By Samantha Alleman

US Food and Drug Administration Approves Use of Colorectal Cancer Screening Test in Younger Adults

On September 23, 2019, the US Food and Drug Administration (FDA) approved a noninvasive colorectal cancer screening test (Cologuard, Exact Sciences Corp) for use in average-risk adults ages 45 years and older, according to a press release published online by the manufacturer. Previously, the stool DNA–based screening test was approved only for adults ages 50 years and older.

In May 2018, the American Cancer Society updated its colorectal cancer screening guidelines to include individuals between the ages of 45 and 49 years, rather than the previously recommended starting age of 50 years, in response to the increasing incidence of colorectal cancer among younger US adults. With this label expansion, the screening test, which uses a biomarker panel to analyze patients' stool samples for 10 DNA markers as well as blood, will become available for approximately 19 million more people in the United States.

Colorectal cancer is the second-leading cause of cancer-related death in the United States, but is treatable when detected in its earlier stages. Regular screening is recommended.

Tenapanor Receives US Food and Drug Administration Approval for Use in Adults With Constipation-Predominant Irritable Bowel Syndrome

On September 12, 2019, the FDA approved tenapanor (Ibsrela, Ardelyx), a locally acting inhibitor of the sodium/hydrogen exchanger 3, in tablet form for the treatment of constipation-predominant irritable bowel syndrome in adults, according to a news release published online on the company's website. Patients should take the 50-mg dose twice daily, both immediately before breakfast and dinner.

Tenapanor was evaluated in 2 randomized, double-blind, placebo-controlled trials, which followed the same design through the first 12 weeks of treatment. Trial 1 then continued for 14 more weeks of double-blind treatment, and Trial 2 included a 4-week randomized withdrawal period. The primary endpoint for both trials was the proportion of patients who experienced at least a 30% reduction in the weekly average abdominal pain score compared with baseline and an increase of at least 1 complete spontaneous bowel movement in a weekly average from baseline, in the same week, for at least 6 of the first 12 weeks.

Both of the tenapanor-treated groups had a higher proportion of responders vs placebo (Trial 1, 37% vs 24%; Trial 2, 27% vs 19%). The most common adverse event was diarrhea (Trial 1, 16% with tenapanor vs 4% with placebo; Trial 2, 15% with tenapanor vs 2% with placebo). Discontinuation rates were low overall (tenapanor, 7.6% vs placebo, 0.8%), and the most common adverse reaction leading to discontinuation was diarrhea (6.5% of tenapanor-treated patients vs 0.7% of placebo-treated patients). Tenapanor is not indicated for patients with known or suspected mechanical gastrointestinal obstruction and in patients younger than 6 years.

More Procedures Needed for Endoscopic Retrograde Cholangiopancreatography Competency

At least 300 hands-on endoscopic retrograde cholangiopancreatography (ERCP) procedures are needed for trainees to achieve competency, according to the results of a prospective study published online on September 10, 2019 ahead of print publication in *Endoscopy*. The previous benchmark was a minimum of 200 procedures.

Dr Keith Siau and colleagues along with the Joint Advisory Group on Gastrointestinal Endoscopy evaluated both the validity of ERCP direct observation of procedural skills (DOPS), a 27-item competency assessment tool, and the development of competency during training. The researchers analyzed ERCP DOPS performed in the United Kingdom between July 2016 and October 2018. Cronbach's alpha was used to measure the reliability of ERCP DOPS, and the contrasting groups method was used to benchmark DOPS scores. To assess learning curves, the percentage of competent scores for each item, domain, and overall rating was averaged and stratified by lifetime procedure count. Multivariable analyses were performed to identify predictors of DOPS competence.

A total of 818 DOPS, including 109 trainees across 80 UK centers, were evaluated. The overall Cronbach's alpha was 0.961. The optimal competency benchmark was defined as achieving competency in 87% of assessed DOPS items (preprocedure, postprocedure management, endoscopic nontechnical skills, cannulation and imaging, and execution of selected therapy) as well as across all items after 200 to 249 procedures (89%). The benchmark for selective cannulation was reached after

performing 300 ERCP procedures (89%), but not for sphincterotomy (80%), stenting (plastic, 73%; metal, 70%), and sphincteroplasty (56%). Predictors of DOPS competence were higher lifetime DOPS count (P=.01), trainee grade (P=.03), easier case difficulty (P<.001), and lifetime procedure count (P=.002).

