CDKN2A (p16INK4a) gene

Associated Syndrome Name: Melanoma-pancreatic cancer syndrome (MPCS)

CDKN2A (p16INK4a) Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Pancreatic	High Risk
Skin	High Risk

CDKN2A (p16INK4a) gene Overview

Melanoma-pancreatic cancer syndrome (MPCS) [1, 2, 3, 4, 5]

- Individuals with *CDKN2A* (p16INK4a) mutations have melanoma-pancreatic cancer syndrome (M-PCS). This condition has previously been known as familial atypical multiple mole melanoma syndrome (FAMMM).
- Patients with M-PCS have a high risk of developing melanoma. Exact estimates of the melanoma risk associated with *CDKN2A* (p16INK4a) mutations vary over a wide range, with higher risks found in patients who have a previous family history of melanoma.
- Patients with M-PCS due to mutations in *CDKN2A* (p16INK4a) may also have a high risk for pancreatic cancer. This risk may not be present in all families with mutations in *CDKN2A* (p16INK4a), so concern about pancreatic cancer risk should be higher for patients who have a family history of this cancer. In addition, patients who have been diagnosed with pancreatic cancer may also have an increased risk for a second primary pancreatic cancer.
- It has been suggested that patients with *CDKN2A* (p16INK4a) mutations have an increased risk for cancers other than melanoma and pancreatic cancer. In particular, several studies have reported an association with tobacco-related cancers such as lung and head and neck. While there are currently no medical management recommendations that address these possible risks, interventions aimed at smoking cessation may be especially important in individuals with *CDKN2A* mutations.
- Although there is a high risk for melanoma and pancreatic cancer in patients with M-PCS, it may be possible to reduce this risk with appropriate medical management, including increased attention to surveillance and lifestyle modifications. Guidelines from expert groups for the management of patients with high risks for these cancers are listed below. Since information about the cancer risks associated with *CDKN2A* (p16INK4a) mutations is relatively new, and there is uncertainty about the best ways to reduce these risks, it may be appropriate to interpret these results in consultation with cancer genetics professionals who have expertise in this emerging area of knowledge.

CDKN2A (p16INK4a) gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Melanoma	To age 50 [1, 3, 5, 6]	14%-50%	0.3%
	To age 80 [1, 3, 5, 6]	28%-76%	1.6%
Pancreatic	To age 70 [3, 4, 6, 7]	Up to 21%	0.6%

CDKN2A (p16INK4a) Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Melanoma	Education about the importance of skin protection, such as sun avoidance, protective clothing and sunscreen. [8, 9]	Infancy	Ongoing

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
	Whole-body skin examinations conducted by the patient or family member.[8, 9]	10 years	Monthly
	Comprehensive skin examination by a dermatologist, with total body photography and dermoscopy.[8, 9, 10]	10 years	Every 6 to 12 months
Pancreatic	Consider available options for pancreatic cancer screening, including endoscopic ultrasonography (EUS) and MRI/magnetic resonance cholangiopancreatography (MRCP). It is recommended that patients who are candidates for pancreatic cancer screening be managed by a multidisciplinary team with experience in screening for pancreatic cancer, preferably within research protocols.[11]	Age 40, or 10 years younger than the earliest age of pancreatic cancer diagnosis in the family	Annually
	Provide education about ways to reduce pancreatic cancer risk, such as not smoking and losing weight.[12]	Individualized	Individualized

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the CDKN2A (p16INK4a) gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

Since there are screening and preventative measures recommended to begin in infancy or early childhood for individuals with *CDKN2A* (p16INK4a) mutations, consideration should be given to the possibility of mutation testing at young ages.

References

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