Background

• The majority of CM patients are diagnosed with early stage disease, but have highly variable prognostics traditionally informed by clinical and pathological features of the primary tumor, including Breslow thickness and ulceration, as well as sentinel lymph node (SLN) positivity. A substantial proportion of melanoma-related deaths occur in traditionally low-risk patients, highlighting the need for additional methods to stratify prognosis.

• The prognostic 31-GEP test stratifies patients as low-risk (Class 1, 1A lowest risk) and high-risk (Class 2, 2B highest risk) for 5-year metastatic risk.11

• Utilizing 31-GEP to guide sentinel lymph node biopsy (SLNB) decisions has been previously published. In patients with T1/T2 melanomas, 46.4% of those Class 1A results have positive SLN, below national guidelines of 5% SLNB consideration.

• Clinically, the 31-GEP has been used to guide intensity of follow-up, use of imaging for surveillance, and consideration of adjuvant therapy.12-16

• We previously published an initial analysis of this cohort showing significantly higher RFS, DMFS, and OS in Class 1 compared to Class 2 with median follow-up of 1.5 years.17

Objectives

Figure 1. Schematic of study objectives and analysis

- Is the 31-GEP a consistent predictor of metastatic risk in a multi-center, prospective cohort of 342 patients?
- Does the 31-GEP add prognostic value beyond the previously published Utility in SLNB guidance18?
- Does the 31-GEP add prognostic value in Cox multivariable analysis including AJCC risk categories?

Methods

• Patients were prospectively enrolled in one of two clinical registries, INTEGRATE (NCT02235587) or EXPAND (NCT03353754) from T1-U.S. dermatological and surgical centers under IRB approval including patient age ≥ 16 years, a CM diagnosis, and successful 31-GEP test result.

• Primary endpoints were recurrence-free survival (RFS), time from diagnosis to any regional or distant (death or recurrence), and distant metastases (DMFS), time from diagnosis to any metastases (DMFS), time to any regional recurrence beyond the regional nodal basin), and overall survival (OS, time from diagnosis to death from any cause). Median event-free follow-up was 3.2 years.

• Patient characteristics were compared by Kruskal-Wallis F or Pearson chi-square tests as appropriate, and survival was estimated by Kaplan-Meier analysis with log-rank test. Multivariable Cox regression analysis included AJCC risk groups (Stage IIA, low risk; Stage III-B, high risk) and 31-GEP Classes.

• This is a follow-up analysis from a previously published initial analysis with a critical alpha value (p value) of 31-GEP 0.01.17 The critical alpha value of this analysis was set to 0.04 to sum the traditional p value of 0.05.

Results

Table 1. Demographics of 342 patients tested with 31-GEP in prospective study

<table>
<thead>
<tr>
<th>Variable</th>
<th>all Cases</th>
<th>Class 1</th>
<th>Class 1A</th>
<th>Class 1B</th>
<th>Class 2</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>68 (18-87)</td>
<td>72 (19-85)</td>
<td>77 (30-87)</td>
<td>64 (23-85)</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>Breslow thickness, mm median (range)</td>
<td>1.2 (0.2-12)</td>
<td>1.0 (0.2-7)</td>
<td>1.0 (0.2-7)</td>
<td>2.5 (0.4-12)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Ultraviolet present</td>
<td>62 (18%)</td>
<td>8 (11%)</td>
<td>15 (19%)</td>
<td>40 (60%)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Familial risk</td>
<td>319 (93%)</td>
<td>337 (99%)</td>
<td>296 (98%)</td>
<td>53 (81%)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Pathologic node status positive</td>
<td>50 (15%)</td>
<td>21 (8%)</td>
<td>19 (8%)</td>
<td>18 (24%)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2. Survival outcomes of 342 patients with CM by 31-GEP class

Table 2. Comparison of recurrence rate to previously published studies

<table>
<thead>
<tr>
<th>Class 1</th>
<th>Class 1A</th>
<th>Class 1B</th>
<th>Class 2</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median follow-up (years)</td>
<td>5.2</td>
<td>5.5</td>
<td>4.7</td>
<td>2.3</td>
</tr>
<tr>
<td>DMFS</td>
<td>95.5% (95.4-95.6)</td>
<td>95.7% (95.6-95.7)</td>
<td>98.8% (98.7-98.9)</td>
<td>99.4% (99.3-99.5)</td>
</tr>
<tr>
<td>OS</td>
<td>98.2% (96.6-99.8)</td>
<td>98.7% (97.5-99.9)</td>
<td>99.8% (99.6-100)</td>
<td>100%</td>
</tr>
</tbody>
</table>

Figure 3. Event rate in Stage I-IIA patients by 31-GEP Class

Table 3. Comparison of T1/T2 survival to previously published study

<table>
<thead>
<tr>
<th>Class 1</th>
<th>Class 1A</th>
<th>Class 2A</th>
<th>Class 2B</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median follow-up (years)</td>
<td>5.2</td>
<td>5.5</td>
<td>4.7</td>
<td>2.3</td>
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</tbody>
</table>

Figure 4. Multivariate analysis of GEP Class and AJCC Stage

Conclusions and Significance

• Patients with 31-GEP Class 2B patients have significantly reduced RFS, DMFS and OS compared to Class 1A and 31-GEP consistently predicts risk of recurrence across stages.

• In patients with T1/T2 melanoma for whom 31-GEP was previously shown to guide SLNB, Class 1A results are associated with favorable prognosis.

• The 31-GEP Class 2B result is a significant, independent predictor of distant metastasis, and mortality compared to higher risk AJCC stages (Stage III-B).

• These prospective results demonstrate the 31-GEP test is an accurate, independent predictor of distant metastasis and may inform the test has previously shown to inform likelihood of recurrence and/or SLN positivity.

References

15. Castle Biosciences, Inc. Friendswood, TX
18. Podlipnik, et al. 2019

Acknowledgements & Disclosures

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