Impella RP System: H140001

Presentation to the Pediatric Advisory Committee
March 7, 2017

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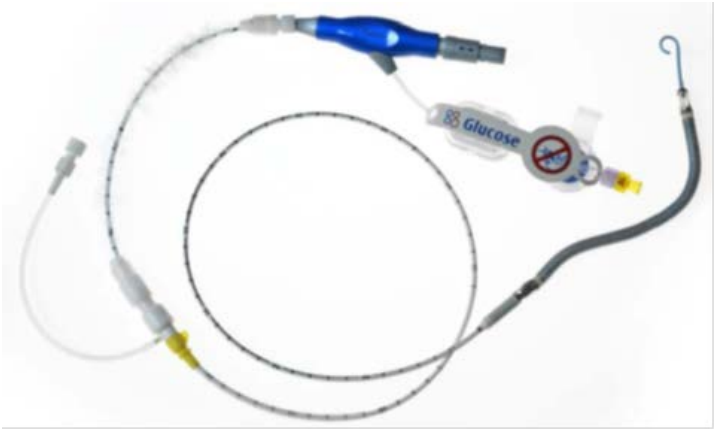
Device Description

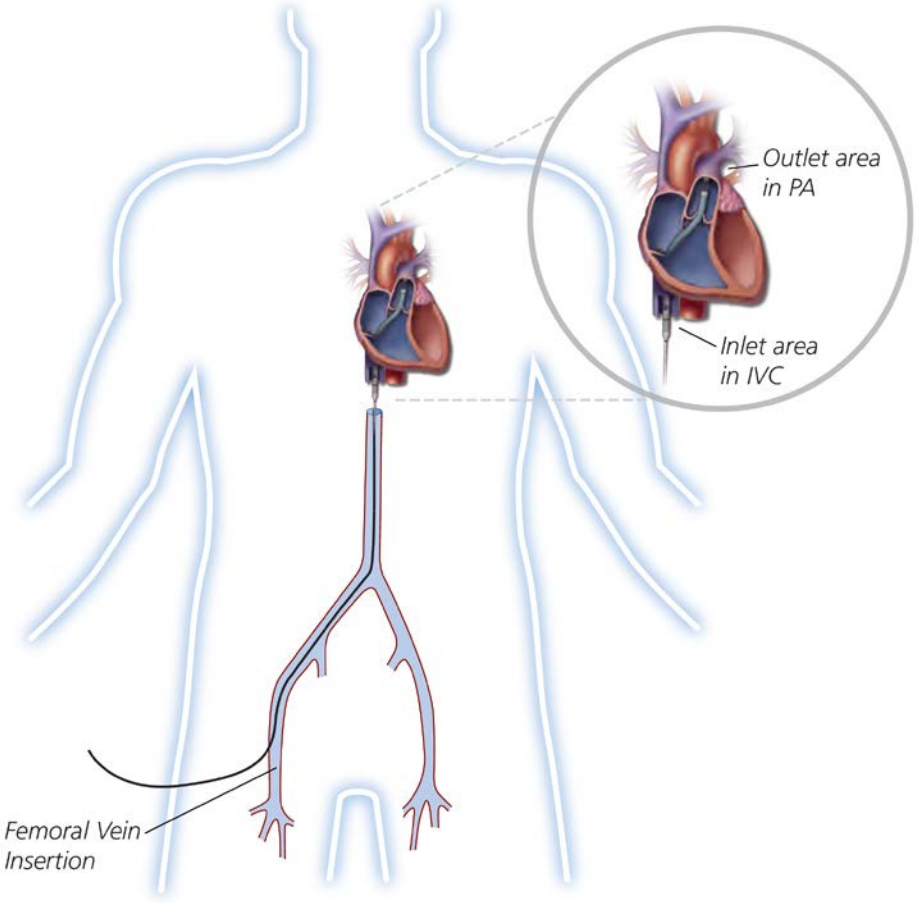
- The Impella RP System is a minimally invasive, miniaturized percutaneous circulatory support system for the right ventricle

- The main component is a 22 French micro-axial flow pump catheter



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 (BSA) ≥1.5 m^2 who develop acute right heart failure or decompensation following left ventricular assist device (LVAD) implantation, myocardial infarction (MI), heart transplant, or open-heart surgery.



