Prospective, Multicenter Evaluation of the 18F Direct Flow Transcatheter Aortic Valve: The DISCOVER Trial

Final Study Enrollment

Caution: The Direct Flow Medical Transcatheter Aortic Valve System has not been approved for use in the USA, Canada or Japan

Potential conflicts of interest

Speaker's name: Professor Joachim Schofer

☑ **I have the following potential conflicts of interest to report:**

Consultant: Direct Flow Medical

Purpose

To report the 30 day outcomes of the Direct Flow Medical Valve in high risk patients with severe aortic stenosis

Designed for TAVR

- **Treat AS with minimal risk of AR**
  - Double-ring design for a tight and durable seal
  - Conforms to anatomy
- **Optimization of Positioning**
  - Full hemodynamic assessment before final detachment
  - Repositionability; distal, proximal and planar
  - Fully retrievable
- **Improved TAVR Procedure**
  - Flexible, low-profile delivery system for reduced vascular complications
  - Fully competent during positioning
  - No post-dilatation or rapid pacing

DISCOVER Trial: *Design*

Study Design

- Prospective, Multicenter, Non-randomized clinical trial
- Corelab adjudicated echo and cath hemodynamics
- MedStar Corelab, Established in 1996 by Neil Weissman, MD
  Served as core lab for over 150 clinical trials, involving over 50 countries with over 25,000 patients

Committees

- Patient Review Committee
- Independent Clinical Events Committee (CEC)
- Independent Data Monitoring Committee (DMC)

Primary Endpoint

Freedom from all-cause mortality from procedure to 30 days

Secondary Endpoints

VARC defined

Corelab Echocardiographic ACC/AHA Classification of AR

	None/Trace	Mild	Mod	Mod-Sev	Severe
Qualitative					
Angiographic grade		1+	2+	3+	4+
Color Doppler jet width	Jet < 1cm in length <10% width and not uniformly seen in all views	Central jet, width < 25% of LVOT	> mild but no signs of severe AR		Central jet, width > 65% LVOT
Doppler vena contracta width (cm)		<.3	.3 -.6		> 0.6
Quantitative (cath or echo)					
Regurgitant volume (ml per beat)		<30	30 - 44	45 - 59	≥ 60
Regurgitant fraction (%)		< 30	30 - 39	40 - 49	≥ 50
Regurgitant orfice area (cm^2)		< .10	.10 - .19	.20 -.29	≥ 0.30
Additional Essential Criteria					
Left ventricular size					Increased

Bonow RO, Carabello BA, Chatterjee K, et al. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice. *J Am Coll Cardiol.* Sep 23 2008;52(13):e1-142.

DISCOVER Trial: *Key Inclusion Criteria*

≥ 70 years old

Severe aortic valve stenosis:

Mean gradient >40 mmHg or peak jet velocity >4.0 m/s

and AVA ≤0.8 cm^2 or AVA index ≤0.5 cm^2/m^2

Native valve annulus diameter is ≥ 19mm or ≤ 26mm (by CT)

Symptomatic aortic valve stenosis (at least one):

