Prediction of Androgen Deprivation Therapy Response Using Laser Captured Microdisection Technique in Patients with Metastatic Prostate Cancer

Introduction and Objective: Prostate cancer (PC) is assumed to be sensitive to androgen deprivation therapy **(**ADT). However, a recent investigation showed that ADT leads some PC to malignant phenotype. The aim of study is to predict ADT response by estimating quantitative androgen receptor (AR) genes expression in selected cells using laser captured microdissection (LCM).

Materials and Methods: The prostate biopsy specimens were obtained from 45 men with bones metastatic PC. The mean serum prostate-specific antigen (PSA) level was 8.6–13700 ng/mL (median 219 ng/mL). Gleason scores (GS) were ≤7 (n = 8), 8 (n = 10), 9 (n = 26), and 10 (n = 1). Extend of disease (EOD) were 1 (n=24), 2 (n=10), 3 (n=9), and 4 (n=2). ADT consisted of medical or surgical castration with or without anti-androgen agents. Tumor and stromal cells were separately collected by LCM (Leica 6500). Total RNA was isolated, cDNA was synthesized, and reverse transcriptase- polymerase chain reaction (RT-PCR) was conducted to assess the AR mRNA expression. We defined PSA nadir less than 0.01 as the good response to ADT. Correlations and area under the curve (AUC) to predict the good response were statistically analyzed using AR expression level and other parameters.

Results: Good responders (n=10) had significantly better cancer-specific survival than non-good responders (n=35) (p = 0.0013). There was no significant difference between ADT response and clinicopathological findings including age, GS, or PSA level. On the other hand, relative AR mRNA expression was significantly increased in both PC foci and stroma adjacent to PC (p=0.003 and 0.015, respectively). AUC of AR mRNA expression in PC was the highest among the parameters (AUC=0.84, p<0.001). Combining clinical and LCM data provided a significantly highly predictive model of good response in logistic model analysis (p< 0.001).

Conclusions: Our findings indicate that AR mRNA levels in cancer cells selectively collected from biopsy specimens by LCM efficiently predicted therapeutic response to ADT. Further analyses of AR down-stream genes might detect more powerful predictors for the strategic PC treatment.