

Data Supplement 2: Any adverse outcomes from the EINSTEIN PE study in relation to simplified Pulmonary Embolism Severity Index score and time period: (A) ≤ 7 days; (B) ≤ 14 days; (C) ≤ 30 days; (D) ≤ 90 days; and (E) full treatment period.

A: ≤ 7 days

PESI Score	Outcome	Rivaroxaban (n = 2,419) n/N (%)	Standard Therapy* (n = 2,412) n/N (%)
0	Recurrent VTE	5/1,256 (0.4)	4/1,333 (0.3)
	Fatal PE	0/1,256 (0.0)	1/1,333 (<0.1)
	All-cause mortality	0/1,256 (0.0)	1/1,333 (<0.1)
	Major bleeding [†]	4/1,254 (0.3)	3/1,329 (0.2)
1	Recurrent VTE	2/919 (0.2)	3/856 (0.4)
	Fatal PE	0/919 (0.0)	1/856 (0.1)
	All-cause mortality	1/919 (0.1)	1/856 (0.1)
	Major bleeding [†]	0/916 (0.0)	5/853 (0.6)
≥ 2	Recurrent VTE	4/244 (1.6)	3/223 (1.3)
	Fatal PE	1/244 (0.4)	2/223 (0.9)
	All-cause mortality	3/244 (1.2)	4/223 (1.8)
	Major bleeding [†]	2/242 (0.8)	3/222 (1.4)

B: ≤ 14 days

PESI Score	Outcome	Rivaroxaban (n = 2,419) n/N (%)	Standard Therapy* (n = 2,412) n/N (%)
0	Recurrent VTE	7/1,256 (0.6)	7/1,333 (0.5)
	Fatal PE	0/1,256 (0.0)	2/1,333 (0.2)
	All-cause mortality	0/1,256 (0.0)	2/1,333 (0.2)
	Major bleeding [†]	6/1,254 (0.5)	6/1,329 (0.5)
1	Recurrent VTE	6/919 (0.7)	6/856 (0.7)
	Fatal PE	1/919 (0.1)	1/856 (0.1)
	All-cause mortality	2/919 (0.2)	2/856 (0.2)
	Major bleeding [†]	1/916 (0.1)	8/853 (0.9)
≥ 2	Recurrent VTE	4/244 (1.6)	5/223 (2.2)
	Fatal PE	1/244 (0.4)	2/223 (0.9)
	All-cause mortality	4/244 (1.6)	5/223 (2.2)
	Major bleeding [†]	2/242 (0.8)	4/222 (1.8)

C: ≤ 30 days

PESI Score	Outcome	Rivaroxaban (n = 2,419) n/N (%)	Standard Therapy* (n = 2,412) n/N (%)
0	Recurrent VTE	10/1,256 (0.8)	9/1,333 (0.7)
	Fatal PE	0/1,256 (0.0)	2/1,333 (0.2)
	All-cause mortality	0/1,256 (0.0)	2/1,333 (0.2)
	Major bleeding [†]	6/1,254 (0.5)	9/1,329 (0.7)
1	Recurrent VTE	9/919 (1.0)	9/856 (1.1)
	Fatal PE	2/919 (0.2)	2/856 (0.2)
	All-cause mortality	7/919 (0.8)	7/856 (0.8)
	Major bleeding [†]	3/916 (0.3)	9/853 (1.1)
≥2	Recurrent VTE	4/244 (1.6)	8/223 (3.6)
	Fatal PE	1/244 (0.4)	2/223 (0.9)
	All-cause mortality	10/244 (4.1)	7/223 (3.1)
	Major bleeding [†]	2/242 (0.8)	7/222 (3.2)

D: ≤ 90 days

PESI Score	Outcome	Rivaroxaban (n = 2,419) n/N (%)	Standard Therapy* (n = 2,412) n/N (%)
0	Recurrent VTE	18/1,256 (1.4)	15/1,333 (1.1)
	Fatal PE	2/1,256 (0.2)	2/1,333 (0.2)
	All-cause mortality	6/1,256 (0.5)	4/1,333 (0.3)
	Major bleeding [†]	9/1,254 (0.7)	11/1,329 (0.8)
1	Recurrent VTE	13/919 (1.4)	12/856 (1.4)
	Fatal PE	2/919 (0.2)	2/856 (0.2)
	All-cause mortality	13/919 (1.4)	11/856 (1.3)
	Major bleeding [†]	6/916 (0.7)	15/853 (1.8)
≥2	Recurrent VTE	6/244 (2.5)	10/223 (4.5)
	Fatal PE	3/244 (1.2)	2/223 (0.9)
	All-cause mortality	14/244 (5.7)	14/223 (6.3)
	Major bleeding [†]	3/242 (1.2)	8/222 (3.6)

E: Full treatment period

PESI Score	Outcome	Rivaroxaban (n = 2,419) n/N (%)	Standard Therapy* (n = 2,412) n/N (%)
0	Recurrent VTE	24/1,256 (1.9)	18/1,333 (1.4)
	Fatal PE	3/1,256 (0.2)	2/1,333 (0.2)
	All-cause mortality	8/1,256 (0.6)	7/1,333 (0.5)
	Major bleeding [†]	11/1,254 (0.9)	16/1,329 (1.2)
1	Recurrent VTE	17/919 (1.8)	15/856 (1.8)
	Fatal PE	3/919 (0.3)	2/856 (0.2)
	All-cause mortality	26/919 (2.8)	19/856 (2.2)
	Major bleeding [†]	10/916 (1.1)	24/853 (2.8)
≥2	Recurrent VTE	9/244 (3.7)	11/223 (4.9)
	Fatal PE	5/244 (2.0)	3/223 (1.3)
	All-cause mortality	24/244 (9.8)	24/223 (10.8)
	Major bleeding [†]	5/242 (2.1)	12/222 (5.4)

*Standard therapy consisted of subcutaneous enoxaparin overlapping with and followed by a vitamin K antagonist (warfarin or acenocoumarol; target international normalized ratio 2.0–3.0).¹

[†]Major bleeding defined according to the Control of Anticoagulation Subcommittee (ISTH SSC 2004): fatal bleeding and/or: symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome; bleeding causing a fall in hemoglobin level of 20 g/L (1.24 mmol/L) or more, or leading to transfusion of ≥ 2 units of whole blood or red cells² (data derived from the safety population).

PE = pulmonary embolism; PESI = Pulmonary Embolism Severity Index; VTE = venous thromboembolism.

References

1. The EINSTEIN–PE Investigators. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. *N Engl J Med* 2012;366:1287-97.
2. Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *J Thromb Haemost* 2005;3:692-4.