Improved prognostic guidance by the 31-gene expression profile test for clinical decisions after a negative lymph node for patients with cutaneous melanoma

Brian Martin PhD1, Christine Bailey, MPH1, Matthew Goldberg, MD1,2, Valentina Petkov, MD, MPH3, Robert Cook, PhD1, Kyle Covington, PhD1, Sarah Kurley, PhD1

1Castle Biosciences, Inc., Friendswood, TX 2Cain School of Medicine at Mount Sinai, New York, NY. 3National Cancer Institute, Surveillance Research Program, Bethesda, MD

Background

Despite a good overall prognosis for patients with a negative SLNB, 10-24% will experience recurrence or metastasis, and melanoma-specific survival (MSS) rates range from 82-99%.1 A subset of these patients (stage IIB-IICC) are currently eligible for adjuvant therapy, though it is unclear which patients will benefit and which patients do not need therapy.3 The recent KEYNOTE-716 trial showed a benefit of adjuvant pembrolizumab in patients with stage IIB-IIIC melanoma (9% RFS improvement), but 80% had an adverse event (16% grade 3 and higher), and 18% discontinued treatment due to adverse events.3

These data underpin a need for prognostic tools beyond clinicopathologic features to identify patients with high-risk tumor staging but low-risk tumor biology, or low-risk tumor staging but high-risk tumor biology, so that patients receive risk-aligned treatment.1,2

Multiple prospective and independent studies have shown that the 31-GEP test is a consistent and independent predictor of survival outcomes in large populations of patients with stage I-II CM, and that clinicians use the 31-GEP to guide patient management decisions.6-10

Objective

In collaboration with the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program (covering 34% of the U.S. population during the study period) this study sought to:

Demonstrate the performance of the 31-GEP to identify patients with high-risk tumor biology in an unselected, clinically tested cohort of patients with a negative lymph node.

Methods

SEER cancer registries linked CM cases diagnosed from 2016-2018 to data for patients with CM who were tested with the 31-GEP (n=3,271). Linkage was mediated by Information Management Services (an Honest Broker for the SEER registries). A de-identified dataset was used for this analysis. A focused analysis of negative lymph node patients was performed. Kaplan-Meier analysis with the log-rank test was used to analyze 3-year melanoma-specific survival (MSS). Multivariable Cox regression was used to identify factors associated with MSS.

Results

Patients with Class 1A results had higher 3-year MSS (Class 1A: 99.7%; Class 1B/2A: 97.8%; Class 2B: 91.8%, p<0.001).

In the subset of patients with IIB-IIIC disease (n=311), no Class 1A (0%, 0/38) patients died from melanoma compared with 6.7% (14/210; 8 IIB, 6 IICC) of Class 2B patients.

Table 1. Multivariable analysis demonstrates independent and significant prognostic information compared to traditional staging factors

<table>
<thead>
<tr>
<th>Melanoma-specific survival</th>
<th>Multivariable HR (95% CI)</th>
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<tbody>
<tr>
<td>31-GEP Class 1A</td>
<td>Reference</td>
</tr>
<tr>
<td>31-GEP Class 1B/2A</td>
<td>5.76 (1.42-23.41)</td>
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<tr>
<td>31-GEP Class 2B</td>
<td>10.50 (2.55-43.28)</td>
</tr>
<tr>
<td>Age (continuous)</td>
<td>1.05 (1.02-1.08)</td>
</tr>
<tr>
<td>AJCC Stage IA</td>
<td>Reference</td>
</tr>
<tr>
<td>AJCC Stage IB</td>
<td>1.48 (0.37-6.01)</td>
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<tr>
<td>AJCC Stage II IA</td>
<td>3.93 (1.10-14.12)</td>
</tr>
<tr>
<td>AJCC IB</td>
<td>3.24 (0.82-12.86)</td>
</tr>
<tr>
<td>AJCC IIC</td>
<td>4.58 (1.09-19.22)</td>
</tr>
</tbody>
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In patients with a negative lymph node, the 31-GEP identifies patients more or less likely to die from their melanoma in the absence of adjuvant therapy, and the 31-GEP is a significant predictor of melanoma-specific death, even when accounting for substage.

The 31-GEP can direct care to patients with high-risk tumor biology who are most likely to benefit from higher intensity management and away from those unlikely to benefit from adjuvant therapies to spare patients from adjuvant therapy-associated adverse events.

Conclusions

Using the 31-GEP results to guide increased clinical management and surveillance for patients at high risk of melanoma-specific death may improve patient outcomes.

References


Acknowledgments & Disclosures

For more information: mgoldberg@castlebiosciences.com

For more information: mgoldberg@castlebiosciences.com

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For more information: mgoldberg@castlebiosciences.com