

Neoadjuvant Chemotherapy of Triple-Negative Breast Cancer: Evaluation of Early Clinical Response, Pathological Complete Response Rates, and Addition of Platinum Salts Benefit Based on Real-World Evidence

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***BRCA* germline mutation testing categorization**

Out of a total of 237 patients, 72 (30%) patients were *BRCA1/2* mutated, 109 (46%) patients were *BRCA1/2* unmutated, and in 56 (24%) patients, the genetic testing was not performed. The age distribution according to *BRCA* testing is shown in Figure S1A. The median age was 37 years in the *BRCA1/2* mutated patients, 44 years in the were *BRCA1/2* unmutated patients and 63 years for untested patients. The untested patients were not indicated to genetic testing following the guidelines for high-risk patients, especially family cancer history was not described. According to a published study[1], the expected prevalence of *BRCA1/2* carriers in women with TNBC diagnosed at age 50 or above is less than 5%. Consequently, the untested patients were considered presumptive noncarriers and analyzed together with *BRCA1/2* noncarriers. Similarly, in the case of unknown *BRCA* status in daily clinical practice, these patients are considered *BRCA1/2* negative.

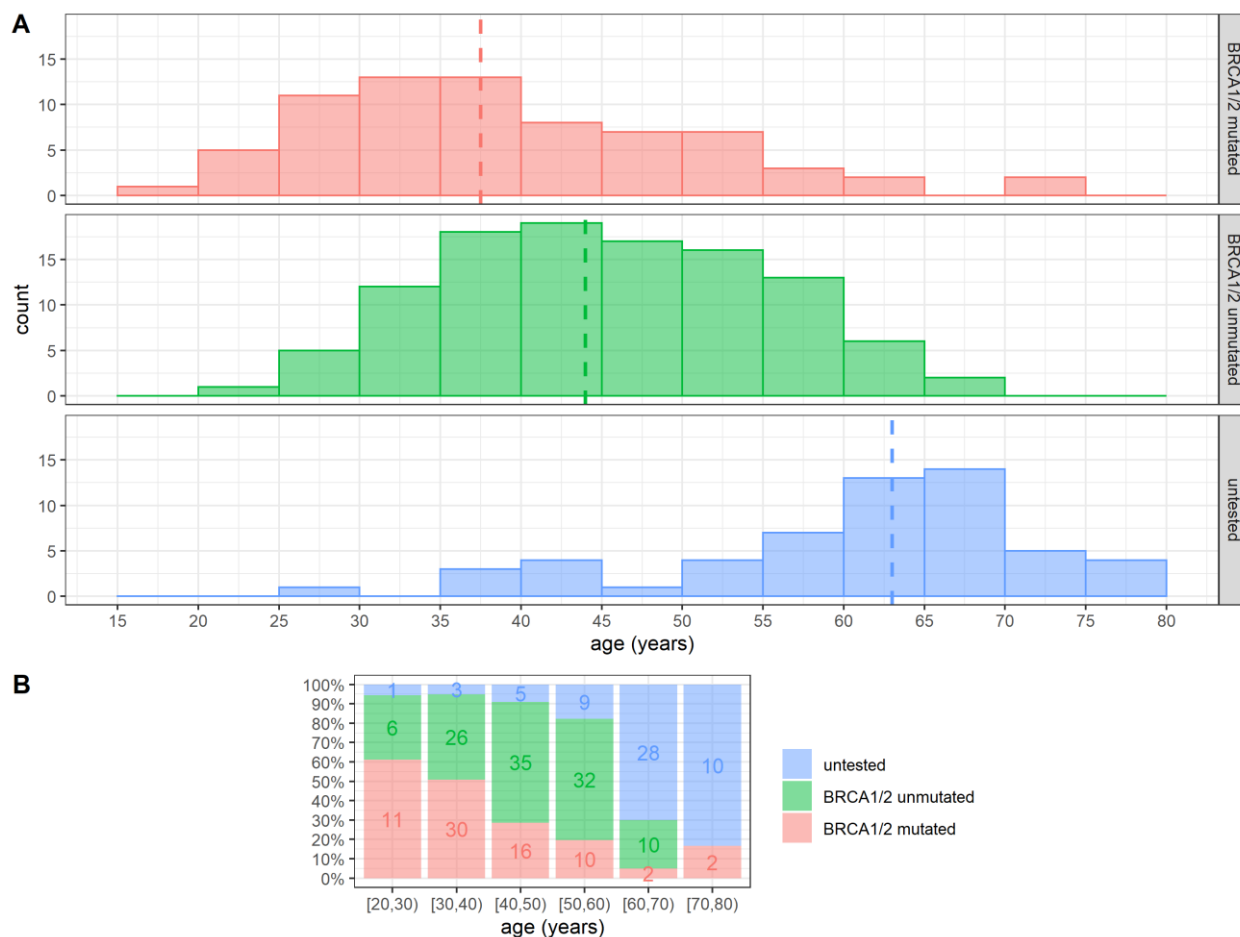


Figure S1. (A) Age distribution according to *BRCA* testing. **(B)** The proportion of *BRCA1/2* mutation in age decade.

- Engel, C.; Rhiem, K.; Hahnen, E.; Loibl, S.; Weber, K.E.; Seiler, S.; Zachariae, S.; Hauke, J.; Wappenschmidt, B.; Waha, A.; et al. Prevalence of Pathogenic *BRCA1/2* Germline Mutations among 802 Women with Unilateral Triple-Negative Breast Cancer without Family Cancer History. *BMC Cancer* 2018, 18, doi:10.1186/s12885-018-4029-y.

Table S1. ECR-adjusted univariable analysis of pCR predictors according to NACT type. NACT, neoadjuvant chemotherapy; BMI, Body mass index

	NACT	N	OR	95% CI	<i>p</i>	<i>p</i> for interaction
