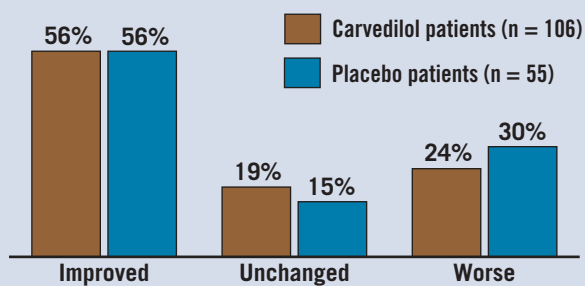


### Carvedilol, Placebo Similar in Pediatric Heart Failure Trial



Note: Totals do not equal 100% because of rounding.  
Source: Dr. Shaddy

## β-Blocker Found Ineffective in First Pediatric Heart Failure RCT

BY BRUCE JANCIN  
Denver Bureau

ATLANTA — Carvedilol proved no better than placebo in the first-ever randomized trial of any therapy for chronic heart failure in children, Dr. Robert E. Shaddy said at the annual meeting of the American College of Cardiology.

Until now, treatment of pediatric heart failure has been based largely on the findings of the landmark heart failure trials in adults, with anecdotal best-guess extrapolation in regard to dosing in children. β-blocker therapy is standard in adult heart failure. But the results of this first multi-center study emphasize that heart

failure in children and adults are in some ways very different conditions, added Dr. Shaddy, professor of pediatric cardiology at the University of Utah, Salt Lake City.

He reported on 161 children with symptomatic systolic heart failure who participated in a 26-center double-blind trial in which they were randomized to one of the following regimens: twice-daily placebo, carvedilol at 0.2 mg/kg b.i.d. to a maximum of 12.5 mg per dose in children weighing more than 62.5 kg, or carvedilol at 0.4 mg/kg b.i.d. to a maximum of 25 mg per dose.

The participants had dilated cardiomyopathy or congenital heart disease. Their median age was 3 years, with a range of 3 months to 17 years. All were on an ACE inhibitor unless they were intolerant. Of the total, 71% had New York Heart Association class II heart failure and 27% had class III disease at baseline, with a median left ventricular ejection fraction of 26%.

The primary study end point was heart failure outcome at 8 months as defined by a composite including death, cardiovascular hospitalization, and change in NYHA class, Ross classification of heart failure, and/or physician global assessment score. The results proved similar in the placebo and combined carvedilol groups because of an unexpectedly robust improvement in the placebo group. (See box.)

In hindsight, this might have been predicted because many in the field think that spontaneous improvement is more frequent in younger children with heart failure.

A prespecified secondary analysis showed differential results for β-blocker therapy based on ventricular anatomy. In patients with a systemic left ventricle, the rate of improvement was 51% with placebo and 64% with carvedilol. By contrast, the 41 patients with a systemic ventricle other than the left ventricle had a 64% rate of improvement with placebo, compared with only 35% with carvedilol.

But it would be difficult to pursue this finding through further controlled trials restricted to children with a systemic left ventricle. It took 4 years to recruit the 161 participants in this initial carvedilol trial. Many parents, physicians, and institutional review boards have ethical reservations about randomizing children with heart failure to placebo, according to Dr. Shaddy.

Discussant Dr. JoAnn Lindenfeld said that although this was a negative study, she was impressed with the trends for reduction in the objective end points of death and cardiovascular hospitalization with carvedilol, even though the trends didn't reach statistical significance.

She cautioned against making too much of the divergent results on the basis of ventricular morphology, particularly in light of the relatively small number of participants without a systemic left ventricle.

It's not clear why a systemic right ventricle wouldn't "respond to a β-blocker. They do in other situations," said Dr. Lindenfeld, professor of medicine at the University of Colorado, Denver.

Dr. Shaddy is a consultant to Glaxo-SmithKline, which sponsored the trial. ■

SAVE THE DATE

CME Accredited

WOMEN'S HEALTH CONGRESS

Improving the Care of Your Female Patients

Presented by: Ob.Gyn. News Family Practice News Clinical Psychiatry News

November 10-12, 2006

The Palace Hotel  
San Francisco,  
California

www.womenshealthcongress.com



The Women's Health Congress is jointly sponsored by the Elsevier Office of Continuing Medical Education and Elsevier/International Medical News Group.

