, 2020**
(n=626)

OBJECTIVE
Evaluate safety & clinical efficacy against control arm in powered study.

RESULTS
Overall neutral; safety consistent with prior studies; large responder population with improvement of QoL and reduction of HF events.[8]

[1]Malek et al. *Int J Cardiol*, 2015; [2]Søndergaard L, et al. *Eur J Heart Fail* 2014; [3]Hasenfuβ et al, *Lancet*, 2016; [4]Kaye D, et al. *Circ Heart Fail* 2016; [5]Unpublished 3-year results on file at Corvia Medical; [6]Feldman et al. *Circulation*, 2018; [7]Shah SJ et al. *JAMA Cardiol*, 2018; [8]Shah SJ et al. *Lancet*, 2022.

REDUCE LAP-HF II study design[1]

PHASE III, MULTI-CENTER, DOUBLE-BLIND, SHAM-CONTROLLED TRIAL

PURPOSE: Evaluate the clinical efficacy and safety of the Corvia Atrial Shunt to improve quality of life and reduce HF related symptoms and events in patients with HFpEF or HFmrEF

Study Population
N = 626 randomized

Symptomatic HF, ongoing GDMT, age ≥40, LVEF ≥40%, preserved RV function, elevated exercise PCWP (≥25 mm Hg) with left-to-right gradient (≥ 5mmHg)

Atrial Shunt Treatment
N=314

Sham Control
NN=312

PRIMARY ENDPOINT

Hierarchical composite of cardiovascular mortality or non-fatal, ischemic stroke through 12m, rate of total HF events (first and recurrent) through 24m & time to first HF event, change in KCCQ score between baseline & 12m

SECONDARY ENDPOINTS

- Composite safety endpoint (MACCRE)
- Rate of HF admissions or IV diuresis, through 24m
- Change in NYHA Class between baseline & 12m
- Change in KCCQ score between baseline & 12m

[1]Berry, N et al. *Am Heart J*, vol. 226 (2020): 222-231

REDUCE LAP-HF II Primary Results

Primary Endpoint	Win Ratio* (95% CI)	p-Value
Composite Endpoint	0.98 (0.8, 1.2)	0.85

Efficacy Endpoints	Treatment (N = 309)	Control (N = 312)	p-Value
CV death or non-fatal ischemic stroke	1% (4 events)	1% (2 events)	0.41
Cardiovascular Death	1% (4 events)	1% (2 events)	0.65
Non-fatal Ischemic Stroke	<1% (1 event)	0% (0 events)	0.32
Total HF events per patient-year	0.28	0.25	0.45
Change in KCCQ-OSS (Mean ± SD)	11.5±22	10.5±21	0.73
Change in NYHA Class	**-0.5 (-1.0, 0.0)**	**0.0 (-1.0, 0.0)**	**0.006**

*In win ratio calculation, all patients are compared with each other in pairwise manner on values of the components in a hierarchical manner (1 = neutral, >1 = treatment better, <1 sham better)

High Exercise PVR + Pacemaker: Key Factors in Clinical Outcomes

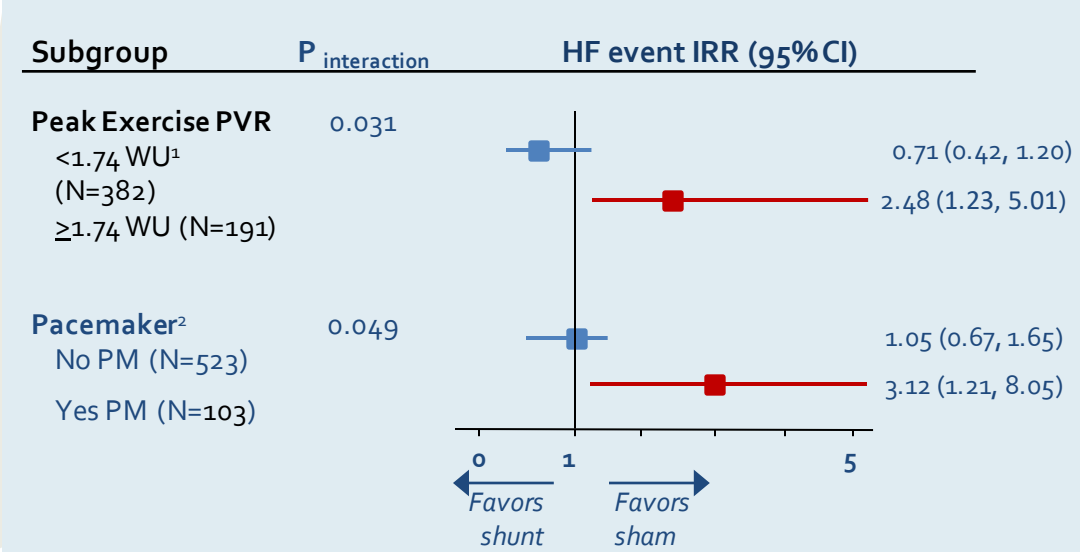
SYSTEMATIC STATISTICAL ANALYSIS IDENTIFIED MOST SIGNIFICANT VARIABLES AFFECTING HF EVENT RATE

