MBD4 Biallelic gene

Associated Syndrome Name: *MBD4*-associated neoplasia syndrome (MANS)

MBD4 Biallelic Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Colorectal	Elevated Risk
Other	Elevated Risk

MBD4 Biallelic gene Overview

MBD4-associated neoplasia syndrome (MANS) [1, 2, 3]

- Individuals with mutations in both copies of *MBD4* (biallelic) have *MBD4*-associated neoplasia syndrome (MANS).
- *MBD4* biallelic mutations have been identified in some individuals with colon polyps, ranging from few to over 100 colon polyps, suggesting a variable polyposis presentation.
- Studies have reported multiple individuals with *MBD4* biallelic mutations who have developed blood disorders such as myelodysplastic syndrome (MDS) and/or acute myelogenous leukemia (AML). The exact size of this risk is unknown.
- Uveal melanoma has been reported in numerous individuals with a mutation in one copy of the *MBD4* gene (monoallelic). However, it is unknown whether individuals with mutations in both copies of the *MBD4* gene are at an increased risk for uveal melanoma.
- Although there are increased risks for cancer in individuals with *MBD4* biallelic mutations, there are interventions that may reduce these risks. Guidelines from the National Comprehensive Cancer Network (NCCN) are listed below. It is recommended that patients with *MBD4* mutations and a diagnosis of MANS be managed by a multidisciplinary team with experience in the prevention and treatment of the cancers associated with *MBD4* mutations.

MBD4 Biallelic gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Colorectal	To age 80[1, 3, 4]	Elevated risk	2.8%
Leukemia	To age 80[1, 4]	Elevated risk	1.1%
Uveal Melanoma	To age 80[2]	Possibly elevated	<0.1%

MBD4 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[1]	18 to 20 years	Every 2 to 3 years
Leukemia	Complete blood count (CBC) with differential[1, 5]	At time of diagnosis of MANS	Every 6 to 12 months
	Bone marrow aspirate and biopsy[5]	At time of diagnosis of MANS	Annually

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Uveal Melanoma	Eye exam[1]	At time of diagnosis of MANS	Annually

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 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 *MBD4* gene, it is almost certain each of their parents and all their children carry at least one of these *MBD4* mutations. Siblings are at very high risk for carrying either one or two *MBD4* mutations. Since even a single *MBD4* mutation can lead to an increased risk for cancer, it is especially important that this information be shared within the family and relatives talk with a healthcare provider about testing. The cancer risk tables that follow provide cancer risks for individuals with mutations in either one (monoallelic) or both (biallelic) copies of the *MBD4* gene.

References

1. Gupta S, et al. NCCN Clinical Practice Guidelines in Oncology® Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, Esophageal, and Gastric. V 1.2026. Jun 16. Available at https://www.nccn.org.
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. Palles C, et al. Germline *MBD4* deficiency causes a multi-tumor predisposition syndrome. Am J Hum Genet. 2022 May 5;109(5):953-960. PMID: 35460607.
4. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2026 May 5]. Available from https://seer.cancer.gov/explorer/.
5. Maese LD, et al. Update on Recommendations for Surveillance for Children with Predisposition to Hematopoietic Malignancy. Clin Cancer Res. 2024 Oct 1;30(19):4286-4295. PMID: 39078402.

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