Pathogenic (or harmful) variants in the PALB2 gene have been associated with increased risk for breast cancer. Other cancer risks associated with pathogenic variants in PALB2 have not been fully established, but studies have suggested increased risks for pancreatic cancer, ovarian cancer, and male breast cancer.

PALB2 pathogenic variants are inherited in an autosomal dominant pattern, meaning that children of someone who carries a pathogenic variant each have a 50% risk to inherit the variant and associated cancer risks. Notably, women and men both have the PALB2 gene and have the same chances to inherit and pass down variants in these genes. Therefore, both sides of the family are important when assessing inherited risk.

Cancer type	Risk in the general population	Risk in PALB2 pathogenic variant carriers
Female breast	12%	33% – 58%

Genetic testing for PALB2

Genetic testing for pathogenic variants in PALB2 are currently available, but there are a few different ways to approach testing:

- *Single site analysis*: Testing specific to a known pathogenic variant in the family
- Full gene sequencing and rearrangement analysis: Comprehensive testing to search for all currently detectable variants in the gene
- Gene panels: Newer, more broadly based gene tests that would include not only the PALB2 gene, but other genes known or suspected to be associated with increased cancer risks

Cancer Screening & Management for PALB2

If you are tested and found to have a pathogenic variant in the PALB2 gene, it is recommended to discuss your management plan with your healthcare team, and if available, to seek consultation through a specialized high-risk clinic. General recommendations are included here based on updated guidelines of the NCCN, but may be tailored to your specific medical and family history.

For women, breast cancer screening recommendations include starting annual mammograms at age 30 with consideration of breast MRI starting at age 30, or 5-10 years prior to the earliest diagnosis of breast cancer in the family, whichever is earlier.

Screening or preventative guidelines for other cancer risks possibly associated with PALB2 pathogenic variants are not clearly established. If there is a history of other cancers in the family, your doctor or healthcare provider may recommend additional, earlier, or more frequent screening for other cancers based on the family history.

PALB2-associated Fanconi Anemia

The above information about cancer risks is relevant for people who have a single pathogenic variant in the PALB2 gene. Importantly, if a child inherits pathogenic variants in both copies the PALB2 gene (one pathogenic variant from mom and one pathogenic variant from dad), this causes a different genetic condition called Fanconi anemia. Fanconi anemia is a rare condition associated with defects of the bone marrow, increased risks for other cancers (e.g. leukemia), as well as some birth defects. Therefore, people with a PALB2 pathogenic variant who are pregnant or planning to have children are recommended to seek genetic counseling to clarify the risk to their children.

Click here to learn more about scheduling a genetic counseling appointment for questions about hereditary cancer predisposition.