Novel Beta-Blocker Reduces Blood Pressure

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May 23, 2006 (New York) — The novel, highly selective, once-daily beta-blocker nebivolol is well tolerated and produces dose-dependent reductions in both systolic and diastolic blood pressure, researchers reported here at the American Society of Hypertension 21st Annual Scientific Meeting.

In a pooled analysis of 2 randomized, 12-week, double-blind trials that compared nebivolol with placebo in 1716 adults with mild to moderate hypertension, "nebivolol showed statistically significant, dose-dependent reductions in the primary end point, trough sitting diastolic blood pressure (DBP), at all doses tested," reported Joel M. Neutel, MD, associate professor of medicine at the University of California in Irvine.

Patients who received the lowest dose (1.25 mg) of nebivolol experienced a 6.9 mm Hg reduction in trough sitting DBP, while those who received the highest dose (40.0 mg) experienced a 10.1 mm Hg decrease in trough sitting DBP. In comparison, patients receiving placebo experienced a 3.8 mm Hg decrease in trough sitting DBP, which was statistically significantly less than the decrease at each dose of nebivolol.

The results were similar for sitting systolic blood pressure (SBP), Dr. Neutel reported. At 1.25, 5.0, 10.0, and 40.0 mg of nebivolol, patients experienced SBP decrements of 2.4, 5.71, 5.71, and 7.6 mm Hg, with each decrease being statistically significantly greater than the 0.7 mm Hg decrease in sitting SBP seen with placebo.

In terms of response rates, 45.8% of patients who received 1.25 mg of nebivolol were considered treatment responders, defined as achieving a sitting DBP less than 90 mm Hg or a reduction of at least 10 mm Hg from baseline. The response rate increased with increasing dose, with 64.5% and 65.1% of patients qualifying as "responders" at the 20.0 mg and 40.0 mg doses, respectively.

Of course, in the aftermath of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), use of beta-blockers as antihypertensive therapy is being carefully reassessed and generally downgraded to adjunctive therapy or for patients with "compelling indications."

Dr. Neutel believes, however, that nebivolol may offer advantages over other beta-blockers in that it is not only highly selective for the beta-1 adrenergic
receptor, but it also exhibits vasodilatation associated with increased endothelial nitric oxide production and release. Its action is mediated through the L-arginine-nitric oxide pathway, he added.

The drug’s "impact on arterial compliance and endothelial function differentiates it from other beta-blockers," Dr. Neutel said. "It acts, in a way, like an [angiotensin-converting enzyme] inhibitor."

The results were borne out in both studies, assessing different dose regimens. In one study, patients were randomly assigned to 12 weeks of treatment with placebo or nebivolol at 1.25 mg, 2.5 mg, 5.0 mg, 10.0 mg, 20.0 mg, or 40.0 mg. In the other study, patients received placebo or nebivolol at 5.0 mg, 10.0 mg, or 20.0 mg.

The mean age of the patients was 54 years, and 55.4% were men. In terms of subgroups, 7.3% of the patients were diabetic and 13.8% were African American; the drug appeared to work equally well in both subgroups.

Dr. Neutel concluded by noting that the drug was well tolerated, with 88.6% of those in nebivolol group and 82.1% of those receiving placebo completing the studies. The rate of adverse events in both the nebivolol and placebo groups was 2.6%.

Ted Okerson, MD, an assistant clinical professor of medicine at the University of California at Irvine, who was not involved with the research, told Medscape that "the drug certainly looks promising.

"It looks like it lowers blood pressure well and in a dose-dependent manner," he said. But the key question, Dr. Okerson said, is whether it improves cardiovascular outcomes, a point with which Dr. Neutel agreed and said is the subject of future phase 3 studies.

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Reviewed by David Good