Genetic Insights: quick reference guide for healthcare providers

This guide is intended to facilitate a discussion between a provider and their patient.

Genetic Insights test results: ***CHEK2*-associated hereditary cancer**

Key results

A variant called c.470T>C (p.Ile157Thr) was found in the *CHEK2* gene.

People with this DNA variant in the *CHEK2* gene have a slightly increased risk of breast cancer in females, prostate cancer in males, and colon cancer in both.

Next steps

Clinical recommendations	Resources
Genetic Insights is a screening test and is 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.	Your patient can schedule a 1-on-1 remote genetic counseling session through their online Genetic Insights Cancer Risk Report at no additional cost.
Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.	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 *CHEK2*-associated hereditary cancer?

DNA variants in the *CHEK2* gene are associated with a higher lifetime risk of certain cancers, often with an earlier age of onset than the general population.[1,2]

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

People with a confirmed *CHEK2* DNA variant are recommended to undergo 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:

Your test showed a specific DNA variant in the *CHEK2* gene. People with this variant have a higher chance of developing certain types of cancer in their lifetime.

Not everyone with this variant develops cancer. The type of cancer and the risk of cancer can vary based on personal or family health history and the specific DNA variant in the *CHEK2* gene.

People with a DNA variant in the CHEK2 gene usually have 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 in the *CHEK2* gene, cascade genetic testing for other family members 18 years 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 people share their results with their biological relatives.

Patient conversation starters:

DNA variants in the *CHEK2* gene run in families. That means the DNA variants 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 this result with your family members is important so that they can talk to a healthcare provider about genetic testing for *CHEK2* DNA variants.

Cancer risk

Select cancer risks in people with a confirmed c.470T>C (p.Ile157Thr) variant in the *CHEK2* gene are listed below. However, research is ongoing to better understand the cancer types linked to the c.470T>C (p.Ile157Thr) variant in the *CHEK2* gene and the associated risks. Therefore, this risk information may change over time.

Cancer type	Approximate lifetime risk in people with the c.470T>C (p.Ile157Thr) *CHEK2* variant	Approximate lifetime risk in the general population
Assigned female at birth:		
Breast	Up to 21%[1]	13%[4]
Assigned male at birth:		
Prostate	Up to 22%[7]	12.1%[6]
Males and females:		
Colon	Up to 7%[1]	4%[5]

Management options

There are options for cancer risk management for people with a DNA variant in the *CHEK2* gene. Clinical guidelines from the National Comprehensive Cancer Network® (NCCN®) for people with a confirmed *CHEK2* DNA variant and no personal history of an associated cancer are listed below.[2,3]

However, screening and management should consider the variable cancer risks depending on the specific *CHEK2* variant identified.[2,3] The risks associated with the *CHEK2* c.470T>C (p.Ile157Thr) DNA variant may not meet a threshold for management change from typical.[2,3]

Cancer type	Guidelines for people with *CHEK2* DNA variant
Breast (assigned female at birth)	Annual mammogram starting at age 40 (or earlier based on family history) Consider breast MRI with contrast starting at age 30-35 (or earlier based on family history Discuss option of risk-reducing options based on family history
Colon	**For individuals with a first-degree relative with colorectal cancer**, colonoscopy screening every 5 years, beginning at age 40 or 10 years prior to age of first-degree relative's age at colorectal cancer diagnosis, whichever is earlier **For individuals with no known family history of colorectal cancer,** colonoscopy screening every 5 years beginning at age 40
Prostate	No recommended changes to standard cancer screening at this time

Patient conversation starters:

People with the *CHEK2* c.470T>C (p.Ile157Thr) DNA variant may need to consider additional cancer screening beyond what is typical. If your test result is confirmed, it is important to work with the right specialists—like a medical oncologist and a geneticist—to find cancer screening options that are right for you.

See NCCN for complete recommendations. 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 *CHEK2*-associated hereditary cancer:

Facing Our Risk of Cancer Empowered (FORCE): FacingOurRisk.org

References

1. Han FF, Guo CL, Liu LH. The effect of CHEK2 variant I157T on cancer susceptibility: evidence from a meta-analysis. *DNA Cell Biol.* 2013 Jun;32(6):329-335. doi:10.1089/dna.2013.1970
2. National Comprehensive Cancer Network®. NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic (Version 1.2023). Accessed December 15, 2022. ww.nccn.org
3. National Comprehensive Cancer Network®. Genetic/Familial High-Risk Assessment: Colorectal (Version 2.2022). NCCN Guidelines®. Accessed December 15, 2022
4. National Cancer Institute. Cancer Stat Facts: Female Breast Cancer. Accessed December 15, 2022. https://seer.cancer.gov/statfacts/html/breast.html
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6. National Cancer Institute: Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Prostate Cancer. Accessed December 15, 2022. https://seer.cancer.gov/statfacts/html/prost.html
7. Wang Y, Dai B, Ye D. CHEK2 mutation and risk of prostate cancer: a systematic review and meta-analysis. *Int J Clin Exp Med.* 2015;8(9):15708-15715. https://www.ncbi.nlm.nih.gov/pubmed/26629066