American College of Gastroenterology (ACG) 2012 Annual Scientific Meeting and Postgraduate Course

Phase 3 Study Validates New Biologic With Gut-Specific Directed Activity

Las Vegas - A new biologic with a unique target of activity appears to be nearing regulatory approval for the treatment of inflammatory bowel diseases (IBD), according to phase 3 data. The drug, called vedolizumab, targets α4β7 integrin, which specifically mediates lymphocyte trafficking to the gut. In separate phase 3 trials in ulcerative colitis (GEMINI I) and Crohn's disease (GEMINI II), the low rate of infectious complications relative to rates typically encountered with tissue necrosis factor (TNF) inhibitors suggest that the unique mechanism of action may be clinically important in the treatment of IBD.

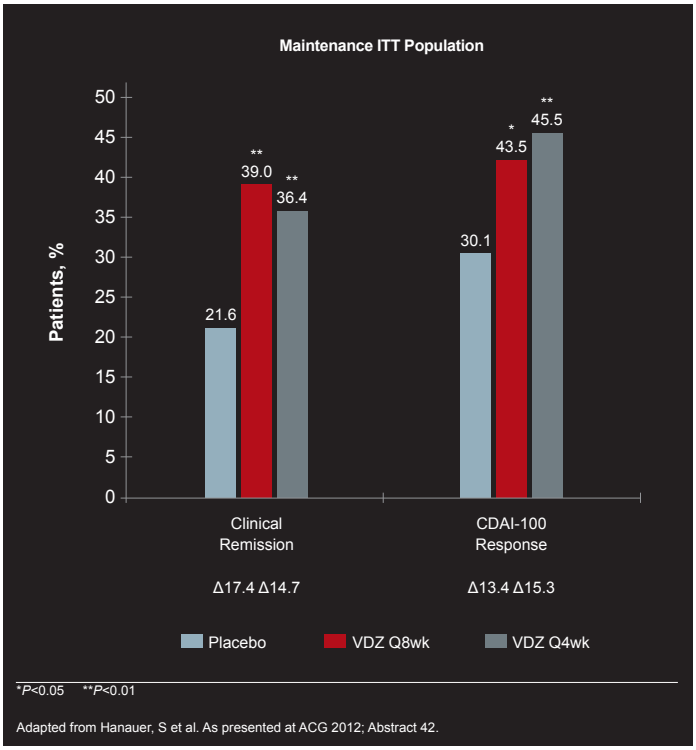
"We speculate that this finding [an absence of infectious complications] may reflect the gut-selective anti-inflammatory effect of this monoclonal antibody," reported Dr. Brian Feagan, Robarts Clinical Trials, Robarts Research Institute, London, Ontario. Delivering the maintenance data from the GEMINI I ulcerative colitis trial, Dr. Feagan reported that the activity of the drug appeared to be similar to that of TNF inhibitors when each is compared to placebo.

In the maintenance phase of GEMINI I trial, the objective was to assess the ability of vedolizumab to maintain a clinical response or remission over 52 weeks in patients who had achieved a clinical response in the induction phase. Prior to entering the induction phase, all patients had failed at least one prior treatment. The 373 participating patients were randomized to vedolizumab every 4 weeks, vedolizumab every 8 weeks, or placebo. The primary outcome of clinical remission was defined as a Mayo score of 2 or less with no individual subscore greater than 1. The study included a number of secondary outcomes, including the mucosal healing.

The advantage for the every-4-week regimen of vedolizumab over placebo was highly statistically significant for the primary outcome of clinical remission (44.8% vs. 15.9%; *P*<0.001) as well as for most secondary outcomes, including mucosal healing (56.0% vs. 19.8%; *P*<0.001) and corticosteroid-free remission (45.2% vs. 13.9%; *P*<0.001). Similar advantages were achieved for most outcomes for the 8-week regimen relative to placebo.

In a separate presentation at the ACG, the maintenance results from the GEMINI II Crohn's disease trial also associated vedolizumab with high rates of activity. Similar in design to the ulcerative colitis trial, GEMINI II also randomized the participating patients to 4- and 8-week regimens of vedolizumab or placebo. Again, all had failed at least one prior therapy before entering the induction phase of GEMINI II and had all had achieved a response on vedolizumab before proceeding to the maintenance phase. Clinical remission rates at 52 weeks in the GEMINI II maintenance study were 39.0%, 36.4%, and 21.6% for the 4-week, 8-week, and placebo arms, respectively (*P*<0.01 for either dose relative to placebo), according to Dr. William Sandborn, Scripps Clinic, University of California, San Diego. The proportion achieving a CDAI-100 response at 52 weeks was 43.5%, 45.5% and 30.1%, respectively (*P*<0.01 for the 4-week and *P*<0.05 for the 8-week regimens vs. placebo). While drug-related side effects were higher on vedolizumab than on placebo, discontinuation rates for adverse events were not (Figure 1).

FIGURE 1 I GEMINI II: Primary and Secondary Outcomes Through 52 Weeks



Adapted from Hanauer, S et al. As presented at ACG 2012; Abstract 42.

Echoing the conclusions of GEMINI I in ulcerative colitis, "vedolizumab proved to be more effective than placebo for maintenance treatment in Crohn's disease in a refractory population with moderately to severely active CD," concluded Dr. Sanborn, who presented these results on behalf of the senior author Dr. Stephen Hanauer, University of Chicago, Illinois. The potential value of vedolizumab in the treatment of Crohn's was substantiated by the fact that almost half the patients in GEMINI II were TNF inhibitor failures. Comparative trials between biologics are needed to explore relative efficacy and safety.

The Medical Xchange.com
Las Vegas, Nevada | October 19-24, 2012

eXtract web exclusive

American College of Gastroenterology (ACG) 2012 Annual Scientific Meeting and Postgraduate Course

NOT FOR DISTRIBUTION