

# Will Rivaroxaban Be Cost-Effective for Prevention of Venous Thromboembolism after Total Hip Replacement in US Patients?

Louis Kwong<sup>1</sup>, Alex Diamantopoulos<sup>2</sup>, Fiona Forster<sup>2</sup>, Nishan Sengupta<sup>3</sup>, Michael Lees<sup>4</sup>  
<sup>1</sup>Harbor-UCLA Medical Center, Torrance, CA, USA; <sup>2</sup>IMS Health, London, UK; <sup>3</sup>Johnson & Johnson, CA, USA; <sup>4</sup>Bayer HealthCare, Uxbridge, UK

## Introduction

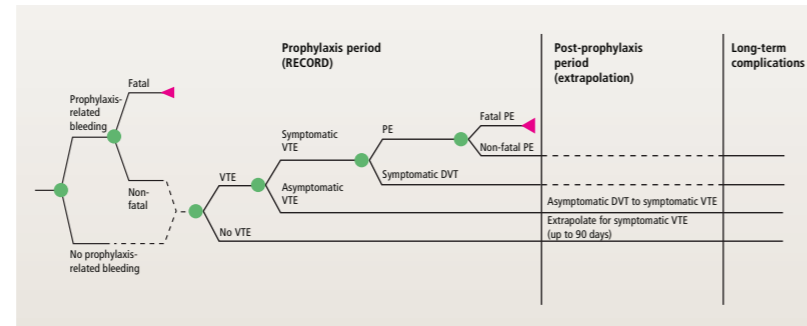
- Rivaroxaban is a novel, oral, direct Factor Xa inhibitor that was submitted for Food and Drug Administration approval for prophylaxis of deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients undergoing total hip or knee replacement (THR or TKR) surgery
  - Rivaroxaban has been approved in Canada and the European Union (in September 2008) for the prevention of venous thromboembolism (VTE) in patients undergoing elective THR or TKR
- The recently published phase III RECORD1 study compared rivaroxaban (10 mg once daily [od]) with subcutaneous (s.c.) enoxaparin (40 mg od) as VTE prophylaxis over 35 days in patients who underwent elective THR<sup>1</sup>
  - The primary outcome (the composite of DVT, non-fatal PE, and all-cause mortality) occurred in 1.1% of rivaroxaban patients and in 3.7% of enoxaparin patients (relative risk reduction [RRR] 70%;  $p < 0.001$ )
- Another phase III study, RECORD2, compared long-term prophylaxis (35 days) with rivaroxaban (10 mg od) with short-term prophylaxis (10–14 days) with s.c. enoxaparin (40 mg od) followed by placebo in patients who underwent THR<sup>2</sup>
  - The primary outcome, which was the same as in RECORD1, occurred in 2.0% of the rivaroxaban group and 9.3% of the enoxaparin followed by placebo group (RRR 79%;  $p < 0.001$ )
- The major bleeding rates observed with these two drugs in the two studies were as follows:
  - In RECORD1, major bleeding rates were 0.3% and 0.1% for rivaroxaban and enoxaparin, respectively ( $p = 0.18$ )<sup>1</sup>
  - In RECORD2, major bleeding rates were similar (0.1%) between the two study groups<sup>2</sup>

## Objective

- To compare the cost-effectiveness of long-term prophylaxis with rivaroxaban with both short- (RECORD2) and long-term (RECORD1) prophylaxis with enoxaparin in patients undergoing THR, from the US payer's perspective

## Methods

- Three economic decision models were developed based on the efficacy and safety parameters from individual as well as combined RECORD1 and 2 studies (Figure 1 is a representation of one such model)
  - This was necessary because of the different treatment durations with enoxaparin (35 days in RECORD1 and 14 days in RECORD2) versus rivaroxaban (35 days)
- The models followed patients for up to 1 year after THR (Figure 1)



