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Recovering hearts. Saving lives.

Notice: FDA Validates Impella RP as Safe and Effective

May 31, 2019

What you need to know:

- FDA issues letter to reinforce benefits of Impella RP
- The survival rate in the Impella RP post-approval study, amongst patients meeting pre-approval study criteria, is similar to the survival rate of the Impella RP pre-approval studies.
- FDA emphasizes importance of early patient selection and device implantation

Dear Healthcare Professional,

In a letter sent to May 21 to healthcare providers, the U.S. FDA validates that Abiomed's Impella RP heart pump is safe and effective for treatment of right heart failure. The letter comes after the FDA examined the results from Abiomed's 18-month post-approval study (PAS) of 42 Impella RP patients.

The data shows a 64% survival rate and 90% heart recovery for the subgroup of PAS patients who met the enrollment criteria of Impella RP's premarket clinical studies. That survival rate is, as the FDA writes in its letter, "similar to the premarket clinical study survival rate," which was 73%. As illustrated in the chart below, a control group humanitarian device exemption (HDE) study of a non-Impella surgical device[1] using the same protocol showed a survival rate of 43%.

FDA Data Source	Survival Rates
Post-approval study (n=14)	64% (9/14)
Premarket clinical studies (RR + CAP + HDE PAS) (n=60)	73% (44/60)
PMA control group data (non-Impella surgical device) (n=24)	43% (10/24)

Importantly, the letter states:

The FDA believes that when the device is used for the currently approved indication in appropriately selected patients the benefits of the Impella RP system continue to outweigh the risks.

The FDA letter emphasizes the need for early patient selection and determines late identification and treatment of cardiogenic shock as the root cause of differences between the survival rate in the pre-market study and the PAS.

Healthcare providers are encouraged to use the Impella RP patient selection checklist (included below), which the FDA and Abiomed collaborated to develop, to assist with proper patient selection to optimize outcomes. Best practices and additional resources are available at www.ProtectedPCI.com.

Impella RP is the most studied right-sided device and the only percutaneous technology with FDA approval for right heart support. Its exclusive FDA approval is a result of five years of research that included:

[1] Humanitarian Device Exemption (HDE) study of surgical VAD is not powered for comparison but uses the same FDA protocol for right ventricular failure. HDE criteria to meet is safe and probable benefit, compared to safe and effective for PMA approval.

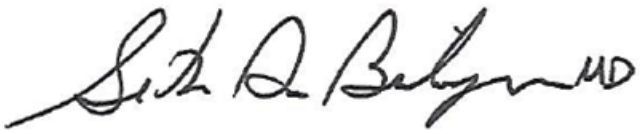
- RECOVER RIGHT, an FDA-approved, prospective, multicenter, single-arm study, which commenced after the company received FDA investigational device exemption (IDE) approval in November 2012 and concluded in 2014.
- HDE approval study, which was completed in January 2015
- A Continuous Access Protocol (CAP)
- FDA post-approval study, initiated after PMA approval in September 2017

It is worth noting the entire family of Impella heart pumps has been recognized by the FDA as safe and effective and has been granted FDA PMA approval -- the highest level of U.S. regulatory approval.

Abiomed is committed to improving patient outcomes by performing post-market patient surveillance and FDA studies, collecting real-world evidence and developing best practices. Abiomed tracks outcomes on nearly 100% of its U.S. patients through its Impella Quality (IQ) Database, helps improve patient outcomes through its Impella Connect cloud-based platform, and prospectively conducts FDA clinical studies through its IRB approved cVAD Study.

Please don't hesitate to reach out with any questions you may have about the Impella RP, or any Impella heart pump.

Sincerely,



Seth Bilazarian

Chief Medical Officer, Abiomed

Impella RP® Heart Pump Patient Selection Criteria Checklist

Treatment with the Impella RP System is appropriate for patients with a body surface area >1.5 m^2, who develop signs of acute right ventricular failure:

1. Within 48 hours post-implantation of an FDA approved surgical LVAD; or
2. Within 48 hours post-heart surgery, post-heart transplant or post-myocardial infarction

The checklists below are based on the exclusion criteria for the Impella RP pre-market clinical study. These checklists are provided to help you determine if Impella RP support is an appropriate treatment for your patient, and if your patient is likely to benefit from Impella RP support.

