

Gy in 28 fractions for level 1–3, and 60 Gy in 24 fractions for level 4. The CTV2 dose was 50.4 Gy in 28 fractions for level 1–3 and 50.4 Gy in 24 fractions for level 4. The size of BTV ranged from 3.1 to 163.6 cc (median 17.1 cc), with 3 patients in level 1, 4 in level 2, 6 in level 3, and 5 in level 4. Treatment planning was performed using the NOMOS Peacock/Corvus system and treatment delivered using a mini-multileaf collimator (MIMiC). The radiation was given 1 fraction per day and 5 days per week. The primary endpoint of the study was acute toxicity. If toxicity was acceptable, dose escalation was planned to go along. Patients were followed every 3 months by clinical examination and MRI or MET-PET/CT after completing IMRT. Median survival time was calculated as a secondary endpoint.

Results: All patients successfully completed the treatment without interruption. Seventeen (94%) patients had acceptable toxicity (grade 0 in 2, grade 1 in 1, grade 2 in 14). Only one (6%) patient in the dose level 3 developed reversible grade 3 toxicity. The median overall survival time for all patients was 13.0 months (95% CI: 8.1 to 17.8). The median progress-free survival time was 6.8 months (95% CI: 4.6 to 9.0). The 1- and 2-year actuarial survival rates were 59.5% and 21.4%, respectively. The 1- and 2-year progress-free survival rates were 18.1% and 9.0%, respectively.

Conclusions: Escalating dose to BTV with 72 Gy in 24 fractions using IMRT for the patients with resected supratentorial high grade gliomas is safe and feasible. Further dose escalation may be investigated.

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1059 Impact of Adjuvant Hormonal Therapy Duration and Timing of Salvage Hormonal Therapy in Prostate Cancer Patients With Unfavorable Prognosis Treated by Radiotherapy. A Secondary Analysis of RTOG 8531

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Purpose/Objective(s): RTOG 85-31 was a randomized trial comparing radiotherapy (RT) alone versus RT plus lifelong adjuvant androgen suppression in unfavorable prognosis carcinoma of the prostate. Since not all patients remained on the protocol mandated long-term hormonal therapy, we examined the effect of hormonal duration in outcome. We also examined the impact of early initiation of salvage hormonal therapy (HT) in relapsing patients randomized to RT alone.

Materials/Methods: The protocol mandated either pelvic RT (60–70 Gy) followed by goserelin 3.6 mg monthly given indefinitely or until disease progression (arm 1) or pelvic RT alone followed by observation and HT at relapse (arm 2). PSA determination was not mandatory at the initiation of the study. There were 477 cases in arm 1 and 468 in arm 2. To avoid potential bias due to early progression in the analysis of arm 1, only patients who were alive with no evidence of disease at the time of voluntary cessation of HT were included, leaving 377 analyzable patients. For the purpose of this analysis, arm 1 patients were divided in groups based on the hormonal therapy duration (HTD), as follows: ≤1 year (27.3%), 1 < and ≤2 years (11.4%), 2 < and ≤4 years (13.3%), 4 < and ≤6 years (10.6%) and >6 years (37.4%). Arm 2 patients were divided in early and late salvage hormonal therapy. The early salvage was defined as receiving HT with a PSA <10 ng/ml prior to HT and late salvage was defined as receiving HT with a PSA ≥10 ng/ml prior to HT. End-points were overall survival, disease-free survival, disease-free survival with PSA <1.5 ng/ml, disease-specific survival and distant failure. Cox-proportional hazards regression model was used to test the outcomes among all groups.

Results: The median follow-up time for surviving patients is over 11 years. The median duration of adjuvant HT was 3.59 years. Adjusted for age and stratification variables, the HTD >6 year group remains the only group significantly associated with having fewer failure events in all measured outcomes. The 5- and 11-year overall survival rates for patients with HTD >6 years was 100 and 77% compared to 67 and 39%, 46 and 17%, 53 and 25%, 89 and 32% for those patients with HTD of ≤1 year, 1 < and ≤2 years, 2 < and ≤4 years, 4 < and ≤6 years, respectively. Of the patients failing RT in arm 2, 132 (51%) initiated early HT and 125 (49%) late HT. The median follow-up of early vs later salvage HT patients was comparable. Pretreatment characteristics show that the early salvage group had significantly fewer nodal disease, post-prostatectomy patients, distant metastases and higher Gleason score. The 5- and 11-year overall survival rates were 86 and 47% for early HT and 65 and 22% for late HT, respectively ($p < 0.0001$). Early initiation of HT was also associated with a significantly improved disease-free survival, disease-free survival with PSA <1.5 ng/ml, local failure, distant failure and cause-specific survival.

Conclusions: Despite the limitations of the retrospective nature of these data, the results from these analyses suggest that the use of HTD for more than 6 years appears to be significantly associated with improvements in all end-points studied and that early salvage HT post-RT failure may result in improved outcomes in patients with unfavorable prostate cancer treated by pelvic RT alone.

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1060 Cardiovascular Mortality Following Androgen Deprivation Therapy in Men With Locally Advanced Prostate Cancer: An Analysis of RTOG 85-31

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Purpose/Objective(s): Gonadotropin-releasing hormone (GnRH) agonists are associated with a greater risk of coronary heart disease and myocardial infarction in men with prostate cancer but little is known about their potential impact on cardiovascular mortality. We assessed the relationship between GnRH agonists and cardiovascular mortality in a large randomized trial of men treated with or without adjuvant goserelin following radiation therapy (RT) for locally advanced prostate cancer.