**Figure 1.** Economic decision model. DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

- The clinical efficacy (DVT, non-fatal PE, and symptomatic VTE events) and safety profiles of both drugs during the period of prophylaxis were obtained from the published RECORD1 and 2 studies, whereas the incidence of VTE up to 90 days after surgery was extrapolated based on epidemiologic data<sup>3</sup>
  - The incidence of recurrent VTE and post-thrombotic syndrome beyond this period was based on clinical data<sup>4</sup>
- The treatment costs for symptomatic VTE and major bleeding were taken from published sources in the US,<sup>5,6</sup> with all costs being inflated to 2007 US\$ (Table 1)

**Table 1.** Selected costs related to VTE and PE (all costs in the model are inflated to 2007 US\$)<sup>5,6,10,11</sup>

Events	Cost (US\$)
<b>Costs related to VTE</b>	
Treating DVT during hospitalization	11,676
Treating PE during hospitalization	16,538
Treating DVT post-discharge	8,180
Treating PE post-discharge	16,538
Treatment of recurrent VTE	13,980
<b>Bleeding (prophylaxis related)</b>	
Major bleeding (fatal or non-fatal)	3,828

Costs are per event. DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

- For costing purposes, the duration of hospitalization for THR (3 days) was obtained from a published US orthopaedic registry<sup>7</sup>
  - It was conservatively assumed that no incremental nurse time or home visit costs were associated with s.c. enoxaparin injection
  - Because major bleeding requires physician visits and potentially an emergency room visit or hospitalization, which are costly, the economic models only included major bleeding costs
- The economic models assumed similar drug acquisition costs to enoxaparin 40 mg od on a daily basis

## Results

- The 1-year economic model based on RECORD2 (versus enoxaparin for 14 days) showed that long-term prophylaxis with rivaroxaban for 35 days was associated with an incremental cost per symptomatic VTE event avoided of US\$5,945 (Table 2)
- The 1-year analysis based on RECORD1, with a 35-day treatment duration for both drugs, showed that rivaroxaban resulted in an average of US\$82 cost saving and a reduction of six symptomatic events, both per 1,000 patients undergoing THR (Table 2)
- Similarly, the combined analysis based on RECORD1 and 2 showed that rivaroxaban resulted in an average of US\$19 cost saving and a reduction of 14 symptomatic events, both per 1,000 patients undergoing THR (Table 2)
  - This improvement was driven primarily by the reduced costs of hospitalization for symptomatic events

**Table 2.** Cost savings based on the 1-year economic model\*

	Oral rivaroxaban (10 mg od)	Subcutaneous enoxaparin (40 mg od)	Incremental
<b>RECORD1</b>	<b>For 35 days</b>	<b>For 35 days</b>	
Cost (US\$)	894.86	977.14	-82.29
Symptomatic VTE events <sup>†</sup>	0.0049	0.0107	-
Symptomatic VTE events avoided <sup>†</sup>	-	-	0.0058
<b>RECORD2</b>	<b>For 35 days</b>	<b>For 10–14 days</b>	
Cost (US\$)	901.53	752.62 <sup>‡</sup>	148.91
Symptomatic VTE events <sup>†</sup>	0.0065	0.0316	-0.0250
ICER (US\$)	5,944.67 <sup>§</sup>	per symptomatic event avoided	
<b>Pooled study</b>			
Cost (US\$)	897.14	915.95	-18.81
Symptomatic VTE events <sup>†</sup>	0.0055	0.0193	-
Symptomatic VTE events avoided <sup>†</sup>	-	-	0.0138

\*It is conservatively assumed that there are no administrative or nursing monitoring costs relevant to the subcutaneous administration of enoxaparin. <sup>†</sup>Events per 1,000 patients undergoing total hip replacement. <sup>‡</sup>Based on 12 days of enoxaparin 40 mg acquisition costs. <sup>§</sup>Estimated number from model; crude incremental calculation (148.91/0.0250) will result in US\$5,956. ICER, incremental cost-effectiveness ratio; od, once daily; VTE, venous thromboembolism.

