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Examining real-world utilisation and associated clinical outcomes of direct oral anticoagulants (DOACs) in patients with atrial fibrillation in Italy

Angel F Valladares, MPH[1]; Rosa Wang, MHA[2]; Joseph Imperato, MS[1]; Sidharth Gupta, BTech[3]; Shantanu Jawla, MPharm[4]; Rüdiger Smolnik, MD[4]; Cathy Chen, MD, MSc[2]; Martin Unverdorben, MD, PhD[2]; Xin Ye, PhD[2]

[1]IQVIA, New York, NY, USA; [2]Daiichi Sankyo Inc., Basking Ridge, NJ, USA; [3]IQVIA, Bengaluru, India; [4]Daiichi Sankyo Europe GmbH, Munich, Germany

INTRODUCTION

- Direct oral anticoagulants (DOACs) are the standard of care for preventing thromboembolism in patients with atrial fibrillation (AF)[1]
- While the prevalence of AF in Italian patients is projected to substantially increase over the next 40 years,[2] no randomised clinical trials have directly compared the safety and efficacy of the four available DOACs in these patients[3]
- The objective of this retrospective cohort study was to compare clinical outcomes at 12 months for each of the four available DOACs among patients with AF in Italy

METHODS

- Adult patients with AF who received their first DOAC prescription between January 2016 and December 2021 were identified from the Italian IQVIA® Longitudinal Patient Database
  - The database contains anonymised patient consultation and treatment data from general practitioners
- Patient characteristics were summarised
- Patients with AF and a DOAC prescription were assigned to a cohort based on their first/earliest DOAC prescription (edoxaban, apixaban, dabigatran, or rivaroxaban cohort)
- A propensity score–matched analysis was conducted to compare clinical outcomes of effectiveness (ischaemic stroke [IS]/systemic embolism [SE]) and safety (any major bleeding [MB]) among edoxaban vs the other 3 DOACs
- Incidence rates of clinical outcomes at 12 months of DOAC use, as well as hazard ratios (HRs; adjusted for gender and age) with 95% confidence intervals (CIs), were computed

RESULTS

- Of the16,747 patients with AF and an index DOAC prescription, 3188 were prescribed edoxaban (19.0%), 5256 apixaban (31.4%), 2981 dabigatran (17.8%), and 5322 rivaroxaban (31.8%: **Figure 1**)
- Baseline demographics and clinical characteristics are shown in **Table 1**
  - The mean age for the patient cohorts were 78.1 years for edoxaban, 78.5 years for apixaban, 75.9 years for dabigatran, and 75.1 years for rivaroxaban
  - The proportion of female patients in the edoxaban cohort (53.6%) was higher than in the dabigatran (43.5%) and rivaroxaban cohorts (47.7%) and similar to that of the apixaban cohort (52.2%)
- Pre-matching, the rate of IS/SE events/100 person-years was numerically lower for the edoxaban cohort (3.9) compared with the apixaban (5.5), dabigatran (6.0), and rivaroxaban (4.1) cohorts; the rate of MB was similar for all DOAC cohorts (**Table 2**)
- Similarly, the edoxaban cohort had the numerically lowest post-matching incidence of IS/SE compared with all other DOAC cohorts (**Table 3**)
- Post-matching, after adjusting for age and sex, the risk for IS/SE (HR, 95% CI) was significantly lower for edoxaban vs apixaban (0.78, 0.61–0.99; *P* <0.05) or dabigatran (0.69, 0.54–0.89; *P* <0.05), whereas edoxaban vs rivaroxaban (0.92, 0.72–1.19) was not (**Figure 2**)
- The adjusted risk of any MB did not significantly differ between DOAC cohorts (**Figure 2**)

In routine clinical practice in Italy, patients with AF receiving a DOAC had a lower incidence of ischaemic stroke/systemic embolism events on edoxaban vs apixaban or dabigatran, with a similar incidence of major bleeding for all four DOACS.

