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Presentation Title: **Analysis of the differential expression of proteolytic factors uPA, PAI-1, and seven tissue kallikreins (hk5,6,7,8,10,11,13) between primary ovarian carcinoma tissues and corresponding omentum metastases**

Presentation Start/End Time: Monday, Apr 18, 2005, 1:00 PM - 5:00 PM

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Antigen levels of proteolytic factors were determined in 142 primary ovarian carcinoma tissues obtained from patients operated on between 1985 and 1999, who were classified as stage FIGO 1 to 4. Proteolytic factors uPA (urokinase-type plasminogen activator), PAI-1 (inhibitor type-1 to uPA) and 7 different tissue kallikreins (hk5,6,7,8,10,11,13) were measured by ELISA and related to total protein content of the tumor tissue extract. These factors were also quantified in corresponding metastasis tissues (omentum). Level differentials were defined as level in metastasis minus level in primary tumor tissue. In pairwise comparison, statistically significant increases in metastasis level compared to primary tumor level were only found for uPA (148% of mean) and hk5 (84% of mean).

In all patients, including those with residual tumor, differences in uPA had significant impact on progression-free survival (PFS), as well as tissue kallikreins hk6,7 and 10 (others were not significant). Larger differentials were associated with disease progression, as shown by univariate Cox models with fractionally ranked level differentials: The hazard ratios for the 75th percentile of these differentials compared to the median were as follows: 1.50 for uPA (1.14 - 1.97); 1.66 for hk6 (1.16 - 2.39); 1.36 for hk7 (1.00 - 1.86); and 1.65 for hk10 (1.16 - 2.34). Some of the impact for uPA, hk6, and hk10 in all patients may be attributable to poorer debulking results (and consequently an increased residual tumor burden) in patients with higher levels in metastasis.

In patients with optimal debulking (i.e., with no macroscopic residual tumor), only the level differentials of hk5,7,8 and 11 had a significant impact on progression free survival. Larger differentials were associated with disease progression: According to univariate Cox models with fractionally ranked level differentials, the hazard ratios for the 75th percentile of these differentials compared to the median were as follows: 2.18 (1.03 - 4.60) for hk5; 2.38 for hk7 (1.08 - 5.27); 2.6 for hk8 (1.15 - 6.01); and 2.03 for hk11 (1.02 - 4.05).

Our results show that serine proteases such as uPA and some of the tissue kallikreins play a clinically meaningful role as prognostic markers in primary ovarian cancer.

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