Angina

Congestive heart failure NYHA Class ≥ II

Syncope

Patient must have logistic EuroSCORE ≥ 20 or co-morbidities

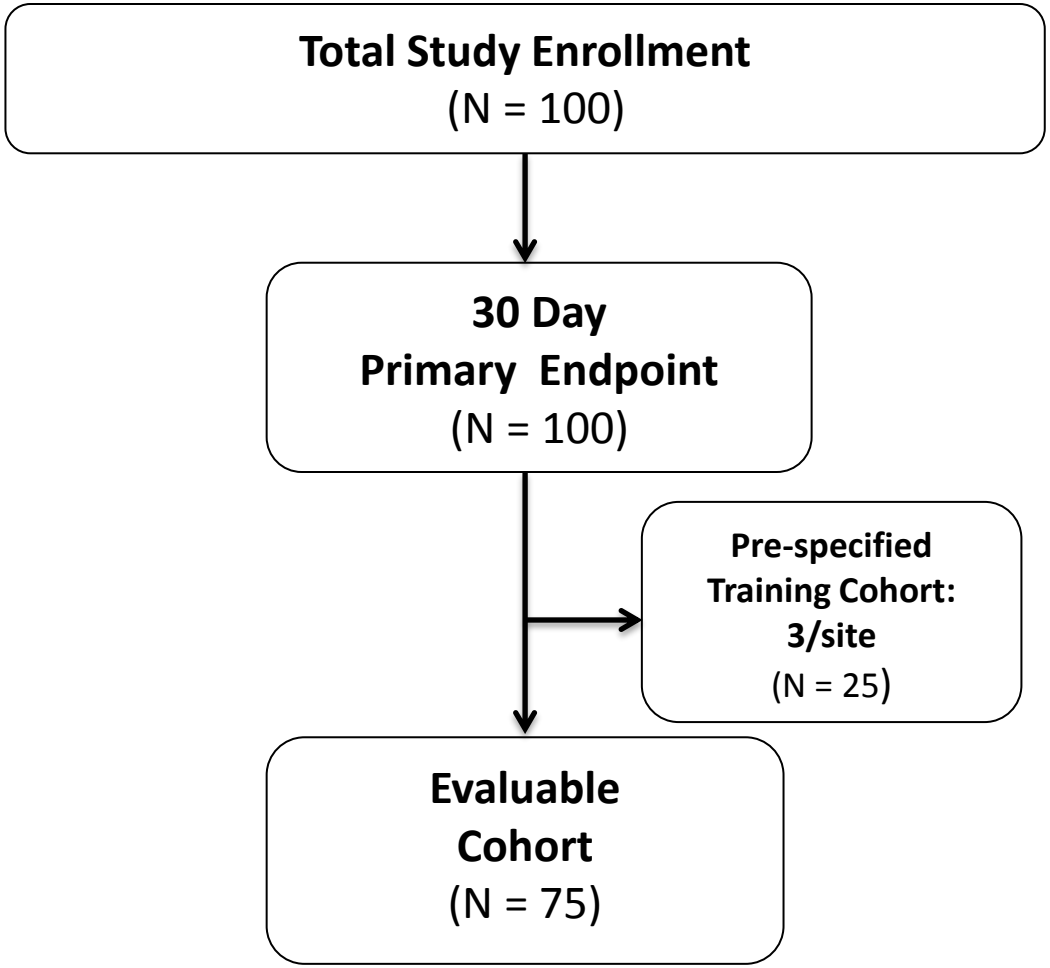
such as: severe COPD, porcelain aorta, previous thorax irradiation

Investigator agreement between interventionalist & surgeon

DISCOVER Trial: *Clinical Sites*

Site #	Country	City	Site/Hospital	Physicians
01	France	Massy	L'Institut Hopitalier Jacques Cartier	Thierry Lefèvre (IC) Mauro Romano (Sx)
02	Germany	Hamburg	Medical Care Center	Joachim Schofer (IC) Klaudija Bijuklic (IC) Michael Schmoeckel (Sx)
03	UK	London	St Thomas' Hospital	Martyn Thomas (IC) Christopher Young (Sx)
04	UK	London	The Heart Hospital	Michael Mullen (IC) John Yap (Sx)
05	France	Toulouse	Clinique Pasteur	Jean Fajadet (IC) Didier Tchetche (IC) Olivier Vahdat (Sx)
06	Italy	Milan	San Raffaele Hospital	Antonio Colombo (IC) Azeem Latib (IC) Francesco Maisano(Sx)
07	Italy	Milan	Ospedale Niguarda Ca' Granda	Silvio Klugmann (IC) Federico DeMarco (IC) Giuseppe Bruschi (Sx)
08	Germany	Trier	Krankenhaus der Barmherzigen	Karl Hauptmann (IC) Ivar Friedrich (Sx)
09	Germany	Bonn	University Hospital Bonn	Eberhard Grube (IC) Georg Nickenig (IC) Fritz Mellert (Sx)

