

Introduction

The expression of the estrogen receptor (ER) and/or the progesterone receptor (PR) is a predictive factor for the response to endocrine treatment and to chemotherapy in primary breast cancer. Knowledge about the prognostic relevance of the PR is rare and partly controversial. Aim of this retrospective study was to analyze the prognostic relevance of PR.

Methods

Between 1995 and 2008, data from 5,144 patients with heterogeneously treated primary breast cancers have been collected in 3 German university hospitals. The laboratories used immunohistochemical assays for the investigation of the ER and PR. The PR-expression was correlated with patient and tumor characteristics. For each outcome parameter overall survival (OS), distant disease free survival (DDFS) and local recurrence free survival (LRFS) cox proportional hazard models were built. Furthermore the effect of the PR status was analyzed according to tumor subgroups.

Results

PR status was associated with a more favourable OS, DDFS and LRFS in the univariate analysis. PR remained an independent prognostic factor for OS and DDFS but not for LRFS in the cox proportional hazard model. For OS and DDFS the prognostic effect of PR appeared to be consistent among the subgroups and was significant for most of them. Comparing subgroups there was a difference between the HR for ER negatives and ER positives. In ER negative tumors the prognostic effect of the PR seemed to be larger (HR=0.40; 95%CI: 0.25-0.63) than in ER positives (HR=0.68; 95%CI: 0.53-0.87). For all other subgroups there appeared to be no interaction between PR status and the other prognostic factors.

Overall survival

Fig. 1: OS for the combination ER/PR

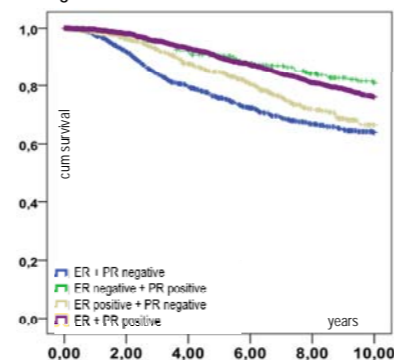


Table 1: Analysis of subgroups with interaction term analysis: OS

	PR negative	PR positive	HR	lower 95% CI	upper 95% CI	p-value	p(interaction)
pT1	849	1904	0.40	0.25	0.63	0.001	0.813
pT2	504	891	0.77	0.52	1.13	0.003	
pT3	63	92	0.50	0.23	1.08	0.081	
pT4	52	71	1.01	0.51	1.99	0.969	
pN0	930	1916	0.75	0.57	0.96	0.047	0.121
pN1	647	1063	0.67	0.48	0.95	0.000	
ductal	1185	2109	0.73	0.55	0.93	0.000	0.852
lobular	172	533	0.78	0.46	1.09	0.055	
other	210	337	0.58	0.37	1.02	0.061	
G1	107	471	0.81	0.42	1.55	0.532	0.368
G2	765	2023	0.42	0.22	0.79	0.000	
G3	707	485	0.67	0.42	0.94	0.015	
ER negative	962	236	0.47	0.36	0.69	0.000	0.090
ER positive	615	2743	0.73	0.61	0.92	0.003	

Distant disease free survival

Fig. 2: DDFS for the combination ER/PR

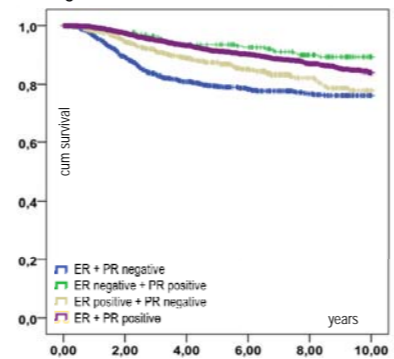


Table 2: Analysis of subgroups with interaction term analysis: DDFS

	PR negative	PR positive	HR	lower 95% CI	upper 95% CI	p-value	p(interaction)
pT1	853	1908	0.68	0.42	0.88	0.041	0.411
pT2	506	897	0.60	0.41	0.75	0.000	
pT3	63	92	0.69	0.25	1.28	0.175	
pT4	52	71	0.66	0.30	1.41	0.284	
pN0	933	1922	0.74	0.58	0.96	0.138	0.212
pN1	650	1067	0.69	0.47	0.74	0.000	
ductal	1200	2117	0.69	0.46	0.75	0.000	0.767
lobular	172	535	0.63	0.38	1.07	0.051	
other	211	337	0.57	0.26	1.31	0.162	
G1	108	475	0.84	0.27	2.71	0.829	0.7
G2	765	2028	0.44	0.24	0.76	0.000	
G3	710	486	0.65	0.38	0.81	0.002	
ER negative	968	238	0.39	0.24	0.63	0.000	0.028
ER positive	615	2751	0.77	0.62	0.93	0.003	

