NTHL1 Biallelic gene

Associated Syndrome Name: *NTHL1* tumor syndrome

NTHL1 Biallelic Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Breast	Elevated Risk
Colorectal	Elevated Risk
Endometrial	Elevated Risk
Other	Elevated Risk

NTHL1 Biallelic gene Overview

NTHL1 tumor syndrome [1, 2, 3, 4, 5, 6]

- Individuals with mutations in both copies of the *NTHL1* gene (biallelic mutations) have *NTHL1* tumor syndrome. Individuals with *NTHL1* tumor syndrome are reported to have approximately 10 to 50 colorectal polyps. These polyps are mostly adenomas, which are associated with an increased risk for colorectal cancer. Although there are as yet no precise estimates of the colorectal cancer risk associated with *NTHL1* tumor syndrome, it is believed that this risk is significantly increased over that in the general population.
- Recent studies have found that women with *NTHL1* tumor syndrome have an increased risk for breast cancer, including a possibly increased risk for multiple primary diagnoses. Although there are as yet no precise estimates of this risk, it may be significantly increased over the risk for women in the general population.
- The small number of individuals identified to date with *NTHL1* tumor syndrome have often been diagnosed with other types of cancer, including endometrial and small bowel cancer and meningiomas of the brain and spinal cord. However, further studies are needed to determine if these (or any other cancers) are conclusively associated with *NTHL1* tumor syndrome.
- Although there are increased risks for cancer in individuals with *NTHL1* tumor syndrome, it may be possible to reduce these risks with appropriate medical management. Guidelines for the medical management of individuals with *NTHL1* tumor syndrome have been developed by the National Comprehensive Cancer Network (NCCN). These are listed below. These guidelines will evolve as we learn more, and it is recommended that patients with *NTHL1* tumor syndrome be managed by a multidisciplinary team with expertise in medical genetics and the care of patients with hereditary cancer syndromes.

NTHL1 Biallelic gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Colorectal	To age 80 [5, 6, 7]	Elevated risk	2.8%
Female Breast	To age 80 [1, 7]	Elevated risk	10.7%
Endometrial	To age 80 [4, 7]	Possibly elevated risk	2.6%
Small Bowel	To age 80 [4, 7]	Possibly elevated risk	0.2%

NTHL1 Biallelic Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Colorectal	Colonoscopy[4]	25 to 30 years	Every 2 to 3 years
	Colorectal surgical evaluation and counseling.[4]	Based on cancer diagnosis and/or polyp number, size and histology	NA
Female Breast	Currently there are no specific medical management guidelines for female breast cancer risk in biallelic mutation carriers. However, the possibility of an increased risk for breast cancer warrants consideration of individualized breast cancer risk-reduction strategies, such as the modification of standard population screening recommendations by starting screening at younger ages and/or performing screenings at greater frequency.[4]	NA	NA
Endometrial	Patient education about the importance of quickly seeking attention for endometrial cancer symptoms, such as abnormal bleeding.[4]	Individualized	NA
	Consider transvaginal ultrasound.[4]	After menopause	Individualized
Small Bowel	Upper endoscopy, including complete visualization of the entire small bowel[4]	Baseline at 30 to 35 years	Every 3 to 5 years

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the *NTHL1* Biallelic gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

Since this patient has mutations in both copies of the *NTHL1* gene, it is almost certain each of their parents and all of their children carry at least one of these *NTHL1* mutations. Brothers and sisters are at very high risk for carrying either one or two *NTHL1* mutations. The cancer risk table that follows provides cancer risks for men and women with mutations in both copies (biallelic) of the *NTHL1* gene. These risks do not apply to relatives who have inherited only a single *NTHL1* mutation (monoallelic).

References

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