

Dose-Response Effect Between P53 Concentrations, Survival and Responsiveness in Patients with Epithelial Ovarian Cancer Treated with Platinum-Based Chemotherapy (Meeting abstract).

Sub-category: [Gynecological Cancer](#)

Category: Gynecological Cancer

Meeting: [1999 ASCO Annual Meeting](#)

Abstract No: 1454

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Abstract: This study was designed to determine whether patients who received adjuvant chemotherapy for epithelial ovarian cancer could be stratified into groups with different prognoses based on the immunoassay-quantified expression levels of two proteins--the p53 tumor suppressor and its downstream mediator WAF1 (p21/CIP1/SDI1)--rather than by conventional immunostaining. The concentrations of both proteins, measured in ovarian tumor extracts from 120 patients, by an immunofluorometric assay developed by the authors (p53) and by a commercially available immunoassay (WAF1), were also compared between groups differing on the basis of treatment response. Whereas p53 levels were elevated in patients with advanced stage disease ($p = 0.02$) or poorly differentiated ($p = 0.03$), suboptimally debulked tumors ($p = 0.02$), as well as in patients who failed to respond to chemotherapy ($p = 0.03$), statistically significant associations between concentrations of p53 and WAF1 were not found. Although also not significantly associated with treatment response and clinicopathologic markers of prognosis, WAF1 expression was suggested to be reduced in more advanced disease. Univariate Cox regression analysis showed that p53 concentrations above the median indicated higher relative risks (RR) for relapse ($p = 0.04$) and death ($p < 0.01$) and provided evidence for a dose-response effect between p53 concentrations and risks for relapse ($p = 0.04$) and death ($p < 0.01$). Multivariate analysis confirmed these observations (RR = 1.50; $p = 0.05$ for relapse and RR = 1.92; $p = 0.03$ for death). WAF1-positivity was not a significant predictor of outcome in survival analysis. In conclusion, p53 expression was an independent indicator of prognosis in ovarian carcinoma patients treated with adjuvant platinum-based chemotherapy and was associated with responsiveness. Prognostic and predictive implications of WAF1 expression in our patients, however, could not be demonstrated.