# Elderly Benefit From Colorectal Cancer Screening

BY FRAN LOWRY
*Orlando Bureau*

ORLANDO — Colorectal cancer screening plays an important role in cancer prevention and detection, not just in the "young-old," but also in the "old-old"—people in their eighties and beyond.

And if a cancer is found, the elderly can also derive considerable benefit from treatments including surgery and chemotherapy, two presenters said at a meeting on gastrointestinal cancers sponsored by the American Society of Clinical Oncology.

A retrospective review of 1,390 patients aged 80 years and older who were screened with colonoscopy at Mount Sinai Medical Center in Miami Beach during the last 26 years showed that the majority of cancers (74%) were caught at an early stage when they were treatable by surgery alone, Dr. Heloisa P. Soares said at the symposium, also sponsored by the AGA Institute, the American Society for Therapeutic Radiology and Oncology, and the Society of Surgical Oncology.

Treatment with chemotherapy for more advanced colon cancer was also beneficial in this elderly population, whose mean age at diagnosis was 85 years, Dr. Soares said.

In all, 98 patients received chemotherapy as part of their treatment. In patients with stage II colon cancer, chemotherapy resulted in a median overall survival of 75 months, compared with 46 months for patients treated with surgery alone. In stage III colon cancer, chemotherapy likewise improved survival, to 49 months vs. 25 months for surgery alone. However, in stage IV colon cancer, survival was similar: 9 months with and 8 months without chemotherapy.

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**DR. SOARES**

"More than 70% of newly diagnosed colon cancer cases are in people older than 70 years. Screening in this population pays off, and so does chemotherapy, especially in the early stages," Dr. Soares said.

In another study presented at the meeting, 161 metastatic colorectal cancer patients aged 80 years or older who were treated with bevacizumab (Avastin) and standard chemotherapy tolerated the regimen as well as their younger counterparts aged 65-79 years, and also had the same progression-free survival. After a median follow-up of 21 months, the median progression-free survival was 10 months for all patients, regardless of their age.

The only risk factors for poor outcome were poor performance status (defined as ECOG [Eastern Cooperative Oncology Group] performance status of grade 2 or greater) and a history of arterial thrombotic events.

These results, from the BRITE (Bevacizumab Regimens Investigation of Treatment Effects and Safety) prospective cohort study, show that advanced age in itself should not be considered a deterrent to treating patients, said Dr. Mark Kozloff of Ingalls Memorial Hospital, Harvey, Ill., and the University of Chicago.

BRITE's large cohort of elderly metastatic colorectal cancer patients offers a unique opportunity to analyze bevacizumab and chemotherapy treatment outcomes in a population that is poorly represented in clinical trials, he said in an interview.

"These were basically all comers, unselected patients with metastatic colorectal cancer who are age 65 and older, and just those patients that we encounter most often in our real-world clinical practices. So these data are reassuring," he said.

Bevacizumab has been shown to prolong overall survival and progression-free survival when added to chemotherapy for metastatic colorectal cancer, but it is associated with an increase in arterial thromboembolic events.

Of 1,953 patients in the observational cohort, 896 patients were aged 65-74 years, 533 were aged 75-79 years, and the rest were aged 80 years or older.

There was a lower median overall survival for patients aged 80 years and older (16 months vs. 21 months for patients aged 65-74, and 20 months for patients aged 75-79) but this might be because of less aggressive treatment in this older cohort, Dr. Kozloff said.

Side effects with bevacizumab—such as gastrointestinal perforations, postoperative bleeding, delayed wound healing, and hypertension—were similar across all age groups.

Dr. Soares disclosed no conflicts of interest. Dr. Kozloff disclosed that he receives research funding from Genentech Inc. The BRITE study was sponsored by Genentech, which developed Avastin. ■

# KRAS Status Predicts Response to Colorectal Ca Treatment

BY FRAN LOWRY
*Orlando Bureau*

ORLANDO — KRAS tumor status has emerged as an important biomarker for the success or failure of therapies for metastatic colorectal cancer and should be assessed before starting treatment, researchers said at a meeting on gastrointestinal cancers sponsored by the American Society of Clinical Oncology.

"Clinicians should definitely start checking for KRAS status in their patients with advanced colorectal cancer. Such testing will become very easy to do in the next few months," Dr. Josep Tabernero, head of the gastrointestinal tumors unit of Vall d'Hebron University Hospital, Barcelona, said at the meeting, which was also sponsored by the AGA Institute, the American Society for Therapeutic Radiology and Oncology, and the Society of Surgical Oncology.

