Nadir PSA Alone or in Combination with Baseline PSA Improves Prediction of Treatment Outcome in Intermediate and High Risk Localized Prostate Cancer Patients Treated by Definitive External Beam Radiotherapy with Androgen Deprivation.

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BACKGROUND: Localized prostate cancer is effectively treated by definitive external beam radiation therapy (EBRT) in combination with androgen deprivation therapy (ADT). The aim of this study is to investigate the effect of known tumor characteristics and parameters of treatment response in predicting biochemical disease-free survival (BFS).

HYPOTHESIS: Composite variables combining tumor characteristics such as baseline PSA (bPSA) and the immediate tumor response parameter nadir PSA (nPSA), could improve our ability to predict biochemical free survival.

METHODS: Between January 1998 and December 2010, 229 patients with localized prostate cancer were treated at our institution by definitive EBRT. Of those, 176 with a National Comprehensive Cancer Network (NCCN) intermediate or high risk categories received both ADT and EBRT and were retained for this study. Median duration of androgen blockade was 6 months (range: 4-28 months); Median radiation dose was 72 Gy (Range: 63-72 Gy). Median follow-up time was 4.93 years (range:0.01-15.34 years). The main study endpoint was BFS.

RESULTS: The median age was 72 years (range: 51-92). Seventy three patients (41.5%) had intermediate and 103 (58.5%) had high risk disease. Thirty patients (17.1%) developed biochemical recurrence (BCR). Monovariate analysis identified radiation dose (p=0.001), age (p=0.007), baseline PSA (p <0.001), Gleason's score (p=0.025), T-stage (p=0.013), and nPSA (p <0.001) as significant variables affecting BCR, while ADT duration (p=0.944), PSA pre-radiation therapy (preRT) (p=0.077), and time to nadir (p=0.671) did not have significant impact on BFS. BFS was significantly higher in the intermediate vs. high risk group with a 10-year rate of 81% vs 59% (p=0.005). The receiver operating characteristic (ROC) curve identified a bPSA of 13 ng/ml and a nPSA of 0.051 ng/ml as optimal cut off values significantly predicting the patients risk of BCR (p=0.003 and 0.018 respectively). Both parameters were also found to be independent determinants of BFS in multivariate cox regression analysis. Patient grouping by bPSA and nPSA identified 3 groups with significant difference in their risk of BFS: A favorable group with a combination of bPSA <13 ng/mL and nPSA <0.051 ng/m, an unfavorable group which included patients with bPSA ≥13 ng/mL and nPSA ≥ 0.051 ng/ml, and an intermediate group

containing only one unfavorable variable (either bPSA ≥13 ng/ml or nPSA ≥ 0.051 ng/ml). BFS rates were 91% for the favorable group, 66% for the intermediate, and 26% for the unfavorable group (p=0.005).

Conclusion: Nadir PSA at 0.051 is a strong independent predictor of BFS in patients with intermediate or high risk prostate cancer treated by definitive EBRT and ADT. Using this treatment outcome variable in combination with the well-established tumor variable bPSA, improves our ability to predict BFS in this group of patients, which might help initiate early and more individualized and adapted therapy for those who have a high predicted risk of recurrence.