

The study results were presented by Bruce L. Rollman, MD, University of Pittsburgh, Pittsburgh, PA, the primary investigator of the study.

Additional reading:

- Rollman BL et al. Telephone-Delivered Collaborative Care for Treating Post-CABG Depression: A Randomized Controlled Trial. *JAMA* 2009;302:2095-2103.
- Rollman BL et al. The Bypassing the Blues Treatment Protocol: Stepped Collaborative Care for Treating Post-CABG Depression. *Psychosomatic Medicine* 2009;71:217-230.
- www.bypassingtheblues.pitt.edu

Results from the J-CHF Study

Results from the Japanese Chronic Heart Failure (J-CHF) study indicate that carvedilol, in doses as low as 2.5 mg/day, can produce long-term beneficial effects in Japanese patients with mild to moderate chronic heart failure (CHF) and reduced left ventricular ejection fraction (LVEF). The results were presented at the American Heart Association 2009 Scientific Sessions in Orlando, FL, by Masatsugu Hori, MD, Osaka University, Osaka, Japan, the principal investigator of the study.

J-CHF was a prospective, randomized, open-label, blinded endpoint study. The objectives were to determine the optimal minimal dose of the beta-blocker carvedilol for Japanese patients with CHF and to determine predictors of response to beta-blocker therapy. A total of 364 subjects aged 20 to 80 years (74% men; mean age ~60 years) with mild to moderate heart failure (New York Association [NYHA] class II or III) and an LVEF \leq 40% were randomly assigned to receive carvedilol 2.5 mg/day (n=118), 5 mg/day (n=116), or 20 mg/day (n=118). Subjects were stratified according to underlying disease, severity, age, gender, and hospital admission status.

The primary study endpoint was a composite of all-cause death and hospitalization for cardiovascular diseases and heart failure. Secondary endpoints included all-cause death, death from heart failure, and sudden death; hospitalization for cardiovascular diseases or heart failure; the need to modify treatment due to worsening of heart failure; aggravation of NYHA class; and changes in LVEF and plasma B type natriuretic peptide (BNP).

There were no significant differences as to the primary endpoint between 2.5 mg/day versus 5.0 mg/day (HR, 0.862; 95% CI, 0.491 to 1.514; $p=0.606$) and 2.5 mg/day versus 20 mg/day (HR, 1.004; 95% CI, 0.583 to 1.731;

$p=0.99$). Differences in the secondary endpoints were also not significant. Adverse events were dose-dependent and increased with higher doses of carvedilol. Increases in discontinuation rates were also dose-dependent (1.7%, 2.6%, and 3.4% in the 2.5-mg, 5-mg, and 20-mg dose groups, respectively). Significantly ($p<0.05$) fewer patients in the 2.5-mg dose group had a change in treatment dose relative to the 20-mg dose group.

LVEF significantly ($p<0.05$) improved in all dose groups but was not dose-dependent (30.4 ± 7.9 vs 42.6 ± 14.5 , 29.8 ± 6.5 vs 42.6 ± 13.6 , and 30.4 ± 7.0 vs 43.2 ± 12.8 for the 2.5-mg, 5.0-mg, and 20-mg/day groups, observation period, and Week 48, respectively). Heart rate (HR) and BNP log significantly ($p<0.05$) decreased in a dose-dependent manner. Multivariate analysis revealed that decreases in HR and BNP during the observation period were predictive of treatment response.

“Our results indicate that therapeutic response to carvedilol shows a high amount of variability between individuals, and we had better select the dose that can achieve reductions in heart rate and/or plasma BNP beyond dosage,” Dr. Hori concluded. He recommended initiating carvedilol at the lowest dose in Japanese patients and increasing the dose incrementally until the desired reductions in HR and/or BNP are achieved and suggested that further study is warranted to understand optimal dosing in different ethnic populations with different genetic backgrounds.

Prof. Marco Metra, MD, University of Brescia, Brescia, Italy, the discussant for the J-CHF study, noted that the results are not in agreement with previous studies, including one by Dr. Hori that used carvedilol in Japanese patients [Hori M et al. *Am Heart J* 2004], which showed a dose-dependent relationship between beta-blocker agents and improved LVEF, as well as improvement of CHF, based on a global assessment by the attending physician. He listed several limitations of the J-CHF study, including not having a placebo group and being underpowered for detecting a dose effect.

Results of the FRANCE Registry

Results from the FRANCE (French Aortic National CoreValve and Edwards) Registry, presented by Helene Eltchaninoff, MD, University of Rouen, Rouen, France, demonstrated high implantation success with excellent and sustained hemodynamic and clinical improvement in high-risk patients with severe aortic stenosis