PS3 Late breaking

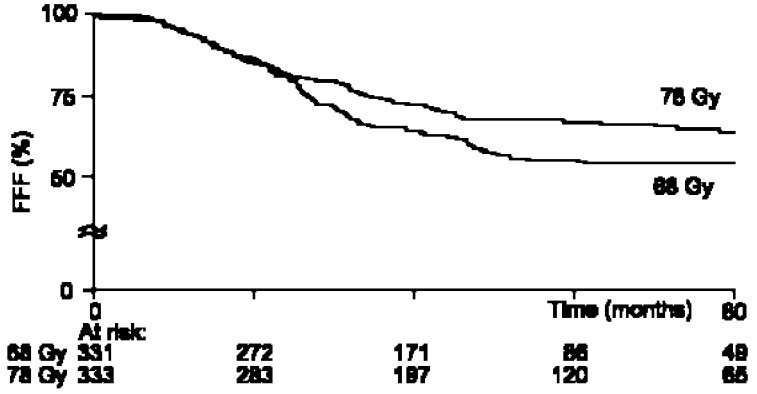
Radiation dose–response in prostate cancer: results of a multicenter randomized phase III trial comparing 68 Gy with 78 Gy

J.V. Lebesque, S.T.H. Peeters[1], W.L.J. van Putten[2], W.D. Heemsbergen[1], A. Slot[3], M.F.H. Dielwart[4], J.M.G. Bonfrer[1], A. van Leenders[2], P.C.M. Koper[2]

[1]The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands; [2]Erasmus Medical Centre, Rotterdam, The Netherlands; [3]Radiotherapy Institute Friesland, Leeuwarden, The Netherlands; [4]Zeeuws Radiotherapy Institute, Vlissingen, The Netherlands

Purpose: To determine whether for prostate cancer patients a radiotherapy dose of 78 Gy improves outcome compared with 68 Gy.

Methods and materials: Between 1997 and 2003, 669 stage T1b–T4N0M0 prostate cancer patients were randomized. Four treatment groups (with specific planning target volumes) were defined based on the probability of seminal vesicle involvement. Stratification was done by hospital, (neo)adjuvant hormonal therapy (HT), age and treatment group. The patients' baseline characteristics were well balanced between both arms [1]. Median initial PSA was 13.0 ng/ml (range 0.4–59.0) and 63% had T1–2 tumors. Differentiation grade was good, moderate and poor in 30%, 55% and 15%, respectively. The 3 prognostic risk groups, low, intermediate and high (Symon et al. [2]), included 18%, 27% and 55% of the patients, respectively. HT was prescribed to 143 intermediate and high risk patients. The primary endpoint was freedom from failure (FFF). Failure was defined as clinical failure (clinical relapse or start new HT) or biochemical failure (ASTRO-definition: 3 consecutive PSA rises with backdating). Patients without failure were censored at last contact or at death. Median follow-up time was 51 months.



Kaplan-Meier curves for both randomization arms showing freedom from failure.

Results: FFF at 5 years was significantly better in the 78 Gy-arm compared with the 68 Gy-arm (64% vs. 54%, $p = 0.025$) (Figure). In all treatment groups FFF was higher in the 78 Gy-arm, but only in group II this difference was significant (83% vs. 60%, $p = 0.006$). Of the three risk groups, intermediate risk patients benefited most from dose-escalation (74% vs. 58%, $p = 0.03$). The gain in the high risk group was smaller (52% vs. 44%, $p = 0.1$), and there was no benefit in the low risk group (84% vs. 86%, $p = 0.7$). No significant differences in overall survival (83% vs. 82%) and freedom from clinical failure (76% vs. 76%) were seen between both arms. Multivariate Cox proportional hazards regression showed that the randomization arm was an independent predictor of FFF, along with initial PSA, differentiation grade, T-stage and HT.

Conclusion: This multicenter randomized trial shows a significantly improved freedom from failure in prostate cancer patients treated to high doses. This benefit was most apparent in intermediate risk patients.

References

[1] Peeters *et al.* IJROBP 2005; 61: 1019–1034.
[2] Symon *et al.* IJROBP 2003; 57: 384–390.