BC CANCER HEREDITARY CANCER
Provincial Health Services Authority

# *PALB2* Cancer Risks and Management

## Overview

People with a pathogenic variant in the *PALB2* gene have a higher chance of developing certain types of cancer compared to the general population. Cancers often happen at a younger age for *PALB2* carriers.

This document summarizes the cancer risks and management recommendations for individuals with a confirmed *PALB2* pathogenic variant.

## Cancer risks associated with *PALB2*

| Cancer Type | *PALB2 (Risk to Age 80)* | General Population |
|---|---|---|
| Breast cancer (female) | 53% | 12.5% |
| Ovarian cancer | 3-5%* | 1 to 2% |
| Breast cancer (male) | 1% | Less than 1% |
| Pancreatic cancer | 2-5% | 1.3% |
| Prostate cancer | Increased but not well quantified | 12.5% |

Contralateral female breast cancer risk reaches 35% at 10 years after a premenopausal ER negative breast cancer.

*However, risk of ovarian cancer before age 50 is below 1% with a *PALB2* pathogenic variant and no family history of ovarian cancer.

## Cancer Screening and Risk Reduction

### Female Breast Cancer

Female Breast Cancer Screening:

- Starting at age 18, females should become familiar with the normal look and feel of their breast tissue and to report any changes to their primary care provider promptly. Regular and consistent breast self-exams can support breast self-awareness and are often most effective when done at the end of menstruation.
- **Annual clinical exam** of the breast and regional nodes from age 30.
- **Annual breast MRI** beginning at age 30 (or 5 years earlier than the youngest diagnosis in the family, whichever is earliest) until age 70.
- **Annual mammograms** beginning at age 30 and continue as long as clinically indicated.

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Female Breast Cancer Prevention:

- Discussion of **risk reducing medication** options and review of potential benefits and side effects is recommended. Medications such as tamoxifen, raloxifene, anastrozole and exemestane may reduce the risk of developing a hormone-receptor positive breast cancer.
- **Risk reducing bilateral mastectomy** (RRBM; removing both breasts) reduces the risk of breast cancer by over 90%. The decision to have RRBM is complex and requires discussion regarding benefits and risks of the surgery in the context of a person's general health, life expectancy and personal health beliefs. Routine breast imaging (mammogram and/or breast MRI) is not required after bilateral mastectomy.

**Ovarian Cancer**

Ovarian Cancer Screening:

Transvaginal ultrasound and/or pelvic exam and/or CA-125 blood test) is **not recommended** in British Columbia as it is proven to be ineffective at detecting cancer early and improving outcomes.

Ovarian Cancer Prevention:

- **Risk-reducing bilateral salpingo-oophorectomy** (RRBSO; removing ovaries and tubes) is an option to consider for people with a pathogenic variant in *PALB2* from age 45-50 or earlier if there is a history of young onset ovarian cancer in the family. If performed before the age of natural menopause it may also reduce the risk of breast cancer with the level of breast cancer risk reduction varying with the age at RRBSO. Hormone replacement therapy is recommended until the natural age of menopause (age 45 to 50) to reduce the bone and cardiac impact of premature menopause.
- **Risk-reducing bilateral salpingectomy (removing fallopian tubes)** has been proposed as a risk-reduction strategy for pre-menopausal women. Recent studies suggest bilateral salpingectomy is safe and feasible, and reduces ovarian cancer risk in the general population by nearly 80% while minimizing adverse effects of early menopause from oophorectomy. Long-term evidence on its effectiveness in cancer prevention in higher risk cohorts is limited and further research is needed.
- **Oral contraceptive pill** (OCP; the birth control pill): Use of the oral contraceptive pill for at least 5 years can reduce the risk of ovarian and endometrial cancer by 50% or more. This protective effect increases with longer use and may last for at least 20 years after stopping. Most studies show a small increase in breast cancer risk, like that seen with hormone replacement therapy. Decisions around using OCP for cancer prevention should involve a careful discussion of risks, benefits, and side effects in the context of the individual's health and contraceptive needs.

**Pancreatic Cancer**

- To lower the risk, avoid or quit cigarette smoking, exercise regularly, limit alcohol, maintain a weight that supports overall health and choose healthy foods and drinks.
- There is no clear data to recommend surveillance with the *PALB2* gene without a diagnosis of pancreatic cancer in a first or second degree relative.
- Begin **screening for type 2 diabetes** at age 40, repeat every 3 years.
- Investigate new onset of diabetes or unexplained changes in diabetic control carefully, with consideration of pancreatic imaging (CT pancreatic protocol or contrast-enhanced MRI/MRCP); refer to GI specialist if any abnormalities are found.

Additional pancreatic screening may be recommended to people who have a close relative with pancreatic cancer and *a PALB2* pathogenic variant. There is more information here: HCP_GuidelinesManuals_FamilialPancreaticCancer.pdf

**Male Breast Cancer**

- Starting at age 35, males should become familiar with the normal look and feel of their breast tissue and to report any changes to their primary care provider promptly. Regular and consistent breast self-exams can support breast self-awareness.
- **Annual clinical exam** of the breast and regional nodes from age 35.

**Prostate Cancer**

Consider annual **digital rectal examination (DRE)** and/or serum **prostate specific antigen test (PSA)** testing as early as 40-45 years of age or 5-10 years before the youngest diagnosis of prostate cancer in the family (whichever is earlier)

The Canadian Urological Association recommends healthcare providers engage in shared decision-making with their patients to come to an individualized screening decision following a thorough discussion on the potential risks and benefits of the PSA test. In BC, PSA testing in asymptomatic men is not an insured benefit.

## High Risk Clinic

Individuals with breast tissue who carry a pathogenic variant in the *PALB2* gene, or are at 50% risk of having inherited one, can be referred to the Hereditary Cancer Program's High Risk Screening Clinic for ongoing cancer risk management and decision support. Read more about the High Risk Clinic.

*Note: In the information above, male/female refers to sex assigned at birth.*

## Family and Reproductive Considerations

### Inheritance

Each child of someone with a *PALB2* pathogenic variant has a 50% chance of inheriting the variant.

Family members are encouraged to contact their local genetics clinic to learn more about whether genetic testing or cancer screening may be helpful for them. Family members who live in British Columbia or the Yukon can contact our program directly at hereditarycancer@bccancer.bc.ca. In BC/Yukon, genetic testing is generally available starting at age 19.

### Fanconi Anemia:

Inheriting a pathogenic variant in *PALB2* from both parents causes Fanconi anemia type N (FA-N). FA-N is a rare condition characterized by progressive bone marrow dysfunction, growth delays, variable congenital malformations and a high risk for leukemia and early onset solid tumours. For there to be a risk of FA-N in offspring, both parents would each have to have a single pathogenic variant in *PALB2*; in such a case, the risk of having an affected child is 25%.

If an individual with a *PALB2* pathogenic variant is planning a family, a review of their partner's family history of cancer may be helpful. Genetic counselling may be offered if there is a concern for the risk of FA-N in children.