

#243 Tumor Specific Activity of Kallikrein 6 Protein is a Prognostic Marker of Ovarian Carcinoma. Barry Roy Hoffman, Dionyssios Katsaros, Andreas Scorilas, Phedias Diamandis, Stefano Fracchioli, Irene A. Rigault de la Longrais, and Eleftherios P. Diamandis. *Mount Sinai Hospital, Toronto, Canada, and University of Turin, Turin, Italy.*

Human kallikrein 6 protein (hK6) is one of the newly discovered members of the human kallikrein-like gene family, a subgroup of serine proteases clustered on chromosome 19q 13.3-13.4. Using a sensitive and specific immunofluorometric assay, we determined the amount of hK6 in extracts of 180 ovarian tumors and correlated specific activity (ng hK6/mg total extract protein) with clinico-pathological variables documented at the time of surgical excision and with outcome [progression free survival (PFS), overall survival (OS)] monitored over a median interval of 60 months. Over this time period, cancer progressed in 54% of the study patients and 34% of the patients died. 35 ng hK6/mg extract protein was selected on the basis of a Chi Square profile related to overall survival as the optimal specific activity to differentiate tumors positive and negative for hK6. 30% of the tumors were positive for hK6 using this criterion. Tumor hK6 specific activity was higher in late stage disease, serous histotype, residual tumor >1 cm and suboptimal debulking (> 1 cm) ($p < 0.05$) whereas there was no relationship with grade or response to chemotherapy. Univariate analysis revealed that patients with positive hK6 tumor levels were more likely than those with negative levels to suffer progressive disease and to die [hazard ratio estimated from the Cox proportional hazard regression model of 1.71 ($p = 0.015$) and 1.88 ($p = 0.022$), respectively]. Survival curves echoed similar findings, namely that patients with positive tumor levels of hK6 relapsed more frequently and died more rapidly ($p = 0.013$ and 0.019 , respectively). Although the adverse prognostic effect of positive hK6 disappeared when the entire database was subjected to multivariate analysis adjusted for stage of disease, tumor grade, residual tumor, histologic type and age, hK6 positivity was retained as an independent prognostic variable in several subgroups of patients, namely those with low tumor grade (grade I and II) and those with optimal debulking of the ovarian carcinoma at the time of initial surgical exploration. Specifically, hazard ratios derived from Cox proportional hazard regression analysis and related to PFS and OS were 4.3 ($p = 0.027$) and 4.1 ($p = 0.023$), respectively, for the low tumor grade group and 3.8 ($p = 0.019$) and 5.6 ($p = 0.011$), respectively, for patients in whom tumor had been optimally debulked. We conclude that tumor kallikrein 6 protein specific activity has utility as a prognostic marker in ovarian cancer, particularly in subgroups of patients with early grade disease and in those in whom less than 1 cm of tumor remains following surgical excision.