

Recommended and non-recommended edoxaban dosing in patients with atrial fibrillation (AF): one-year clinical events from the Global ETNA-AF non-interventional study (NIS)

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Background: In AF patients on direct oral anticoagulants (DOAC), safety and effectiveness vary with dose. This might impact treatment decisions.

Purpose: To investigate the effects of dosing of the DOAC edoxaban in AF patients on safety and effectiveness during 1-year observation in a real-world setting.

Methods: The Global ETNA-AF NIS included 26,823 patients. Baseline data by edoxaban dosing (60mg/30mg) and their influences on the safety (major bleeding [MB], clinically relevant non-major bleeding [CRNMB]), and effectiveness (stroke, systemic embolism, myocardial infarction [MI], death) were investigated (Table).

Results: Figure shows the breakdown by dose (60mg vs 30mg) and recommended (rec) vs non-recommended (non-rec) dosing. Patients on non-rec 30mg vs on rec 60mg edoxaban were older (mean \pm SD: 74 \pm 9 vs 70 \pm 9

y); had lower creatinine clearance (72.2 \pm 20.6 vs 85.8 \pm 26.8 mL/min); and had more comorbidities, history of MB (2.1% vs 1.1%), and strokes (11.0% vs 8.6%). Non-rec 60mg vs rec 30mg patients were younger (75 \pm 9 vs 78 \pm 9 y), had fewer comorbidities, history of MB (1.2% vs 2.6%), and strokes (10.2% vs 16.4%). In non-rec 30mg vs rec 60mg, MB was not lower and ischaemic events were not higher. In non-rec 60mg vs rec 30mg, no increase in MB, CRNMB or ischaemic events was seen.

Conclusion: Edoxaban was prescribed at the label recommended dose in the vast majority of patients. Non-rec 30mg patients were sicker than rec 60mg patients while non-rec 60mg patients were less sick than rec 30mg patients. Overall event rates were low, and ischaemic event rates of non-rec 30mg and bleeding event rates of non-rec 60mg were not numerically higher than that of corresponding rec dosing groups.

Clinical events, N (%/yr)	No dose reduction criteria met		≥ 1 dose reduction criterion met	
	Rec. 60 mg (N=12,708)	Non-rec. 30 mg (N=3,016)	Non-rec. 60 mg (N=1,640)	Rec. 30 mg (N=9,459)
Major bleeding (ISTH)	92 (0.77)	31 (1.13)	18 (1.19)	132 (1.61)
ICH	31 (0.26)	5 (0.18)	1 (0.07)	38 (0.46)
Major GI bleeding	32 (0.27)	21 (0.76)	6 (0.39)	81 (0.98)
CRNMB	177 (1.48)	42 (1.53)	25 (1.65)	226 (2.76)
Ischaemic stroke/TIA	113 (0.94)	20 (0.72)	16 (1.05)	126 (1.53)
Haemorrhagic stroke	20 (0.17)	3 (0.11)	1 (0.07)	32 (0.39)
MI	42 (0.35)	8 (0.29)	5 (0.33)	31 (0.38)
Systemic embolism	8 (0.07)	1 (0.04)	1 (0.07)	12 (0.15)
All-cause mortality	214 (1.78)	79 (2.86)	54 (3.54)	398 (4.82)
CV mortality	99 (0.82)	37 (1.34)	21 (1.38)	142 (1.72)

