Biomarkers

**207P BIOMARKER ANALYSES OF A PHASE I/II STUDY OF NANOPARTICLE ALBUMIN-BOUND PACLITAXEL PLUS CISPLATIN IN THE TREATMENT OF ADVANCED NASOPHARYNGEAL CARCINOMAS**

W. Liang, L. Zhao, X. Wu, Y. Huang, H. Zhao, Z. Li
Department of Medical Oncology, Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, Guangzhou, CHINA

**Aim:** A phase I/II study of nanoparticle albumin-bound paclitaxel (nab-paclitaxel) plus cisplatin in the treatment of advanced nasopharyngeal carcinomas (NPC) has been completed (NCT01735409). Here we reported the outcomes of biomarker analyses.

**Methods:** The tumor tissues and baseline blood sample of all included patients were prospectively collected. The expression of secreted protein acidic and rich in cysteine (SPARC), excision repair cross-complementation group (ERCC1), β-tubulin III and Breast cancer 1 (BRCA1) were examined by immunohistochemical (IHC) staining. The single nucleotide polymorphism (SNP) of ATP-binding cassette B1 (ABCB1) 2677 was detected by DNA sequencing. RECIST 1.1 was used to evaluate the response and CTC AE 4.0 was used to assess the toxicity.

**Results:** A total of 69 patients with advanced NPC were enrolled. The overall objective response rate (ORR) was 66% (42/64) and median progression free survival (PFS) was 9 months (95% CI 6-12). Stromal-vascular SPARC over-expression indicated significantly better response (74% vs. 29%, OR = 7.1, 95% CI 1.2 to 41.1; \( P = 0.03 \)) and prolonged PFS (9 vs. 3 months, \( P = 0.01 \)). However, SPARC expression on the tumor cells as well as other biomarkers including β-tubulin III, ERCC1 and BRCA1 failed to show substantial predictive value. ABCB1 2677 homozygous genotype (GG/TT) indicated inferior tumor response (OR = 0.5, 95% CI 0.2 to 1.8; \( P = 0.33 \)) and higher incidence of Grade 3/4 toxicity (OR = 1.3, 95% CI 0.4 to 4.7; \( P = 0.69 \)) but without significance. The above results were confirmed by adjusting for history of chemotherapy and dose level in the multivariate analysis. Additionally, those with simultaneously low tumoral β-tubulin III, ERCC1 and BRCA1 expression and ABCB1 2677 heterozygotes represented significantly greater tumor response rate (100% vs. 64%, \( P = 0.04 \)) and longer PFS (\( P = 0.03 \)).

**Conclusions:** SPARC expression in the stromal-vascular, rather than that on the tumor cells, predicts the sensitivity of patients to nab-paclitaxel plus cisplatin. Other markers (β-tubulin III, ERCC1, BRCA1) failed to show significant predictive value. ABCB1 2677 loci SNP were not associated with efficacy and toxicity. In addition, we showed some evidences that combination of biomarkers may improve the predictive accuracy.

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