

Xarelto® Reduces Symptomatic VTE and Death Following Knee or Hip Replacement Surgery

Last Updated Thursday, 05 February 2009

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Leverkusen, December 8, 2008 -

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"Swelling

in the leg and shortness of breath are symptoms that can herald venous thromboembolism, which, in turn, can result in long-term complications or death," said Dr. A.G.G. Turpie, Professor of Medicine, McMaster University, Canada, and Principal Investigator for the RECORD program.

"As a physician, one of my goals is to reduce patients' risk of complications, and these data show that Xarelto has the ability to reduce the composite of symptomatic VTE and all cause mortality by half when compared to enoxaparin."

Analysis Confirms Significant Benefit in Clinical Outcomes

The

RECORD studies evaluated Xarelto (10 mg given as one tablet, once-daily) in the prevention of VTE following elective total knee replacement surgery (TKR) or total hip replacement surgery (THR) against enoxaparin at various doses and treatment durations. The pooled analysis had a primary composite efficacy endpoint of symptomatic VTE [symptomatic deep vein thrombosis (DVT) and symptomatic non-fatal pulmonary embolism (PE)] and all-cause mortality, which was analyzed at three different time points:

- The total study duration pool: day 42 post-TKR and day 65 post-THR, including a 30-day follow-up period after study drug discontinuation;

- The total treatment duration pool:
12±2 days following TKR and 35±4 days following THR, including 5 weeks rivaroxaban treatment in RECORD2 compared to 2 weeks enoxaparin treatment followed by placebo for 3 weeks;
- The head-to-head treatment pool: 12±2 days post surgery.

At

all three time points, patients treated with rivaroxaban demonstrated a statistically significant reduction of more than 50% in the composite primary efficacy endpoint compared to patients treated with enoxaparin. Specifically, there was a 51% relative risk reduction (RRR) in those treated with rivaroxaban vs. those treated with enoxaparin (0.8% vs. 1.6%, respectively, $p < 0.001$) in the total study duration pool; a 58% RRR in the total treatment duration pool (0.6% vs. 1.3%, respectively, $p < 0.001$) and a 52% RRR for those treated with rivaroxaban vs. those treated with enoxaparin (0.5% vs. 1.0%, respectively, $p < 0.001$) in the head-to-head treatment pool.

These

findings confirm the results of the four individual RECORD studies, which demonstrated the superior efficacy of Xarelto for preventing total VTE [composite of DVT, non-fatal PE, all-cause mortality], both in head-to-head comparisons with enoxaparin (RECORD1, 3 and 4) as well as when comparing extended-duration (5 weeks) Xarelto with short-duration (2 weeks) enoxaparin in RECORD2. In all four trials, Xarelto and enoxaparin had similar safety profiles.

The

four pre-specified treatment-emergent bleeding safety endpoints in the pooled analysis were assessed at two time points: the total treatment duration pool and in the head-to-head treatment pool of 12±2 days post surgery.

Xarelto

demonstrated low bleeding rates, which were not statistically significantly different in comparison to enoxaparin for three of the four pre-specified safety endpoints (major bleeding, major bleeding including surgical site bleeding and any bleeding) at both time points:

- Rates of major bleeding at total treatment duration were 0.4% vs. 0.2% (p=0.076) and at 12±2 days were 0.3% vs. 0.2% (p=0.175) for Xarelto and enoxaparin, respectively.

- Combined rates of surgical site bleeding added to major bleeding at total treatment duration were 1.8% vs. 1.4% (p=0.063) and at 12±2 days were 1.7% vs. 1.4% (p=0.082) for Xarelto and enoxaparin, respectively.

- Rates of any bleeding at total treatment duration were 7.0% vs. 6.5% (p=0.255) and at 12±2 days were 6.6% vs. 6.2% (p=0.376) for Xarelto and enoxaparin, respectively.

Results

for the composite endpoint of major and clinically relevant non-major bleeding were also low but statistically significantly different for the total treatment duration time period [12±2 days following TKR and 35±4 days following THR, including extended (5 weeks) Xarelto treatment in RECORD2 compared to short-term (2 weeks) enoxaparin, followed by placebo for 3 weeks] with 3.2% for Xarelto vs. 2.5% for enoxaparin (p=0.039). However, the rates were not statistically significantly different in the head-to-head treatment pool of 12±2 days, which included the majority of reported bleeding cases in these criteria, 2.8% for Xarelto vs. 2.5% for enoxaparin (p=0.186).

"The combination of the efficacy and the safety profile of Xarelto may help change clinical practice to more accurately reflect established anticoagulation guidelines which are in place to protect patient lives," said Dr. Turpie. "All the results reported from the RECORD program strengthen my belief that direct Factor Xa inhibition with Xarelto has the potential to revolutionize the way we prevent the formation of dangerous blood clots."

Multiple Presentations Highlight Efficacy

During a separate plenary session and ASH media briefing, Dr. Turpie presented

results from the RECORD4 trial, which demonstrated that Xarelto is the only oral anticoagulant to show clinical benefit in the head-to-head comparison against the U.S.-approved regimen of enoxaparin. Xarelto (10 mg once-daily) provided a statistically significant 31% RRR in total VTE events compared to enoxaparin (30 mg twice-daily) [6.9% vs. 10.1%, respectively ($p=0.012$)]. Rates of major bleeding, the main safety endpoint, were low in both treatment groups.

About Xarelto® (rivaroxaban)

Xarelto is approved for use in the European Union for the prevention of VTE in adult patients who have undergone elective total hip or knee replacement surgery. Additional filings are under review with regulatory agencies in more than 10 other countries worldwide, including the United States.

The extensive clinical trial program supporting Xarelto makes it the most studied oral, direct Factor Xa inhibitor in the world today. More than 60,000 patients are expected to be enrolled into the Xarelto clinical development program, which will evaluate the product in the prevention and treatment of a broad range of acute and chronic blood-clotting disorders including VTE treatment, stroke prevention in patients with atrial fibrillation and VTE prevention in hospitalized, medically ill patients.

Xarelto was invented in Bayer's Wuppertal laboratories in Germany, and is being jointly developed by Bayer HealthCare and Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

About Bayer HealthCare

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contribution to medical progress and strives to improve the quality of life. Find more information at www.bayerscheringpharma.de.

Additional Information:

Copies of the abstracts may be viewed online at www.hematology.org/meetings/abstracts.cfm

To learn more about thrombosis please visit www.thrombosisadviser.com and to learn more about Xarelto please visit www.xarelto.com

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