PS5-04-21: Impact of Germline *BCRA* Variants in the Neoadjuvant Treatment

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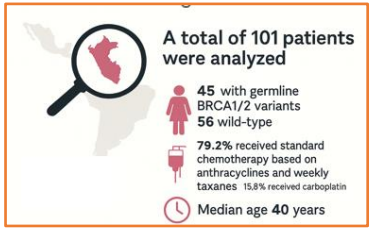
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Background

Carriers of pathogenic *BRCA1* and *BRCA2* variants often develop breast cancers with distinct pathological features, frequently associated with more aggressive phenotypes such as triple-negative tumors. Previous studies have reported greater benefit from chemotherapy and higher rates of pathological complete response in this population. Objective: To evaluate the response to neoadjuvant therapy and survival outcomes in breast cancer patients with germline *BRCA*1/2 variants compared with those with wild-type phenotypes.

Methods and Materials

Women diagnosed with breast cancer and referred for genetic evaluation at the National Institute of Neoplastic Diseases (INEN, Lima) between August 2013 and March 2020 were included. Eligible participants meeting clinical criteria were enrolled in the inter-institutional protocol INEN13-48: *Hereditary and Familial Cancer Study in the Peruvian Population*, as part of the project *Molecular Genetic Studies in Cancer Patients and Their Relatives* (IRB #96144, City of Hope). Genetic testing was performed at the City of Hope (COH).

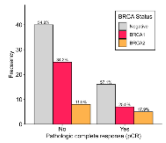


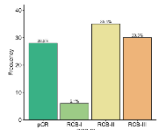
Results

Table 1. Baseline clinicopathological characteristics of breast cancer patients according to pathological complete response (pCR)

Characteristic	Overall N = 101[1]	pCR		p-value[2]
		No N = 74[1]	Yes N = 27[1]	
BRCA status				0.5
Negative	56 (55.4%)	40 (54.8%)	16 (57.1%)	
BRCA1	32 (31.7%)	25 (34.2%)	7 (25.0%)	
BRCA2	13 (12.9%)	8 (11.0%)	5 (17.9%)	
Clinical Stage				0.6
II	32 (31.7%)	22 (30.1%)	10 (35.7%)	
III	69 (68.3%)	51 (69.9%)	18 (64.3%)	
Subtype				0.062
HR+/HER2-	18 (18.2%)	17 (23.3%)	1 (3.8%)	
HER2+	11 (11.1%)	8 (11.0%)	3 (11.5%)	
Triple negative	70 (70.7%)	48 (65.8%)	22 (84.6%)	
Unknown	2	0	2	
RCB				
pCR	28 (28.3%)	0 (0.0%)	28 (100.0%)	
RCB-I	6 (6.1%)	6 (8.5%)	0 (0.0%)	
RCB-II	35 (35.4%)	35 (49.3%)	0 (0.0%)	
RCB-III	30 (30.3%)	30 (42.3%)	0 (0.0%)	
Unknown	2	2	0	
Treatment regimen				0.8
Anthracycline → Taxane	80 (79.2%)	57 (78.1%)	23 (82.1%)	
Carboplatin-based	16 (15.8%)	11 (15.1%)	5 (17.9%)	
Anthracycline-only	4 (4.0%)	4 (5.5%)	0 (0.0%)	
Taxane-only	1 (1.0%)	1 (1.4%)	0 (0.0%)	

[1] n (%)
[2] Fisher's exact test; Pearson's Chi-squared test





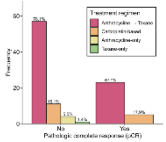
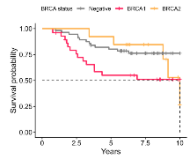
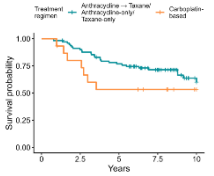


Table 2. Logistic regression analysis of clinicopathological and genetic factors associated with pathological complete response (pCR) in breast cancer

Characteristic	N	Event N	OR	95% CI	p-value
Age at Diagnosis	101	28	1	0.95–1.05	0.98
BRCA1/2 Status	101	28			
Negative					
BRCA1/2			0.91	0.34–2.18	0.88
BRCA status	101	28			
Negative					
BRCA1			0.7	0.26–1.89	0.49
BRCA2			1.56	0.42–5.44	0.49
FH of Breast Cancer	101	28			
No			—	—	
Yes			0.59	0.16–1.82	0.39
Clinical Stage	101	28			
II			—	—	
III			0.78	0.31–2.00	0.59
Subtype	99	26			
HR+/HER2-			—	—	
HER2+			6.37	0.69–147	0.13
Triple negative			1.73	1.45–105	0.059
Treatment regimen	101	28			
Anthracycline → Taxane/Anthracycline only/Taxane only					
Carboplatin-based			1.23	0.35–3.77	0.73

Abbreviations: CI = Confidence Interval, OR = Odds Ratio





Overall Survival

Characteristic	N	HR	95% CI	p-value
BRCA status	101			
Negative				
BRCA1		2.37	1.14–4.92	0.021
BRCA2		1.39	0.50–3.87	0.5
FH of Breast Cancer	101			
No		—	—	
Yes		2.07	1.01–4.26	0.048
Clinical Stage	101			
II		—	—	
III		1.23	0.60–2.12	>0.9
Subtype	99			
HR+/HER2-		—	—	
HER2+		2.19	0.49–9.80	0.3
Triple negative		2.85	0.80–8.79	0.11
First-Degree Family History (BC/OC/PC/PCa)	101			
No		—	—	
Yes		2.20	1.11–4.45	0.025
Regimen	101			
Anthracycline → Taxane/Anthracycline-only/Taxane-only		—	—	
Carboplatin-based		1.89	0.80–4.96	0.15

Abbreviations: CI = Confidence Interval, HR = Hazard Ratio

Discussion

A total of 101 patients were analyzed, including 45 with germline *BRCA*1/2 variants and 56 wild-type. Patients received standard chemotherapy based on anthracyclines and weekly taxanes (79.2%); only a minority had access to carboplatin (15.8%) due to public policy and approval restrictions. The median age (40 years) was comparable between groups, as all participants were enrolled in the hereditary breast cancer screening program. No significant differences were observed in pathological complete response (pCR) between *BRCA* variant carriers and wild-type patients. However, a correlation was noted between pCR and the triple-negative subtype (p=0.053). Regarding overall survival, *BRCA*1 carriers had poorer outcomes, with a hazard ratio of 2.37, whereas *BRCA*2 carriers showed survival outcomes similar to wild-type breast cancer patients. It is likely that the pCR results in BRCA mutation carriers were not optimal due to the limited use of carboplatin, a drug that has shown significantly improved response rates in other studies. Overall survival data are still under follow-up.

Conclusions

In this cohort of 101 breast cancer patients, *BRCA*1 carriers had worse overall survival (median 10 years, HR 2.37) compared with *BRCA*2 and wild-type patients, despite similar pCR rates. Pathological complete response was mainly associated with the triple-negative subtype. Limited access to carboplatin likely contributed to suboptimal responses in BRCA mutation carriers, underscoring the need for broader availability of platinum-based therapy.

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