NAT platinum / nonplatinum		68 / 169	3.14	[1.57;6.58]	<0.001	
Early clinical response						0.896
yes / no	platinum	43 / 25	21.33	[6.01;103.5]	<0.001	
	nonplatinum	126 / 43	18.64	[5.41;117.4]	<0.001	
Age (10-years)						0.200
	platinum	68	1.30	[0.74;2.36]	0.362	
	nonplatinum	169	0.85	[0.65;1.11]	0.244	
Age (years)						0.016
≥ 45 / < 45	platinum	24 / 44	4.53	[1.06;31.5]	0.041	
	nonplatinum	104 / 65	0.60	[0.30;1.20]	0.151	
Menopausal status						0.108
peri-post / pre	platinum	16 / 52	3.07	[0.62;23.4]	0.177	
	nonplatinum	92 / 77	0.69	[0.35;1.36]	0.287	
BMI (kg/m²)						0.653
≥ 30 / < 30	platinum	9 / 59	4.05	[0.57;40.3]	0.166	
	nonplatinum	39 / 130	2.23	[0.99;5.17]	0.052	
BRCA						0.951
mutated / undetected	platinum	48 / 20	0.92	[0.12;4.79]	0.928	
	nonplatinum	24 / 145	1.04	[0.39;2.74]	0.941	
Baseline cT						0.074
T3-T4d / T1-T2	platinum	16 / 52	1.28	[0.31;5.98]	0.735	
	nonplatinum	44 / 125	0.27	[0.09;0.68]	0.005	
Baseline cN						0.567
N1-N3 / N0	platinum	33 / 35	0.80	[0.24;2.80]	0.723	
	nonplatinum	96 / 73	1.19	[0.60;2.38]	0.611	
Grade						0.585
3 / 2	platinum	57 / 8	0.99	[0.14;6.01]	0.989	
	nonplatinum	138 / 28	1.74	[0.69;4.68]	0.242	
Ki-67						0.035
≥ 65% / < 65%	platinum	48 / 18	5.15	[1.24;24.7]	0.024	
	nonplatinum	115 / 49	0.90	[0.42;1.94]	0.790	
Dose-dense AC						0.945
yes / no	platinum	19 / 49	0.84	[0.22;3.20]	0.791	
	nonplatinum	16 / 153	0.90	[0.28;2.77]	0.879	
Early change from baseline cT						0.171
undecreased from any T /	platinum	29 / 27	0.69	[0.13;4.10]	0.688	
decreased from T1-T2	nonplatinum	52 / 85	0.45	[0.15;1.26]	0.010	
decreased from T3-T4d /	platinum	12 / 27	1.57	[0.30;10.6]		
decreased from T1-T2	nonplatinum	32 / 85	0.24	[0.08;0.64]		
Early change from baseline cN						0.140
decreased from N1-N3 /	platinum	12 / 35	0.60	[0.14;2.82]	0.763	
N0	nonplatinum	53 / 73	2.00	[0.94;4.32]	0.003	
undecreased from N1-N3 /	platinum	21 / 35	1.17	[0.23;8.78]		
N0	nonplatinum	43 / 73	0.30	[0.08;0.91]		

