DGK.

Multizentrische klinische Ergebnisse und laufende klinische Studien

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Führt die IASD Implantation…

- zu einer Rechtsherzbelastung?
- zu mehr Schlaganfällen?
- zu einem dauerhaften li.-re. Shunt?

Ist die IASD Implantation…

Sicher ?

- zu reduziertem LAP?
- zu einer Verbesserung der Symptomatik?
- Zu weniger Krankenhauseinweisungen?

Effektiv ?

REDUCE LAP-HF study design

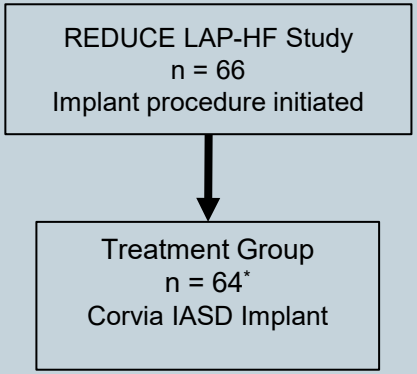
Prospective, multi-center, non-randomized, open label, single-arm study

Purpose

Evaluate Corvia Atrial Shunt safety and performance for patients with elevated left atrial pressure who remain symptomatic despite appropriate medical management.

Enrollment

Subjects enrolled at 21 sites in the UK, Netherlands, Belgium, France, Germany, Austria, Denmark, Czech Republic, Australia, and New Zealand.



Follow-up

Patients will be followed for 1 year and then annually for 3 years after index procedure and implant.

Endpoints

1ary safety endpoints:

- MACCE or
- Systemic embolic event (excl. pulmonary thromboembolism), or
- Explant within 6 months of implant

1ary device performance endpoints:

- Successful implant (deployed at intended location during index procedure)
- PCWP reduction & proof of left to right flow through the device at 6 months

*2 patients not implanted as a result of 1) trans-septal puncture complication without further sequelae, and 2) perceived unsuitable atrial septal anatomy

REDUCE LAP-HF: MACCE and Device performance

MACCE EVENT	SIX MONTHS %	ONE YEAR %
DEATH	0	4.7 (3/64)
STROKE	0	1.5 (1/64) (Pt. Died)
MI	0	0
SYSTEMIC EMBOLIC EVENT	0	0
IMPLANT REMOVAL	0	0

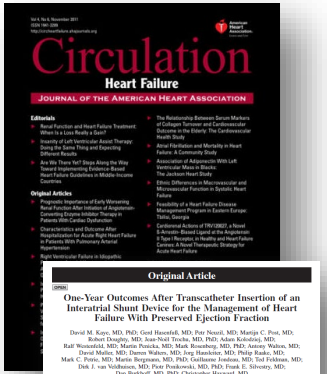
EFFECTIVENESS	SIX MONTHS %	ONE YEAR %
L→ R SHUNT FLOW (ECHO)	100 (49/49)	100 (48/48)
R→ L SHUNT FLOW (ECHO)	0	0
QP:QS	1.27 ± 0.24	1.28 ± 0.25

Kaye D., Hasenfuß G., Neuzil P., et al. Circ Heart Fail. 2016;9:e003662

One-Year Outcomes After Transcatheter Insertion of an Interatrial Shunt Device for the Management of Heart Failure With Preserved Ejection Fraction

Implantation of an interatrial shunt device was successful, safe and well tolerated, reduces left atrial pressure during exercise and may be a novel strategy for the management of HFpEF.

- Sustained improvements in:
  - NYHA class (P<0.001)
  - QOL – MLWHF (P<0.001)
  - 6-minute walk distance (P<0.01)
- Sustained reduction in workload-corrected exercise PCWP at 6 months and one year (p<0.01)
- 95% survival at one year
- Sustained device patency confirmed at 6 months and one year by left-to-right shunting
- No evidence of device-related complications



Vol 9 November 16, 2016
12-mo results

Vol 387 March 26, 2016
6-mo results

REDUCE LAP-HF | study design

Phase 2, randomized, blinded, sham-controlled trial

Purpose

Evaluate the peri-procedural safety and potential effectiveness (mechanistic effect) of the Corvia Atrial Shunt in HF patients with LVEF >40%, elevated left sided filling pressures, and who remain symptomatic despite optimal Guideline Directed Medical Therapy (GDMT).

