Impella Right Percutaneous (RP) System: H140001

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Device Description

• The Impella RP System is a minimally invasive, miniaturized percutaneous circulatory support system for the right ventricle.
• The main components are a 22 French (F) micro-axial flow pump catheter and The Impella Automated Control Unit
• Designed to provide > 4 Liters (L) of Flow/min
IMPELLA RP Axial Flow Pump
Rapidly Deployable Right-Sided Percutaneous Support

Outlet Area in Main Pulmonary Artery (PA)
Inlet Area in Inferior Vena Cava (IVC)
Femoral Vein Insertion

11F Catheter Diameter
>4L Greater than 4L/minute
22F Pump Motor
Inlet Area
Unique 3D Cannula Design
Outlet Area

3D CT Human Anatomic Fitting Studies – Appropriate for Body Surface Area (BSA) ≥ 1.5m²*

*verified by human use
Indication for Use

The Impella RP System is indicated for providing circulatory assistance for up to 14 days in pediatric or adult patients with a body surface area ≥1.5 m² who develop acute right heart failure or decompensation following left ventricular assist device implantation, myocardial infarction, heart transplant, or open-heart surgery.

Likely Population Examples*:

- Patients implanted with a long-term left ventricular assist device (LVAD) for either bridge-to-transplant or destination therapy who require emergent right ventricular assist device (RVAD).
- Patients who developed right ventricular failure (RVF) as a result of acute myocardial infarction (AMI).
- Heart transplant patients with RVF who require emergent RVAD following transplantation.
- Patients with RVF due to post-cardiotomy cardiogenic shock

*Examples in red = likely plausible pediatric populations
Annual Distribution Number (ADN)

• The humanitarian use designation (HUD) was approved with an ADN = 4,000

• Number of Impella devices sold in the US in 2015: 292

• Number of devices implanted in the US in 2015: 143 implants (0 in pediatric patients)
RECOVER RIGHT TRIAL
A non-randomized safety study

Not Eligible N=145
- 53.8% No RVF
- 8.2% INTERMACS 1 or End Organ Failure
- 4.2% Another RVAD used
- 2.8% Deep Vein Thrombosis or IVC Filter
- 2.8% Heparin Induced Thrombocytopenia
- 2.1% AMI with complications
- 26.6% Other

Assessed for Eligibility
N=175

Enrolled
N=30

Cohort A
n=18
RVF post LVAD insertion

Cohort B
n=12
5 RVF post AMI Shock
2 RVF post cardiotomy
5 RVF post transplant

All 30 enrolled patients were treated with the Impella RP and were followed to 30 days post pump removal or hospital discharge, whichever was longer.
Pre-Procedural Characteristics

Major Patient Characteristics*

- Mean age 59.2
  - Range: 24 - 86 years
- Male 77%
- 40% African American
- Mean BSA 1.94 ± 0.22m²
  - Range 1.5-2.56m²
- 93% NYHA Class III or IV
- Prior History
  - Coronary artery Disease – 67%
  - Congenital Heart Disease – 12.5%
  - Congestive Heart Failure – 88.5%
  - Diabetes 53%
  - Stroke/Transient Ischemic Attack 16.7%

Major Hemodynamic Characteristics*

- Number of Inotropes 3.2/patient
- Mean Cardiac Index 1.8 ± 0.2 l/min/m²
- Pulmonary Capillary Wedge Pressure 17.5 ± 7.3 mmHg
- Right Atrial Pressure 19.3 ± 3.9 mmHg
- Mean Arterial Pressure 70.5 ± 14.3 mmHg
- Heart Rate 90.2 ± 20.5 beats per minute

* No significant differences between Cohorts A and B unrelated to Cohort assignment
Procedural Characteristics Safety and Probable Benefit

Procedural Characteristics:

Primary Endpoint:
Survival at 30 days or discharge post device removal (whichever is longer), or to induction of anesthesia to the next therapy

<table>
<thead>
<tr>
<th>Event</th>
<th>All Patients</th>
<th>Cohort A (N=18)</th>
<th>Cohort B (N=12)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive @ 30 days % (n)</td>
<td>73 % (22/30)</td>
<td>83.3 % (15/18)</td>
<td>58.3 % (7/12)</td>
<td></td>
</tr>
<tr>
<td>Alive @ Discharge % (n)</td>
<td>70 % (21/30)</td>
<td>77.8 % (14/18)</td>
<td>58.3 % (7/12)</td>
<td></td>
</tr>
<tr>
<td>Alive at 30 day/DC/next therapy % (n)</td>
<td>73 % (22/30)</td>
<td>83.3 % (15/18)</td>
<td>58.3 % (7/12)</td>
<td></td>
</tr>
</tbody>
</table>

Additional Safety Endpoints:

<table>
<thead>
<tr>
<th>Safety Endpoints</th>
<th>All Patients</th>
<th>Cohort A (N=18)</th>
<th>Cohort B (N=12)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>26.7 % (8/30)</td>
<td>16.7 % (3/18)</td>
<td>41.7 % (5/12)</td>
<td>0.129</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>60.0 % (19/30)</td>
<td>55.6 % (10/18)</td>
<td>66.7 % (8/12)</td>
<td>0.543</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>13.3 % (4/30)</td>
<td>18.7 % (3/18)</td>
<td>8.3 % (1/12)</td>
<td>0.511</td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>0.0 % (0/30)</td>
<td>0.0 % (0/18)</td>
<td>0.0 % (0/12)</td>
<td></td>
</tr>
<tr>
<td>Tricuspid &amp; Pulmonary Valve Dysfunction*</td>
<td>3.3 % (1/30)</td>
<td>5.8 % (1/18)</td>
<td>0.0 % (0/12)</td>
<td>0.408</td>
</tr>
</tbody>
</table>

