Results Not Robust

Nebivolol from page 1

professor of medicine, division of cardiovascular medicine, Duke University, Durham, N.C. He said he struggled with the vote, however, because he thought SENIORS was a good trial and commended the company and investigators for enrolling patients over age 70. Heart failure studies of metoprolol and carvedilol were in younger patients.

The panel was asked whether the data on carvedilol and metoprolol could be considered supportive evidence for nebivolol’s beneficial effects in heart failure. However, panelists were “skeptical about automatically assigning benefit to the class of beta-blockers,” said Dr. Harrington, also director of the Duke Clinical Research Institute.

“I found the class effect argument with beta-blockers a little more challenging to accept given a lot of differences between these agents,” he continued. “There are differences among beta-blockers that may make them a different type of drug to draw class comfort from,” he said, adding that they “do a lot of different things with different receptors.”

Panelist Dr. Darren McGuire of the University of Texas Southwestern Medical Center, Dallas, said he was convinced “of the integrity of the study processes,” and he recommended “the study is strong, the results are strong.”

The analysis also showed a strong association between severity of heart failure symptoms and risk for new-onset diabetes in patients with higher New York Association Class heart failure faced a greater risk for developing diabetes than did patients with less severe heart failure symptoms, Dr. Ankit Rathod said at the annual scientific sessions of the American Heart Association.

The hypothesis is a causal link between heart failure and diabetes is the neurohormonal, sympathetic activation that characterizes heart failure. This leads to norepinephrine release, which can trigger insulin resistance and hence increased susceptibility to developing diabetes, said Dr. Rathod, an internist at Wayne State University in Detroit. In addition, patients with more severe heart failure symptoms have reduced activity, which might exacerbate insulin resistance and the risk for developing diabetes.

“I believe the connections between insulin resistance and neurohormonal activation are a real phenomenon,” said Dr. Clyde W. Yancy, medical director of the Baylor Heart and Vascular Institute at Baylor University Medical Center in Dallas. Treatment with drugs that block neurohormonal activation also cut development of diabetes, such as with ramipril in the HOPE study (N. Engl. J. Med. 2000;342:145-153) and treatment with carvedilol in the CAPRICORN study (Lancet 2001;357:1385-90), he said.

Dr. Rathod collected data from the more than 4,900 people enrolled into the Framingham Offspring Study in 1971. He analyzed associations excluded people with a history of diabetes or heart failure at enrollment, and those who had missing data on their subsequent rate of new-onset diabetes. The 4,614 people included in the study had an average age of 35; about half were women.

During an average follow-up of 24 years, 123 developed heart failure, and 468 developed new-onset diabetes. Forty-one of the 123 patients (33%) who developed heart failure later developed diabetes, compared with 427 new cases of diabetes among the other 4,491 people (10%).

In a multivariate analysis that adjusted for baseline demographic and clinical differences, including drug treatments and baseline blood glucose levels, patients who first developed heart failure had a statistically significant 2.5-fold increase in risk for later developing diabetes compared with the people who did not have heart failure.

Dr. Rathod and Dr. Yancy said they had no conflicts of interest.

Nebivolol

The differences among beta-blockers made the class effect argument ‘a little more challenging to accept.’

Dr. HARRINGTON

Heart Failure Boosts Risk For New-Onset Diabetes

BY MITCHEL L. ZOLER

ORLANDO — Patients with heart failure had a greater than twofold increased risk of developing diabetes compared with people without heart failure in a review of more than 4,600 individuals in the Framingham Offspring Study.

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Dr. Rathod and Dr. Yancy said they had no conflicts of interest.

Gout Associated With Worse Heart Failure Outcomes

BY MITCHEL L. ZOLER

ORLANDO — Gout boosted the risk of death or hospitalization for heart failure in an observational, case-control study of more than 150,000 patients with heart failure.

Patients with heart failure and gout who were on long-term allopurinol treatment had a significantly reduced risk for death or heart failure hospitalization, Dr. George Thanassoulis said at the annual scientific sessions of the American Heart Association.

Allopurinol exerts its benefit for heart failure outcomes not by lowering blood levels of uric acid, but by inhibiting oxidative stress and the endothelial dysfunction that oxidative stress produces, said Dr. Thanassoulis, a cardiologist at Boston University and the Framingham (Mass.) Heart Study.

He suggested that allopurinol inhibits xanthine oxidase, the same action that also blunts uric acid production.

The study used administrative health record data from Quebec residents aged older than 65 years. Cases were 14,327 people hospitalized for heart failure but without another heart failure hospitalization during the 3 years before the index episode, a restriction that helped ensure a uniform level of heart failure severity among the patients. Controls were 143,255 people in the Quebec database matched to the cases by follow-up duration and by calendar year.

The average age was 79 years among the cases and 77 years among the controls. Cases and controls were evenly split among men and women. Identification of gout relied on hospitalization, a physician visit, or a diagnostic code in the medical record.

During an average follow-up of 2 years, the rate of death or new heart failure hospitalization was 63% higher in the patients with gout than in those without gout, a statistically significant difference in an analysis that controlled for several demographic and clinical variables including age, gender, comorbidities, and medications.

The rate of death or heart failure hospitalization was even higher in patients who had acute gout, with a twofold higher risk in the adjusted analysis. The researchers defined acute gout as hospitalization or a physician visit for gout within 60 days of the index heart failure event.

Another pair of analyses looked at the impact of allopurinol treatment. Among patients with an index heart failure event who also had gout treatment with allopurinol, there was a significant 24% reduction in the subsequent rate of death or heart failure hospitalization in the adjusted analysis. This benefit was limited to the patients on chronic allopurinol treatment for more than 30 days. Patients on allopurinol for 30 days or less showed no significant reduction in mortality or new heart failure hospitalizations.

The allopurinol analysis also showed no link between the drug and outcomes for the entire heart failure population studied, suggesting that benefit from allopurinol is not general for all heart failure patients, only those with gout.

Dr. Thanassoulis and his associates had no conflicts of interest to disclose.