Facilitate design of pivotal trial.

Enrollment

22 centers across the US, Europe, & Australia.

Participants enrolled n = 94

↓

Participants randomized n = 44

Treatment n = 22	Control n = 22
@ 1m visit n = 21*	@ 1m visit n = 22

Follow-up

at 1 month and then annually for a total of 5 years after index procedure or implant.

Endpoints

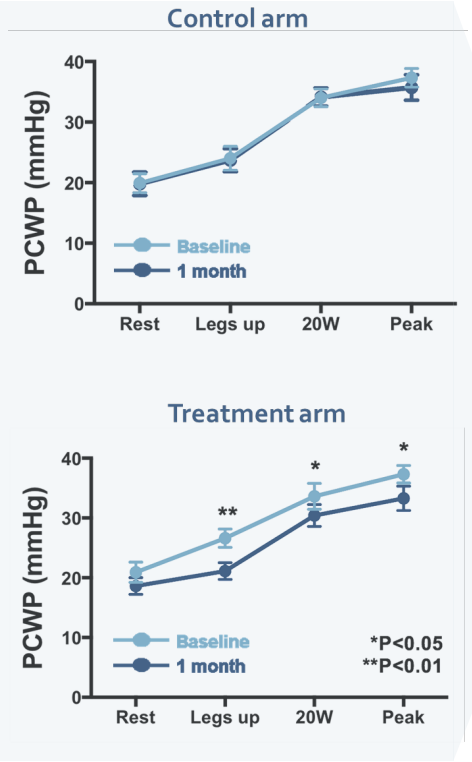
- Change in supine exercise PCWP compared to control group at 1 month
- % of patients that experience major adverse cardiac, cerebrovascular embolic, or renal events (MACCRE)

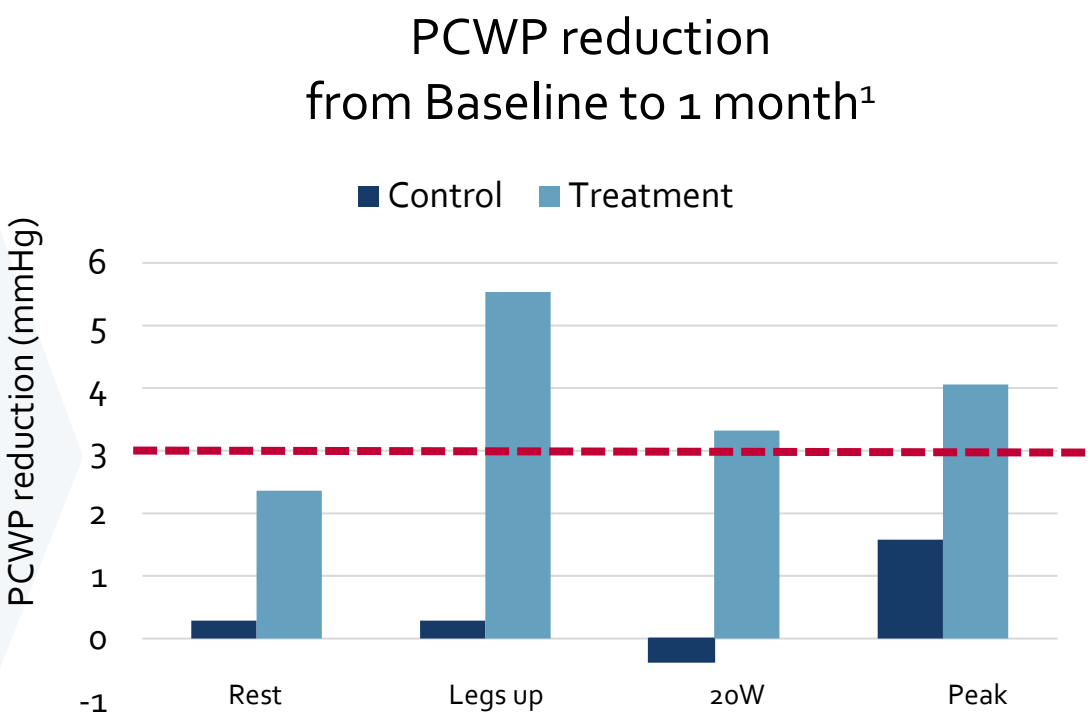
primary objective: to evaluate mechanistic efficacy (lowering of PCWP with exercise) and periprocedural safety

