**Longer-Term Androgen Deprivation Therapy Improves Cancer-Specific Survival in Patients With Gleason Score 9-10 Prostate Adenocarcinoma: An Individual Patient-Level Meta-analysis of RTOG 8531, 8610, and 9202**

A.U. Kishan,1 X. Wang,2 K.A. Sandler,3 N. Nickols,4 M.L. Steinberg,5 and C.R. King1;

*1Department of Radiation Oncology, University of California, Los Angeles, Los Angeles, CA, 2Department of Medicine, University of California, Los Angeles, Los Angeles, CA, 3David Geffen School of Medicine at UCLA, Los Angeles, CA, 4Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 5University of California, Los Angeles, Los Angeles, CA*

**Purpose/Objective(s):** It has been suggested that Gleason grade 5 prostate carcinoma (PCa) is less responsive to androgen deprivation therapy (ADT) than lower grade PCa. Three randomized trialsdRTOG 8531, 8610, and 9202dhave examined the effect of ADT utilization and duration when used in concert with definitive radiotherapy (RT). The purpose of this study was to evaluate the effect of ADT on clinical outcomes of patients with Gleason score (GS) 9-10 PCa, who by definition had Gleason grade 5- containing PCa.

**Materials/Methods:** Patients enrolled in RTOG 8531 were randomized to lifelong ADT vs. RT alone, those in RTOG 8610 to short-term ADT (STADT, 4 mos) vs. RT alone, and those in RTOG 9202 to long-term ADT (LTADT, 28 mos) vs. STADT. Data was obtained from the NRG via a data sharing agreement to allow for analysis of a total of 351 patients enrolled on these protocols who had GS 9-10 PCa. For overall survival (OS) and distant metastasis-free survival (DMFS), patient-level data were used to obtain hazard ratio (HR) and standard error estimates of pair-wise treatment effects after fitting multivariate Cox proportional hazards models adjusting for age, GS (9 or 10) and T-stage. For cancer- specific survival (CSS), HRs were obtained by fitting cause-specific competing risk models to the data. A Network Meta-Analysis (NMA) approach was adopted for pair-wise meta-analysis of all pairs of treatments. Along with analyzing within-trial comparisons between two treatments, the NMA framework enables incorporation of indirect comparisons constructed from two trials that have one treatment in common.

**Results:** The median follow-up was 6.01 years. Overall, lifelong ADT was associated with significantly improved DMFS, CSS, and OS when compared with RT alone and STADT; only DMFS was improved with lifelong ADT versus LTADT. LTADT offered significantly higher DMFS than STADT ADT, but not RT alone. Though not statistically sig- nificant, the HRs for STADT vs. RT alone were in the direction of an inferior effect on all three outcomes.

**Conclusion:** GS 9-10 PCa appear to show a temporal dose-response to ADT, contrary to the hypothesis that grade 5 cancers are relatively hormone-insensitive. The inferior outcomes with STADT are likely the result of a small sample size. The extension of these findings in the modern era of dose-escalated radiotherapy constitutes an area of future study.