The DISCOVER Trial
3-Year Results

Evaluation of the Direct Flow Medical® Transcatheter Aortic Valve System for the Treatment of Patients with Severe Aortic Stenosis in extreme risk patients
Potential conflicts of interest

Speaker's name: Federico DeMarco, MD

• I have the following potential conflicts of interest to report:
  – Consultant to Direct Flow Medical Inc.
**Designed for Improved Outcomes**
- Non-metallic, double-ring design
- Conforms to anatomy for a better seal

**“Fine-tunable”**
- Early valve assessment during positioning
- Adjustable at the annulus site
- Fully repositionable and retrievable

**Controlled TAVI Procedure**
- Fully functional throughout procedure
- Same flexible DS for all valve sizes
Study Design

- Prospective, multicenter, non-randomized clinical study

Patient Population

- Extreme risk patients with severe aortic stenosis

Independent Bodies

- Clinical Events Committee (CEC)
- Echo Corelab, MedStar Health, Washington DC

Follow Up: 30 days, 6 months, yearly up to 5 years

Primary Endpoint:

- Freedom from all-cause mortality from procedure to 30 days

Secondary Endpoint:

- Device success
The DISCOVER Trial
Clinical Study Sites

The Heart Hospital
M. Mullen, J. Yap

St Thomas’ Hospital
J. Hancock, M. Thomas, C. Young

L’Institut Hopitalier Jacques Cartier
T. Lefèvre, M. Romano

Clinique Pasteur
J. Fajadet, D. Tchetche, O. Vahdat

San Raffaele Hospital
A. Colombo, A. Latib, F. Maisano, O. Alfieri

Medical Care Center Hamburg
J. Schofer, K. Bijuklic, M. Schmoeckel

University Clinic Bonn
E. Grube, G. Nickenig, F. Mellert

Krankenhaus der Barmherzigen Brüder Trier
K. Hauptmann, I. Friedrich

Ospedale Niguarda Ca’ Granda
S. Klugmann, F. De Marco
S. Nava, G. Bruschi
### Baseline Patient Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean</th>
<th>± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>83.1</td>
<td>± 5.9</td>
</tr>
<tr>
<td>Male (%)</td>
<td>50.0</td>
<td></td>
</tr>
<tr>
<td>STS Score (%)</td>
<td>9.7</td>
<td>± 8.7</td>
</tr>
<tr>
<td>Logistic Euro SCORE I (%)</td>
<td>22.5</td>
<td>± 11.3</td>
</tr>
<tr>
<td>Characteristic (n=100)</td>
<td>(%)</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>NYHA III or IV</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Previous CABG</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Chronic Renal Insufficiency</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation/Flutter</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Porcelain Aorta</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Pre-existing Pacemaker</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>
The DISCOVER Trial
Patient Disposition

Procedure / Enrollment (n = 100)

30-day known status (n = 100/100)
- 5 study exits
  - 3 withdrawals
  - 2 non-implants

1-year known status (n = 95/100)
- 1 study exit / withdrawal

2-year known status (n = 94/100)
- 4 study exits / withdrawals

3-year known status (n = 90/100)
### Device Success Component (n=100)

<table>
<thead>
<tr>
<th>Component</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful vascular access, delivery and deployment of the device</td>
<td>98%</td>
</tr>
<tr>
<td>and successful retrieval of the delivery system</td>
<td></td>
</tr>
<tr>
<td>Correct positioning of a single prosthetic heart valve into the</td>
<td>97%</td>
</tr>
<tr>
<td>proper anatomical location</td>
<td></td>
</tr>
<tr>
<td>Intended performance of the prosthetic heart valve: Mean aortic valve</td>
<td>93%</td>
</tr>
<tr>
<td>gradient &lt;20 mmHg or peak velocity &lt;3 m/s, without moderate or severe</td>
<td></td>
</tr>
<tr>
<td>prosthetic valve AR</td>
<td></td>
</tr>
<tr>
<td>Only one valve implanted in the proper anatomical location</td>
<td>97%</td>
</tr>
<tr>
<td>Combined Device Success</td>
<td>92%</td>
</tr>
</tbody>
</table>
The DISCOVER Trial
Freedom from All-cause Mortality