Feldman et al, *Circ Hear Fail*. 2016

*1 pt exited the study

REDUCE LAP-HF I – PCWP reduction

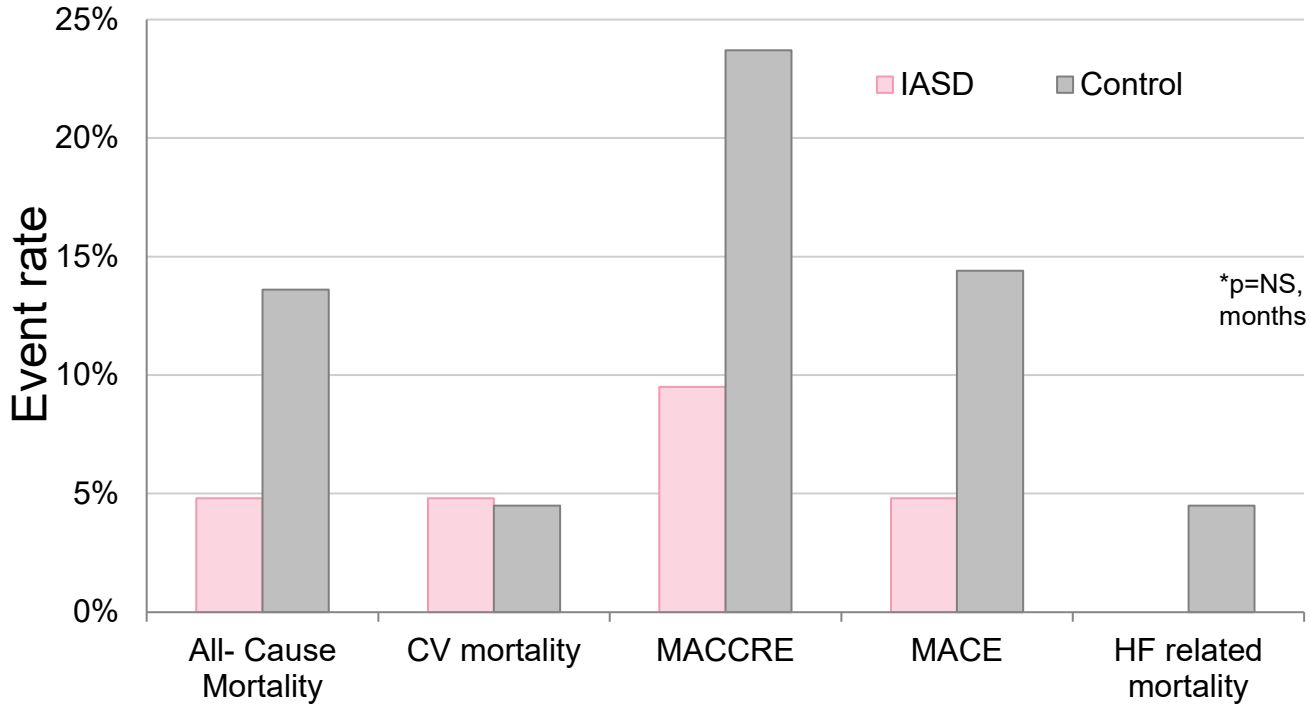




A 3mmHg reduction in PCWP has been reported to decrease mortality[2].

