**Background**

- Management of patients with melanoma involves multiple decision points during clinical care, all of which, in line with guidelines, should be aligned with a patient’s risk for poor outcomes. The 31-gene expression profile (GEP) was developed and validated to predict a patient’s risk of recurrence and further validated to precisely predict a patient’s individual risk for a positive SLNB.
- An SLNB risk threshold weighs surgical risks against those of missing a positive SLN. Current guidelines recommend a 5% risk threshold for considering SLNB in patients with cutaneous melanoma (T1a with high-risk features, T1a-HR-T4). 1,2
- A 5% threshold indicates that, in a group of 20 similar patients foregoing SLNB, 19 would have a negative result, with one missed positive SLN (19:1 negative:positive ratio). 2,3 Any novel test to identify patients who can forego SLNB should increase the ratio of negative-to-missed positive nodes (Figure 1).
- A second GEP test was developed to identify patients at low risk of SLN metastasis, CP-GEP, but is not available for survival prognostication. 11,12

**Results**

**Clinical Impact and Objective**

- Patient management decisions, including the decision to undergo SLNB, should be risk-appropriate to the individual being considered for treatment. Currently, national guidelines recommend patients consider SLNB when risk reaches a 5% threshold, broadly identified by T-stage (T1a with high-risk features and greater). Thus, by guidelines, an allowable threshold for true negatives to false negatives when foregoing SLNB is 19:1, and any test used to guide this decision should be superior to this benchmark.
- To compare the utility of the i31-GEP and CP-GEP for SLNB guidance with the current standard of care in T1b-T2 cutaneous melanoma.

**Figure 2. Only the i31-GEP performs better than standard of care at identifying those who can safely forgo SLNB (T1b-T2)**

<table>
<thead>
<tr>
<th>Test</th>
<th>TN</th>
<th>FN</th>
<th>Ratio (TN:FN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>i31-GEP</td>
<td>134</td>
<td>5</td>
<td>30:1 (154:5)</td>
</tr>
<tr>
<td>Standard</td>
<td>19</td>
<td>1</td>
<td>19:1 (19:1)</td>
</tr>
<tr>
<td>CP-GEP</td>
<td>60</td>
<td>4</td>
<td>15:1 (60:4)</td>
</tr>
</tbody>
</table>

1: GEP results adapted from Whitman et al. JCO PO 2021 2: CP-GEP results obtained from Youssaf et al. JCO 2021 2: TN: True-negative, FN: False negative.

CP-GEP would miss more positive nodes per 100 ‘low-risk’ patients (n=6; 100/15) than using the current standard of 5% (n=5), while i31-GEP would miss less than the standard (n=3; 100/30) and half as much as CP-GEP.

**Figure 1. Current guidelines suggest considering SLNB when the risk of a positive biopsy is ≥5% (T1a-HR-T4)**

For every 20 similar patients who are eligible for SLNB, if you do not perform the SLNB...

- 19 patients would have had a negative SLN
- 1 patient would have had an undetected positive SLN
- 19:1 negative-to-missed positive ratio at 5% risk threshold

Any new test must do better than this when selecting patients to forego SLNB.

**Conclusions**

- Standard of care suggests that at a 5% risk threshold, for every 20 patients not getting an SLNB, one positive node will be missed (19:1 true-to-false negative). To be safe and clinically useful, any new test must do better.
- i31-GEP: 30:1 true-to-false negative SLNB ratio is better than using standard of care for identifying patients who may safely forego SLNB.
- CP-GEP: 15:1 true-to-false negative SLNB ratio is worse than using standard of care.
- The i31-GEP is the only test to offer both SLNB risk prediction and risk of recurrence, metastasis, or death prognostication.

**Methods**

- We compared the performance of two GEP tests, the i31-GEP (n=763) and the CP-GEP (U.S. validation cohort; n=153 [includes three T1a]),2 in patients with T1b-T2 tumors, with known SLNB results, to determine if either test increased the ratio of negative-to-missed positive nodes.

**References**


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The integrated 31-gene expression profile (i31-GEP) test for cutaneous melanoma outperforms CP-GEP at identifying patients who can safely forego sentinel lymph node biopsy.