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Age at Diagnosis of Breast Cancer for Women with Pathogenic Variants in *BARD1*, *RAD51C*, and *RAD51D*

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Background

- Pathogenic variants (PVs) in *BARD1*, *RAD51C*, and *RAD51D* confer an increased lifetime risk of approximately two-fold for breast cancer.[1]
- The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend that PV carriers undergo yearly mammogram with consideration of breast MRI, starting at age 40.[2]

OBJECTIVE: We investigated the median age at diagnosis for women with breast cancer who carry a PV in *BARD1*, *RAD51C*, or *RAD51D* and compared that to the recommended screening age in the NCCN Guidelines® for these and other breast cancer-associated genes.[2]

Methods

- This study included women with a personal history of breast cancer who were tested with the MyRisk multi-gene panel from Myriad Genetics between September 2013 and March 2024 and who were found to carry a single PV in *BARD1*, *RAD51C*, or *RAD51D*.
- Patients were evaluated for age at first breast cancer diagnosis.
- Women identified with PVs in *ATM*, *CHEK2*, *PALB2*, *BRCA1*, and *BRCA2* over the same time period were evaluated for comparison.
- Clinical information was collected from provider-completed test request forms.

References: **1.** Breast Cancer Association Consortium, et al. Breast Cancer Risk Genes - Association Analysis in More than 113,000 Women. *N Engl J Med.* 2021 384:428-439.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. V.3.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed August 15, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Disclosures: DC, JW and SSR authors were employees of Myriad Genetics, Inc. at the time of this study and received salaries and stock as compensation.

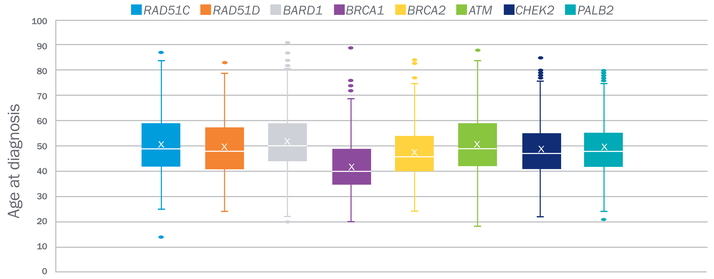
Results

- A total of 1,485 women (defined as identifying as female at birth) had a PV in *BARD1, RAD51C,* or *RAD51D*.
- The median age of first breast cancer diagnosis was 51, 49, and 48 years, respectively, for these genes **(Table 1)**.
  - For all three genes, the earliest age at first diagnosis was between 14 and 24 years.
- The median ages at first diagnosis were similar to those of women with a PV in *ATM* (50 years), *CHEK2* (49 years), *PALB2* (49 years), and *BRCA2* (47 years), and older than those with a PV in *BRCA1* (42 years) **(Figure 1)**.

Table 1. Age at first breast cancer diagnosis by PV

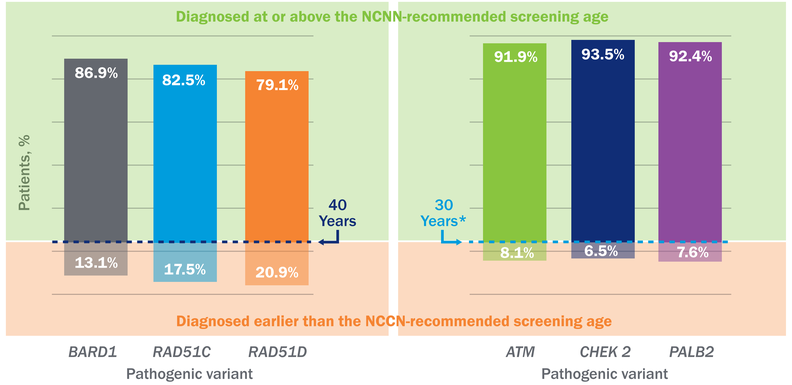
Gene with PV	Total number of PV carriers, n (%)	Earliest age at first BC diagnosis, y	Median age at first BC diagnosis, y
Evaluated PV Group	1,485 (100)		
BARD1	692 (46.6)	20	51
RAD51C	502 (33.8)	14	49
RAD51D	291 (19.6)	24	48
Comparison PV group	19,165 (100)		
ATM	2,802 (14.6)	18	50
CHEK2	4,239 (22.1)	16	49
PALB2	2,356 (12.3)	21	49
BRCA1	4,538 (23.7)	17	42
BRCA2	5,230 (27.3)	22	47

Figure 1. Mean age at first breast cancer diagnosis by PV



- A substantial number of *BARD1*, *RAD51C*, and *RAD51D* PV carriers were diagnosed earlier than the the National Comprehensive Cancer Network® (NCCN®)-recommended screening age of 40 years;[2] percentages were higher than for comparator PV carriers diagnosed earlier than their respective NCCN Guideline-recommended screening age of 30–35 years[2] **(Figure 2)**.

Figure 2. Percentages of PV carriers diagnosed with breast cancer earlier than the recommended screening age



*Percentages calculated using the lower end of the 30–35-year recommended age range.

Conclusions

- For women with a PV in *BARD1, RAD51C,* and *RAD51D*, the median age at first breast cancer diagnosis was similar to that of other breast cancer-associated genes.
- Collectively, our data suggest that a starting breast cancer screening age similar to that recommended for genes such as *ATM* and *CHEK2* (age 30–35) may be suitable for women with PVs in *BARD1*, *RAD51C*, or *RAD51D*.