UT Southwestern Harold C. Simmons Comprehensive Cancer Center | NCI Designated Comprehensive Cancer Center

BAP1 Mutations

What You Should Know About *BAP1* Mutations

Individuals with mutations the *BAP1* gene have a genetic condition known as "*BAP1* hereditary cancer predisposition syndrome". Individuals with *BAP1* mutations have an increased lifetime risk for cancers such as uveal melanoma, malignant mesothelioma, cutaneous melanoma and renal cell carcinoma. Most individuals with a *BAP1* mutation develop multiple non-cancerous skin lesions. It has been estimated that up to 85% of individuals with a *BAP1* mutation will develop cancer by 65 years of age.

Cancer Risks Associated with a *BAP1* Mutation

- Uveal Melanoma: Uveal melanoma (UM) is a cancer of the eye. The lifetime risk for UM in individuals with *BAP1* mutations is estimated to be up to 31%. UM is the most commonly reported finding in *BAP1* mutation carriers with the earliest reported age of diagnosis (16 years). UM tends to be more aggressive with a higher risk for metastasis compared to UM that occurs in the general population.
- Malignant Mesothelioma: The lifetime risk for malignant mesothelioma (MMe) is estimated at 22% for individuals with *BAP1* mutations. Some studies have suggested that survival in individuals with BAP1-related MMe is longer compared to those with MMe in the general population. Evidence suggests that environmental asbestos exposure increases the risk for MMe in *BAP1* mutation carriers.
- Cutaneous Melanoma: The lifetime risk for cutaneous melanoma with *BAP1* mutations has been estimated at 13% and multiple primary cutaneous melanomas are common.
- Clear Cell Renal Cell Carcinoma: Individuals with *BAP1* mutations are at increased risk for renal cell carcinoma with the lifetime risk estimated at 10%.
- Basal Cell Carcinoma: Studies shown an increased risk for basal cell carcinoma with *BAP1* mutations. Exact risks remain unclear, but multiple primary basal cell carcinomas are common.

Risks to Family Members

Mutations in the *BAP1* gene are inherited in an autosomal dominant fashion. This means that children, brothers, sisters, and parents of individuals with a *BAP1* mutation have a 1 in 2 (50%) chance of having the mutation as well. Individuals with a *BAP1* mutation may develop one type cancer, more than one type of cancer, or no cancer at all. Both males and females can inherit a familial *BAP1* mutation and can pass it on to their children.

Managing Cancer Risks

Management for cancer risks associated with *BAP1* mutations may be individualized. Recommendations may include:

Uveal Melanoma (UM)

- Annual dilated eye examinations with ophthalmic imaging by an ocular oncologist beginning at age 11
- High-risk monitoring for metastasis if a uveal melanoma is diagnosed (liver-directed imaging every 3-6 months and pulmonary imaging 1-2 times per year)

- Those with any pigmented lesions should be referred to an ocular oncologist for follow-up or treatment.

Malignant Mesothelioma (MMe)

- Annual physical examination is recommended.
- Evaluation of the peritoneum and pleura with abdominal MRI may be considered during screening for renal cell carcinoma.
- There are conflicting recommendations for spiral chest CT for asymptomatic individuals with a history of exposure to asbestos, due to the possible increased risk of cancer from radiation exposure.

Cutaneous Melanoma

- Annual full-body dermatologic examinations are recommended starting at age 20 years
- Skin self-exam following ABCDE melanoma characteristics
- Regular use of sun protection

Clear Cell Renal Cell Carcinoma (ccRCC)

- Annual abdominal ultrasound examination is recommended.
- Annual urinalysis and abdominal MRI every two years may be considered.

Agents/circumstances to avoid

- Uveal melanoma: avoid arc-welding. There is currently no data to suggest a benefit of sunglasses for reduction of UM risk.
- Malignant mesothelioma: avoid asbestos exposure and smoking.
- Cutaneous melanoma and BCC: limit sun exposure, use sunscreen and protective clothing, and have regular dermatologic examinations.

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