[1]Feldman et al, *Circulation*, 2018;137(4):364-375. [2] Zile MR, et al. CircHeart Fail 2017 Jan;10(1):e003594

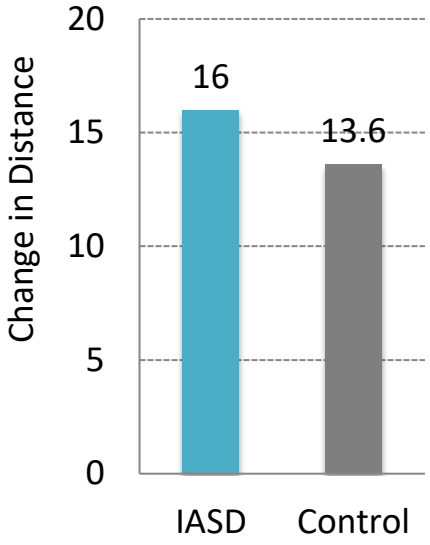
REDUCE LAP-HF I – 12 months: safety profile

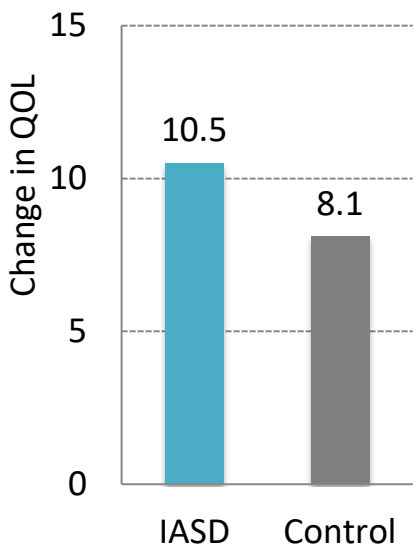


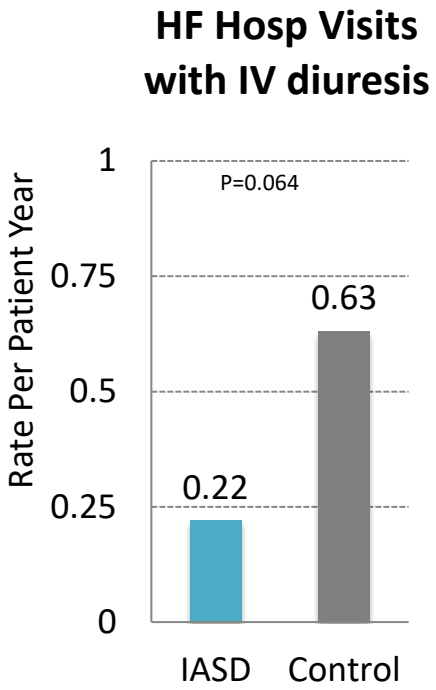
*p=NS, for safety outcomes at 12 months

Shah SJ et al AMA Cardiol. 2018 Oct; 3(10): 968–977.

