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New results help predict treatment response in colorectal cancer

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Genetic testing can identify a group of patients with advanced colorectal cancer who are likely to survive on average twice as long if treated with the drug cetuximab, late breaking results show.

At the 33rd Congress of the European Society for Medical Oncology (ESMO) in Stockholm, Dr. Christos Karapetis from Flinders University in Australia reports on a genetic analysis of 394 patients who took part in a phase III study comparing the monoclonal antibody cetuximab with best supportive care.

The latest analysis compared the effect of mutations in the K-Ras gene on overall survival and progression-free survival. The gene encodes a protein that is a key component of cellular signalling pathways, conveying extracellular growth signals from the cell surface to the nucleus. When growth factors bind to cell surface receptors, including epidermal growth factor receptor (EGFR), K-Ras is temporarily activated, facilitating regulated cell growth and proliferation.

The K-Ras gene is mutated in up to 35% of colorectal cancers. These mutations keep K-Ras stuck in its active form, switching on signalling without the requirement for EGFR stimulation.

Dr. Karapetis and colleagues found that patients with mutated forms of K-Ras had a median overall survival of 4.6 months when treated with cetuximab, and 4.5 moths with supportive care. In contrast, among those with wild-type forms, overall survival jumped to 9.5 months when

treated with cetuximab, compared to 4.8 months with best supportive care.

The results show that determining K-Ras mutation status should be considered a new standard of care for selecting patients for targeted therapies against EGFR, the authors say.

Also at the congress, Professor Eric Van Cutsem from University Hospital Gasthuisberg, Leuven in Belgium will present data on the impact of K-Ras mutations from the Crystal study, in which patients were randomized to either the chemotherapy combination "FOLFIRI" or FOLFIRI plus cetuximab, in first line metastatic colorectal cancer.

Professor Van Cutsem recently reported that the combination of cetuximab and FOLFIRI significantly improves progression free survival and response rate in patients with a K-Ras wild type. In Stockholm he will present new data on survival in the Crystal trial.

"Overall survival in all patients included in the trial was identical in both treatment arms. There was however a strong trend towards a longer survival in patients with a K-Ras wild type tumor treated with cetuximab/FOLFIRI," he said. The median survival was 24.9 months for patients who received the cetuximab combination, versus 21.0 months (HR: 0.84). The overall survival results in patients with K-Ras mutant tumors did not differ in the two study arms.

In another study, Dr. Miriam Koopman from the University Nijmegen Medical Centre St. Radboud in The Netherlands, reports that the number of tumor cells found circulating in the blood of patients with advanced colorectal cancer is another valuable predictor of survival.

Her group studied 467 patients who were being treated within a prospective clinical trial (CAIRO2 of the Dutch Colorectal Cancer

Group) with chemotherapy plus bevacizumab, with or without the addition of cetuximab. In each patient they measured levels of circulating tumor cells before treatment, and at different stages during treatment.

"Circulating tumor cell (CTC) level might be an indicator of the aggressiveness of disease," Dr. Koopman explained. "Thus, a high CTC level before initiating therapy in metastatic colorectal cancer patients is an inferior prognostic factor in our study."

The results show that the median progression-free survival time for patients with less than three CTC in every 7.5mL of blood was 10.5 months, compared to 8.2 months for those with three or more. Furthermore the median overall survival time for patients with less than three CTC in every 7.5mL of blood was 22.2 months, compared to 13.7 months for those with three or more.

"In our study CTC in metastatic colorectal cancer patients proves to be an early prognostic marker," Dr. Koopman said. "Prospective trials are needed to investigate whether a change in therapy based on CTC is beneficial."

Source: European Society for Medical Oncology