Brief Summary of the Circulatory System Devices Panel Meeting – February 18, 2016

Introduction

The Committee met on February 18, 2016 to discuss and make recommendations concerning clinical trial, post approval study (PAS) design and physician training requirements for leadless cardiac pacemaker device technology. Specifically, the Committee was asked to make recommendations on the acceptability of adverse event rates in acute and chronic time frames, indications for use for this device type, manufacturer-required training and necessary elements for PAS collection.

General Device Description

Leadless pacemakers (LPs) are single-chamber, fully implantable devices that provide sensing and pacing to the right ventricle. These devices are indicated for use in patients who may benefit from rate-responsive pacing to support cardiac output during varying levels of activity.

Panel Deliberations/FDA Questions

QUESTION #1

The panel discussed the rates of acute (during and within 30 days of implantation) adverse events observed for LPs as compared to transvenous pacemakers. The panel felt that cardiac perforation rates for LPs should be consistent with published perforation rates of transvenous pacemakers. Other adverse events that were of concern consisted of: pericardial effusion, dislodgement, embolization (i.e. acute migration during implant necessitating retrieval), serious groin complications necessitating repair or transfusions, cardiac mortality, and infection.

The panel discussed subgroups that may have possible increased risk of a cardiac perforation during the implant procedure and determined that no subgroup should be excluded from receiving this device.

The panel agreed that implanting physicians must be adequately trained/informed regarding adverse events and appropriate patient selection.

QUESTION #2

The panel was asked to make recommendations on the appropriate PAS design.

The panel agreed that the acute events should be captured through collection of post-approval data, include groin complications, hematoma, vascular issues, perforations, infection, acute electrical performance, and mortality.

The panel agreed that the sample size needed to capture acute complications should be around 1,741 subjects enrolled, which assumes a complication rate of 1% with a confidence interval width of +/- 0.5%. The panel recognized that due to attrition of this sample size, 500 patients would complete 9 years of follow-up and about 200 cases of EOL would be observed.

In terms of long-term performance of leadless pacemakers, the Panel was asked to consider the following points:

a. the difficulty in implementing such a study;
b. patients lost to follow-up over the course of a long study;
c. the ability to characterize end of life device failures; and
d. the ability to accurately collect device disposition when a new device is placed.

With this in mind, the panel noted that the PAS should capture as much information as possible, including: unanticipated and anticipated adverse events, battery longevity, device-device interactions (including interactions with MRI and cardioversion), infection, device erosion, and thrombus formation.

The panel agreed that based on the current PAS paradigm for cardiac leads, a complication-free rate (including deaths) can be used as the endpoint for long-term performance assessment of LPs. The panel also determined that 8-9 years of follow-up would be necessary for LPs.

The panel agreed that collecting observational data on the following scenarios for device EOL is appropriate:

- Explant Leadless Pacemaker and implant
    - another LP
    - a transvenous pacemaker system
    - an ICD (in the event the patient develops an indication for one)
- Turn OFF the existing LP and implant
    - an adjacent LP
    - an adjacent transvenous pacemaker
    - an adjacent ICD (in the event the patient develops an indication for one)

The panel also recommended that a PAS must capture device removal/extraction experience including how often it is attempted, success rates, and associated complications.

Furthermore, the panel agreed that the PAS design should incorporate data collection for patients who receive a LP as a replacement for a transvenous system.

The panel revisited the necessary PAS sample size needed to capture long-term performance and again agreed that 1,741 subjects should be enrolled. The panel recognized that due to attrition of this sample size, 500 patients would complete 9 years of follow-up and about 200 cases of EOL would be observed.

QUESTION #3

The panel confirmed that labeling should be device-specific and incorporate all experience on long-term performance and EOL options to date, noting limitation of data available at the time of approval.

QUESTION #4

The panel discussed and agreed that indications for transvenous, single chamber (VVI) pacemakers apply to this class of devices. The panel agreed that guidance for certain populations are already in place under the AHA/ACC/HRS guidelines.

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