Supplemental Table 1: Summary of safety and efficacy of DOACs for the prevention of stroke and SEE in patients with NVAF [19-22]

	Primary efficacy endpoint[a]		Primary safety outcome[b]	
	N, n (%)	HR (95% CI) *P* value	N, n (%)	HR (95% CI) *P* value
RE-LY				
Dabigatran 110 mg BID	6015, 182 (1.53)	0.91 (0.74–1.11) 0.34	6015, 322 (2.71)	0.80 (0.69–0.93) 0.003
Dabigatran 150 mg BID	6076, 134 (1.11)	0.66 (0.53–0.82) <0.001	6076, 375 (3.11)	0.93 (0.81–1.07) 0.31
Warfarin	6022, 199 (1.69)		6022, 397 (3.36)	
ROCKET AF				
Rivaroxaban 20 mg QD[c]	7081, 269 (2.10)	0.88 (0.75–1.03) 0.12	7111, 1475 (20.70)	1.03 (0.96–1.11) 0.44
Warfarin	7090, 306 (2.40)		7125, 1449 (20.30)	
ARISTOTLE				
Apixaban 5 mg BID[d]	9120, 212 (1.27)	0.79 (0.66–0.95) 0.01	9088, 327 (2.13)	0.69 (0.60–0.80) <0.001
Warfarin	9081, 265 (1.60)		9052, 462 (3.09)	
ENGAGE AF-TIMI 48				
Edoxaban 60 mg QD	7035, 182 (1.18)	0.79 (0.63–0.99)[e] <0.001[f]	7012, 418 (2.75)	0.80 (0.71–0.91) <0.001
Edoxaban 30 mg QD	7034, 253 (1.61)	1.07 (0.87–1.31)[e] 0.005[f]	7002, 254 (1.61)	0.47 (0.41–0.55) <0.001
Warfarin	7036, 232 (1.50)		7012, 524 (3.43)	

[a]For RE-LY, ROCKET AF, ARISTOTLE, and ENGAGE AF-TIMI 48, the primary efficacy endpoint was stroke or SEE.

[b]For RE-LY, ARISTOTLE, and ENGAGE AF-TIMI 48, the primary safety endpoint was major bleeding; for ROCKET AF, the primary safety endpoint was major or clinically relevant nonmajor bleeding.

[c]15 mg QD in patients with creatinine clearance 30–49 mL/min.

[d]2.5 mg BID in patients meeting 2 or more of the following criteria: age ≥80 years, body weight ≤60 kg, or serum creatinine ≥15 mg/L.

[e]97.5% CI.

[f]P value for noninferiority.

ARISTOTLE, Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation; BID, twice daily; DOACs, direct-acting oral anticoagulants; ENGAGE AF-TIMI 48, Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48; HR, hazard ratio; N, number of total patients; n, number of events;

NVAF, nonvalvular atrial fibrillation; QD, once daily; RE-LY, Randomized Evaluation of Long-Term Anticoagulation Therapy; ROCKET AF, Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation; SEE, systemic embolic event; VKA, vitamin K antagonist.

Supplemental Table 2: Summary of safety and efficacy of DOACs for the treatment and secondary prevention of VTE [28-32]

	Primary efficacy endpoint[a]		Primary safety outcome[b]	
	N, n (%)	HR (95% CI) *P* value[c]	N, n (%)	HR (95% CI) *P* value
RE-COVER I/II				
Dabigatran 150 mg BID[d]	2553, 60 (2.4)	1.09 (0.76–1.57) NR	2553, 37 (1.4)	0.73 (0.48–1.11) NR
Heparin/VKA	2554, 55 (2.2)		2554,51 (2.0)	
EINSTEIN-DVT				
Rivaroxaban[e]	1731, 36 (2.1)	0.68 (0.44–1.04) <0.001	1718, 139 (8.1)	0.97 (0.76–1.22) 0.77
Heparin/VKA	1718 51 (3.0)		1711 138 (8.1)	
EINSTEIN-PE				
Rivaroxaban[e]	2419, 50 (2.1)	1.12 (0.75–1.68) 0.003	2412, 249 (10.3)	0.90 (0.76–1.07) 0.23
Heparin/VKA	2413 44 (1.8)		2405 274 (11.4)	
AMPLIFY				
Apixaban[f]	2609, 59 (2.3)	0.84 (0.60–1.18) <0.001	2676, 15 (0.6)	0.31 (0.17–0.55) <0.001
Heparin/VKA	2635 71 (2.7)		2689, 49 (1.8)	
Hokusai-VTE				
Edoxaban 60 mg QD[d,g]	4118, 130 (3.2)	0.89 (0.70–1.13) <0.001	4118, 349 (8.5)	0.81 (0.71–0.94) 0.004
Heparin/VKA	4122, 146 (3.5)		4122, 423 (10.3)	

[a]For Hokusai-VTE, AMPLIFY, and RE-COVER I/II, the primary efficacy endpoint was first recurrent VTE or VTE-related death; for EINSTEIN-DVT and EINSTEIN-PE, the primary efficacy endpoint was recurrent VTE.

[b]For Hokusai-VTE, EINSTEIN-PE, and EINSTEIN-DVT, the primary safety endpoint was major or clinically relevant nonmajor bleeding; for AMPLIFY and RECOVERI/II, the primary safety endpoint was major bleeding.

[c]P value for noninferiority.

[d]With a parenteral anticoagulation lead-in.

[e]15 mg BID for 3 weeks followed by 20 mg QD.

[f]10 mg BID for the first 7 days followed by 5 mg BID for 6 months.

[g]30 mg QD in patients with creatinine clearance 30–50 mL/min or body weight ≤60 kg, or receiving concomitant potent P-glycoprotein inhibitors.

AMPLIFY, Apixaban for the Initial Management of Pulmonary Embolism and Deep-Vein Thrombosis as First-Line Therapy; BID, twice daily; CI, confidence interval; DOACs, direct-

acting oral anticoagulants; DVT, deep vein thrombosis; HR, hazard ratio; N, number of total patients; n, number of events; NR, not reported; PE, pulmonary embolism; QD, once daily; VKA, vitamin K antagonist; VTE, venous thromboembolism.