GASTRO-HEP News

By Samantha Alleman

Obeticholic Acid Drug Receives Accelerated Approval Recommendation From FDA Advisory Committee

The Gastrointestinal Drugs Advisory Committee of the US Food and Drug Administration (FDA) recently recommended the accelerated approval of the obeticholic acid drug Ocaliva (Intercept Pharmaceuticals) for the treatment of primary biliary cholangitis (PBC) in patients who are intolerant to treatment with ursodeoxycholic acid (UDCA) or in combination with UDCA for patients who do not respond to UDCA alone. If approved, the drug would provide an alternative treatment option for PBC for the first time in almost 2 decades.

The 17 to 0 panel vote for accelerated approval, granted to products that treat life-threatening or serious diseases, was based on data from 2 phase 2 studies and 1 phase 3 study, all of which showed significant efficacy in comparison with placebo.

Pruritus was the most common treatment-related adverse event throughout all 3 trials; 8 patients in the phase 3 study discontinued drug use owing to pruritus. The drug, administered orally, is available in 5-mg and 10-mg tablets. The suggested dosing regimen is 5 mg daily for 3 months, titrated up to 10 mg daily. According to an FDA briefing, transaminase and bilirubin elevations were related to doses higher than 10 mg daily.

Intercept Pharmaceuticals is currently conducting a phase 4 trial to confirm results of the phase 3 trial. Patients will be followed for at least 6 years, until 121 total primary endpoint events have accumulated.

Infliximab Biosimilar Safe for Long-term Maintenance of Crohn's Disease and Ulcerative Colitis

The infliximab (Remicade, Janssen) biosimilar CT-P13 (Celltrion) is safe and effective in the induction and maintenance of patients with Crohn's disease (CD) and ulcerative colitis (UC), according to results of a prospective, nationwide, multicenter, observational cohort study presented at the European Crohn's and Colitis Organisation 2016 Congress on March 17, 2016. The efficacy of the biosimilar was influenced by prior exposure to anti–tumor necrosis factor (TNF) therapy. CT-P13, which received support from the Arthritis Drugs Advisory Committee of the FDA for all indications of the original drug in February, has been shown to be effective in the remission of inflammatory bowel diseases.

Dr Krisztina Gecse and colleagues enrolled 291 patients in the study, including 184 with CD and 107 with UC; age at disease onset was 23 years (median, 19-34) and 28 years (median, 22-39), respectively. No patients had received infliximab within a year prior to receiving the biosimilar. Of patients with CD, 49% had ileocolonic disease locations, 41% had complicated disease behavior, 35% had perianal disease, 32% had colonic disease location, and 23% had previously undergone surgery. Of patients with UC, 59% had left-sided or extensive colitis, 25% had previously received anti-TNF therapy in CD, 14% had previously received anti-TNF therapy in UC, and 8% had proctitis.

Biochemical response, clinical remission, and clinical response were evaluated at weeks 14, 30, and 54. One hundred of the total enrolled patients achieved the endpoint of 54 weeks. Clinical remission was achieved by 55% of CD patients and 59% of UC patients at week 14; by 57% of CD patients and 46% of UC patients at week 30; and by 47% of CD patients and 53% of UC patients at week 54. Clinical response was achieved by 83% and 78% of CD and UC patients, respectively, at week 14; by 77% and 69% of CD and UC patients at week 30; and by 58% and 64% of CD and UC patients by week 54. Patients in either group who had previously undergone anti-TNF therapy reported lower response and remission rates at weeks 14, 30, and 54.

Adverse events included infusion reactions in 21 patients (6.6%) and infections in 23 patients (7.9%); 1 patient died.

FDA Approves Blood-Based Colorectal Cancer Screening Test

The FDA approved Epi proColon (Epigenomics AG), a blood-based test, for use in colorectal cancer screening, according to a press release published online on April 13, 2016. The test is used to detect Septin9 methylation, an indicator of colorectal cancer, in DNA that has been isolated from the plasma of the patient. Colorectal cancer is the second-leading cause of cancer death in the United States.

The qualitative, in vitro, diagnostic test is indicated for use in average-risk patients who do not wish to undergo guideline-recommended screening methods such as colonoscopy and stool-based fecal immunochemical tests, and can be performed as part of a routine office visit. Changes in diet and medication are not necessary for the test. The blood sample can be analyzed by a local or regional diagnostic laboratory.

Epi proColon was originally recommended for FDA approval in 2014, but several panel members were concerned about its effectiveness and efficacy, especially in comparison with the fecal immunochemical test. According to a statement from the manufacturer, the recent FDA approval was based on results of 3 clinical studies.

