

Supplementary Materials: Expression of AR-V7 (Androgen Receptor Variant 7) Protein in Granular Cytoplasmic Structures Is an Independent Prognostic Factor in Prostate Cancer Patients

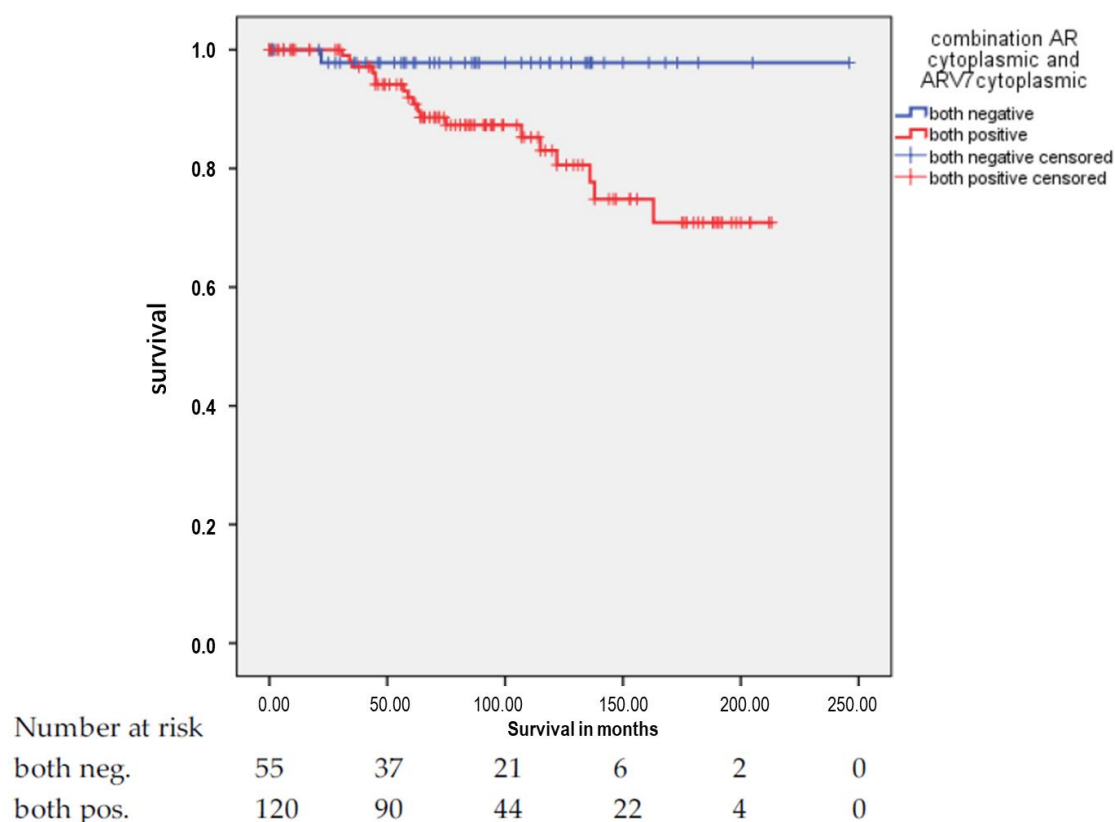


Figure S1. Kaplan-Meier analysis: Combination of AR cytoplasmic staining and AR-V7 cytoplasmic staining and its association with RFS. Combination of AR cytoplasmic and AR-V7 cytoplasmic protein expression at comparing both positive vs both negative was associated with RFS ($p = 0.025$, log rank test).

Table S1. Detailed staining results for AR and AR-V7.