DISCOVER Trial: *Enrollment*



DISCOVER Trial: *All Patients (N=100)*

Baseline Patient Characteristics

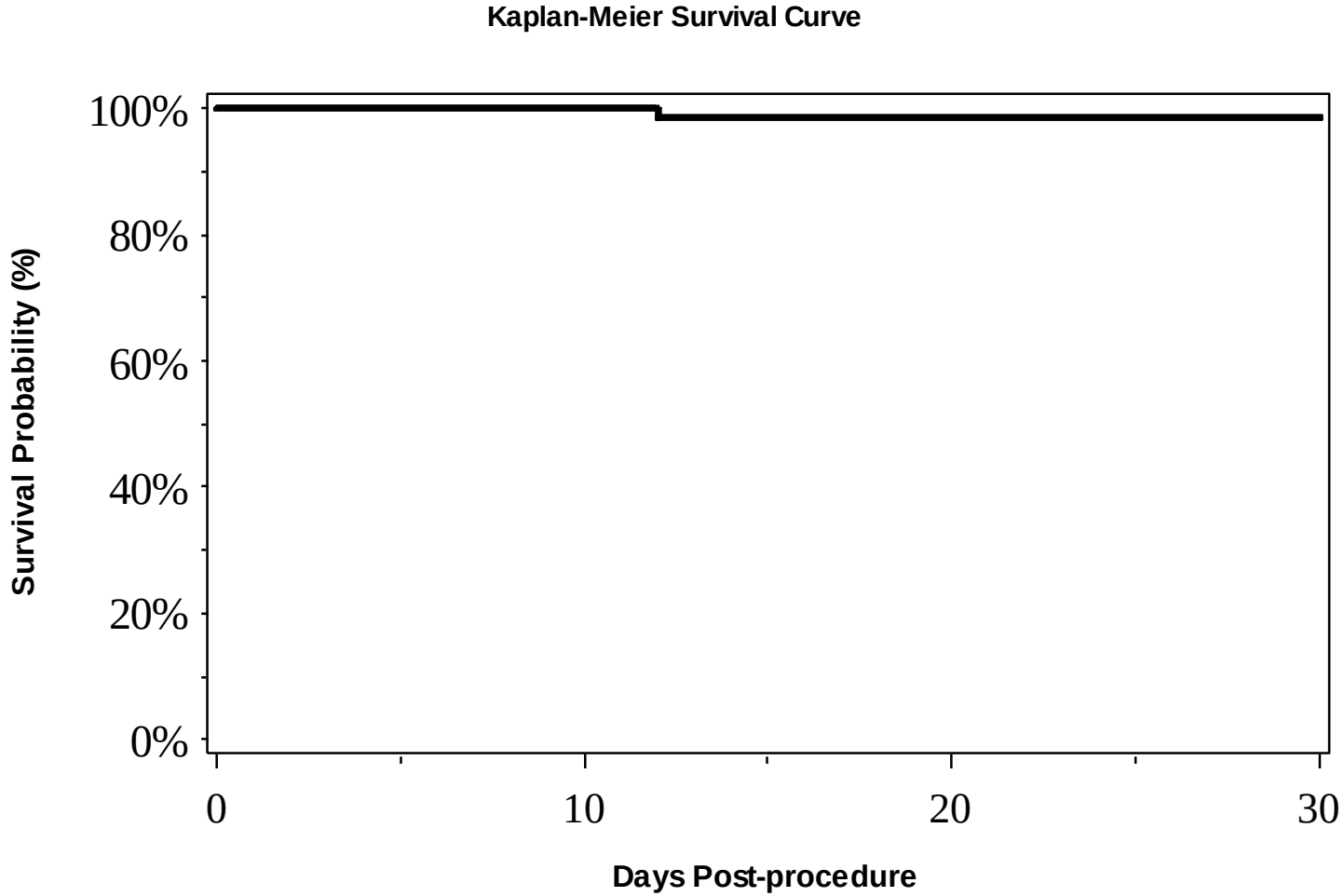
Characteristic	Results N =100
Age (yrs, mean & range)	83.1 (63 – 95)
Female	50% (n=50)
Logistic EuroSCORE (mean)	22.5 ± 11.3 [n=99]

Note: Some study data in this presentation is unmonitored and CEC adjudications are not yet all complete.

