JACCRO Newsletter

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JACCRO CC-11 のバイオマーカー試験の成果が ESMO Open に掲載されました

試験にご協力頂いた先生方、参加頂いた患者様ご家族の方に改めて感謝いたします。

ORIGINAL RESEARCH

Dynamic changes in *RAS* gene status in circulating tumour DNA: a phase II trial of first-line FOLFOXIRI plus bevacizumab for *RAS*-mutant metastatic colorectal cancer (JACCRO CC-11)

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Background: Few prospective studies have used liquid biopsy testing in *RAS*-mutant metastatic colorectal cancer (mCRC), and its clinical significance remains unknown. Therefore, this study aimed to carry out a biomarker analysis by liquid biopsy using updated data of the phase II trial of FOLFOXIRI plus bevacizumab as first-line chemotherapy for *RAS*-mutant mCRC.

Materials and methods: A total of 64 patients who received modified FOLFOXIRI regimen (irinotecan 150 mg/m^2, oxaliplatin 85 mg/m^2, levofolinate 200 mg/m^2, and fluorouracil 2400 mg/m^2) plus bevacizumab biweekly were enrolled. The primary endpoint was the objective response rate (ORR). Plasma samples were collected at pre-treatment, 8 weeks after treatment, and progression in participants included in the biomarker study. The levels of circulating tumour DNA (ctDNA) and specific *KRAS* and *NRAS* variants were evaluated using real-time PCR assays.

Results: There were 62 patients (median age: 62.5 years, 92% performance status 0, 27% right side) who were assessable for efficacy and 51 for biomarker analysis. ORR was 75.8% (95% confidence interval 65.1% to 86.5%). The median progression-free survival was 12.1 months, and the median overall survival (OS) was 30.2 months. In 78% of patients, *RAS* mutations disappeared in the ctDNA at 8 weeks after treatment; these patients tended to have better outcomes than those with *RAS* mutations. Interestingly, *RAS* mutations remained undetectable during progression in 62% of patients. Survival analysis indicated that the median OS from progression was significantly longer in patients with *RAS* mutation clearance than in those with *RAS* mutation in the ctDNA at disease progression (15.1 versus 7.3 months, hazard ratio: 0.21, $P = 0.0046$).

Conclusions: Our biomarker study demonstrated no *RAS* mutations in ctDNA at disease progression in 62% of patients with *RAS*-mutant mCRC. Both OS and post-progression survival were better in patients with clearance of *RAS* mutations in ctDNA after triplet-based chemotherapy.

Key words: colorectal cancer, *RAS* mutation, FOLFOXIRI plus bevacizumab, liquid biopsy