



## Brief Summary of the Circulatory System Devices Panel Meeting – July 21, 2011

### **Introduction:**

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on July 21, 2011 to discuss, make recommendations, and vote on information related to HDE H100004 for the Berlin Heart EXCOR Pediatric Ventricular Assist Device (VAD).

The EXCOR VAD is intended to provide mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients. Pediatric candidates with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support may be treated using the EXCOR Pediatric.

### **Panel Deliberations/FDA questions:**

The Panel discussed the primary effectiveness endpoint results noting the differences in survival rates between patients treated with the EXCOR VAD and those in the control group who were treated with extracorporeal membrane oxygenation (ECMO). Survival rates were in favor of the EXCOR VAD and the panel specifically noted that observational data showed that patients could remain on this device for longer periods of time compared to the time patients were on ECMO. The panel believed that the device meets a critical need for patients with end stage heart failure who are awaiting a transplant.

The Panel felt that the secondary effectiveness endpoint results were supportive of clinical conclusions resulting from the primary effectiveness endpoint. The data showed that transplant eligibility is maintained while the need for other supportive measures that require sedation and limit patient mobility are diminished.

The Panel commented on the primary safety endpoint and agreed that the overall rate of serious adverse events (SAE) was less in the EXCOR patients compared to the ECMO patients. The panel specifically noted the clinical significance of the higher, acute stroke rates and neurologic outcomes that were observed in patients treated with the EXCOR. Despite a 29% stroke rate, approximately 90% of pediatric patients were successfully transplanted. However, it was concluded that stroke rates and neurological outcomes are serious issues that need to be investigated further in the setting of a post-approval study. The panel also suggested that strokes and their outcomes must be better defined and that more data are necessary to understand the impact of pediatric antiplatelet therapy and drug efficacy for this patient population.

The Panel agreed that the rate of pump changes could be independent of the stroke rate and does not seem to be a quality metric for strokes. Visible thrombus is an important clinical finding and steps should be

taken to prevent thrombus build up in the pump and to determine its cause. The Panel recommended that the relationship between visible thrombus and stroke rate requires further study to better understand their effects on long term outcomes.

The Panel discussed the number of pediatric transplant centers and the number of patients that might be implanted in a given year. There was agreement that a precise and thorough training program should be required for site initiation.

The Panel concluded that all available clinical data for all patients in the study should be clearly summarized in a specific clinical section of the labeling, including survival data regarding patients with single ventricle circulation and those who have had use of pre-implant ECMO. The panel agreed that the labeling should not include contraindications and enough data should be included to allow physicians to make an informed decision based on patient selection factors that may lead to optimal success and outcomes in these complex patients. Specific inclusion of the eligibility criteria used for study patients in this trial should be included as a guide for optimal patient selection.

The Panel also discussed the post-approval study (PAS) design and considered 2 elements of the study: 1) follow-up of current IDE patients and 2) enrollment of a new cohort with important baseline data with follow-up beyond explant. They agreed that the overall EXCOR data from this trial would be an appropriate comparator for the PAS given the limitations of the ELSO registry and the lack of any other suitable comparators. The Panel felt that the overall AE rate used as a baseline for this PAS should be substantially less than the 0.25 per patient day on support, and that the proposal for future performance goals should be informed by the results of patients in the IDE. Participation in existing registries or design of a distinct registry for tracking of these patients for acute and long-term outcomes was also thought to be of critical importance. The Panel proposed that approximately 5 year data should be collected on stroke, pump thrombus and longer-term neurologic and quality of life outcomes to adequately assess the longer-term impact of device implantation.

#### **Vote:**

#### **Voting Question 1:**

The Panel voted **16 to 0 that the data does show** there reasonable assurance that the Berlin Heart EXCOR Pediatric Device is safe for use in patients as a bridge to cardiac transplantation for pediatric patients who meet the criteria specified in the proposed indication.

#### **Voting Question 2:**

The Panel voted **16 to 0 that there is** reasonable assurance that the Berlin Heart EXCOR Pediatric Device provides probable benefit as a bridge to cardiac transplantation for pediatric patients who meet the criteria specified in the proposed indication.

#### **Voting Question 3:**

The Panel voted **16 to 0 that the benefits** of the Berlin Heart EXCOR Pediatric Device for use in patients as a bridge to cardiac transplantation for pediatric patients who meet the criteria specified in the proposed indication **do outweigh the risks** of the Berlin Heart EXCOR Pediatric Device for use in patients as a bridge to cardiac transplantation for pediatric patients who meet the criteria specified in the proposed indication.

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