The 31-gene expression profile outperforms AJCC in stratifying risk of recurrence in patients with stage I cutaneous melanoma

Sebastian Podlipnik, MD1, Valentina I. Petkov, MD, MPH2, Jung S. Byun, PhD, MPH3, Christine Bailey, MPH4, Robert W. Cook, PhD5, Kelli Ahmed, PhD5, Brian Martin, PhD5, Susana Puig, MD1,4,5

1Department of Dermatology, Hospital Clinic of Barcelona, Barcelona, Spain, 2Surveillance Research Program, National Cancer Institute, Bethesda, Maryland, USA, 3Castle Biosciences, Inc, Friendswood, Texas USA, 4Department of Dermatology, University of Barcelona, Barcelona, Spain, 5Centro de Investigación Biomédica en Red de Enfermedades Raras, CIBERER, Instituto de Salud Carlos III, Barcelona, Spain

Background

1The American Joint Committee on Cancer (AJCC) staging stratifies patients with cutaneous melanoma (CM) according to risk of poor outcomes1. Patients with stage I CM are considered low risk for recurrence and melanoma-specific death1.  
2Although most patients with stage I CM will have good outcomes, many will experience recurrence and due to the large number of patients diagnosed with stage I disease (~70% of newly diagnosed patients), this group accounts for about one third of melanoma deaths2,3.  
3Additional methods, such as molecular risk stratification tests, that better identify which patients are truly low risk versus those who may benefit from increased clinical surveillance are needed to improve patient care.  
4The 31-gene expression profile (31-GEP) test has been consistently shown in multiple retrospective and prospective trials to be an independent predictor of survival outcomes across all staging subgroups4-10. A second GEP test, CP-GEP, has been developed for CM prognostication11.

Objective

1Demonstrate the added value of using the 31-GEP test to stratify risk of recurrence (Table 1) and melanoma-specific death (Figure 1) in patients with stage I CM compared to using AJCC staging alone.

Methods

1We analyzed recurrence-free survival data for patients with stage I CM who were tested with the 31-GEP and were enrolled in previous prospective and retrospective studies (n=1261) and stage I patient melanoma-specific survival data provided by Surveillance, Epidemiology, and End Results (SEER) registries (diagnosis 2013-2018) that were linked to data for patients who were 31-GEP tested (n=5651).  
2SEER linkage was mediated by Information Management Services (an Honest Broker for the SEER registries). A de-identified dataset was used for this analysis.  
3AJCC and CP-GEP survival data were analyzed from previously published reports2,10.

Results

Table 1. Recurrence-free survival rate stratification by 31-GEP, AJCC, and CP-GEP in patients with stage I melanoma

<table>
<thead>
<tr>
<th>Group</th>
<th>5-year RFS</th>
<th>Recurrences</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-GEP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class IA</td>
<td>97.3% (96.1-98.5%)</td>
<td>2.3% (25/965)</td>
</tr>
<tr>
<td>Class IB/2A</td>
<td>88.6% (83.9-93.7%)</td>
<td>9.3% (21/226)</td>
</tr>
<tr>
<td>Class 2B</td>
<td>77.3% (66.9-89.2%)</td>
<td>18.6% (13/70)</td>
</tr>
<tr>
<td>AJCC10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IA</td>
<td>93.3% (93.1-94.7%)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Stage IB</td>
<td>87.6% (85.4-89.9%)</td>
<td>Not reported</td>
</tr>
<tr>
<td>CP-GEP10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>92.9% (88.0-95.8%)</td>
<td>8.3% (350/2530)</td>
</tr>
<tr>
<td>High risk</td>
<td>86.0% (76.6-91.8%)</td>
<td>12.9% (12/93)</td>
</tr>
</tbody>
</table>

Figure 1. 31-GEP improves melanoma-specific survival stratification over AJCC staging alone among patients with stage I CM

Clinical Impact

1The 31-GEP test provided independent and significant prognostic information in addition to AJCC staging.  
2Using the 31-GEP in combination with staging factors to guide treatment and clinical management plans can improve patient care by identifying stage I patients who are truly at low risk of poor outcomes and those at high-risk who should consider more aggressive management plans.

Conclusions

1In patients with stage I CM, the 31-GEP adds valuable prognostic information to AJCC staging to better stratify 5-year RFS and MSS2,10.  
2Incorporating 31-GEP testing into clinical practice can help guide better risk-aligned care in a population considered low risk by staging by identifying high-risk patients who may be missed using only AJCC criteria.

Acknowledgments & Disclosures

1 OLB, JWC, KA, and BM are employees and shareholders of Castle Biosciences, Inc.  
2 SEER, 31, and CP are in disclosures.

References


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