BRAF mutant and RAS mutant patients treated with FOLFIRI plus Bevacizumab or FOLFIRI plus Cetuximab. Role of ETS and molecular markers in FIRE-3 (AIO KRK-0306)

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Background: The FIRE-3 study (AIO KRK-0306) was initiated as a randomized multicenter trial to compare the efficacy of FOLFIRI plus cetuximab or FOLFIRI plus bevacizumab as first-line treatment in metastatic colorectal cancer (mCRC) patients. BRAF and RAS mutations were determined as baseline analysis. The primary end points were overall response rate (ORR) and progression-free survival (PFS) compared to FOLFIRI plus bevacizumab. However, the sample size was not sufficient to determine an association between the use of targeted therapies and the presence of RAS or BRAF mutations.

Methods: Patients treated within the FIRE-3 trial were retrospectively treated for BRAF and RAS mutations using FFPE tumor material supplied by participating centers, and results were reevaluated for the present study. BRAF and RAS mutations were analyzed using a validated next-generation sequencing (NGS) approach. The Kaplan-Meier method was used to calculate the median survival times of BRAF and RAS mutant patients treated with FOLFIRI plus cetuximab or FOLFIRI plus bevacizumab. The log-rank test was used to compare the survival distributions.

Results: BRAF mutations were detected in 29% of patients (n=592), with 19% (n=362) of the tumors showing a BRAF V600E mutation. RAS mutations were found in 36% of patients (n=655), with 31% (n=551) showing a RAS mutation.

Conclusions: In patients with BRAF V600E mutation and RAS mutational status, a significant improvement in overall survival (OS) and progression-free survival (PFS) was observed compared to FOLFIRI plus cetuximab. This suggests that BRAF and RAS mutations may be important biomarkers for the selection of patients who may benefit from targeted therapies.

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