Updated December 2019 (NCCN v1.2020)

MRE11A Mutations

Cancer Risks and General Management Recommendations

***MRE11A* Mutation Carrier Cancer Risks**	**General Population Lifetime Cancer Risks**	**Surveillance/Management Recommendations[3]**
Female Breast[1] 37.2% (3-fold of general population risk)	12.4%	*Surveillance and Surgery* • Insufficient evidence for intervention with breast MRI. • Insufficient evidence for intervention with risk-reducing mastectomy (RRM). • Family history and other personal factors (e.g. breast density), in conjunction with the presence of a *MRE11A* mutation, should be considered when evaluating medical management options. • These options should be discussed with a physician to determine the most appropriate management.
Ovarian Cancer[2] Unknown	1.3%	*Surgery* • Insufficient evidence to make any recommendations for risk-reducing salpingo-oophorectomy (RRSO). • Risk management for ovarian cancers should be based on an individual's personal and family history. • These options should be discussed with a physician to determine the most appropriate management.

Some studies have proposed an increased risk for breast cancer in females with a *MRE11A* mutation (lifetime risk of 37.2%, 3-fold of general population risk).[1] However, others have found no increased risk for breast cancer. It is currently unknown if there is an increased risk for ovarian cancer in individuals with a *MRE11A* mutation.[2] Additionally, it is currently unknown if *MRE11A* mutations cause a predisposition to other cancers. Current NCCN guidelines assert that there is insufficient evidence to make any recommendations for breast MRI, risk-reducing mastectomy (RRM), or risk-reducing salpingo-oophorectomy (RRSO) based on *MRE11A* mutation status alone.[1] An individual's personal and family history should be considered in developing an appropriate surveillance and management plan.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *MRE11A* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- Rarely, children inherit *MRE11A* mutation from both parents. Individuals with two *MRE11A* mutations have ataxia-telangiectasia-like disorder (ATLD), an autosomal recessive neurodegenerative disorder affecting multiple body systems.[4] Parents who each carry a *MRE11A* mutation have a 25% cancer for a child with ATLD with every pregnancy.
    - *MRE11A* genetic testing for the partner of an individual with a *MRE11A* mutation may be appropriate to clarify the risk of having children with ATLD.
- 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

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2. Walsh T, Casadei S, Lee MK, Pennil CC, Nord AS, Thornton AM, 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.
3. Genetic/Familial High Risk Assessment: Breast, Ovarian, and Pancreatic (Version 1.2020). *NCCN Clinical Practical Guidelines in Oncology (NCCN Guidelines).* 2019.
4. Taylor, A.M., Groom, A., and Byrd, P.J. (2004). Ataxia-telangiectasia-like disorder (ATLD)-its clinical presentation and molecular basis. DNA Repair (Amst.) 3, 1219–1225.