

Screening Reduces Cancer Deaths in Lynch Syndrome

BY BRUCE K. DIXON
Chicago Bureau

Colorectal and endometrial cancers are the most frequent malignancies in people with Lynch syndrome, with respective cumulative risks of 60%-80% and 30%-50%.

The good news from a Dutch study is that a comprehensive screening program may cut the incidence of colorectal cancer (CRC) in this high-risk population by 70% (Gastroenterology 2006;130:665-71).

Cancer mortality in a large cohort of Lynch syndrome patients was compared with that in the general Dutch population by computation of the standard mortality ratio (SMR)—which is observed deaths/expected deaths—and absolute excess risk of death.

Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer, is a rare disorder that usually causes the development of colorectal, endometrial, and other forms of cancer.

The study evaluated the effectiveness of a large-scale cancer surveillance program. More than 2,700 individuals in 140 families fulfilled the selection criteria for being mutation carriers, putative carriers, or first-degree relatives of carriers.

The SMR for CRC decreased significantly between 1960 and 2004, from 32 to

10. In contrast, there was no significant change in the SMRs for all other cancers, including endometrial cancer (EC).

Among those who did not have a surveillance colonoscopy (1,073 patients), the SMR was 23.9, versus 6.5 for the group that had the test. The death rate for all cancers—barring CRC—was higher among women than men.

"The most frequent causes of death in the total cohort were CRC, EC, brain tumor, lung cancer, and cancer of the stomach," the authors said. Although the CRC death rate decreased after initiation of the registry and screening program, the SMR increased significantly for cancers of the small bowel, brain, kidney, ovaries, pancreas, and stomach.

"A striking finding in the present study," the authors observed, "was that there was no difference in EC mortality between relatives from *hMLH1/hMSH2* and *hMSH6* (germ line mutation) families despite the reported higher risk of EC in *MSH6* mutation carriers compared with the risk in *MLH1* and *MSH2* mutation carriers" (Gastroenterology 2004;127:17-25).

"Although the observed decrease in CRC mortality since the start of large-scale surveillance programs is encouraging, the mortality because of this cancer is still relatively high," and thus long-term studies are needed, they wrote. ■

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Panitumumab Found to Slow Metastatic Colorectal Cancer

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Twice-weekly doses of the investigational monoclonal antibody panitumumab reduced short-term disease progression by 46% in previously treated patients with metastatic colorectal cancer, Dr. Marc Peeters reported at the annual meeting of the American Association for Cancer Research.

After 8 weeks of twice-weekly 6-mg/kg doses of panitumumab plus the best standard of care, 49% of 231 patients were alive and had no disease progression, compared with 30% of 232 patients who received the best standard of care without panitumumab, said Dr. Peeters of Ghent (Belgium) University Hospital.

Disease progression continued to be slower in patients treated with panitumumab, compared with the standard-care group until about 20 weeks of treatment, and more panitumumab-treated patients remained alive after 32 weeks of treatment, compared with the standard therapy group.

Panitumumab, which is being developed by Amgen Inc., targets the epidermal growth factor receptor.

The randomized study included 463 patients aged 27-82 years of age, with a median age of 62 years. Overall, 67% of the patients had colon cancer, and 33% had rectal cancer, and all but one patient had undergone at least two chemotherapy regimens. Other demographic and clinical characteristics were similar between the groups.

Skin rash, the most common adverse event, was reported in about 90% of the panitumumab patients and in 9% of the

standard group. Other side effects that were more common among panitumumab patients included fatigue, abdominal pain, nausea, and diarrhea. No treatment-related deaths were reported.

"This is the first randomized controlled phase III study comparing a monoclonal antibody with best supportive care in chemoresistant patients," Dr. Peeters noted. "These data support further investigations with panitumumab, and additional studies are ongoing," he said.

Dr. James Abbruzzese, of the University of Texas M.D. Anderson Cancer Center in Houston, was the study's discussant at the meeting. The results were unsurprising, he said. "The objective response rate was very consistent with prior phase II studies."

