FDA Panel Backs Cryoablation for Atrial Flutter

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GAITHERSBURG, MD. — The majority of a federal advisory panel recommended that a cryoablation system be approved for treating atrial flutter in adults, under certain conditions that include a postmarketing study of treatment recipients conducted by the manufacturer to further evaluate its safety and efficacy.

If approved, the device, the CryoCor Cryoablation System, would be the first cryoablation device approved in the United States for treating atrial flutter.

At a recent meeting, the Food and Drug Administration's circulatory system devices panel voted 8-2 that the device was "approvable with conditions," for treating isthmus-dependent atrial flutter in patients aged 18 years and older. Two conditions for approval pertained to labeling issues for the device and requirements for training of physicians and their staffs in how to use the console and manipulate the catheter. The third condition was that the manufacturer, San Diego–based CryoCor Inc., conduct a postmarketing registry study of patients treated with the device, to follow the short-term and longer-term adverse events and clinical effectiveness in a real-world setting.

Despite reservations about the design and results of the clinical trial submitted for approval, the majority of the panel agreed that the data presented by the company had shown that there was "reasonable assurance" that the device was safe and effective for treating right isthmus-dependent atrial flutter. The main issue was that the clinical trial did not compare the device with a control group, but instead compared it with established safety and efficacy objective performance criteria (OPC) for current standard ablation treatment modalities, agreed upon by the FDA and company.

Dr. David Slotwiner, an electrophysiologist at Long Island Jewish Medical Center, New Hyde Park, N.Y., said that he believed that the data demonstrated that the device was safe and effective for treating the proposed indication. But like others on the panel, he strongly agreed that it was not appropriate to use the OPC for such studies and that in the future, these devices be studied in randomized, controlled trials that include a comparator group of patients.

The FDA usually follows the advice of its advisory panels, which are not binding. The FDA decision is expected in August, according to CryoCor, which is now conducting a study of the system for treating atrial fibrillation.

The system includes a console and a percutaneous catheter, which ablates cardiac tissue by freezing it, using nitrous oxide. In the pivotal study conducted at 24 U.S. sites, 160 patients, with documented, symptomatic isthmus-dependent atrial flutter and with at least one episode within the previous 6 months, were treated with the system. (Exclusion criteria included structural heart disease, unstable heart failure symptoms, and having undergone ablation for atrial flutter previously.)

Acute effectiveness, defined as the proportion of patients achieving bidirectional block across the cavotricuspid isthmus, was 87.5% (140 of 160 patients), which met the goal of more than 80% acute effectiveness rate. The primary safety end point, serious adverse events within 7 days of the procedure, was not met; however, the rate was 5.6%, more than twice as high as the prespecified goal of 2.5%. Dr. Randall Brockman, the FDA's primary reviewer of the application, said that although the primary safety end point was not met, the agency believed that the events that occurred were similar to those that would be expected for patients with atrial flutter.

Chronic effectiveness, based on evaluations by the blinded core lab adjudication of patient event recordings, was 81.6%, which did not meet the prespecified chronic effectiveness goal of 90%.

One of the two panelists voting against approval, cardiac surgeon Norman S. Kato, said there was insufficient evidence to satisfy the objective performance criteria. He also pointed out that atrial flutter usually is not a life-threatening problem, and that a 2- to 2.5-fold higher complication rate "in a situation where the disease is not life threatening is a problem."

Also voting against approval was the panel's statistician, Sharon-Lise Normand, Ph.D., of Harvard School of Public Health, Boston, who said that the data did not support approval and also remarked that she was concerned that "subjective opinions" were behind many of the votes for approval. ■