POLD1 gene

Associated Syndrome Name: Polymerase proofreading-associated polyposis (PPAP)

POLD1 Summary Cancer Risk Table

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

POLD1 gene Overview

Polymerase proofreading-associated polyposis (PPAP) [1, 2, 3, 4, 5]

- *POLD1* mutations have been found in individuals with early onset colorectal cancer, large numbers of adenomatous colorectal polyps, and/or significant family histories of colorectal cancer. Although there are as yet no precise estimates of the colorectal cancer risk associated with mutations in *POLD1*, it is believed that the risk is significantly increased over that in the general population.
- Some families with *POLD1* mutations include individuals with a wide range of other cancers, including some with multiple primary tumors. In particular, there is some evidence for an increased risk for endometrial cancer in women with mutations in *POLD1*. Further studies are needed to determine which cancers are conclusively associated with *POLD1* gene mutations.
- Although there is an increased risk for colorectal cancer in individuals with PPAP due to mutations in *POLD1*, it may be possible to reduce this risk with appropriate medical management. Guidelines for the medical management of patients with PPAP have been developed by the National Comprehensive Cancer Network (NCCN). These are listed below. These guidelines will evolve as we learn more about PPAP, and it is recommended that patients with a *POLD1* mutation and a diagnosis of PPAP be managed by a multidisciplinary team with expertise in medical genetics and the care of patients with hereditary cancer syndromes.

POLD1 gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Colorectal	To age 70[1, 2, 3, 4, 5, 6]	50%	1.9%
Endometrial	To age 70[1]	Elevated risk	1.9%
Small Bowel	To age 70[1]	Possibly elevated risk	0.1%

POLD1 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[3]	25 to 30 years, or 2 to 5 years younger than the earliest colorectal cancer diagnosis in the family if it is under age 25	Every 2 to 3 years

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
	Colorectal surgical evaluation and counseling.[3]	Based on cancer diagnosis and/or polyp number, size and histology	NA
Endometrial	Patient education about the importance of quickly seeking attention for endometrial cancer symptoms, such as abnormal bleeding.[3]	Individualized	NA
	Consider transvaginal ultrasound.[3]	After menopause	Individualized
Small Bowel	Upper endoscopy[3]	Baseline at 30 to 35 years, or earlier if there is a family history of small bowel cancer	Based on polyp number, size and histology

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 POLD1 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.

References

1. Palles C, et al. The clinical features of polymerase proof-reading associated polyposis (PPAP) and recommendations for patient management. Fam Cancer. 2022 21:197-209. PMID: 33948826.
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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.
4. Buchanan DD, et al. Risk of colorectal cancer for carriers of a germ-line mutation in *POLE* or *POLD1*. Genet Med. 2018 20:890-895. Erratum in: Genet Med. 2018 Feb 01. PMID: 29120461.
5. Palles C, et al. Germline mutations affecting the proofreading domains of *POLE* and *POLD1* predispose to colorectal adenomas and carcinomas. Nat Genet. 2013 45:136-44. PMID: 23263490.
6. 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/.

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