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In an open-label, phase I, multicenter study, Dr. Tabernero and colleagues evaluated the efficacy of cetuximab (Erbitux) given either once a week or once every 2 weeks, in 52 patients with epidermal growth factor receptor (EGF-R)–expressing metastatic colorectal cancer. Cetuximab was administered as a single agent over a 6-week period, and then FOLFIRI (irinotecan/5-fluorouracil [5-FU]/folinic acid [FA]) was added to the regimen.

The researchers also determined KRAS status in tumor samples from 48 of the patients, and correlated this status with overall response and progression-free survival.

The patients had had no prior exposure to EGF-R–targeting therapy, no previous chemotherapy (including adjuvant therapy) for metastatic colorectal cancer within 6 months of study entry, and no surgery or radiation treatment within 4 weeks of study entry.

The results showed that cetuximab 500 mg/m$^2$ given once every second week was feasible and convenient, but only the patients with wild-type KRAS tumors benefited.

The 29 patients with wild-type KRAS tumors had an overall response rate of 28%, compared with 0% for the 19 patients with mutant KRAS tumors when cetuximab was given as single agent. Once FOLFIRI was added to cetuximab, patients with wild-type KRAS tumors had an overall response rate of 55%, compared with 32% for those with mutant KRAS tumors.

The median progression-free survival for patients with wild-type KRAS tumors was 9 months, compared with 6 months for patients with mutant KRAS tumors (hazard ratio 0.47).

"This is the first time that the predictive value of the KRAS status has been demonstrated in patients treated with cetuximab and chemotherapy in the first-line setting of patients with advanced colorectal cancer," Dr. Tabernero said.

In another study presented at the meeting, KRAS status influenced clinical response to treatment with panitumumab (Vectibix) in patients with chemotherapy-refractory metastatic colorectal cancer.

In a phase III trial that randomized 463 patients to panitumumab plus best supportive care (n = 231) or best supportive care alone (n = 232), the benefit of panitumumab was confined to patients with wild-type KRAS tumors. Patients with mutant KRAS tumors showed no benefit, said Dr. Rafael G. Amado at a press briefing. Dr. Amado works for Amgen Inc., which makes panitumumab.

The median progression-free survival for the 124 patients with wild-type KRAS who were treated with panitumumab was 12 weeks, compared with 7 weeks for the 84 patients who had mutant KRAS. The median progression-free survival for patients randomized to best supportive care only was 7 weeks, regardless of KRAS status.

The response rate for wild-type KRAS patients treated with panitumumab was 17%, and 34% had stable disease. In contrast, the response rate for mutant KRAS patients treated with panitumumab was 0%, and 12% had stable disease.

The median overall survival was longer in patients with wild-type KRAS than in those with mutant KRAS tumors, regardless of treatment arm. The median survival of patients with wild-type KRAS tumors receiving panitumumab was 8 months, versus 5 months for those in the mutant KRAS group. In the best-supportive-care arm, the median survival for patients with wild-type and mutant KRAS tumors was 8 months and 4 months, respectively.

"Over 75% of patients in the best-supportive-care arm in both KRAS groups went on to receive panitumumab in a crossover protocol, which likely confounded the survival results," Dr. Amado noted.

In an interview, he commented on the significance of his study's results. "These findings are important because, by testing for KRAS mutations, physicians may now be able to identify patients who are more likely to respond to panitumumab treatment and avoid unnecessary side effects, as well as expense, to those who are unlikely to respond."

He added that being able to pinpoint subgroups of patients according to KRAS status or other biomarkers will become increasingly important for directing cancer treatment.

"The field of oncology will continue to undergo further segmentation as diseases are catalogued according to molecular alterations, and drugs will be developed to specifically interdict pathways that are active for specific categories of tumors within the same type of cancer."

To date in the United States, no tests have been approved by the Food and Drug Administration for testing KRAS in tumor samples. The test used in the panitumumab study, called the DxS KRAS, has a CE marking (a mandatory conformity marking in the European market). Amgen is currently collaborating with the maker of the test, DxS Ltd., to guide this test through the regulatory process of the FDA, Dr. Amado said.

Dr. Tabernero disclosed that he is a consultant to and receives honoraria from several pharmaceutical companies, including Merck KGaA, which sponsored his study. Dr. Amado is an employee of Amgen and owns stock in the company. ■