Gene Expression Testing for Melanoma Ready for Prime Time?

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Disclosures

Dr. Sondak is a compensated consultant for Alkermes, Bristol Myers Squibb, Eisai, Merck, Novartis, Regeneron and Replimune and receives research funding from Neogene Therapeutics.

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Agents that have not been FDA approved or are used for purposes other than the label indications may be discussed in this presentation.
Role of GEP for Melanoma

An Established Role in Uveal Melanoma

But uveal melanoma is very different from cutaneous melanoma:
- Incomplete pathology analysis
- No lymphatic drainage
- Limited treatment options
- No approved adjuvant therapy

Role of GEP for Cutaneous Melanoma

Potential Roles in Cutaneous Melanoma

• Diagnostic adjunct to conventional histopathologic analysis
• Prognostication beyond currently available clinicopathologic prognostic factors
• Prediction of lymph node metastasis in clinically node-negative patients
• Selection for sentinel node biopsy
• Selection for adjuvant therapy in node-positive or node-negative patients
• Determining intensity of surveillance for recurrence
Role of GEP for Cutaneous Melanoma

Potential Roles in Cutaneous Melanoma

• Diagnostic adjunct to conventional histopathologic analysis

Farberg AS et al. Skin 2020;4:523
Role of GEP for Cutaneous Melanoma

Potential Roles in Cutaneous Melanoma

- Diagnostic adjunct to conventional histopathologic analysis

➢ How do we deal with a lesion that is histologically benign but has a malignant GEP signature or vice versa?
Role of GEP for Cutaneous Melanoma

Potential Roles in Cutaneous Melanoma

• Diagnostic adjunct to conventional histopathologic analysis

➢ How do we deal with a lesion that is histologically benign but has a malignant GEP signature or vice versa?

Final Diagnosis
SKIN, "LEFT UPPER ARM/SOULDER", WIDE EXCISION:

Extensive melanoma in situ, with adnexal extension, margins clear.
Multifocal and diffuse actinic keratosis.
Dermal scar.

Note: SOX-10 immunostain highlights residual melanoma in situ but fails to highlight evidence of melanoma in situ at any of the inked lateral margins of excision. Multiple deeper levels were examined. Melanocytic hyperplasia in sun-damaged skin is present throughout the specimen and blends intimately with melanoma in situ.
Role of GEP for Cutaneous Melanoma

Potential Roles in Cutaneous Melanoma

• Diagnostic adjunct to conventional histopathologic analysis

➢ How do we deal with a lesion that is histologically benign but has a malignant GEP signature or vice versa?

➢ Will a GEP that discriminates normal nevi from obvious melanomas apply equally well to ambiguous lesions, especially of unusual histologic types (eg: Spitzoid, desmoplastic melanomas)?
Role of GEP for Cutaneous Melanoma

Potential Roles in Prognostication

FIG 2. Survival outcomes of patients with stage I-III CM by 31-GEP results. RFS, DMFS, and OS were estimated by Kaplan-Meier analysis and P-values determined by logrank test. Tables beneath the graphs show survival rates and number of events in each GEP class: CM, cutaneous melanoma; DMFS, distant metastasis-free survival; GEP, gene expression profile; CS, overall survival; RFS, recurrence-free survival.

Hsueh EC et al. *JCO Precision Oncol* 2021;5:589
Role of GEP for Cutaneous Melanoma

Potential Roles in Prognostication

Gershenwald JG et al. *CA Cancer J Clin* 2017;67:474
Role of GEP for Cutaneous Melanoma

Potential Roles in Prognostication

Most patients with a low-risk AJCC stage I designation received a low-risk class 1 31-GEP result (n = 201) and had good survival outcomes (NPV of 96%). However, the patients with stage I disease and a class 2 result (n = 17) had increased rates of recurrence (18% vs 4%), distant metastasis (18% vs 1%), and death (6% vs 2%) compared to those with class 1 tumors.

