Table 3. Venous thromboembolism initial treatment: comparison of NOAC phase III trials

	RE-COVER I RE-COVER II	EINSTEIN-DVT EINSTEIN-PE	AMPLIFY	Hokusai-VTE
Comparison	Dabigatran 150 mg bd vs LMWH/ warfarin	Rivaroxaban 15 mg bd 21 days, then 20 mg od vs LMWH/warfarin or VKA	Apixaban 10 mg bd 7 days, then 5 mg bd vs LMWH/ warfarin	Edoxaban 60 mg od 30 mg od[1] vs LMWH/warfarin
Patients, n	RE-COVER I: 2,564 RE-COVER II: 2,568	EINSTEIN-DVT: 3,449 EINSTEIN-PE: 4,832	5,400	8,292
Study design	Double blind, double dummy	Open-label	Double blind,	Double blind, double dummy
Patient age, years	55.0 (median) 54.7	55.8 (mean) 57.9	57.2	55.8 (mean)
Unprovoked VTE, %	NS	60.9 64.7	89.8	65.9
Cancer, %	4.8	7.0	2.5	9.2
Heparin lead-in	At least 5 days	None	None	At least 5 days
Treatment duration	6 months	Pre-specified 3, 6, or 12 months	6 months	Flexible 3–12 months
Recurrent VTE or VTE-related death HR (95% CI)*	1.10 (0.65–1.84) 1.08 (0.64–1.80)	0.68 (0.44–1.04) 1.12 (0.75–1.68)	0.84 (0.60–1.18)	0.89 (0.70–1.13)
Major bleeding HR (95% CI)*	0.82 (0.45–1.48) 0.69 (0.36–1.32)	0.65 (0.33–1.30) 0.49 (0.31–0.79)	0.31 (0.17–0.55)	0.84 (0.59–1.21)
Major or clinically relevant non-major bleeding HR (95% CI)*	0.63 (0.51–0.77) 0.62 (0.45–0.84)	0.97 (0.76–1.22) 0.90 (0.76–1.07)	0.44 (0.36–0.55)	0.81 (0.71–0.94)
Intracranial bleeding, % (warfarin/VKA)	0.1 (0.2)	NS	0.1 (0.2)	0.1 (0.4)
Gastrointestinal bleeding,% (warfarin/VKA)	4.0 (2.8)	NS	0.3 (0.7)	NS

All comparisons versus LMWH/warfarin or vitamin K antagonist.

*Data for apixaban are presented as relative risk (95% CI)

[1]Dose of 30 mg od in patients with one of CrCl 15–50 mL/min, weight ≤60kg or concomitant treatment with potent P-glycoprotein inhibitors.

bd = twice per day; HR = hazard ratio; LMWH = low molecular weight heparin; NOAC = non-vitamin K oral anticoagulant; NS = not stated; od = once daily; VKA = vitamin K antagonist; VTE = venous thromboembolism