DISCOVER Trial: *All Patients (N=100)*

Primary Endpoint

Freedom from all-cause mortality within 30 days: **99%**

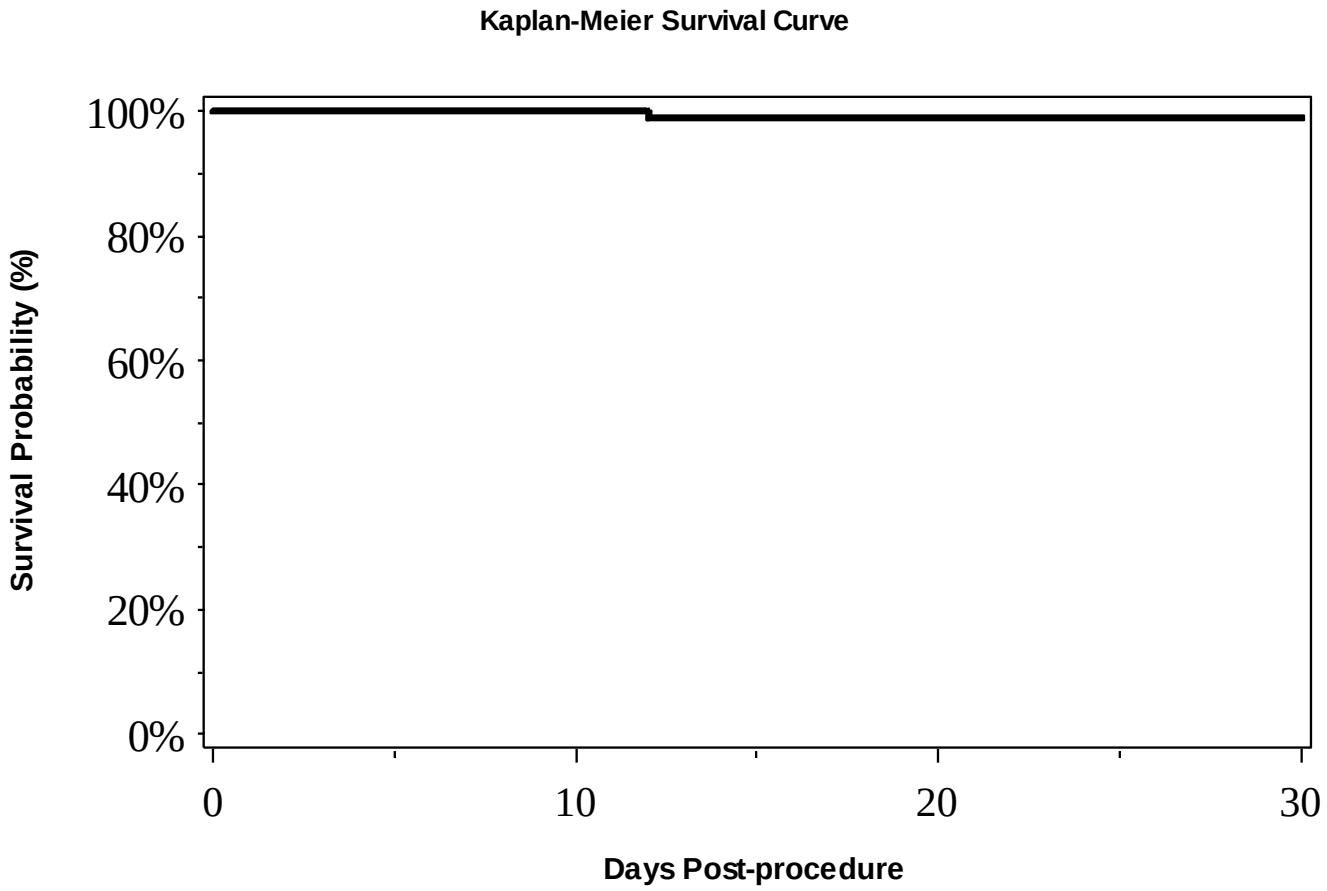


1 death at 12 days due to complications from pneumonia

DISCOVER Trial: *All Patients (N=100)*

Cardiovascular Mortality

Freedom from cardiovascular mortality (VARC) within 30 days: **99%**



DISCOVER Trial: *Evaluable Cohort*

Implanted Valve and Vessel Diameters

Implanted Valve Size	N=75
25 mm (19 – 24 mm annulus)	44
27 mm (> 24 – 26.5 mm annulus)	31

Native Valve Diameter	N=75
Mean Diameter Treated	23.6

Vessel Access Dimensions	N=75
Minimum Diameter Treated	5.2 mm

DISCOVER Trial: *Evaluable Cohort*

Procedure Summary

Total Procedure Time (mean skin to skin)	57.7 min
Pre Dilatations (mean per patient)	1.5
Post Dilatations	0
Valve Positioning and Echo and Angiographic Assessment	14 ±14 min
Retrieval (6 due to sizing and 2 pull through)	8
Rapid Pacing During Implantation	0

DISCOVER Trial: *Evaluable Cohort*

Device Success Secondary Endpoint

VARC Device Success	**91%** (67/74)
Successful vascular access, delivery and deployment and retrieval of delivery system	99% (74/75)
Position of the device in proper location	99% (74/75)
Intended performance: Mean gradient <20 mmHg or Peak velocity <3 m/s, without moderate or severe AR	93% (68/73)
One valve implanted	100%

