

tract submission and selecting abstract review committee members and chairs for each descriptor within the section. Collectively, these committees are responsible for reviewing the 4,500 abstracts submitted to the AGA Institute each December for presentation at DDW.

“My goals for the council are to be responsive to the needs of the AGA membership, to continue to build international representation, and for our hard work and dedication to continue to be displayed at DDW each May,” says Polk. “As chair of this group, I am

very grateful for the tremendous efforts of the individuals serving on AGA Institute Council and for the AGA Institute staff’s support for the council’s many activities.”

Further details can be found at www.gastro.org.

Genetic Risk Factor for Liver Disease for Patients With Cystic Fibrosis

A genetic analysis indicates that a certain gene variation in patients with cystic fibrosis may significantly increase their risk of developing severe liver disease, according to a study in the September 9 issue of *JAMA*.

A small fraction (about 3% to 5%) of patients with cystic fibrosis develop severe liver disease characterized by cirrhosis with portal hypertension (CFLD). Previous research has suggested that genetic variability that is not associated with the cystic fibrosis transmembrane conductance regulator (CFTR) gene may contribute to the risk for severe liver disease.

Jaclyn R. Bartlett, PhD, of the University of North Carolina at Chapel Hill, and colleagues examined 9 vari-

ants in 5 genes previously studied in CFLD to determine the association between non-CFTR genetic variations and CFLD. The initial study compared genetic variations in candidate genes in persons with CFLD ($n = 124$) and in control patients without CFLD ($n = 843$), with a second study testing these findings in different populations of patients with ($n = 136$) and without ($n = 1,088$) CFLD.

This international collaboration compiled the largest number of samples ever from cystic fibrosis patients with severe liver disease.

The researchers found that of the 5 genes studied, “only the SERPINA1 Z allele was significantly associated with CFLD and portal hypertension. This polymorphism is relatively uncommon in CF [about 2.2 percent of patients with CF are carriers], but the odds ratio for association with severe

liver disease is relatively high [about 5 times higher] for the contribution of a genetic modifier to a mendelian disorder. . . . Moreover, the estimated population-attributable risk among patients with CF is 6.7 percent. From a clinical perspective, a rare variant with large penetrance (such as the Z allele) may be more useful than a common variant with low penetrance in screening for genetic polymorphisms,” the researchers note.

“The identification of the SERPINA1 Z allele as the first marker for the development of severe liver disease in CF illustrates the possibility of identifying CF risk factors early in life, conceptually as a secondary component of neonatal screening after the diagnosis of CF is confirmed,” the authors conclude.

For more details, see “Genetic modifiers of liver disease in cystic fibrosis,” *JAMA* 2009;302:1076–1083.

FDA Issues Early Communication About Ongoing Safety Review of Weight Loss Drug Orlistat

The US Food and Drug Administration (FDA) announced that it is reviewing new safety information regarding reports of liver-related adverse events in patients taking orlistat. Orlistat is marketed in the United States as a prescription product, Xenical, and as an over-the-counter (OTC) product, Alli.

Xenical (orlistat 120 mg) was approved as a prescription product by FDA in 1999 for obesity manage-

ment in conjunction with a reduced caloric diet, and to reduce the risk of regaining weight after prior weight loss. In 2007, Alli (orlistat 60 mg) was approved for OTC use for weight loss in overweight adults (≥ 18 years) in conjunction with a reduced calorie, low-fat diet. Currently, orlistat is approved for marketing in approximately 100 countries. In January 2009, a nonprescription version of orlistat was approved for sale in the European Union.

Between 1999 and October 2008, 32 reports of serious liver injury,

including 6 cases of liver failure, in patients using orlistat were submitted to FDA’s Adverse Event Reporting System. Thirty of the 32 reports occurred outside the United States. The most commonly reported adverse events were jaundice, weakness, and abdominal pain. Hospitalization was reported in 27 of the 32 cases.

In addition to the 32 reported cases, this issue was discussed at the CDER Drug Safety Oversight Board in April 2009, and the FDA says it is reviewing other data on

suspected cases of liver injury submitted by the manufacturers of orlistat. The agency points out that analysis of these data is ongoing and no definite association between liver injury and orlistat has been established at this time. Other symptoms may include abdominal pain, nausea, vomiting, light-colored stools, itching, brown urine, or loss of appetite.

The FDA notes it is not advising health care professionals to change

their prescribing practices with orlistat. Consumers currently taking Xenical should continue to take it as prescribed and those using OTC Alli should continue to use the product as directed.

The agency urges both health care professionals and consumers to report side effects from the use of orlistat (both Alli and Xenical) to the FDA's MedWatch Adverse Event Reporting program either online, or by regular mail, fax, or phone:

- Online: <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>
- Regular Mail: use postage-paid FDA form 3500 and mail to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787
- Fax: 800-FDA-0178
- Phone: 800-FDA-1088

Stories by Les Lang