

## NEWSBRIEFING 4

### 172 Hypofractionation For Prostate Cancer: Interim Results Of A Randomized Trial

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**Purpose/Objective(s):** Prostate cancer has been hypothesized to have a low  $\alpha/\beta$  ratio based on several, but not all, retrospective analyses. A low  $\alpha/\beta$  ratio, particularly a value of  $<3$ , supports a rationale for hypofractionation. If the  $\alpha/\beta$  ratio were lower than that of the surrounding normal tissues, there would be a therapeutic gain by increasing the effects on the tumor relative to the surrounding normal tissues. We performed a Phase III randomized intensity modulated radiotherapy (IMRT) dose escalation trial using hypofractionation, assuming an  $\alpha/\beta$  ratio of 1.5. The primary hypothesis was that a calculated 8 Gy difference in equivalent 2.0 Gy fractions would significantly improve biochemical failure (BF) without increasing bladder or rectal side effects, and that using hypofractionation the treatment could be delivered in approximately 2.5 weeks less time.

**Materials/Methods:** Between 2002 and 2006, 303 of 307 (goal 300) assessable patients were entered into the trial. Of these, 152 were assigned to receive standard intensity modulated radiotherapy (SIMRT) to 76 Gy at 2.0 Gy/fraction and 151 to receive hypofractionated IMRT (HIMRT) to 70.2 Gy at 2.7 Gy/fraction. The hypofractionation regimen was hypothesized to be equivalent to 84.4 Gy in 2.0 Gy fractions. The selection of an 8 Gy difference was based on a large retrospective database showing a pronounced dose response from 76 to 84 Gy. There were 34 (18 SIMRT and 16 HIMRT) of 200 intermediate risk patients who received short term androgen deprivation (STAD) for a median of 4 mo and 102 (50 SIMRT and 52 HIMRT) of 103 high risk patients in the HIMRT arm who received long term AD (LTAD) for a median length of 24.5 mo. A minimum of 95% of the target volumes received the prescription dose and the pelvic lymph nodes were treated in the high risk patients. The primary endpoint is ASTRO biochemical failure. Median follow-up is 39 mo.

**Results:** There was no significant difference between the treatment arms in the distribution of patients by T-category, Gleason score, pretreatment initial PSA, or use of STAD or LTAD. The 5 yr BF rates for the SIMRT and HIMRT arms were 19% and 14% using the ASTRO definition ( $p=0.2$ ) and 21% and 17% using the nadir+2 definition ( $p=0.7$ ). For the SIMRT and HIMRT arms, 5 year grade 2 or higher GI toxicity was 8% and 6% ( $p=0.5$ ) and GU toxicity was 17% and 25% ( $p=0.2$ ).

**Conclusions:** At the time of this planned initial interim analysis, there is no difference in patient outcome or toxicity for men treated with SIMRT vs HIMRT. If there remains no difference between the treatment arms with longer follow-up, the  $\alpha/\beta$  ratio could be above 3 (possibly even 6.5 or higher), which could translate into reduced efficacy for aggressive hypofractionation regimens. Nonetheless, the data suggest that patients may be treated with HIMRT with similar results in 2.5 weeks less.

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