

# Prucalopride

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# Prucalopride: An Opportunity to Simultaneously Address Gastroparesis and Chronic Constipation

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I commend Carbone et al. (1) for their excellent work in performing the long-awaited trial examining the effects of prucalopride in gastroparesis. Prucalopride is registered for the treatment of chronic idiopathic constipation, but there is no reimbursement for this medication in several countries. Considering the currently available evidence, there seems to be a rationale for using prucalopride particularly in patients who suffer from both symptoms of gastroparesis and chronic constipation.

Gastroparesis and chronic constipation seem to occur frequently in the same patient: A recent retrospective study analyzing 206 patients showed that patients with gastroparesis are more likely to have slow colon transit (assessed by radiopaque marker testing) than patients with dyspeptic symptoms but normal gastric emptying (64.7% vs 28.1%). Conversely, patients with slow colon transit were more likely to have delayed than normal gastric emptying (55.0% vs 20.7%) (2). When measuring transit times using wireless motility capsules, extragastric transit delays

were seen in >40% of 209 patients with suspected gastroparesis (3).

Prucalopride has previously been shown to accelerate gastric emptying (in addition to overall colon transit) in patients with chronic constipation (4). Furthermore, Carbone et al. describe an increase in stool frequency and increased incidence of diarrhea during prucalopride treatment albeit the increased frequency was not sustained. The 4-week treatment period might be too short, however, in terms of establishing efficacy in constipation. It would be interesting to know whether patients who scored high on constipation on the Patient Assessment of Gastrointestinal Disorders Symptom Severity Index had greater improvement in their upper gastrointestinal (GI) symptoms as well on prucalopride. This would suggest a more generic effect on GI motility, although the sample size might be too small to adequately answer this question. For future trials, it would be interesting to preselect patients with concurrent gastroparesis and chronic constipation to increase therapeutic efficacy.

Another open question is related to the fact that no firm association was seen between symptom improvement and the apparent acceleration of gastric emptying. This observation has been matter of debate for some time (5). It is therefore tempting to assume that mechanisms unrelated to prokinetic effects are involved in the therapeutic effect of prucalopride. For instance, previous studies have shown that prucalopride diminished perception of luminal distension by gas, and this was hypothesized to be related to an antinociceptive effect (6). Such effects could be important when interpreting beneficial effects of prucalopride on bloating (which was seen through all 4 weeks of treatment in the daily diaries) and the only item significantly improved in terms of quality of life in the Carbone study: clothing. Bloating is also frequently associated with lower GI disorders, such as irritable bowel syndrome, and hence can originate from other parts than the gastroduodenal region. In constipation trials with prucalopride, there was a large effect size

seen for the improvement in bloating, akin to a decrease in incomplete bowel movements (7). The clinical benefit of prucalopride in gastroparesis may therefore not be the results of a more intuitive prokinetic effect but rather primarily related to a decreased perception of bloating.

## CONFLICTS OF INTEREST

**Guarantor of the article:** Daniel Keszthelyi, MD, PhD.

**Specific author contributions:** D.K. wrote the article.

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**Potential competing interests:** None to report.

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