

Table 1: Patient- and treatment-related characteristics of the study population (n=62)

Characteristics before primary radiotherapy	Number	Percentage/range /SD	Missing, n (%)
Primary therapy			0
Iodine-125 brachytherapy	14	(23%)	
EBRT, 60 Gy, 30 fractions	4	(6%)	
EBRT, 64.4 Gy, 28 fractions	24	(39%)	
EBRT, 66 Gy, 33 fractions	7	(11%)	
EBRT, 70 Gy, 35 fractions	3	(5%)	
IMRT, 76 Gy, 38 fractions	1	(2%)	
Other EBRT schedule	9	(15%)	
Age at primary treatment, mean (\pm SD)	63	(5.3)	1 (1.6%)
Initial PSA before primary (ng/ml), median (range)	16.6	(2.6-66.9)	7 (11.3%)
Primary T-stage			0
T1	11	(17.7%)	
T2	30	(48.4%)	
T3	21	(33.9%)	
Differentiation grade primary tumor			3 (4.8%)
Gleason 2-6	29	(46.8%)	
Gleason 7	27	(43.5%)	
Gleason 8-10	3	(4.8%)	
Number of biopsies, median (range)	6	(4-14)	31 (50%)
Pre-salvage characteristics			
PSA-nadir (ng/ml) after primary, median (range)	1.1	(0.02-12.9)	8 (12.9%)
Disease-free survival interval from primary (months), mean (\pm SD)	51	(31)	11 (17.7%)
Interval primary – salvage (months), mean (\pm SD)	67	(32)	0
Age at salvage treatment (years), mean (\pm SD)	69	(5.3)	0
PSA pre-salvage (ng/ml), median (range)	8.6	(0.1-92.6)	1 (1.6%)
PSADT, median (range)	11.3	(3.2-31.7)	6 (9.7%)
PSA-density (ng/ml/cc), median (range)	0.37	(0.01-7.12)	4 (6.5%)
PSA-velocity (ng/ml/year), median (range)	3.8	(0.5-33.1)	11 (17.7%)
ADT pre-salvage			0
Bicalutamide	19	(31%)	
Nilutamide	1	(2%)	
Leuproreline	1	(2%)	
Duration of ADT use			0
3 months pre-salvage	16	(26%)	
2, 7, 9, 15 and 25 months pre-salvage	1 each	(8%)	
Dosimetry parameters (n=28)			
D90 (Gy), median (range)	167	(154-200)	NA
V100 (%), median (range)	98	(92-100)	
V150 (%), median (range)	48	(22-84)	

Outcome characteristics			
BF (Phoenix definition)	43	(69%)	0
Response to salvage treatment	51	(82%)	0
PSA-nadir after salvage (ng/ml), median (range)	0.71	(0.01-13.8)	1 (1.6%)
Follow-up (months) from salvage, median (range)	74	(5-138)	0
Abbreviations: EBRT=external beam radiotherapy; IMRT=intensity modulated radiotherapy; PSADT=PSA doubling time; ADT=androgen deprivation therapy; D90=minimal dose in 90% of the prostate; V...=volume (as percentage of total volume) of the prostate receiving ...% dose (100% dose equals 145 Gy); NA=not applicable; BF=biochemical failure.			

Table 2: biochemical disease free survival estimates subdivided by prognostic variables from Kaplan-Meier analysis. P-values are derived from the log-rank statistic.

Factor	bDFS estimate	p-value
Primary therapy		
EBRT	5 y: 27%	
I-125	5 y: 30%	0.96
iPSA		
0-10 ng/ml	5 y: 33%	
10-20 ng/ml	5 y: 31%	
>20 ng/ml	5 y: 20%	0.42
T-stage primary		
T1	5 y: 27%	
T2	5 y: 30%	
T3	5 y: 24%	0.60
Differentiation primary		
Gleason 2-6	5 y: 33%	
Gleason 7	5 y: 22%	
Gleason 8-10	5 y: 0%	0.06
Nadir after primary		
≤1 ng/ml	5 y: 31%	
>1 ng/ml	5 y: 28%	0.33
DFSI after primary		
<36 months	5 y: 0%	
≥36 months	5 y: 39%	<0.01
Age at salvage		
>65-years	5 y: 33%	
≤65-years	5 y: 14%	0.21
ADT use before salvage		
Yes	5 y: 31%	
No	5 y: 27%	0.96
Pre-salvage PSA		
≤10 ng/ml	5 y: 40%	
>10 ng/ml	5 y: 13%	<10 ⁻³
PSADT		
>10 months	5 y: 44%	
≤10 months	5 y: 5%	<0.0001
PSA-density		
≤0.25 ng/ml/cc	5 y: 57%	
>0.25 ng/ml/cc	5 y: 16%	<0.001
PSA-velocity		
≤3 ng/ml/year	5 y: 64%	
>3 ng/ml/year	5 y: 0%	<0.0001
Nadir after salvage		
≤1.0 ng/ml	5 y: 50%	
>1.0 ng/ml	5 y: 0%	<10 ⁻⁶