Hsueh EC et al. JCO Precision Oncol 2021;5:589
Role of GEP for Cutaneous Melanoma

Potential Roles in Prognostication

**TABLE 1** Patient cohort characteristics by gene expression profiling class

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Class 1A (n = 144) n (%)</th>
<th>Class 1B/2A (n = 92) n (%)</th>
<th>Class 2B (n = 125) n (%)</th>
<th>p Value</th>
<th>All patients (n = 361) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Median (IQR)</td>
<td>63.6</td>
<td>68.2</td>
<td>69.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>75</td>
<td>41</td>
<td>40</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>69</td>
<td>51</td>
<td>85</td>
<td>205 (56.8)</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>Median (IQR)</td>
<td>13.3</td>
<td>14.9</td>
<td>15.8</td>
<td>0.54</td>
</tr>
<tr>
<td>Primary site</td>
<td>Head and Neck</td>
<td>28</td>
<td>15</td>
<td>23</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>Trunk</td>
<td>43</td>
<td>20</td>
<td>48</td>
<td>111 (30.75)</td>
</tr>
<tr>
<td></td>
<td>Extremities</td>
<td>73</td>
<td>57</td>
<td>50</td>
<td>180 (50.0)</td>
</tr>
<tr>
<td>Breslow thickness</td>
<td>Median (IQR)</td>
<td>1.05 (0.8–1.5)</td>
<td>1.525 (1.1–2.6)</td>
<td>3 (1.95–5)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Present</td>
<td>14</td>
<td>22</td>
<td>79</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>130</td>
<td>70</td>
<td>46</td>
<td>246 (68.1)</td>
</tr>
<tr>
<td>AJCC</td>
<td>Stage 1</td>
<td>109 (75.7)</td>
<td>47 (51.1)</td>
<td>22 (17.6)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Stage 2</td>
<td>19 (13.2)</td>
<td>34 (37.0)</td>
<td>68 (54.4)</td>
<td>121 (33.5)</td>
</tr>
<tr>
<td></td>
<td>Stage 3</td>
<td>16 (11.1)</td>
<td>10 (10.9)</td>
<td>36 (28.8)</td>
<td>62 (17.2)</td>
</tr>
<tr>
<td>SLNB</td>
<td>Performed</td>
<td>106 (74.3)</td>
<td>78 (84.8)</td>
<td>89 (71.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>14 (13.1)</td>
<td>7 (9.0)</td>
<td>32 (36.0)</td>
<td>53 (19.3)</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>92 (64.0)</td>
<td>71 (91.0)</td>
<td>57 (64.0)</td>
<td>220 (80.3)</td>
</tr>
</tbody>
</table>

_IQR_ interquartile range; _AJCC_ American Joint Committee on Cancer Staging; _SLNB_ sentinel lymph node biopsy

### Role of GEP for Cutaneous Melanoma

#### Potential Roles in Prognostication

<table>
<thead>
<tr>
<th>AJCC stage</th>
<th>Class 1A ($n = 144$)</th>
<th>Class 1B/2A ($n = 92$)</th>
<th>Class 2B ($n = 125$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a ($n = 33$)</td>
<td>31</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1b ($n = 145$)</td>
<td>78</td>
<td>46</td>
<td>21</td>
</tr>
<tr>
<td>2A ($n = 53$)</td>
<td>12</td>
<td>18</td>
<td>23</td>
</tr>
<tr>
<td>2B ($n = 33$)</td>
<td>5</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>2C ($n = 35$)</td>
<td>2</td>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>3A ($n = 10$)</td>
<td>6</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3B ($n = 18$)</td>
<td>7</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>3C ($n = 34$)</td>
<td>3</td>
<td>3</td>
<td>28</td>
</tr>
</tbody>
</table>

