Response to a letter to the Editor by Prof Platonov and Prof Holmqvist

Prof Platonov and Prof Holmqvist have correctly observed that ICD implantation may not be a valid surrogate end point for proarrhythmia in patients with atrial fibrillation (AF) using class 1 or class 3 antiarrhythmic drugs because ICD implantations often are made as primary prevention without any serious arrhythmic events having taken place.

The reason why I included ICD implantation in the end point was to increase the number of events for the statistical analysis because AF patients using antiarrhythmic drugs represent a selected section of relatively young and healthy patients. It was both unwise and unnecessary for me to do so.

Relatively few patients using dronedarone or flecainide had a medical history suggesting an indication for an ICD for primary prevention; 19.0 % of dronedarone users and 6.5 % of flecainide users had a previous diagnosis of either heart failure or myocardial infarction.

Among 6 dronedarone patients who received an ICD, 2 also had a concurrent diagnosis of ventricular tachycardia/ventricular fibrillation. Among the flecainide patients, all 3 of those who got an ICD also had a concurrent diagnosis of ventricular tachycardia/ventricular fibrillation. Thus, primary prevention as a cause for ICD implantation in these patients did not play a significant role.

Exclusion of new implantation of ICD from the main composite end point has very small effect on the results (Table 1). Reexamination of data using a new composite end point consisting of arrhythmic death, resuscitation, ventricular fibrillation, and sustained ventricular tachycardia shows that dronedarone use remains to be associated with lower risk than sotalol (HR 0.55, 95% CI 0.34-0.90). Flecainide use remains neutral, whereas amiodarone is associated with higher risk than sotalol but slightly less so than previously.

Hopefully, this reduces some of the confusion and makes interpretation of the study findings easier.

Sincerely

Leif Friberg, MD, PhD
Associate Professor of Cardiology
Department of Clinical Sciences, Karolinska Institutet at Danderyd University Hospital, Stockholm, Sweden

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Leif Friberg, MD, PhD
Dept. of Clinical Sciences
Karolinska Institutet at Danderyd University Hospital
Stockholm, Sweden
E-mail: *leif.friberg@ki.se*

Table 1. End point events and hazards ratios with and without new implantation of ICD as part of the composite end point

	Main end point counting new implantation of ICD			Main end point not counting new implantation of ICD		
	Events	Events/1000 risk years	HR (95% CI)	Events	Events/1000 risk years	HR (95% CI)
Sotalol n=16,137	163	3.5 (3.0-4.0)	Ref	152	3.2 (2.7-3.8)	Ref
Amiodarone n=10,541	281	20.6 (18.3-23.2)	2.61 (2.02-3.38)	163	11.81 (10.1-13.8)	2.01 (1.50-2.70)
Dronedarone n=8254	26	2.5 (1.7-3.7)	0.58 (0.37-0.90)	22	2.1 (1.4-3.3)	0.55 (0.34-0.90)
Flecainide n=7925	63	2.6 (2.0-3.3)	0.95 (0.69-1.32)	63	2.6 (2.0-33.3)	1.08 (0.77-1.52)
Disopyramide n=1966	22	3.5 (2.3-5.4)	1.30 (0.83-2.05)	19	3.1 (1.9-4.8)	1.20 (0.74-1.95)

Send to Gelle Divinagracia
gelle.divinagracia@elsevier.com
Author's reply to letter to the Editor by Platonov