Clinical relevance of kallikrein-related peptidase 6 (KLK6) and 8 (KLK8) mRNA expression in advanced serous ovarian cancer.

Abstract:
Most members of the kallikrein-related peptidase family have been demonstrated to be dysregulated in ovarian cancer and modulate tumor growth, migration, invasion, and resistance to chemotherapy. In the present study, we assessed the mRNA expression levels of KLK6 and KLK8 by quantitative PCR in 100 patients with advanced serous ovarian cancer FIGO stage III/IV. A pronounced correlation between KLK6 and KLK8 mRNA expression (rs = 0.636, p< 0.001) was observed, indicating coordinate expression of both peptidases. No significant associations of clinical parameters with KLK6, KLK8, and a combined score KLK6+KLK8 were found. In univariate Cox regression analysis, elevated mRNA levels of KLK6 were significantly linked with shortened overall survival (OS) (hazard ratio [HR] = 2.07, p = 0.007). While KLK8 values were not associated with patients’ outcome, high KLK6+KLK8 values were significantly associated with shorter progression-free survival (HR = 1.82, p = 0.047) and showed a trend towards significance in the case of OS (HR = 1.82, p = 0.053). Strikingly, in multivariable analysis, elevated KLK6 mRNA values, apart from residual tumor mass, remained an independent predictive marker for poor OS (HR = 2.33, p = 0.005). As KLK6 mRNA and
protein levels correlate, KLK6 may represent an attractive therapeutic target for potent and specific inhibitors of its enzymatic activity.