The trial versus amiodarone. The Dionysos double-blind trial included 504 patients aged 28 to 90 years (mean: 64 years) who had atrial fibrillation for more than 72 hours (2,3). After randomisation, they were treated for at least 6 months with either dronedarone (400 mg twice a day) or amiodarone (600 mg/day for 4 weeks, then 200 mg/day). Treatment failure was defined as recurrence of fibrillation, or premature discontinuation due to adverse effects, or a lack of efficacy at 12 months. Failure was significantly more frequent with dronedarone than with amiodarone (75.1% versus 58.8%) (3). Reports of this trial released by the company and the European Medicines Agency do not provide details concerning adverse effects.

The placebo-controlled trial. The Athena double-blind trial included 4630 patients with paroxysmal or persistent atrial fibrillation, atrial flutter, or sinus rhythm after cardioversion, and at least one of the following risk factors: age of at least 70 years, hypertension, diabetes, previous stroke or embolism, left atrial diameter at least 50 mm on echocardiography, or left ventricular ejection fraction less than or equal to 40% (2-7). The exclusion criteria included permanent atrial fibrillation and class IV heart failure based on the NYHA classification (a). The patients were randomised to receive either dronedarone (400 mg twice a day) or placebo for at least a year.

The all-cause mortality rate was about 6% at two years, with no significant difference between the groups (5).

Heart-failure patients: excess mortality?

The Andromeda double-blind trial included patients hospitalised for symptomatic heart failure (NYHA class III or IV) who had a marked reduction in the left ventricular ejection fraction (35% maximum) but without arrhythmia (2,8). They were randomised to receive either dronedarone (400 mg twice a day) or placebo.

The trial was intended to include 1000 patients, but it was halted when an interim analysis of 627 patients monitored for an average of 7 months showed excess mortality in the dronedarone group (25 deaths, versus 12 in the placebo group; p=0.03) (8).

Given the different selection criteria used in the two trials in heart failure, (patients in the Athena trial were less severely ill), it is impossible to draw firm conclusions from these conflicting results.

Fewer short-term adverse effects

The company’s report of adverse effects is based on data for 3282 patients treated with dronedarone and 2875 patients given placebo (3).

Comparison with amiodarone. In the trial comparing dronedarone and amiodarone, the overall incidence of adverse effects was similar with the two drugs. However, various disorders were less frequent with dronedarone than with amiodarone, including thyroid disorders, mainly hypothyroidism (3 cases