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NCCN Clinical Practice Guidelines in Oncology
(NCCN Guidelines®)

Melanoma: Cutaneous

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PRINCIPLES OF SENTINEL LYMPH NODE BIOPSY (SLNB)

General Principles (continued)

- SLNB should be discussed with all patients with clinical stage IB or II melanoma, with the following considerations:
  - For patients with a melanoma Breslow depth of <0.8 mm without ulceration (T1a) or other adverse features, the probability of a positive SLN is <5%. NCCN does not generally recommend SLNB for these patients unless there is significant uncertainty about the adequacy of microstaging (eg, positive deep margins or limited sampling of a larger lesion).
  - For patients with clinical stage IB, T1b melanoma (Breslow depth <0.8 mm with ulceration or 0.8–1 mm with or without ulceration), or T1a lesions with Breslow depth >0.5 mm and other adverse features (age ≤42 years, head/neck location, lymphovascular invasion, and/or mitotic index ≥2/mm^2), the probability of a positive SLNB is 5% to 10%, with additive increased risk when multiple adverse features are present. NCCN recommends discussing and considering SLNB for these patients.
  - For patients with stage IB (T2a) or II (T2b and higher) melanoma, the probability of a positive SLN is generally >10%. However, there are subsets of patients (non-mitogenic, or older age) for whom the probability of a positive SLN is substantially lower.[3,4] NCCN recommends discussing and offering SLNB for these patients.
  - Regardless of a patient's risk of a positive SLNB, if the patient is medically unfit or is unlikely to act on the information that the SLNB would provide (eg, pursue surveillance nodal basin US, undergo CLND, consider adjuvant therapy, and/or change follow-up schedules), then it is reasonable to forego SLNB.
  - Predictive GEP testing to differentiate melanomas at low versus high risk for nodal metastasis should not replace surgical oncology discussion of pathologic staging with SLNB in eligible patients. Findings of the prospective Merlin_001 trial suggest that CP-GEP testing may be used in select patients with T1b ± T2a melanoma to support shared decision-making, when a patient or provider would decide against SLNB if the true risk was <10%. A high-risk result in that scenario would portend a 3 times higher risk of SLN involvement based on trial results.[5] Alternative GEP tests for SLNB risk prediction are not recommended outside of the context of a clinical study or trial based on current data. Additional prospective investigation and outcomes data (including impact of missing a positive SLNB) will further inform the utility of GEP tests, multivariable nomograms/risk calculators (eg, melanomarisk.org.au/snlland; mskcc.org/nomograms/melanoma/sentinel_lymph_node_metastasis), and other decision analytical models for SLNB risk prediction.[6-8] Existing GEP tests for SLNB risk prediction should be prospectively compared with no-cost, contemporary models that incorporate readily available CP variables.[9-19]
- Although the accuracy of SLNB may be lower after a prior wide excision, rotational flap, or skin graft closure of a primary melanoma, it may be considered selectively in this setting, particularly for non-head and neck primary melanomas.
- In the setting of an isolated in-transit metastasis or local recurrence of a primary melanoma without clinically or radiographically evident regional nodal or distant metastases, SLNB may be considered, if it will affect the decision for adjuvant therapy.

References

Note: All recommendations are category 2A unless otherwise indicated.

FOOTNOTES FOR WORKUP AND PRIMARY TREATMENT

[e] Molecular analysis for *BRAF* or MGPT of the primary lesion is not recommended for patients with cutaneous melanoma unless required to guide adjuvant or other systemic therapy or consideration of clinical trials. See Principles of Biomarker Testing (ME-C).

[l] In patients with pure desmoplastic melanoma (≥90% of invasive melanoma associated with prominent stromal fibrosis), SLNB positivity is less common compared to mixed desmoplastic/nondesmoplastic and conventional melanoma subtypes. Variability across studies in the rate of SLNB positivity in desmoplastic melanoma may be due to lack of standardized criteria for defining pure desmoplastic melanoma, histopathologic reproducibility, and/or reporting. In the setting of these conflicting reports, the role of SLNB in patients with pure desmoplastic melanoma remains controversial.

