

Certolizumab Pegol Approved for Treatment of Moderate-to-Severe Crohn's Disease

The US Food and Drug Administration (FDA) recently approved certolizumab pegol (Cimzia, UCB) for reduction of the signs and symptoms of Crohn's disease and maintenance of clinical response in adult patients with moderate-to-severe active disease who have not responded to conventional therapy. According to a press release from the manufacturer, FDA approval was based upon safety and efficacy data from clinical trials in more than 1,500 patients with Crohn's disease. In each pivotal study, a statistically significant greater proportion of patients with moderate-to-severe Crohn's disease achieved and sustained clinical response with certolizumab pegol for up to 6 months, versus patients taking placebo. The majority of patients in remission after initial dosing were able to maintain their remission without dose escalation.

Certolizumab pegol, a PEGylated anti-tumor necrosis factor- α antibody, is dosed subcutaneously every 4 weeks after initial dosing of 1 injection every 2 weeks for the first 3 injections. According to the FDA, the most common side effects of certolizumab pegol are headache, upper respiratory infections, abdominal pain, injection site reactions, and nausea. As with all biologic therapies for Crohn's disease, which affect the body's immune system, patients taking certolizumab pegol are at increased risk for adverse effects including serious infections. Unlike other anti-tumor necrosis factor- α agents, which have been associated with increased risk of lymphomas and other malignancies, the certolizumab pegol trials did not reveal an increased risk of tumors. However, the FDA noted that the studies were modest in size and of relatively short duration and that further postmarketing studies and clinical trials would be needed to obtain long-term safety data.

Hepatic Functional Impairment in Compensated Chronic Hepatitis C

Recently, researchers sought to define hepatic impairment using quantitative liver function tests and then correlate the results with disease severity in patients with chronic hepatitis C. This study was conducted by Greg T. Everson, MD, of the University of Colorado School of Medicine in Denver, Colorado, and associates at various institutions. It included 285 adult patients with chronic hepatitis C and was published in the May

issue of *Alimentary Pharmacology and Therapeutics*. All patients were subsequently enrolled in the Hepatitis C Antiviral Long-term Treatment Against Cirrhosis Trial. Of these patients, 171 had fibrosis (defined as Ishak fibrosis stages 2–4), 114 had cirrhosis (defined as stage 5 or 6), and none had experienced clinical decompensation. Twelve quantitative liver function tests were used to assess the spectrum of hepatic microsomal, mitochondrial, and cytosolic functions as well as hepatic and portal blood flow.

The researchers found that 26–63% of patients with fibrosis and 45–89% of patients with cirrhosis had hepatic impairment according to the quantitative liver function tests. The patients with cirrhosis experienced the greatest impairment, with a P value ranging from .15 to $<.0001$. In addition, cholate Cl_{oral} , cholate shunt, and perfused hepatic mass were shown to correlate with cirrhosis, stage of fibrosis ($r=-0.51, +0.49, -0.51$), varices, and variceal size ($r=-0.39, +0.36, -0.41$). The study also revealed that 91% of patients with medium- or large-sized varices could be identified by a perfused hepatic mass of less than 95 and a cholate shunt of more than 35%. The authors concluded that hepatic impairment is common in compensated patients with fibrosis or cirrhosis due to chronic hepatitis C and that cholate shunt, cholate Cl_{oral} , and perfused hepatic mass could identify patients at risk for cirrhosis or varices.

Computed Tomography for the Detection of Large-Bowel Obstruction

A study presented at the 2008 Annual Meeting of the American Roentgen Ray Society, held recently in Washington, DC, investigated the use of computed tomography (CT) in the detection of large-bowel obstruction and identification of the site and cause of obstruction. Researchers at the University of South Manchester in Manchester, United Kingdom, examined 42 patients identified for follow-up after the detection of large-bowel obstruction, large-bowel dilatation, or pseudoobstruction.