DGK. REDUCE LAP-HF I – 12 months: secondary outcomes



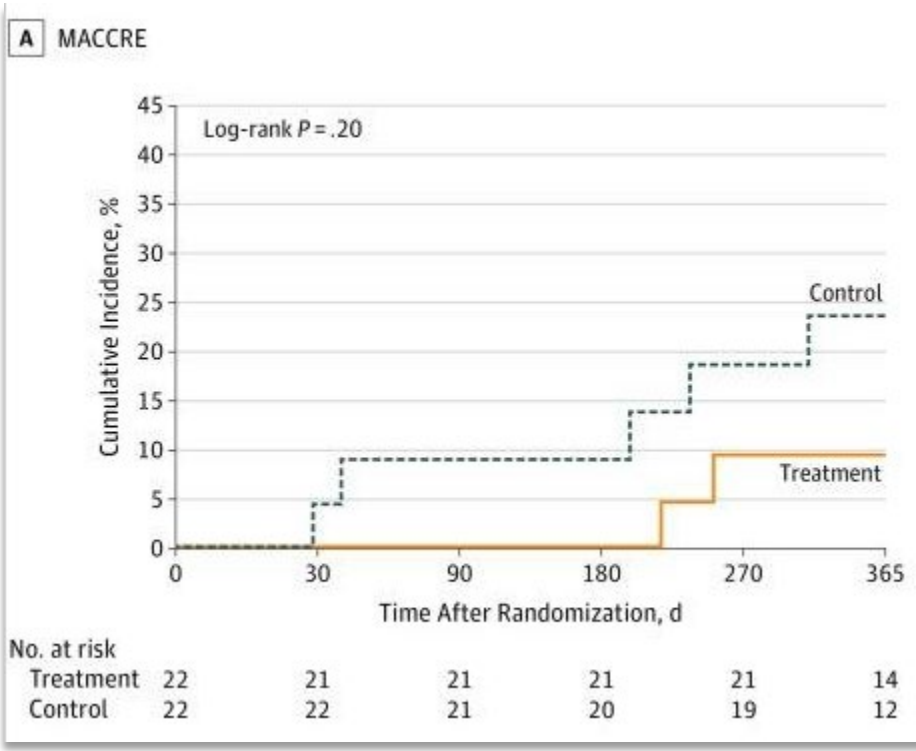


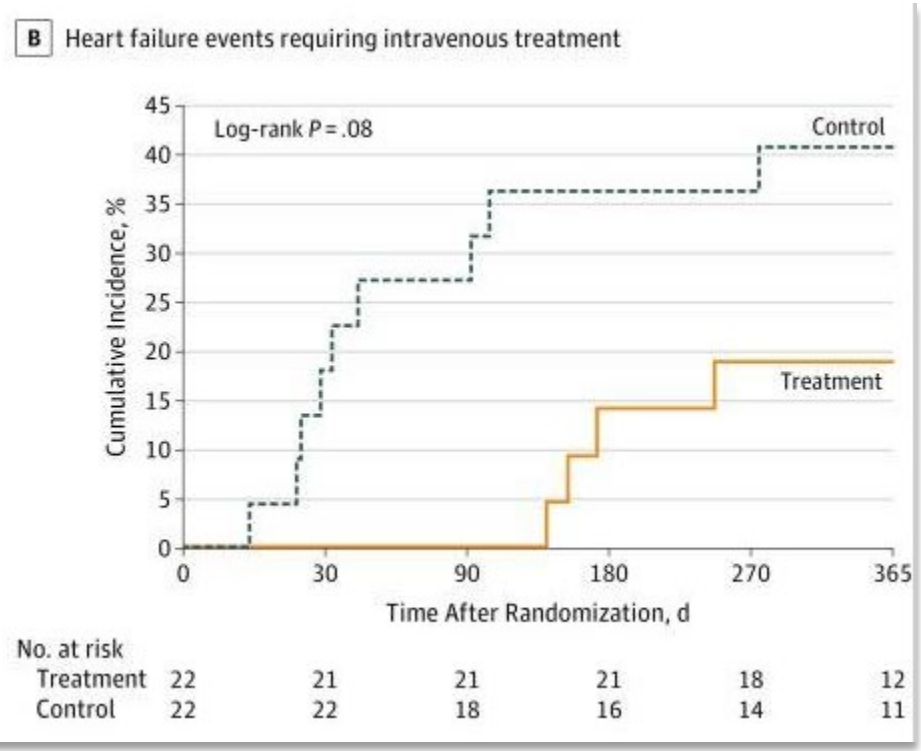


Shah SJ et al AMA Cardiol. 2018 Oct; 3(10): 968–977.

65% fewer HF events with iv *d*iuresis per patient year

REDUCE LAP-HF I – 12 months: timing of events





Shah SJ et al AMA Cardiol. 2018 Oct; 3(10): 968–977.

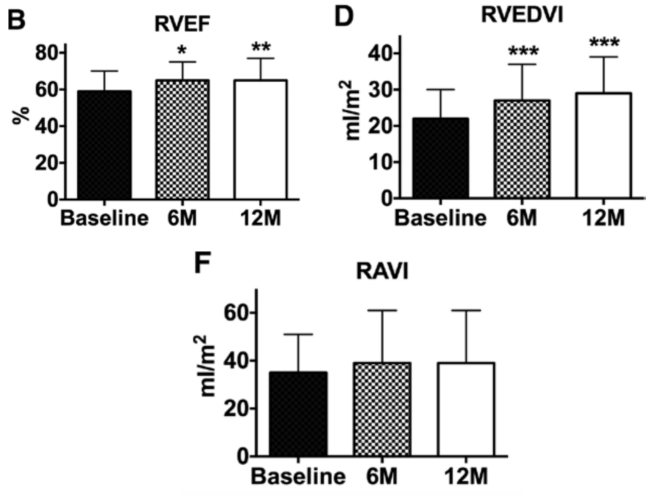
REDUCE LAP-HF I – safety after 12 months