AJCC American Joint Committee on Cancer Staging; GEP gene expression profiling

Role of GEP for Cutaneous Melanoma

Potential Roles in Prognostication

Product-Limit Survival Estimates

<table>
<thead>
<tr>
<th>AJCC stage</th>
<th>Any recurrence n (%)</th>
<th>Distant metastatic recurrence n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n = 178)</td>
<td>7 (3.9)</td>
<td>5 (2.8)</td>
</tr>
<tr>
<td>2 (n = 121)</td>
<td>28 (23.1)</td>
<td>14 (11.6)</td>
</tr>
<tr>
<td>3 (n = 62)</td>
<td>14 (22.5)</td>
<td>10 (16.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GEP class</th>
<th>Any recurrence n (%)</th>
<th>Distant metastatic recurrence n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A (n = 144)</td>
<td>10 (6.9)</td>
<td>4 (2.8)</td>
</tr>
<tr>
<td>1B/2A (n = 92)</td>
<td>10 (10.9)</td>
<td>6 (6.5)</td>
</tr>
<tr>
<td>2B (n = 125)</td>
<td>29 (23.2)</td>
<td>19 (15.2)</td>
</tr>
</tbody>
</table>

AJCC American Joint Committee on Cancer Staging; GEP gene expression profiling

Recurrence Free Survival (RFS)

# Role of GEP for Cutaneous Melanoma

## Potential Roles in Prognostication

<table>
<thead>
<tr>
<th>Variable</th>
<th>Variable</th>
<th>Univariate HR (95% CI)</th>
<th>p Value</th>
<th>Multivariate HR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEP class</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1A</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1B/2A</td>
<td>1.758 (0.878–3.561)</td>
<td>0.118</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2B</td>
<td>3.485 (1.932–6.285)</td>
<td>&lt; 0.0001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head and neck</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trunk</td>
<td>0.564 (0.317–1.001)</td>
<td>0.051</td>
<td></td>
<td>0.586 (0.264–1.299)</td>
<td>0.1879</td>
</tr>
<tr>
<td>Extremities</td>
<td>0.328 (0.190–0.569)</td>
<td>&lt; 0.0001</td>
<td></td>
<td>0.358 (0.162–0.793)</td>
<td>0.0114</td>
</tr>
<tr>
<td>Breslow thickness</td>
<td>Millimeters</td>
<td>1.085 (1.050–1.121)</td>
<td>&lt; 0.0001</td>
<td>1.187 (1.100–1.280)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Present</td>
<td>2.741 (1.731–4.341)</td>
<td>&lt; 0.0001</td>
<td>2.571 (1.364–4.846)</td>
<td>0.0035</td>
</tr>
<tr>
<td>Mitoses</td>
<td>Continuous</td>
<td>1.057 (1.023–1.092)</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLNB</td>
<td>Positive</td>
<td>2.323 (1.284–4.201)</td>
<td>0.005</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*HR* hazard ratio; *CI* confidence interval; *GEP* gene expression profiling; *SLNB* sentinel lymph node biopsy

Role of GEP for Cutaneous Melanoma

Potential Roles in Prognostication

This study found that the prognostic ability of DecisionDx-Melanoma and MelaGenix to predict recurrence among patients with localized melanoma varied by AJCC stage and appeared to be poor for patients with stage I disease. Additional, more rigorously structured research appears to be needed to better quantify the association of GEP tests with melanoma outcomes and to demonstrate clinical utility.

Marchetti MA et al. JAMA Dermatol 2020;156:953
Role of GEP for Cutaneous Melanoma

Potential Roles in Cutaneous Melanoma

- Prognostication beyond currently available clinicopathologic prognostic factors
- Prediction of lymph node metastasis in clinically node-negative patients

Does the intensity of follow-up surveillance imaging actually lead to a better outcome in patients at high risk of recurrence or just increase the time with known disease without improving outcomes?
Role of GEP for Cutaneous Melanoma

Potential Roles in Prognostication

• Prediction of lymph node metastasis in clinically node-negative patients

➢ There is relatively widespread agreement that patients with at least a 5% risk of having a positive sentinel node should undergo sentinel node biopsy