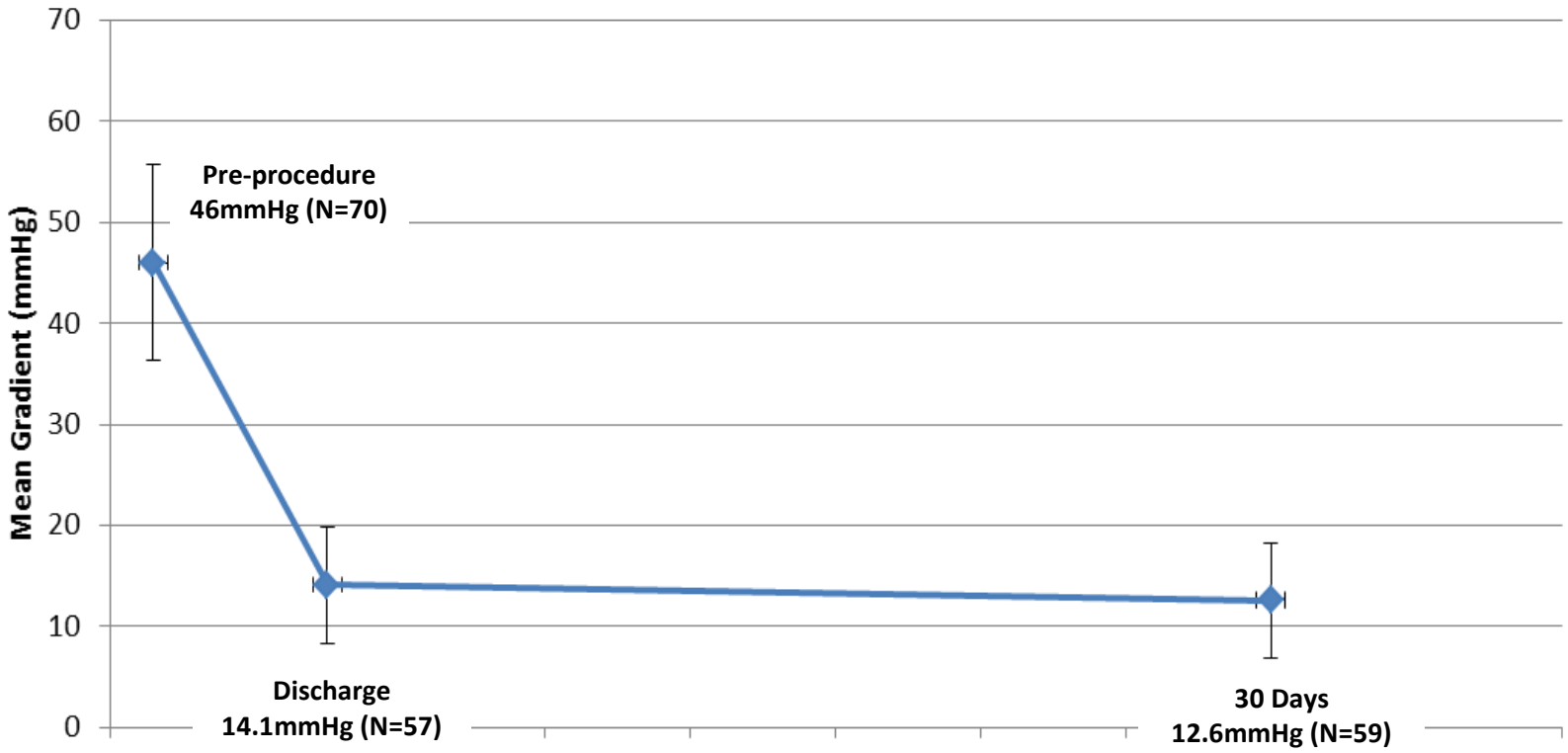
DISCOVER Trial: *Evaluable Cohort*

Patient Safety

Combined Safety Endpoint Freedom From Event (per patient)	**89%** (67/75)
All Cause Mortality	1.3% (1/75)
Major Stroke	2.7% (2/75)
Life Threatening or Disabling Bleeding	4% (3/75)
AKI (acute kidney injury) – Stage 3	0% (0/75)
Peri-procedural MI	1.3% (1/75)
Major Vascular Complications	2.7% (2/75)
Repeat Procedure for Valve related dysfunction	1.3% (1/75)
New Pacemaker	16% (12/75)

