# Antiarrhythmics Reduce Postablation Arrhythmias

BY SHERRY BOSCHERT
*San Francisco Bureau*

SAN FRANCISCO — Giving antiarrhythmic medications in the 6 weeks after ablation for atrial fibrillation cut the rate of clinically significant arrhythmias and the need for cardioversion or hospitalization.

The Antiarrhythmics After Ablation of Atrial Fibrillation (5A) study findings provide the first evidence to support prescribing antiarrhythmics to reduce arrhythmias occuring after ablation, and were contrary to expectations, Dr. Jean-Francois Roux said at the annual meeting of the Heart Rhythm Society. He said he has no association with companies making the medications studied.

The trial was halted early after data on 110 of a planned 160 patients showed significant benefits from the postprocedure antiarrhythmics. The nonblinded study randomized 53 patients undergoing ablation to start antiarrhythmia therapy the night of the procedure, using propafenone or flecainide for those with structural heart disease, or dofetilide or sotalol if they had heart disease. The other 57 received only atrioventricular nodal blocking agents after ablation.

Nine patients (17%) in the antiarrhythmics group and 23 (40%) in the control group developed clinically significant atrial arrhythmias or couldn't tolerate the medications, said Dr. Roux of the University of Pennsylvania, Philadelphia, and associates. Significant arrhythmias were defined as atrial fibrillation for more than 24 hours, arrhythmias requiring initiating or changing antiarrhythmic medication, or arrhythmia-related hospitalizations or electrical cardioversions.

Patients were monitored transtelephonically for 4 weeks postablation and seen 6 weeks after the procedure. Their mean age was 55 years; 71% were men. The groups' baseline characteristics were similar, with an average left atrial size of 4.2 cm, normal left ventricular ejection fractions, and prior atrial fibrillation for an average of 71 months in the medication group and 81 months in the controls. Before ablation, around 94% of patients used antiarrhythmic therapy, and 25% of each group had undergone previous atrial ablation. Three patients in the treated group stopped therapy due to side effects such as severe fatigue, rash, and headaches.

Using the end points of arrhythmias for more than 24 hours or cardioversion or hospitalization for arrhythmia, rates still were significantly lower in the treated group (6 patients; 11%), compared with the control group (15; 26%). Patients will be tracked for 6 and 12 months to see how the postablation therapy affects long-term arrhythmia rates.

Patients treated with amiodarone in the 3 months before ablation were excluded. A separate study compares postablation therapy with amiodarone or dronedarone. ■

# *Patients With Systemic Sclerosis Should Undergo Screen for PAH*

BY SHARON WORCESTER
*Southeast Bureau*

The incidence of pulmonary arterial hypertension in patients with systemic sclerosis is 0.61 per 100 patient-years, according to data on 384 patients in a longitudinal study presented at the annual meeting of the European League Against Rheumatism in Paris.

**Right heart catheterization is necessary to confirm pre-capillary PAH.**

**DR. HACHULLA**

The prevalence of pulmonary arterial hypertension (PAH) in a cohort of patients from the ItinerAir-HTAP registry, which is a 3-year, multicenter study of patients with systemic sclerosis, was found to be 7.85% (confidence interval range, 5.70-10.00), prompting this study to determine the incidence of PAH over 3 years of follow-up, explained Dr. Eric Hachulla of Hôpital Claude Huriez, Lille, France.

The patients underwent Doppler echocardiography screening for PAH. PAH was suspected in those with peak velocity of tricuspid regurgitation (VTR) of 2.8-3 m/sec and unexplained dyspnea, or with VTR greater than 3 m/sec, according to Dr. Hachulla.

Right heart catheterization (RHC) was used to confirm the presence of pulmonary hypertension.

The patients, 87% of whom were women, had a mean age of 53 years and were followed for a mean of 41 months.

Pulmonary hypertension was found in 18 patients (incidence of 1.37 per 100 patient-years).

Of those 18 patients, 8 were found to have pre–capillary pulmonary hypertension identified by RHC, and 8 had post–capillary hypertension detected despite the absence of left heart dysfunction on echocardiography (incidence of 0.61 per 100 patient-years for both groups).

The remaining two patients had pulmonary hypertension resulting from severe interstitial lung disease, Dr. Hachulla noted.

The findings show that post–capillary pulmonary hypertension is common in systemic sclerosis, which indicates that RHC is necessary to confirm pre-capillary PAH, he concluded. ■

# Dronedarone Reduced Cardiac Risks From Atrial Fibrillation

BY SHERRY BOSCHERT
*San Francisco Bureau*

SAN FRANCISCO — An investigational agent, dronedarone, reduced by 24% the risk of hospitalization for cardiovascular problems or death from any cause in moderate- to high-risk patients with atrial fibrillation or flutter in the largest study of any antiarrhythmic medication for atrial fibrillation.

