Counterpulsation Therapy Benefits Heart Failure

BY BRUCE JANCIN
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ORLANDO — A standard 7-week course of enhanced external counterpulsation therapy in patients with heart failure who are on optimal pharmacotherapy improves their exercise duration, quality of life, and New York Heart Association class for at least 6 months afterward, according to the results of a randomized trial presented at the annual meeting of the American College of Cardiology.

"We believe these results suggest that EECP provides adjunctive therapy in patients with New York Heart Association [NYHA] class II-III heart failure receiving optimal pharmacologic therapy," said Arthur M. Feldman, M.D., chairman of the steering committee for the Prospective Evaluation of EECP in Congestive Heart failure (PEECH) trial.

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EECP therapy is synchronized to the individual patient's cardiac cycle, inflating the cuffs when the heart is resting and deflating the cuffs just before the heart beats. These pulses counter to the heart beat, increase blood flow to the heart muscle, and decrease the heart's workload.

PEECH involved 187 patients with systolic heart failure (HF) and a mean ejection fraction of 26% who were randomized at 29 medical centers to optimal drug therapy alone or in combination with 35 hour-long EECP sessions over 7 weeks.

Patients were unblinded as to their treatment allocation, as were their treating physicians; however, a separate group of blinded investigators performed all patient evaluations, explained Dr. Feldman, professor and chairman of the department of medicine at Thomas Jefferson University, Philadelphia.

The primary study end point was at least a 60-second improvement in exercise duration at follow-up 6 months after the last EECP session. This was achieved in 35% of the EECP group and 25% of controls, a significant difference.

However, there was no between-group difference in a predefined alternative primary end point, the percentage of patients achieving at least a 1.25-mL/kg per minute increase in peak oxygen consumption (VO_2).

Exercise duration improved by a mean of 25 seconds in the EECP group, whereas it declined by 10 seconds among controls. To put this 35-second difference into perspective, Dr. Feldman said randomized trials of cardiac resynchronization therapy show it typically results in roughly a 50-second differential in exercise duration, compared with sham therapy.

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DR. FELDMAN

Improvement in NYHA class was a secondary PEECH end point. At 6 months, 31% of the EECP group, and only 14% of controls showed at least a one-class improvement.

Another secondary end point was quality of life as measured in terms of change from baseline in scores on the Minnesota Living with HF questionnaire.

One month after completion of the EECP sessions, treated patients had a mean 8.9-point improvement, compared with a 3.4-point gain in controls. The quality of life advantage favoring the EECP group remained significant at 3 months, but not at 6 months.

EECP was well tolerated, although one patient developed a pulmonary embolism that investigators believed was therapy related.

Discussant Andrew D. Michaels, M.D., characterized the PEECH results as "mixed."

"The trial met one of two primary end points. It's somewhat concerning that the end points that were met—namely increased exercise duration, improved quality of life, and improvement in [NYHA] class—are all subject to the placebo effect," added Dr. Michaels of the University of California, San Francisco.

Dr. Feldman said that although EECP resulted in a significant gain in VO_2 in an earlier pilot study, the PEECH population may have been biased against realizing a similar benefit because they were predominantly NYHA class II and hence didn't have a long way to go to reach an essentially normal response.

EECP utilizes a series of ECG-synchronized inflatable cuffs wrapped around the legs. The cuffs swiftly inflate at onset of diastole and rapidly deflate at onset of systole, providing hemodynamic effects similar to intraaortic balloon counterpulsation, including increased coronary artery blood flow along with afterload reduction.

EECP is approved for the treatment of stable angina and the average physician payment under Medicare is $138.34 per session.

Both Dr. Feldman and Dr. Michaels are consultants to Vasomedical Inc., which markets EECP systems and sponsored the PEECH trial. ■

FDA Panel Narrowly Votes Down AbioCor Artificial Heart

BY RICHARD A. PIZZI
Contributing Writer

GAITHERSBURG, MD. — The AbioCor total artificial heart did not meet the Food and Drug Administration's humanitarian-device exemption requirements, according to the FDA's Circulatory Systems Devices Panel. The vote was 7-6 against, with one abstention.

The committee determined that the device maker Abiomed's submission under the humanitarian-device exemption standards was inadequate. Concerns were based on undefined anticoagulation treatment protocols and the lack of quality of life data. The panel stressed the need for more extensive studies demonstrating the device's safety.

The AbioCor Implantable Replacement Heart is the first fully implantable artificial heart for severe end-stage heart failure patients who are younger than 75 years, not transplant candidates at the time of assessment, and in biventricular failure not treatable by a destination-therapy left ventricular–assist device. The device is designated as a last resort for a small patient population with a poor prognosis of survival within 30 days.

Abiomed submitted data from a clinical trial spanning slightly more than 3 years, from 2001 through 2004. The device was implanted into a total of 14 patients. The trial was initially designed to assess patient survival at 2 months.

The panel was concerned about the lack of quality of life data, and they stressed the need for more extensive safety studies because of a high stroke incidence.

Two patients died during implantation, and two others died before the 60-day end point. Three of the patients who survived more than 60 days had strokes prior to 60 days. A device failed in one patient at 5 months, and in another patient, the device wore out expectedly at 17 months. (The average runtime during bench tests was 18.8 months.) Complications included postoperative bleeding requiring reoperation and neurologic events.

Two patients improved enough to be discharged from the hospital—one to the patient's home and the other to a hotel near the hospital.

Although a humanitarian-device exemption is similar in both form and content to an FDA premarket approval application, requiring reasonable assurance of safety and probable benefit, it is exempt from the effectiveness requirements of a premarket approval. The sponsor's representatives stressed this distinction during their presentations to the panel and emphasized the groundbreaking nature of the technology. The FDA's presentation to the panel offered a somewhat mixed evaluation of the device. Biomedical engineer Eric Chen, the FDA's lead reviewer, asserted that the device met the humanitarian device exemption's requisite standards for biocompatibility, electrical safety, and manufacturing, but he said there are still concerns about reliability. Julie Swain, M.D., leading the FDA's clinical review team, said "This device is a real dilemma." She asserted that the relationship between risk and benefit was very difficult to ascertain, "due to a lack of validated quality of life and functional data."

Discussion among panel members echoed the uncertainties of the FDA review team. Joanne Lindenfeld, M.D., director of heart transplantation at the University of Colorado, Denver, said, "Safety is the biggest concern here. We see enormous [incidence of] death due to stroke." Dr. Lindenfeld said that she could not support the device because she was "unconvinced that we've settled the issue of bleeding and stroke." Thomas B. Ferguson, M.D., of Washington University, St. Louis, spoke to concerns about anticoagulation, telling the sponsor's representatives that he would "like to be reassured that you are totally convinced that … all has been done to minimize the device as a clot producer."

The FDA usually follows the recommendations of its advisory panels but is under no statutory obligation to do so. ■