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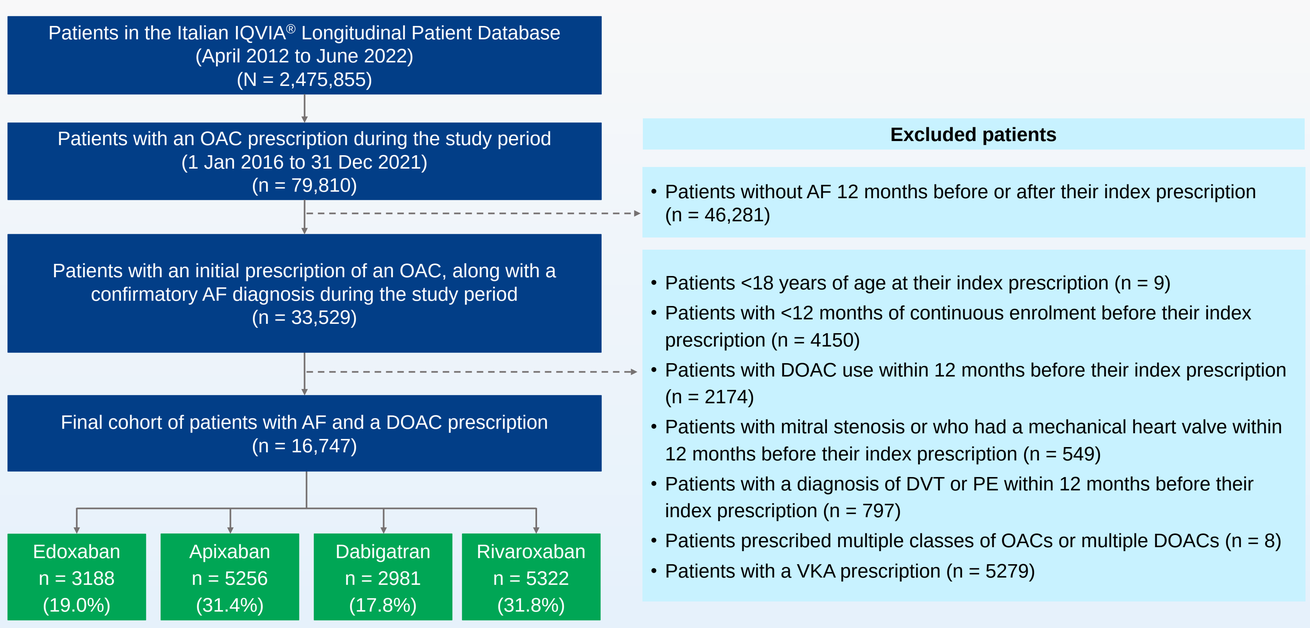
TABLES AND FIGURES

Figure 1. Patient selection



AF, atrial fibrillation; DOAC, direct oral anticoagulant; DVT, deep vein thrombosis; OAC, oral anticoagulant; PE, pulmonary embolism; VKA, vitamin K antagonist.

Table 1. Patient baseline characteristics by DOAC treatment (N=16,747)[a]

	Edoxaban (n = 3188)	Apixaban (n = 5256)	Dabigatran (n = 2981)	Rivaroxaban (n = 5322)
Age, years				
Mean (SD)	78.1 (9.8)	78.5 (9.7)	75.9 (9.9)	75.1 (10.5)
Median (Q1, Q3)	79.0 (72.0, 85.0)	80.0 (73.0, 85.0)	77.0 (70.0, 83.0)	76.0 (69.0, 83.0)
≤64 years	275 (8.6)	445 (8.5)	368 (12.3)	806 (15.1)
65–74 years	769 (24.1)	1137 (21.6)	819 (27.5)	1478 (27.8)
≥75 years	2144 (67.3)	3674 (69.9)	1794 (60.2)	3038 (57.1)
Sex				
Female	1710 (53.6)	2743 (52.2)	1297 (43.5)	2537 (47.7)
Male	1478 (46.4)	2513 (47.8)	1684 (56.5)	2785 (52.3)
$CHADS_2$ score, mean (SD)	2.0 (0.9)	2.0 (0.9)	1.9 (0.9)	1.8 (0.9)
CHA_2DS_2-VASc score, mean (SD)	3.5 (1.2)	3.6 (1.2)	3.3 (1.3)	3.2 (1.3)
Charlson Comorbidity Index				
0	1775 (55.7)	2666 (50.7)	1651 (55.4)	3034 (57.0)
1	848 (26.6)	1484 (28.2)	837 (28.1)	1366 (25.7)
2	325 (10.2)	630 (12.0)	299 (10.0)	543 (10.2)
>2	240 (7.5)	476 (9.1)	194 (6.5)	79 (7.1)
Vascular disease	235 (7.4)	521 (9.9)	297 (10.0)	465 (8.7)
Stroke/transient ischaemic attack	146 (4.6)	324 (6.2)	179 (6.0)	224 (4.2)
Bleeding history or predisposition	19 (0.6)	48 (0.9)	22 (0.7)	19 (0.4)
Hypertension	2928 (91.8)	4830 (91.9)	2695 (90.4)	4779 (89.8)
Congestive heart failure	243 (7.6)	442 (8.4)	187 (6.3)	315 (5.9)
Diabetes mellitus	623 (19.5)	1097 (20.9)	584 (19.6)	1051 (19.8)
Renal disease	104 (3.3)	239 (4.6)	72 (2.4)	173 (3.3)
Cancer	180 (5.7)	314 (6.0)	141 (4.7)	277 (5.2)
Medications				
Antiplatelets	323 (10.1)	691 (13.2)	325 (10.9)	548 (10.3)
NSAIDs	275 (8.6)	437 (8.3)	243 (8.2)	480 (9.0)
H_2-receptor antagonists	49 (1.5)	95 (1.8)	35 (1.2)	85 (1.6)
Proton pump inhibitors	1446 (45.4)	2507 (47.7)	1343 (45.1)	2300 (43.2)
ACEI-ARB	1361 (42.7)	2428 (46.2)	1309 (43.9)	2228 (41.9)
Amiodarone	294 (9.2)	542 (10.3)	264 (8.9)	486 (9.1)
Statins	1125 (35.3)	1920 (36.5)	1124 (37.7)	1919 (36.1)

Data are shown as n (%) unless otherwise noted. [a]Pre-matching.