A Trial With Dronedarone to Prevent Hospitalization or Death in Patients With Atrial Fibrillation (ATHENA trial) randomized 4,628 patients at 551 sites in 37 countries to treatment with dronedarone 400 mg b.i.d. or placebo, with a follow-up of at least 1 year. The overall rate of treatment-related adverse events did not differ between groups, and 30% in each group discontinued treatment prematurely, Dr. Stefan H. Hohnloser reported at the annual meeting of the Heart Rhythm Society.

**The results have raised hopes that physicians may soon have a safer alternative to amiodarone for treating atrial fibrillation.**

The results have raised hopes that physicians may soon have a safer alternative to amiodarone for treating atrial fibrillation. Dronedarone's mechanism of action is similar but without the iodine moiety of amiodarone, which can cause hyperthyroidism, among the drug's other side effects.

The study was funded by Sanofi Aventis, which makes dronedarone.

The drug also showed significant benefits compared with placebo in several predefined secondary outcomes, including a 29% reduction in deaths from cardiovascular causes, a difference that mainly was due to a significant 45% decrease in the risk of cardiac arrhythmic deaths, said Dr. Hohnloser, lead investigator in the study and professor of medicine at J.W. Goethe University, Frankfurt, Germany. He has no association with Sanofi Aventis other than receiving research funding.

There was no significant difference between groups in cardiac nonarrhythmic deaths.

Cardiovascular-related hospitalizations were reduced 29% in the dronedarone group compared with placebo, mainly because of a 37% decrease in admissions to treat atrial fibrillation and a 30% reduction in admissions to treat acute coronary syndromes.

The study enrolled patients with paroxysmal or persistent atrial fibrillation who were at least 75 years of age or were at least 70 years of age with one or more additional risk factors, such as drug treatment for hypertension, diabetes, prior stroke or transient ischemic attack, enlarged left atrium, or depressed left ventricular function.

The cohort represents "the typical elderly atrial fibrillation population at risk for hospitalization," Dr. Hohnloser noted. The mean age was 72 years, and 47% were female. At randomization, 25% were in atrial fibrillation, 60% had structural heart disease, 86% were being treated for hypertension, 30% had coronary artery disease, 16% had valvular heart disease, and 6% had nonischemic cardiomyopathy. A history of New York Heart Association (NYHA) functional class II or III was found in 21%, and 12% had ejection fractions below 45%. Only 6% were so-called lone atrial fibrillators.

The study excluded patients with recently decompensated heart failure or NYHA class IV heart failure, among others, because a previous study of dronedarone in heart failure was cancelled prematurely when it became clear that more patients on dronedarone were dying.

In the ATHENA trial, the beneficial effects of dronedarone for the treatment of atrial fibrillation or flutter held steady across clinically important subgroups, with no difference on the basis of the presence or absence of class II or III heart failure, age, gender, or ejection fractions if divided into quartiles. Results also did not vary by the presence or absence of structural heart disease or of atrial fibrillation at baseline, or by the use of some antihypertensive agents.

At baseline, medication use was similar between groups, with 71% on β-blockers, 70% on ACE inhibitors, 39% on statins, 60% on vitamin K antagonists for anticoagulation therapy, and 44% on antithrombotic therapy with aspirin.

Side effects were seen in 69% of patients on placebo and 72% on dronedarone. Only GI side effects were significantly more common with dronedarone (26%), compared with placebo (22%).

No differences were seen in skin-related side effects, thyroid-related events, or serious adverse events. Dronedarone interferes with the tubular secretion of creatinine, which produced a 5% increase in blood levels of creatinine, compared with a 1% increase on placebo.

Sanofi Aventis plans to resubmit a new drug application to the Food and Drug Administration and a dossier to the European Medicines Agency in late 2008 based on the ATHENA data. The FDA in August 2007 turned down a request for approval that had relied on two previous trials using a combined end point of all-cause hospitalizations or deaths.

The ATHENA trial's primary combined end point of cardiovascular-related hospitalizations or all-cause mortality has never been used in studies of antiarrhythmic agents, which is why the company chose to compare dronedarone with placebo. A separate comparison with amiodarone is ongoing—the Efficacy and Safety of Dronedarone Versus Amiodarone for Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation (DIONYSOS) trial. ■