Background

- Sentinel lymph node biopsy (SLNB) is recommended to assess prognosis in cutaneous melanoma (CM) patients.
- The decision to perform SLNB is guided by high-risk histopathologic features. The procedure is not recommended for the population in which the rate of SLN positivity is <5%1,2.
- Using formalin-fixed, paraffin-embedded CM tumor samples, a 31-gene expression profile (31-GEP) test has been previously demonstrated to accurately determine risk of recurrence and metastasis for CM patients in multiple retrospective and prospective studies3-10. The 31-GEP test categorizes metastatic risk as Class 1A, 1B, 2A, and 2B. Class 1A tumors have the lowest risk, Class 1B/2A is associated with intermediate risk, and Class 2B confers the highest risk for recurrence and/or death.

- To use the 31-GEP test along with clinical features to identify patients who are more likely to exhibit SLN positivity (i.e. risk of recurrence to the SLN node) and those who have a low rate of positivity and could potentially avoid the procedure.

Methods

- Gene expression data for the 31-gene and clinical features for a development cohort (n=946) and two prospective validation cohorts (n=584 and n=837) of CM patients were collected.
- The 31-GEP test was performed in a CAP-accredited/CUA-certified laboratory using high-throughput RT-PCR assays as previously described3-10.
- Survival analysis was performed on a long term follow-up (25 years if no recurrence) retrospective cohort (n=690). Endpoints included recurrence-free survival (RFS), defined as time to either a regional or distant metastatic event; distant metastasis-free survival (DMFS), defined as time to any metastatic event beyond the regional basin; overall survival (OS) and melanoma-specific survival (MSS), defined as time from diagnosis to death documented as specifically resulting from melanoma.

Model Development

- Goal: Identify CM population with <5% SLN positivity rate
- Stage 1: Modeling to optimize prediction of SLN status, including: 
  - Neural networks 
  - Self-organizing maps 
  - Support vector machines 
  - Tree based models
- Stage 2: Evaluation of recurrence algorithm (31-GEP) in combination on clinical factors

Best performing model

Table 1. Demographics of the validation cohort (n=1421) and T1/2 cases (n=1065)

<table>
<thead>
<tr>
<th>Attribute in validation cohort</th>
<th>Summary (n=1421)</th>
<th>T1/2 cases (n=1065)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (range)</td>
<td>57.4 (18-94)</td>
<td>57.4 (18-94)</td>
</tr>
<tr>
<td>Sex</td>
<td>74.0% male</td>
<td>70.1% male</td>
</tr>
<tr>
<td>Race</td>
<td>63.6% White</td>
<td>61.5% White</td>
</tr>
<tr>
<td>T Stage</td>
<td>63.6% T1-2</td>
<td>63.6% T1-2</td>
</tr>
<tr>
<td>Ulceration present</td>
<td>87.3%</td>
<td>87.3%</td>
</tr>
<tr>
<td>Mitotic rate ≥1/mm</td>
<td>46.9%</td>
<td>46.9%</td>
</tr>
<tr>
<td>Breslow depth: Mean mm (SD)</td>
<td>4.8 (2.0-12.5)</td>
<td>4.5 (2.0-12.5)</td>
</tr>
<tr>
<td>N stage</td>
<td>23.6% pN0</td>
<td>23.6% pN0</td>
</tr>
<tr>
<td>SLNB positivity (%)</td>
<td>5.4%</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

Conclusions

- The 31-GEP test can identify patients with different risks of SLN positivity.
- A Class 1A GEP test result, with Breslow thickness and age, can be useful in identifying a patient population with <5% likelihood of a positive SLN and thus has potential utility in guiding SLNB decisions in CM patients.
- Results from the long-term outcome cohort analysis show that T1-T2 tumors with a Class 1A GEP signature have a good prognosis, which suggests this patient population may be able to safely avoid the SLNB procedure. This is consistent with the low rate of recurrence observed for Class 1A patients in prior studies of the test.

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References


Disclosures

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