Annual Distribution Number (ADN)

- The HDE was approved with an ADN = 4,000
- Number of Impella RP devices sold in the US in 2016: 339
- Number of Impella RP devices implanted in the US in 2016: 288 implants (8 in pediatric* patients)

*Pediatric: Age < 22 years

Impella RP Post Approval Studies (PAS)

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

PAS 1: Impella RP Prospective Study

- Design: Prospective, single arm, multicenter study
- Sample: 30 adult (≥ 18 years old) patients at 15 sites
- Indications: Patients with BSA ≥1.5m^2 with acute right ventricular failure or decompensation following:
  - LVAD implantation
  - Myocardial Infarction
  - Heart transplant or
  - Open heart surgery (post-cardiotomy cardiogenic shock)

Impella RP PAS1 (cont'd)

PAS 1: Impella RP Prospective Study

- Follow-up: 30 and 180 days post explant
- Primary Endpoint: Survival at 30 days post device explant or hospital discharge (whichever is longer), or to induction of anesthesia for next therapy
- Enrollment status:
  - 26 patients currently enrolled (Age: range 21-81yrs, mean 60yrs)
  - Includes 1 patient age 21 years (within the CDRH pediatric age range)

Impella RP PAS1 (cont'd)

Treatment Outcomes for Enrolled patients (N=26)

Outcome	Count (n)
Met primary endpoint (Weaned and alive at 30 days post explant or hospital d/c, induction of anesthesia for next therapy)	**18**
Discharged and alive at 180 days	13
Died 31 to 180 days	3
Discharged alive, not yet 180 days	1
Transitioned to next therapy*	1
Died prior to meeting primary endpoint	8
Died in hospital or prior to 30 days	9*
Total deaths	12

*1 patient died in hospital prior to 30 days after successful transition to next therapy and is counted with the 9 early (30 days) deaths

Impella RP PAS1 (cont'd)

Study findings:

- Primary endpoint rate of 69.2% (18/26) for this PAS is comparable to the survival rate in the RECOVER Right IDE Study – 73% (22/30)
- Single Pediatric Aged Patient (21 yo male):
  - treated for RVF post LVAD (non-ischemic cardiomyopathy)
  - transitioned to Centrimag device for RV Support
  - discharged following a successful wean – now post 180 days
- Adverse Events
  - Major bleeding 42% (11/26)
  - Hemolysis 35% (9/26)
  - Pulmonary Embolism 0% (0/26)
- All adverse events including death adjudicated by the CEC
  - No device or procedure AE's in Pediatric patient
  - Definitely related to device and procedure - 1 Major bleeding and 2 Hemolytic events
  - Probably related to device and procedure – 1 death

Impella RP PAS1 (cont'd)

Death Summary – Probably related to device & procedure

Patient: 72 year old female admitted with shortness of breath, severe LVF, RVF and an ejection fraction (LVEF) of 10%

Hospital Course:

- LVAD and Impella RP were implanted
- Developed compartment syndrome of right leg after Impella RP placement which required fasciotomy
- Impella RP was explanted on Day 6 of placement
- Patient also developed MSOF (liver, kidney and respiratory failure)

Outcome: Death - sepsis due to cardiogenic shock

Impella RP PAS2

PAS 2: Impella RP Pediatric Study

- Design: Retrospective, single arm, multicenter
- Sample: All pediatric patients supported with Impella RP over 5 years until 15 pediatric patients at a minimum of 5 sites are enrolled
- Indications: Patients age 15-17 (BSA ≥1.5m^2) with acute right ventricular failure or decompensation following:
  - LVAD implantation
  - Myocardial Infarction
  - Heart transplant or
  - Open heart surgery (post-cardiotomy cardiogenic shock)

Impella RP PAS2 (cont'd)

PAS 2: Impella RP Pediatric Study

- Follow-up: 30 and 180 days post explant
- Primary Endpoint: Survival at 30 days post explant or hospital discharge (whichever is longer) or to induction of anesthesia for next therapy
- Enrollment Status:
  - One site approved for general HUD use has enrolled 1 pediatric patient since the last PAC meeting
  - Two pediatric sites trained to use the Impella RP

Impella RP PAS2 (cont'd)

Patient: A 16 year old male diagnosed with arrhythmogenic right ventricular dysplasia (ARVD) who experienced cardiac arrest at home

