IN THE PIPELINE

Updates on Promising Agents in Development for Gastroenterology & Hepatology

Vedolizumab Approved as Second-line Therapy for Moderate-to-Severe IBD

Vedolizumab (Entyvio, Takeda Pharmaceuticals) was approved by the US Food and Drug Administration (FDA), on May 20, 2014, for the management of moderate-to-severe ulcerative colitis and Crohn's disease in patients whose disease inadequately responds to one or more standard therapies. Vedolizumab is an integrin receptor antagonist and, therefore, has the ability to block migration of circulating inflammatory cells that target the gastrointestinal tract; however, integrin receptor antagonists have been associated with progressive multifocal leukoencephalopathy (PML). Although no cases of PML were observed in vedolizumab clinical trials, the FDA suggests that patients receiving vedolizumab be monitored for any new onset or worsening of neurologic signs and symptoms and any adverse effects be reported to MedWatch.

FDA to Consider Gastroenterologic Indication for Calcium Channel Blocker

A cream formulation of diltiazem hydrochloride (Dolizem, Ventrus Biosciences), a topical calcium channel blocker, will be the subject of a type B pre–New Drug Application (NDA) meeting this month between the FDA and the agent's manufacturer. Diltiazem hydrochloride cream, which, heretofore, was prepared via compounding, has been shown to reduce the pain of anal fissures, normalize internal anal sphincter pressure, and reduce anal maximal resting pressure. Although the US Department of Health and Human Services guidelines on anal fissures list topical calcium channel blockers as a preferred agent prior to attempting surgery, no approved, readily available topical formulation yet exists. Assuming all goes well during the pre-NDA meeting, Ventrus Biosciences plans to file an NDA in the latter half of 2014, with an anticipated Prescription Drug User Fee Act date planned for the latter half of 2015.

Ramucirumab Approved for Advanced Gastric Cancers

The recombinant human immunoglobulin G1 monoclonal antibody ramucirumab (Cyramza, Eli Lilly) has been approved for treatment of advanced or metastatic gastric and gastroesophageal junction adenocarcinoma in patients currently or previously treated with fluoropyrimidine- or platinum-containing chemotherapy. The approval was based on a randomized, placebo-controlled trial that showed a survival advantage and slowing of tumor growth with ramucirumab vs placebo. The mechanism of action is inhibition of blood supply to the tumor. Ramucirumab is delivered via a bimonthly 60-minute intravenous infusion. Its labeling carries a black box warning of risk of hemorrhage.

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Dr Dubinsky has been a consultant for Prometheus Laboratories, AbbVie, Janssen, UCB, and Takeda and has received research support from Janssen.

Suggested Reading

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Siegel CA, Siegel LS, Hyams JS, et al. Real-time tool to display the predicted disease course and treatment response for children with Crohn's disease. *Inflamm Bowel Dis.* 2011;17(1):30-38.

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