GASTRO-HEP News

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US Food and Drug Administration Approves Infliximab Biosimilar

On December 14, 2017, the US Food and Drug Administration (FDA) approved the infliximab (Remicade, Janssen) biosimilar infliximab-qbtx (Ixifi, Pfizer) for all relevant indications for the reference product. Two other infliximab biosimilars, infliximab-abda (Renflexis, Merck) and infliximab-dyyb (Inflectra, Pfizer), previously received FDA approval.

The biosimilar received approval based in part on the results of the REFLECTIONS B537-02 study, a phase 3, multinational, randomized, double-blind, 2-arm, parallel-group study that compared the safety, efficacy, and immunogenicity of the biosimilar and the reference product in patients with active rheumatoid arthritis. The study found that the biosimilar demonstrated a high degree of similarity to the reference product. Infliximab-qbtx is approved to treat patients with ankylosing spondylitis, pediatric and adult Crohn's disease, plaque psoriasis, psoriatic arthritis, rheumatoid arthritis, and ulcerative colitis.

According to the prescribing label for infliximab-qbtx, the most common adverse events are abdominal pain, headache, infections (eg, pharyngitis, sinusitis, upper respiratory), and infusion-related reactions. The biosimilar is contraindicated in doses greater than 5 mg/kg in patients with moderate to severe heart failure and in patients who have previously had a severe hypersensitivity reaction to infliximab products or who have a known hypersensitivity to inactive components of the biosimilar.

Fecal Microbiota Transplantation Effective Long Term in Patients With Recurrent *Clostridium difficile* Infection

Fecal microbiota transplantation (FMT) is a safe and effective treatment in the long term compared to antibiotic therapy in patients with recurrent *Clostridium difficile* infection (CDI), according to the results of a retrospective, comparative, observational, follow-up study published online on December 11, 2017 ahead of print publication in *Alimentary Pharmacology & Therapeutics*. FMT also improved gastrointestinal symptoms and quality of life compared to antibiotic therapy.

Dr Jonna Jalanka and colleagues followed 84 patients with recurrent CDI for an average of 3.8 years. Forty-five patients underwent FMT, and 39 received antibiotics. The 2 groups were matched in age range (23-91 years vs 22-91 years, respectively), sex (female/male, 35/10 vs 31/8, respectively), and number of episodes before treatment (3.5 vs 3.9, respectively). The patients were evaluated with a retrospective questionnaire.

No statistical difference was found between the 2 treatment groups in terms of the incidence of severe diseases, including autoimmune diseases, cancer, diabetes, gastrointestinal polyps, and inflammatory bowel disease (IBD). The most reported conditions were migraine (4 in each group) and dementia (3 in each group). Patients in the FMT group reported fewer upper gastrointestinal tract symptoms and more regular bowel function compared to patients in the antibiotic group. Additionally, FMT-treated patients had significantly faster improvements in their bowel habits and noted improved mental health following treatment. Patients in both treatment groups expressed willingness to undergo FMT for de novo CDI compared to other treatment options, and 97.6% of patients in the FMT treatment group stated that they would prefer initial treatment with FMT as opposed to antibiotics.

Hepatitis B Vaccine Receives Approval From the US Food and Drug Administration

On November 10, 2017, the FDA approved a hepatitis B vaccine (Heplisav-B, Dynavax) indicated for all known subtypes of the hepatitis B virus. The vaccine, which is the first and only 2-dose vaccine for hepatitis B, was rejected in 2013 and 2016 due to various safety concerns. A postmarketing study will compare the new vaccine with a currently licensed hepatitis B vaccine (Engerix-B, GlaxoSmithKline) over 2.5 years for the risk of immune-mediated diseases and acute myocardial infarctions to address further safety concerns.

The new vaccine received a 12-to-1 vote of approval from the Vaccines and Related Biological Products Advisory Committee in July 2017, with 3 committee members abstaining in favor of administering the vaccine to patients age 18 years and older. The shorter dosing schedule of the new vaccine compared with competitors (2 doses in 1 month vs 3 doses in 6 months) was considered by the committee members to improve patient adherence.

The vaccine is contraindicated in patients who have experienced severe allergic reactions to any hepatitis B vaccine or component of Heplisav-B, including yeast. The most common adverse events reported within 7 days of vaccination were fatigue, headache, and injection site pain.

