

SUPPLEMENTARY MATERIAL**Clinical characteristics, prescription patterns and clinical outcomes of patients with extended therapy with direct oral anticoagulants for unprovoked venous thromboembolism. Insights from the RIETE Registry**

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**A full list of the RIETE investigators is given in the Appendix.*

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Supplementary Table 1. Baseline characteristics of the patients and VTE-related outcomes during extended therapy, according to prescribed drugs and doses.

	Rivaroxaban		Apixaban	
	Reduced doses	Full doses	Reduced doses	Full doses
Patients, N	334	1,693	587	1,135
Demographics,				
Male sex	199 (60%)	1,048 (62%)	274 (47%) [‡]	644 (57%)
Age >75 years	127 (38%) [‡]	342 (20%)	301 (51%) [‡]	361 (32%)
Body weight <60 kg	34 (10%)*	117 (6.9%)	107 (18%) [‡]	107 (9.4%)
Initial presentation,				
Isolated DVT	127 (38%)	556 (33%)	208 (35%) [‡]	307 (27%)
Comorbidities,				
Hypertension	176 (54%) [†]	727 (45%)	347 (63%) [†]	582 (55%)
Diabetes	52 (16%)*	179 (11%)	99 (18%)	186 (18%)
Chronic lung disease	36 (11%)	142 (8.4%)	63 (11%)	95 (8.4%)
Chronic heart failure	26 (8.0%)	89 (5.5%)	43 (7.9%)	65 (6.4%)
Anemia	67 (20%) [†]	226 (13%)	131 (22%)*	202 (18%)
CrCl levels <50 mL/min	81 (24%) [‡]	141 (8.3%)	165 (28%) [‡]	161 (14%)
Concomitant drugs,				
Antiplatelets	11 (3.6%)	59 (3.9%)	19 (3.8%)	32 (3.3%)
Corticosteroids	25 (8.1%)	81 (5.5%)	41 (8.3%)	66 (6.9%)
Statins	83 (26%)	330 (21%)	182 (34%)*	295 (29%)
Countries,				
Spain	163 (49%)*	710 (42%)	324 (55%)	569 (50%)
Rest of Europe	139 (42%)*	832 (49%)	239 (41%)	494 (44%)
America	13 (3.9%)	89 (5.3%)	14 (2.4%)*	53 (4.7%)
Asia or Africa	19 (5.7%)	62 (3.7%)	10 (1.7%)	19 (1.7%)
Hospital size,				
501-1,000 beds	128 (38%)	657 (39%)	263 (45%) [‡]	359 (32%)
≤500 beds	73 (22%)*	465 (27%)	143 (24%) [‡]	378 (33%)
>1,000 beds	132 (40%)*	569 (34%)	181 (31%)	398 (35%)
Outcomes (rates),				
VTE recurrences	1.58 (0.40-4.30)	3.28 (2.27-4.59)	1.19 (0.38-2.86)	0.94 (0.38-1.96)
Major bleeding	1.05 (0.18-3.46)	0.63 (0.26-1.32)	0.59 (0.10-1.96)	0.78 (0.29-1.74)
Death	1.57 (0.40-4.28)	1.48 (0.84-2.42)	2.96 (1.51-5.28)	1.57 (0.80-2.79)

Comparisons between reduced doses and full doses: *p<0.05, †p<0.01; ‡p<0.001.

Abbreviations: VTE, venous thromboembolism; DVT, deep vein thrombosis; CrCl, creatinine clearance.

Supplementary Table 2. Treatment details in patients receiving reduced- or full-dose DOACs for extended therapy of unprovoked VTE.

	All patients	Reduced doses	Full doses	Odds ratio (95%CI)
Patients, N	3,749	921	2,828	
Year of the index VTE,				
2013-2016	1,050 (28%)	213 (23%)	837 (30%)	0.72 (0.60-0.85)
2017-2020	1,713 (46%)	442 (48%)	1,271 (45%)	1.13 (0.97-1.31)
2021-2023	986 (26%)	266 (29%)	720 (25%)	1.19 (1.01-1.40)
Therapy before Day 180,				
Direct oral anticoagulants,	3,569 (95%)	855 (93%)	2,714 (96%)	0.54 (0.40-0.74)
Full doses	3,047 (81%)	334 (36%)	2,714 (96%)	0.02 (0.02-0.03)
Reduced doses	522 (14%)	521 (57%)	0	-
Rivaroxaban	1,933 (52%)	312 (34%)	1,621 (57%)	0.38 (0.33-0.45)
Apixaban	1,608 (43%)	516 (56%)	1,092 (39%)	2.03 (1.74-2.35)
Edoxaban	23 (0.6%)	23 (2.5%)	0	-
Dabigatran	5 (0.1%)	4 (0.4%)	1 (0.04%)	12.3 (1.38-110)
Vitamin K antagonists	101 (2.7%)	38 (4.1%)	63 (2.2%)	1.89 (1.25-2.85)
Other drugs	79 (2.1%)	28 (3.0%)	51 (1.8%)	1.71 (1.07-2.72)
Therapy beyond Day 180,				
Median days of therapy (IQR)	240 (179-240)	240 (183-240)	240 (178-240)	
Rivaroxaban, any dosage	2,027 (54%)	334 (36%)	1,693 (60%)	0.38 (0.33-0.44)
20 mg daily	1,693 (45%)	0	1,693 (60%)	-
15 mg daily	130 (3.5%)	130 (14%)	0	-
10 mg daily	204 (5.4%)	204 (22%)	0	-
Apixaban, any dosage	1,722 (46%)	587 (64%)	1,135 (40%)	2.62 (2.25-3.06)
5 mg twice daily	1,135 (30%)	0	1,135 (40%)	-
2.5 mg twice daily	573 (15%)	573 (62%)	0	-
2.5 mg once daily	14 (0.4%)	14 (1.5%)	0	-

Abbreviations: DOACs, direct oral anticoagulants; VTE, venous thromboembolism; IQR, inter-quartile range; CI, confidence intervals.