Updated December 2019 (NCCN v1.2020)

BRIP1 Mutations

Cancer Risks and General Management Recommendations

***BRIP1* Mutation Carrier Cancer Risks**	**General Population Lifetime Cancer Risks**	**Surveillance/Management Recommendations[7]**
Ovarian Cancer[1,2] 5.8-18%	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 *BRIP1* mutations[6] *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: There is a potential increased risk for women with a *BRIP1* mutation to develop breast cancer (including triple negative breast cancer).[3,4,7] Data are conflicting regarding the risk of breast cancer in women with a *BRIP1* mutation; with one study showing a two-fold increased risk (~25% lifetime risk), [1] and another more recent study showing no increased risk.[5] The lifetime risk to develop breast cancer in men with *BRIP1* mutations is currently unknown. Current NCCN guidelines (v1.2020) state that there is insufficient evidence to recommend modified breast cancer risk management based on *BRIP1* mutation status alone. An individual's personal and family history should be considered in developing an appropriate surveillance plan.

Other Cancer Risks: *BRIP1* mutations may be associated with other increased cancer risks but data are limited at this time. Recommendations for screening for other cancers should be based on family history and general population screening guidelines.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *BRIP1* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- Rarely, individuals may inherit two *BRIP1* mutations (one from each parent) which causes Fanconi Anemia, Complementation Group J (FANCJ).
  - FANCJ is characterized by physical abnormalities, growth retardation, progressive bone marrow failure, and a high risk for cancer.
  - *BRIP1* genetic testing for the partner of an individual with a *BRIP1* mutation may be appropriate to clarify the risk of having children with FANCJ.
- 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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3. Couch FJ, Hart SN, Sharma P, et al. Inherited mutations in 17 breast cancer susceptibility genes among a large triple-negative breast cancer cohort unselected for family history of breast cancer. *J Clin Oncol*. 2015;33(4):304–311.
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7. NCCN v1.2020 Genetic/Familial High Risk Assessment: Breast, Ovarian, and Pancreatic.