[o] Based on the current evidence, the NCCN Melanoma Panel does not recommend incorporation of commercially available prognostic GEP tests into melanoma care. The routine use of GEP to predict patient outcome according to specific AJCC-8 melanoma stage (before or after SLNB) requires further prospective investigation in large, contemporary datasets of unselected patients. Moreover, since there is a low probability of metastasis in stage IA melanoma and a high proportion of false-positive results using these tests, GEP testing should not guide clinical decision-making in this subgroup.

[p] Predictive GEP tests to differentiate melanomas at low versus high risk for nodal metastasis should not replace surgical oncology discussion of pathologic staging with SLNB in eligible patients. Findings of the prospective Merlin_001 trial suggest that clinicopathologic (CP)-GEP testing may be used in select patients with T1b ± T2a melanoma to support shared decision-making, when a patient or provider would decide against SLNB if the true risk was <10%. A high-risk result in that scenario would portend a 3 times higher risk of SLN involvement based on trial results (Hieken TJ, et al. JAMA Surg 2025;160:1358-1366). Alternative GEP tests for SLNB risk prediction are not recommended outside of the context of a clinical study or trial based on current data.

[q] Principles of Imaging–Workup (ME-D).

[r] Nodal basin ultrasound (US) is not a substitute for SLNB. Consider nodal basin US prior to SLNB for patients with melanoma with an equivocal regional lymph node physical exam. Abnormal or suspicious findings on nodal basin US should be confirmed histologically, whenever possible. Negative nodal basin US is not a substitute for biopsy of clinically suspicious lymph nodes.

[s] Decision not to perform SLNB may be based on significant patient comorbidities, patient preference, or other factors (such as advanced age and/or poor functional status).

[t] SLNB is an important staging tool. A positive SLNB upstages melanoma to stage III and is associated with significantly decreased melanoma-specific survival (MSS) (Montcreif MD, et al. J Clin Oncol 2022;40:3940-3951). While SLNB has not been proven to provide improved relapse-free survival (RFS) or overall survival (OS), it is associated with improved control of regional nodal disease (Crystal JS, et al. JAMA Surg 2022;157:835-842). SLNB status may aid adjuvant therapy decisions in clinically node-negative patients.

[u] The likelihood of a positive SLNB may also be informed by the use of multivariable nomograms/risk calculators (eg, melanomarisk.org.au/snlland; mskcc.org/nomograms/melanoma/sentinel_lymph_node_metastasis). However, some validation studies suggest nomogram underestimation of SLN-positivity risk for probabilities ≤10%, with no current models offering clinical utility at risk thresholds ≤8%, which may limit their predictive value in this lower risk category (Maddineni S, et al. Ann Surg Oncol 2024;31:2737-2746; Drebin HM, et al. J Am Coll Surg 2024;238:23-31; Olofsson Bagge R, et al. JAMA Surg 2024;159:260-268; Drebin HK. Ann Surg Oncol 2025;32:1463-1472). In a prospective trial of 1802 patients, the Merlin Assay CP-GEP test showed an overall negative predictive value (NPV) of 92.9% (94.8% for T1b and 91.9% for T2a melanoma), similar to that of current SLNB risk nomograms. Additional prospective investigation and outcomes data (including impact of missing a positive SLNB) will further inform the utility of GEP tests, multivariable nomograms/risk calculators, and other decision analytical models for SLNB risk prediction (Hieken TJ, et al. JAMA Surg 2025;160:1358-1366; Yamamoto M, et al. Curr Med Res Opin 2023;39:417-423; Miller JR 3rd, et al. JAMA Netw Open 2023;6:e236356; Bartlett EK. Ann Surg Oncol 2025;32:1429-1442). See Principles of Biomarker Testing (ME-C).

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