S20-1 Significant effects of polymorphisms in CYP2D6 and ABCC2 on clinical outcomes of adjuvant tamoxifen therapy for Japanese breast cancer patients

◯Taisei MUSHIRODA[1]

[1]RIKEN Center for Genomic Medicine

The clinical efficacy of tamoxifen is suspected to be influenced by the activity of drug-metabolizing enzymes and transporters involved in the formation, metabolism and elimination of its active forms. We investigated association of polymorphisms in the pharmacokinetics-related genes to clinical outcome of patients with tamoxifen treatment.

We genotyped 282 hormone receptor-positive, invasive breast cancer patients receiving tamoxifen monotherapy. *CYP2D6* variants were significantly associated with shorter recurrence-free survival (P = 0.000036, hazard ratio (HR) 9.52 in patients with 2 variant alleles vs without variant allele). In addition, a significant association was found at rs3740065 in *ABCC2* (P = 0.00017, HR 10.64 in patients with AA vs GG genotypes). The number of risk alleles of *CYP2D6* and *ABCC2* showed cumulative effects on recurrence-free survival. The patients carrying 4 risk alleles showed 45-times higher risk of recurrence compared to those with ≤1 risk allele.