**Androgen Deprivation Therapy and Overall Survival for Gleason 8 Versus Gleason 9-10 Prostate Cancer**

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**Purpose/Objective(s):** While the addition of androgen deprivation therapy (ADT) to external beam radiation therapy is known to improve overall survival in Gleason 8-10 prostate cancer, it has been hypothesized that Gleason 9-10 disease, which is less differentiated than Gleason 8 disease, may be less sensitive to ADT. To investigate this idea, we examined the association between ADT and overall survival for Gleason 8 versus Gleason 9-10 prostate cancer.

**Materials/Methods:** We identified 20,139 men in the National Cancer Database diagnosed with localized or locally advanced, Gleason 8-10 prostate cancer from 2004 through 2011 who received external beam radiation therapy, with follow-up obtained through 2012. Patients with clinical evidence of nodal or metastatic disease were excluded. Cox proportional hazards regression was used to examine the association between ADT and overall survival.

**Results:** Median follow-up was 4.0 years. 78.2% (9,509) of the 12,160 men with Gleason 8 disease and 86.6% (6,908) of the 7,979 men with Gleason 9-10 disease received ADT. On multivariable analysis, ADT was associated with a significant improvement in overall survival for Gleason 8 patients (adjusted hazard ratio 0.79, 95% confidence interval 0.71-0.88, P<0.001) but not Gleason 9-10 patients (adjusted hazard ratio 0.96, 95% confidence interval 0.83-1.10, P=0.532), with a significant interaction (*P*interaction=0.020). When considering Gleason 9-10 patients separately as Gleason 9 and Gleason 10, a higher Gleason score correlated with a greater adjusted hazard ratio for the association between ADT and overall survival (*P*interaction =0.012).

**Conclusion:** In contrast to the significant survival advantage of ADT for Gleason 8 disease, our results strongly suggest that Gleason 9-10 disease may be less sensitive to ADT and that a higher Gleason score predicts lesser sensitivity. Consideration should be given to treatment intensification for Gleason 9-10 patients through enrollment in clinical trials or potentially adding novel antiandrogens or docetaxel, which have shown efficacy in both castration-resistant and castration-sensitive settings.