* based on echocardiographic core lab analysis
Hemodynamic Outcomes

![Graph showing average cardiac index and average LVAD flow/minute with significance levels P<0.0001 and P=0.004.](image)

![Graph showing average CVP (mmHg) with significance level P<0.0001.](image)

![Graph showing average time of Impella support with pump implant.](image)
Hemolysis, Right Ventricular (RV) Function and Survival

Historical Comparison:
Impella RP (Recover Right) vs. CentriMag RV Assist System (RVAS)

Right ventricular function changes from baseline to 30 day or discharge
## Pediatric Extrapolation

### Table 3: Calculated BSA versus age for pediatric patients

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>BSA</th>
<th>Age (years)</th>
<th>BSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>1.57</td>
<td>19</td>
<td>1.86</td>
</tr>
<tr>
<td>16</td>
<td>1.64</td>
<td>20</td>
<td>1.93</td>
</tr>
<tr>
<td>17</td>
<td>1.71</td>
<td>21</td>
<td>2.00</td>
</tr>
<tr>
<td>18</td>
<td>1.79</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 4: Safety endpoint outcomes analysis from the RECOVER RIGHT trial

<table>
<thead>
<tr>
<th>Safety Endpoints</th>
<th>Patients having BSAs similar to the pediatric cohorts (15-21 years old) (N=16)</th>
<th>All Patients (N=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>25.0% (4/16)</td>
<td>26.7% (8/30)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>68.7% (11/16)</td>
<td>60.0% (18/30)</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>18.8% (3/16)</td>
<td>13.3% (4/30)</td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>0.0% (0/16)</td>
<td>0.0% (0/30)</td>
</tr>
<tr>
<td>Tricuspid and Pulmonary Valve Dysfunction*</td>
<td>6.3% (1/16)</td>
<td>3.3% (1/30)</td>
</tr>
</tbody>
</table>

### Table 2: Safety endpoint outcomes for each BSA tercile (for the 2 pertinent pediatric indications)

(Pediatric Indications = Post Transplant and Post LVAD BTT)

<table>
<thead>
<tr>
<th>Safety Endpoints</th>
<th>Low Range 1.6&lt;BSA≤1.9 (N=7)</th>
<th>Mid Range 1.9&lt;BSA≤2.1 (N=9)</th>
<th>Upper Range BSA&gt;2.1 (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>28.6% (2/7)</td>
<td>22.2% (2/9)</td>
<td>0.0% (0/9)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>71.4% (5/7)</td>
<td>66.7% (6/9)</td>
<td>44.4% (4/9)</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>14.3% (1/7)</td>
<td>22.2% (2/9)</td>
<td>11.1% (1/9)</td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>0.0% (0/7)</td>
<td>0.0% (0/9)</td>
<td>0.0% (0/9)</td>
</tr>
<tr>
<td>Tricuspid and Pulmonary Valve Dysfunction*</td>
<td>14.3% (1/7)</td>
<td>0.0% (0/9)</td>
<td>0.0% (0/9)</td>
</tr>
</tbody>
</table>
Regulatory History

• Humanitarian Use Device (HUD) designation: July 13, 2012

• Investigational Device Exemption (IDE) approval: November 8, 2012

• Humanitarian Device Exemption (HDE) approval: January 23, 2015
Impella RP Post Approval Studies (PAS)

Two (2) PAS are required to monitor the safety and probable benefit

• **PAS 1**: Impella RP Prospective Study
  
  o prospective, single arm, multicenter study
  
  o patients with acute right ventricular failure or decompensation after left ventricular assist device implantation, post myocardial infarction, post heart transplant or open heart surgery with body surface area ≥ 1.5m²
Impella RP PAS1 (cont’d)

- **PAS 1**: Impella RP Prospective Study
  - Sample size: 30 patients at 15 sites in the US
  - Follow-up: 30 and 180 days post explant
  - Enrollment status: 13 patients currently enrolled (Age: range 46-81yrs, mean 63yrs)
• **PAS 2: Impella RP Pediatric Study**

  - Retrospective, single arm, multicenter

  - Pediatric patients < 18 yrs, body surface area $\geq 1.5\text{m}^2$ that develop right ventricular failure after left ventricular assist device implantation, post myocardial infarction, heart transplant or heart surgery supported with the Impella RP
Impella RP PAS2 (cont’d)

- **PAS 2:** Impella RP Pediatric Study
  
  - Sample size: up to 15 pediatric patients or all pediatric patients supported with Impella RP at a minimum of 5 sites over 5 yrs (whichever comes first)
  
  - Enrollment: 2 pediatric sites have been trained and received IRB approval for HUD use of the device as of 1/15/16
  
  - No patient has been enrolled
Literature Results

• **Literature Search** – Date 1/23/2015- 11/30/2015
  - No published studies on the Impella RP other than a publication on the data submitted to FDA for the HDE approval (the RECOVER RIGHT Study)
Impella RP
Medical Device Report (MDR) Review

MDR Search Criteria:
• Brand Name: Impella RP
• Date Report Entered: January 23, 2015 – November 30, 2015

Search Results: 2 MDRs
• There were NO pediatric patients
  o Type of Event: 1 death and 1 serious injury
  o Patient Age and Gender: 2 males both 54 years of age
  o Reporting Country: US
FDA Recommends and Question to the PAC

FDA recommends continued surveillance and will report the following to the PAC in 2017:

- Annual distribution number
- PAS follow-up results
- Literature review
- MDR review

Question: Does the Committee agree with FDA’s conclusions and recommendations?