➢ Are there better ways to estimate the risk of sentinel node positivity in a patient than Breslow thickness, ulceration and mitotic rate?
Role of GEP for Cutaneous Melanoma

Patient Selection for SLNB

- A large group of patients with T1b and T2a melanomas likely have less than a 5% risk of sentinel node positivity, and some T1a melanomas likely have a 5% or greater risk
  - Gene expression profiles
    - Generic (“high-risk” melanoma identification)
    - Specific (“high-risk” for nodal dissemination)
Role of GEP for Cutaneous Melanoma

Patient Selection for SLNB

• A large group of patients with T1b and T2a melanomas likely have less than a 5% risk of sentinel node positivity, and some T1a melanomas likely have a 5% or greater risk

➢ A GEP that reliably identified a substantial number of patients as not requiring sentinel node biopsy would potentially be cost-effective
### Role of GEP for Cutaneous Melanoma

**Patient Selection for SLNB**

**Table 4:** Average Performance of the Combined Clinicopathologic and Gene Expression Profile Model, Across T Categories, Trained in Double-Loop Cross-Validation

<table>
<thead>
<tr>
<th>T Category</th>
<th>P</th>
<th>SY</th>
<th>SP</th>
<th>NPV (95% CI)</th>
<th>PPV</th>
<th>ACC</th>
<th>bACC</th>
<th>SLNKR (95% CI)</th>
<th>ER</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1b</td>
<td>0.03</td>
<td>0.41</td>
<td>0.82</td>
<td><strong>0.98 (0.95 to 1.00)</strong></td>
<td>0.07</td>
<td>0.80</td>
<td>0.61</td>
<td>0.80 (0.74 to 0.86)</td>
<td>0.02</td>
</tr>
<tr>
<td>T2a</td>
<td>0.13</td>
<td>0.80</td>
<td>0.53</td>
<td><strong>0.95 (0.91 to 0.98)</strong></td>
<td>0.21</td>
<td>0.56</td>
<td>0.66</td>
<td>0.48 (0.42 to 0.54)</td>
<td>0.03</td>
</tr>
<tr>
<td>T2b</td>
<td>0.17</td>
<td>0.94</td>
<td>0.27</td>
<td>0.96 (0.91 to 1.00)</td>
<td>0.21</td>
<td>0.38</td>
<td>0.66</td>
<td>0.24 (0.14 to 0.34)</td>
<td>0.01</td>
</tr>
<tr>
<td>T3a</td>
<td>0.31</td>
<td>0.99</td>
<td>0.12</td>
<td>0.98 (0.95 to 1.00)</td>
<td>0.33</td>
<td>0.38</td>
<td>0.55</td>
<td>0.08 (0.03 to 0.12)</td>
<td>0.00</td>
</tr>
<tr>
<td>T3b</td>
<td>0.43</td>
<td>1.00</td>
<td>0.07</td>
<td><strong>1.00 (0.97 to 1.00)</strong></td>
<td>0.45</td>
<td>0.47</td>
<td>0.54</td>
<td>0.04 (0.00 to 0.09)</td>
<td>0.00</td>
</tr>
</tbody>
</table>

**Note:** The operating point of the model was determined in each training set to yield an NPV of 97.5% and was fixed to that value in the corresponding test set.

**Abbreviations:** ACC, accuracy; bACC, balanced accuracy; ER, error rate; NPV, negative predictive value; P, fraction of patients with positive sentinel lymph nodes (prevalence); PPV, positive predictive value; SLNKR, sentinel lymph node biopsy reduction rate; SP, specificity; SY, sensitivity.

