P-IS-1 ERCC1 polymorphism : a predictive factor of resistance to first－line platinum－based chemotherapy in epithelial ovarian cancer

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Objectives : ERCC1 is a DNA repair gene associated with resistance to DNA damaging agents. In this study we hypothesized that the polymorphism of ERCC1 Asn118Asn (C->T) might affect the platinum-resistance of epithelial ovarian cancer patients who received platinum-taxane chemotherapy postoperatively.
Methods : Using the SNapShot assay, polymorphism in ERCC1 was assessed in 60 patients.
Platinum-resistance was defined as progression on platinum-based chemotherapy or recurrence within 6 months of completing therapy. The Pearson Chi-square test, Fisher's exact test, and Mann-Whitney test were used to compare the genotypes and clinicopathological variables between the resistant and non-resistant groups. Then, multivariate logistic regression analysis was performed to adjust for confounding effect between the variables.
Results : Although not significant, platinum-resistance was less frequently observed in the patients with the C/T + T/T genotypes (P = 0.064). Moreover, a multivariate analysis showed that the C/T + T/T genotypes constituted an independent predictive factor of reduced risk for platinum-resistance in ovarian cancer (Odds Ratio 0.17, 95%Confidence Interval 0.04-0.74, P = 0.018). No significant correlation was observed between overall survival and ERCC1 polymorphism.
Conclusions : Our results suggest that the genotyping of the ERCC1 polymorphism Asn118Asn may be useful in predicting platinum-resistance of epithelial ovarian cancer patients, however, these findings require prospective confirmation.

P-IS-2 PDZK1 is a potential target for 1q21-q22 amplification frequently detected in drug resistant ovarian cancer

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[Objective] Prognosis of ovarian cancer patients are deeply affected by chemotherapy response after cytoreductive surgery. Our purpose is to find characteristic genetic changes that define chemotherapy resistant phenotype in ovarian cancer.
[Methods] We detected whole chromosomal changes by comparative genomic hybridization (CGH) in 28 ovarian cancer specimens removed at first surgery before chemotherapy. Expression of candidate genes, including PDZ domain containing 1 (PDZK1), on amplified chromosomal region was detected by quantitative real time PCR. [Results] Amplification of 1q21-q22 appears significantly frequent (p = 0.0183) in chemoresistant tumors (9/14) than chemosensitive tumors (2/14). Those who harbour 1q21-q22 amplification showed deteriorated 5 year survival rate (35%) than patients without the aberration (49%). No patients with PDZK1 over expressed tumor reached to 2 years survival, while 33%patients with low expression achieved 5 year survival. [Conclusion] PDZK1 is known to interact with cMOAT and reported to have role in multi-drug resistance. Our results indicate that acquired PDZK1 overexpression with 1q21-q22 chromosomal amplification during carcinogenesis have critical role in forming drug refractory ovarian cancer.