

Angiotensin-Receptor Blockers in Patients with Atrial Fibrillation

Irbesartan fails to reduce adverse event rates in ACTIVE I participants.

In 2005, [a meta-analysis](#) of angiotensin-converting enzyme (ACE) inhibitor and angiotensin-receptor blocker (ARB) trials suggested that blockade of the renin-angiotensin-aldosterone system (RAAS) prevents atrial fibrillation (AF) in patients with heart failure (HF) or left ventricular dysfunction. In the industry-sponsored ACTIVE I trial, investigators randomized patients with permanent AF or at least two episodes of AF in the previous 6 months to irbesartan or placebo. The two primary endpoints were the composite of myocardial infarction, stroke, and death from vascular causes, (1) including and (2) not including hospitalization for HF. A secondary endpoint was recurrence of AF in patients who were in sinus rhythm at study entry.

At baseline, the mean systolic blood pressure (BP) of the 9016 participants (mean age, 70; 61% men) was 138 mm Hg, and about 60% were taking an ACE inhibitor. During a median follow-up of 4.5 years, the systolic BP reduction in the irbesartan group was 3 mm Hg greater than in the placebo group. The risks for the primary endpoints and for recurrent AF did not differ significantly between the two groups. Although the rate of first hospitalization for a cardiovascular event was similar in the groups, the total cardiovascular hospitalization rate was significantly lower in the irbesartan group. However, significantly more irbesartan patients than placebo patients discontinued study treatment because of symptomatic hypotension.

Comment: Exploratory findings are often intriguing, but they always require careful testing. ACTIVE I did not validate the suggested benefit of adding an ARB to the regimen of these AF patients, many of whom were already taking an ACE inhibitor. A new exploratory finding — the reduction in cardiovascular hospitalization rate with irbesartan — will in turn need to be formally tested before it can be considered strong evidence.

— [Harlan M. Krumholz, MD, SM](#)

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