Budesonide Equal to Mesalamine in Crohn's

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FROM GASTROENTEROLOGY

Budesonide was found noninferior to, but not better than, mesalamine for inducing remission of mildly to moderately active Crohn's disease in an international phase III clinical trial, Dr. Andreas Tromm and his colleagues reported.

In addition, once-daily dosing with 9 mg of budesonide was as effective as was the standard regimen of 3-mg doses taken three times daily. "From a clinical practice perspective, it would seem justified to recommend the budesonide 9-mg once-daily regimen, since this would be expected to improve adherence," said Dr. Tromm of Evangelisches Hospital Hattingen (Germany) and his associates (Gastroenterology 2011 February [doi:10.1053/j.gastro.2010.11.004]).

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Recent guidelines from the European Crohn's and Colitis Organisation recommend budesonide as more effective than mesalamine for mildly active, localized ileocecal Crohn's disease, and also recommend that budesonide or systemic corticosteroids are preferable for treating moderately active localized ileocecal disease. Budesonide has a superior adverse effect profile and is better able to preserve adrenal function and bone mass, the authors wrote.

"However, only a single randomized study [involving only 182 subjects] a decade ago has directly compared the efficacy and safety of budesonide versus mesalamine for the management of active Crohn's disease," they added. No studies have explored the use of different dosing regimens.

Dr. Tromm and his colleagues performed a double-blind phase III clinical trial in which adults with mildly to moderately active Crohn's disease were randomly assigned to receive eudragit-L-coated mesalamine tablets 4.5 g/day (153 patients), 3-mg budesonide capsules three times per day (79 patients), or one 9-mg oral budesonide capsule once daily (77 patients), for 8 weeks. The study subjects were followed every 2 weeks at 46 gastroenterology clinics.

The mean Crohn's Disease Activity Index (CDAI) score was higher in both budesonide groups than in the mesalamine group, and both budesonide groups had a higher proportion of patients with CDAI scores over 300. Also, both budesonide groups had more patients with extraintestinal manifestations of Crohn's disease. Otherwise there were no meaningful differences among the study groups in clinical characteristics.

The primary efficacy end point was clinical remission (a CDAI score of 150 or less) at the conclusion of the trial. Remission occurred in 70% of the patients taking budesonide, compared with 62% of those taking mesalamine. This difference was not statistically significant but did meet the criteria for noninferiority in effectiveness.

More physicians rated budesonide as achieving "therapeutic success" or "therapeutic benefit" than mesalamine, but this difference also did not reach statistical significance.

Remission rates did not differ significantly between the once-daily (67%) and thrice-daily (72%) budesonide groups, nor did any other efficacy end points. "Although tested in only an exploratory sense, these data suggest that once-daily or thrice-daily administration does not affect the efficacy of budesonide," Dr. Tromm and his colleagues said.

The subgroup of female patients demonstrated a greater clinical response to budesonide (75% remission) than to mesalamine (57%). "Whether this finding reflects a genuine treatment effect remains uncertain, since other studies of budesonide for active Crohn's disease have observed no gender-specific effects," they noted.

The greatest difference in treatment response was seen in the subgroups of patients who had high CDAI scores or high CRP levels at baseline, indicating greater severity of inflammation. Sixty-six percent of patients with high baseline CDAI scores remitted with budesonide, compared with only 49% of those with high CDAI scores who took mesalamine. The remission rate was 65% with budesonide for patients with high baseline CRP levels, compared with only 52% with mesalamine.

Median time to treatment response and median time to remission did not differ among the three treatment groups. Similarly, the median decrease in CDAI scores did not differ, and it was significant with all three of the drug regimens.

Adverse events occurred in 39% of patients taking t.i.d. budesonide, 47% of those taking once-daily budesonide, and 47% of those taking mesalamine. The corresponding rates of adverse events suspected to be drug related were 10%, 12%, and 7%.

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