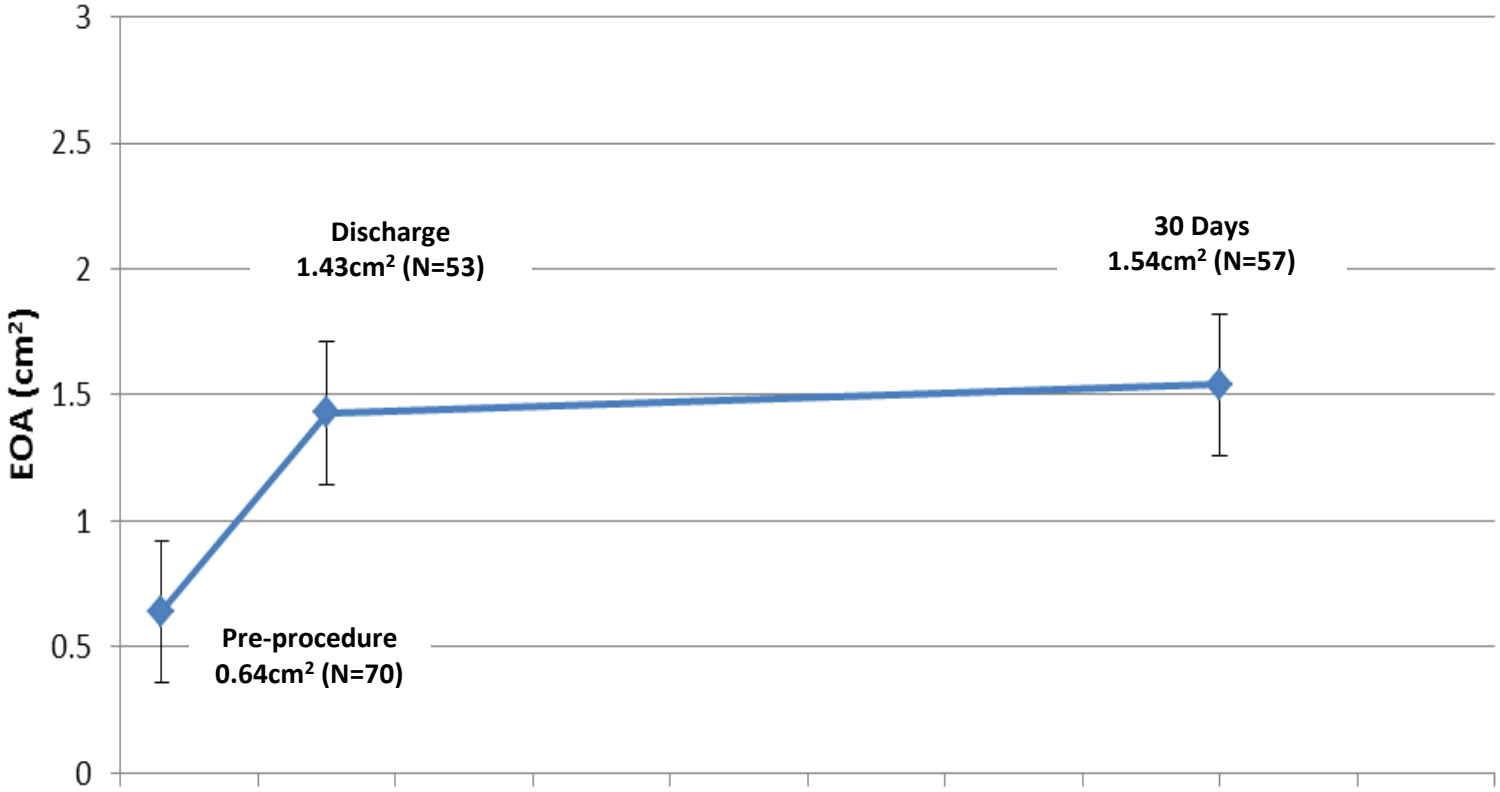
DISCOVER Trial: *Evaluable Cohort*

Echocardiographic Gradient by Core Lab



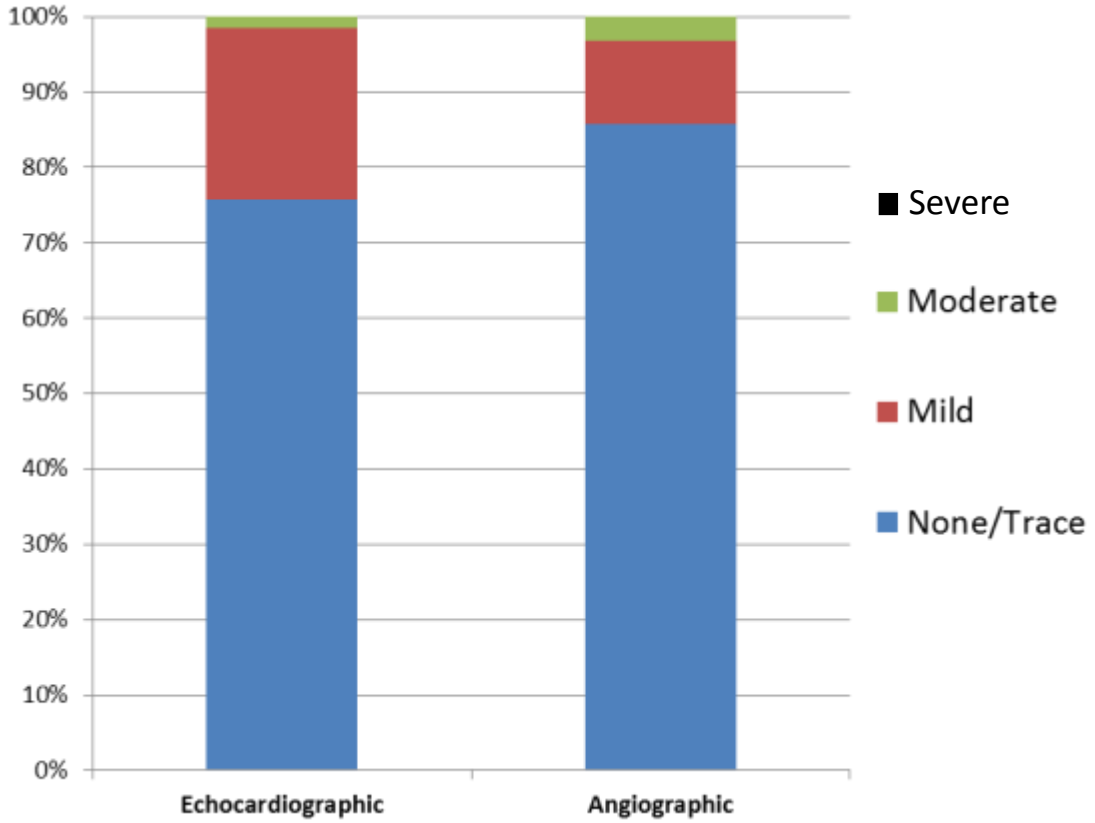
DISCOVER Trial: *Evaluable Cohort*

Echocardiographic EOA by Core Lab



