Genetic Insights: quick reference guide for healthcare providers

This guide is intended to facilitate a discussion between providers and their patients.

Genetic Insights test results: ***POLD1*-associated hereditary cancer**

Key results

A pathogenic or likely pathogenic variant associated with an increased risk of colon cancer was found in the *POLD1* gene.

Next steps

Clinical recommendations	Resources
Genetic Insights is a screening test and not intended for diagnosis. A follow-up genetic test should be performed in a clinical setting before any other action is taken.	**Ready to order?** Check with your institution and/or patient's insurance about the preferred testing laboratory. Blueprint Genetics® offers hereditary cancer testing. To confirm this test result, **targeted variant testing** for the variant identified is available. You can order a confirmation test here: Blueprint Genetics/TVT **Have questions?** Call **1.866.GENE.INFO** (1.866.436.3463) to speak to a specialized Quest genetic counselor or geneticist available to healthcare providers to discuss test selection and results.
Refer your patient to a genetic counselor specializing in hereditary cancer. *Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.*	Your patient can schedule a 1-on-1 remote genetic counseling session through their online Genetic Insights Cancer Risk Report at no additional cost. To find a genetic counselor with expertise in hereditary cancer practicing in your patient's area for an in-person session, please visit FindAGeneticCounselor.NSGC.org

Patient conversation starters:

Patient conversation starters summarize the preceding information in plain language to support meaningful conversations between you and your patient.

FindAGeneticCounselor.NSGC.org

Your Genetic Insights test is a screening test. The next step is to have your result confirmed with a second genetic test.

It's also important that you talk with a genetic counselor. Genetic counselors are experts in genetics and can help you understand this result and potential next steps.

You can access a genetic counselor through your online Genetic Insights dashboard at no additional cost to you, and we can discuss a referral to a local genetic counselor.

Visit QuestDiagnostics.com/Genetic-Health-Screening for more information about this test.

What is *POLD1*-associated hereditary cancer?

DNA variants in the *POLD1* gene are associated with a higher lifetime risk of adenomatous polyps and colon cancer, and possibly other cancers, often with an earlier age of onset than the general population.[1,2]

While precise cancer risk estimates still need to be determined, males with a *POLD1* variant may have up to a 90% chance of developing colon cancer by age 70 (95% CI; 33%-99%).[1] Females with a *POLD1* variant may have up to an 82% risk of colon cancer by age 70 (95% CI; 26%-99%).[1] This is significantly higher than the typical lifetime risk of approximately 4%.[3]

However, colon cancer risks may vary based on family history, the specific DNA variant identified, and other factors.

People with a confirmed *POLD1* DNA variant are recommended to consider undergoing more frequent cancer screening, typically starting at earlier ages than in the general population.[2]

See the Management options section for more detail.

Patient conversation starters:

People with a DNA variant in the *POLD1* gene have a higher than typical chance of developing colon cancer. But not everyone with a DNA variant will develop cancer.

People with a DNA variant in the *POLD1* gene should have cancer screenings earlier in life and more often than typical. This increases the chance that if cancer develops, it's detected as early as possible.

What this result means for family members

Family members may have the same DNA variant. The DNA variant was most likely inherited from a parent. Full siblings and children have a 50% chance of having this variant.

In people with a confirmed DNA variant on the *POLD1* gene, cascade genetic testing for other family members 18 and older may help inform their risks and screening protocols.

A genetic counselor can help determine the most appropriate testing options. Therefore, it is strongly recommended that individuals share these results with their biological relatives.

Patient conversation starters:

DNA variants run in families. That means the DNA variant in *POLD1* can be inherited or passed down from parents to their children. Your close relatives, like your parents, full siblings, and children, have a 50% (or 1 in 2) chance of having the same DNA variant.

Other relatives might also have the same DNA variant. Sharing these results with your family members is important so they can decide if they want to have genetic testing.

Management options

There are options for cancer prevention and early detection for people with *POLD1*-associated hereditary cancer. Clinical guidelines from the National Comprehensive Cancer Network® (NCCN®) in people with this variant and no personal history of an associated cancer include[2]:

Cancer type	Guidelines for people with a *POLD1* DNA variant
Colon	Begin colonoscopy at age 25-30 and repeat every 2-3 years if negative If polyps are found, colonoscopy every 1-2 years with consideration of surgery if colon polyp burden becomes unmanageable by colonoscopy Surgical evaluation if appropriate

Patient conversation starters:

It's recommended that people with a DNA variant in *POLD1* have cancer screenings earlier and more often than typical. This way, cancer is more likely to be caught in the early stages when it's most treatable.

In fact, colon cancer can even be prevented if pre-cancerous colon polyps are found and removed during a colonoscopy.

If your DNA result is confirmed, it's important to work with the right specialists, like a medical oncologist or gastroenterologist and a geneticist, to find cancer screening and risk-reducing options that are right for you.

See NCCN for complete recommendations including recommendations during childhood.[2] Recommendations may change over time. If the test result is confirmed, local centers for excellence in hereditary cancer should be consulted for further clinical management.

Additional resources

The following patient advocacy groups have additional information and resources about *POLD1*-associated hereditary cancer:

Colorectal Cancer Alliance: CCAlliance.org
Fight Colorectal Cancer: FightColorectalCancer.org
FORCE: Facing Our Risk of Cancer Empowered: FacingOurRisk.org

References

1. Buchanan DD, Stewart JR, Clendenning M, et al. Risk of colorectal cancer for carriers of a germ-line mutation in POLE or POLD1. *Genet Med*. 2018;20(8):890-895. doi:10.1038/gim.2017.185
2. National Comprehensive Cancer Network®. Genetic/Familial High-Risk Assessment: Colorectal (Version 2.2022). NCCN Guidelines®. Accessed December 13, 2022. www.nccn.org
3. National Cancer Institute: Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Colorectal Cancer. Accessed October 31, 2022. https://seer.cancer.gov/statfacts/html/colorect.html