

Title: Pooled Analysis of Rivaroxaban after Total Hip and Knee Replacement: Effects of Co-medications

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Introduction: The RECORD program investigated the oral, direct Factor Xa inhibitor rivaroxaban for venous thromboembolism (VTE) prevention after total hip or knee replacement. Patients (N=12,729) were randomized to receive rivaroxaban 10 mg once daily (od) or enoxaparin 40 mg od (RECORD1–3), or 30 mg 12 hourly (RECORD4). RECORD2 compared 31–39 days' rivaroxaban with 10–14 days' enoxaparin followed by placebo. The other studies were head-to-head comparisons. Pooled analyses of RECORD1–4 evaluated the effect of rivaroxaban on efficacy and safety endpoints. The present prespecified analysis explored potential drug–drug interactions with specified co-mediations.

Methods: The co-mediations investigated were non-steroidal anti-inflammatory drugs (NSAIDs) and platelet aggregation inhibitors (PAIs), including acetylsalicylic acid (ASA). The analysis assessed on-treatment, adjudicated bleeding events including the composite of major and clinically relevant non-major (CRNM) bleeding. Time after surgery was stratified into three periods (days 1–3, 4–7, and 7 onwards). Bleeding rates, with and without co-mediations (rate ratios), were calculated separately for rivaroxaban and enoxaparin/placebo groups.

Results: Co-medication use with rivaroxaban or enoxaparin may result in non-significant increases in bleeding events. Rate ratios for concomitant use of NSAIDs (major and CRNM bleeding, 1.28 [95% confidence interval {CI} 0.94–1.73] vs 0.90 [95% CI 0.63–1.28]) or PAIs/ASA (major and CRNM bleeding, 1.11 [95% CI 0.55–2.55] vs 1.13 [95% CI 0.47–2.75]) were not significantly different between rivaroxaban and enoxaparin groups.

Conclusion: Co-medication use with rivaroxaban or enoxaparin resulted in non-significant increases in bleeding events. However, rate ratios were not significantly different between rivaroxaban and enoxaparin groups.