BC CANCER HEREDITARY CANCER
Provincial Health Services Authority

CDKN2A Cancer Risks and Management

Overview

Pathogenic variants in *CDKN2A* confer an increased risk to develop malignant melanoma, pancreatic cancer, and possibly other cancer types (e.g. sarcoma, nervous system tumours). This condition may also be referred to as Familial Atypical Multiple Mole Melanoma Syndrome (FAMMM).

This document summarizes the cancer risks and management recommendations for individuals with a confirmed *CDKN2A* pathogenic variant.

Cancer risks associated with *CDKN2A*

The lifetime cancer risks associated with *CDKN2A* vary widely across published studies. The **melanoma** risk by age 80 is estimated at **28-76%,** compared to the 1-2% lifetime risk in the general Canadian population. In addition to *CDKN2A* genetic status, a person's melanoma risk depends on additional personal risk factors (e.g. skin type, nevi, atypical mole/dysplastic nevi, UV exposure, prior radiation, history of melanoma) and familial risk factors (e.g. family history of melanoma).

The **pancreatic cancer** risk by age 80 is estimated **greater than 15%,** compared to the 1.3% lifetime risk in the general population. There is evidence that tobacco smoking significantly increases pancreatic cancer risk.

Cancer Screening and Risk Reduction

Melanoma

There remains a lack of consensus on dermatologic management and surveillance guidelines for individuals carrying *CDKN2A* pathogenic variants.

We recommend the following:

- **Self-examination**: monthly self-examination of the skin either alone or with the assistance of a relative to look for abnormalities in growth, shape or coloring.
- **Clinical skin exam**: total body skin examination (including scalp, genital area, oral mucosa, and nails) every 6 months by a Dermatology specialist, including mole mapping (or full body photographs), dermoscopic examination of clinically atypical nevi and review of ABCDE features (Asymmetry, Border irregularity, Color

variegation, Diameter >6mm, Evolution). In BC, mole mapping is not an insured benefit. For those with additional personal or familial melanoma risk factors, more frequent skin exam can be considered.
- **Limit exposure to UV light:** avoid excess sun exposure, wear a hat, sunglasses, and long protective clothing, apply sunscreen with SPF of 30 or more and labeled "broad-spectrum", and avoid tanning beds and sun lamps.

Children in families with *CDKN2A* pathogenic variants may begin skin screening at age 10.

First-degree relatives of a person with melanoma who test negative for a familial *CDKN2A* pathogenic variant are still at risk for developing melanoma and should continue annual clinical skin exam and monthly self-examination.

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.
- Annual diabetes screen from age 40 (fasting glucose or HbA1C).
- Investigate new onset 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 found.
- Consider annual imaging with alternating endoscopic ultrasound (EUS) and contrast-enhanced MRI/MRCP screening **starting at age 40 or 10 years before** the youngest diagnosis of pancreatic cancer in the family. Screening may continue to age 75, then reassessed based on clinical status.
- Refer to experienced, high-volume GI center for baseline assessment and discussion of current surveillance methods:
    - St. Paul's Hospital/Pacific Gastroenterology and Associates (tel: 604.688.6332; fax: 604.689.2004)
    - Vancouver General Hospital (tel: 604.875.5474; fax: 604. 628.2419)
    - Interior: KGA Gastroenterology (tel: 250.763.6433; fax 250.763.3818)
    - Vancouver Island: Pacific Digestive Health (tel: 250.412.1864; fax: 1.888.398.7091).

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

Family and Reproductive Considerations

Inheritance

Each child of someone with a *CDKN2A* 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 10.