Abbreviations: EBRT=external beam radiotherapy; bDFS=biochemical disease-free survival;
iPSA=initial PSA before primary treatment; PSADT=PSA doubling time.

Table 3: Univariable and multivariable Cox proportional hazards regression analysis

Univariable analysis		Multivariable analysis			
Factor	HR (95% CI)	p-value	HR (95% CI)	Corrected (shrinkage factor 0.86)	p-value
Primary therapy I-125 versus EBRT	0.96 (0.47-1.95)	0.91	-		-
Initial dose >64.4 Gy versus ≤64.4 Gy	1.90 (0.86-4.19)	0.11	-		-
iPSA	1.01 (0.99-1.03)	0.49	-		-
T-stage 2 versus 1	0.69 (0.31-1.53)	0.36	-		-
3 versus 1	0.70 (0.30-1.62)	0.40	-		-
Differentiation Gleason 7 versus 2-6	1.44 (0.75-2.78)	0.27	-		-
Gleason 8-10 versus 2-6	2.70 (0.64-11.43)	0.18	-		-
Year of primary treatment	0.99 (0.97-1.002)	0.10	-		-
Year of salvage treatment	0.90 (0.84-0.97)	0.01	0.91 (0.84-0.99)	0.92 (0.86-0.99)	0.03
ADT use	1.02 (0.53-1.96)	0.96	-		-
ADT duration	1.05 (0.95-1.15)	0.33	-		-
PSA-nadir after primary	1.16 (1.02-1.31)	0.02	-		-
DFSI	0.98 (0.97-0.99)	<0.001	0.98 (0.97-0.999)	0.99 (0.97-0.999)	0.04
Age at salvage	0.94 (0.88-0.99)	0.02	-		-
PSA pre-salvage	1.02 (1.01-1.04)	0.006	-		-
PSADT	0.91 (0.85-0.96)	0.001	0.93 (0.88-0.99)	0.94 (0.89-0.99)	0.03
PSA-density	1.29 (1.02-1.63)	0.03	Excluded, MC		-
PSA-velocity	1.09 (1.05-1.14)	<0.0001	Excluded, MC		-
PSA-nadir after salvage	1.33 (1.18-1.51)	<10 ⁻⁵	Excluded, redundancy		-

Abbreviations: HR=hazard ratio; iPSA=initial prostate specific antigen (before primary treatment); ADT=androgen deprivation therapy; DFSI=disease-free survival interval; PSADT=PSA doubling time; MC=multicollinearity. P-values are based on the Wald test-statistic.

Table 4: Biochemical disease free survival percentages of different levels of the predictor variables at 3 years follow-up

Variable level	DFSI	24 months	48 months	72 months	96 months
PSADT					
6 months		17% (9-26)	27% (9-48)	38% (10-67)	50% (11-81)
12 months		28% (18-39)	40% (19-60)	51% (20-76)	61% (21-86)
18 months		41% (31-52)	52% (31-70)	62% (32-82)	71% (33-90)
24 months		54% (44-63)	64% (44-78)	72% (45-87)	79% (46-93)
30 months		65% (56-72)	73% (57-84)	79% (57-91)	84% (58-95)
36 months		74% (66-79)	80% (67-88)	85% (68-93)	89% (68-96)
42 months		81% (75-85)	86% (76-92)	89% (76-95)	92% (76-97)
48 months		86% (82-89)	90% (82-94)	92% (83-97)	94% (83-98)

Abbreviation: DFSI=disease-free survival interval; PSADT=PSA doubling time. 95% confidence intervals are listed after the survival proportions