Episodic Amiodarone Flops for Atrial Fibrillation

BY BRUCE JANCIN
Denver Bureau

DENVER — Episodic amiodarone therapy is a losing strategy for maintenance of sinus rhythm in patients with persistent atrial fibrillation, according to the first randomized trial comparing this approach to continuous amiodarone.

"Episodic amiodarone therapy is no option for pharmacologic rhythm control," Dr. Isabelle C. Van Gelder declared at the annual meeting of the Heart Rhythm Society.

She presented the results of the Continuous Versus Episodic Amiodarone Therapy for Prevention of Permanent Atrial Fibrillation (CONVERT) trial. In this multicenter Dutch study, 206 patients with persistent atrial fibrillation (AF) underwent cardioversion followed by a loading dose of amiodarone at 600 mg/day for 4 weeks and were then randomized to continuation of the antiarrhythmic agent at 200 mg/day or discontinuation of amiodarone. The patients in the episodic treatment arm who experienced AF recurrences went back on amiodarone for up to 1 month following each cardioversion.

Contrary to the investigators' expectation, CONVERT showed that episodic amiodarone brings significantly more morbidity, not less.

Amiodarone is widely recognized as the most effective antiarrhythmic agent at maintaining sinus rhythm in AF patients. It is also the antiarrhythmic drug least likely to cause proarrhythmias. But amiodarone causes a wide variety of noncardiac side effects in what has been thought to be a cumulative dose-related fashion. The hypothesis in CONVERT was episodic amiodarone would be as effective as continuous therapy at suppressing AF, because the drug has a very long half-life of up to 100 days, but that episodic therapy would be associated with markedly less toxicity.

Contrary to expectation, however, CONVERT showed that episodic amiodarone brings significantly more morbidity, not less, said Dr. Van Gelder of the University of Groningen (the Netherlands).

After a median 1.8 years of follow-up, 32% of the episodic amiodarone group and 25% on continuous therapy had progressed to permanent atrial fibrillation. In the episodic treatment arm, 70% experienced AF recurrences and cardioversions, compared with 39% of controls. The primary CONVERT end point—a composite of adverse drug-related cardiac and noncardiac effects—occurred at a rate of 21.5 cases per 100 person-years with episodic therapy and 16.7 cases per 100 person-years with continuous amiodarone, a nonsignificant difference.

"What was surprising to us was there were more events related to underlying heart disease in the episodic amiodarone group. They had more hospitalizations for heart failure because of atrial fibrillation after discontinuation of amiodarone and not that much rate control," Dr. Van Gelder explained.

Indeed, 13% of patients in the episodic amiodarone arm experienced an end point related to AF or underlying heart disease, compared with only 3% on continuous amiodarone.

The most common amiodarone-related adverse events were hypo- and hyperthyroidism, which occurred in 9% on episodic therapy and 7% on continuous amiodarone, and sinus bradycardia or other cardiovascular events, which occurred in 5% on episodic and 3% on continuous therapy. Rash, GI side effects, and neurologic events each occurred in 1%-3% of the continuous amiodarone group and no one on episodic treatment. No pulmonary or hepatic complications were noted in the study.

The influential Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) and Dutch Rate Control Versus Electrical Cardioversion (RACE) trials suggested that rate control may be preferable to rhythm control in many AF patients. However, rhythm control remains first-line therapy in a substantial number, including those whose AF is highly symptomatic, relatively young patients with a reversible tachycardia myopathy, and those with poor ventricular rate control during AF, Dr. Van Gelder noted. ■