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: ***PALB2*-associated hereditary cancer**

Key results

A DNA variant associated with an increased risk of breast cancer in females and males was found in the *PALB2* gene. Risks for pancreatic and ovarian cancer may also be increased.

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 genetics 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 *PALB2*-associated hereditary cancer?

DNA variants in the *PALB2* 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 *PALB2* 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:

PALB2-associated hereditary cancer is caused by a DNA variant in the *PALB2* gene.

People with *PALB2*-associated hereditary cancer have a higher than typical chance of developing certain cancers, especially breast cancer. Not everyone with a DNA variant will develop cancer.

People with this variant should have cancer screenings earlier in life and more often than typical. This increases the chance that if cancer develops, it's found as soon 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.[1]

In people with a confirmed DNA variant in the *PALB2* gene, cascade genetic testing for other family members 18 years and older may help inform their risks and screening protocols.[2]

Children of biological parents who both have a DNA variant in the *PALB2* gene are at risk for having a genetic condition called Fanconi anemia.[2]

A genetic counselor can help determine the most appropriate testing options for family members.

Therefore, it is strongly recommended that people share their results with their biological relatives and reproductive partners.

Patient conversation starters:

The DNA variant in the *PALB2* gene runs in families. It can be inherited or passed down from parents to their children.

Your close relatives, like your parents, full siblings, and children each 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 is important so family members can decide if they want to have genetic testing.

Cancer risk

Select estimated cancer risks in people with a confirmed variant in the *PALB2* gene compared to the general population are included below. Individual cancer risks may be higher or lower depending on the specific variant identified in addition to personal and family health history. Associated cancers and risks may change over time as medical research advances.

Cancer type	Approximate risk by age 80 with *PALB2* variant	General population risk
Assigned female at birth:		
Breast	Up to 60%[1-3]	13%[4]
Ovarian	Up to 5%[1]	1.2%[5]
Assigned male at birth:		
Breast	1%[1]	0.1%[6]
Males and females:		
Pancreas	2%-3%[1]	1.6%[7]

Management options

There are options for cancer prevention and early detection for people with a confirmed *PALB2* DNA variant. Select clinical guidelines from the National Comprehensive Cancer Network® (NCCN®) for people with a confirmed *PALB2* DNA variant and no personal history of an associated cancer include[2]:

Cancer type	Guidelines for people with *PALB2* DNA variant
Breast (assigned female at birth)	Annual mammogram and breast MRI at age 30 (or earlier based on family history) Discuss option of risk-reducing mastectomy
Breast (assigned male at birth)	Males should discuss management with a hereditary cancer specialist. There are currently no evidenced-based recommendations for breast cancer screening in males
Ovarian	Discuss management based on family history and consider risk reduction options
Pancreatic	Consider pancreatic cancer screening based on family history

Patient conversation starters:

It's recommended that people with a DNA variant in the *PALB2* gene 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. If your result is confirmed, it's important to work with the right specialists, like a medical oncologist and a geneticist, to find cancer screening and risk-reducing 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 *hereditary cancer risk:*

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

Susan B. Komen Foundation: Komen.org

Foundation for Women's Cancer: FoundationForWomensCancer.org

References

1. Yang X, Leslie G, Doroszuk A, et al. Cancer risks associated with germline PALB2 pathogenic variants: an international study of 524 families. *J Clin Oncol*. 2020;38(7):674-685. doi:10.1200/JCO.19.01907
2. National Comprehensive Cancer Network®. NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic (Version 3.2023). Accessed February 15, 2023. www.nccn.org
3. Antoniou AC, Casadei S, Heikkinen T, et al. Breast-cancer risk in families with mutations in PALB2. *N Engl J Med*. 2014;371(6):497-506. doi:10.1056/NEJMoa1400382
4. National Cancer Institute. Cancer Stat Facts: Female Breast Cancer. Accessed August 12, 2022. https://seer.cancer.gov/statfacts/html/breast.html
5. National Cancer Institute. Cancer Stat Facts: Ovarian Cancer. Accessed August 12, 2022. https://seer.cancer.gov/statfacts/html/ovary.html
6. American Cancer Society. Key Statistics for Breast Cancer in Men. Accessed August 12, 2022. https://www.cancer.org/cancer/breast-cancer-in-men/about/key-statistics.html
7. National Cancer Institute. Cancer Stat Facts: Pancreatic Cancer. Accessed August 12, 2022. https://seer.cancer.gov/statfacts/html/pancreas.html

This information is not a substitute for medical advice, diagnosis, or treatment. The diagnosis or treatment of any disease or condition may be based on personal history, family history, symptoms, a physical examination, laboratory test results, and other information considered important by a healthcare provider.

Individuals should talk with a healthcare provider about the meaning of genetic test results and before stopping, starting, or changing any medication or treatment.

Genetic Insights is a test developed and performed by Quest Diagnostics. The test results are not diagnostic and do not determine overall chances of developing a disease or health condition. The tests are not cleared or approved by the US Food and Drug Administration.

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