Adding cetuximab to chemotherapy enables patients with advanced colorectal cancer, liver metastasis to undergo surgery

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New results from a clinical trial conducted in Shanghai, China, indicate that adding cetuximab (Erbitux) to standard chemotherapy enables some patients with otherwise inoperable liver metastases due to colorectal cancer have their metastases surgically removed. Such surgery can be curative, and is generally critical to long-term survival. While this combination regimen is a standard treatment option for many patients with advanced colorectal cancer, this is the first randomized study to explore its impact on inoperable liver metastases.

The study, published April 8 in the *Journal of Clinical Oncology*, also suggests that, compared to chemotherapy alone, combination of cetuximab and chemotherapy improves tumor shrinkage and extends survival, even for patients with inoperable liver metastases who cannot undergo surgery.

"Our study suggests that in Chinese patients adding cetuximab to chemotherapy may effectively reduce tumor burden and increase the possibility of surgically removing liver metastases, improving survival and quality of life, " said senior study author Jianmin Xu, MD, PhD, a surgeon at the Zhongshan Hospital, Fudan University, in Shanghai, China. "While our study evaluated only Chinese patients, these findings may also be relevant for patients in North America and Europe."

Colorectal cancer is the third most common cause of cancer death in the

United States. At least two thirds of those deaths are due to tumor cells spreading (metastasizing) to the liver. Patients with colorectal cancer who develop liver metastases have a grave prognosis, with a median survival time of only 20 months despite chemotherapy.

The liver is often the first site of metastatic disease and may be the only site of spread in as many as 30-40 percent of patients with advanced colorectal cancer. Approximately 50 percent of patients with colorectal cancer develop liver metastases during the course of the disease. This study focused on patients who had liver metastases at the time of initial diagnosis of colorectal cancer, which account for 15-25 percent of all patients with liver metastases. Surgical removal of metastasis offers the only chance for long-term survival for these patients. Prior studies found that nearly half of patients are alive five years after removal of liver metastases. However, only 10-20 percent of patients with liver metastases are candidates for surgery. The current practice guidelines recommend giving "downsizing" chemotherapy or chemotherapy and targeted therapy combination regimens (for example, cetuximab) with the goal of "converting" initially inoperable metastases to operable tumors. This trial is the first study specifically designed to determine if adding cetuximab to chemotherapy would help "convert" initially inoperable tumors to operable ones.

In this Phase III clinical trial , patients with stage IV colorectal cancer spread only to the liver were randomly assigned to receive chemotherapy with cetuximab (Group A) or chemotherapy alone (Group B). They received either the FOLFIRI (leucovorin, fluorouracil and irinotecan) or the mFOLFOX6 (leucovorin, fluorouracil, and oxaliplatin) chemotherapy drug combination. Both regimens are standard treatment options for colorectal cancer with comparable efficacy but different side effects.

After treatment, 26 percent of patients (18 out of 70) became eligible

for surgery to remove liver metastases in Group A compared to only 7 percent (5 out of 68) in Group B. Patients in Group A who underwent surgery to remove such metastases lived significantly longer (46.4 months), on average, than those who were not able to have surgery (25.7 months). Compared to chemotherapy alone, combination treatment significantly increased liver tumor shrinkage rates (57 versus 29 percent) and the predicted 3-year overall survival rates (41 percent versus 18 percent). Overall, the median survival time for patients in Group A was 30.9 months compared with 21 months for those in Group B.

Cetuximab belongs to a class of drugs known as EGFR inhibitors. Such drugs block specific molecular pathways involved in tumor growth. This study included only patients with a so-called wild-type (normal) KRAS gene, because cetuximab is known to be ineffective against tumors with alterations in the KRAS gene. About 60 percent of all people with colorectal cancer have a normal, unchanged KRAS gene. ASCO recommends routine testing for KRAS gene alterations before giving anti-EGFR therapy.

Provided by American Society of Clinical Oncology

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