

PROGNOSTIC AND PREDICTIVE VALUE OF p53 AND WAF1 EXPRESSION IN EPITHELIAL OVARIAN CANCER (Meeting abstract).

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Abstract: WAF1 is an inhibitor of cell cycle progression and of DNA replication whose expression is regulated by the p53 tumor suppressor gene. While p53 alteration, detected as mutation of the p53 gene or as accumulation of mutant p53 protein, is a common feature of ovarian carcinoma and may identify patients with unfavorable prognosis and resistance to chemotherapy, the prognostic and predictive significance of possibly decrease WAF1 expression levels has not been investigated. Tumor tissues from 148 consecutive patients with primary epithelial ovarian carcinoma were assayed both for WAF1 protein using colorimetric immunoassay and for p53 protein using an immunofluorimetric assay developed by the authors. Detailed clinicopathologic information, as well as patient response to treatment, were collected and related to p53 and WAF1 concentrations in the tumor extracts. Statistical analyses used to reveal these associations included contingency tables and Cox proportional hazard regression analysis. Elevated p53 concentrations were associated with advanced stage ($p = 0.002$) and high grade disease ($p = 0.05$), the presence of residual tumor ($p = 0.005$) in suboptimally debulked patients ($p = 0.008$), and elevated post-operative CA-125 values ($p = 0.004$). p53-positivity was also more common in patients who did not respond completely to chemotherapy ($p = 0.05$) and whose tumors had lower WAF1 levels ($p = 0.06$). Trends also suggested that WAF1 positivity was associated with endometrioid histotype, optimal debulking surgery, small residual tumor and high CA-125 pre-operative values. while p53 positivity was a significant indicator of increased risk for relapse. p53-positivity indicated poorer prognosis in patients given chemotherapy ($p = 0.01$) and was suggestive of increased risk of treatment failure ($p = 0.01$) while WAF1 expression was not associated with treatment outcomes. These results strongly suggest the prognostic and predictive value of p53 protein accumulation in ovarian cancer while the functional status of the WAF1 protein accumulation needs further investigation.