SO-14 The prognostic impact of KRAS G12C mutation in patients with metastatic colorectal cancer: A multicenter retrospective observational study

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Background: KRAS is one of the most frequently mutated oncogenes in colorectal cancer (CRC). Recently, a novel therapy targeting KRAS G12C mutation has demonstrated promising activities for corresponding advanced solid tumors including metastatic CRC (mCRC). However, the prognostic impact of the KRAS G12C mutation remains unclear in patients with mCRC. Therefore, the aim of this study was to evaluate the prognostic impact of KRAS G12C mutation in mCRC in a large cohort of real-world data.

Methods: We retrospectively reviewed medical records of patients with mCRC who received the first-line chemotherapy between January 2005 and December 2017 at four large oncology facilities in Japan. Patient characteristics and survival outcomes were compared between the patients with KRAS G12C and non-G12C mutations.

Results: Among 2,457 patients with mCRC, a total of 1,632 patients met selection criteria. Of these, 696 patients had KRAS exon 2 mutations. In terms of the distribution of KRAS exon 2 mutations, the following six mutations accounted for the majority of them (% of all population [n = 1632]): KRAS G12D (16.0%, n = 261), G13D (9.8%, n = 160), G12V (9.3%, n = 151), G12C (2.8%, n = 45), G12S (2.2%, n = 36), and G12A (1.9%, n = 31). Patient characteristics were not significantly different between patients with the KRAS G12C and non-G12C mutations. At a median follow-up of 64.8 months, patients with the KRAS G12C mutation showed significantly shorter first-line progression-free survival (PFS; median, 9.4 vs. 10.8 months, hazard ratio [HR]: 1.47, 95% confidence interval [CI] 1.08-2.01; P = 0.015) and overall survival (OS; median, 21.1 vs. 27.3 months, HR: 1.50, 95% CI 1.08-2.08, P = 0.015) than those with non-G12C mutations. Multivariate analysis also showed that KRAS G12C mutations were significantly associated with shorter first-line PFS (adjusted HR, 1.43; 95% confidence interval [CI], 1.04—1.96, P=0.030) and OS (adjusted HR, 1.42; 95% CI, 1.01—2.00, P=0.044).

Conclusions: We demonstrated that KRAS G12C mutation was significantly correlated with shorter first-line PFS and OS compared to non-G12C mutations. These findings indicate the importance of a stratified treatment targeting KRAS G12C mutation in mCRC.

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