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

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Background

- The American Joint Committee on Cancer (AJCC) staging stratifies patients with cutaneous melanoma (CM) according to risk of poor outcomes[1]. Patients with stage I CM are considered low risk for recurrence and melanoma-specific death[1].
- Although 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 deaths[2, 3].
- Additional 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.
- The 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 subgroups[4-10]. A second GEP test, CP-GEP, has been developed for CM prognostication[11].

Objective

- Demonstrate 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

- We 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).
- SEER linkage was mediated by Information Management Services (an Honest Broker for the SEER registries). A de-identified dataset was used for this analysis.
- AJCC and CP-GEP survival data were analyzed from previously published reports[2,10].

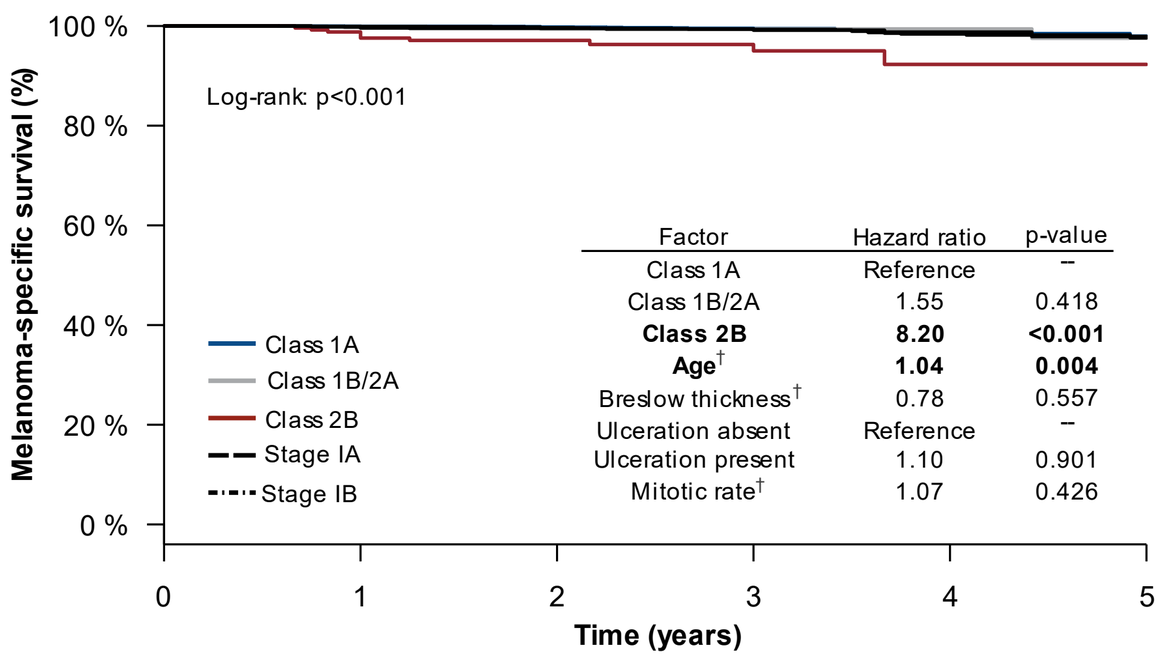
Results

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

Group	5-year RFS	Recurrences
31-GEP		X^2=389.86, p<0.001
Class 1A	97.3% (96.1-98.5%)	2.3% (25/965)
Class 1B/2A	88.6% (83.8-93.7%)	9.3% (21/226)
Class 2B	77.3% (66.9-89.2%)	18.6% (13/70)
AJCC[2]		Not reported
Stage IA	93.3% (93.1-94.7%)	Not reported
Stage IB	87.6% (85.4-89.9%)	Not reported
CP-GEP[10]		X^2=1.77, p=0.184
Low risk	92.9% (88.0-95.8%)	8.3% (25/301)
High risk	86.0% (76.6-91.8%)	12.9% (12/93)

[2]Garbe et al. 2022. JCO. [11]Amaral et al. 2022. EJC.

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



Group	5-year MSS (95% CI)	Deaths, % (n/N)
Class 1A (n=4,526)	98.0% (96.7-99.2%)	0.5% (22/4,526)
Class 1B/2A (n=865)	97.5% (93.9-100%)	0.6% (5/865)
Class 2B (n=260)	92.3% (86.2-98.8%)	3.8% (10/260)
Stage IA (n=4,097)	97.6% (96.2-99.0%)	0.6% (26/4,097)
Stage IB (n=1,554)	97.9% (95.9-99.9%)	0.7% (11/1,554)

†Continuous variables. Unknown ulceration status HR=0, p=0.997. Class 1A, Class 1B/2A, Stage IA, and Stage IB lines overlap.

- A 31-GEP Class 2B was associated with a 7.6-fold increased death rate relative to a Class 1A result and a 5.4-fold increase relative to stage IB CM.

Clinical Impact

- The 31-GEP test provided independent and significant prognostic information in addition to AJCC staging.
- Using 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

- In patients with stage I CM, the 31-GEP adds valuable prognostic information to AJCC staging to better stratify 5-year RFS and MSS[2,10].
- Incorporating 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.

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- CNB, RWC, KA, and BM are employees and shareholders of Castle Biosciences, Inc.
- SP, VIP, JB, and SP have no disclosures.

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