

Melanoma

Genetic Risk, Cutaneous

No germline biomarker testing is recommended by NCCN with the exception of risk stratification. Genetic counseling and testing if any of the following are indicated:

When and what should be tested?

- Upon or before presentation
- Peripheral blood, saliva or buccal mucosa swab

Who should be tested?

- Consider genetic counseling referral for p16/CDKN2A mutation testing in the presence of 3 or more invasive cutaneous melanomas, or a mix of invasive melanoma, pancreatic cancer, and/or astrocytoma diagnoses in an individual or family.
- Multigene panel testing that includes CDKN2A is recommended for patients with invasive cutaneous melanoma who have a first-degree relative diagnosed with pancreatic cancer
- Presence of germline mutations or polymorphisms predisposing to melanoma (eg, CDKN2a, CDK4, MC1R, BAP1 [especially for uveal melanoma], TERT, MITF, PTEN, and potential other genes with increased melanoma risk (eg CHEK2, BRCA 1/2, BLM, ATM).
- Family or personal history of 2 or more invasive cutaneous melanomas; family or personal history of at least 2 non-cutaneous cancers, especially pancreatic, renal, bladder, GI, and/or breast cancer; family history of astrocytoma; uveal melanoma; and/or mesothelioma. .
- CDKN2a, CDK4, MC1R, BAP1 (including uveal), TERT, MITF, PTEN, xeroderma pigmentosum

FDA/NCCN Approved

- CDKN2a
- CDK4
- MC1R
- BAP1
- TERT
- MITF
- PTEN

Emerging

Multigene panel testing for p16/CDKN2A mutation testing

Melanoma

Genetic Risk, Uveal

No germline biomarker testing is recommended by NCCN with the exception of risk stratification. Genetic counseling and testing if any of the following are indicated:

When and what should be tested?

- Upon or before presentation
- Peripheral blood, saliva or buccal mucosa swab

Who should be tested?

- Early age at diagnosis (<30 years of age)
- History of other primary cancers in the patient
- Family or personal history of other cancers known to be associated with a hereditary syndrome:
 - BAP1: RCC, basal cell, HCC, mesothelioma, cutaneous melanoma, cholangiocarcinoma, meningioma
 - BRCA, PALB2: breast, ovarian, or pancreatic cancers

FDA/NCCN approved – Risk of distant metastasis

Low Risk

- Disomy 3
- Gain of function chromosome 6p
- *EIF1AX* mutation
- PRAME(-)

Medium Risk

- *SF3B1* mutation
- PRAME(+)

High risk

- Monosomy 3
- Gain of chromosome 8q
- *BAP1*

FDA/NCCN approved – Risk of development of uveal melanoma

- *BAP1*
- *MBD4*
- *PALB-2*

Emerging

Melanoma

Cutaneous (somatic)

When and what should be tested?

- Treatment eligible
- Metastatic disease
- At time of initial diagnosis or recurrence
- Tissue or liquid



FDA/NCCN approved stage III

- *BRAF*

FDA/NCCN approved stage IV*

- BRAF V600E, BRAF V600K, BRAF V600R,M,D,G
- NTRK 1,2,3
- TMB
- dMMR
- KIT
- NRAS
- ALK
- ROS1
- RET
- HER2
- MRD

Emerging

Melanoma

Uveal (somatic)

When and what should be tested?

- Treatment eligible
- Unresectable or metastatic disease
- At time of initial diagnosis or recurrence
- Tissue or liquid (liquid only at recurrence unless another tissue biopsy obtained)

FDA/NCCN approved

- HLA-A *02:01
- For metastatic disease:
 - BRAF V600E
 - NTRK 1/2/3
 - RET
 - TMB
 - dMMR
 - MRD

Emerging