Updated December 2019 (NCCN v1.2020)

RAD51D Mutations

Cancer Risks and General Management Recommendations

***RAD51D* Mutation Carrier Cancer Risks**	**General Population Lifetime Cancer Risks**	**Surveillance/Management Recommendations[1]**
Ovarian Cancer[2,3] 7-14%	1-2%	*Surgery* • Consider risk-reducing salpingo-oophorectomy (RRSO) at age 45-50 years, or earlier based on ovarian cancer family history ○ Insufficient evidence exists to recommend an optimal age for RRSO • Further pathological examination of the ovarian specimen on RRSO can yield greater detection of ovarian cancer, and should be considered in individuals with *RAD51D* mutations[4] *Surveillance* • For women who have not elected RRSO, transvaginal ultrasound combined with serum CA-125 for ovarian cancer may be considered at their clinician's discretion • The benefit of ovarian cancer surveillance is uncertain at this time

Breast cancer: The lifetime risk to develop breast cancer in women with a *RAD51D* mutation is currently unknown. Some studies indicate the *RAD51D* gene may not be associated with breast cancer at all,[5] but other studies show that it could be a low penetrant gene for breast cancer.[6] Current NCCN guidelines (v1.2020) state that there is a potential increased risk for triple-negative breast cancer, however there is insufficient evidence to recommend modified breast cancer risk management based on *RAD51D* mutation status alone. An individual's personal and family history should be considered in developing an appropriate surveillance plan.

Treatment: *RAD51D* mutation carriers may be sensitive to specific chemotherapy agents and thus may benefit from therapies suggested for *BRCA1* and *BRCA2* carriers, such as poly ADP ribose polymerase (PARP) inhibitors.

Other Cancer Risks: Preliminary evidence of an association between *RAD51D* mutations in prostate cancer has been proposed.[7] However, this association has not been completely established and more information is needed.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *RAD51D* 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

1. NCCN v1.2020 Genetic/Familial High Risk Assessment: Breast, Ovarian, and Pancreatic.
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4. Powell CB, et al. 2005. Risk-reducing salpingo-oophorectomy in BRCA mutation carriers: role of serial sectioning in the detection of occult malignancy. *Journal of Clinical Oncology.* 23(1):127-132.
5. Osher DJ et al. Mutation analysis of RAD51D in non-BRCA1/2 ovarian and breast cancer families. Br J Cancer. 2012; 106(8):1460-3.
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7. Pritchard, C.C. et al. “Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer.” *The New England journal of medicine* 375.5 (2016): 443–453. *PMC*. Web. 22 Feb. 2018.