Committee for Medicinal Products for Human Use Recommends Marketing of Budesonide for Eosinophilic Esophagitis

On November 10, 2017, the Committee for Medicinal Products for Human Use of the European Medicines Agency recommended granting a marketing authorization in the European Union for budesonide (Jorveza, Dr Falk Pharma GmbH) for the treatment of adults with eosinophilic esophagitis. No medicine is currently authorized to treat this condition in the European Union. The drug received orphan medicinal product designation from the European Medicines Agency on August 5, 2013.

The locally acting glucocorticosteroid will be available in 1-mg orodispersible tablets. In clinical trials, the most commonly reported adverse events were fungal infections of the esophagus and oral cavity, including the pharynx, occurring in approximately 30% of treated patients. The majority of infections were treated with antifungal medications, and no patient discontinued use of budesonide due to infection. Additional adverse events included dyspepsia, gastroesophageal reflux disease, headache, interaction with CYP3A4 inhibitors, lipedema, nausea, and reduced cortisol levels.

The European Commission will review the opinion of the Committee for Medicinal Products for Human Use and decide whether to move forward with a marketing authorization for budesonide throughout the European Union.

Thiopurine and Anti–Tumor Necrosis Factor Therapies for Inflammatory Bowel Disease Linked to Higher Lymphoma Risk

Treatment of IBD with anti–tumor necrosis factor (TNF) monotherapy, thiopurine monotherapy, or combination therapy was associated with a small but statistically significant increased risk of lymphoma compared with nonusers, according to a nationwide cohort study based on French National Health Insurance databases.

Results of the study were published online on November 7, 2017 ahead of print publication in *JAMA*. Dr Magali Lemaitre and colleagues evaluated data from 189,289 adult patients diagnosed with IBD between January 1, 2009 and December 31, 2013. Patients were followed up until December 31, 2015, at which time they were classified as being exposed to anti-TNF therapy alone, thiopurine therapy alone, or combination therapy, or as being unexposed. The primary outcome was incident lymphoma.

A total of 336 cases of lymphoma occurred during the study. Among patients treated with therapy, the incidence rate (IR) of lymphoma was highest in those exposed to combination therapy (14 cases; IR per 1000 person-years, 0.95; 95% CI, 0.45-1.45), followed by those exposed to thiopurine monotherapy (70 cases; IR, 0.54; 95% CI, 0.41-0.67) and anti-TNF monotherapy (32 cases; IR, 0.41; 95% CI, 0.27-0.55). The IR was lowest among unexposed patients (220 cases; IR, 0.26; 95% CI, 0.23-0.29).

Study limitations include short follow-up for combination therapy (8 months) and the possibility of the association between combination therapy and increased lymphoma risk reflecting high levels of inflammation instead of treatment.

Glecaprevir/Pibrentasvir Yields High Sustained Virologic Response in Patients With Hepatitis C Virus Infection and Chronic Kidney Disease

The combination of glecaprevir/pibrentasvir (Mavyret, AbbVie) in patients with hepatitis C virus (HCV) infection and severe chronic kidney disease (CKD) yielded a sustained virologic response (SVR) in nearly all patients 12 weeks following treatment. Patients with both HCV infection and advanced CKD have limited treatment options, causing a majority of these patients to remain untreated.

Results of the multicenter, open-label, phase 3 trial were published online on October 12, 2017 ahead of print publication in the *New England Journal of Medicine*. Dr Edward Gane and colleagues enrolled 104 patients with HCV genotype 1 infection (52%), genotype 2 infection (16%), genotype 3 infection (11%), genotype 4 infection (19%), and genotype 5 or 6 infection (2%) in combination with stage 4 or 5 CKD to evaluate the safety and efficacy of glecaprevir/pibrentasvir. Patients had either previously received treatment containing interferon or pegylated interferon, ribavirin, sofosbuvir (Sovaldi, Gilead) or a combination of these medications, or were treatment-naive. Patients received 3 doses of glecaprevir (100 mg) and pibrentasvir (40 mg) daily for 12 weeks. The primary endpoint was SVR12.

SVR12 was achieved in 102 of 104 patients (98%; 95% CI, 95-100). No patient experienced virologic failure during treatment or virologic relapse following the end of treatment. SVR12 was similar across all genotypes. Fatigue, nausea, and pruritus were reported in at least 10% of the patients. Serious adverse events were reported in 24% of the patients, although none were attributed to the study treatment. Of the 4 patients who discontinued treatment due to adverse events, 3 achieved SVR12.