Bellomo D et al. *JCO Precision Oncol* 2020;4:319
### Role of GEP for Cutaneous Melanoma

**Patient Selection for SLNB**

Table 2 Performance of the CP-GEP model

<table>
<thead>
<tr>
<th></th>
<th>T1–T3 (n = 175)</th>
<th>T1 (n = 11)</th>
<th>T2 (n = 94)</th>
<th>T3 (n = 70)</th>
<th>T4 (n = 35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP-GEP high risk</td>
<td>133</td>
<td>1</td>
<td>66</td>
<td>66</td>
<td>35</td>
</tr>
<tr>
<td>True positive</td>
<td>43</td>
<td>0</td>
<td>14</td>
<td>29</td>
<td>9</td>
</tr>
<tr>
<td>False positive</td>
<td>90</td>
<td>1</td>
<td>52</td>
<td>37</td>
<td>26</td>
</tr>
<tr>
<td>CP-GEP low risk</td>
<td>42</td>
<td>10</td>
<td>28</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>True negative</td>
<td>38</td>
<td>10</td>
<td>25</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>False negative</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Sensitivity**
- T1–T3: 91.5% (95% CI: 80.1–96.6)  
- T1: 0% (95% CI: 70.1–100)  
- T2: 96.7% (95% CI: 83.3–99.4)  
- T3: 100% (95% CI: 70.1–100)  
- T4: 0%

**Specificity**
- T1–T3: 29.7% (95% CI: 22.5–38.1)  
- T1: 90.9% (95% CI: 62.3–98.4)  
- T2: 32.5% (95% CI: 23.1–43.5)  
- T3: 7.5% (95% CI: 2.6–19.9)  
- T4: 0%

**PPV**
- T1–T3: 32.3% (95% CI: 25.0–40.7)  
- T1: 0% (95% CI: 14.2–42.1)  
- T2: 21.2% (95% CI: 13.1–32.5)  
- T3: 43.9% (95% CI: 32.6–55.9)  
- T4: 25.7%

**NPV**
- T1–T3: 90.5% (95% CI: 77.9–96.2)  
- T1: 100% (95% CI: 72.2–100)  
- T2: 89.3% (95% CI: 72.8–96.3)  
- T3: 75.0% (95% CI: 30.1–95.4)  
- T4: 0%

CP-GEP, Clinopathological Gene Expression Profile; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

Prospектив Registry Study of a Primary Melanoma Gene-Signature to Predict Sentinel Lymph Node (SN) status and Determine its Prognostic Value for more Accurate Staging of SN-Negative Melanoma Patients

**Study Objective:**
Determine (1) predictive capability of CP-GEP model to identify primary cutaneous melanoma patients who can safely forgo sentinel lymph node biopsy and (2) to predict recurrence of melanoma after a negative sentinel node biopsy.

**Study Design:**
Multi-center non-interventional clinical study with a consortium of surgical oncologists to prospectively validate the utility in high volume clinics. Results will be blinded to both patients and clinicians.

**Study Population:**
Newly diagnosed primary cutaneous melanoma patients who are elected to undergo a sentinel lymph node biopsy.

**Target #patients:**
2,132 patients from 8 to 10 US institutions

**Enrollment period:**
1.5 years (Starting end Q4/2020)

**Inclusion criteria**
- Newly diagnosed melanoma:
  - T1b-T3 (BT <4.0mm) N0M0
  - T1a (BT <0.8 mm) with other adverse features (very high mitotic index [>2/mm2], young age [<40 years], lymphovascular invasion, combination of these factors)
- Male or female, age ≥18 years
- Elected to undergo SLN biopsy per treating physician’s recommendation

**Exclusion criteria**
- Melanoma pathology report & diagnostic biopsy tissue unavailable
- Documented clinical apparent nodes at diagnosis
- Distant metastatic disease clinically present at primary diagnosis
- Any prior or concurrent primary invasive melanoma mapping to same draining lymph node basin
- Documented prior history of primary invasive melanoma of T1b or greater at any site within last 5 years before current diagnosis
- Previous surgery in draining lymph nodes basin of current primary melanoma
- Ocular, vulvar, perianal, and mucosal melanoma and melanocytic tumors of uncertain malignant potential (MELTUMP) or atypical Spitz tumors
Prospective Registry Study of a Primary Melanoma Gene-Signature to Predict Sentinel Lymph Node (SN) status and Determine its Prognostic Value for more Accurate Staging of SN-Negative Melanoma Patients

