Radical Prostatectomy 15-year Overall and Prostate Cancer Specific Mortality: A Novel Analysis of Radiation Therapy and Androgen Deprivation

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1. Introduction

Although the most common cancer, prostate cancer (PC) is remarkable for its long natural life history and modest lethality when compared to other cancers. Despite recurrence rates of 20-40% following definitive therapy, PC specific survival 25-years post-surgery even in high-grade cancers is only approximately 50%.

Post-treatment, salvage radiation therapy with ADT (sRT/ADT) has been shown to reduce biochemical recurrence (BCR) following radical prostatectomy (RP). Direct comparison of patients receiving sRT/ADT versus ADT monotherapy has not been published. The present study seeks to compare overall survival and prostate cancer specific survival between sRT/ADT versus ADT monotherapy.

2. Materials and Methods

A retrospective cohort analysis of 1,865 patients undergoing RP from June 2002 and September 2019 was conducted. 410 patients experienced BCR. 410 (22%) experienced post-RP BCR, defined as two consecutive PSA>0.2 ng/dl (n=362) or those undergoing adjuvant therapy (n=46). Patients were managed with concurrent sRT+ADT (n=91), ADT alone (n=156) or active observation only (AO, n=136).

Our main outcome measure was the difference in OS and PCSS in men undergoing sRT/ADT versus ADT groups, estimated by Kaplan-Meier survival analysis and cox regression. Ad hoc of OS/PCSS analysis was conducted combining AS (all candidates for sRT) as part of sRT/ADT.

3a. Results, Patient Demographics

**Table 1: Patient demographic characteristics of RT+ADT with AO versus ADT groups**

Treatment	ADT	ADT+RT	AS	Overall	all	ADT vs ADT+RT	ADT+RT vs AS
	Count (%)	Count (%)	Count (%)	Count (%)	p-value	p-value	p-value
N, all patients	156 (8.4%)	91 (4.9%)	136 (7.3%)	1865 (100%)			
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	p value	p value	p value
Age, years	65.1 (7.1)	62.7 (7.0)	63.5 (7.3)	62.2 (7.5)	0.023	0.02	0.433
Adj Pre-PSA, ng/mL	14.6 (20.8)	9.8 (7.8)	8.4 (5.7)	7.5 (9.2)	< 0.001	0.066	0.116
SHIM	17.2 (7.8)	18.0 (7.4)	19.8 (7.1)	19.4 (7.1)	0.017	0.661	0.081
EBL	99.0 (42.3)	92.0 (30.5)	102.2 (48.4)	99.0 (41.0)	0.203	0.175	0.076
BMI	27.4 (4.0)	27.4 (3.6)	27.0 (3.8)	27.0 (3.5)	0.674	0.773	0.449
Prostate Weight	55.4 (21.8)	51.2 (15.7)	51.4 (21.3)	53.3 (20.6)	0.183	0.235	0.916
Follow Up, years	7.2 (4.4)	7.8 (4.3)	7.5 (4.0)	5.9 (4.3)	0.61	0.097	0.642
Time to Death, years	7.8 (4.1)	8.6 (3.4)	6.9 (2.7)	7.2 (4.4)	0.499	0.513	0.166
Time to Earliest Treatment	2.4 (3.3)	2.5 (3.3)	NA	2.9 (7.6)		0.825	
Current PSAdt, months	6.4 (5.6)	10.7 (12.3)	26.0 (19.9)	15.6 (16.9)	< 0.001	0.003	< 0.001
	Count (%)	Count (%)	Count (%)	Count (%)	p-value	p value	p value
Margins	65 (41.7%)	35 (38.5%)	36 (26.5%)	292 (15.7%)	0.02	0.638	0.056
p-stage					< 0.001	0.851	< 0.001
pT2	38 (24.5%)	24 (26.4%)	67 (49.3%)	1281 (68.7%)			
pT3/T4	117 (75.5%)	67 (73.6%)	69 (50.7%)	583 (31.3%)			
Gleason Grade Group					< 0.001	0.613	< 0.001
1	0 (0.0%)	1 (1.1%)	17 (12.5%)	503 (27.0%)			
2	30 (19.2%)	14 (15.4%)	48 (35.3%)	758 (40.6%)			
3	39 (25.0%)	29 (31.9%)	43 (31.6%)	340 (18.2%)			
4	13 (8.3%)	8 (8.8%)	17 (12.5%)	82 (4.4%)			
5	74 (47.4%)	39 (42.9%)	11 (8.1%)	182 (9.8%)			
PSAdt Group, months					< 0.001	0.015	< 0.001
>12	14 (12.2%)	20 (32.8%)	108 (79.4%)	151 (45.8%)			
6 to 12	27 (23.5%)	13 (21.3%)	23 (16.9%)	68 (20.6%)			
<6	74 (64.3%)	28 (45.9%)	5 (3.7%)	111 (33.6%)			
DT Pattern					< 0.001	0.596	< 0.001
Increasing	20 (12.8%)	23 (25.3%)	96 (70.6%)	139 (36.2%)			
Decreasing	62 (39.7%)	28 (30.8%)	37 (27.2%)	127 (33.1%)			
NA	74 (47.4%)*	40 (44.0%)*	4 (2.9%)**	118 (30.7%)			
PCSM	21 (13.5%)	8 (8.8%)	0 (0.0%)	33 (1.8%)	< 0.001	0.483	< 0.001
Dead	37 (23.7%)	12 (13.2%)	13 (9.6%)	133 (7.1%)	0.003	0.14	0.392

