

New drug to help common bowel disease

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(Medical Xpress)—An international team led by University of Adelaide researchers has identified the mechanism of pain relief of a new drug for treating Irritable Bowel Syndrome with Constipation (IBS-C), based on nonclinical studies, and quantified its effectiveness in pain relief in human trials.

Published in the journal *Gastroenterology*, the study describes the pain mechanism of action for Linaclotide, a recently approved drug for the treatment of <u>chronic abdominal pain</u> and constipation in adult IBS-C patients.

IBS is a potentially debilitating condition with abdominal pain, bloating, diarrhoea and/or constipation. It affects up to 15% of western populations, costing millions of dollars annually in Australia alone in lost productivity and health care. Approximately one third of IBS patients are diagnosed as having IBS-C.

"This is a significant finding and very good news for IBS-C sufferers," says study leader Dr Stuart Brierley, NHMRC RD Wright Biomedical Fellow in the University's Nerve-Gut Research Laboratory. "IBS affects many people, particularly women, on a daily basis and has a significant impact on their quality of life. Abdominal pain is often the most troubling symptom to IBS patients and has been

the most difficult symptom to treat.

"The drug is effective in relieving abdominal pain associated with IBS-C and is already available and registered for use by IBS-C patients in the



USA and Europe. It is yet to go through the regulatory process in Australia."

The research is a collaboration between the Nerve-Gut Research Laboratory, (University of Adelaide) and Ironwood Pharmaceuticals Inc, the developers of Linaclotide. Linaclotide is a new class of medicine and is the only treatment for IBS-C currently registered with the European Medicines Agency; it is also the first prescription treatment available in over six years for adults with IBS-C in the US.

Linaclotide binds the receptor domain of guanylate cyclase-C on the inner lining of the intestines. It is marketed by Ironwood and Forest Laboratories Inc as Linzess® in the US and by Ironwood and Almirall SA as Constella in Europe. Ironwood has partnerships through which it is conducting clinical trials of Linaclotide in China and Japan. Ironwood is exploring partnership opportunities for advancing Linaclotide in unpartnered territories, including Australia and New Zealand.

Dr Brierley, in the Nerve-Gut Research Laboratory, collaborated with Ironwood to further investigate how Linaclotide acts within the gastrointestinal tract to reduce abdominal pain. It had been shown to increase the secretion of fluids into the intestine and improve transit through the gastrointestinal tract. However, initial trials had shown that it also reduced abdominal pain associated with IBS-C, independently of its action on improving constipation.

Pre-clinical studies by the Nerve-Gut Research Laboratory showed that Linaclotide inhibits pain nerve endings in the intestine through a novel physiological pathway localised to the gastrointestinal tract. "The study also showed the analgesic effect translated into clinical findings in humans," says Dr Brierley. "IBS-C patients given the drug orally showed significant improvement in abdominal pain over those given placebo during a 26-week trial."



Provided by University of Adelaide

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