UT Southwestern Harold C. Simmons Comprehensive Cancer Center | NCI Designated Comprehensive Cancer Center

PALB2 Mutations

What you should know about *PALB2* mutations

Individuals with a *PALB2* mutation have an increased lifetime risk for breast, pancreas, and possibly other cancers. Exact lifetime cancer risks for individuals with one mutation in this gene are not fully understood, but more specific information becomes available with ongoing research.

Cancer risks associated with a *PALB2* mutation

- Breast Cancer: Females with one *PALB2* mutation have a 33-58% chance to develop breast cancer in their lifetime. Males with one *PALB2* mutation are also at increased risk to develop breast cancer, but their exact risk is unknown at this time. Family history has been found to impact breast cancer risk.
- Pancreatic Cancer: Both males and females with one *PALB2* mutation have an increased risk for pancreatic cancer, but the exact risk is unknown at this time.
- Ovarian Cancer: There is a potential increased risk for ovarian cancer in females with a *PALB2* mutation, but evidence is still insufficient at this time.

Risks to family members

Mutations in the *PALB2* gene are inherited in an autosomal dominant manner. This means that children, brothers, sisters, and parents of individuals with a *PALB2* mutation have a 1 in 2 (50%) chance of having the mutation as well. Both males and females can inherit a familial *PALB2* mutation and can pass that it on to their children.

When an individual inherits two *PALB2* mutations (one from each parent), this causes a syndrome called Fanconi Anemia (FA). FA is associated with physical abnormalities, childhood leukemia, and other cancers.

Managing cancer risks

The following surveillance is recommended by the National Comprehensive Cancer Network (NCCN v2.2020).

Breast Cancer

- For females, annual mammogram beginning at age 30 (or 5-10 years before the youngest breast cancer diagnosis in the family, but no later than age 30) with consideration of annual breast MRI with contrast.
- Currently, there are no consensus management guidelines for male breast cancer. Males with a *PALB2* mutation are encouraged to discuss family history and breast cancer surveillance options (i.e. clinical breast exam) with their medical providers to determine an appropriate surveillance regimen.

- Data on the benefit of risk-reducing mastectomy based on *PALB2* mutation status alone is limited, but the option of a risk-reducing mastectomy should be discussed.

Pancreatic Cancer

- For individuals with a first- or second-degree relative diagnosed with pancreatic cancer, consider surveillance beginning at age 50 (or ten years younger than the earliest diagnosis of pancreatic cancer in the family) using annual abdominal MRI/MRCP, EUS, and/or enrollment in research protocols
- In the absence of a close family history of pancreatic cancer, no pancreatic screening is currently recommended

Ovarian Cancer

- Evidence is insufficient to recommend management based on *PALB2* mutation status alone; management should be based on personal risk factors and family history

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