Cetuximab did not add significant benefit to NORDIC FLOX regimen in first line treatment of mCRC

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Adding the targeted drug cetuximab to a three-drug chemotherapy regimen for first-line treatment of metastatic colorectal cancer does not improve response rate, progression-free survival or overall survival, researchers reported at the 35th Congress of the European Society for Medical Oncology (ESMO) in Milan, Italy.

Professor Kjell Magne Tveit from Oslo University Hospital, Norway, reported the unexpected results from the NORDIC VII study, which included 566 patients from Sweden, Denmark, Norway, Finland and Iceland who were randomly assigned to either a combination of 5-fluorouracil plus folinate plus oxaliplatin (NORDIC FLOX), FLOX plus cetuximab until disease progression, or FLOX intermittently plus continuous cetuximab.

"The finding that cetuximab did not add any significant benefit to the FLOX regimen (fluorouracil, folinate and oxaliplatin) was unexpected," Prof Tveit said. "Cetuximab has a documented beneficial effect in later stages of metastatic colorectal cancer, when given alone or together with chemotherapy. We expected that similar findings would be found in early stage when given together with an oxaliplatin regimen."

Among the whole study population, there were no statistically significant differences between the treatment groups in terms of response rate, progression-free survival or overall survival, the NORDIC VII

researchers found.

The lack of significant benefit also applied to sub-groups of patients with mutant and wild-type versions of the KRAS gene. "Some recent studies have shown that the beneficial effect of cetuximab was limited to the group of patients without KRAS-mutations. However, unexpectedly, we could not find a significant clinical effect in this specific group either," Prof Tveit said.

The new results come after mixed results from trials in which cetuximab was added to chemotherapy as first-line treatment in colorectal cancer. In the Phase-III CRYSTAL study, cetuximab combined with an irinotecan-based combination known as FOLFIRI had a positive effect. Similarly, cetuximab was beneficial when combined with FOLFOX in the Phase-II OPUS study.

However, the recent Phase-III COIN study, also using oxaliplatin combination as standard, did not show a positive effect of adding cetuximab.

"The results from our study and the COIN study together really question whether cetuximab has a clinically significant effect in first line when combined with oxaliplatin," Prof Tveit said. "Altogether, we think that the place for anti-EGFR drugs in first-line treatment for metastatic colorectal cancer is still questionable."

"Our results do not support the use of cetuximab in first line when given together with an oxaliplatin regimen. The results of trials combining cetuximab with an irinotecan regimen, as well as results from panitumumab-studies in first line, seem to be more positive. However, we conclude that these drugs are not fully established as part of standard first-line treatment of metastatic colorectal cancer."

Dr Josep Tabernero of the Vall d'Hebron University Hospital in Barcelona, Spain commented that the results of this study add to a growing body of evidence regarding the role of cetuximab in the treatment of patients with metastatic colorectal cancer in the first-line setting.

"Although the results of this study have not met the expectations of gastrointestinal medical oncologists, they have to be analyzed in the context of other studies," he said. "The only way to analyze all these separate pieces of information is to develop meta analysis of all of them."

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