BC CANCER HEREDITARY CANCER
Provincial Health Services Authority

BRIP1 Cancer Risks and Management

Cancer risks associated with *BRIP1*

Studies suggest that females with a truncating pathogenic variant in the *BRIP1* gene have a moderately increased lifetime risk to develop ovarian cancer (primarily high grade serous adenocarcinoma) with a median age of diagnosis of 65. A relative risk of 4.94 [95% CI 4.07-6.00] confers an absolute risk of 5-15% (to age 80) compared to the general population risk of 1-2%.

Current evidence does not support an increased risk of breast cancer for female *BRIP1* pathogenic variant carriers.

There are no well-established increased cancer risks for males who carry a *BRIP1* pathogenic variant.

Cancer Screening and Risk Reduction

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.

Ovarian Cancer Prevention:

- **Risk-reducing bilateral salpingo-oophorectomy** (RRSO; removing ovaries and tubes) is an option to consider for people with a pathogenic variant in *BRIP1* typically from age 45-50 (or earlier if there is a first or second degree relative with young onset ovarian cancer in the family). Hormone replacement therapy is recommended until age 50 to reduce the bone and cardiac impact of premature menopause. Decisions about ongoing use should be made with a specialized healthcare provider. Pathology must be done by SEE-FIM protocol.
- **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. Pathology must be done by SEE-FIM protocol.

- **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. 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.

Female Breast Cancer:
General population breast cancer screening is sufficient for females with pathogenic *BRIP1* variants who do not have a close family history of breast cancer.

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

Family and Reproductive Considerations

Inheritance
Each child of someone with a *BRIP1* 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 *BRIP1* pathogenic variant from both parents causes Fanconi anemia type J (FA-J). FA-J 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-J in offspring, both parents would each have to have a single pathogenic variant in *BRIP1*; in such a case, the risk of having an affected child is 25%.

If an individual with a *BRIP1* 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-J in children.