JACCRO Newsletter

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JACCRO CC-13AR が ESMO OPEN に掲載されました

東北大学腫瘍内科 大内康太先生を筆頭著者として「RAS 野生型転移性大腸がん患者における一次治療の Biomarker としての Genome-wide メチル化検索の有用性について」が 2025 年 5 月 6 日付けで ESMO OPEN に掲載されました。

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ORIGINAL ARTICLE

Genome-wide DNA methylation status as a biomarker for clinical outcomes of first-line treatment in patients with *RAS* wild-type metastatic colorectal cancer: JACCRO CC-13AR

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Background: Several retrospective studies have demonstrated an association between genome-wide DNA methylation status (GWMS) and clinical outcomes after treatment with anti-epidermal growth factor receptor antibody in metastatic colorectal cancer (mCRC). This biomarker study evaluated the association of GWMS with clinical outcomes in mCRC patients who were enrolled in a randomized phase II DEEPER trial of comparing modified (m)-FOLFOXIRI plus bevacizumab (Bev) and m-FOLFOXIRI plus cetuximab (Cet) as first-line treatment.

Patients and methods: GWMS was measured using tumor tissues which were collected from patients with tissue samples available in the DEEPER trial. In addition, tumor tissues were classified into high-methylated colorectal cancer (HMCC) and low-methylated colorectal cancer (LMCC) groups. The correlation between GWMS and survival was analyzed by comparing progression-free survival (PFS) and overall survival (OS) between the two different groups of GWMS.

Results: Of the 137 patients, 15 were classified into the HMCC group, and 122 were classified into the LMCC group; 71 patients were treated with Bev, and 66 were treated with Cet. In the Bev arm, OS was significantly shorter in the HMCC group than in the LMCC group (median 24.2 versus 48.9 months, $P = 0.03$). In the Cet arm, both PFS and OS were significantly shorter in the HMCC group than in the LMCC group (median 4.0 versus 14.3 months, $P < 0.01$ and median 13.6 versus 42.7 months, $P < 0.01$). The interaction tests revealed that GWMS was a significant predictor of PFS and OS in the Cet arm.

Conclusions: GWMS was associated with survival in *RAS* wild-type mCRC patients treated with initial chemotherapy. Also, it may serve as a predictor for selection of molecular-targeted antibodies in first-line treatment.

Key words: colorectal cancer, biomarker, predictive factor, anti-EGFR treatment, genome-wide DNA methylation status