**NRG Oncology RTOG 0415: A Randomized Phase III Non-Inferiority Study Comparing Two Fractionation Schedules in Patients with Low-Risk Prostate Cancer**

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**Purpose/Objective(s):** To determine whether the efficacy of a hypofractionated (H) schedule is no worse than a conventional (C) schedule in men with low-risk prostate cancer.

**Materials/Methods:** The trial opened to accrual in April 2006 and closed in December 2009. One thousand one hundred fifteen men with low-risk prostate cancer (clinical stage T1-2a, Gleason ≤6, PSA <10) were randomly assigned 1:1 to a conventional (C) schedule (73.8 Gy in 41 fractions over 8.2 weeks) or to a hypofractionated (H) schedule (70 Gy in 28 fractions over 5.6 weeks). The trial was designed to establish with 90% power and alpha = 0.05 that (H) results in 5-year disease-free survival (DFS) that is not lower than (C) by more than 7% (hazard ratio (HR) < 1.52). Secondary endpoints reported include: freedom from biochemical recurrence (FFBR), and overall survival. At the third planned interim analysis (July 2015), the NRG Oncology Data Monitoring Committee recommended that the results of the trial be reported.

**Results:** One thousand one hundred and one protocol eligible men were randomized: 547 to C and 554 to H. Median follow-up is 5.9 years. Baseline characteristics were not different according to treatment arm. Median age = 65 yrs; median pretreatment PSA = 5.4 ng/mL. At the time of analysis there were 185 DFS events; 99 in the C arm and 86 in the H arm. The estimated seven-year disease-free survival is 75.6% (95% CI 70.3 - 80.1) in the C arm and 81.8% (77.5 - 85.3) in the H arm. The DFS HR (C/H) is 0.85 (0.64 - 1.14). Comparison of biochemical recurrence (HR = 0.77, (0.51 - 1.17)) and overall survival (HR = 0.95, (0.65 - 1.41)) also met protocol non-inferiority criteria. Grade ≥ 3 GI toxicity is 3.0% (C) vs. 4.6% (H), Relative risk (RR) for H vs. C 1.53, (95% CI 0.86 - 2.83); grade ≥ 3 GU toxicity is 4.5% (C) vs. 6.4% (H), RR = 1.43 (0.86 -2.37).

**Conclusion:** In men with low-risk prostate cancer, 70 Gy in 28 fractions over 5.6 weeks is non-inferior to 73.8 Gy in 41 fractions over 8.2 weeks.