AR Cytoplasm			AR Nuclear			AR-V7 Cytoplasm			AR-V7 Granular		
IRS	Frequency	Percentage	IRS	Frequency	Percentage	IRS	Frequency	Percentage	Percentage per TCs	Frequency	Percentage of all
0.00	120.00	29.3	0.00	38.00	9.30	0.00	14.00	3.40	0.00	260.00	63.40
0.67	2.00	0.5	0.67	1.00	0.20	0.67	1.00	0.20	2.50	1.00	0.20
1.00	50.00	12.2	1.00	12.00	2.90	1.00	6.00	1.50	5.00	1.00	0.20
1.33	2.00	0.5	1.33	1.00	0.20	1.50	5.00	1.20	10.00	41.00	10.00
1.50	11.00	2.7	1.50	10.00	2.40	2.00	33.00	8.00	15.00	2.00	0.50
2.00	97.00	2.7	2.00	34.00	8.30	2.50	8.00	2.00	20.00	37.00	9.00
2.33	1.00	0.2	2.33	1.00	0.20	3.00	39.00	9.50	25.00	1.00	0.20
2.50	23.00	5.60	2.50	12.00	2.90	3.50	12.00	2.90	30.00	25.00	6.10
3.00	54.00	13.20	2.67	1.00	0.20	4.00	69.00	16.80	40.00	11.00	2.70
3.50	11.00	2.70	3.00	43.00	10.50	4.50	8.00	2.00	45.00	1.00	0.20
3.67	1.00	0.20	3.50	11.00	2.70	5.00	28.00	6.80	50.00	8.00	2.00
4.00	23.00	5.60	4.00	74.00	18.00	5.33	2.00	0.50	60.00	9.00	2.20
4.50	2.00	0.50	4.50	11.00	2.70	5.50	3.00	0.70	70.00	4.00	1.00
5.00	2.00	0.50	5.00	28.00	6.80	6.00	66.00	16.10	80.00	3.00	0.70
5.50	2.00	0.50	5.33	1.00	0.20	6.50	1.00	0.20	90.00	1.00	0.20
6.00	8.00	2.00	5.50	2.00	0.50	7.00	16.00	3.90	sum missing all	405.00	98.80
sum	409.00	99.80	6.00	72.00	17.60	7.50	8.00	2.00		5.00	1.20
missing	1.00	0.20	6.50	3.00	0.70	7.67	2.00	0.50		410.00	100.00
all	410.00	100.00	7.00	8.00	2.00	8.00	31.00	7.60			
			7.33	1.00	0.20	8.50	7.00	1.70			
			7.50	8.00	2.00	8.67	1.00	0.20			
			8.00	18.00	4.40	9.00	24.00	5.90			
			8.50	2.00	0.50	10.00	3.00	0.70			
			9.00	16.00	3.90	10.50	7.00	1.70			
			10.00	1.00	0.20	12.00	12.00	2.90			
			12.00	1.00	0.20	sum	406.00	99.00			
		sum/all		410.00	100.00	missing	4.00	1.00			
					all		410.00	100.00			

Table S2. Bivariate correlations between immunohistochemical staining for AR/AR-V7 and clinic-pathological and molecular parameters.

