

**Appendix Table. Active or completed trials evaluating use of direct oral anticoagulants (DOACs) in children with a venous thromboembolism event (VTE).** All are multi-center, open-label, active-controlled, randomized trials.

Patient exclusion criteria was consistent across most trials and criteria included the following: active bleeding or bleeding risk contraindicating anticoagulant therapy, estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m<sup>2</sup>, hepatic disease which is associated with either: coagulopathy leading to a clinically relevant bleeding risk or liver biomarkers above designated thresholds, platelet count < 50 x 10<sup>9</sup>/L, sustained uncontrolled hypertension, life expectancy < 3 months, concomitant use of strong inhibitors of both cytochrome P450 isoenzyme 3A4 (CYP3A4) and P-glycoprotein (P-gp), concomitant use of strong inducers of CYP3A4, childbearing potential without proper contraceptive measures, pregnancy or breast feeding

<b>Trial (Trial No)</b>	EINSTEIN-Jr (NCT02234843)	Apixaban for the Acute Treatment of VTE in Children (NCT02464969)	Hokusai Study in Pediatric Patients with Confirmed VTE (NCT02798471)	Open Label Study Comparing Efficacy and Safety of Dabigatran Etexilate to Standard of Care in Paediatric Patients with VTE (NCT01895777 )
<b>Phase</b>	Phase 3 (Complete, published)	Phase 4 (Recruiting)	Phase 3 (Recruiting)	Phase 3 (Complete, unpublished)
<b>Intervention</b>	Rivaroxaban	Apixaban	Edoxaban	Dabigatran
<b>Control</b>	LMWH, fondaparinux, or warfarin	LMWH, UFH or warfarin	LMWH, UFH, fondaparinux, warfarin	LMWH, fondaparinux, warfarin
<b>Numbers</b>	500 (recruited)	250 (goal)	274 (goal)	263 (recruited)
<b>Ages</b>	Birth-17 years	Birth-17 years	Birth-17 years	Birth-17 years
<b>Primary Outcomes</b>	<u>Efficacy:</u> Recurrent symptomatic VTE <u>Safety:</u> Major or clinical relevant non-major bleeding	<u>Efficacy:</u> Composite of 1) confirmed recurrent VTE and 2) VTE related mortality <u>Safety:</u> Composite of 1) major and 2) clinically relevant non-major bleeding	<u>Efficacy:</u> 1) Symptomatic recurrent VTE and 2) VTE-related mortality and 3) thrombus extension	<u>Efficacy:</u> 1) Complete thrombus resolution, 2) freedom from recurrent VTE, 3) freedom from mortality related to VTE
<b>Secondary Outcomes</b>	Composite of recurrent VTE and deterioration on repeat imaging Composite of recurrent VTE and major bleeding	Composite of 1) confirmed recurrent VTE and 2) VTE-related mortality Apixaban concentration and anti-Xa levels	Major and clinically relevant non-major bleeding Composite of 1) symptomatic recurrent VTE, 2) VTE-related mortality, and 3) major and 4) clinically relevant non-major bleeding Pharmacokinetics/pharmacodynamics	Frequent of switch of type of anticoagulation therapy All bleeding events All-cause mortality Pharmacokinetic/pharmacodynamics of dabigatran