Efficacy and safety of dronedarone vs placebo in patients with atrial fibrillation or atrial flutter across a spectrum of renal function: post hoc analyses of the EURIDIS-ADONIS trials

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Background/Introduction: The use of antiarrhythmic drugs in patients with chronic kidney disease (CKD) is complex because impaired renal clearance can cause increased drug levels, and risk of intolerance or adverse events. Since CKD commonly co-occurs with atrial fibrillation/atrial flutter (AF/AFL), it is important to establish efficacy and safety for such drugs when used in AF/AFL patients with CKD.

Purpose: To evaluate the efficacy and safety of dronedarone in patients with AF or AFL across different levels of renal function.

Methods: This post hoc analysis evaluated pooled data from two multicentre, double-blind, randomised (2:1) trials of rhythm control with dronedarone 400 mg twice daily vs placebo. Primary endpoint was time to first recurrence of AF or AFL. Renal function (estimated glomerular filtration rate [eGFR]) was assessed with the CKD-Epidemiology Collaboration equation. Patients were grouped by eGFR strata. Log-rank testing and Cox regression were used to compare time to events between treatment groups.

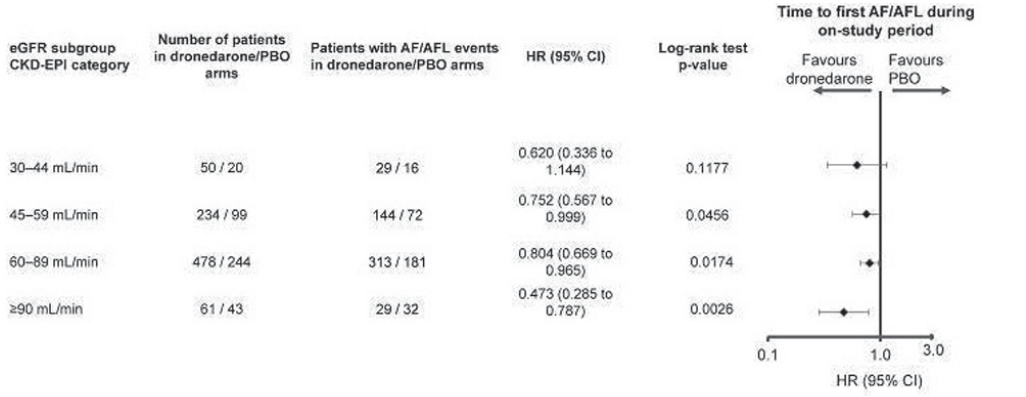
Results: Most (85%) patients had mild or mild-to-moderate decrease in eGFR (Table 1). Median time to first AF recurrence was significantly longer in the dronedarone vs placebo group for all eGFR subgroups except the 30–44 mL/min group (Figure 1), where the trend was consistent; however, the small population size may have precluded meaningful analyses in this subgroup. Serious adverse events, deaths, and treatment discontinuations did not differ notably between each group irrespective of eGFR strata.

Conclusions: This analysis confirms the efficacy and safety of dronedarone in patients with AF across a wide spectrum of renal function.

Table 1

	eGFR 30–44 mL/min		eGFR 45–59 mL/min		eGFR 60–89 mL/min		eGFR ≥90 mL/min	
	Placebo (n=20)	Dronedarone (n=50)	Placebo (n=99)	Dronedarone (n=234)	Placebo (n=244)	Dronedarone (n=478)	Placebo (n=43)	Dronedarone (n=61)
Age at BL, years, mean (SD)	76.7 (6.9)	73.3 (7.5)	67.7 (7.9)	68.8 (8.4)	60.4 (10.3)	61.4 (9.5)	52.4 (11.4)	50.5 (11.6)
Sex at BL, male, %	45.0	44.0	54.5	58.1	76.2	76.6	69.8	85.2
Structural heart disease at BL, %	65.0	63.3	39.6	50.6	38.9	38.3	34.9	25.0
Coronary heart disease at BL, %	35.0	38.0	23.2	23.5	16.8	23.2	9.3	13.1
Hypertension at BL, %	70.0	70.0	68.7	68.6	43.9	57.5	32.6	34.4
Pt with any serious TEAE, %	35	34	27	24	22	18	30	13
Death (any cause), %	10	8	1	1	0	0	0	0
Pt with any TEAE leading to discontinuation, %	25	28	4	9	7	8	9	7

Placebo group: n=406; Dronedarone group: n=823. BL, baseline; CI, confidence interval; Pt, patient; SD, standard deviation; TEAE, treatment emergent adverse event.



AF, atrial fibrillation; AFL, atrial flutter; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PBO, placebo

Figure 1

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