PALB2 gene

Associated Syndrome Name: *PALB2*-associated cancer risk

PALB2 Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Breast	High Risk
Male Breast	Elevated Risk
Ovarian	Elevated Risk
Pancreatic	Elevated Risk

PALB2 gene Overview

PALB2-associated cancer risk [1, 2, 3]

- Women with *PALB2* mutations have a risk for breast cancer that is significantly increased over the 12.5% lifetime risk for women in the general population of the United States. Estimates of this risk vary and may be strongly influenced by other factors such as family history and when she was born. The highest risks for breast cancer seem to be in women with a family history of breast cancer and those who were born more recently.
- Women with *PALB2* mutations have an increased risk for ovarian cancer. The 5% estimate in the Cancer Risk Table below is for women in the United Kingdom, where ovarian cancer is almost twice as common as in the United States. Therefore, risk may be lower for women in the United States. There is also evidence that the risk may be higher in women with a family history of ovarian cancer.
- Men and women with *PALB2* mutations have a small increased risk for pancreatic cancer. Pancreatic cancer screening is only recommended for individuals with a *PALB2* mutation if there have been past diagnoses of pancreatic cancer in the family.
- Men with *PALB2* mutations have an increased risk for male breast cancer. Although the breast cancer risk is significantly increased over that for men without *PALB2* mutations, the absolute risk of male breast cancer remains small.
- There is some evidence that men and women with mutations in *PALB2* have an increased risk for gastric cancer. However, at this time, the evidence is not conclusive and there are no management recommendations for gastric cancer risk.
- Although there are increased risks for cancer in men and women with mutations in *PALB2*, there are interventions that may reduce these risks. Guidelines from the National Comprehensive Cancer Network (NCCN) that may apply are listed below. Since information about the cancer risks associated with *PALB2* mutations is relatively new, and there is still some uncertainty about the best ways to reduce these risks, it may be appropriate to interpret these results in consultation with cancer genetics experts in this emerging area of knowledge.

PALB2 gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Female Breast	To age 50[1, 4]	17%	2.1%
	To age 80[1, 4]	53%	10.7%
	Second primary within 10 years of first breast cancer diagnosis[5, 6]	5%	3.5%
Pancreatic	To age 80[1, 4]	2%-3%	1.1%
Ovarian	To age 80[1, 4]	5%	0.9%
Male Breast	To age 80[1, 4]	1%	0.1%

PALB2 Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of

each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Female Breast	Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Periodic, consistent breast self-examination (BSE) may facilitate breast awareness.[7]	Individualized	NA
	Clinical encounter, including clinical breast exam, ongoing risk assessment and risk-reduction counseling[7]	When genetic risk is identified, but not before age 21	Every 6 to 12 months
	Mammography and breast MRI with contrast[8]	Age 30, or modified to a younger age based on family history	Annually
	Consider risk-reducing mastectomy.[8]	Individualized	NA
	Consider additional risk-reduction strategies.[7, 8]	Individualized	NA
Pancreatic	For patients with a family history of pancreatic cancer, consider available options for pancreatic cancer screening, including the possibility of endoscopic ultrasonography (EUS) and MRI/magnetic resonance cholangiopancreatography (MRCP). It is recommended that patients who are candidates for pancreatic cancer screening be managed by a multidisciplinary team with experience in screening for pancreatic cancer, preferably within research protocols.[9]	Age 50, or 10 years younger than the earliest age of pancreatic cancer diagnosis in the family	Annually
	Provide education about ways to reduce pancreatic cancer risk, such as not smoking and losing weight.[10]	Individualized	Individualized
Ovarian	Consider bilateral salpingo-oophorectomy (BSO).[8]	After 45 years	NA
Male Breast	Currently there are no specific medical management guidelines for male breast cancer risk in mutation carriers. However, the increase in risk warrants consideration of options for male breast cancer screening, such as patient breast awareness education and clinical breast examinations.[7, 8]	Individualized	NA
For Patients With A Cancer Diagnosis	For patients with a gene mutation and a diagnosis of cancer, targeted therapies may be available as a treatment option for certain tumor types (e.g., platinum chemotherapy, PARP-inhibitors)[10, 11]	NA	NA

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the *PALB2* gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

In rare instances, an individual may inherit mutations in both copies of the *PALB2* gene, leading to the condition Fanconi anemia, complementation group N (FANCN). This condition is extremely rare, but is thought to include physical abnormalities, growth retardation, progressive bone marrow failure and a high risk for cancer. The children of this patient are at risk of inheriting FANCN only if

the other parent is also a carrier of a *PALB2* mutation. Screening the other biological parent of any children for *PALB2* mutations may be appropriate.[12]

References

1. Yang X, et al. Cancer Risks Associated With Germline *PALB2* Pathogenic Variants: An International Study of 524 Families. J Clin Oncol. 2020 38:674-685. PMID: 31841383.
2. Lott PC, et al. Resolving gastric cancer aetiology: an update in genetic predisposition. Lancet Gastroenterol Hepatol. 2018 3:874-883. PMID: 30507471.
3. Ajani JA, et al. NCCN Clinical Practice Guidelines in Oncology®: Gastric Cancer. V 1.2023. Mar 10. Available at https://www.nccn.org.
4. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2023 Mar 24]. Available from https://seer.cancer.gov/explorer/.
5. Morra A, et al. The impact of coding germline variants on contralateral breast cancer risk and survival. Am J Hum Genet. 2023 Mar 2;110(3):475-486. PMID: 36827971.
6. Giannakeas V, et al. The risk of contralateral breast cancer: a SEER-based analysis. Br J Cancer. 2021 Aug;125(4):601-610. PMID: 34040177.
7. Bevers TB, et al. NCCN Clinical Practice Guidelines in Oncology®: Breast Cancer Screening and Diagnosis. V 1.2022. Jun 2. Available at https://www.nccn.org.
8. Daly M et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast, Ovarian and Pancreatic. V 3.2023. Feb 13. Available at https://www.nccn.org.
9. Goggins M, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. Gut. 2020 69:7-17. PMID: 31672839.
10. Tempero MA, et al. NCCN Clinical Practice Guidelines in Oncology®: Pancreatic Adenocarcinoma. V 2.2022. Dec 6. Available at https://www.nccn.org.
11. Schaeffer E, et al. NCCN Clinical Practice Guidelines in Oncology®: Prostate Cancer. V 1.2023. Sep 16. Available at https://www.nccn.org.
12. Reid S, et al. Biallelic mutations in *PALB2* cause Fanconi anemia subtype FA-N and predispose to childhood cancer. Nat Genet. 2007 39:162-4. PMID: 17200671.

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