BAP1 gene

Associated Syndrome Name: *BAP1*-tumor predisposition syndrome (*BAP1*-TPDS)

BAP1 Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Other	High Risk
Renal	High Risk
Skin	High Risk

BAP1 gene Overview

BAP1-tumor predisposition syndrome (*BAP1*-TPDS) [1, 2, 3, 4, 5, 6]

- Individuals with *BAP1* mutations have *BAP1*-tumor predisposition syndrome (*BAP1*-TPDS).
- The most common cancer diagnosed in individuals with *BAP1*-TPDS is melanoma of the eye (uveal melanoma). There is also a high risk for melanomas of the skin (cutaneous melanoma).
- The risk for basal cell skin cancer is increased in individuals with *BAP1* mutations. Although basal cell skin cancer is common in the general population, individuals with *BAP1*-TPDS are more likely to be diagnosed at younger ages, and with multiple tumors.
- Individuals with *BAP1*-TPDS have a high risk for malignant mesothelioma, a cancer that occurs in the lungs, abdomen, or skin. Asbestos exposure is a well-known environmental risk factor for mesothelioma and it is believed that individuals with *BAP1*-TPDS may be especially susceptible to asbestos exposure.
- Individuals with *BAP1*-TPDS have a high risk for clear cell renal cell carcinoma, a type of kidney cancer.
- Cancers in individuals with *BAP1*-TPDS often develop at relatively young ages and individuals may develop more than one type of cancer.
- Estimates of the risks for different types of cancer in individuals with *BAP1*-TPDS are listed in the Cancer Risk Table, but these estimates are based on small numbers of cases and are likely to change as we learn more about this condition.
- Benign skin tumors known as *BAP1*-inactivated melanocytic tumors (BIMT) are likely to be the first sign of *BAP1*-TPDS in most patients. These are not cancers, but may have the potential to become melanomas.
- Studies have suggested that *BAP1*-TPDS could also include an increased risk for a wide variety of other cancers, including hepatocellular carcinoma, cholangiocarcinoma, meningioma, breast, thyroid, lung, and others. However, more studies are needed to determine exactly which cancers are more common in people with *BAP1* mutations.
- Individuals with *BAP1*-TPDS may have an increased risk for other clinical findings, including nail abnormalities and lesions in the spleen.
- There is a lack of data on whether radiation exposure from CT imaging increases the risk of cancer in individuals with *BAP1* gene mutations. Some experts recommend limiting radiation exposure from medical imaging if possible.
- Although there are high cancer risks for patients with *BAP1*-TPDS, there may be interventions that can reduce these risks. Guidelines for kidney-specific screening from the National Comprehensive Cancer Network (NCCN) for the medical management of patients with *BAP1*-TPDS are listed below. There are currently no professional society medical management recommendations for patients with *BAP1*-TPDS for the additional cancers, but suggestions from experts who study the condition are provided below. Since *BAP1*-TPDS is a complex condition with risks for multiple types of cancer, and evolving recommendations for screening, patients with a *BAP1* mutation should be managed by a multidisciplinary team with expertise in medical genetics and the care of patients with hereditary cancer syndromes.

BAP1 gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Uveal Melanoma	Percentage of mutation carriers affected[1, 2, 3, 4, 7]	25%-36%	<0.1% to age 80
Malignant Mesothelioma	Percentage of mutation carriers affected[1, 2, 3, 4, 7]	20%-25%	<0.1% to age 80
Cutaneous Melanoma	Percentage of mutation carriers affected[1, 2, 3, 4, 7]	13%-17%	1.6% to age 80

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Renal	Percentage of mutation carriers affected[2, 3, 4, 7]	5%-10%	1.4% to age 80
Basal Cell Skin Cancer	Percentage of mutation carriers affected[2, 3, 4, 7]	6%-10%	20% to age 70
Other - Non-malignant features of *BAP1*-TPDS	All ages[1, 2]	*BAP1*-TPDS is associated with benign skin tumors known as BIMTs (see Overview)	NA

BAP1 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)
Uveal Melanoma	Currently there are no specific medical management guidelines for uveal melanoma risk in mutation carriers. However, expert groups have suggested consideration of screening including eye examinations and imaging by an ocular oncologist. It may also be desirable to avoid risk factors for uveal melanoma, such as arc welding and exposure to sunlight without UV protective sunglasses.[1, 3, 8]	11 years	Annually
Malignant Mesothelioma	Currently there are no specific medical management guidelines for malignant mesothelioma risk in mutation carriers. However, expert groups have suggested consideration of individualized monitoring for symptoms of malignant mesothelioma, and/or consideration of abdominal MRI or CT imaging.[1, 8]	30 years	NA
Cutaneous Melanoma	Currently there are no specific medical management recommendations for skin melanoma risk in mutation carriers. However, the increased risk for melanoma warrants consideration of risk-reduction strategies, including frequent self-examination of the skin, consideration of clinical skin examinations, and minimizing exposure to the sun and other sources of UV radiation.[1, 3, 8, 9, 10]	18 years	Annually
Renal	Abdominal MRI (preferred) or CT, with and without IV contrast.[11]	30 years, or 10 years younger than the earliest renal cancer diagnosis in the family	Every 2 years
Basal Cell Skin Cancer	Currently there are no specific medical management recommendations for basal cell skin cancer risk in mutation carriers. However, the increased risk for melanoma warrants consideration of risk-reduction strategies, including frequent self-examination of the skin, consideration of clinical skin examinations, and minimizing exposure to the sun and other sources of UV radiation.[1, 3, 8, 9, 10]	18 years	Annually

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Other - Non-malignant features of *BAP1*-TPDS	Currently there are no specific medical management guidelines for BIMTs in mutation carriers. However, expert groups have suggested it may be appropriate for these tumors to be monitored by a dermatologist along with monitoring for melanoma and basal cell cancer.[1, 3, 8]	18 years	Annually

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 BAP1 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 *BAP1* mutations carry a risk for complications in children and there are some screenings that may begin in children, consideration should be given to the possibility of mutation testing in childhood.

References

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