Effect of alirocumab on incidence of atrial fibrillation after acute coronary syndromes: insights from ODYSSEY OUTCOMES

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Background: Atrial fibrillation (AF) is a marker of risk in patients presenting with acute coronary syndromes (ACS). The potential effect of inhibiting proprotein convertase subtilisin/kexin type 9 (PCSK9) on the incidence of AF is unknown.

Methods: The ODYSSEY OUTCOMES trial compared randomized treatment with the PCSK9 inhibitor alirocumab or placebo in patients with recent ACS and residual dyslipidaemia despite optimal statin therapy. The current analysis determined: 1) whether alirocumab treatment influenced incident AF; 2) whether a history of AF influenced the risk of major adverse cardiovascular events (MACE); and 3) whether there was interaction between AF at baseline and randomized treatment on MACE. AF was determined from the medical history and investigator reports of adverse events.

Results: Of 18,924 participants, 662 (3.5%) had a history of AF at randomization and 18,262 (96.5%) had no history of AF. Of the latter category, 499 (2.7%) had incident AF. Older age, randomization in South America or Eastern Europe, history of heart failure or myocardial infarction, and higher body mass index were factors associated with incident AF. Treatment with alirocumab or placebo did not influence incident AF (2.2% vs 2.6%, respectively; hazard ratio 0.90, 95% confidence interval 0.75–1.08; Figure). Patients with a history of AF had a greater burden of comorbidities, including cerebrovascular disease, peripheral artery disease, hypertension and heart failure; they also had higher rates of MACE (Table). There was no significant interaction between AF and randomized treatment on risk of MACE (P interaction=0.78)

Conclusions: Although treatment with alirocumab did not significantly modify the risk of incident AF after ACS in this analysis, future studies with more sensitive and systematic methods of ascertainment may be warranted. History of AF is a strong predictor of risk of recurrent MACE after ACS.

Table 1. Clinical outcomes according to history of AF (intention-to-treat population)

Event	Events (events per 100 patient-years)		HR (95% CI)
	No history of AF	History of AF	
CV death, MI, stroke, hospitalization for UA	1810 (3.7)	145 (8.8)	2.4 (2.0–2.8)
CV death	459 (0.9)	52 (2.8)	3.4 (2.6–4.6)
MI	1305 (2.6)	97 (5.8)	2.1 (1.7–2.6)
Stroke	240 (0.5)	23 (1.3)	2.8 (1.8–4.3)
Hospitalization for UA	95 (0.2)	2 (0.1)	0.6 (0.1–2.4)
All-cause death	652 (1.3)	74 (4.0)	3.4 (2.6–4.3)
Hospitalization for HF	304 (0.6)	51 (2.9)	4.8 (3.5–6.5)