The Risk of Contralateral Breast Cancer in Women with *PALB2*-Associated Breast Cancer

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Introduction

- Women with a germline pathogenic variant (PV) in *PALB2* have lifetime risk of breast cancer exceeding 40%
- Preliminary evidence of poor breast cancer survival in women with *PALB2* PV
- Limited evidence on risk of contralateral breast cancer risk in women with *PALB2*-associated breast cancer
- Unclear if breast cancer treatment should be personalized for women with *PALB2*-associated breast cancer

Study Objectives

1. To describe the clinical characteristics of *PALB2*-associated breast cancer
2. To estimate the risk of contralateral breast cancer in women with *PALB2* PVs
3. To identify factors predictive of contralateral breast cancer risk in women with *PALB2*-associated breast cancer

Methods

PALB2 Study

Prospective

Questionnaire Participants
- Informed Consent
- Baseline Questionnaire
- Follow-Up Qs every 2 years for 10 years
- Family history questionnaire
- Consent to collect medical records and genetic test results

Retrospective

Data-only Participants
- Medical chart review only
- Site sends de-identified data

Eligibility Criteria

- Breast cancer stage 0 to IV
- Diagnosed in 2000 or later
- *PALB2* pathogenic (or likely pathogenic) variant

Excluded:
- Previous diagnosis of any cancer (other than non-melanoma skin)

Variables Collected

- Demographic Characteristics
- *PALB2* variant
- Clinical Characteristics (histological subtype, size, nodal status, grade, hormone status)
- Treatment Details (surgery, radiation, chemotherapy, adjuvant treatments)
- New cancers
- Oophorectomy and salpingectomy
- Vital status (cause of death)

Results

Table 1: Clinical and Demographic Characteristics of Sample (n=888)

	Mean (range) or Frequency (%)
Follow-up mean (years)	5.6 (0.1-24.0)
Age at diagnosis mean (years)	49.3 (22-83)
Laterality	
Bilateral	36(4.1)
Unilateral	851(95.9)
Missing	1
TNM Stage	
0	57(7.3)
1	267(34.3)
2	311(40.0)
3	118(15.2)
4	25(3.2)
Unknown	110
Estrogen Receptor Status	
Positive	602(73.6)
Negative	216(26.4)
Unknown	70
Progesterone Receptor Status	
Positive	513(65.1)
Negative	275(34.9)
Unknown	100
Her 2 Status	
Positive	87(11.8)
Negative	631(85.4)
Equivocal	21(2.8)
unknown	149
Histology	575(64.8)
Ductal	57(6.4)
Lobular	5(0.6)
Medullary	25(2.8)
Other	63(7.1)
Unknown	163(18.4)

Table 2: Cumulative Risks of CBC

Years From Diagnosis	All Subjects	<50 Years at Diagnosis	≥50 Years at Diagnosis
5 Years	3.7%	4.7%	2.6%
10 Years	12.9%	13.6%	12.1%
15 Years	26.4%	19.5%	34.8%

Results

Figure 1a: Cumulative Incidence of CBC; Figure 1b: by ER Status

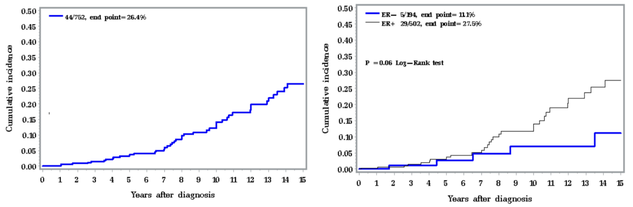


Table 3: Relative Risks of CBC Associated with Selected Factors

Variable	CBC case/total	Univariate RR (95%CI) p-value	Multivariate[a] RR (95%CI) p-value
Age at Diagnosis			
<40	7/149	1.0	1
40-49	18/258	1.50(0.62-3.62) 0.37	1.56(0.62-3.94) 0.35
≥50	28/343	1.59(0.69-3.66) 0.28	1.94(0.80-4.66) 0.14
Oophorectomy			
No	45/586	1.0	1
Yes	2/120	0.17(0.04-0.70) 0.01	0.17(0.04-0.71) 0.02
Missing	6/46		
Chemotherapy			
No	21/222	1	1
Yes	30/514	0.59(0.33-1.04) 0.07	0.73(0.38-1.41) 0.35
Missing	2/16		
Tamoxifen			
No	28/483	1.0	1
Yes	25/269	1.10(0.64-1.89) 0.73	1.02(0.53-1.94) 0.96
ER Status			
Negative	8/194	1.0	1
Positive	33/502	1.79(0.82-3.89) 0.14	1.15(0.45-2.93) 0.77
Missing	12/56		
Grade			
I/II	31/352	1.0	1
III	10/309	0.30(0.14-0.63) 0.002	0.30(0.13-0.69)0.005
Missing	12/90		
Nodal Status			
Negative	31/502	1.0	1
Positive	14/194	0.95(0.51-1.80) 0.88	1.03(0.52-2.07) 0.93
Missing	8/56		

Results

Table 4: Relative Risks of CBC Associated with Selected Factors for 502 ER+ Subjects

Variable	CBC case/total	Univariate RR (95%CI) p-value	Multivariate[a] RR (95%CI) p-value
Age at Diagnosis			
<40	2/110	1	1
40-49	12/187	3.70(0.82-16.80) 0.09	5.31(1.11-25.5) 0.04
≥50	19/203	3.86(0.90-16.61) 0.07	4.32(0.95-19.6) 0.06
Oophorectomy			
No	29/392	1.0	1
Yes	1/86	0.11(0.02-0.83) 0.03	0.10(0.01-0.74) 0.02
Missing	3/24		
Chemotherapy			
No	16/182	1	1
Yes	17/317	0.53(0.53-1.27) 0.76	0.66(0.30-1.45) 0.30
Missing	0/3		
Tamoxifen			
No	10/257	1	1
Yes	23/245	1.27(0.60-2.70) 0.53	1.06(0.47-2.39) 0.89
Grade			
I/II	26/306	1	1
III	4/166	0.17(0.05-0.60) 0.01	0.14(0.04-0.53) 0.004
Missing	3/30		
Nodal Status			
Negative	21/336	1	1
Positive	12/154	1.24(0.60-2.53) 0.56	1.10(0.48-2.50) 0.83
Missing	0/12		

Conclusions

- High 15-year risk of contralateral breast cancer in women with *PALB2*-associated breast cancer
- Bilateral mastectomy may be considered for surgical treatment
- For women with ER-positive tumors, oophorectomy significantly reduces the risk of contralateral breast cancer
- Women with *PALB2*-associated breast cancer should be counselled on risk of contralateral breast cancer at the time of surgical decision making
- These data highlight the importance of genetic testing at the time of breast cancer diagnosis

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