Local recurrence free survival

Fig. 3: LRFS for the combination ER/PR

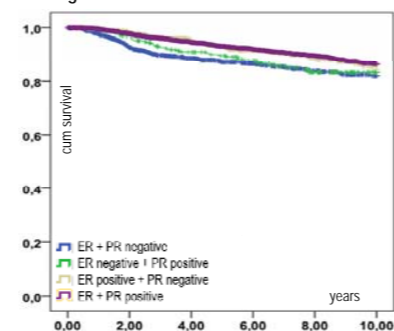


Table 3: Analysis of subgroups with interaction term analysis: LRFS

	PR negative	PR positive	HR	lower 95% CI	upper 95% CI	p-value	p(interaction)
pT1	852	1911	0.99	0.69	1.42	0.995	0.125
pT2	506	896	0.76	0.51	1.13	0.234	
pT3	63	92	0.66	0.27	0.88	0.146	
pT4	52	71	0.82	0.16	1.92	0.377	
pN0	933	1924	1.12	0.78	1.60	0.528	0.044
pN1	649	1069	0.69	0.48	1.00	0.052	
ductal	1199	2118	0.66	0.40	1.11	0.349	0.808
lobular	172	537	0.91	0.50	1.68	0.802	
other	211	338	0.73	0.36	1.59	0.435	
G1	107	476	0.67	0.24	1.30	0.191	0.105
G2	765	2030	0.50	0.12	1.82	0.334	
G3	710	487	1.08	0.64	1.72	0.728	
ER negative	967	240	0.67	0.36	1.30	0.648	0.844
ER positive	615	2753	0.72	0.62	1.21	0.420	

Conclusion

PR positivity results in a similarly favourable prognosis in ER negative and ER positive patients. ER positivity alone does not seem to be sufficient to define a group of patients with the most favourable prognosis. On the contrary, patients with ER positive, PR negative tumors have a significantly deteriorated prognosis and seem to be a patient group, which should be investigated concerning drug resistance mechanisms.

Table 4: Description of the patient characteristics

variable		N (PR negative)	% (PR negative)	N (PR positive)	% (PR positive)	N (Total)	% (Total)	P-value
pT	pT0 or pTis (after neoadjuvant chemotherapy)	124	6.9	26	0.8	150	2.9	<0.001
	pT1	976	54.6	2161	64.4	3137	61.0	
	pT2	562	31.4	994	29.6	1556	30.2	
	pT3	66	3.7	99	2.9	165	3.2	
	pT4	60	3.4	76	2.3	136	2.6	
pN	total	1788	100.0	3356	100.0	5144	100.0	
	pN0	1064	59.5	2158	64.3	3222	62.6	0.001
	pN1	724	40.5	1198	35.7	1922	37.4	
histology	total	1788	100.0	3356	100.0	5144	100.0	
	invasive ductal	1289	72.9	2245	67.7	3534	69.5	<0.001
	lobular	232	13.1	684	20.6	916	18.0	
grading	total	248	14.0	387	11.7	635	12.5	
	1,00	111	6.7	493	15.9	604	12.7	<0.001
	2,00	790	48.0	2090	67.6	2880	60.7	
	3,00	746	45.3	511	16.5	1257	26.5	
estrogen receptor	total	1647	100.0	3094	100.0	4741	100.0	
	ER negative	1092	61.2	282	8.4	1374	26.8	<0.001
	ER positive	691	38.8	3064	91.6	3755	73.2	
chemotherapy	total	1783	100.0	3346	100.0	5129	100.0	
	no chemotherapy	700	46.7	1820	66.9	2520	59.7	<0.001
	chemotherapy	800	53.3	900	33.1	1700	40.3	
endocrine treatment	total	1500	100.0	2720	100.0	4220	100.0	
	no endocrine treatment	1012	69.9	1054	40.6	2066	51.1	<0.001
	endocrine treatment	435	30.1	1542	59.4	1977	48.9	
radiotherapy	total	1447	100.0	2596	100.0	4043	100.0	
	no radiotherapy	411	29.2	772	30.6	1183	30.1	0.373
	radiotherapy	997	70.8	1755	69.4	2752	69.9	
pre-/postmenopausal	total	1408	100.0	2527	100.0	3935	100.0	
	premenopausal	503	29.2	1008	31.5	1511	30.7	0.091
	postmenopausal	1219	70.8	2191	68.5	3410	69.3	
total		1722	100.0	3199	100.0	4921	100.0	

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