転移性大腸がんの遺伝子（Abstract #: 2）

KRAS遺伝子に変異のない転移性大腸がん患者はファーストラインの一部としてcetuximabを用いた治療がより有効である

Patients who have no mutations in the KRAS gene are more likely to respond to cetuximab as part of their first-line therapy for metastatic colorectal cancer

腫瘍細胞のKRAS遺伝子に変異のない転移性大腸がん患者は変異のある患者よりも、ファーストラインの一部としてcetuximabを用いた治療がより有効であるとAmerican Society of Clinical Oncology学会で発表された。今回のスタディでは、CRYSTALトライアルの患者1,198人中587人の組織検体を用いて、このサブグループの患者がcetuximabにより有益性がより多く得られるかを評価した。変異は35.6%の患者の腫瘍において認められた。KRAS遺伝子が正常であった患者のうち治療が有効であったのはcetuximabを追加した化学療法群で59.3%（約半分の腫瘍縮小）であったのに対し、従来の化学療法のみの群では43.2%であった。変異のある患者においては、これらの治療群間で奏効率に差はなかった。全ての患者のデータを解析したオリジナルのスタディでは、FOLFIRIとcetuximabの併用により進行リスクが15%低下した。

Full Text

Patients whose tumor cells have no mutations in the KRAS gene are more likely to respond to cetuximab as part of their first-line therapy for metastatic colorectal cancer, according to a presentation at the annual meeting of the American Society of Clinical Oncology.

"While our initial study indicated that cetuximab has the potential to become part of the standard treatment for patients with newly diagnosed metastatic colorectal cancer, this study helps us to identify which patients are most likely to benefit from adding the drug to treatment," said Eric Van Cutsem, MD, PhD, professor at the University Hospital Gasthuisberg in Leuven, Belgium, and the study's first author.

"KRAS testing should be routinely conducted in all colorectal cancer patients immediately after diagnosis to ensure the best treatment strategies for the individual patient."

KRAS mutations, which are found in 30 to 45 percent of all colorectal tumors, have previously been shown to predict whether patients will benefit from agents that block epidermal growth factor receptors in the second-line or later setting.

The CRYSTAL trial was the first randomized study to compare patients who received chemotherapy alone to those who received chemotherapy plus cetuximab as part of initial therapy. Researchers presented data last year that showed addition of cetuximab to FOLFIRI chemotherapy resulted in longer progression-free survival than treatment with the combination chemotherapy alone.

The current study is an extension of the CRYSTAL trial that sought to determine whether certain subsets of patients benefited more from the addition of cetuximab than others.
Researchers had access to tumor material from 587 of the 1,198 patients in the original trial and used these samples to determine each patient tumor's KRAS status.

KRAS mutations were detected in 35.6 percent of patients' tumors. Investigators found that among patients with normal KRAS, 59.3 percent responded to treatment with chemotherapy and cetuximab (their tumors shrank by more than half), compared with 43.2 percent who responded to chemotherapy alone. Among patients with mutated KRAS in their tumors, there was no difference in response rates between those who received chemotherapy alone and those who received chemotherapy and cetuximab.

In the overall study, which analyzed data for all patients, the addition of cetuximab to FOLFIRI resulted in a 15-percent decreased risk for progression. When KRAS was evaluated, the normal KRAS gene group was shown to have a 32-percent decreased risk for progression with the addition of cetuximab. Patients with a mutation in KRAS did not get an additional benefit from addition of cetuximab to chemotherapy.

ASCO2008 特集