Patients and Materials/Methods: Between 1987 and 1992, 945 eligible men with locally advanced prostate cancer were enrolled on a phase III trial (RTOG 85-31) and randomized to RT and adjuvant goserelin (Arm I) or RT alone (Arm II). Cox regression analyses were performed to evaluate the relationship between treatment arm and cardiovascular mortality. Covariates included age, prevalent cardiovascular disease (CVD), hypertension (HTN), diabetes (DM), body mass index (BMI), race, Gleason score, clinical stage, history of prostatectomy, and nodal involvement.

Results: After a median follow-up of 8.1 years, there were a total of 117 cardiovascular-related deaths. There was no GnRH agonist treatment-related increase in cardiovascular mortality. At 5 years, cardiovascular mortality for men treated with adjuvant goserelin was 4.1% vs 6.5% for men treated without adjuvant goserelin (Gray's $p = 0.17$). In multivariate analyses, treatment arm was not significantly associated with an increased risk of cardiovascular mortality [adjusted hazard ratio (HR) = 0.68, 95% confidence interval (CI) 0.43–1.05, $p = 0.08$] (Table 1). Notably, results were similar when censoring subjects at the time of salvage GnRH agonist therapy [HR = 0.92, 95% CI 0.54–1.55, $p = 0.74$], when applying alternative definitions of cardiovascular mortality, and when imputing missing data. Traditional cardiac risk factors, including prevalent CVD and DM, were significantly associated with greater cardiovascular mortality.

Conclusions: GnRH agonists do not appear to increase cardiovascular mortality in men with locally advanced prostate cancer. Further studies are warranted to evaluate the adverse effects of GnRH agonists in patient populations with a lower risk of cancer-specific mortality.

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Table 1: Multivariate analyses of cardiovascular mortality without censoring and with censoring at time of salvage GnRH agonist therapy (n = 716)

Covariate	Comparison	Without Censoring			With Censoring		
		HR	(95% CI)	p-value	HR	(95% CI)	p-value
Treatment arm	Arm II vs. Arm I	-0.68	(0.43, 1.05)	0.082	-0.92	(0.54, 1.55)	0.74
Age	<70 vs. ≥70	-1.89	(1.14, 3.12)	0.013	-1.62	(0.90, 2.91)	0.11
Race	Black vs. Other	-1.06	(0.48, 2.32)	0.88	-1.81	(0.61, 5.33)	0.28
Prevalent CVD	No vs. Yes	-2.58	(1.63, 4.10)	<0.0001	-2.96	(1.70, 5.13)	0.0001
Prevalent HTN	No vs. Yes	-1.50	(0.96, 2.36)	0.077	-1.71	(1.01, 2.91)	0.048
Prevalent DM	No vs. Yes	-2.38	(1.38, 4.11)	0.002	-2.80	(1.50, 5.24)	0.001
BMI	<25	—			—		
	≥25, <30	0.92	(0.55, 1.55)	0.76	0.89	(0.48, 1.64)	0.70
	≥30	0.87	(0.44, 1.74)	0.69	0.96	(0.44, 2.13)	0.93

HR = Hazard ratio, CI = confidence interval.

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1061 Does Adjuvant Hormonal Therapy Improve Freedom From Biochemical Relapse in Prostate Cancer Patients Receiving Dose-Escalated Radiation Therapy? An Analysis of RTOG 94-06

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Purpose/Objective(s): The purpose of this study was to determine if adjuvant hormonal therapy (HT) had an effect on freedom from biochemical failure (bNED) in prostate cancer patients receiving dose-escalated radiation therapy (DRT).

Materials/Methods: We analyzed 920 prostate cancer patients who enrolled on RTOG 94-06, a phase I/II dose escalation trial, and whose mean planning target volume (PTV) dose exceeded 73.8 Gy (mean dose = 78.0 Gy, maximum = 84.0 Gy). Men were broken down into risk groups: low (prostate-specific antigen (PSA) ≤10 ng/ml, Gleason score 2–6, and T-stage ≤T2a), intermediate (a group of patients who are not in the other two groups), and high (PSA > 20, or Gleason score >7, or T stage >T2b). One hundred and four men initiated HT between 2 to 3 months prior to DRT, and completed all HT within 3 months after DRT. Sixty-seven high-risk patients received HT for a longer duration. We defined biochemical failure using the Phoenix definition (the occurrence of a post-treatment PSA greater than the nadir +2 ng/ml or the initiation of salvage HT).

Results: At 5 years, the bNED rates after DRT alone were 85% (95% confidence interval (CI):80%-91%), 82% (95% CI: 75%-88%), and 69% (95% CI: 58%-80%) for low, intermediate, and high risk patients ($p < 0.0003$). After HT + DRT, the rates correspond to 83% (95% CI: 71%-95%) and 76% (95% CI: 65%-86%) for low and intermediate risk patients, respectively. In the high risk group, the rates were 69% (95% CI: 61%-77%) and 71% (95% CI: 60%-83%) for HT + RT and LHT + RT, respectively. A Cox-proportion hazards regression model (after adjusting for pre-treatment PSA, biopsy Gleason score, length of follow-up, and T stage) did not reveal a significant effect on bNED for the addition of HT to DRT.

Conclusions: Adjuvant HT did not appear to improve bNED survival in patients receiving DRT. The lack of benefit was seen in all risk groups.

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