Left vs. Right: Primary Tumor Location Predicts Survival in Metastatic Colorectal Cancer

Cancer Originating on the Left Side of the Colon Is Associated With Longer Survival, Versus the Right Side
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ASCO Perspective

“This is the largest study to date of tumor location in colorectal cancer, and it strongly suggests that this unexpected factor could answer some long-standing questions about why certain patients do better than others,” said ASCO President Julie M. Vose, MD, MBA, FASCO, ASCO President. “It is also an important reminder, in this exciting era of precision medicine, that genomics is not the only source of insight into how cancers should be studied and treated.”

ALEXANDRIA, Va. – A retrospective analysis of data from a large, federally funded clinical trial finds that the location of the primary tumor within the colon predicts survival and may help inform optimal treatment selection for patients with metastatic colorectal cancer. The study was featured in a press briefing today and will be presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

The data show that patients whose primary tumors originate on the left side of the colon (the descending colon, sigmoid colon, and rectum) survive significantly longer than those whose tumors originate on the right side (the cecum and ascending colon).

“While previous studies had suggested that tumor location may impact clinical colorectal cancer outcomes, the effect we observed in this analysis appears to be far greater than we expected,” said lead study author Alan P. Venook, MD, Professor of Medicine at the University of California, San
Francisco. “These findings will likely change the way we approach colorectal cancer treatment and research, even as we seek to more deeply understand the biology driving the difference in outcomes between right- and left-sided cancers.”

**About the Study**

Researchers retrospectively evaluated data from the Phase III CALGB/SWOG 80405 clinical trial, a federally funded clinical trial designed to compare bevacizumab and cetuximab in combination with chemotherapy as initial therapy for metastatic colorectal cancer.

For the primary analysis, researchers identified data from 293 patients with right-sided primary tumors and 732 patients with left-sided primary tumors. This analysis included only patients without a mutated \textit{KRAS} gene, which is a known biomarker of response to certain colorectal cancer therapies (cetuximab is approved only for treating \textit{KRAS} wild-type tumors).

**Key Findings**

In this patient population, those with left-sided tumors had longer median overall survival (33.3 months), compared to those with right-side tumors (19.4 months). Among patients who received cetuximab, patients with left-sided tumors lived 36 months, while those with right-sided tumors lived 16.7 months. Similar trends were observed among patients receiving another treatment, bevacizumab: overall survival was 31.4 months and 24.2 months for patients with left- and right-sided tumors, respectively.

**Location May Predict Optimal Treatment Selection**

While the original trial found no significant advantage in overall or progression-free survival in patients treated with bevacizumab or cetuximab, this analysis suggests that the relative effectiveness of cetuximab and bevacizumab may differ depending on primary tumor location. Researchers are in the process of examining the molecular biology that presumably underlies these findings.

Among patients with right-sided tumors, treatment with bevacizumab was associated with longer survival than that of cetuximab (24.2 months vs. 16.7 months). Conversely, among patients with left-side tumors, treatment with cetuximab was associated with longer overall survival than bevacizumab (36 months vs. 31.4 months).

**Even in KRAS-Mutated Tumors, Left-Sided Tumors Are Associated With Improved Survival**

Because the CALGB/SWOG trial was initiated before \textit{KRAS} mutation status was known to be an important factor in use of cetuximab, there was a smaller population of patients who had \textit{KRAS}
mutations (an additional 213). In this separate analysis, researchers found that those with left-sided tumors also lived longer compared to patients with right-sided tumors (median overall survival: 30.3 months vs. 23.1 months).

This study received funding and support from BMS, Genentech, and Imclone in collaboration with the National Cancer Institute.

View the full abstract.

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