ACEI-ARB, angiotensin-converting enzyme inhibitor-angiotensin receptor blocker; $CHADS_2$, Congestive heart failure, Hypertension, Age ≥75, Diabetes, Stroke (doubled); CHA_2DS_2-VASc, Congestive heart failure, Hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65 to 74, and Sex category (female); NSAID, nonsteroidal anti-inflammatory drug; Q1, first quartile; Q3, third quartile; SD, standard deviation.

Table 2. Clinical outcomes at 12 months for all DOACs

Event rate	Pre-matching incidence			
	Edoxaban n = 3188	Apixaban n = 5256	Dabigatran n = 2981	Rivaroxaban n = 5322
Effectiveness				
IS/SE	**3.9**	**5.5**	**6.0**	**4.1**
Safety				
Any MB	**0.9**	**1.0**	**0.8**	**0.8**
Major GI bleeding	0.4	0.3	0.4	0.3
ICH	0.2	0.5	0.3	0.2
Other MB	0.2	0.3	0.1	0.2

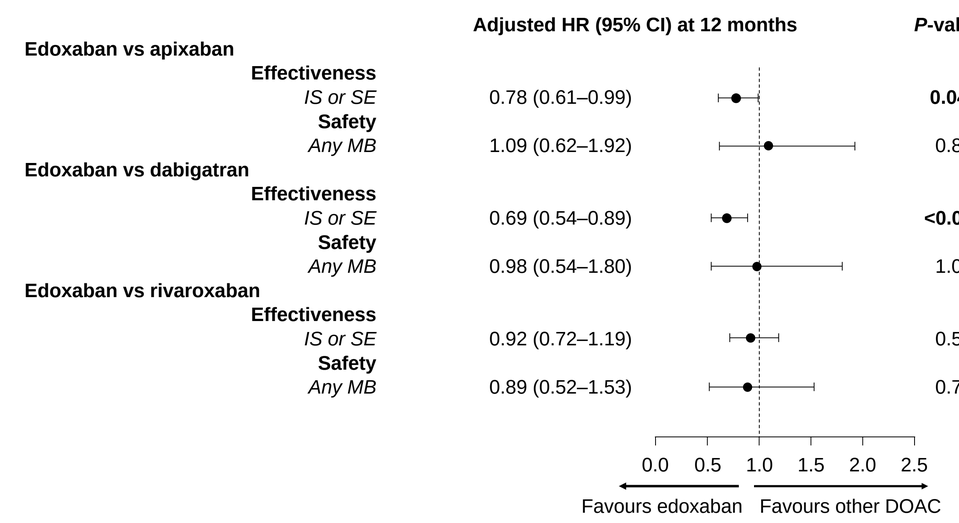
N=16,747.
Data shown as event rate per 100 person-years.
DOAC, direct oral anticoagulant; GI, gastrointestinal.

Table 3. Clinical outcomes at 12 months: edoxaban vs other DOACs

Event rate	Post-matching incidence					
	Edoxaban vs apixaban		Edoxaban vs dabigatran		Edoxaban vs rivaroxaban	
	Edoxaban (n = 3187)	Apixaban (n = 3187)	Edoxaban (n = 2739)	Dabigatran (n = 2739)	Edoxaban (n = 3185)	Rivaroxaban (n = 3185)
Effectiveness						
IS/SE	**3.9**	**5.1**	**4.1**	**6.0**	**3.9**	**4.3**
Safety						
Any MB	**0.9**	**0.8**	**0.8**	**0.9**	**0.9**	**1.0**
Major GI bleeding	0.4	0.2	0.4	0.4	0.4	0.3
ICH	0.2	0.5	0.2	0.4	0.2	0.3
Other MB	0.2	0.1	0.2	0.1	0.2	0.3

N=16,747.
Data shown as event rate per 100 person-years.
DOAC, direct oral anticoagulant; GI, gastrointestinal; ICH, intracranial haemorrhage; IS, ischaemic stroke; MB, major bleeding; SE, systemic embolism.

Figure 2. Clinical outcome HRs at 12 months: edoxaban vs other DOACs



AF, atrial fibrillation; CI, confidence interval; DOAC, direct oral anticoagulant; HR, hazard ratio; IS, ischaemic stroke; MB, major bleeding; SE, systemic embolism.

CONCLUSIONS

In routine clinical practice in Italy, the adjusted risk for IS/SE was significantly lower among patients with AF treated with edoxaban vs apixaban or dabigatran; no significant differences were observed between edoxaban and rivaroxaban

The adjusted risk of MB was similar between DOACs

These results suggest some effectiveness advantages of edoxaban over apixaban and dabigatran for preventing thromboembolism in Italian patients with AF without any differences in safety

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DISCLOSURES

AFV, **JI**, and **SG** are employees of IQVIA; **RW**, **CC**, **MU,** and **XY** are employees of Daiichi Sankyo; **SJ** and **RS** are employees of Daiichi Sankyo Europe GmbH.

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