**Hypofractionated vs Conventionally Fractionated Radiotherapy for Prostate Cancer: 5-year Oncologic Outcomes of the Dutch Randomized Phase 3 HYPRO Trial**

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**Purpose/Objective(s):** Hypofractionated treatment might increase the radiobiological tumor dose without increasing toxicity due to the reported high radiation-fraction sensitivity of prostate cancer. Here, we present the first results on oncologic outcome from the Dutch randomized hypofractionation trial (HYPRO).

**Materials/Methods:** Between March 2007- December 2010, we conducted a multicenter, randomized phase 3 superiority trial, including intermediate-to high risk patients with localized T1b-4NX-0MX-0 prostate cancer. Inclusion criteria were a PSA concentration ≤60 ng/ml, and a WHO performance status <3. Patients were randomly assigned (1:1) to receive conventional treatment with 39 fractions of 2 Gy in 8 weeks (5 fractions per week), or hypofractionated treatment with 19 fractions of 3.4 Gy in 6.5 weeks (3 fractions per week). Randomization was done with a minimization procedure, stratified by risk group and treatment center. The primary endpoint is relapse-free survival (RFS) after treatment. Relapse is defined as biochemical relapse (Phoenix definition), clinical relapse, locoregional or distant relapse, or start of hormonal therapy, whichever occurs first. The aim of this trial was to detect an absolute reduction of 10% of the relapse rate at 5 years in the hypofractionation arm. The Kaplan-Meier method was used to calculate RFS probabilities and Cox regression analysis was applied to compare the RFS between the treatment arms. Analyses were based on intention-to-treat. An α of 0.05 was considered the level of statistical significance.

**Results:** Of the enrolled 820 patients, 804 men were included in this analysis. Median follow-up was 60 months. Androgen deprivation therapy (ADT) was prescribed to 534 patients (66%). The 5-year RFS rates were 77% for conventional treatment and 80% for hypofractionated treatment (p=0.36). The adjusted hazard ratio (HR) was 0.86 (95% CI 0.63-1.16). Factors associated with RFS in multivariate analysis were Gleason score ≤7 (HR=0.46, 95% CI 0.32-0.66, p<0.001), long-term ADT (≥12 months) versus none (HR=0.50, 95% CI 0.31-0.80, p=0.004), and high risk (>25%) of seminal vesicle involvement according to the updated Partin tables (HR=2.59, 95% CI 1.36-4.93, p=0.004).

**Conclusion:** Hypofractionated radiotherapy (19 fractions of 3.4 Gy) resulted in higher RFS rates, but the difference was not statistically significant. These results show no evidence of superiority of hypofractionation over conventional treatment.