Table S2. Univariable and multivariable analysis of pCR predictors according to NACT type for early responders.
NACT, neoadjuvant chemotherapy; BMI, Body mass index

		Univariable analysis					Multivariable analysis			
	NACT	N	OR	95% CI	<i>p</i>	<i>p</i> for inter.	OR	95% CI	<i>p</i>	<i>p</i> for inter.
NAT platinum / nonplatinum		43 / 126	3.20	[1.52;7.16]						
Age (10-years)						0.187				
	platinum	43	1.29	[0.64;2.81]	0.480					
	nonplatinum	126	0.78	[0.58;1.02]	0.071					
Age (years)						0.014				0.013
≥ 45 / < 45	platinum	13 / 30	6.00	[0.96;117]	0.056		16.9	[1.54;721]	0.017	
	nonplatinum	75 / 51	0.53	[0.26;1.09]	0.086		0.75	[0.33;1.68]	0.481	
Menopausal status						0.222				
peri-post / pre	platinum	7 / 36	2.31	[0.33;46.5]	0.431					
	nonplatinum	67 / 59	0.61	[0.30;1.22]	0.162					
BMI (kg/m^2)						0.683				
≥ 30 / < 30	platinum	4 / 39	1.03	[0.12;22.2]	0.978					
	nonplatinum	29 / 97	1.78	[0.77;4.20]	0.176					
BRCA						0.911				
mutated / undetected	platinum	39 / 4	0.97	[0.04;8.59]	0.978					
	nonplatinum	18 / 108	1.12	[0.41;3.07]	0.827					
Baseline cT						0.082				
T3-T4d / T1-T2	platinum	9 / 34	1.26	[0.25;9.51]	0.793					
	nonplatinum	24 / 102	0.22	[0.07;0.61]	0.003					
Baseline cN						0.602				
N1-N3 / N0	platinum	17 / 26	0.72	[0.18;2.98]	0.643					
	nonplatinum	70 / 56	1.09	[0.54;2.21]	0.811					
Grade						0.422				
3 / 2	platinum	35 / 5	0.62	[0.03;4.91]	0.680					
	nonplatinum	103 / 21	1.66	[0.64;4.50]	0.298					
Ki-67						0.014				0.004
≥ 65% / < 65%	platinum	34 / 8	7.78	[1.51;47.6]	0.014		24.8	[2.59;770]	0.004	
	nonplatinum	89 / 34	0.79	[0.36;1.75]	0.568		0.77	[0.31;1.89]	0.574	
Dose-dense AC						0.790				
yes / no	platinum	13 / 30	1.21	[0.28;6.42]	0.803					
	nonplatinum	13 / 113	0.94	[0.29;2.99]	0.911					
Early change from baseline cT						0.211				0.841
undecreased from any	platinum	7 / 27	0.88	[0.15;7.07]	0.957		0.26	[0.01;5.13]	0.558	
T / decreased from T1-T2	nonplatinum	17 / 85	0.54	[0.18;1.54]	0.006		0.31	[0.09;1.06]	0.011	
decreased from T3-T4d	platinum	9 / 27	1.23	[0.23;9.53]			0.45	[0.04;6.63]		
/ decreased from T1-T2	nonplatinum	24 / 85	0.20	[0.06;0.56]			0.21	[0.06;0.66]		
Early change from baseline cN						0.064				0.020
decreased from N1-N3	platinum	12 / 26	0.60	[0.13;2.87]	0.767		0.57	[0.04;7.57]	0.266	
/ N0	nonplatinum	52 / 56	1.85	[0.86;4.02]	<0.001		2.73	[1.14;6.93]	0.003	
undecreased from N1-N3 / N0	platinum	5 / 26	1.20	[0.14;25.9]			6.96	[0.39;407]		
	nonplatinum	18 / 56	0.14	[0.02;0.57]			0.27	[0.04;1.23]		