Dronedarone Cut Morbidity, Deaths in Atrial Fib

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DALLAS — The novel investigational antiarrhythmic agent dronedarone reduced by 27% the 1-year combined incidence of hospitalization or death compared with placebo in a large group of patients with paroxysmal or persistent atrial fibrillation, Dr. Stefan H. Hohnloser reported at the annual scientific sessions of the American Heart Association.

He presented a posthoc analysis of two pivotal phase III, double-blind, randomized trials totaling 1,237 patients with atrial fibrillation: the European trial in atrial fibrillation or flutter patients receiving dronedarone for the maintenance of sinus rhythm (EURIDIS) and the American-Australian trial with dronedarone in atrial fibrillation or atrial flutter patients for the maintenance of sinus rhythm (ADONIS).

In EURIDIS/ADONIS, the combined 1-year rate of all-cause hospitalization or mortality was 30.9% with placebo, compared with 22.8% in patients who received dronedarone at 400 mg b.i.d. The rate of death or hospitalization for a cardiovascular cause was 19.2% with placebo and 16.1% with dronedarone, added Dr. Hohnloser, professor of medicine and director of clinical electrophysiology at JW Goethe University in Frankfurt.

This potential major clinical benefit—and Dr. Hohnloser stressed that 'potential' needs to be emphasized because this was a posthoc analysis—distinguishes dronedarone from the various antiarrhythmic agents currently marketed for maintenance of sinus rhythm, all of which have been shadowed by safety concerns.

The reduction in morbidity and mortality identified post hoc in EURIDIS/ADONIS is now being further explored in a definitive prospective double-blind study: a trial to assess the efficacy of dronedarone 400 mg b.i.d. for the prevention of cardiovascular hospitalization or death from any cause in patients with atrial fibrillation/atrial flutter (ATHENA). Results of the 3,700-patient ATHENA are due in late 2007.

In the previously reported primary efficacy outcomes in EURIDIS/ADONIS, the recurrent atrial fibrillation rate was cut by 22% and 28%, respectively, with dronedarone.

The combined 1-year rate of all-cause hospitalization or mortality was 30.9% with placebo, versus 22.8% in the dronedarone group.

Dronedarone is an amiodarone derivative designed to provide the efficacy of the parent drug without its toxicities. Sanofi-Aventis has applied to the Food and Drug Administration and to European authorities for marketing approval for dronedarone for maintenance of sinus rhythm and ventricular rate control in patients with atrial fibrillation or flutter.

The potential reduction in morbidity and mortality noted with dronedarone in EURIDIS/ADONIS, coupled with new evidence presented at the AHA meeting to the effect that the drug is effective not only for rhythm control but for rate control as well, suggests dronedarone may provide an important new treatment approach in atrial fibrillation, according to Dr. Hohnloser.

Dr. Jean-Marc Davy reported that in the double-blind efficacy and safety of dronedarone for the control of ventricular rate (ERATO) trial, dronedarone provided additional rate control in patients not adequately controlled with standard agents including β-blockers, calcium channel blockers, and/or digitalis.

ERATO involved 174 patients with permanent atrial fibrillation and a baseline heart rate in excess of 80 bpm despite standard rate-control agents. They were randomized to dronedarone at 400 mg b.i.d. or placebo while continuing on their previous medications.

The primary study end point—heart rate as assessed by 24-hour Holter monitoring on day 14—was reduced by a mean of 11.7 bpm with dronedarone, compared with baseline, but was unchanged in the placebo arm. Maximal exercise ventricular rate was reduced by 24.5 bpm in the dronedarone arm, added Dr. Davy of Arnaud de Villeneuve Hospital in Montpellier, France.

Dr. Hohnloser and Dr. Davy are consultants to Sanofi-Aventis. ■