PROSTATE CANCER

Post-ADT PSA kinetics predict survival

Androgen deprivation therapy (ADT) is the most effective available treatment for metastatic hormone-sensitive prostate cancer (HSPC). Although pretreatment PSA kinetics are good indicators of survival, little information exists on the prognostic significance of PSA kinetics after treatment initiation. A study from the Dana-Farber Cancer Institute, Boston, MA, has now produced evidence that a short time to PSA nadir (TTN) after initiation of ADT is an independent predictor of poor survival in patients with metastatic HSPC.

“...a short time to PSA nadir ... is an independent predictor of poor survival...”

“We noticed several patients with metastatic prostate cancer in our own experience who had a very fast drop in their PSA after LHRH [luteinizing hormone-releasing hormone] therapy, reaching a nadir pretty quickly, only to recur at a later date,” explains Toni Choueiri, lead author on the paper. The researchers decided to investigate the observation further, using a longitudinal database of patients who were treated for

prostate cancer at their institution. They analyzed data from 179 patients treated with ADT for metastatic HSPC (median age was 64 years at the start of treatment). PSA level at ADT initiation, nadir PSA, TTN, and PSA decline (PSAD) were analyzed in relation to overall survival. After a median follow-up of 4 years, 63 patients died. The median overall survival was 7 years. Univariate analysis indicated that Gleason score >7, PSA ≥ 47.2 ng/ml at ADT initiation, PSA nadir ≥ 0.2 ng/ml, PSAD >52 ng/ml per year and TTN <6 months were all associated with reduced overall survival. PSA nadir, TTN and Gleason score remained significant predictors of survival in multivariate analysis. The association between TTN and survival was limited to those patients with PSA nadir >0.2 ng/ml. The group with rapid PSAD had much higher baseline PSA levels than the group with slow PSAD, and patients with rapid PSAD or short TTN were also less likely to achieve a PSA nadir <0.2 ng/ml.

“This is the first report to demonstrate that a faster time to reach a PSA nadir after the initiation of ADT was associated with shorter survival duration in men with metastatic HSPC,” says Choueiri. The authors hypothesize that the rapid fall in

PSA might be caused by the effect of ADT on PSA transcription rather than on cancer cell viability. Alternatively, they suggest that the treatment selected for an aggressive, androgen-independent subset of cancer cells. This retrospective study highlights the need for prospective investigations into the utility of PSA kinetics in predicting survival in prostate cancer patients undergoing treatment.

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Original article Choueiri, T. K. *et al.* Time to prostate-specific antigen nadir independently predicts overall survival in patients who have metastatic hormone-sensitive prostate cancer treated with androgen-deprivation therapy. *Cancer* 115, 981–987 (2009).