

Title: Timing of symptomatic venous thromboembolism and bleeding events after total knee arthroplasty: A pooled analysis of rivaroxaban studies

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Introduction: The risk of venous thromboembolism (VTE) remains a major concern beyond the standard period of hospitalization of about 4 days after total knee arthroplasty (TKA). A pooled analysis of the RECORD3 and RECORD4 studies evaluated the efficacy, safety, and timing of events with rivaroxaban compared with enoxaparin for the prevention of VTE after TKA.

Methods: Patients (N=5,679) were randomized to receive oral rivaroxaban 10 mg once daily starting postoperatively or subcutaneous enoxaparin 40 mg once daily starting preoperatively (European Union regimen; RECORD3) or enoxaparin 30 mg every 12 hours starting postoperatively (North American regimen; RECORD4) for 10–14 days. The primary efficacy endpoint was the composite of symptomatic VTE and all-cause mortality, and this was analyzed over the treatment period. The safety endpoints were treatment-emergent major bleeding, major bleeding including surgical-site bleeding, major bleeding plus clinically relevant non-major (CRNM) bleeding, and any bleeding. The incidence and timing of the safety endpoints were assessed after the first dose of study medication and up to 2 days after the last dose.

Results: Rivaroxaban significantly reduced symptomatic VTE and all-cause mortality compared with enoxaparin regimens (0.73% vs 1.71%, respectively; $p=0.001$) with no significant differences in major bleeding (0.62% vs 0.36%, $p=0.185$) or composite of major plus CRNM bleeding (3.13% vs 2.48%, $p=0.145$). The majority of venous thromboembolic events occurred after day 4 for both regimens (rivaroxaban: 70%; enoxaparin: 68%). For the composite of major plus CRNM bleeding events, 44% occurred after day 4 with rivaroxaban regimens and 38% occurred after day 4 with enoxaparin regimens.

Conclusion: Rivaroxaban significantly reduced symptomatic VTE and all-cause mortality compared with enoxaparin regimens after TKA, with no significant difference in bleeding events between regimens. Major plus CRNM bleeding was more likely to occur before day 4, whereas the majority of symptomatic venous thromboembolic events occurred after day 4. These results highlight the importance of continuing thromboprophylaxis beyond the normal time of hospital discharge for TKA.