DISCOVER Trial: *Evaluable Cohort*

Echo and Angiographic Aortic Regurgitation by Core Lab



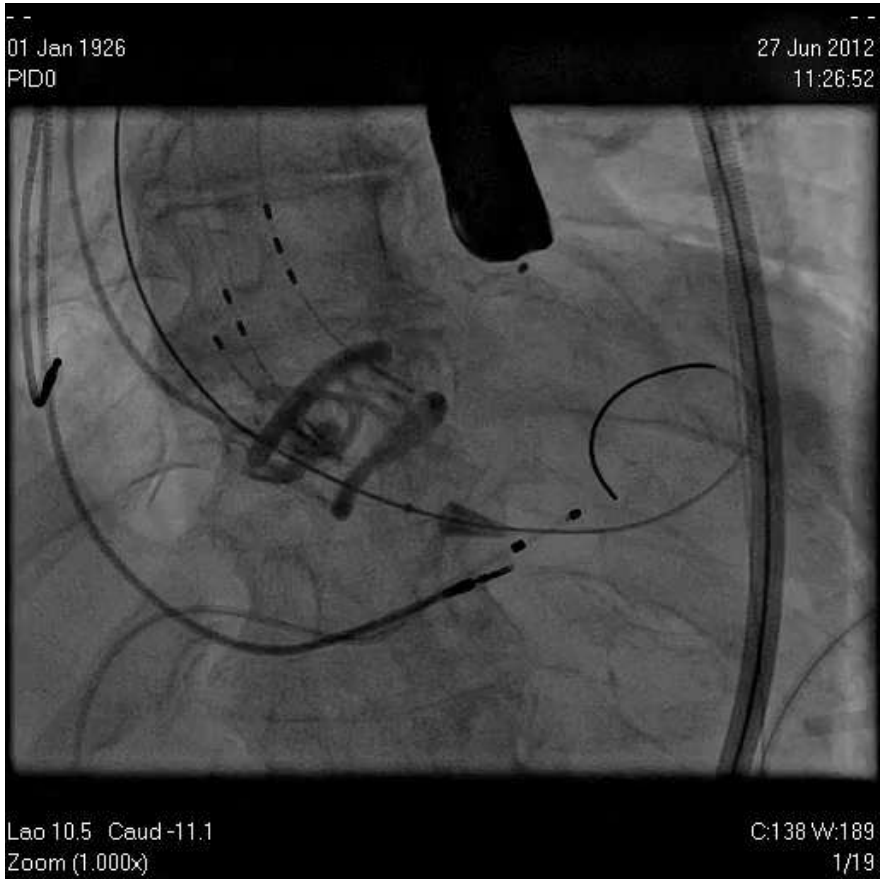
Aortic Regurgitation	Post Procedure ≤ Mild	Post Procedure None/Trace
Echocardiographic (N=74)	99%	73%
Angiographic (N=63)	97%	86%