Safety

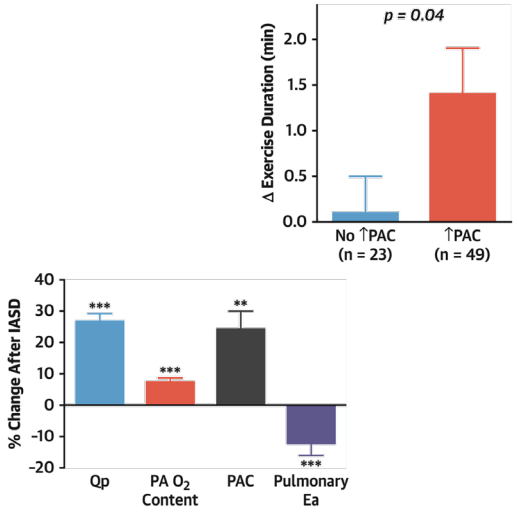
- Device patency confirmed in all patients
- No device embolization / migration
- no strokes or transient ischemic attacks in the IASD-treated patients
- none of the IASD-treated participants developed persistent or permanent atrial fibrillation or atrial flutter through 12 months
- No differences in major adverse cardiac, cerebrovascular, or renal events (MACCRE)
- RV size slightly enlarged at 6 months, but stable at 12 months. RV function preserved.

Shah SJ et al AMA Cardiol. 2018 Oct; 3(10): 968–977.

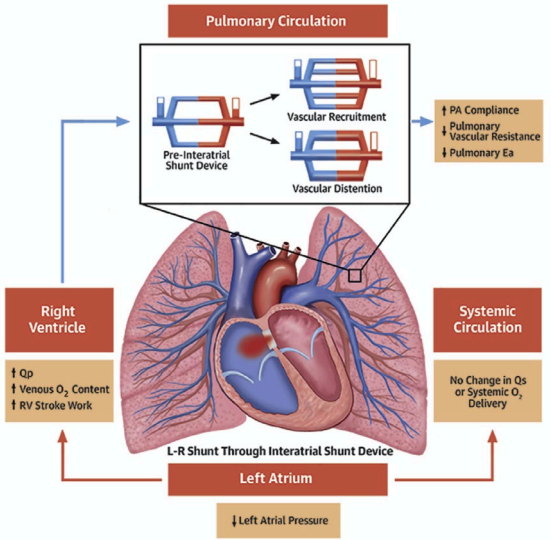
Right ventricular and pulmonal effects



No change in RV parameters between 6- and 12-months post implant[1]



Shunt implant correlated with increases in pulmonary blood flow (Qp), pulmonary artery oxygen saturation, pulmonary artery compliance (PAC), and reduction in arterial elastance (pulmonary Ea). **Patients with increased PAC had a significant increase in exercise duration.**[2]



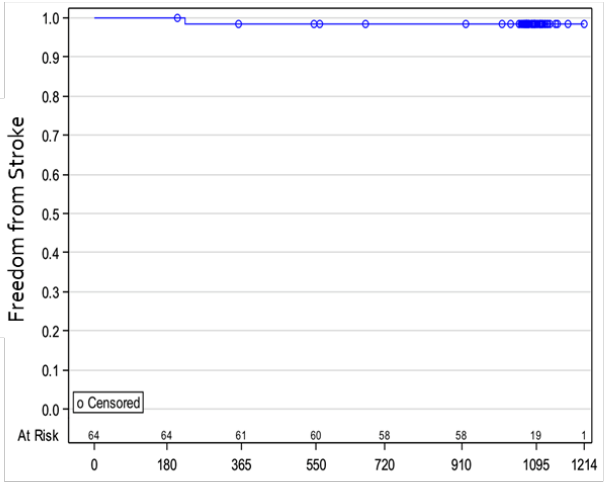
Improved pulmonary vascular function may be due to enhanced perfusion of pulmonary circulation or pulmonary vasodilation due to increased blood oxygen content.[2]

[1]Kaye D, et al. *Circ Heart Fail* 2016;
[2]Obokata et al, *JACC,* 2019

Incidence of stroke

Anticoagulation

- All get ASA 81 mg po qd indefinitely
- If on anticoagulation (e.g., DOAC, warfarin, clopidogrel) continue for at least 6 months
- If not on anticoag, Rx with clopidogrel x 6 mo.



