Updated December 2019 (NCCN v1.2020)

NBN Mutations

Cancer Risks and General Management Recommendations

NBN management recommendations are based on data derived from the truncating Slavic founder mutation (c.657del5). Current data suggest that breast cancer risks are not increased for other mutations in the *NBN* gene.[1]

***NBN* c.657del5 Mutation Carrier Cancer Risks**	**General Population Lifetime Cancer Risks**	**Surveillance/Management Recommendations[1]**
Female Breast Up to 30%[2]	12.4%	*Surveillance* • Annual mammogram with consideration of tomosynthesis and consider breast MRI with contrast beginning at age 40 • Age to initiate breast surveillance may be modified based on family history, typically 5-10 years earlier than the youngest breast cancer diagnosis in the family, but no later than age 40 *Surgery* • Insufficient evidence to support risk-reducing mastectomy based on *NBN* mutation status alone; management should be based on personal risk factors and family history

Other Cancer Risks: There may be other cancer risks associated with *NBN* mutations for which we do not yet have sufficient evidence to warrant intervention, including prostate,[3-5] ovarian,[6,7] colorectal,[8] pancreatic, [9] and gastric cancers,[5] as well as hematologic malignancies.[5,10,11] Further research is needed to make conclusions about these cancer risks. NCCN does note that while there may be a potential increased risk for ovarian cancer, there is insufficient evidence to recommend a risk-reducing salpingo-oophorectomy. Instead, patients should be managed on their personal risk factors and family history.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *NBN* 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 *NBN* mutation (one from each parents) which causes Nijmegen breakage syndrome (NBS).
    - NBS is a condition characterized by short stature, microcephaly, distinctive facial features, recurrent respiratory tract infections, an increased risk of cancer, intellectual disability, and other health problems.[12]
    - *NBN* genetic testing for the partner of an individual with an *NBN* mutation may be appropriate to clarify the risk of having children with NBS.
- 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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