Ambry Genetics®

Clinician Management Resource for *PALB2*

This overview of clinical management guidelines is based on this patient's positive test result for a *PALB2* gene mutation. Unless otherwise stated, medical management guidelines used here are limited to those issued by the National Comprehensive Cancer Network® (NCCN®)[1] in the U.S. Please consult the referenced guideline for complete details and further information.

Clinical correlation with the patient's past medical history, treatments, surgeries and family history may lead to changes in clinical management decisions; therefore, other management recommendations may be considered. Genetic testing results and medical society guidelines help inform medical management decisions but do not constitute formal recommendations. Discussions of medical management decisions and individualized treatment plans should be made in consultation between each patient and his or her healthcare provider, and may change over time.

SCREENING/SURGICAL CONSIDERATIONS[1]	AGE TO START	FREQUENCY
Female Breast Cancer		
Breast Screening ▪ Mammography ▪ Breast MRI with and without contrast	30 years old, or 5-10 years before the earliest known breast cancer in the family	Every 12 months
Discuss option of risk-reducing mastectomy	Individualized	N/A
Male Breast Cancer		
Consider breast self-exam training and education	35 years old	Periodic and consistent
Consider clinical breast exam	35 years old	Every 12 months
Consider mammogram screening	50 years or 10 years before the earliest known male breast cancer in the family (whichever comes first)	Every 12 months
Pancreatic Cancer		
For individuals with exocrine pancreatic cancer in >1 first-or second-degree relative on the same side of the family (or presumed to be from the same side of) as the identified pathogenic/likely pathogenic germline variant, consider pancreatic cancer screening using contrast-enhanced MRI/MRCP and/or EUS.*	50 years (or 10 years younger than the earliest exocrine pancreatic cancer diagnosis in the family)	Annually (with consideration of shorter intervals if worrisome abnormalities seen on screening)
Ovarian Cancer		
Consider risk-reducing salpingo-oophorectomy	Starting at age 45-50 years	N/A
Other		
Counsel for risk of autosomal recessive condition in offspring	Individualized	N/A

* For individuals considering pancreatic cancer screening, the panel recommends that screening be performed in experienced high-volume centers. The panel recommends that such screening only take place after an in-depth discussion about the potential limitations to screening, including cost, the high incidence of benign or indeterminate pancreatic abnormalities, and uncertainties about the potential benefits of pancreatic cancer screening. Most small cystic lesions found on screening will not warrant biopsy, surgical resection, or any other intervention.

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. V2.2024. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed September 27, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

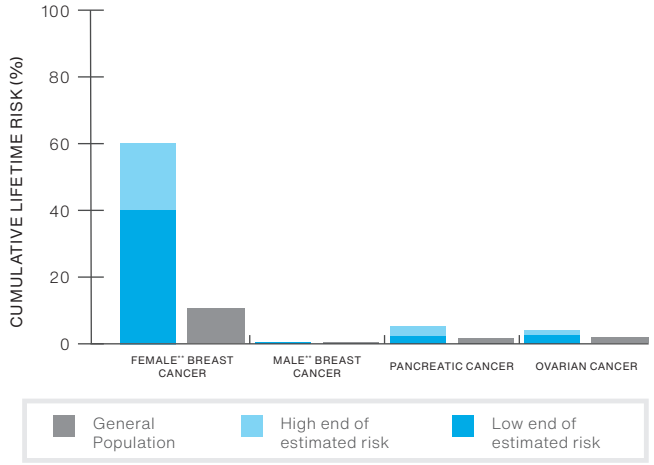
Understanding Your Positive *PALB2* Genetic Test Result

INFORMATION FOR PATIENTS WITH A PATHOGENIC MUTATION OR VARIANT, LIKELY PATHOGENIC

5 Things To Know

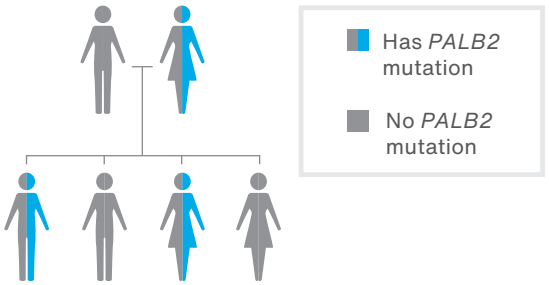
1	*PALB2* mutation	Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the *PALB2* gene.
2	Cancer risks	You have an increased chance to develop breast cancer, ovarian cancer, pancreatic cancer, and possibly other types of cancer although evidence is insufficient.
3	What you can do	Risk management decisions are very personal. There are options to detect cancer early or lower the risk to develop cancer. It is important to discuss these options with your doctor and decide on a plan that works for you.
4	Other medical concerns	Individuals with *PALB2* mutations may have an increased risk to have a child with Fanconi anemia, but only if their partner also carries a mutation in the *PALB2* gene. Fanconi anemia is a rare condition that can cause specific physical characteristics, bone marrow failure, and an increased risk of certain cancers.
5	Family	Family members may also be at risk – they can be tested for the *PALB2* mutation that was identified in you. It is recommended that you share this information with your family members so they can learn more and discuss with their healthcare providers.

PALB2 Mutation Lifetime Cancer Risks*



PALB2 Mutations in the Family

There is a 50/50 random chance to pass on a *PALB2* mutation to each of your children. The image below shows that everyone can carry and pass on these mutations, regardless of their sex at birth.



* Because risk estimates vary in different studies, only approximate risks are given. Cancer risks will differ based on individual and family history.
** Refers to sex assigned at birth

RESOURCES

- Ambry's hereditary cancer site for families patients.ambrygen.com/cancer
- Bright Pink brightpink.org
- FORCE facingourrisk.org
- ICARE Inherited Cancer Registry InheritedCancer.net
- Imerman Angels imermanangels.org
- Susan G. Komen Foundation komen.org
- Genetic Information Nondiscrimination Act (GINA) ginahelp.org
- National Society of Genetic Counselors nsgc.org
- Canadian Association of Genetic Counsellors cagc-accg.ca

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *PALB2* result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.

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