MBD4 Monoallelic gene

Associated Syndrome Name: *MBD4*-associated cancer risk

MBD4 Monoallelic Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Other	Elevated Risk

MBD4 Monoallelic gene Overview

MBD4-associated cancer risk [1, 2, 3]

- Individuals with a mutation in only one copy of the *MBD4* gene (a monoallelic mutation) may have an elevated risk for uveal melanoma. However, the data are not conclusive and there are currently no medical management guidelines to address these possible risks.
- Individuals with mutations in both of their copies of the *MBD4* gene (biallelic mutations) have a condition known as *MBD4*-associated neoplasia syndrome (MANS), which is associated with an increased risk for colorectal polyps, colorectal cancer, blood disorders, and uveal melanoma. This patient does not have a diagnosis of MANS, but may have relatives who are at risk for this condition. Please see the Information for Family Members section below for details.
- Currently there are no medical management guidelines for patients with a single *MDB4* mutation. However, this may change as we learn more, and therefore patients with monoallelic *MBD4* mutations may benefit from consultation with healthcare providers who have expertise in medical genetics and the care of patients with hereditary cancer syndromes.

MBD4 Monoallelic gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Uveal Melanoma	To age 80[1, 2]	Elevated risk	<0.1%

MBD4 Monoallelic 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)
Uveal Melanoma	Currently there are no specific medical management guidelines for uveal melanoma risk in monoallelic mutation carriers. However, the increased risk for uveal melanoma warrants consideration of risk reduction strategies, including eye exam and UV-protective eyewear.[3]	Individualized	NA

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 MBD4 Monoallelic 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.

This patient carries a single *MBD4* mutation (monoallelic). This patient's relatives are at risk for carrying a single *MBD4* mutation, or mutations in both copies of *MBD4* (biallelic). Relatives who have inherited mutations in both copies of *MBD4* have an increased risk for colorectal polyps, colorectal cancer, certain blood disorders, and uveal melanoma. Genetic testing may be appropriate for close family members to determine whether they are at an increased risk for these cancers.

References

1. Derrien AC, et al. Germline *MBD4* Mutations and Predisposition to Uveal Melanoma. J Natl Cancer Inst. 2021 Jan 4;113(1):80-87. PMID: 32239153.

2. Villy MC, et al. Familial uveal melanoma and other tumors in 25 families with monoallelic germline *MBD4* variants. J Natl Cancer Inst. 2024 Apr 5;116(4):580-587. PMID: 38060262.

3. Gupta S, et al. NCCN Clinical Practice Guidelines in Oncology® Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric. V 1.2025. Jun 13. Available at https://www.nccn.org.

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