Identified significant interactions....

- PA systolic pressure @ 20W exercise
- Indexed RA volume
- Sex

...which led to a focus on pulmonary vascular and RV health and a systematic identification of most significant factors

- **Peak PVR**
- **Pacemakers**

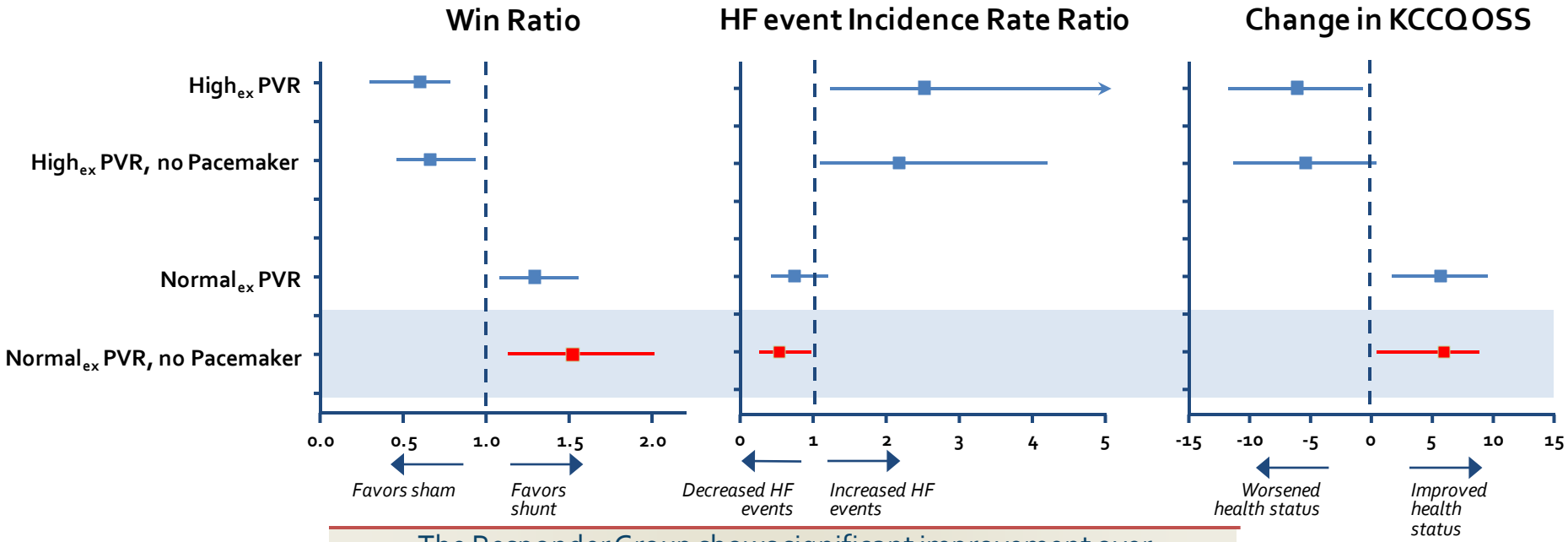


High exercise pulmonary vascular resistance (PVR) and presence of a pacemaker result in a 2-3 x increased risk of HF events

[1]Upper tertile, which roughly corresponds to peak exercise in a healthy adult >55 years (≤1.8WU); [2]Includes CRT

Identification of Responder Subgroup

PATIENTS WITH NORMAL EXERCISE PVR AND NO PACEMAKER DERIVED SIGNIFICANT CLINICAL BENEFIT



The Responder Group shows significant improvement over sham control in Win ratio, HF event IRR, and KCCQ-OSS.

