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CDKN2A Mutations

Cancer Risk and Management Recommendations

Cancer Type	*CDKN2A*-associated lifetime cancer risks	General Population Lifetime Cancer Risks	Management Recommendations[1,2]

Melanoma	28-76% in the United States (varies by geographic location)[3-5]	2.5%	*Screening*
			• Presently, there are no formal guidelines for managing families with hereditary melanoma risk. The following methods are suggested for high-risk families:
			  ○ Clinical skin examinations every 6-12 months from age 10 and monthly skin self-examination beginning in childhood.[1,2] Depending on the individual, screening may be recommended at an increased interval.
			  ○ Skin surveillance programs should include evaluation of the scalp, as well as oral and genital mucosa. Digital dermoscopy and clinical photography can be helpful for monitoring these patients.[1]
			Surgery/Treatment
			• Biopsy and/or removal of suspicious moles is necessary. Melanoma vaccines have been developed, but have failed to prove efficacious to date.[6] Individuals with malignant melanoma may consider participating in clinical trials.
			Lifestyle Modifications
			• Individuals with *CDKN2A* mutations should reduce their amount of sun exposure and exposure to sources of ultraviolet radiation. If exposure is unavoidable, they should wear protective clothing (long-sleeved shirts, hats, sunglasses, etc.) and apply sunscreen with Sun Protection Factor (SPF) of 30 or higher at regular intervals during time of exposure.[7]

Pancreatic Cancer	17-58%[4,8]	1.6%	*Screening* • Consider pancreatic cancer screening including annual contrast-enhanced MRI/MRCP and/or EUS, with consideration of shorter screening intervals for individuals found to have worrisome abnormalities on screening beginning at age 40 or

			10 years younger than the earliest exocrine pancreatic cancer diagnosis in the family, whichever is earlier.[9] *Lifestyle Modifications* • Smoking is known to increase pancreatic cancer risk. It is essential for individuals with *CDKN2A* mutations to avoid smoking.[4,10] • Diet and general health are also thought to influence pancreatic cancer risk, so it is important to maintain a healthy diet (fruits, vegetables, whole grains, low in fat), exercise, and maintain a healthy weight. • Other risk factors for pancreatic cancer include diabetes and chronic pancreatitis.

Other Cancer Risks: *CDKN2A* mutations may be associated with other increased cancer risks, particularly those related to tobacco use, but data are limited at this time.[4,10] Recommendations for screening for other cancers should be based on family history and general population screening guidelines.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *CDKN2A* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- For carriers of a known mutation, assisted reproduction (with or without egg or sperm donation), pre-implantation genetic testing, and prenatal diagnosis options exist.
- All family members are encouraged to pursue genetic counseling to clarify their risks. Family members can visit www.FindAGeneticCounselor.com to find genetic services near them.

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