- Sensitivity analyses including the costs associated with home nursing time (for administration of s.c. enoxaparin in patients unable to self-inject) or training patients to self-administer s.c. enoxaparin showed potential for more cost savings if patients receive oral rivaroxaban (Table 3)
  - Published data suggest that home nursing visits for prophylaxis after hospital discharge cost US\$100 for a course of enoxaparin<sup>8</sup>

**Table 3.** Cost savings including one-time home healthcare nursing costs related to injection

	Oral rivaroxaban (10 mg od)	Subcutaneous enoxaparin (40 mg od)	Incremental
<b>RECORD1</b>			
Cost (US\$)	894.78	1,076.82	-182.05
Symptomatic VTE events*	0.0049	0.0107	-
Symptomatic VTE events avoided*	-	-	0.0058
<b>RECORD2</b>			
Cost (US\$)	901.35	851.70	49.65
Symptomatic VTE events*	0.0065	0.0316	-0.0251
ICER (US\$)	1,981 <sup>†</sup>	per symptomatic event avoided	
<b>Pooled study</b>			
Cost (US\$)	897.03	1,015.42	-118.39
Symptomatic VTE events*	0.0055	0.0193	-
Symptomatic VTE events avoided*	-	-	0.0138

\*Events per 1,000 patients undergoing total hip replacement. <sup>†</sup>Estimated number from model; crude incremental calculation (49.65/0.0251) will result in US\$1,978. ICER, incremental cost-effectiveness ratio; od, once daily; VTE, venous thromboembolism.

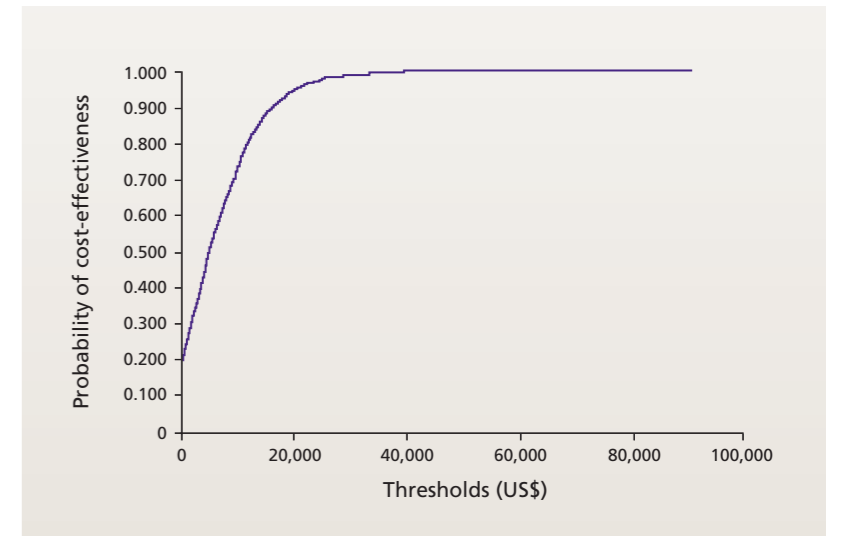
- Probabilistic sensitivity analyses (PSA) based on RECORD1 and on the pooled analysis of RECORD1 and 2 suggested that 35 days of rivaroxaban might be a cost-saving therapy option based on statistically significant reduction in symptomatic VTE events and assuming similar drug acquisition costs
- PSA based on RECORD2 (i.e. extended prophylaxis with rivaroxaban versus short-term prophylaxis with enoxaparin) suggested that rivaroxaban might be a cost-effective treatment option in 80% of cases (Figure 2) and that it might save cost in the remaining 20% of cases

## References and Disclosures

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**Figure 2.** Probabilistic sensitivity analysis for RECORD2. Cost-effectiveness acceptability curve: 35 days' rivaroxaban versus 12 days' enoxaparin.

## Conclusions

- Despite the clinical benefits of extended prophylaxis for up to 5 weeks with enoxaparin, and its recommendations in the guidelines,<sup>9</sup> its use is limited in current US clinical practice<sup>7</sup>
- Based on this analysis, oral rivaroxaban given for 35 days has the potential to be cost-effective based on its superior efficacy over 12 days of enoxaparin in patients undergoing THR
- With more than 150,000 US patients having hip replacement surgery annually, potentially significant benefits could be associated with the use of rivaroxaban

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