Bosentan Safe, Effective in Children With PAH

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BARCELONA — Bosentan was safe and appeared effective for treating pulmonary arterial hypertension in children with congenital heart disease in a retrospective, open-label study with 48 patients.

The results suggest that treatment with bosentan "may improve long-term outcomes" in children with pulmonary arterial hypertension (PAH) related to congenital heart disease, Dr. Erika B. Rosenzweig and her associates reported in a poster at a joint meeting of the European Society of Cardiology and the World Heart Federation.

PAH is a rare but potentially life-threatening condition that can occur in infants and children as persistent pulmonary hypertension of the newborn, as idiopathic or primary PAH, or in association with congenital heart disease or chronic lung disease.

At follow-up, 36% of the 48 patients with PAH related to congenital heart disease had an improved functional class, 55% remained the same, and 10% worsened.

Treatment with an oral calcium channel blocker can initially be effective, but eventually another treatment is often needed. Continuous infusion of epoprostenol is effective, but chronic central venous access can be a problem, and the drug has many adverse effects.

Bosentan is an oral agent that's been effective in adults with PAH, and so was tested in a total of 86 children, including 38 with idiopathic disease and 48 with PAH associated with congenital heart disease. Results from all 86 patients were reported a year ago (J. Am. Coll. Cardiol. 2005;46:697-704); the new report focused entirely on results from the subgroup with congenital heart disease.

The treated children ranged in age from 1 to 18 years, with an average age of 11. They were treated from May 2001 to April 2003 at two centers: New York–Presbyterian Hospital, and Children's Hospital in Denver.

Four different target bosentan dosages were used depending on each patient's weight. For children who weighed less than 10 kg, the target dosage was 15.6 mg b.i.d.; for those weighing 10-20 kg, the target was 31.25 mg b.i.d.; for those weighing 20-40 kg, the target was 62.5 mg b.i.d.; and for children weighing more than 40 kg, the target was 125 mg b.i.d. Patients received half the their target dosage for the first 4 weeks of treatment, and if it was well tolerated the dosage was then increased to the target level.

Intravenous epoprostenol or subcutaneous treprostinil was added for patients who had clinically significant deterioration while on bosentan. Eighteen of the 48 patients in this subgroup received an add-on prostanoid, while 30 patients received monotherapy with bosentan.

Baseline and follow-up data on functional class assessments were available for 42 patients. Follow-up functional assessments, using World Health Organization criteria, were done after an average of 12 months of treatment (range was 3-23 months).

At follow-up, 15 of the patients (36%) had an improved functional class, 23 (55%) remained the same, and 4 (10%) worsened, reported Dr. Rosenzweig, a pediatric cardiologist at New York–Presbyterian Hospital, and her associates.

Hemodynamic assessments at baseline and follow-up were available for 24 patients. The average follow-up time was 10 months (range was 3-20 months). Pulmonary arterial pressure fell by an average of 7 mm Hg.

The efficacy shown by these findings was very similar to the efficacy reported last year for the entire group of 86 patients studied. Two of the 48 patients died during follow-up, both because of worsening pulmonary arterial hypertension.

Bosentan was well tolerated. No patient in this subgroup had a symptomatic increase in liver enzymes. Two patients were taken off of bosentan because of symptomatic arterial desaturation; in one of these patients arterial oxygen saturation normalized once bosentan treatment stopped.

The study was partially sponsored by Actelion, the company that markets bosentan (Tracleer). ■