Freedom from CVA	Pilot study (n=11)	REDUCE LAP-HF (n=64)	REDUCE LAP-HF I (n=22)	Combined (n=97)
1 year	100%	98.5%	100%	**99%**
2 year	100%	98.5%	100%	**99%**
3 year	100%	98.5%	95.5%	**98%**
4 year	100%	97%^	95.5%	**96%**
5 year	100%	97%*	TBD	---

^ Median FY 44.4M * Median FU of 68.7M

Open-label study (n=64) showed low risk of stroke through 4 years of follow-up.[1]

Similar results across 3 studies with a combined 96% freedom from CVA through 4 years of follow-up.[1-5]

[1] Unpublished results on file at Corvia Medical [2] Malek et al, *Int J Cardiol*, 2015. [3] Søndergaard L, et al. *Eur J Heart Fail* 2014. [4] Hasenfuß et al, *Lancet*, 2016. [5] Kaye D, et al. *Circ HF* 2016.

Corvia IASD trials - summary

Pilot Study
Observational study
(n=11)

REDUCE LAP-HF
Observational study
(n=64)

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

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

IASD therapy ist technisch sicher durchführbar und sicher hinsichtlich Rechtsherzbelastung und Schlaganfallrisiko. Sie führt zu einer relevanten Senkung des LAP und zeigt vielversprechende Ergebnisse zu HF Symptomatik und Hospitalisierung.

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

RESULTS
Available 2022.

[1]Malek et al, *Int J Cardiol*, 2015; [2]Søndergaard L, et al. *Eur J Heart Fail* 2014; [3]Hasenfuß et al, *The 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.

REDUCE LAP-HF II study design

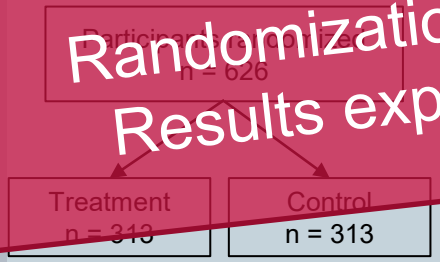
Randomized, double-blinded, sham-controlled, multi-center trial

Purpose

Evaluate the clinical efficacy and safety of the Corvia Atrial Shunt in HF patients with LVEF >40%, elevated left sided filling pressures, and who remain symptomatic despite optimal Guideline Directed Medical Therapy (GDMT).

Enrollment

up to 60 US sites and 28 sites in Europe, Australia and Japan. Start date was Q2 2017. Enrollment is complete.



Follow-up

1 year and annually for a total of 5 years after index procedure or implant.

Cross-over to treatment group allowed at ≥24 months post-procedure. If patient crosses over they are followed for an additional 5 years.

Primary Endpoint

- Composite of:
  - cardiovascular mortality or first non-fatal, ischemic stroke through 12m
  - Rate of HF admissions or IV diuresis, up to 24m
  - Change in KCCQ score between baseline & 12m

Randomization completed – Results expected in 2022

Berry et al. *Am Heart J*, 2020

Reduce LAP-HF III (PMCF) Study design

OBSERVATIONAL, MULTI-CENTER, SINGLE-ARM, POST-MARKET CLINICAL FOLLOW-UP STUDY

Purpose	Enrollment	Follow-up	Select Outcome Measures
Collect post market data in consecutive patients treated with the Corvia Atrial Shunt to further evaluate efficacy, safety and quality of life outcomes as a new treatment for patients with heart failure in a “real world” practice setting.	Up to 500 subjects treated at up to 50 sites in Europe.	Patients will be followed for 1 year and then annually for 5 years after index procedure and implant.	• Implant procedure failures • Device and or procedure related serious adverse cardiac events through 30 days • Embolic stroke through 60 months • All cause, CV and HF related mortality through 60 months • Newly acquired persistent or permanent AF or atrial flutter through 60 months. • NYHA, KCCQ, EQ-5D, 6MWT at all follow-up timepoints • HF hospitalizations through 60 months

Vielen Dank!

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