

Supplementary Table 2. Relationship between the clinical events and the observed plasma concentrations or predicted Cmax, Cmin, and AUC for apixaban, rivaroxaban and edoxaban.

		Apixaban	
Dosage	2.5 mg BID	5 mg BID	
Stroke and systemic embolization	CI: 189 (1.9 h) (Cmax 168, Cmin 87, AUC 3,224)	CI: 326 (4.5 h) (Cmax 308, Cmin 156, AUC 5,900)	
	CI: 124 (4.9 h) (Cmax 124, Cmin 51, AUC 2,238)	CI: 217 (3.2 h) (Cmax 220, Cmin 85, AUC 3,900)	
Major bleeding	CB: 354 (3.1 h) (Cmax 252, Cmin 159, AUC 5,168)	TH: 233 (5.2 h) (Cmax 223, Cmin 73, AUC 3,760)	
	GIB: 316 (2.4 h) (Cmax 207, Cmin 70, AUC 3,540)	EP: 311 (3.4 h) (Cmax 247, Cmin 44, AUC 3,600)	
	GIB: 98 (4.5 h) (Cmax 148, Cmin 77, AUC 2,800)		
Non-major bleeding	EP: 236 (2.2 h) (Cmax 188, Cmin 69, AUC 3,292)	BH: 362 (4.0 h) (Cmax 299, Cmin 134, AUC 5,540)	
	EP: 225 (3.8h) (Cmax 190, Cmin 109, AUC 3,794)	SB: 272 (4.4 h) (Cmax 220, Cmin 54, AUC 3,480)	
	HS: 143 (3.7 h) (Cmax 171, Cmin 81, AUC 3,214)	EP: 404 (3.2 h) (Cmax 278, Cmin 103, AUC 4,880)	
		GG: 69 (3.6 h) (Cmax 164, Cmin 52, AUC 2,760)	

CI: cerebral infarction; CB: cerebral bleeding; GIB: gastrointestinal bleeding; TH: traumatic hematoma; EP: epistaxis; HS: hemosputum; BH: bleeding of haemorrhoid; SB: subcutaneous bleeding; GG: gingival bleeding, RI: renal infarction; HU: haematuria.

Observed plasma concentration (ng/ml), h: hours after oral ingestion ((predicted Cmax (ng/ml), Cmin (ng/ml), and AUC (ng/ml/h⁻¹))

Rivaroxaban

Dosage	10 mg QD	15 mg QD
Stroke and systemic embolization	CI: 191 (4.2h) (Cmax 191, Cmin 23, AUC 2,120)	RI: 21 (24.0 h) (Cmax 216, Cmin 22, AUC 2,541) CI: 52 (14.0 h) (Cmax 172, Cmin 15, AUC 2,206)
Major bleeding		GIB: 297 (3.8 h) (Cmax 292, Cmin 32, AUC 3,047) CB: 34 (24.0 h) (Cmax 230, Cmin 34, AUC 2,830) GIB: 258 (5.3 h) (Cmax 277, Cmin 29, AUC 2,903)
Non-major bleeding	SB: 52 (1.0 h) (Cmax 81, Cmin 15, AUC 1,395) HU: 139 (18.0 h) (Cmax 245, Cmin 77, AUC 2,266) SB: 291 (3.1 h) (Cmax 280, Cmin 17, AUC 2,343) HS: 59 (24.0 h) (Cmax 222, Cmin 56, AUC 2,473)	HU: 393 (2.5 h) (Cmax 380, Cmin 25, AUC 3,244) EP: 340 (2.1 h) (Cmax 342, Cmin 28, AUC 3,187) SB: 85 (1.4 h) (Cmax 113, Cmin 24, AUC 2,067) EP: 61 (16.5 h) (Cmax 635, Cmin 9, AUC 4,279)

Edoxaban

Dosage	30 mg QD	60 mg QD
Stroke and systemic embolization		
Major bleeding		
Non-major bleeding		SB: 158 (1.7 h) (Cmax 155, Cmin 45, AUC 1,414) GIB: 171 (3.2 h) (Cmax 192, Cmin 8, AUC 931) EP: 250 (2.9 h) (Cmax 263, Cmin 21, AUC 1,538) GIB: 275 (2.3 h) (Cmax 265, Cmin 11, AUC 1,229)