Drug trial shows promise for treating constipation caused by pain medicines

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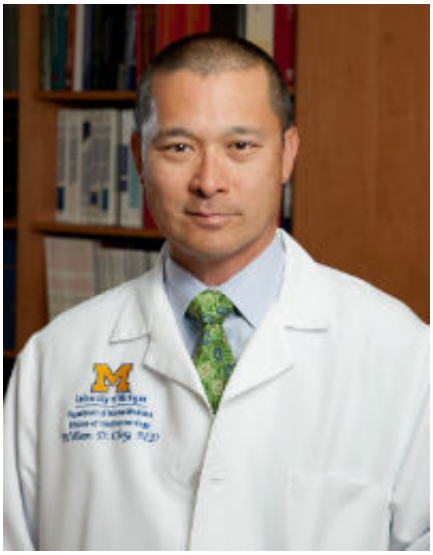

Dr. William Chey of the University of Michigan Health System leads a study of investigational drug to treat opioid-induced constipation. Credit: University of Michigan Health System

Pain medicines often lead to constipation for patients seeking long-term pain relief, but an investigational once-daily drug may help, according to study led by the University of Michigan Health System.

Globally, approximately 28 million to 35 million, or nearly half, of patients taking opioids for long-term pain develop constipation. Laxatives provide sub-optimal relief.

The results of two pivotal Phase 3 studies – KODIAC-4 and KODIAC-5 of naloxegol, an investigational treatment for opioid-induced constipation (OIC) – were published online first in the *New England Journal of Medicine*.

A 25 mg dose of the investigational drug naloxegol safely increased bowel movements among opioid-induced constipation sufferers, compared to a placebo, and the effects were maintained over a 12-week treatment period.

"The studies showed rapid and sustained improvement for these patients, without compromising their pain management," says lead study author and gastroenterologist William Chey, M.D., professor of internal medicine at the U-M Health System.

Naloxegol is an investigational peripherally-acting mu-opioid receptor antagonist, which has been specifically designed for the treatment of opioid-induced constipation (OIC), a common and often debilitating side effect of prescription medicines used to treat osteoarthritis and chronic back pain.

Opioids play an important role in chronic pain relief by binding to mu-receptors in the brain, blocking the brain's ability to perceive brain. But they also bind to mu-receptors in the bowel, contributing to constipation.

Naloxegol is designed to block the binding of opioids to receptors in the gastrointestinal tract without impacting the opioid receptors in the brain.

The Phase III studies known as KODIAC, enrolled 652 people in one trial and 700 in another. The 12-week, multicenter, randomized, double blind, placebo-controlled pivotal trials evaluated 12.5 mg and 25 mg doses of naloxegol, once-daily.

The most commonly reported adverse effects with naloxegol were abdominal pain, diarrhea, nausea, vomiting, flatulence and appeared to be dose-ordered, occurring more commonly in the 25 mg group.

Most adverse events were mild to moderate in severity and occurred shortly after initiation of naloxegol. There was one major cardiovascular adverse event in the 25 mg treatment group, one in the 12.5 mg treatment group and two among those in the placebo group.

A New Drug Application (NDA) for naloxegol was accepted by the US Food and Drug Administration on Nov. 19, 2013. Naloxegol is also under regulatory review with health agencies in the European Union and Canada.

Provided by University of Michigan Health System