According to the researchers, CT revealed large-bowel obstruction in 31 patients, pseudo-obstruction in 8 patients, and indeterminate results in 3 patients. Of the 31 patients with large-bowel obstruction, 27 were confirmed by surgery or endoscopy. Of the 8 patients with pseudo-obstruction, no surgical/endoscopic intervention

was needed and the diagnosis was confirmed by follow-up. Of the 3 patients with indeterminate CT results, 2 were later found to have carcinomas and 1 had a negative laparotomy. The causes of the large-bowel obstruction ranged from the common (carcinoma, volvulus, diverticular stricture) to the rare (hernias, inflammatory stricture, gallstone obstruction at unusual sites). When diagnosing large-bowel obstruction, the sensitivity and specificity of CT was determined to be 94% and 100%. Sathi Sukumar, MD, lead author of the study, noted, "The results of this study could simplify the diagnostic process dramatically. A large number of patients in our study were frail or unwell, so it is particularly important in this group that diagnosis is achieved with the least invasive and quickest method possible."

Infection Risks for Patients With Inflammatory Bowel Disease

As published in the April issue of *Gastroenterology*, researchers from the Mayo Clinic in Rochester, Minnesota, the Centre Hospitalier Regional Universitaire in Lille, France, and the National University of Ireland, in Galway, Ireland, conducted a study to identify and quantify the clinical factors related to opportunistic infections in patients with inflammatory bowel disease (IBD). The researchers studied 100 consecutive IBD patients with opportunistic infections and then matched two IBD patients without any history of opportunistic infection as controls for each case. The researchers used conditional logistic regression to evaluate the relationship between putative risk factors and opportunistic infections, which was presented in terms of odds ratios (OR) and 95% CIs.

Using univariate analysis, the researchers found that use of corticosteroids (OR, 3.4; 95% CI, 1.8–6.2), azathioprine/6-mercaptopurine (OR, 3.1; 95% CI, 1.7–5.5), and infliximab (OR, 4.4; 95% CI, 1.2–17.1) were individually associated with significantly increased odds for opportunistic infection. Multivariate analysis revealed that use of any one of these drugs produced an OR of 2.9 (95% CI, 1.5–5.3) compared to the use of 2 or 3 of these drugs in combination, which produced an OR of 14.5 (95% CI, 4.9–43) for opportunistic infection. The

relative risk of opportunistic infection was found to be the highest in IBD patients older than 50 years of age (OR, 3.0; 95% CI, 1.2–7.2, relative to IBD patients 24 years of age or younger). There were no deaths from opportunistic infection during the study. The authors concluded that increased risk of opportunistic infections was associated with older age and immunosuppressive medications, particularly when used in combination, although the absolute risk of opportunistic infection in IBD patients has yet to be determined. Edward Loftus, MD, one of the authors of the study, noted, "This study shows that patients with inflammatory bowel disease who are on immunosuppressive medications should have a low threshold for seeking medical attention at any sign of infection, such as cough or fever."

In Brief

In a prospective study of patients with chronic hepatitis C virus genotype 2 infection who have achieved rapid virologic response, an 8-week regimen of combination antiviral therapy with peginterferon and ribavirin yielded an increase in the relapse rate, indicating the limitation of reducing treatment under 12 weeks in patients with genotype 2 and rapid virologic response. (*Liver Int.* 2008 Apr 1 [Epub ahead of print].)

According to a prospective study, infliximab is efficacious in controlling severe pediatric Crohn's disease; however, to induce and maintain clinical remission, repeated infliximab infusions are required, with the need for dose adjustment in a substantial number of patients. (*J Pediatr Gastroenterol Nutr.* 2008;46:293-298.)

A prospective study demonstrated that dyspeptic symptoms coexist in a subset of nonerosive reflux disease patients, but the prevalence and severity of the symptoms appears to be independent of esophageal acid exposure. (*Eur J Gastroenterol Hepatol.* 2008;20:264-268.)