HeartMate II Approved As Destination Therapy

BY ELIZABETH MECHCATIE

The approval of the HeartMate II, the continuous-flow left ventricular assist device, has been expanded to include its use as destination therapy for people with severe heart failure who are not acceptable candidates for heart transplantation.

The device can now be used in patients with New York Heart Association class IIIB or IV end-stage left ventricular failure, who have received optimal medical therapy for at least 45 of the last 60 days, according to the statement issued by the manufacturer, Thoratec Corp.

The Food and Drug Administration and Thoratec Corp. announced the approval of the Heart Mate II left ventricular assist device (LVAD) in late January.

It was first approved by the FDA in April 2008 for use as a bridge to transplantation in cardiac transplant candidates at risk of imminent death from nonreversible left ventricular heart failure. The HeartMate II is markedly smaller than previously available devices, including Thoratec's HeartMate XVE, the only other LVAD approved for destination therapy. The HeartMate XVE, a pulsatile flow LVAD, was first approved for use as a bridge to transplantation.

"Its smaller size and mobility should allow more patients, including women and men of smaller stature, access to treatment," Dr. Jeffrey Shuren, director of the FDA's Center for Devices and Radiological Health, said in the agency's approval statement.

The HeartMate II Destination Therapy study, a randomized trial sponsored by Thoratec, compared the HeartMate II with the HeartMate XVE in 200 patients (median age 64 years) with advanced heart failure who were ineligible for cardiac transplantation.The primary end point—survival at 2 years free of disabling stroke and reoperation to repair or replace the device—was met by 62 (46%) of the 134 patients who received the Heart Mate II, compared with 7 (11%) of the 66 who received the HeartMate XVE (N. Engl J. Med. 2009;361:2241-51).

"In addition, data collected in a separate registry of smaller-stature women and men indicated that the device worked well in this specific population," the FDA statement said.

As a condition of FDA approval, Thoratec is required to conduct a postmarketing study evaluating the device's performance. The data will be entered into the Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS), which is managed by the FDA; the National Heart, Lung, and Blood Institute; the Center for Medicare & Medicaid Services; and participating hospitals and manufacturers. The study will follow 247 patients for 2 years, and will collect data on outcomes, adverse events, functional status, and quality of life, according to Thoratec. ■

MY TAKE

Smaller Device Yields Big Results

With this approval, the current state-of-the-art nonpulsatile LVAD can be offered to all appropriate patients without the confines of an investigational study. The approval validates the concept that the smaller LVAD devices confer benefits, compared with the pulsatile device, and it opens up the way to their further development.

Small-stature adults, and many women, are too small for the HeartMate XVE. The HeartMate II is a smaller, nonpulsatile pump, so more patients are eligible candidates. And as the HeartMate II Destination Therapy study showed, there's less morbidity associated with the surgical operation because of the smaller size, which is a big advantage.

Despite better survival and fewer infections with the HeartMate II compared with the HeartMate XVE, the stroke rate was not different, and that's a concern. Investigators will focus more on the mechanisms behind stroke and the resultant anticoagulation strategies.

Typically, destination-therapy patients have class IV heart failure, a low ejection fraction, and poor exercise tolerance, but are not transplant candidates—perhaps because they have had cancer recently, are too old, or have other comorbidities.

Efforts are underway at the NHLBI to study VAD therapy in less ill patients, to determine if patients can be identified as candidates for LVAD therapy before they get desperately ill and need a transplant, or before they are as sick as current LVAD candidates. The HeartMate XVE has shown wear and tear after 1-1½ years of use, but there are people who have had the HeartMate II for more than 3 years.

Considering how far we have come with cardiac resynchronization therapy devices and implantable cardioverter defibrillators—which once were huge, bulky devices that have gotten smaller and smaller and eventually will not even have leads—this is certainly what we expect to happen with LVADS as well.

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Newly Approved LVAD Alternative to Heart Transplantation

BY BRUCE JANCIN

SNOWMASS, COLO. — The Food and Drug Administration's recent approval of Thoratec Corp.'s HeartMate II left ventricular assist device as destination therapy—that is, as an alternative to heart transplantation—is a landmark development heralding a long-awaited era of lifetime mechanical circulatory support in patients with terminal heart failure, experts said at a conference sponsored by the American College of Cardiology.

"This represents a significant step forward and now becomes a realistic option in the treatment of patients with advanced heart failure," said Dr. Clyde W. Yancy, the president of the American Heart Association, at the conference.

"When I went to the Cleveland Clinic in 1978, we believed that we were just about ready to have an effective mechanical cardiac replacement. And, honestly, one of the most disappointing parts of my career is that for a long time we really didn't make much progress in that area. Basically, the devices just weren't good enough. The pumps fell apart. There was a high incidence of stroke, bleeding, and infection. It made for very poor quality of life," observed Dr. Bruce Lytle, professor and chairman of the department of cardiothoracic surgery at the Cleveland Clinic Foundation.

The HeartMate II has not solved all those problems, but it does represent a great improvement over earlier-generation devices. "Mechanical replacement really does now appear to be on the cusp of being able to offer real benefit to at least some patients with severe heart failure," Dr. Lytle said.

Dr. Yancy explained that the technologic breakthrough that has finally brought destination therapy to the fore is the development of small, reliable, totally implantable left ventricular assist devices (LVADs) featuring continuous-flow rotary pumps.

The HeartMate II is 'a realistic option in the treatment of patients with advanced heart failure.'

DR. LYTLE

'Outcomes with the HeartMate II are not nearly as good as with heart transplantation.'

DR. FOWLER

The HeartMate II is the prototype. It earned FDA approval as destination therapy on the strength of a 200-patient, multicenter, randomized trial in which it was compared with its predecessor, the HeartMate XVE, which uses a pulsatile-flow pump.

The primary study end point—survival at 2 years free of disabling stroke or reoperation to replace or repair the pump—was achieved in 46% of HeartMate II recipients and 11% of those who got the pulsatile-flow device. Two-year actuarial survival was 58% in the HeartMate II group, compared with 24% on the pulsatile-flow device (N. Engl. J. Med. 2009;361:2241-51). Two-year survival in medically managed patients with similarly advanced heart failure is typically less than 10%, noted Dr. Yancy, medical director of the Baylor Heart and Vascular Institute and chief of cardiothoracic transplantation at Baylor University Medical Center, Dallas.

Dr. Michael B. Fowler cautioned that outcomes with the HeartMate II are not nearly as good as with heart transplantation, which has a 1-year survival of roughly 85% and a 10-year survival of 50%. But heart transplantation is available to only 2,000 patients per year because of the very limited donor organ supply.

It is clear from observational registry data that LVADs need to be implanted relatively early in the course of end-stage heart failure to achieve the best long-term survival. In one large registry, older age, shock, and right-heart failure as reflected in ascites or increased bilirubin at device implantation were significant predictors of shortened survival (J. Heart Lung Transplant. 2009;28:44-50), said Dr. Fowler, professor of medicine and director of the heart failure program at Stanford (Calif.) University. He noted that the HeartMate II has not solved the problem of device-associated thromboembolism: The rate of disabling stroke in the randomized trial was 11% in the HeartMate II arm and 12% with the pulsatile-flow LVAD. ■

Disclosures: *Dr. Yancy and Dr. Lytle indicated they have no relevant financial interests. Dr. Fowler disclosed that he serves as a consultant to Medtronic, AstraZeneca, GlaxoSmithKline, Merck, and Scios.*