Updated December 2019 (NCCN v3.2019 Colon and NCCN v1.2020 Breast)

Monoallelic/Heterozygous *MUTYH* Mutations

Heterozygous (monoallelic) *MUTYH* mutations may be associated with a moderately increased risk for colorectal cancer. Individuals who inherit two *MUTYH* mutations, one from each parent (biallelic), have a condition called *MUTYH*-associated polyposis (MAP). MAP is characterized by increased risks for colon polyps, as well as colon and gastric cancers.

Individuals who have one *MUTYH* mutation do not have MAP themselves, but they are carriers of MAP. Carriers are not known to exhibit features of MAP, but may have increased risks for colon cancer. A carrier may have a child with MAP if his or her partner is also a carrier.

Cancer Risks and General Management Recommendations

Cancer Type	*MUTYH* (Heterozygous) Mutation Carrier Lifetime Cancer Risks	General Population Lifetime Cancer Risks	Surveillance/Management Recommendations[1]
Colorectal[2]	Up to 2-fold (~9%)	4.5%	For individuals with a first-degree relative (i.e., parent, child, sibling) with CRC: • Colonoscopy screening every 5 years, beginning at age 40 (or 10 years prior to the age of first-degree relative's age at colorectal cancer diagnosis) For individuals with no first-degree relative with CRC: • Uncertain if specialized surveillance is warranted • General population CRC screening recommended, at minimum

Breast Cancer: Current NCCN guidelines (v1.2020)[3] state that there is insufficient evidence for breast cancer interventions based on a heterozygous *MUTYH* mutation alone. An individual's personal and family history should be considered in developing an appropriate screening plan.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *MUTYH* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- Individuals who inherit two *MUTYH* mutations, one from each parent, are at risk to develop MAP. If both parents are carriers of an *MUTYH* mutation, each of their children has a 25% chance to have MAP.
    - MAP is characterized by increased risks for colon polyps, as well as colon and gastric cancers.
- All family members should have full *MUTYH* gene analysis rather than single-site testing for the known mutation given that 1-2% of the general population of individuals with Northern European ancestry carries a common *MUTYH* mutation.
- 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 may visit www.FindAGeneticCounselor.com to find genetic services near them.

References

1. Genetic/Familial High-Risk Assessment: Colorectal (version 3.2019). National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Website. https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf.
2. Jones, N. et al. Increased colorectal cancer incidence in obligate carriers of heterozygous mutations in MUTYH. *Gastroenterology*. 2009;137(2),725-726.
3. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic (version 1.2020). National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Website. https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf.