Five Year Results of a Randomized External Beam Radiotherapy Hypofractionation Trial for Prostate Cancer

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Purpose/Objective(s): Based on the assumption that the α/β ratio for prostate cancer is low at 1.5 Gy, a randomized trial was devised with a dose escalation strategy. We hypothesized that using hypofractionation to deliver the equivalent of an 8 Gy difference in 2 Gy fractions would significantly improve biochemical failure (BF) without increasing bladder or rectal side effects. The trial compared 76 Gy in conventional 2.0 Gy fractions (CIMRT) to 70.2 Gy in 2.7 Gy fractions (HIMRT), which was estimated to be equivalent to 84.4 Gy in 2.0 Gy fractions. The results of a planned analysis are described.

Materials/Methods: There were 303 of 307 (goal 300) assessable patients entered between 2002 and 2006. Of these, 152 were assigned to receive CIMRT and 151 to receive HIMRT. Median follow-up for those alive is greater than 60 months in both arms. The rates of BF using the Nadir+2 ng/mL definition and clinical failure, consisting of either local-regional failure or distant metastasis (LRF/DM), and death without failure were estimated by the method of cumulative incidence (CI) allowing for competing risk. Patients without failure who died more than 6.5 months after last PSA assessment were censored at the time of last PSA follow up. Only patients who died within 6.5 months of last PSA assessment were treated as competing risk events at the time of death. Grey's test was used to compare CI rates by treatment arm.

Results: No significant differences were seen between the treatment arms in terms of the distribution of patients by T-category, Gleason score, pretreatment initial PSA, use of androgen deprivation therapy (ADT) or length of ADT. There were 41 BFs with 20 in the CIMRT group and 21 in the HIMRT group. Six BFs occurred within 6.5 months of either LRF or DM, with the earliest event time used as failure time. Competing risk events are comprised of 1 LRF, 2 DM and 4 deaths. The 5-year CI rates of BF were 14.4% (95%CI: 8.8 to 21.5%) for CIMRT, and 13.9% (95%CI: 8.4 to 20.9%) for HIMRT. Rates for LRF/DM were 1.0% and 1.3% for CIMRT and HIMRT at 5 years. Considering any failure, the 5-year CI rates for CIMRT were 15.4% (95%CI: 9.5 to 22.7%) and 15.3% (95%CI: 9.5 to 22.4%) for HIMRT. There were no statistically significant differences in late toxicity between the arms. The grade 2 or higher toxicities for the CIMRT and HIMRT arms were 8.9 and 13.8 (p=0.2) for GU and 4.1 and 5.9% (p=0.5) for GI.

Conclusions: The anticipated failure rate of 15% in the HIMRT arm was accurate, but fewer failures were seen in the CIMRT arm at the time of this planned analysis. With a median follow-up of 5 years, there remain no statistically significant differences between the

treatment arms in terms of BF, any failure, or late side effects. HIMRT is a reasonable option for men with intermediate to high risk prostate cancer.