Prucalopride for Treatment of Chronic Constipation: A Systematic Review and Meta-analysis

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Background: Chronic constipation (CC) is a challenging, albeit common, condition that impairs quality of life and, because of its high prevalence and chronicity, consumes significant healthcare resources. Our understanding of the pathophysiology of constipation remains incomplete, and available therapies have limited efficacy. Prucalopride is the first selective, high-affinity 5-HT_4 agonist, with a predominantly enterokinetic effect, translating into a significant clinical efficacy.
Aim: To perform a systematic review and meta-analysis of the large clinical trials using prucalopride to treat patients affected by CC in order to assess its efficacy.
Methods: MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials as well as abstracts from the major American, European and Asian meetings were searched up to November 2012. Large (≥ 250 patients) randomized controlled trials (RCTs) in adult patients with CC, treated with prucalopride, were included. Risk of bias for RCTs was assessed as described in the Cochrane handbook. Relative risks (with 95% CI) were computed using a random effects model in order to provide a more conservative estimate. The outcomes assessed were the number of patients with an average increase of ≥3 SCBM (at both 4 and 12 weeks), the number of patients with an average increase of ≥1 SCBM (at 12 weeks), the number of patients rating their treatment as extremely or quite a bit effective, the Improvement ≥1 PAC-SYM satisfaction from baseline as well as the use of laxative (both oral and enemas). Results were analyzed only if, for each variable considered, data were available from at least 3 RCTs.
Results: Five studies, comparing different doses of prucalopride to placebo, were identified. They included more than 2500 patients, most (up to 92.5 %) of whom were female. All studies were at low risks of bias. The results are shown in Table 1.
Conclusions: Prucalopride is effective for treating CC and also improves significantly the quality of life. The two regimens tested (i.e. 2 mg and 4 mg daily) provide a similar clinical benefit, with no evidence of dose-response effect.
style="height:45px; text-align:center; width:170px"> **RR: 2.20**
(95% CI: 1.68 to 2.88)

	Prucalopride 2 mg daily *versus* Placebo	Prucalopride 4 mg daily *versus* Placebo	Prucalopride 4 mg daily *versus* 2 mg daily
Patients with an average increase of ≥3 SCBMs at week 4	**RR: 2.20** (95% CI: 1.68 to 2.88)	**RR: 2.33** (95% CI: 1.53 to 3.56)	**RR: 1.13** (95% CI: 0.73 to 1.77)
Patients with an average increase of ≥3 SCBMs at week 12	**RR: 2.45** (95% CI: 1.94 to 3.07)	**RR: 2.32** (95% CI: 1.73 to 2.87)	**RR: 1.01** (95% CI: 0.83 to 1.22)
Patients with an average increase of ≥1 SCBMs at week 12	**RR: 1.82** (95% CI: 1.59 to 2.08)	**RR: 1.78** (95% CI: 1.51 to 2.09)	**RR: 1.03** (95% CI: 0.91 to 1.17)
Patients with an average increase of ≥1 SBMs at week 12	**RR: 1.71** (95% CI: 1.57 to 1.87)	**RR: 1.75** (95% CI: 1.56 to 1.96)	**RR: 1.02** (95% CI: 0.89 to 1.16)
Patients rating their treatment as extremely or quite a bit effective at week 12	**RR: 2.23** (95% CI: 1.66 to 2.99)	**RR: 1.87** (95% CI: 1.53 to 2.30)	**RR: 0.97** (95% CI: 0.83 to 1.42)
Improvement ≥1 PAC-SYM satisfaction from baseline at week 12	**RR: 1.78** (95% CI: 1.48 to 2.14)	**RR: 1.53** (95% CI: 1.11 to 2.10)	**RR: 0.92** (95% CI: 0.72 to 1.17)
Number of bisacodyl tablets taken/week, during the 12 weeks of the study (mean)	**-0.345** (95% CI: -0.437 to -0.252)	**-0.355** (95% CI: -0.488 to -0.223)	**-0.016** (95% CI: -0.124 to -0.093)
Number of enemas used/week, during the 12 weeks of the study (mean)	**-0.183** (95% CI: -0.276 to -0.091)	**-0.183** (95% CI: -0.291 to -0.074)	**0.05** (95% CI: -0.104 to 0.113)