Hospital Course:

- Resuscitated in the ER, Inotropes given
- Echocardiograph: significant RVF and depressed LVEF
- Left-sided assist device (Impella CP) implanted followed by Impella RP
- Hemodynamics stabilized, inotropes were reduced
- Impella CP and RP explanted 7 days after implant

Outcome: Neurologically intact, discharged home

Impella RP PAS2 (cont'd)

Plans to Increase Pediatric PAS Enrollment

- Abiomed is prioritizing recruitment of new Impella RP HUD sites at high volume specialized pediatric centers
  - 6 specialized pediatric centers identified
  - Next 1-3 months, contact investigators
  - 3-12 months (2017) enroll patients at pediatric HUD sites and adult HUD sites
  - Target enrollment for 2017 (Year 3): 5 to 6 patients
  - Enrollment per year (Year 4 and 5): 4 to 5 patients to achieve enrollment goal of 15 patients total

Summary Information for non-Study Pediatric Patients Treated in the US (n=6)

Age (mean, range) years	18.8, 18-20
Gender	
Male	3
Female	2
Unknown	1
Indication for Use	
RVF following:	
LVAD implantation (Bridge to transplant)	1
Post Cardiotomy Cardiogenic Shock	2
Pulmonary Embolism/Pulmonary Hypertension	1
Cardiac Transplant (rejection)	1
Unknown	1
Outcome (at end of ICU Support)	
Successfully weaned	3
Patient Died	2
Unknown	1

Literature Results

- **Literature Search** – Date 12/1/2015- 11/30/2016
  - 1 case report and 1 study based on the data submitted to FDA for the HDE approval (the RECOVER Right IDE Study)

Literature Results Cont'd

Case report (Morgan 2016)

- 70 year-old female with a history of non- ischemic dilated cardiomyopathy, EF of 10–15%, NYHA class IV, stage D, end-stage HF refractory to optimal medical therapy
  - HeartWare VAD implantation as a destination therapy
  - RV failure developed intra-operatively
  - Impella RP placed percutaneously
  - Improvement in MAP, increase in LVAD flow, reduction in RV size and improvement in hemodynamics
  - No device-related complications, discharged POD 14

JA Morgan et al. Percutaneous Right Ventricular Assist Device Support in a Patient Supported by an LVAD. ASAIO J. 2016 Jul-Aug;62(4)

Medical Device Report (MDR) Review

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March 7, 2017

Abiomed Impella RP
Medical Device Report (MDR) Review

MDR Search Criteria:

- Brand Name: Impella RP
- Date Report Entered: December 1, 2015 – November 30, 2016

Search Results: 6 MDRs

- **There were NO pediatric* patients reported in the MDRs**
  - Patient Gender: Male: 5 (83%), Female: 1 (17%)
  - Patient Age: Range: 44 – 68 years; Mean 59 years
  - Reporting Country: US (5 MDRs), OUS (1 MDR)
  - Type of Event: 1 death and 5 serious injuries

*Pediatric: Age < 22 years

Reported Problems by Type of Event in 2017 Analysis Compared to 2016 Analysis

	MDR Count 2017 Analysis (n=6) (12/1/2015-11/30/2016)		MDR Count 2016 Analysis (n=2) (1/23/2015 – 11/30/2015)	
Reported Problem	**Death**	**Injury[1]**	**Death**	**Injury[1]**
Thrombosis/Clot in the Device	1	1	0	1
Device Detachment	0	2	0	0
Bleeding	0	1	1	0
Positioning Issue	0	1	0	0

[1]Serious Injury per regulatory definition (CFR803.3) includes an event that is life-threatening or results in permanent impairment of a body function or permanent damage to a body structure or necessitates medical or surgical intervention(s) to preclude permanent impairment of a body function or permanent damage to a body structure.

Summary of MDR Review

- There were no pediatric patients reported in the MDRs
- The thrombosis, hemolysis, bleeding and positioning issues are addressed in the IFU and are known complications of this type of device
- Corrective actions have been implemented by the firm related to device detachments
- There was one MDR related to an adult PAS patient
- No other safety concerns at this time

FDA Recommendations and Question to the PAC

FDA recommends continued surveillance and will report the following to the PAC in 2018:

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

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