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• Ocular, vulvar, perianal, and mucosal melanoma and melanocytic tumors of uncertain malignant potential (MELTUMP) or atypical Spitz tumors

Statistical formulation and statistical analysis plan of the objectives

Primary objective: To establish the predictive capability of CP-GEP to identify primary cutaneous melanoma patients who can safely forgo SLNB. Performance statistics for CP-GEP will be calculated; these include Negative Predictive Value (NPV), Positive Predictive Value (PPV), Sensitivity and Specificity, and their 95% confidence intervals. Any subset of patients defined by T category (only T1b and higher) or AJCC 8 stage (e.g., stage I and stage IIA) who have a risk of SLN metastasis where the upper bounds of the 95% confidence interval <5% will be considered as a group who can safely forgo SLNB.
Role of GEP for Cutaneous Melanoma

Potential Roles in Cutaneous Melanoma

Selecting patients for adjuvant therapy

- Improved discrimination of risk of recurrence
- Prediction of response/resistance to therapy and selection of treatment
  - BRAF targeted therapy vs immunotherapy
  - Single-agent vs combination immunotherapy
The current problem with adjuvant therapy

Even though we know some people are benefiting, we don’t know who they are!
Role of GEP for Cutaneous Melanoma

Selecting Patients for Adjuvant Therapy

OBS

SEL

ALL

CONCLUSIONS

Resected stage IIA melanoma is characterized by a relatively favorable long-term prognosis. Indiscriminate adjuvant therapy in this population may confer a small survival benefit, but is associated with significant cost and patient morbidity. The use of 31-GEP to risk-stratify patients has the potential to marginally improve cost-benefit over a universal adjuvant approach, with a small trade-off in 10-year overall survival. However, the prognostic impact of 31-GEP beyond standard clinicopathologic factors is necessary.

At present, based on this model, the routine use of 31-GEP to risk-stratify patients with IIA melanoma for adjuvant therapy cannot be recommended.

Role of GEP for Cutaneous Melanoma

Conclusions

Prognostic Gene Expression Profiling in Cutaneous Melanoma
Identifying the Knowledge Gaps and Assessing the Clinical Benefit

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Role of GEP for Cutaneous Melanoma

Conclusions

**FINDINGS** The MPWG members are optimistic about the future use of prognostic GEP testing to improve risk stratification and enhance clinical decision-making but acknowledge that current utility is limited by test performance in patients with stage I disease. Published studies of GEP testing have not evaluated results in the context of all relevant clinicopathologic factors or as predictors of regional nodal metastasis to replace sentinel lymph node biopsy (SLNB). The performance of GEP tests has generally been reported for small groups of patients representing particular tumor stages or in aggregate form, such that stage-specific performance cannot be ascertained, and without survival outcomes compared with data from the American Joint Committee on Cancer 8th edition melanoma staging system international database. There are significant challenges to performing clinical trials incorporating GEP testing with SLNB and adjuvant therapy. The MPWG members favor conducting retrospective studies that evaluate multiple GEP testing platforms on fully annotated archived samples before embarking on costly prospective studies and recommend avoiding routine use of GEP testing to direct patient management until prospective studies support their clinical utility.

Role of GEP for Cutaneous Melanoma

Conclusions

CONCLUSIONS AND RELEVANCE More evidence is needed to support using GEP testing to inform recommendations regarding SLNB, intensity of follow-up or imaging surveillance, and postoperative adjuvant therapy. The MPWG recommends further research to assess the validity and clinical applicability of existing and emerging GEP tests. Decisions on performing GEP testing and patient management based on these results should only be made in the context of discussion of testing limitations with the patient or within a multidisciplinary group.
