S100A9 and EGFR Gene Signatures Predict Disease Progression in Bladder Cancer Patients after Chemotherapy

Introduction and Objective: In a gene expression profile analysis carried out in an earlier study by our group, IL1B, S100A8, S100A9, and EGFR were shown to be important mediators of MIBC progression. The aim of the present study was to investigate the ability of these gene signatures to predict disease progression after chemotherapy in patients with locally recurrent or metastatic MIBC.
Material and Methods: Patients with locally recurrent or metastatic MIBC who received chemotherapy were enrolled in the study. In addition, 69 primary MIBC samples were analyzed. The expression signatures of four genes were measured by real-time PCR. The prognostic effect of these genes was evaluated by Kaplan-Meier analysis and Cox regression.
Results: Two of the four genes, S100A9 and EGFR, were determined to significantly influence disease progression ($p=0.023$, $p=0.045$, respectively). Based on a ROC curve, a cutoff value (36.1683) for disease progression was determined. The time to progression was significantly different between the good- and poor-prognostic signature groups, both in all patients and in the subgroup of those who had previously undergone cystectomy ($p<0.001$, respectively). In multivariate Cox regression analysis, gene signature was the only factor that significantly influenced disease progression in these patients (HR: 5.380, CI: 1.570–18.436, $p=0.007$). Patients in the good-prognostic signature group had a significantly longer cancer-specific survival time than those in the poor-prognostic signature group ($p=0.010$).
Conclusions: The gene signatures S100A9 and EGFR may be useful markers for predicting chemoresponse in patients with locally recurrent or metastatic MIBC.

Keywords: Urinary Bladder Neoplasms; Drug Resistance, Neoplasm; Receptor, Epidermal Growth Factor; Urinary Bladder