

BARD1 Mutations

Cancer Risks and General Management Recommendations

There are currently no national consensus guidelines outlining specific clinical management recommendations for individuals who carry a *BARD1* gene mutation. Additionally, exact lifetime cancer risks associated with *BARD1* mutations are unknown at this time. Current literature may be specific to one particular *BARD1* mutation and/or ethnic population.

Cancer Type	<i>BARD1</i> Mutation Carrier Cancer Risks	General Population Lifetime Cancer Risks	Surveillance/Management Recommendations
Female Breast Cancer	Potential Increase (including triple negative breast cancer)	12.4%	<ul style="list-style-type: none">• Insufficient evidence to support intervention based on <i>BARD1</i> mutation status alone.¹• Discuss family history and personal risk factors with a physician to determine appropriate surveillance and management options.• Limited data has been published regarding an increased risk of breast cancer associated with <i>BARD1</i> gene mutations²⁻⁵; two large case-control studies reported approximately two fold risk.^{6,7}
Ovarian Cancer	Unknown	1.3%	<ul style="list-style-type: none">• Insufficient evidence to offer ovarian cancer screening or risk reducing surgery based on <i>BARD1</i> mutation status alone.¹• Discuss family history and personal risk factors with a physician in ovarian cancer risk management decision-making.• Studies have reported <i>BARD1</i> mutations in patients with ovarian cancer but the data is limited at this time and may be impacted by type of gene mutation.⁸⁻¹¹

Other Cancer Risks: It is currently unknown if *BARD1* mutations cause a predisposition to other cancers. At this time, there are no known cancer risks for men with a *BARD1* mutation. Patients are encouraged to contact our office every 1-2 years to determine if there is any new information related to the associated risks and clinical management of individuals with *BARD1* mutations.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *BARD1* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- For carriers of a known mutation, assisted reproduction (with or without egg or sperm donation), pre-implantation genetic testing, and prenatal diagnosis options exist.
- All family members are encouraged to pursue genetic counseling to clarify their risks. Family members can visit www.FindAGeneticCounselor.com to find genetic services near them.

References

*please note that some references may be specific to one particular mutation and/or ethnic population

1. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 1.2020. 2019.
2. De Brakeleer S, De Greve J, Loris R, et al. Cancer predisposing missense and protein truncating BARD1 mutations in non-BRCA1 or BRCA2 breast cancer families. *Human mutation*. 2010;31(3):E1175-1185.
3. Ghimenti C, Sensi E, Presciuttini S, et al. Germline mutations of the BRCA1-associated ring domain (BARD1) gene in breast and breast/ovarian families negative for BRCA1 and BRCA2 alterations. *Genes Chromosomes Cancer*. 2002;33(3):235-242.
4. Gonzalez-Hormazabal P, Reyes JM, Blanco R, et al. The BARD1 Cys557Ser variant and risk of familial breast cancer in a South-American population. *Mol Biol Rep*. 2012;39(8):8091-8098.
5. Karppinen SM, Heikkinen K, Rapakko K, Winqvist R. Mutation screening of the BARD1 gene: evidence for involvement of the Cys557Ser allele in hereditary susceptibility to breast cancer. *Journal of medical genetics*. 2004;41(9):e114.
6. Kurian AW, Hughes E, Handorf EA, et al. Breast and Ovarian Cancer Penetrance Estimates Derived From Germline Multiple-Gene Sequencing Results in Women. *JCO Precision Oncology*. 2017(1):1-12.
7. Couch FJ, Shimelis H, Hu C, et al. Associations Between Cancer Predisposition Testing Panel Genes and Breast Cancer. *JAMA Oncol*. 2017;3(9):1190-1196.
8. Ratajska M, Antoszewska E, Piskorz A, et al. Cancer predisposing BARD1 mutations in breast-ovarian cancer families. *Breast cancer research and treatment*. 2012;131(1):89-97.
9. Sauer MK, Andrulis IL. Identification and characterization of missense alterations in the BRCA1 associated RING domain (BARD1) gene in breast and ovarian cancer. *Journal of medical genetics*. 2005;42(8):633-638.
10. Pennington KP, Swisher EM. Hereditary ovarian cancer: beyond the usual suspects. *Gynecologic oncology*. 2012;124(2):347-353.
11. Walsh T, Casadei S, Lee MK, et al. Mutations in 12 genes for inherited ovarian, fallopian tube, and peritoneal carcinoma identified by massively parallel sequencing. *Proc Natl Acad Sci U S A*. 2011;108(44):18032-18037.