Translating Evidence into Practice: Primary Cutaneous Melanoma Guidelines. Sentinel Lymph Node Biopsy

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Disclosures

I do not have any relationships with industry

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Guidelines of care for the management of primary cutaneous melanoma

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The incidence of primary cutaneous melanoma has been increasing dramatically for several decades. Melanoma accounts for the majority of skin cancer—related deaths, but treatment is nearly always curative with early detection of disease. In this update of the guidelines of care, we will discuss the treatment of patients with primary cutaneous melanoma. We will discuss biopsy techniques of a lesion clinically suspicious for melanoma and offer recommendations for the histopathologic interpretation of cutaneous melanoma. We will offer recommendations for the use of laboratory and imaging tests in the initial workup of patients with newly diagnosed melanoma and for follow-up of asymptomatic patients. With regard to treatment of primary cutaneous melanoma, we will provide recommendations for surgical margins and briefly discuss nonsurgical treatments. Finally, we will discuss the value and limitations of sentinel lymph node biopsy and offer recommendations for its use in patients with primary cutaneous melanoma.

(J Am Acad Dermatol 2011;65:332-47.)

Key words: biopsy; follow-up; melanoma; pathology report; sentinel lymph node biopsy; surgical margins.
 Sentinel Lymph Node Biopsy

- AAD recommendations
- Impact AJCC 8th Ed staging
- Contrast with current NCCN guidelines
- Future/new role of SLNB
Sentinel Lymph Node Biopsy

- Sentinel Lymph Node
- Afferent Lymphatic Vessel
- Primary Melanoma
Sentinel Lymph Node Biopsy

**AAD:**

- Status of SLN is **most important prognostic indicator** for disease-specific survival in patients with primary cutaneous melanoma.

Melanoma-specific Survival by SLN Status

- **Negative**: 85.1±1.5%
- **Positive**: 62.1±4.8%

Disease-specific survival over time (months) with a log-rank test showing a significant difference (p<0.0001).

While there is interest in newer prognostic molecular techniques such as gene expression profiling to differentiate melanomas at low versus high risk for metastasis, routine (baseline) **prognostic genetic testing of primary cutaneous melanomas (before or following sentinel lymph node biopsy [SLNB]) is not recommended** outside of a clinical study (trial).
2011 AAD Guidelines of Care – Sentinel Lymph Node Biopsy (SLNB) for Primary Cutaneous Melanoma

- **Tis/T1a**, SLNB is **not** recommended
- **T1b 0.76-1.00 mm thickness**, discuss SLNB
- **T1b ≤ 0.75 mm thickness**, SLNB should not be considered
  - unless other adverse parameters in addition to ulceration and mitotic rate are present, such as angiolymphatic invasion, positive deep margin, or young age
- **> 1.0 mm thickness**, SLNB should be considered

### 8th Edition AJCC T-Classification

<table>
<thead>
<tr>
<th>T Class.</th>
<th>Thickness (mm)</th>
<th>Ulceration Status</th>
<th>Stage (cN0)</th>
<th>SLN Positivity</th>
<th>Stage (pN0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>&lt; 0.8</td>
<td>a - without ulceration</td>
<td>IA</td>
<td>&lt;5%</td>
<td>IA</td>
</tr>
<tr>
<td>T1</td>
<td>&lt; 0.8</td>
<td>b - with ulceration</td>
<td>IB</td>
<td>5-10%</td>
<td>IA</td>
</tr>
<tr>
<td>T1</td>
<td>0.8 – 1.0</td>
<td>b – w/ or w/o ulceration</td>
<td>IB</td>
<td>5-10%</td>
<td>IA</td>
</tr>
<tr>
<td>T2</td>
<td>&gt;1.0 – 2.0</td>
<td>a - without ulceration</td>
<td>IB</td>
<td>≥10%</td>
<td>IIA</td>
</tr>
<tr>
<td>T2</td>
<td>&gt;1.0 – 2.0</td>
<td>b - with ulceration</td>
<td>IIA</td>
<td></td>
<td>IIA</td>
</tr>
<tr>
<td>T3</td>
<td>&gt;2.0 – 4.0</td>
<td>a - without ulceration</td>
<td>IIA</td>
<td></td>
<td>IIA</td>
</tr>
<tr>
<td>T3</td>
<td>&gt;2.0 – 4.0</td>
<td>b - with ulceration</td>
<td>IIB</td>
<td></td>
<td>IIB</td>
</tr>
<tr>
<td>T4</td>
<td>&gt; 4.0</td>
<td>a - without ulceration</td>
<td>IIB</td>
<td></td>
<td>IIB</td>
</tr>
<tr>
<td>T4</td>
<td>&gt; 4.0</td>
<td>b - with ulceration</td>
<td>IIC</td>
<td></td>
<td>IIC</td>
</tr>
</tbody>
</table>

