Updated December 2019 (NCCN v1.2020)

RAD50 Mutations

Cancer Risks and General Management Recommendations

- There are currently no national consensus guidelines outlining specific clinical management recommendations for individuals who carry a *RAD50* gene mutation. Additionally, exact lifetime cancer risks associated with *RAD50* mutations are unknown at this time.
- Some studies have proposed an increased risk for breast cancer in females with a *RAD50* mutation (lifetime risk of ~24-36%).[1-4] However, others have found no increased risk for breast cancer.[5-7] Additionally, some studies have proposed an increased ovarian cancer risk in individuals with a *RAD50* mutation.[8,9] However, the studies are small, and data remains limited. At this time, it is unknown if individuals with *RAD50* gene mutations are at increased risk for 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 *RAD50* mutation status alone.[10] An individual's personal and family history should be considered in developing an appropriate surveillance plan.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *RAD50* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- It has been proposed that individuals who inherit two pathogenic *RAD50* mutations, one from each parent, are at risk for a rare genetic condition known as Nijmegen breakage syndrome-like disorder (NBSLD).
    - NBSLD is characterized by chromosomal instability, radiosensitivity, neurodevelopmental disease, and immunodeficiency[11].
    - *RAD50* genetic testing for the partner of an individual with an *RAD50* mutation may be appropriate to clarify the risk of having children with NBSLD.
- 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:

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