IDENTIFYING PATIENTS THAT MAY BENEFIT FROM THE ADDITION OF BICALUTAMIDE TO SALVAGE RADIATION THERAPY IN THE SETTING OF BIOCHEMICAL FAILURE AFTER RADICAL PROSTATECTOMY: A POST-HOC ANALYSIS OF RTOG 9601 TRIAL DATA

Natalija Kovacevic, M.D. [1], Akshay Sood, M.D.[1], Jacob Keeley, M.S.[1], Deepansh Dalela, M.D.[1], Sohrab Arora, M.Ch.[1], Isaac Palma-Zamora, M.D. [1], Marcus Jamil, M.D. [1], Wooju Jeong, M.D.[1], Quoc-Dien Trinh, M.D. [2], Craig Rogers, M.D.[1], James Peabody, M.D.[1], Mani Menon, M.D.[1], Firas Abdollah, M.D.[1]

[1]Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI; [2]Brigham and Women's Hospital, Harvard Medical School, Boston, MA

INTRODUCTION

- More than 170,000 men in the U.S. are diagnosed with prostate cancer each year, and about half of those patients choose radical prostatectomy as the initial treatment.
- Nearly one-third of these patients will develop disease relapse, which manifests as a rise in serum level of PSA (biochemical failure).
- It is generally agreed that salvage radiation therapy (sRT) improves outcomes in patients that experience biochemical failure after radical prostatectomy.
- However, 50% of patients treated with sRT alone will have disease progression within 5 years.
- Adding anti-androgen therapy (AAT) improves outcomes further, but not in all.
- In this study we aimed to elucidate which patients derive benefit from a combination of bicalutamide and sRT.

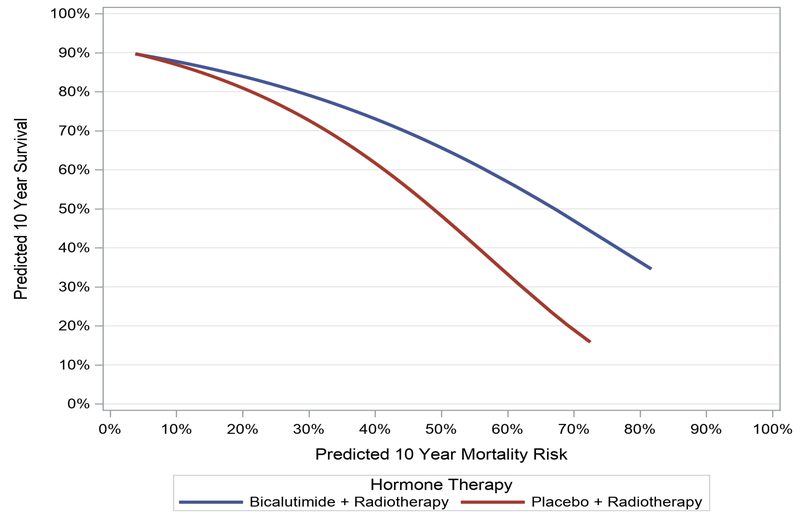
MATERIALS AND METHODS

- Study design: post-hoc analysis of RTOG 9601 trial patients (n=760), obtained from NCI's National Clinical Trials Network.
- Covariates: covariates were categorized as reported in the original trial, and consisted of age, race, Karnofsky performance score, pathologic Gleason score, pathological T (pT) stage, surgical margin status, pre-sRT PSA (<0.7 versus 0.7-1.5 versus >1.5-4.0 ng/ml), and receipt of bicalutamide versus placebo.
- Patients were stratified into 2 groups, those that received sRT alone and those that received both sRT and bicalutamide.
- Analysis: Interaction between 10-yr predicted mortality probability and AAT/no AAT was plotted using locally-weighted methods controlling for all baseline factors; a two sided p<0.05 was considered significant.

Table: Baseline characteristics in prostate cancer disease patients experiencing biochemical failure after radical prostatectomy receiving sRT alone vs sRT and bicalutamide. (RTOG 9601 trial data)

Patient characteristics	Bicalutamide; (n=384)	Placebo; (n=376)	p value
Age in years; n (%)			
<60 years	99 (25.8)	88 (23.4)	0.749
60 to 69 years	192 (50)	194 (51.6)	
>=70 years	93 (24.2)	94 (25)	
Race; n (%)			
Whites	344 (89.6)	324 (86.2)	0.268
Blacks	28 (7.3)	40 (10.6)	
Others	12 (3.1)	12 (3.2)	
Karnofsky performance score; n (%)			
<=90	88 (22.9)	96 (25.5)	0.400
100	296 (77.1)	280 (74.5)	
pGleason score; n (%)			
Unknown	1 (0.3)	1 (0.3)	0.859
2-6	111 (28.9)	103 (27.4)	
7	205 (53.4)	208 (55.3)	
8-10	67 (17.5)	64 (17.0)	
pT stage; n (%)			
pT2	128 (33. 3)	120 (31.9)	0.677
pT3	256 (66. 7)	256 (68.1)	
Surgical margins; n (%)			
Negative surgical margins	96 (25)	95 (25.3)	0.933
Positive surgical margins	288 (75)	281 (74.7)	
PSA at Study Entry; n (%)			
<0.7 ng/ml	210 (54.7)	195 (51.9)	0.601
0.7 - 1.5 ng/ml	119 (31)	118 (31.4)	
>1.5 - 4.0 ng/ml	55 (14.3)	63 (16.8)	
Completion of Protocol Hormone Therapy; n (%)			
Did not complete hormone therapy	126 (32.8)	118 (31.4)	0.673
Completed hormone therapy	258 (67.2)	258 (68.6)	

Figure: Interaction between 10-yr predicted mortality probability and AAT/no AAT. The blue line represents bicalutamide and AAT while the red line represents sRT alone (RTOG 9601 trial data)



RESULTS

- Of the 760 patients that were part of the RTOG 9601 trial, 376 (49.5%) received sRT alone while the remaining 384 (50.5%) received both sRT and bicalutamide.
- Baseline characteristics of patients in the two groups were well-matched (Table).
- The median follow-up was 12 years.
- The lines for bicalutamide and no AAT separated at 10-yr predicted mortality risk of 10%, indicating that patients with a predicted 10-yr mortality risk of 10% or greater will benefit from addition of bicalutamide (**Figure**).
- Cox-regression analysis demonstrated that patients undergoing combination bicalutamide and sRT (HR= 1.34, 95% CI 1.18-1.52) had 16% lower hazard of mortality as compared to patients undergoing sRT alone (HR= 1.51, 95% CI 1.36-1.67) for every 10% increment in predicted mortality risk (p<0.001).

CONCLUSIONS

- In patients with biochemical failure after RP, only patients with mortality risk of 10% or greater benefit from addition of AAT to sRT.
- Combining bicalutamide and sRT shows a 16% added survival benefit for every 10% incremental increase in 10-yr mortality risk.
- These data may facilitate patient counseling and shared treatment selection.

REFERENCES

- Boorjian SA, Karnes RJ, Crispen PL, Rangel LJ, Bergstralh EJ, Blute ML. Radiation therapy after radical prostatectomy: impact on metastasis and survival. J Urol 2009; 182: 2708–14.
- Shipley WU, Seiferheld W, Lukka HR, et al. Radiation with or without antiandrogen therapy in recurrent prostate cancer. N Engl J Med 2017;376:417-428.
- Stephenson AJ, Scardino PT, Kattan MW, et al. Predicting the outcome of salvage radiation therapy for recurrent prostate cancer after radical prostatectomy. J Clin Oncol 2007;25:2035-41.