Biomarkers

38P Single-nucleotide polymorphisms of DPYD predict adverse events associated with 5-fluorouracil in patients with gastrointestinal cancer

Department of Surgery, Tohoku University Hospital, Sendai, Japan

Aim/Background: The aim of this study was to investigate the association between 5-fluorouracil (5-FU)-related adverse events (AEs) in Japanese patients with gastrointestinal cancer treated with 5-FU and the patients' genotypes of DPYD.

Methods: Sequence analyses of 20 polymorphisms in DPYD were performed using genomic DNA extracted from peripheral blood mononuclear cells of 103 patients with gastric (n = 34) or colorectal (n = 69) cancer. The 5-FU-related AEs of in these 103 patients were evaluated based on the medical records of patients in each of three groups: the intravenous administration group (i.v. group, n = 51), oral administration group (p.o. group, n = 106), and all-regimens group (both i.v. and p.o. group, n = 157). The associations between the incidence of AEs and each genotype were statistically analyzed.

Results: Three single-nucleotide polymorphisms (SNPs) of DPYD were identified; c.496A > G (n = 7), c.1905 + 1G > A (n = 1), and c.2303C > A (n = 3), those of which were all heterozygote. Among them, five of seven c.496A > G individuals suffered from grade 3 neutropenia (n = 1), fatigue (n = 3), and diarrhea (n = 2). One of three c.2303C > A individuals suffered from grade 3 neutropenia and fatigue. The one c.1905 + 1G > A individual suffered from grade 4 neutropenia and grade 3 hyperbilirubinemia. The patients in the all-regimens group carrying any one of three DPYD SNPs showed statistically significant associations with the incidence of AEs of any type and fatigue. A similar trend was observed in the p.o. group, but not in the i.v. group.

Conclusions: These findings suggest that the DPYD SNPs c.496A > G, c.1905 + 1G > A, and c.2303C > A might be predictive factors for the occurrence of severe 5-FU-related AEs.

Disclosure: All authors have declared no conflicts of interest.