Dr. Abbruzzese, who was not financially associated with the study, reviewed the data and noted that the hazard ratio for panitumumab was significantly lower during the first weeks of care, stabilized to 0.5 at about 5 weeks, and then tapered off after about 20 weeks.

Although the long-term survival rates were no longer significantly different between the two groups, "the impact of panitumumab during the early weeks of treatment was substantial, and prevented patients from progressing or dying during that period of time," he said. Panitumumab's impact on disease progression after 20 weeks remains uncertain, and may suggest some emergent resistance over time, he noted.

Panitumumab is being incorporated into investigational front-line cancer therapy regimens, and future research will examine its long-term effects. ■

Colorectal Cancer Screening Is Often Under Radar of Medicare Consumers

BY BRUCE K. DIXON
Chicago Bureau

Medicare consumers are underutilizing colorectal cancer screening, according to the authors of a National Cancer Institute study conducted after initiation of the Medicare colorectal cancer screening benefit.

The study, conducted in North and South Carolina, relied on data from a 2001 telephone survey of a random sample of 2,004 eligible Medicare consumers. The analysis was based on the 1,901 with no history of CRC (Am. J. Prev. Med. 2006;30:313-9).

The strongest predictors of adherence to Medicare-covered testing intervals were elevated CRC risk, having a checkup in the past year, and having a usual source of care. The influence of a physician's recommendation also was evident.

"Almost all of the Medicare

consumers who had received CRC tests indicated that they had also received a physician recommendation, while only 7% who had never been tested reported receiving a recommendation," said Carrie N. Klabunde, Ph.D., of the National Cancer Institute, and her associates.

Overall, 72% of Medicare consumers reported receiving a recommendation to have a CRC test. Of those who had never been tested, lack of knowledge or awareness of the need for CRC screening, followed by the physician's not ordering the test, were the most commonly cited reasons.

When asked about colonoscopy, half of those interviewed said they had never heard of it. Similarly, 62% had never heard of fecal occult blood testing and 63% had never heard of sigmoidoscopy.

"These results are especially concerning because over 90% of

consumers reported having a usual source of health care, and nearly 90% had a routine or preventive health care visit in the past 12 months," the authors said.

In a separate analysis, the investigators found that only 57% of whites and 39% of blacks reported adhering to current Medicare-covered testing intervals, and one-quarter of whites and nearly one-half of blacks had "never" been tested.

"Despite the increased risk for CRC due to age, and insurance coverage for screening and treatment through Medicare, almost half of enrollees are not current with CRC screening recommendations," the authors said (Am. J. Prev. Med. 2006;30:320-6).

"Improving initial test use among African American Medicare consumers is a necessary step toward increased compliance with guideline-based testing," they said. ■

Insulin Levels, Lifestyle May Affect Colon Cancer Risk

WASHINGTON — Elevated insulin levels and lifestyle factors were significantly associated with an increased risk of colon cancer in both white and African American subjects in a population-based study, Temitope O. Keku, Ph.D., reported at the annual meeting of the American Association for Cancer Research.

The study included 231 African Americans with colon cancer and 360 African American controls, along with 297 white patients with colon cancer and 530 white controls in North Carolina.

Cancer patients of both races reported eating significantly more food, compared with controls. Whites with cancer were significantly more likely than controls to report a high-fat diet, while African Americans with cancer were significantly more likely than controls to report NSAID use, Dr. Keku and

her colleagues at the University of North Carolina at Chapel Hill wrote in a poster.

Comparison of the highest and lowest quartiles for insulin-like growth factor I showed a threefold increased risk of colon cancer among African Americans and a 1.6-fold increased risk among whites in the highest quartiles compared with the lowest quartiles.

Elevated insulin and C-peptide levels were positively associated with cancer in both races, as were elevated IGF-I levels, higher body mass index, and low levels of physical activity. In addition, high levels of IGF-I significantly increased the risk of colon cancer in overweight or obese subjects.

These interactions suggest that lifestyle and dietary factors may modify the link between insulin resistance and colon cancer, regardless of race.

—Heidi Splete