Probability of Event-Free Survival (%)

Days
The DISCOVER Trial
Freedom from Cardiovascular Mortality

Probability of Event-Free Survival (%)

Days
The DISCOVER Trial

Freedom from All-cause Mortality and Major Stroke

Probability of Event-Free Survival (%) vs. Days
# The DISCOVER Trial

## Procedure and Valve Related Safety

<table>
<thead>
<tr>
<th>Event Rate (%)</th>
<th>0 – 30 Days</th>
<th>31 D – 1 Y</th>
<th>1 Y – 2 Y</th>
<th>2 Y – 3 Y</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General safety</strong></td>
<td>(n=100)</td>
<td>(n=96)</td>
<td>(n=85)</td>
<td>(n=75)</td>
</tr>
<tr>
<td>Life threatening or disabling bleeding</td>
<td>3.0</td>
<td>2.1</td>
<td>2.4</td>
<td>0.0</td>
</tr>
<tr>
<td>AKI – Stage 2 or 3</td>
<td>2.0</td>
<td>2.1</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>MI peri-procedural and spontaneous</td>
<td>1.0</td>
<td>1.0</td>
<td>0.0</td>
<td>2.7</td>
</tr>
<tr>
<td><strong>Valve related safety</strong></td>
<td>(n=98)</td>
<td>(n=96)</td>
<td>(n=85)</td>
<td>(n=75)</td>
</tr>
<tr>
<td>Repeat procedure for valve related dysfunction</td>
<td>1.0*</td>
<td>0.0</td>
<td>0.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Valve thrombosis/leaflet immobility</td>
<td>0.0</td>
<td>1.0†</td>
<td>1.2</td>
<td>1.3</td>
</tr>
<tr>
<td>Valve migration</td>
<td>1.0*</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Valve endocarditis</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Coronary Artery obstruction requiring intervention</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>1.3†</td>
</tr>
</tbody>
</table>

*same event †same patient
The DISCOVER Trial
Mean Pressure Gradient &
Effective Orifice Area

Paired Data

Mean Pressure Gradient*
(mmHg)

EOA (cm²)

Baseline
30D – D/C
1 – 3+ Years

n=60
n=79

0,66
1,48
13,3
13,7
45,2

0
40
80

0
1
2
3

0
20
40
60

* Full Bernoulli formula
The DISCOVER Trial
Paravalvular AR

Paired Data (n=75)

Discharge – 30D *

- None/Trace: 83%
- Mild: 17%

1 – 3+ Years *

- None/Trace: 75%
- Mild: 25%

* latest available follow-up

Note: Data from subjects implanted with DFM only
The DISCOVER Trial
NYHA Clinical Improvement

Baseline (N=97)
- Class I: 38%
- Class II: 58%
- Class III: 4%
- Class IV: 4%

30 days (N=92)
- Class I: 58%
- Class II: 35%
- Class III: 7%
- Class IV: 4%

1 year (N=81)
- Class I: 46%
- Class II: 50%
- Class III: 4%
- Class IV: 8%

2 year (N=71)
- Class I: 51%
- Class II: 41%
- Class III: 8%
- Class IV: 4%

3 year (N=53)
- Class I: 58%
- Class II: 38%
- Class III: 4%
- Class IV: 4%
Sustained & durable valve performance at 3 years

• Freedom from *all-cause mortality*
  • 89.6% at 1 years
  • 81.1% at 2 years
  • *68.5% at 3 years*

• Freedom from *cardiovascular mortality*
  • 82.6% at 3 years

• No moderate/severe PVL and 75% of patients with none/trace PVL

• *96% of patients in NYHA class I/II*