DISCOVER Trial: *Conclusions*

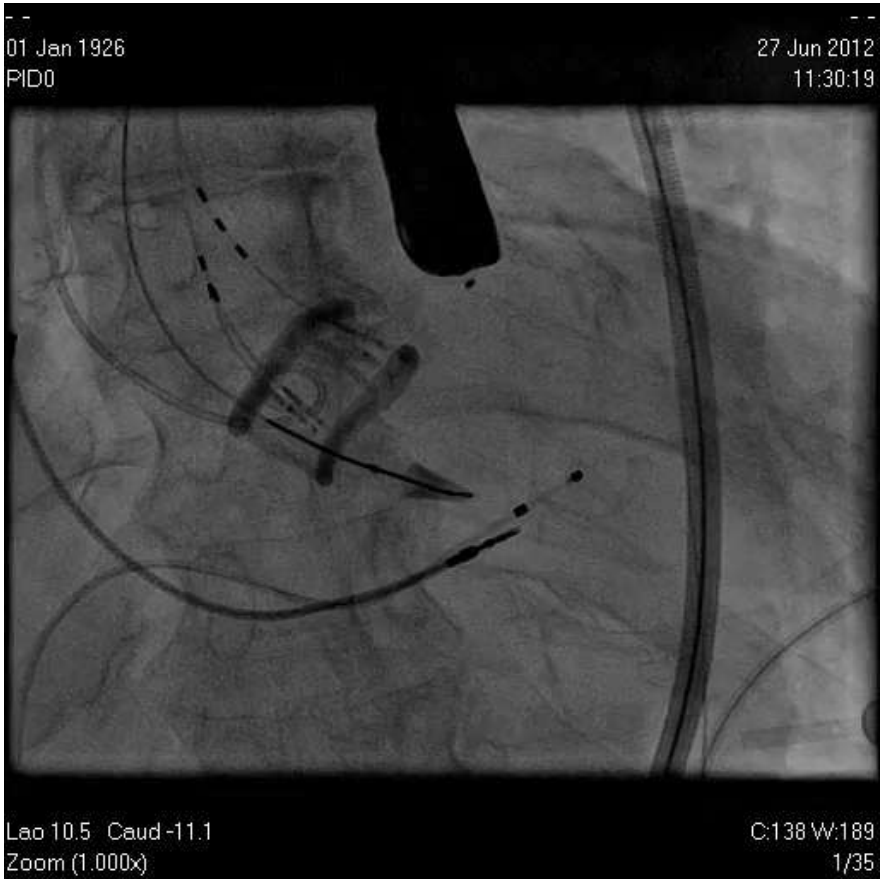
The Direct Flow Valve:

- **Achieved 99% freedom from all cause mortality at 30 days, the Primary Endpoint**
- **Achieved 91% VARC defined Device Success and 89% Combined Safety endpoints**
- **Can be safely and effectively used to treat high and extreme surgical risk patients with aortic stenosis and complex anatomy**
- **Provides hemodynamic stability during implantation**
- **Allows controlled positioning, repositioning and safe retrieval**
- **Virtually eliminates aortic regurgitation**

Direct Flow Reposition



Initial Valve Placement
AR Grade Moderate



Final Valve Placement
AR Grade None

Corelab Angiographic Classification of AR

None/Trace Minimal regurgitant jet seen. Clears rapidly from proximal chamber with each beat.

Mild (1+) Moderate opacification of proximal chamber, clearing with subsequent beats.

Moderate (2+) Intense opacification of proximal chamber, becoming equal to that of the distal chamber.

Severe (3 to 4+) Intense opacification of proximal chamber, becoming more dense than that of the distal chamber. Opacification often persists over the entire series of images obtained.

Davidson C, Bonow, R Cardiac Catheterization in Braunwald Heart Disease 9th Edition, 2012