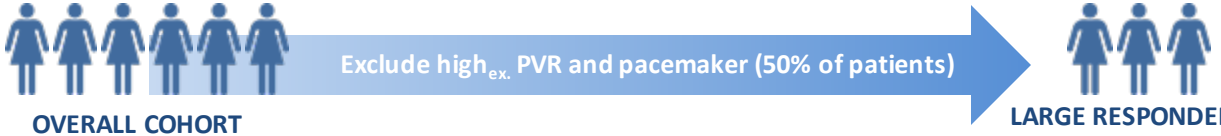
High Exercise PVR + Pacemaker: Key Factors in Clinical Outcomes

Patients with high exercise PVR and Pacemakers in this study had common comorbidities:

- worse RV strain
- lower TAPSE
- larger RA
  and/or
- more TR

Primary Endpoint Responder Group

PATIENTS WITH NORMAL EXERCISE PVR AND NO PACEMAKER DERIVE SIGNIFICANT HF AND QOL BENEFIT

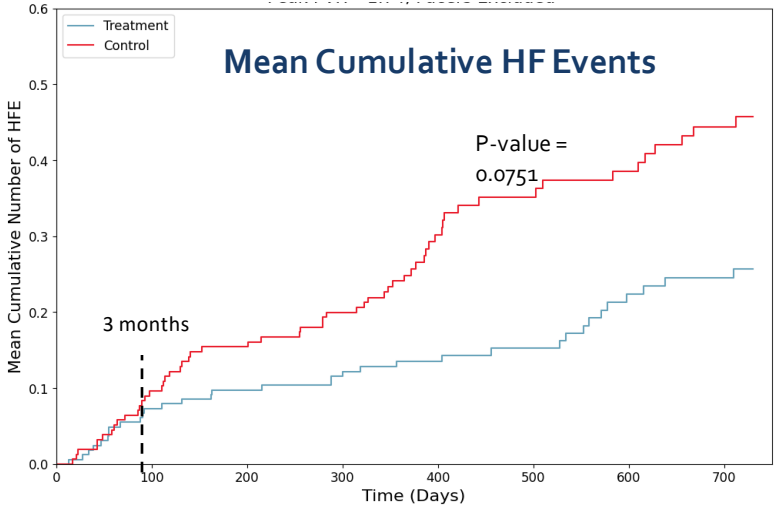


Responder Group	Variable	Treatment (N=161)	Sham Control (N=152)	Win Ratio	P-Value
Peak PVR < 1.74 no pacemaker	Composite Endpoint (KCCQ Threshold=5)			**1.5**	**0.007**
	CV death or non-fatal ischemic stroke	1.24% (2 events)	0% (0 events)	-	0.17
	Total HF events per patient-year	**0.12**	**0.22**	-	**0.007**
	Change in KCCQ-OSS (Mean ± SD)	**15.5 ± 22.2 (153)**	**10.0 ± 20.6 (141)**	-	**0.01**

HF Events in Responder Group

SIGNIFICANT REDUCTION IN TOTAL HF EVENTS FOR TREATED PATIENTS

HF event curves for shunt therapy and sham control arms begin to separate around 3 months



TREATMENT	At risk	161	160	160	160	117	103	95	85
CONTROL	At risk	152	152	150	150	101	86	83	75

[1]Up to 24 months follow-up

CRT22 REDUCE LAP-HF II Summary

- REDUCE LAP-HF II is the largest interventional device therapy trial (n=626) in HFpEF, the largest unmet need in cardiology
- The study has significantly advanced the understanding of patient selection, and we have established criteria that identify a responder group, which represent >50% of the trial population
- Patients with normal exercise pulmonary vascular resistance (PVR <1.74) and without a pacemaker derived significant clinical benefit from the shunt
  - 45% reduction in the rate of HF events (0.12 vs. 0.22 events per patient-year, p = 0.007)
  - 55% greater improvement in health status over sham (+5.5 points, p = 0.01) as assessed by KCCQ overall summary score, including 40% more patients with a very large (>20 points) quality of life improvement
- There is biological plausibility for the criteria defining the subgroup and is further supported by congruence in clinical outcomes, including a reduction in the HF event rate and an improvement in health status (both KCCQ and NYHA class)
- Exercise hemodynamic phenotyping played a critical role in defining the responder group