Low bleeding and stroke rates with minor age-dependent increase confirm the safety and effectiveness of edoxaban in patients with atrial fibrillation across age groups: Two-year results from ETNA-AF

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Background: Age is a risk factor for ischemic stroke and bleeding in patients with atrial fibrillation (AF). The large dataset from the global prospective, noninterventional ETNA-AF program allows for analysis of the impact of age on clinical events in AF patients treated with edoxaban.

Purpose: Evaluate the safety and effectiveness of edoxaban by age subgroups and the impact of age on clinical events.

Methods: Baseline patient characteristics, thromboembolic and bleeding events, and mortality data were collected from patients with 2-year follow-up in ETNA-AF program and analyzed in defined age subgroups. Cox regression analysis was conducted using age as a continuous variable and clinical events as outcome variables.

Results: A total of 27,617 patients were categorized into four age subgroups: <65, 65-74, 75-84 and ≥85 years. Patient demographics and baseline characteristics are shown in the Table. Percentage of male, mean body weight, and mean creatinine clearance decreased with age, whereas percentages of patients with heart failure, patients on reduced dose edoxaban 30 mg, mean stroke and bleeding risk scores increased with age. The annualized rates of ischemic stroke and major bleeding increased with age, yet remained low. Importantly, the rate of intracranial hemorrhage was low across age groups, including the ≥85 years group. The hazard ratio (HR) for ischemic stroke was 1.041 (95%CI 1.028-1.053), ie. with a 1-year increase in age, the risk of ischemic stroke increased by 4.1%. The HRs for other clinical events were: major bleeding 1.044 (95%CI 1.033-1.055), intracranial hemorrhage 1.027 (95%CI 1.007-1.046), major gastrointestinal bleeding 1.065 (95%CI 1.048-1.081), all-cause mortality 1.086 (95%CI 1.079-1.093).

Conclusion: Two-year follow-up data from the global ETNA-AF program support the use of edoxaban as a safe and effective treatment for AF patients across all age groups, including the very elderly, in routine clinical care. The impact of age on the risk of ICH was smaller than that of ischemic stroke and major bleeding.

	<65 yr (N = 4,278)	≥65-74 yr (N = 9,396)	≥75-84 yr (N = 10,728)	≥85 yr (N = 3,214)
Age [years], mean (SD)	57.3 (6.6)	69.9 (2.9)	79.1 (2.8)	87.9 (2.8)
Male, %	72.5	61.9	53.9	42.2
Weight [kg], mean (SD)	80.6 (20.3)	73.0 (17.7)	68.0 (16.0)	60.1 (14.9)
CrCL [mL/min], mean (SD)	101.8 (33.7)	75.3 (22.3)	57.9 (18.1)	42.5 (14.3)
CHA_2DS_2-VASc, mean (SD)	1.6 (1.1)	2.8 (1.2)	4.1 (1.2)	4.4 (1.3)
Mod. HAS-BLED≠, mean (SD)	1.4 (1.0)	2.5 (1.1)	2.7 (1.0)	2.7 (1.0)
2-year clinical events				
Major Bleeding (ISTH)	0.49	0.84	1.16	1.88
%/yr [95% CI]	[0.35; 0.68]	[0.70; 0.99]	[1.00; 1.32]	[1.51; 2.30]
Intracranial Hemorrhage	0.18	0.26	0.31	0.46
%/yr [95% CI]	[0.09; 0.30]	[0.18; 0.34]	[0.23; 0.40]	[0.29; 0.69]
Major GI Bleeding	0.22	0.34	0.60	1.19
%/yr [95% CI]	[0.13; 0.36]	[0.26; 0.44]	[0.49; 0.72]	[0.90; 1.53]

	<65 yr (N = 4,278)	≥65-74 yr (N = 9,396)	≥75-84 yr (N = 10,728)	≥85 yr (N = 3,214)
Any Stroke %/yr [95% CI]	0.54 [0.38; 0.73]	0.79 [0.66; 0.94]	1.15 [1.00; 1.32]	1.53 [1.21; 1.92]
Ischemic Stroke %/yr [95% CI]	0.38 [0.26; 0.56]	0.59 [0.47; 0.71]	0.89 [0.76; 1.04]	1.21 [0.92; 1.56]
Hemorrhagic Stroke %/yr [95% CI]	0.12 [0.06; 0.23]	0.19 [0.13; 0.27]	0.23 [0.16; 0.31]	0.32 0.18; 0.52]
All-cause Death %/yr [95% CI]	1.05 [0.83; 1.32]	1.82 [1.62; 2.04]	3.51 [3.25; 3.80]	9.08 [8.27; 9.96]
CV Death (sensitivity) %/yr [95% CI]	0.51 [0.36; 0.70]	0.83 [0.69; 0.98	1.65 [1.47; 1.84]	4.16 [3.62; 4.77]

≠Excluding labile INR.