* No PSAdt as treatment was initiated based on very rapid PSA progression
** Not enough PSA's prior to non-cancer specific death (n=2), lost to follow-up (n=1), and after BCR (n=1).

Table 2a: Univariate and Multivariate Models

Figure 1a. Prostate cancer specific survival (p=0.39) and overall survival (p=0.082) of the RT+ADT vs. ADT groups
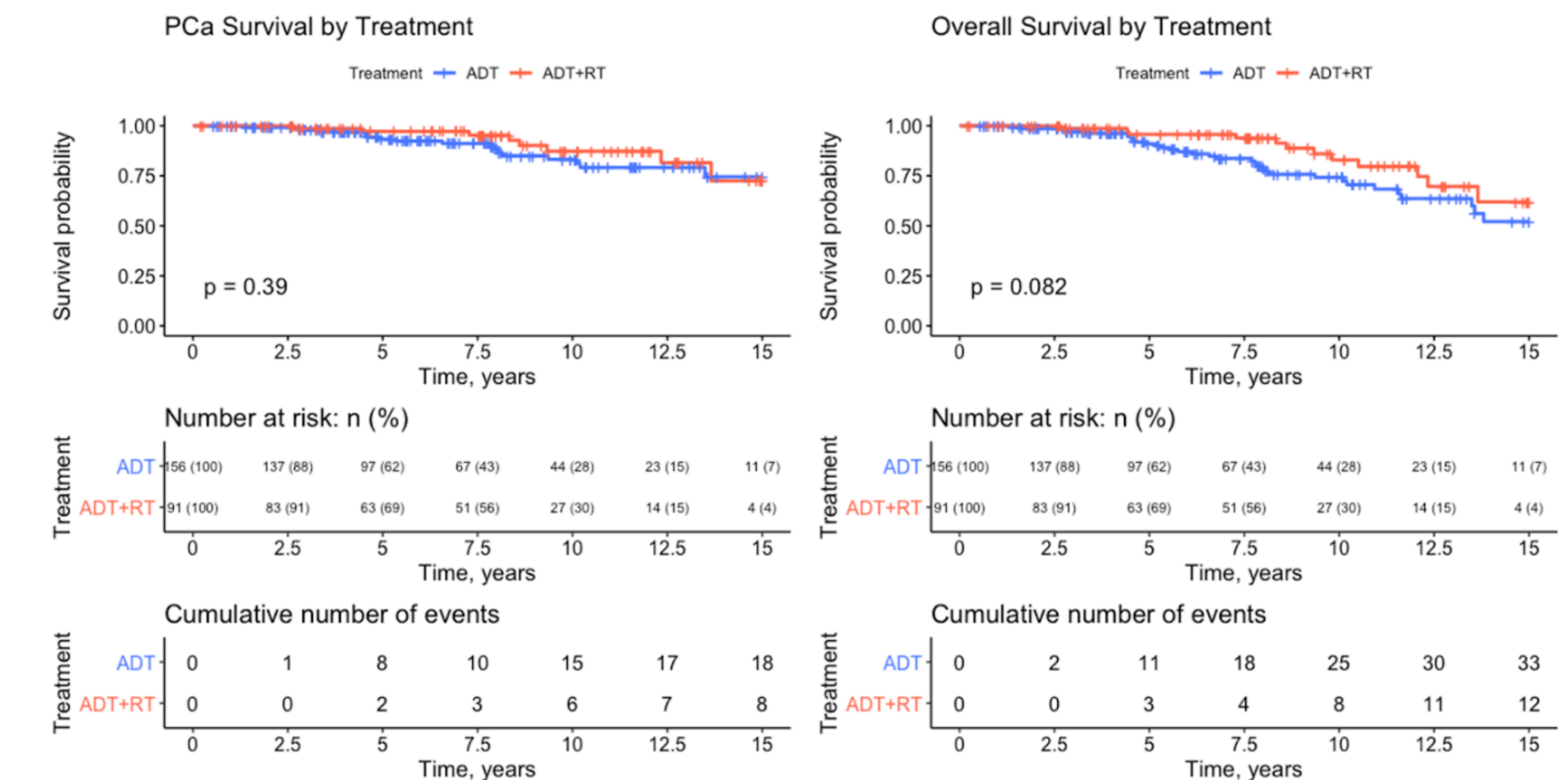
Figure 2a. Prostate cancer specific survival (p=0.0016) and overall survival (p=0.0045) of the RT+ADT with AO vs. ADT groups
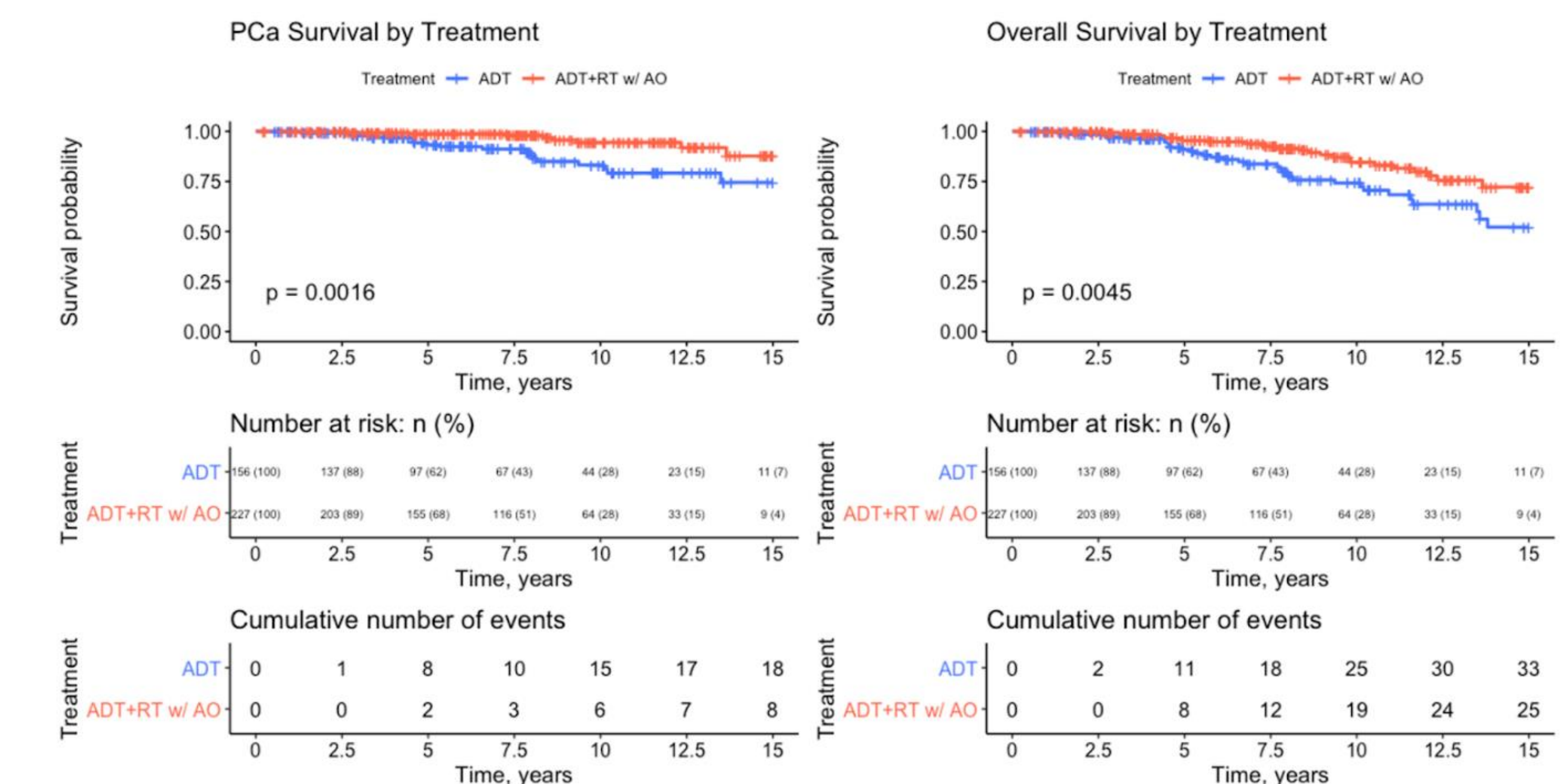
4. Conclusions

Of the 410 BCR patients, 138 (34%) were managed with AS, with 92% OS and 100% PCSS. Kaplan-Meier analysis demonstrated no significant difference between RT+ADT and ADT monotherapy in OS (p=0.060) or PCSS (p=0.336). Only in ad-hoc analysis did the AS + sRT/ADT group demonstrate improved OS/PCSS (p<0.001) compared to ADT monotherapy. This outcome is consistent with our experience with AS patients with a DT greater than 12 months, suggesting that a significant percentage of recurrences can be managed with observation alone.