(continued on page 320)

by several factors, including sample handling, timing of sample collection, concomitant medications, presence of vedolizumab, and underlying disease. For these reasons, comparison of the incidence of antibodies to ENTYVIO with the incidence of antibodies to other products may be misleading.

DRUG INTERACTIONS

Natalizumab

Because of the potential for increased risk of PML and other infections, avoid the concomitant use of ENTYVIO with natalizumab.

TNF Blockers

Because of the potential for increased risk of infections, avoid the concomitant use of ENTYVIO with TNF blockers.

Live Vaccines

Live vaccines may be administered concurrently with ENTYVIO only if the benefits outweigh the risks *[see Warnings and Precautions]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ENTYVIO during pregnancy. Information about the registry can be obtained by calling 1-877-TAKEDA7 (1-877-825-3327).

Pregnancy Category B:

Risk Summary

There are no studies with ENTYVIO in pregnant women. No fetal harm was observed in animal reproduction studies with intravenous administration of vedolizumab to rabbits and monkeys at dose levels 20 times the recommended human dosage. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the benefits to the mother outweigh the risk to the unborn child.

Clinical Considerations

Any adverse pregnancy effect from ENTYVIO would likely be greater during the second and third trimesters of pregnancy. Monoclonal antibodies are transported across the placenta in a linear fashion as pregnancy progresses, with the largest amount transferred during the third trimester.

Animal Data

A reproduction study has been performed in pregnant rabbits at single intravenous doses up to 100 mg/kg administered on gestation Day 7 (about 20 times the recommended human dosage) and has revealed no evidence of impaired fertility or harm to the fetus due to vedolizumab. A pre- and post-natal development study in monkeys showed no evidence of any adverse effect on pre- and post-natal development at intravenous doses up to 100 mg/kg (about 20 times the recommended human dosage).

Nursing Mothers

It is unknown whether vedolizumab is present in human milk. Vedolizumab was detected in the milk of lactating monkeys. Exercise caution when administering vedolizumab to a nursing woman.

Pediatric Use

Safety and effectiveness of ENTYVIO in pediatric patients have not been established.

Geriatric Use

Clinical trials of ENTYVIO did not include sufficient numbers of subjects aged 65 and over (46 Crohn's and ulcerative colitis patients aged 65 and over were treated with ENTYVIO during controlled Phase 3 trials) to determine whether they respond differently from younger subjects. However, no overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients.

Distributed by:
Takeda Pharmaceuticals America, Inc.
Deerfield, IL 60015

U.S. License No. 1898

For more information, go to www.ENTYVIO.com or call 1-877-825-3327

Issued: May 2014

VMB245 R1_Brf L-BZV-0514-7

(continued from page 289)

GASTRO-HEP News

The screening test will be marketed in the United States under a joint agreement with Polymedco, the strategic partner of Epigenomics AG. The test is already available in Europe, China, and select other countries.

Hepatocellular Carcinoma More Common in Hepatitis C Virus Patients Taking Direct-Acting Antiviral Agents

Patients with hepatitis C virus (HCV) and cirrhosis developed hepatocellular carcinoma (HCC) within weeks of beginning treatment with direct-acting antiviral (DAA) agents, according to the results of a retrospective cohort study presented on April 14, 2016 by Dr Stefano Brillanti at the International Liver Congress. Similar results from a study by Dr María Reig and colleagues were published online on April 12, 2016 in the *Journal of Hepatology*. Data from both studies also revealed that patients with a history of HCC who are taking DAA therapy have the highest risk of developing a tumor.

Dr Brillanti and colleagues enrolled 344 patients with HCV and cirrhosis who were treated with DAA agents and followed for 24 weeks. Of the 344 patients, 237 had HCV genotype 1 infection, 191 were treatment-experienced, and 59 had been successfully treated for HCC. Patients with active HCC were excluded at baseline and at 12 and 24 weeks after treatment.

Twenty-six patients (7.6%) were diagnosed with HCC during follow-up, including 17 of the 59 patients with previous HCC. No connection was found between recurrence and treatment response, DAA regimen, or HCV genotype. In both groups of patients (those who developed HCC vs those who did not), the sustained virologic response rate at 12 weeks was 89%. Within the group with prior HCC, recurrence developed in patients who were younger (56 vs 73 years), were more treatment-experienced (88.2% vs 61.9%), and had more advanced fibrosis at baseline.

According to Dr Brillanti, DAA agents are not directly responsible for the development of HCC; however, patients with HCV who are taking DAA agents should be closely monitored.