NEWS BRIEFING 3

22 A Phase III Trial Employing Conformal Photons with Proton Boost In Early Stage Prostate Cancer: Conventional Dose (70.2gye) Compared To High Dose Irradiation (79.2 GyE): Long-term Updated Analysis of Proton Radiation Oncology Group (PROG)/American College Of Radiology (ACR) 95-09

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Purpose/Objective(s): Randomized trial to test the hypothesis that increasing radiation dose to men with early stage prostate cancer above conventional levels improves clinical outcomes.
Materials/Methods: Patients with T1b-T2b prostate cancer and a PSA of <15ng/ml were randomized to receive a boost to the prostate alone using conformal protons (either lateral or perineal fields) of either 19.8 or 28.8 Gray equivalent (GyE). All pts then received 50.4Gy at 1.8Gy per fraction using 3-D conformal photons to the prostate, seminal vesicles, and peri-prostatic tissues. No pt received androgen suppression with their radiation. Local failure (LF), Biochemical failure (BF) defined by ASTRO consensus or Phoenix definitions, and overall survival (OS) were used as outcomes. The Kaplan-Meier estimation with log-rank test was used for the OS rate and the cumulative incidence estimation with Gray's test was used for LF and BF rates.
Results: 391 eligible pts with median follow-up of 8.9 years. 197 received 70.2 GyE (conventional dose) and 196 79.2 GyE (high dose). Median age at diagnosis 67 years and median PSA 6.3. 75.3% had Gleason scores of 6 or less, 15.3% GS 7, and 8.4% GS 8-10. 61.2% had T1c tumors. Men in the high does arm were less likely to have LF than the conventional arm with hazard ratio of 0.57(95% CI: 0.43, 0.74). Ten-year ASTRO BF rates (with backdating) were 35.3% (95% CI=27.9, 43.6) for conventional dose and 16.3% (95% CI=9.8, 22.7) for high dose (*p=0.0001*). For low risk disease (n=227, 58% of total): 10-year BF rate was 29.0% in the conventional dose arm and 6.1% in the high dose arm (p=<0.0001). There was a trend in the same direction for the smaller group of intermediate risk patients (n=144, 37% of total; 44.6 vs. 28.6, p=0.06). 11% patients subsequently required androgen deprivation for recurrence in the conventional dose arm compared with 6% in the high-dose arm (p=0.047). There remains no difference in OS between the arms (83.4(high-dose) vs. 78.4, *p=0.41*). 2.1% of patients in the both arms experienced late urinary or rectal toxicity grade $\geq$3. The cumulative incidence of any grade $\geq$2 late toxicity was 29.4% and 39.4% respectively (p=0.045). Parallel quality of life studies have shown similar levels of satisfaction with bowel and urinary function in both arms.
Conclusions: This RCT shows a long-term advantage in terms of freedom from biochemical failure for men with low and intermediate risk prostate cancer receiving high dose versus conventional dose conformal radiation delivered with mixed proton and photon beams. This advantage was achieved without any associated increase in grade $\geq$3 late urinary or rectal morbidity.

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