Valsartan May Cut New-Onset Atrial Fibrillation

BY BRUCE JANCIN
Denver Bureau

BARCELONA — Valsartan-based antihypertensive therapy significantly reduced new-onset atrial fibrillation, compared with amlodipine in 15,314 randomized hypertensive patients, Dr. Roland Schmieder reported at the joint meeting of the European Society of Cardiology and the World Heart Federation.

The incidence of new-onset atrial fibrillation was a prespecified secondary end point in the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial. As such, although the results are extremely promising, they have to be viewed as hypothesis generating rather than the sort of compelling evidence that upends guidelines and transforms clinical practice.

But the new VALUE data add to a growing body of evidence from retrospective analyses of other major clinical trials in heart failure and hypertension that suggest that angiotensin II receptor blockers (ARBs) and ACE inhibitors may offer a specific therapeutic advantage over other drug classes in terms of reduced rates of atrial fibrillation, commented Dr. Schmieder of the University of Erlangen (Germany).

The new VALUE data are unique in that they showed a degree of mean blood pressure lowering in the valsartan arm that was actually several millimeters of mercury less than in the amlodipine arm. Thus, unlike in other studies reported to date, the reduction in new-onset atrial fibrillation in the ARB-treated group can't be ascribed to greater blood pressure lowering and consequent better unloading of the heart, he explained.

The incidence of at least one documented occurrence of new-onset atrial fibrillation was 3.67% in the valsartan arm of VALUE, 16% less than the 4.34% rate in amlodipine-treated patients.

Moreover, the incidence of persistent atrial fibrillation during 4 years of follow-up in the 31-country trial was 1.35% in the valsartan group, compared with 1.97% with amlodipine, for a 32% relative risk reduction.

Unlike in other studies, the reduction in new-onset atrial fibrillation in the ARB-treated group can't be ascribed to greater blood pressure lowering.

The significant difference in new-onset atrial fibrillation could not be explained by differences between groups; patients in the two treatment arms were essentially identical in terms of baseline atrial fibrillation risk factors and other characteristics. There were no differences between the groups in terms of other medications used at baseline or during the study.

Serial ECGs showed no difference between the two study arms in terms of reduction of left ventricular hypertrophy. Finally, the reduced incidence of atrial fibrillation couldn't be attributed to differences in on-treatment heart rate or serum potassium.

Having examined and rejected these various possibilities, Dr. Schmieder concluded that the most likely explanation for the observed outcome difference is the well-documented antifibrotic and anti-inflammatory effects of ARBs.

Discussant Dr. Andreas Goette pronounced this theory "very reasonable." It is supported by solid experimental evidence that angiotensin-II has a proarrhythmic effect. It is known to cause oxidative stress along with collagen deposition and other deleterious structural changes in the atria, he said.

What is needed now are prospective data from large ongoing randomized clinical trials in which atrial fibrillation is a primary end point, rather than a secondary one as in VALUE.

One such study well underway is the Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events (ACTIVE I).

The study is testing the hypothesis that the angiotensin II receptor blocker irbesartan is superior to placebo when added to other antihypertensive agents in patients with atrial fibrillation, noted Dr. Goette of University Hospital, Magdeburg, Germany.

The VALUE trial is sponsored by Novartis Pharmaceuticals, the maker of valsartan (Diovan). ■