• Transition to **risk based** recommendations

• If risk of positive sentinel lymph node is:
  • **<5%**, NCCN does not recommend SLNB
    • Clinical stage IA, T1a, without other adverse features, including positive deep margin.
  • **5-10%**, NCCN recommends discussing and considering SLNB
    • Clinical stage IB, T1b (or T1a with adverse features)
  • **≥10%**, NCCN recommends discussing and offering SLNB
Indication for Sentinel Lymph Node Biopsy for Cutaneous Melanoma in 2018

• Prognosis

• Consider additional surgery (completion lymph node dissection)
  • DeCOG-SLT
  • MSLT-2

• Consider adjuvant systemic therapy
Completion Dissection or Observation for Sentinel-Node Metastasis in Melanoma

Multicenter Selective Lymphadenectomy Trial-II

- 1934 patients with nodal metastasis determined by pathological assessment or RT-PCR (~12%)
- Randomized to completion lymph node dissection (CLND) vs active nodal basin surveillance
  - Clinical and ultrasound exam q4 mos x yrs 1-2; q6 mos yrs 3-5
  - 46.6% trunk, 39.7% extremities, 13.7% head and neck
- Immediate completion lymph node dissection:
  - Increased rate of regional disease control
  - Provided prognostic information (non-sentinel node positivity)
  - Did not increase melanoma-specific survival
MSLT-II Considerations

- Tumor burden bias
- Location – morbidity of nodal recurrence
- Reliability of active nodal basin surveillance
- Prognostic information (stage IIIA)
- Adjuvant systemic therapy – separate discussion
Adjuvant Dabrafenib plus Trametinib in Stage III BRAF-Mutated Melanoma


Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma

NCCN Guidelines Version 1.2018
Melanoma

CLINICAL/PATHOLOGIC STAGE

<table>
<thead>
<tr>
<th>Stage IIIA (sentinel node positive)</th>
<th>WORKUP*</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Consider imaging¹ for baseline staging (category 2B)</td>
<td></td>
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<tr>
<td>• Imaging¹ to evaluate specific signs or symptoms</td>
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<table>
<thead>
<tr>
<th>Stage IIIB/C (sentinel node positive)</th>
<th>WORKUP*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging¹ for baseline staging and to evaluate specific signs or symptoms</td>
<td></td>
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</table>

| Stage III (clinically positive node[s]) | See ME-5 |

PRIMARY TREATMENT

| Active nodal basin surveillance⁵ or Complete lymph node dissection (CLND)⁵ |

ADJUVANT TREATMENT

Observation or

Nivolumab or resected stage III B/C (category 1) (preferred adjuvant immunotherapy regimen)³ or

Dabrafenib/trametinib for patients with BRAF V600 activating mutation and SLN metastasis >1 mm (category 1) or

High-dose ipilimumab for SLN metastasis >1 mm¹,⁵ (category 1) or

Interferon alfa³