Right Ventricular Failure (RVF) is defined as:

- A cardiac index <2.2 l/min/m^2 despite continuous infusion of high dose inotropes

AND ANY OF THE FOLLOWING:

- CVP > 15 mmHg or
- CVP/PCWP or LAP > 0.63 or
- Moderate to severe global RV dysfunction on echocardiography defined as one of the following criteria:
  - Global RV hypokinesis
  - TAPSE score of ≤ 14 mm
  - Right ventricular diameter at basis > 42 mm
  - Right ventricular short axis (or mid-cavity) diameter > 35 mm

High dose inotropes is defined as:

- Dobutamine of ≥ 10 µg/kg/min or equivalent for more than 15 minutes (120 minutes for milrinone) and/or administration of more than one inotrope/ vasopressor medication

Has your patient received a surgical LVAD within 48 hrs and has any of the following?	Has your patient had cardiac surgery, heart transplant or AMI within 48 hrs and has any of the following?
☐ INTERMACS I patients (crash and burn with worsening lactate levels or acidosis)	☐ Patients in profound cardiogenic shock, i.e., SBP < 75mmHg and CI < 1.3 l/min/m^2 despite two or more high dose inotropes, PH<7.1 not corrected by 100 Ml NaHCO3, DIC, anoxic brain Injury or CGS >24 hrs
☐ Evidence of end-organ failure (bilirubin >5 or creatinine >4 within 24 hrs of implant)	☐ Ami with acute mechanical complication (VSD, ventricular rupture or pap rupture)
☐ Evidence of acute neurologic injury	☐ Unsuccessful revascularization of RCA
☐ Active infection defined as two of the following (WBC >12,5000 or positive blood culture or fever)	☐ Active infection defined as two of the following (WBC >12,5000 or positive blood culture or fever)
☐ RA, RV or PA thrombus	☐ RA, RV or PA thrombus
☐ Prosthetic valves In the right heart	☐ Prosthetic valves in the right heart
☐ Structural tricuspid disease	☐ Structural tricuspid disease
☐ ASD or PFO (unrepaired)	☐ ASD or PFO (unrepaired)
☐ Pulmonary valve stenosis or insufficiency	☐ Pulmonary valve stenosis or insufficiency
☐ Severe pulmonary hypertension (PAS>60mmHg)	☐ Severe pulmonary hypertension (PAS>60mmHg)
☐ Documented DVT and/or presence of IVC filter	☐ Documented DVT and/or presence of IVC filter
☐ Anatomic abnormalities precluding insertion	☐ Anatomic abnormalities precluding insertion
☐ PA conduit	☐ PA conduit
☐ Patients on right-sided support or ECMO	☐ Patients on right-sided support or ECMO
☐ Current Pulmonary Embolism	☐ Current Pulmonary Embolism
☐ Aortic Dissection or Marfan Syndrome	☐ Aortic Dissection or Marfan Syndrome
☐ Allergy or intolerance to contrast	☐ Allergy or intolerance to contrast
☐ HIT or sickle cell disease	☐ HIT or sickle cell disease
☐ Existing congenital heart disease that would preclude placement	☐ Existing congenital heart disease that would preclude placement
If your patient received a surgical LVAD >48 hrs ago, or you checked any of the above boxes, your patient is not a candidate	**If your patient had cardiac surgery, heart transplantation, or AMI > 48 hrs ago, or you checked any of the above boxes, your patient is not a candidate**

If you have questions about the appropriate selection of a patient for Impella RP support, or patient management, contact Abiomed's 24 Hour Clinical Support Center at (800-422-8666)

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Right-Side Support
The Impella RP® System is indicated for providing temporary right ventricular support for up to 14 days in patients with a body surface area ≥1.5 m^2, who develop acute right heart failure or decompensation following left ventricular assist device implantation, myocardial infarction, heart transplant, or open-heart surgery.

Important Risk Information for Impella RP System

CONTRAINDICATIONS
The Impella RP System is contraindicated for patients with the following conditions: Disorders of the pulmonary artery wall that would preclude placement or correct positioning of the Impella RP device. Mechanical valves, severe valvular stenosis or valvular regurgitation of the tricuspid or pulmonary valve. Mural thrombus of the right atrium or vena cava. Anatomic conditions precluding insertion of the pump. Presence of a vena cava filter or caval interruption device, unless there is clear access from the femoral vein to the right atrium that is large enough to accommodate a 22 Fr catheter.

POTENTIAL ADVERSE EVENTS
The potential adverse effects (eg, complications) associated with the use of the Impella RP System: Arrhythmia, Atrial fibrillation, Bleeding, Cardiac tamponade, Cardiogenic shock, Death, Device malfunction, Hemolysis, Hepatic failure, Insertion site infection, Perforation, Phlegmasia cerulea dolens (a severe form of deep venous thrombosis), Pulmonary valve insufficiency, Respiratory dysfunction, Sepsis, Thrombocytopenia, Thrombotic vascular (non-central nervous system) complication, Tricuspid valve injury, Vascular injury, Venous thrombosis, Ventricular fibrillation and/or tachycardia.

In addition to the risks above, there are other **WARNINGS** and **PRECAUTIONS** associated with Impella RP. Learn more visit:
www.abiomed.com/important-safety-infomation

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