VIOXX® Relieved Pain and Improved Clinical Outcomes in Patients Undergoing Total Knee Replacement Surgery, New Study Showed

Study Published in JAMA Demonstrated that Patients Receiving VIOXX Before and After Surgery Used Opioids Less Frequently

WHITEHOUSE STATION, NJ, USA, 12 November 2003 – In a new study of patients undergoing total knee replacement, the COX-2 inhibitor VIOXX® (rofecoxib), when given before surgery and continued through recovery, effectively controlled pain and reduced the need for opioids following surgery. In addition, the study demonstrated that patients receiving VIOXX experienced greater satisfaction and improved clinical outcomes, including better function in the knee during recovery. Results are published in today's issue of the Journal of the American Medical Association (JAMA).[1]

"In our study, not only were more patients satisfied with the level of pain relief achieved with VIOXX immediately after their knee replacement surgery, but they actually enjoyed an improved range of motion in the joint and required less physical therapy," said Asokumar Buvanendran, M.D., Assistant Professor, Department of Anesthesiology at Rush-Presbyterian-St. Luke's Medical Center, Rush University, Chicago, Illinois, and lead investigator of the study. "Coupled with the post-operative reduction in opioid consumption, these results suggest that VIOXX may be an effective component of operative pain management when initiated before surgery and continued through recovery."

The randomized, double-blind, placebo-controlled study involved 70 patients scheduled to undergo total knee replacement. All prior non-steroidal anti-inflammatory drug (NSAID) therapy was discontinued 14 days prior to surgery. Patients received either VIOXX 50 mg (n=35) or placebo (n=35) 24 hours before and one to two hours before surgery. Following surgery, patients received either VIOXX 50 mg or placebo daily from days one to five, and VIOXX 25 mg or placebo daily from days six to 14. A total of 66 patients completed the study, with 33 patients in each treatment arm.

The primary objective of the study was to determine whether pre-operative use of VIOXX reduced the amount of post-operative opioid consumption. The secondary objective was to determine if pre-operative use of VIOXX was associated with improved clinical outcomes (and/or decreased side effects) in this setting.

The study was an investigator-initiated research study conducted at Rush-Presbyterian-St. Luke's Medical Center in Chicago, Illinois, and supported by a medical school grant from Merck, Sharpe & Dohme.

VIOXX reduced the need for opioids after surgery

Immediately following surgery, patients were able to control the level of epidural analgesic medicine that they received. Pain was judged on the visual analog scale (VAS), with zero meaning "no pain" and 10 representing "the worst imaginable pain." Patients were instructed to maintain their pain score between two and four. After one hour, if patients were still experiencing a high level of pain (with scores between four and ten) and the maximum amount of epidural analgesic medicine was already given, patients were allowed to request intravenous morphine.

During the post-operative hospital stay, pain scores for the replaced knee were lower for patients taking VIOXX than those taking placebo (median VAS score was 2.2 for VIOXX versus 3.5 for placebo, $p<0.001$). Significantly fewer patients taking VIOXX consumed epidural medicine compared to those receiving placebo ($p=0.003$). Additionally, during the first 24-hour post-operative period, those patients receiving VIOXX requested 50 percent fewer doses of intravenous morphine compared with those patients receiving placebo ($p=0.02$).

Other clinical outcomes improved with VIOXX

In the study, patients receiving VIOXX experienced meaningful improvements in other clinical measures compared to placebo. Specifically:

- *Nausea and Vomiting*: On the first post-operative day, patients randomized to VIOXX had an approximate 75 percent reduction in the incidence of vomiting compared to those receiving placebo (6 percent versus 26 percent, $p=0.047$). The incidence of nausea after surgery also was lower in patients receiving VIOXX, with 24 percent suffering nausea compared to 44 percent of those receiving placebo ($p=0.08$). Additionally, anti-emetic use with intrave-

nous odansetron to help relieve nausea and vomiting was significantly less in patients taking VIOXX, an approximate 57 percent reduction, compared to those taking placebo (18 percent versus 41 percent, p=0.04).

- *Flexing of the Replaced Knee*: The ability to flex the replaced knee following surgery, an important measure of outcome, also was greater in patients receiving VIOXX. For example, 67 degrees of flexion is needed to walk, 83 degrees to climb stairs, 90 degrees to descend stairs, 93 degree to rise from a chair and a full range of 106 degrees is required to tie one's shoes. At discharge from the hospital, patients taking VIOXX demonstrated greater knee functionality compared to those taking placebo (mean 84.2 degrees for patients receiving VIOXX versus 73.2 degrees for those receiving placebo, p=0.03). In addition, patients taking VIOXX demonstrated an earlier achievement of 90 degrees of flexion compared to placebo (p=0.05) and had a greater range of motion at one month (mean 109.3 degrees for patients receiving VIOXX versus 100.8 degrees for those receiving placebo, p=0.01) at just one month post-operation.

Patients reported satisfaction with the level of pain relief provided by VIOXX

Patient satisfaction also was assessed in the study, using a five-point scale where one represented "no efficacy" and five represented "excellent efficacy." Overall, patients rated a higher satisfaction for VIOXX in terms of pain relief at discharge versus placebo (4.3 versus 3.3, p=0.03). The difference in satisfaction for VIOXX measured at discharge from the hospital persisted at two weeks and then again at a one-month follow-up.

Reference

1. *Buvanendran A et al. Effects of Perioperative Administration of a Selective Cyclooxygenase 2 Inhibitor on Pain Management and Recovery of Function After Knee Replacement. JAMA 2003;190:2411-2418.*