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Comparative Study of DNA Repair and Cell Proliferation Markers in High Grade Neuroendocrine Carcinoma of the Uterine Cervix and Small Cell Carcinoma of the Lung

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Background: The optimal treatment for high grade neuroendocrine carcinoma of the uterine cervix (cNEC) remains undetermined. Most patients (pts) are treated with chemotherapy regimens used for small cell lung cancer (SCLC) because of both tumors' histological similarity and aggressive behavior. DNA replication and DNA damage repair processes could play a role in determining the tumors' behavior and responses to treatment.

Methods: The rate of expression of thymidine kinase (TK), thymidylate synthetase (TS), proliferating cell nuclear antigen (PCNA), replication protein A (RPA), Ki-67, and DNA excision repair protein (ERCC-1) in tumor specimens from 20 pts with cNEC and 15 pts with SCLC seen at our institution in 1977-2010 was determined by using immunohistochemical methods. No pre-selection criteria other than the primary pathological diagnosis were used. Unpaired t-test analysis was performed and two-tailed P values were calculated to compare the means of the two groups.

Results: RPA and Ki-67 were expressed at significantly higher levels in SCLC than in cNEC (P=0.04 and 0.002, respectively). No significant difference in the expression of TK, TS, PCNA or ERCC-1 was found between the two groups. The mean percent of positive cells and standard error of the mean for SCLC vs. cNEC were 74.7% (9.4) and

48.3% (7.7) for RPA, 49.9% (8.4) and 16.9% (5.3) for Ki-67, 49.7% (10.8) and 58.4% (6.4) for TK, 45.0% (11.3) and 25.3% (6.7) for TS, 56.6% (7.9) and 64.5% (5.9) for PCNA, and 43.5% (9.3) and 29.9% (7.8) for ERCC-1, respectively. Eight pts (53.3%) with SCLC expressed very high levels of RPA (>80% cells positive), vs. only 2 pts (10%) with cNEC. High levels of Ki-67 expression (>80% cells positive) were observed in 4 pts (26.6%) with SCLC; none of the patients with cNEC had such high levels.

Conclusion: RPA and Ki-67 are both expressed at significantly higher levels in SCLC than in cNEC. The mean expression rate, although not statistically significant, possibly due to the small sample size, was higher in SCLC than in cNEC for all analyzed markers, with the sole exception of PCNA. Further studies are needed to determine possible correlation between these markers and clinical outcomes, including survival, as well as response to therapy.