Updated December 2019

Monoallelic/Heterozygous *NTHL1* Mutations

Individuals who inherit two (biallelic) *NTHL1* mutations, one from each parent, have *NTHL1*–associated polyposis and may develop numerous colorectal polyps that can become cancerous if left untreated.

Individuals who have one *NTHL1* mutation (heterozygous/monoallelic) do not have *NTHL1*-associated polyposis, and are instead referred to as carriers. Carriers are not known to exhibit features of *NTHL1*-related conditions, but they can potentially have children who are affected.

Currently, there are limited data regarding cancer risks in individuals with a monoallelic *NTHL1* mutation. Additionally, there are no consensus guidelines for modified management for individuals with a monoallelic *NTHL1* mutation. Cancer surveillance and management should be based on personal risk factors and family history.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, children, and siblings) have a 50% chance to inherit the familial *NTHL1* mutation. Second-degree relatives (i.e., grandparents, aunts/uncles, nieces/nephews) have 25% chance to inherit the familial mutation.
- Individuals who inherit two *NTHL1* mutations, one from each parent, are at risk to develop *NTHL1*-associated polyposis. If both parents are carriers of an *NTHL1* mutation, each of their children has a 25% chance to have *NTHL1*-associated polyposis.
    - *NTHL1*-associated polyposis is an adult-onset hereditary cancer predisposition syndrome characterized by the development of multiple colon polyps, as well as increased risks for colon and possibly other cancers.
- 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.