4. Rungoe C, et al. Gut 2012;Suppl:[Abstract]OP225.
5. Storm HH, et al. Dan Med Bull 1997;44:535–539.

Conflicts of interest
The authors disclose no conflicts.

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Budesonide MMX and Mesalamine to Induce Remission in Patients With Ulcerative Colitis

Dear Sir:

We read with interest about the randomized, controlled trial (RCT) by Sandborn et al,[1] which deserve some comments concerning the methodology and the interpretation of the results.

First, the authors compared the efficacy of Budesonide MMX (9 and 6 mg/d) with mesalamine 2.4 g/d or placebo to induce remission in patients with active mild to moderate ulcerative colitis (UC). When a new drug must be evaluated versus an old treatment, the main rule is to choose the most appropriate dosage of the comparison drug. In 1987, Schroeder et al[2] showed that oral 5-aminosalicylic acid therapy in a dosage of 4.8 g/d was an effective therapy to induce remission in active UC. Two successive metaanalyses of the all RCTs of mesalamine confirmed that ≥3 g/d are needed to achieve the best result.[3,4] Therefore, the comparison in this trial was not appropriate.

Second, the clinical and combined remission (clinical and endoscopic) data observed in this study with mesalamine tablets (34% and 12%, respectively) are at variance with those of published RCTs. Leifeld et al,[5] in a pooled analysis of 4 RCTs of 3 g/d of mesalamine, showed that tablets were able to obtain a clinical remission in 71% and endoscopic remission in 48% of patients. In the discussion, the authors state that mesalamine 2.4 g/d is not more effective than placebo, when this statement seems debatable according to the analysis previously quoted.[5]

Considering that mesalamine is an effective drug in mild-to-moderate, active UC, before introducing budesonide MMx as a standard treatment for mild to moderate UC, it is advisable to design a trial which compare budesonide MMX with an effective dose of mesalamine.

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1. Sandborn WJ. Gastroenterology 2012;143:1218–1226.
2. Schroeder KW, et al. N Engl J Med 1987;317:1625–1629.
3. Ford AC, et al. Am J Gastroenterol 2011;106:601–616.
4. Sutherland L. Cochrane Database Syst Rev 2006;2:CD000544.
5. Leifeld, et al. Aliment Pharmacol Ther 2011;34:1115–1122.

Conflicts of interest
The authors disclose no conflicts.

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Reply. We appreciated Criscuoli, Sinagra, and Cottone's comments regarding our manuscript, "Once-Daily Budesonide MMX Extended-Release Tablets Induce Remission in Patients with Mild to Moderate Ulcerative Colitis: Results from the CORE I Study."[1] Their primary concern surrounds the dose of Asacol utilized in the study (2.4 g/d) and the performance of the drug in the clinical trial that was designed to examine the efficacy of MMX budesonide for mild to moderately active ulcerative colitis.

There is now abundant evidence that there are not clinically important differences in dose response between 2.4 and 4.8 g/d for the 2 different dose forms of delayed-release mesalamine, Asacol[2–4] and Lialda,[5,6] in patients with mild to moderately active ulcerative colitis. Based on these large, randomized, controlled trials and the original trial by Sninsky et al,[7] which showed that Asacol at doses of both 1.6 and 2.4 g/d was more effective than placebo, we believe that Asacol 2.4 g/d is an effective dose.

Furthermore, the primary goals of our study were to demonstrate the efficacy of budesonide MMX relative to placebo and to establish a dose response. Those goals were achieved in this study. The nonpowered Asacol reference arm was included at the request of European regulatory authorities, and was the approved dose at the time the study protocol was designed and approved. The study was not powered to demonstrate either superiority or noninferiority of Asacol relative to MMX budesonide; therefore, no conclusions can be drawn regarding the relative efficacy of these 2 agents. Last, the trial was not powered to demonstrate the superiority of Asacol relative to placebo; therefore, no conclusions can be from our data regarding the efficacy of Asacol.

We stand by the conclusion of our study, that budesonide MMX 9 mg/d is effective for induction of remission in patients with mild to moderately active ulcerative colitis.

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