Mixed Results with Telmisartan in ACE-Intolerant Patients with Diabetes or High-Risk Vascular Disease

The angiotensin receptor blocker (ARB) telmisartan did not reduce the primary composite of cardiovascular (CV)death, myocardial infarction (MI), stroke, or hospitalization for heart failure in patients with diabetes or high-risk vascular disease who are unable to tolerate standard treatment with angiotensin-converting enzyme (ACE) inhibitors, researchers report.

Findings from the TRANSCEND trial (Telmisartan Randomized AssessmeNt Study in aCE iNtolerant subjects with cardiovascular Disease; NCT00153101) were presented in Munich at the 2008 European Society of Cardiology Congress in a late-breaking clinical trial session.

While telmisartan treatment did not reach statistical significance compared with placebo for the primary outcome of the study, it did significantly reduce the composite of CV death, heart attack, or stroke, as reported by investigator Koon Teo, MD, Michael G. DeGroote School of Medicine, McMaster University, Hamilton, Ontario, Canada. "Even though the benefit was moderate, there was an impact on a wide range of outcomes. Because a large proportion of people are unable to tolerate an ACE inhibitor, the use of telmisartan among such patients could become clinically important," he added.

Following a 3-week run-in period, 5926 subjects who were ACE-intolerant were randomized to receive telmisartan 80 mg/day (n=2954) or placebo (n=2972) plus other proven therapies. Patient characteristics were similar in both groups. Mean age was 66.9 ± 7.3 years, 43% was female, 76% had hypertension, and 35.7% had diabetes. Mean blood pressure was 141.0 ± 16.6/81.9 ± 10.1 mm Hg. Fasting plasma glucose was 6.50 ± 2.44 mmol/L. Mean total cholesterol was 5.09 ± 1.16 mmol/L (91.6 +/- 20.9 mg/dL).

Subjects were assessed at 6 weeks, 6 months, and every 6 months thereafter. Primary outcome events were adjudicated by a blinded central committee. The authors noted that because most of the subjects entered the trial with pre-existing CV disease, deaths were classified as CV-related unless an unequivocal noncardiovascular cause was determined.

The median duration of follow-up was 56 months. The researchers were able to ascertain vital status in 5908 (99.7%) of the subjects. Of the 2122 (80.8%) telmisartan subjects who were still using the drug at the end of the study, 2086 (79.4%) were on a full dose and 36 (1.4%) were on a reduced dose.

Nonstudy ARBs were used by 54 (1.8%) of the telmisartan subjects and 84 (2.9%) of placebo subjects at Year 1, increasing to 152 (5.8%) and 200 (7.6%), respectively, by the end of the study. Other nonstudy blood pressure-lowering drugs were used less frequently in patients who were randomized to telmisartan compared with placebo: diuretics, 888 (33.7%) versus 1059 (40.0%; p<0.0001); calcium channel blockers, 1003 (38.0%) versus 1215 (45.9%; p<0.0001); beta-blockers, 1492 (56.6%) versus 1561 (59.0%; p=0.081); and alpha-blockers, 140 (5.3%) versus 197 (7.5%; p=0.0002). The use of statins (1683 [63.6%] vs 1671 (63.1%]; p=0.588) and antiplatelet agents (2025 [76.8%] vs 2040 [77.0%]; p=0.831) were similar in both cohorts following randomization, and the rates remained constant during the study.

Throughout the study, mean blood pressure was lower in the telmisartan cohort than in the placebo cohort, with a weighted mean difference between the groups of 4.0 ± 19.6/2.2 ± 12.0 mm Hg.

A total of 465 (15.7%) of the patients who were randomized to telmisartan experienced a primary endpoint event (death, heart attack, stroke, or hospitalization for heart failure), compared with 504 (17%) patients in the placebo group (HR 0.92, 95% CI, 0.81-1.05; p=0.22).

For one of the prespecified secondary outcomes—a composite of CV death, MI, or stroke—386 (13.0%) of the patients who were assigned telmisartan experienced events, compared with 440 (14.8%) who were assigned placebo (HR 0.87, 95% CI, 0.76-1.00; p=0.048). The investigators reported that 894 (30.3%) of the telmisartan subjects were hospitalized for a CV reason, compared with 980 (33.0%) of the placebo subjects (RR 0.92, 95% CI, 0.85-0.99; p=0.025).

Fewer subjects in the telmisartan group tended to discontinue their study medication compared with the placebo group, (639 [21.6%] vs 705 [23.8%]; p=0.055). The most common cause of permanent discontinuation, hypotensive symptoms, occurred in 29 (0.98%) patients in the telmisartan group and 16 (0.54%) in the placebo group (p=0.049).

The authors concluded, "Telmisartan was well tolerated in patients unable to tolerate ACE inhibitors. Although the drug had no significant effect on the primary outcome of the study, which included hospitalizations for heart failure, it modestly reduced the risk of the composite outcome of cardiovascular death, myocardial infarction, or stroke."

Results of this study were published simultaneously online in *The Lancet*.