

**NEW INVESTIGATIONAL STUDY HIGHLIGHTS BENEFIT OF  
LOW-DOSE KYTRIL<sup>®</sup> FOR THE PREVENTION OF  
POST-OPERATIVE NAUSEA AND VOMITING (ponv)**

*-- Kytril<sup>®</sup> Demonstrated to be Effective at Dosage of 0.1 mg --*

**Nutley, NJ (December 7, 2002)** – In an investigational study, clinical data shows Roche's Kytril<sup>®</sup> (granisetron) to be effective in the prevention of post-operative nausea and vomiting (PONV) at doses as low as 0.1 mg. These data were presented today at the 56<sup>th</sup> Annual Post Graduate Assembly in Anesthesiology. Kytril is a selective, 5-hydroxytryptamine type 3 (5-HT<sub>3</sub>) receptor antagonist class of antiemetic. Intravenous Kytril is indicated for the prevention and treatment of PONV at a dosage of 1 mg. Kytril is also approved for the prevention of chemotherapy and radiation induced nausea and vomiting.

Researchers led by Dr. Robert D'Angelo of Wake Forest University, Baptist Medical Center, Department of Anesthesiology, presented results of a pilot, multicenter, randomized, double-blind dose-ranging study of intravenous Kytril in the prevention of PONV in patients undergoing abdominal hysterectomy. Kytril was shown to be more effective than placebo in the prevention of PONV at doses of 0.1 mg, 0.2 mg, and 0.3 mg. The benefit of Kytril over placebo was similar to the efficacy of other 5-HT<sub>3</sub>-receptor antagonists. Additionally, there was no evidence of a dose response relationship between the three ascending doses of Kytril versus placebo. All three doses (0.1, 0.2 and 0.3 mg) provided similar efficacy. This means that a minimum dose of 0.1 mg for the prevention of PONV may make higher doses unnecessary in many patients.

"The results of this study are important as they show effective dose of antiemetics that can substantially prevent post-operative nausea and vomiting," said Dr. Tong J. Gan Associate Professor, Director, Clinical Research, Department of Anesthesiology, Duke University Medical Center and an investigator in the study. "Additionally, there is a cost benefit to administering a low dose as long as efficacy is not compromised."

In this study, 121 women between the ages of 18 and 64 years, scheduled to undergo elective open abdominal hysterectomy requiring general anesthesia, were randomized to receive a single dose of intravenous Kytril at 0.1 mg, 0.2 mg, 0.3 mg or placebo. The proportion of patients in each dose group with no vomiting episodes in the 0-6 hour interval after administration of study medication was higher in the Kytril treatment groups (0.1 mg, 94 percent; 0.2 mg, 96 percent;

0.3 mg, 91 percent) compared to the placebo group (77 percent). The proportion of patients requiring the use of rescue medication over 0-6 hours was lowest in the Kytril treatment group, (0.1 mg, 29 percent; 0.2 mg, 41 percent, 0.3 mg 30 percent) compared to the placebo group (60 percent). The mean time to first rescue medication administration was shorter in the placebo group (4 hours) compared to the Kytril treatment group (0.1 mg, 13.5 hours; 0.2 mg, 12.2 hours; and 0.3 mg, 13.2 hours). In addition, the proportion

of patients with total control (no vomiting, no moderate/severe nausea, and no use of rescue medication over 0-6 hours) was higher in the Kytril treatment groups (0.1 mg, 65 percent; 0.2 mg 56 percent; 0.3 mg, 67 percent) compared to placebo (33 percent). The proportion of patients with no vomiting episodes in the 0-24 hour interval was similar in all treatment groups.

The most common adverse events in the treatment groups were: gastrointestinal disorders, general disorders and administration site reactions. The proportion of patients reporting at least one adverse event was similar across treatment groups (placebo, 90 percent, 0.1 mg, 84 percent; 0.2 mg, 78 percent; 0.3 mg, 88 percent).

### **PONV**

PONV remains a frequent and unpleasant experience for patients undergoing surgery. On average, 20 to 30 percent of surgical subjects suffer from PONV symptoms, depending on individual subject factors, type and duration of anesthesia and type of surgery. PONV can result in dehydration, electrolyte imbalances, prolongation of stay in the recovery room, unanticipated hospital admissions and loss of work.

### **About Kytril**

Kytril is a selective blocking agent of the serotonin 5-HT<sub>3</sub> receptor. Studies have indicated that this serotonin receptor is an important link in nausea and vomiting associated with chemotherapy and radiation therapy. Serotonin is believed to act on the vagus nerve to trigger nausea and vomiting. Kytril blocks receptors on the vagus nerve, thereby reducing and sometimes eliminating patient nausea and vomiting. Kytril can cause headache, constipation, weakness, drowsiness or diarrhea. As with any cancer therapy, there is a risk of side effects. Those observed with the use of Kytril are usually manageable and reversible with dose modification or interruption.

The FDA first approved Kytril injection in December 1993 for chemotherapy-induced nausea and vomiting (CINV). Kytril oral tablets were approved in July 1999, for use in radiation therapy-induced nausea and vomiting (RINV). In August 2002, Kytril received an additional indication for the prevention and treatment of post-operative nausea and vomiting (PONV).

More information is available at [www.kytril.com](http://www.kytril.com)

### **About Roche**

Hoffmann-La Roche Inc. (Roche), based in Nutley, N.J., is the U.S. prescription drug unit of the Roche Group, a leading research-based health care enterprise that ranks among the world's leaders in pharmaceuticals and diagnostics. Roche discovers, develops, manufactures and markets numerous important prescription drugs that enhance people's health, well-being and quality of life. Among the company's areas of therapeutic interest are: dermatology; genitourinary disease; infectious diseases, including influenza;

inflammation, including arthritis and osteoporosis; metabolic diseases, including obesity and diabetes; neurology; oncology; transplantation; vascular diseases; and virology, including HIV/AIDS and hepatitis C.

For more information on the Roche pharmaceuticals business in the United States, visit the company's web site at: <http://www.rocheusa.com>.

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