POLE gene

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

POLE Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK	
Colorectal	High Risk	

POLE gene Overview

Polymerase proofreading-associated polyposis (PPAP) ^{1, 2, 3, 4, 5}

- POLE 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 POLE, it is believed that the risk is significantly increased over that in the general population.
- Individuals with POLE mutations are often found to have small bowel and gastric fundic gland adenomas.
- Some families with POLE mutations include individuals with a wide range of cancers, including some with multiple primary
 tumors. In particular, there are reports of an increased risk for brain tumors (glioblastomas and astrocytomas), endometrial,
 small bowel, and ovarian cancer in individuals with mutations in POLE. Further studies are needed to determine if these (or
 any other cancers) are conclusively associated with POLE gene mutations.
- Although there is an increased risk for colorectal cancer in individuals with PPAP due to mutations in *POLE*, 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 *POLE* 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.

POLE gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Colorectal	To age 70 ^{2, 3, 4, 5, 6}	90%	1.8%

POLE 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 ²	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
	Colorectal surgical evaluation and counseling. ²	Based on cancer diagnosis and/or polyp number, size and histology	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 POLE 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

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- 5. 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.
- 6. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2025 Apr 1]. Available from https://seer.cancer.gov/explorer/.

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