[O27-4] O27-4: Oncology (2)
Chairs: Takayasu Kurata, Japan / Etienne Chatelut, France
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[O27-4-4] UGT1A1 polymorphism may be a prognostic indicator of stage I ovarian clear cell carcinoma patients treated with irinotecan

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Background
Homozygous UGT1A1*6 and *28 or compound heterozygous UGT1A1*6/*28 are known to be poor metabolizers of irinotecan, having a higher risk of severe adverse events. The appropriate irinotecan dose that takes into account UGT1A1 polymorphisms is still controversial. We investigated whether UGT1A1 polymorphisms are related with irinotecan treatment outcome of ovarian cancer.

Methods
Eleven patients of stage I clear cell ovarian cancer who received irinotecan as first-line chemotherapy were recruited to this study, and their UGT1A1 genotypes were examined. The chemotherapy regimen included administration of 60 mg/m² irinotecan on days 1, 8, and 15; and 60 mg/m² cisplatin on day 1 repeated every 4 weeks. Progression-free survival (PFS), overall survival (OS) and adverse events were analyzed retrospectively.

Results
Three patients harbored UGT1A1*1/*6 while another three harbored UGT1A1*1/*28. Five patients were classified as wild-type (UGT1A1*1/*1). Two patients with a wild-type genotype experienced recurrence and one died of tumor progression, whereas no recurrence or death was observed in patients with heterozygous genotypes. The median OS and PFS rates of the heterozygous group were both 88.5 months (range: 63.4–145.8 months), whereas these rates were 83.3 months (range: 44.8–149.0 months) and 83.3 months (range: 16.8–149.0 months) in the wild-type group, respectively. Heterozygous group tended to have a better prognosis because no recurrence or death occurred, although no significant difference was observed (PFS (p=0.101) or OS (p=0.221)) likely because of the small sample size. On the other hand, adverse events tended to be more severe in patients with UGT1A1*6 and *28. All 6 patients in the heterozygous group had neutropenia of grades 3, whereas 2 patients had grade 3 and another 3 had grade 2 neutropenia in the wild-type group (p=0.061).

Conclusions
Our results speculate that UGT1A1 polymorphisms may be a prognostic marker of irinotecan treatment. If this results will be verified in a prospective study with a larger population, it is worth considering that the irinotecan dose can be increased to optimal levels of efficacy in UGT1A1 wild-type patients.

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