Updated December 2019 (NCCN v2.2020)

RAD51C Mutations

Cancer Risks and General Management Recommendations

***RAD51C* Mutation Carrier Cancer Risks**	**General Population Lifetime Cancer Risks**	**Surveillance/Management Recommendations[1]**
Ovarian Cancer 5-9%[2,3]	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 *RAD51C* 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

Other cancer risks: The lifetime risk to develop breast cancer in women with a *RAD51C* mutation is currently unknown. Some studies indicate the *RAD51C* gene may not be associated with breast cancer at all,[5,6] but other studies suggest that it could be a low penetrant gene for breast cancer.[6] Current NCCN guidelines (v2.2020) 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 *RAD51C* mutation status alone. An individual's personal and family history should be considered in developing an appropriate surveillance plan.

Treatment: *RAD51C* 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.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *RAD51C* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- Rarely, individuals inherit two *RAD51C* mutations (one from each parent), and may develop Fanconi Anemia (FA).
  - FA is characterized by physical abnormalities as well as pediatric leukemia and other cancers.
  - *RAD51C* genetic testing for the partner of an individual with a *RAD51C* mutation may be appropriate to clarify the risk of having children with FA.
- 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, including reproductive 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. PMID: 15625367.[4] Pelttari L et al. RAD51C is a susceptibility gene for ovarian cancer. Hum Mol Genet. 2011; 20(16):3278-88. PMID 21616938.
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