Persistence to edoxaban treatment in patients with atrial fibrillation: Analysis from the Global ETNA-AF programme

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BACKGROUND

- Many studies report suboptimal persistence to NOAC treatment among patients with atrial fibrillation (AF), which may reduce treatment effectiveness and negatively impact clinical outcomes[1-3]
- Data collected in routine clinical care, such as in the Global ETNA-AF programme, may provide insight into factors associated with treatment persistence

OBJECTIVE

- To evaluate the persistence to edoxaban treatment in a large, unselected, real-world population from the Global ETNA-AF programme

METHODS

- The Global ETNA-AF programme is a predefined integration of prospective, observational, non-interventional regional studies from Europe (NCT02944019), Japan (UMIN000017011), Korea/Taiwan (NCT02951039), Thailand (NCT03247569) and Hong Kong (NCT03247582) to evaluate the safety and effectiveness of edoxaban in patients with AF[4-6]
- Patients were stratified into subgroups based on patterns of persistence defined during the first year (**Figure 1**)
- Baseline patient characteristics and clinical outcomes that occurred during the second year of follow-up were compared across these patient subgroups (**Figure 1**)

RESULTS

- Mean age, creatinine clearance, CHA_2DS_2-VASc, and HAS-BLED score at baseline were similar across patient groups (**Table 1**)
- The SUS + PERD group had a higher percentage of patients with a history of stroke or intracranial hemorrhage (15.4%) compared with the PERD (10.0%), SUS (11.5%), and PERS (12.5%) groups (**Table 1**)
- Patients in the SUS + PERD group had a higher rate of a history of bleeding (8.3%) than those in the in the SUS (6.0%), PERD (5.3%), or PERS (3.8%) groups (**Table 1**)
- The type of AF varied across groups (**Figure 2**)
  - The PERD group had the highest proportion of patients with paroxysmal AF (55.3%) and the lowest proportion of patients with long-standing persistent AF (6.2%), compared with the other patient groups
- Overall persistence was high with 78.1% of patients continuing to use edoxaban through the first year of follow-up
  - This persistence in ETNA-AF was higher than rates reported in GLORIA-AF at 2 years (70.9%) and XANTUS at 1 year (77.4%), despite a more compromised health profile[7,8]
- All-cause death was lower in patients in the PERS and SUS groups (annualised event rate = 2.99 %/year and 3.26 %/year, respectively) compared with patients who discontinued edoxaban (PERD, 5.98 %/year; SUS + PERD, 4.77 %/year. All other clinical event rates were similar across the levels of persistence (**Figures 3 and 4**)
- Patients who continued on edoxaban (PERS, 0.32 %/year) had a lower rate of major GI bleeding than those who suspended (SUS, 0.45 %/year) or permanently discontinued edoxaban treatment (PERD, 0.55 %/year)
- Of patients who were in the PERD group, 10.5% switched to VKA and 32.6% switched to another NOAC; in the SUS + PERD group, 4.6% switched to VKA and 17.4% switched to another NOAC

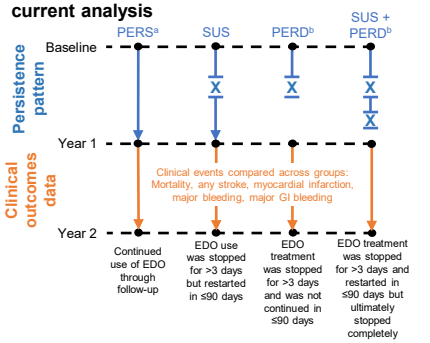
CONCLUSIONS

- Treatment with edoxaban in routine clinical practice is associated with high persistence (78.1%) at 2 years
- Persistence to edoxaban treatment was associated with better survival in the second year
- Further investigation is ongoing to determine the specific causes and consequences of edoxaban suspension and discontinuation to improve personalization of thromboembolic prophylaxis in patients with AF

In this subanalysis of the Global ETNA-AF programme, persistence to edoxaban treatment was high and associated with better survival in the second year

FIGURES

Figure 1. Patient subgroups and data included in current analysis



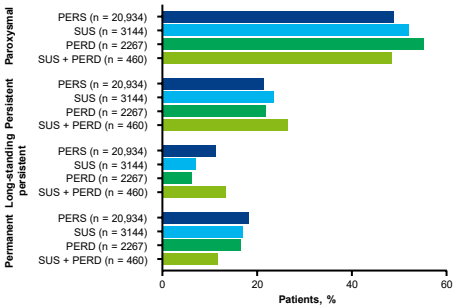
[a]The PERS group includes patients that died while receiving EDO.
[b]Patients that discontinued edoxaban and started another treatment are included.
EDO, edoxaban; GI, gastrointestinal; PERD, permanent discontinuation; PERS, persistence; SUS, suspension; SUS + PERD, suspension and permanent discontinuation.

