BC CANCER HEREDITARY CANCER
Provincial Health Services Authority

RAD51C Cancer Risks and Management

Overview

People with a pathogenic variant in the *RAD51C* gene have a higher chance of developing certain types of cancer compared to the general population. Cancers often happen at a younger age for *RAD51C* carriers.

This document summarizes the cancer risks and management recommendations for individuals with a confirmed *RAD51C* pathogenic variant.

Cancer risks associated with *RAD51C*

RAD51C is a moderate penetrance **ovarian cancer** susceptibility gene. Females who are carriers of a single pathogenic *RAD51C* variant have an **estimated lifetime risk to develop ovarian cancer of 11%** (95% CI: 6%-21%). This compares to the general population risk of 1-2%.

RAD51C pathogenic variants also confer a moderate risk for **female breast cancer**. In general, pathogenic variants in this gene are reported to confer a **lifetime risk of 21%** (95% CI: 15%-29%) compared to general population risk of 12.5%.

At this time, there are no known increased cancer risks for males with pathogenic variants in *RAD51C*.

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 at detecting cancer early and improving outcomes.

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. Individuals wishing to pursue this option should be referred to an expert center to discuss the risks and benefits and consider participation in a clinical trial. 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 Surveillance

- Starting at age 18, females should become familiar with the normal look and feel of their breast tissue and report any changes to their primary care provider promptly. Regular and consistent breast self-exams can support breast self-awareness and are most effective when done at the end of menstruation.
- **Annual clinical exam** of the breast and regional nodes from age 30.
- **Annual mammograms** beginning at age 40 and continue as long as clinically indicated.

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

Family and Reproductive Considerations

Inheritance

Each child of someone with a *RAD51C* 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 *RAD51C* pathogenic variant from both parents causes Fanconi anemia type O (FA-O). FA-O 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-O in offspring, both parents would each have to have a single pathogenic variant in *RAD51C*; in such a case, the risk of having an affected child is 25%.

If an individual with a *RAD51C* 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-O in children.