Noninvasive Colon Cancer Test Granted US Food and Drug Administration Breakthrough Status

The FDA has granted a test for the early detection of colon polyps and colon cancer (LifeKit Prevent Colorectal Neoplasia Test, Prescient Metabiomics) its Breakthrough Device status, according to a press release published online on September 4, 2019 by the company. Breakthrough status allows the company to receive additional agency input as it finalizes test development as well as expedites the review process.

The Breakthrough Device status is the first designation for a noninvasive diagnostic test designed to detect precancerous polyps and early-stage carcinomas, as other available noninvasive tests primarily detect full-blown cancer and require programs that rely on colonoscopies to prevent colon cancer. The test uses a noninvasive collection swab to analyze stool-based microbial DNA and RNA biomarkers that are associated with neoplasia. A positive result suggesting the presence of colorectal adenomas or cancer should be followed by a diagnostic colonoscopy and, if needed, polypectomy.

US Food and Drug Administration Recommends Transition to Disposable Duodenoscopes

The FDA recommends duodenoscope manufacturers and health care facilities begin transitioning from duodenoscopes with fixed endcaps to those with disposable components, or to fully disposable duodenoscopes when they become available, in order to lessen the risk of patient infection, according to a safety communication published online by the FDA on August 29, 2019. Interim results of postmarket surveillance studies found persistent high levels of contamination and difficulty with cleaning these devices for reuse, leading to infections and deaths.

Health care facilities are advised to stop using fixed endcap models such as TJF-160F/VF, TJF-Q180V, PJF-160, and JF-140F (Olympus Corporation); ED-530XT (Fujifilm Medical Systems USA); and ED-3490TK (Pentax Medical). The FDA is working with manufacturers to increase the supply of disposable caps and to develop new designs that will further decrease or eliminate the risk of patient infection. Two duodenoscopes with disposable endcaps have already been cleared by the FDA, model ED-580XT (Fujifilm Corporation) and model ED34-i10T (Pentax Medical), and other firms have announced plans to develop fully disposable duodenoscopes.

The FDA will require new postmarket studies for manufacturers and will request real-world contamination rates in duodenoscope labeling.

Serious Liver Injury Associated With Hepatitis C Virus Infection Treatments in Patients With Advanced Liver Disease

The use of hepatitis C virus (HCV) infection treatments glecaprevir/pibrentasvir (Mavyret, AbbVie), elbasvir/grazoprevir (Zepatier, Merck), and sofosbuvir/velpatasvir/voxilaprevir (Vosevi, Gilead) in patients with moderate to severe liver impairment has resulted in rare cases of worsening liver function or liver failure, according to a drug safety communication published online by the FDA on August 28, 2019. The direct-acting antiviral drug combinations, all of which contain an HCV protease inhibitor, are FDA-approved to treat chronic HCV infection in patients with no or mild liver impairment (Child-Pugh class A) and are not indicated for use in patients with advanced liver disease (Child-Pugh class B or C) or other serious liver problems.

A total of 63 cases were reported to the FDA Adverse Event Reporting System databases or identified in literature through January 8, 2019. In the majority of cases, liver failure or decompensation typically occurred within the first 4 weeks of starting treatment. Discontinuing the medication led to symptom resolution or improvement of new onset worsening of liver function for most patients. Some cases reported patients with no cirrhosis or compensated cirrhosis with mild liver impairment who had decreased platelets at baseline or an increase in the pressure within the portal vein responsible for carrying blood from the digestive organs to the liver. Other patients had preexisting risk factors (eg, alcohol abuse, liver cancer, serious medical illnesses associated with liver problems), which may have contributed to clinical worsening of liver function or liver failure when receiving these HCV infection treatments.

The FDA continues to monitor this safety concern and recommends health care providers prescribe glecaprevir/pibrentasvir, elbasvir/grazoprevir, and sofosbuvir/velpatasvir/voxilaprevir as indicated in the prescribing information for patients with no or mild liver impairment. The severity of liver disease should be assessed at baseline, and patients should be monitored for signs and symptoms of worsening liver function, ceasing medication when liver decompensation becomes present or as clinically indicated.