Table 1. Baseline patient characteristics[a]

	PERS[b] n = 20,934	SUS n = 3144	PERD n = 2267	SUS + PERD n = 460
Region				
Europe, n (%)	10,014 (47.8)	1696 (53.9)	1325 (58.4)	129 (28.0)
Japan, n (%)	8628 (41.2)	957 (30.4)	489 (21.6)	268 (58.3)
ASCA (with Hong Kong), n (%)	2292 (10.9)	491 (15.6)	453 (20.0)	63 (13.7)
Age, mean (SD)	73.9 (9.5)	72.9 (9.5)	72.3 (11.4)	73.0 (11.2)
Sex, male, n (%)	12,039 (57.5)	1904 (60.6)	1341 (59.2)	289 (62.8)
Weight, kg, mean (SD)	71.8 (18.0)	74.0 (18.5)	74.0 (18.1)	68.0 (18.2)
CrCl, (calculated) mL/min, mean (SD)	68.9 (28.0)	70.9 (29.8)	69.8 (31.3)	65.5 (29.7)
CHA_2DS_2-VASc, mean (SD; calculated)	3.29 (1.48)	3.20 (1.49)	3.12 (1.62)	3.29 (1.71)
Mod. HAS-BLED, mean (SD)	2.70 (1.04)	2.68 (1.07)	2.55 (1.14)	2.74 (1.21)
History of stroke or ICH if any, n (%)	2624 (12.5)	363 (11.5)	226 (10.0)	71 (15.4)
Any stroke, n (%)	3351 (16.0)	471 (15)	287 (12.7)	85 (18.5)
History of bleeding, if any, n (%)	793 (3.8)	189 (6.0)	121 (5.3)	38 (8.3)
Major bleeding, n (%)	332 (1.6)	58 (1.8)	42 (1.9)	13 (2.8)
GI bleeding (major or CRNM), n (%)	162 (0.8)	50 (1.6)	43 (1.9)	7 (1.5)
Hepatic impairment at baseline, n (%)	86 (0.4)	15 (0.5)	16 (0.7)	1 (0.2)
Comorbidities, n (%)				
Chronic obstructive pulmonary disease	1116 (5.3)	212 (6.7)	163 (7.2)	19 (4.1)
Diabetes mellitus	4941 (23.6)	745 (23.7)	507 (22.4)	106 (23.0)
Hypertension	15,733 (75.2)	2363 (75.2)	1610 (71.0)	317 (68.9)
Heart Failure	4052 (19.4)	629 (20.0)	468 (20.6)	124 (27.0)
Myocardial infarction	763 (3.6)	130 (4.1)	93 (4.1)	24 (5.2)
Peripheral artery disease	443 (2.1)	99 (3.1)	69 (3.0)	15 (3.3)

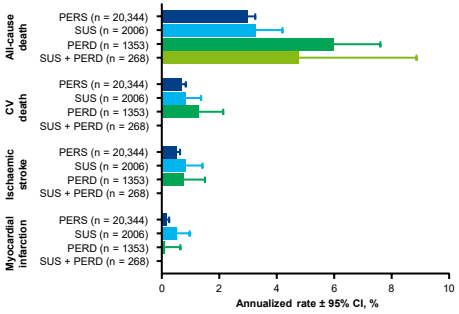
[a]Baseline characteristics were evaluated based on 2-year classification to PERS/SUS/PERD/SUS + PERD.
[b]Persistent = no suspension and no permanent discontinuation.
AF, atrial fibrillation; ASCA, Asia, South and Central America; CHA_2DS_2-VASc, Congestive Heart Failure, Hypertension, Age ≥75 Years, Diabetes Mellitus, Prior Stroke or Transient Ischaemic Attack or Thromboembolism; CrCl, creatinine clearance; CRNM, clinical relevant nonmajor; GI, gastrointestinal; HAS-BLED, Hypertension, Abnormal Renal and Liver Function, Stroke, Bleeding, Labile INR, Elderly, Drugs or Alcohol; ICH, intracranial haemorrhage; NOAC, non–vitamin K oral anticoagulant; PERD, permanent discontinuation; PERS, persistence; SD, standard deviation; SUS, suspension; SUS + PERD, suspension and permanent discontinuation; VKA, vitamin K antagonist.

Figure 2. Type of AF at baseline across patient groups[a]



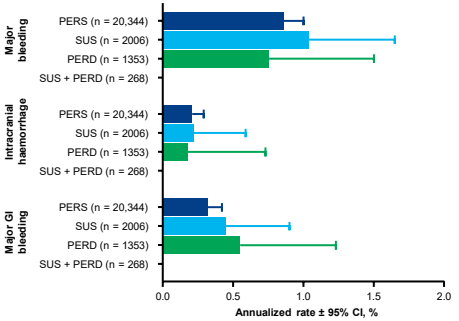
[a]Baseline characteristics were evaluated based on 2-year classification to PERS/SUS/PERD/SUS + PERD.
AF, atrial fibrillation ; PERD, permanent discontinuation; PERS, persistence; SUS, suspension; SUS + PERD, suspension and permanent discontinuation.

Figure 3. Annualised rates of effectiveness outcomes



CV, cardiovascular; PERD, permanent discontinuation; PERS, persistence; SUS, suspension; SUS + PERD, suspension and permanent discontinuation.

Figure 4. Annualised rates of safety outcomes



Values of 0 in the SUS + PERD group are the result of small sample size and events occurring in the first year of follow-up.
GI, gastrointestinal; PERD, permanent discontinuation; PERS, persistence; SUS, suspension; SUS + PERD, suspension and permanent discontinuation.

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