			AR IRS Nuclear	AR IRS Cytoplasmic	AR-V7 IRS Cytoplasmic	AR-V7 Granular Percent
Spearman- Rho	AR IRS nuclear	Correlation coefficient (Cc)	1.000	0.652**	0.401**	−0.109*
		Sig. (2-sided)		<0.001	<0.001	0.028
		N	410	409	406	405
	AR IRS cytoplasmic	Cc	0.652**	1.000	0.482**	−0.081
		Sig. (2-sided)	<0.001		<0.001	0.102
		N	409	409	405	404
	AR-V7 IRS cytoplasmic	Cc	0.401**	0.482**	1.000	−0.173**
		Sig. (2-sided)	<0.001	<0.001		<0.001
		N	406	405	406	405
	AR-V7 granular percent	Cc	−0.109*	−0.081	−0.173**	1.000
		Sig. (2-sided)	0.028	0.102	<0.001	
		N	405	404	405	405
	Age at diagnosis	Cc	−0.002	0.011	0.056	−0.014
		Sig. (2-sided)	0.971	0.832	0.261	0.776
		N	410	409	406	405
	pT	Cc	0.102*	0.160**	.152**	−0.169**
		Sig. (2-sided)	0.038	0.001	0.002	0.001
		N	410	409	406	405
	pN	Cc	−0.026	0.077	.116*	−0.125*
		Sig. (2-sided)	0.600	0.125	0.021	0.012
		N	402	401	398	397
	pM	Cc	0.043	0.073	0.051	0.025
		Sig. (2-sided)	0.400	0.152	0.320	0.631
		N	390	389	386	385
	Lymph invasion	Cc	0.000	0.070	0.143**	−0.044
		Sig. (2-sided)	0.993	0.200	0.009	0.421
		N	335	334	332	332
	Vaskular invasion	Correlation coefficient	0.067	−0.041	−0.047	−0.024
		Sig. (2-sided)	0.178	0.411	0.353	0.626
		N	403	402	399	398
	GS at prostatectomy	Cc	0.076	0.146**	0.167**	−0.147**
		Sig. (2-sided)	0.140	0.004	0.001	0.004
		N	381	380	377	376
	Perineural invasion	Cc	0.112*	0.142**	0.271**	−0.187**
		Sig. (2-sided)	0.028	0.005	<0.001	<0.001
		N	383	382	379	378
	Follow-up time RFS	Cc	0.081	0.094	0.062	−0.013
		Sig. (2-sided)	0.100	0.058	0.214	0.789
		N	410	409	406	405
	RFS	Cc	0.087	0.122*	0.083	−0.204**
		Sig. (2-sided)	0.079	0.014	0.094	<0.001
		N	410	409	406	405
	Follow-up time OS/DSS	Cc	0.094	0.122*	0.083	−0.073
		Sig. (2-sided)	0.056	0.013	0.096	0.142
		N	410	409	406	405
	OS	Cc	0.036	0.048	−0.040	−0.052
		Sig. (2-sided)	0.464	0.334	0.423	0.298
		N	410	409	406	405
	DSS	Cc	0.067	0.057	0.027	−0.059
		Sig. (2-sided)	0.178	0.253	0.594	0.232

	N	410	409	406	405
Follow-up time metastasis	Cc	0.075	0.118*	0.050	−0.046
	Sig. (2-sided)	0.131	0.017	0.319	0.357
Metastasis	N	410	409	406	405
	Cc	0.059	0.088	0.092	−0.173**
	Sig. (2-sided)	0.231	0.076	0.063	<0.001
CK20 IRS cytoplasmic	N	410	409	406	405
	Cc	0.222**	0.154**	0.116*	0.029
	Sig. (2-sided)	<0.001	0.002	0.019	0.556
	N	409	408	405	404

*, Correlation is on the 0.05 level significant (2-sided). **Correlation is on the 0.01 level significant (2-sided). Bonferroni correction $\alpha = 0.0025$ (since 20 parameters: $0.05/20 = 0.0025$). Abbreviations: Cc-correlation coefficient; Sig.-significance, AR-androgen receptor; pT-pathological tumor stage; pathological nodal stage; pM-pathological metastasis stage; RFS-relapse free survival, OS-overall survival; DSS-disease-specific survival; IRS-immunoreactive score. Values below 0.0025 are in bold.

Table S3. Univariate Cox's regression analysis: Association of clinicopathological and molecular parameters with RFS.

Parameter	univariate Cox's regression analysis		
	N	RFS	
		HR	p
	410		
>65 years vs. ≤65 years	194 vs. 216	1.18	0.581
Pathological tumor stage	410		
pT2 vs. pT3+4	174 vs. 236	1.37	0.041
Gleason sum at prostatectomy	410		
GS6	213	reference	
GS7	108	5.02	<0.001
GS8-10	60	4.85	<0.001
Perineural invasion	383		
Pn positive vs. Pn negative	236 vs. 147	2.44	0.013
CK20	408		
negative vs. positive	303 vs. 105	1.25	0.556
AR cytoplasm	409		
IRS > 2 vs. IRS ≤2	127 vs. 282	1.32	0.370
AR nuclear	410		
IRS > 2 vs. IRS ≤2	314 vs. 96	1.39	0.417
AR-V7 cytoplasm	406		
IRS > 2 vs. IRS ≤2	347 vs. 59	6.87	0.057

Values $p < 0.05$ are in bold.



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