Analysis Shows Treatment Response to Mesalamine Associated With Rapid Mucosal Healing in Patients With Moderately Active Ulcerative Colitis

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Combined data analysis from two trials demonstrated that treatment success is associated with mucosal healing in patients with moderately active ulcerative colitis who received either 2.4 or 4.8 grams of mesalamine per day. By 6 weeks, 67% of patients achieved both treatment success and mucosal healing, while only 5% achieved treatment success without demonstrating mucosal healing. The results were presented by University of Chicago researcher David T. Rubin, MD, at the annual scientific meeting of the American College of Gastroenterology (ACG).

According to the American College of Gastroenterology guidelines, the goals for treating active UC are to treat symptoms as well as mucosal inflammation. The mucosa is the innermost layer of the gastrointestinal tract and plays a primary role in digestion and absorption. When UC flares up, the mucosal lining of the lower GI tract (specifically the colon and rectum) becomes inflamed, leading to symptoms such as diarrhea, rectal bleeding, abdominal cramping, and an urgent need to go to the bathroom. Characteristic mucosal changes of UC seen on endoscopy include loss of vascular pattern, granularity, friability, and ulceration. Clinicians may evaluate symptom improvement as well as endoscopic improvement to determine whether a UC patient's flare is improving. Historically, however, the correlation between mucosal healing and clinical improvement has been uncertain, and therefore the relevance of demonstrating mucosal healing has been unclear.

"Importantly, this analysis demonstrates that there is an association between successful treatment of ulcerative colitis and achievement of mucosal healing," said lead author Dr. Rubin, Assistant Professor of Medicine, section of Gastroenterology.

This study analysis was based on results from the ASCEND (Assessing the Safety and Clinical Efficacy of a New Dose of 5-ASA) I and II studies -- sponsored by Procter & Gamble Pharmaceuticals, which markets the drug mesalamine under the brand name Asacol(R). The ASCEND studies were two Phase III, multi-center, double-blind randomized active-control studies designed to compare delayed-release mesalamine 2.4 g/day (marketed 400mg tablets) to mesalamine 4.8 g/day (investigational 800mg) tablets in patients with active UC for 6 weeks. The primary endpoint in these studies was treatment success defined as improvement in the Physician's Global Assessment (PGA) and improvement in one clinical assessment [rectal bleeding, stool frequency, endoscopy findings, Patient Functional Assessment (PFA)] and no worsening in any of the other clinical assessments. A total of 423 patients with moderately active UC (defined as a baseline PGA score of 2) were eligible for the primary endpoint analysis in the ASCEND studies. Among those patients with moderately active UC, the results showed that 72% of patients taking 4.8 g/day and 58% of patients taking 2.4 g/day achieved treatment success (p<0.05).

An additional analysis of 391 patients with moderately active UC (baseline PGA score of 2) and baseline endoscopy score greater than or equal to 2 showed that delayed-release mesalamine induced endoscopically measured mucosal healing in patients with moderately active UC (80% and 68%, respectively for 4.8 g/day and 2.4 g/day at 6 weeks). Mucosal healing was defined as endoscopy score of 0 (intact vascular pattern, no friability or granularity) or 1 (erythema; diminished or absent vascular markings; mild granularity; friability). The newest analysis of these same patients, presented at the ACG meeting this week, demonstrates that response to therapy with delayed-release mesalamine (meeting the primary endpoint) correlates with mucosal healing. Another analysis demonstrated that mucosal healing and PFA correlated poorly. This may be due to the fact that UC patients' general well-being involves more than mucosal healing.

Both doses of mesalamine were well tolerated, with adverse events comparable between 2.4 grams (400 mg tablet) per day and 4.8 grams (800 mg investigational tablet) per day. In pivotal clinical studies of mildly to moderately active UC, the most frequent adverse events reported for mesalamine and placebo, respectively, were headache (35% vs 36%), abdominal pain (18% vs 14%), eructation (16% vs 15%), pain (14% vs 8%), and nausea (13% vs 15%).

About Ulcerative Colitis

Ulcerative colitis involves inflammation of the lining of the colon and rectum. It varies in clinical severity with patients having mild, moderate or severe disease. Treatment depends on the extent and severity of disease.

It causes flares followed by periods of remission. During a flare, in which the rectum or colon become inflamed, people experience symptoms such as diarrhea, rectal bleeding, abdominal cramping and an urgent need to go to the bathroom. Flares can vary in duration and intensity.

While ulcerative colitis is a lifelong condition, flares can be controlled with medication.
Ulcerative colitis affects people of all ages, but often is diagnosed during early adulthood. The causes of this condition are unknown, but may involve heredity, infection or the immune system.

About Asacol(R) (mesalamine) Delayed-Release Tablets 400 mg

Asacol is indicated for the treatment of mildly to moderately active UC (the indicated dosage is two 400 mg tablets tid for 6 weeks) and for the maintenance of remission of UC (the indicated dosage is 1.6 g/day in divided doses).

Asacol was well-tolerated in clinical studies. Overall, the incidence of adverse events with Asacol was comparable to placebo.

In pivotal clinical studies of mildly to moderately active UC, the most frequent adverse events reported for Asacol and placebo, respectively, were headache (35% vs 36%), abdominal pain (18% vs 14%), and eructation (16% vs 15%); for the maintenance of remission of UC, the most frequent adverse events were headache (50% vs 50%), rhinitis (42% vs 36%), and diarrhea (35% vs 50%).

Asacol is contraindicated in patients with hypersensitivity to salicylates. Caution should be exercised when using Asacol in patients with known renal dysfunction or history of renal disease. It is recommended that all patients have an evaluation of renal function prior to initiation of Asacol tablets and periodically while on Asacol therapy. As with other mesalamine-containing products, serious adverse events may occur with Asacol. Please visit [http://www.pgpharma.com/pi/US-Asacol.pdf](http://www.pgpharma.com/pi/US-Asacol.pdf) for full prescribing information.

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