Thiopurine May Cut Colorectal Ca Risk in IBD

BY MICHELE G. SULLIVAN

CHICAGO — Thiopurine therapy appears to prevent colorectal neoplasias in patients with long-term, extensive inflammatory bowel disease, reducing the risk of cancer or high-grade dysplasia by more than 70%.

The finding from a large French prospective cohort study casts a new light on the usual concern about the immunosuppressive effect of thiopurine, Dr. Philippe Seksik said at the annual Digestive Disease Week.

"Thiopurines could increase the risk of colorectal cancer via their immunosuppressive effect, or through their anti-inflammatory effect [they] could reduce the risk of colorectal cancer," said Dr. Seksik of Saint-Antoine Hospital, Paris. "Our data raise the hypothesis that the anti-inflammatory effect of thiopurines on colonic mucosa has a much greater impact on the risk of colorectal cancer than the putative deleterious effect of its drug-induced immunosuppression."

Dr. Seksik and his colleagues examined the risk of colorectal cancer in the national CESAME (Cancers et Sur-Risque Associé aux Maladies Inflammatoires Chroniques Intestinales en France) study. CESAME is a cross-sectional French cohort study that prospectively assesses the risk of cancers in patients with irritable bowel diseases. The study recruited 19,500 patients from 2004 to 2005, and followed them through December 2007. Dr. Seksik's analysis included follow-up data from 85% of the cohort.

The patients' mean age at recruitment was 40 years (range, 1-96 years). The mean duration of the disease was 8 years, although again, the range was very wide, including a disease duration of up to 65 years. In all, 11,760 patients (60%) had Crohn's disease; of these, 15% had long-standing extensive colitis, defined as a disease duration of more than 10 years with more than 50% of the colonic mucosa involved. The remaining 40% of the cohort had ulcerative colitis or an unclassified inflammatory bowel disease; of these, 37% had long-standing extensive colitis.

In those with long-standing extensive colitis, thiopurine reduced the risk of new neoplasia by 72%.

DR. SEKSIK

In the entire cohort, there were 36 incident cases of colorectal cancer and 21 high-grade dysplasias. Among patients with long-standing extensive colitis, there were 21 new cancers and 8 high-grade dysplasias.

At study inclusion, 36% of the patients were on immunosuppressive therapy. Of those, 30% were taking azathioprine or 6-mercaptopurine, 4% methotrexate, and 5% a tumor necrosis factor antagonist. Among all thiopurine-exposed patients, there were nine incident cases of colorectal cancer and three cases of high-grade dysplasia. Among only those with long-standing colitis, there were five colorectal cancers and one case of high-grade dysplasia.

On multivariate analysis examining the risk of colorectal neoplasia associated with sex, age, disease duration, and extensive colitis, the presence of extensive colitis significantly increased the risk of neoplasia sevenfold, compared with the expected number of cases obtained from the national French cancer registries.

When the team examined the association between thiopurine therapy and neoplasia, they found a nonsignificant risk reduction of 43%, compared with patients who had never taken a thiopurine. The effect was much more powerful when the analysis was restricted to those with long-standing extensive colitis; thiopurine exposure reduced the risk of new neoplasia by 72%—a 3.5-fold decrease from the rate seen in thiopurine-naive patients.

Researchers are still uncertain about the mechanism of protection, Dr. Seksik said. "The protective effect could be due to a nonspecific anti-inflammatory effect, or it could be a drug-specific, antineoplastic action on the inflammation-dysplasia-cancer sequence." Dr. Seksik said that he had no relevant financial disclosures. ■