Genitourinary Malignancies

Oral presentations (Mon, 24 Sep, 10.45−12.15)
Prostate cancer

4000 ORAL

Update of the results of the Dutch multicenter randomized phase III trial comparing 68 Gy of external beam radiotherapy with 78 Gy for localized prostate cancer

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Background: After a median follow-up of 51 months, The Dutch Multicenter Randomized Phase III Trial has shown that dose escalation from 68 to 78 Gy in patients with localized prostate cancer significantly improves Freedom From Failure (FFF) but without statistically significant differences in Freedom From Clinical Failure (FFCF) and Overall Survival (OS).
Purpose: We report on the results of the updated analysis after a median follow-up of 69 months.
Patients and Methods: Between June 1997 and February 2003, 669 patients with stage T1a-4 prostate cancer were included in this Multicenter Randomized Trial comparing 68 with 78 Gy. Follow-up data were available until June 2006. The median follow-up time was 69 months (range 9–115 months). The primary end point was FFF, which was defined as clinical or biochemical failure, according to the American Society of Therapeutic Radiation Oncology definition. The secondary end points were FFCF, OS, Gastrointestinal (GI) and Genitourinary (GU) toxicities.
Results: After a median follow-up of 69 months, FFF is still significantly better in the 78-Gy arm compared with the 68-Gy arm (7-year FFF rate, 57% v 45%, respectively), with an adjusted hazard ratio of 0.75 (P = 0.015). However, no differences in OS (75% v 74% at 7 years, HR = 0.93, P = 0.66) and FFCF (70% v 69% at 7 years, HR = 0.99, P = 0.96) were observed. The cumulative incidence of late GU toxicity of RTOG/EORTC grade 2 or higher was the same in both arms (36% at 5 years and 40% at 7 years), while the cumulative incidence of late GI toxicity of RTOG/EORTC grade 2 of higher was increased in the 78-Gy arm (36% v 25% at 7 years, P = 0.04).
Conclusion: This Dutch Multicenter Randomized Trial confirms that high-dose radiotherapy is beneficial for localized prostate cancer in terms of FFF, but not in terms of FFCF and OS. Late GU toxicity was similar in both treatment arms, but there is a higher rate of late GI toxicity in the 78-Gy arm.

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PSA decrease at the end of the course of radiotherapy for prostate cancer has a significant impact on biochemical failure and clinical recurrence

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Background: The objective was to identify early failure predictors in patients (pts) receiving external beam radiotherapy (EBRT) for prostate cancer. All pts had a PSA at the 6th week (PSA6wRT) of RT (at 60 Gy).
Materials and Methods: From 1990 to 2004, 409 pts with localized prostate cancer were treated by EBRT without androgen deprivation. Median pretreatment PSA (PSApreRT) was 13 ng/mL (0.5–133). Clinical stages were: T1 (26%), T2 (60%), and T3 (14%). Gleason scores were: 4−6 (59%), 7 (31%) and 8−10 (10%). Prognosis was classified as low risk (24%), intermediate (39%) and high risk (37%). The prostate was to receive 65 Gy (2.5 Gy/day, 4 times a week) (34%) or 70 Gy (2 or 2.5 Gy/day) (66%).
Results: The median follow-up was 57 months (6–190). The median ratio of: PSA6wRT / PSApreRT (RAT) was 71% (1–374). The 5-year biochemical disease free survival (DFS) rates by RAT (<71% or >71%) were: 66% (95% CI: 58−74) and 56% (95% CI: 48−64) (Log rank, p = 0.048), respectively. The 5-year clinical (local or metastases) DFS rates by RAT (<71% or >71%) were: 96% (95% CI: 93−99) and 85% (95% CI: 79−91), respectively (p = 0.03). Multivariate analysis of biochemical failure (nadir + 2 ng/ml) and clinical failure were performed using: disease-risk group, total dose (65 Gy vs. 70 Gy), dose/fraction (2 Gy vs 2.5 Gy) and RAT. The Cox model selected disease-risk group and RAT (as continues values and median value) as independent factors that have an adverse effect on biochemical and clinical control. The corresponding hazard ratios are presented in the table.

Factors	p	HR	95% CI
Biochemical DFS			
Disease-risk group	<0.0001	2.49	1.91−3.25
PSA6wRT/PSApreRT >71%	0.010	1.59	1.12−2.25
Clinical DFS			
Disease-risk group	<0.0001	2.64	1.54−4.54
PSA6wRT/PSApreRT >71%	0.012	2.45	1.22−4.9

Conclusions: PSA6wRT / PSApreRT predicts for biochemical and clinical failure in localized prostate cancer EBRT. This parameter could be used to propose adjuvant treatment following EBRT, in case of high: PSA6wRT / PSApreRT.

4002 ORAL

Six months versus three years concomitant and adjuvant hormonal treatment with external beam irradiation for locally advanced prostate cancer: Results of the EORTC randomized Phase III trial 22961

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Background: After EORTC trial 22863, 3 years of endocrine treatment has become standard adjuvant treatment to 3-D external beam irradiation (EBRT) for locally advanced prostate cancer. In EORTC trial 22961 70 Gy EBRT and 6 months of combined androgen deprivation (SADT arm) was randomly compared to the same treatment followed by 2.5 years of further treatment with LH-RH agonist (62% triptoreline) monotherapy (LADT arm) with the aim to show non inferior survival and possibly earlier recovery of testosterone resulting in improved quality of life on the SADT-arm.
Material and Methods: Eligible patients had T1c-2b N1−2 or pN1−2, or T2c-4 N0−2 M0 prostate cancer (UICC 1992) with PSA < 150 ng/ml. Non-inferior survival was defined as a morality hazard ratio (HR) alpha 1.35 for SADT vs LADT. Non inferiority at 80% power and 1-sided alpha=0.05 required 275 deaths. A stopping boundary was applied at 1-sided alpha=0.018. Event-free rates are estimated by Kaplan-Meier and compared with the LogRank test.
Results: 970 patients were randomized (483 SADT and 487 LADT). At 5.2 years median follow-up, 173 patients had died (100 vs 73). After an interim analysis conducted in September 2006, the Independent Data Monitoring Committee recommended the disclosure of the study results. The patient characteristics were well balanced: median age 69 years, WHO PS 0 in 83.4%, most patients had T2c-T3 N0 disease. Progression (mostly biochemical and/or bone progression) occurred in 220 cases (159 on SADT vs 61 on LADT) and was treated by secondary hormonal manipulation. The 5-year overall survival rate was 85.3% on LADT and 80.6% on SADT (HR = 1.43, 96.4% CI: 1.04−1.98), and failed to prove non-inferiority (the lower bound of the CI being >1.0). Clinical progression-free survival was significantly worse on SADT with 5-year event-free rate of 68.9% vs 81.8% on LADT (HR = 1.93, P < 0.0001). Likewise, the 5-year biochemical progression-free survival rate was 58.9% on SADT vs 78.3% on LADT (HR = 2.29, P < 0.0001). Updated results will be available for presentation at the meeting.
Conclusions: The study aimed at demonstrating non-inferior survival with 6 months ADT compared to 3 years adjuvant ADT after irradiation for patients with locally advanced prostate cancer. However, the data observed so far indicate that survival with short term ADT is worse than 3-years ADT. Progression-free survival was also shorter on SADT.