

Improving patient selection for adjuvant therapy: Considerations for the role of the 31-gene expression profile test

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Background

- Guidelines for cutaneous melanoma suggest patients with stage I-IIA are low-risk and those with stage IIB-III are high-risk for recurrence and death.¹
- Pembrolizumab was approved in late 2021 for stage IIB-IIC disease; however, a minimal survival difference at 12 months relative to placebo and an associated high adverse event (AE) rate (7% RFS benefit vs. an absolute 12% more grade ≥ 3 adverse events) suggests refinement in patient selection for therapy is needed.²
- Identifying stage IIB-IIC patients who have high survival rates without adjuvant therapy can improve the benefit to risk ratio of adjuvant therapy.
- The 31-gene expression profile (31-GEP) test for cutaneous melanoma (CM) is a validated risk stratification molecular tool that stratifies patients with stage I-III CM into groups at low (Class 1A), intermediate (Class 1B/2A), and high (Class 2B) risk of recurrence, metastasis, and death.³⁻⁹

Clinical Implications & Objectives

- Identifying patients with stage IIB-IIC melanoma who have high survival rates without adjuvant therapy could lead to reduced numbers of patients receiving unnecessary adjuvant therapy in the current melanoma landscape.
- Understanding which patients truly need adjuvant therapy could, most importantly, lead to a reduction in adjuvant therapy-related adverse events as well as reduce healthcare costs.
- Objective:** Validate the performance of the 31-GEP for risk stratification in an unselected and prospectively tested cohort of patients who may benefit from better selection for adjuvant therapy.

Results

Figure 1. Risk stratification for melanoma specific survival of patients with stage I-III CM by the 31-GEP (n=4687)

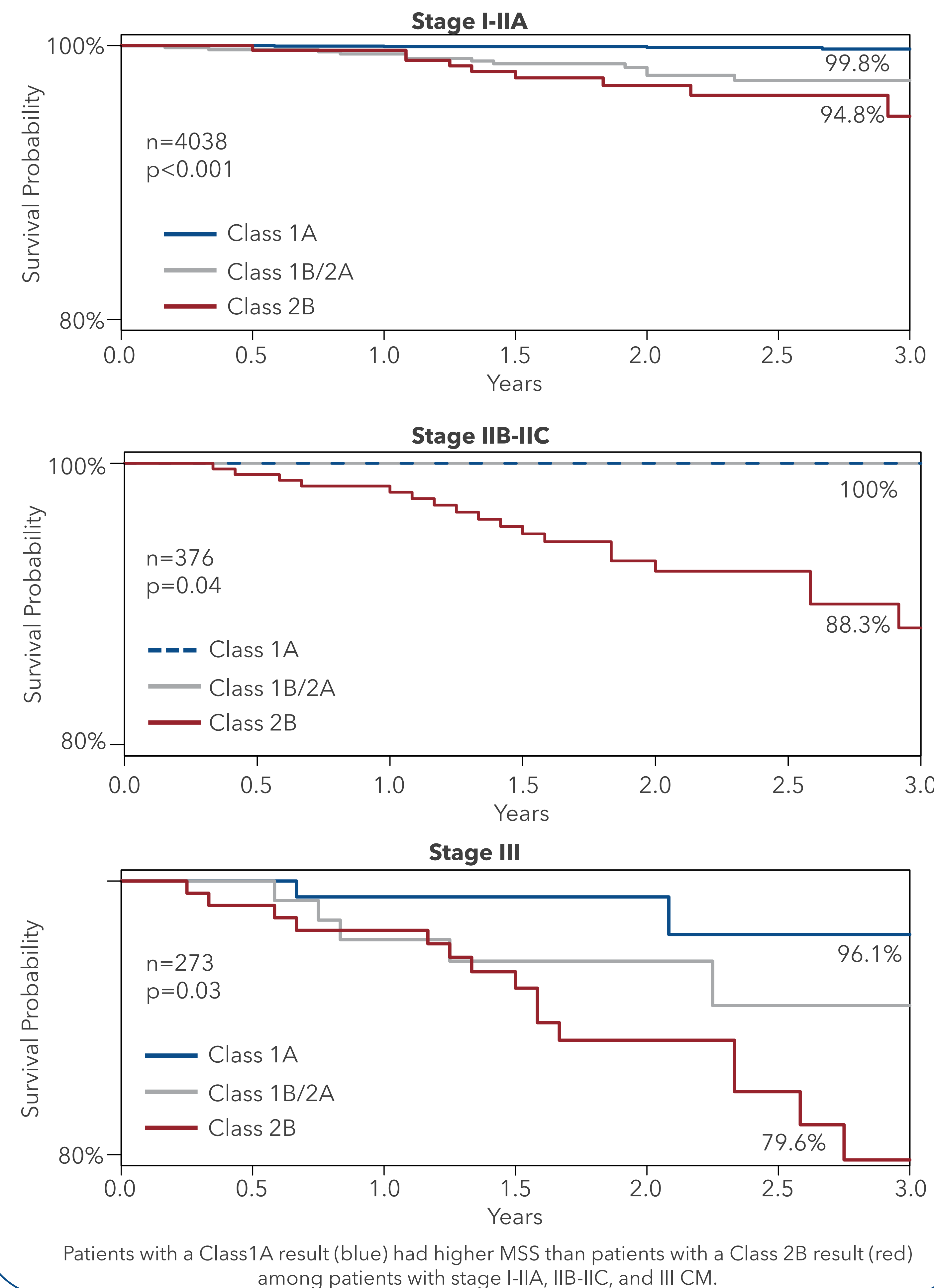


Table 1. Univariate and multivariable analysis for melanoma-specific survival for patients linked to SEER data registry.

Melanoma-specific survival	Univariate HR (95% CI)	Multivariable HR (95% CI)
Class 1A	Reference	Reference
Class 1B/2A	10.25 (4.31-24.38)	4.86 (1.97-12.03)
Class 2B	28.25 (12.69-62.89)	7.00 (2.70-18.00)
Age (continuous)	1.06 (1.04-1.08)	1.05 (1.03-1.07)
Ulceration absent	Reference	Reference
Unknown ulceration	1.16 (0.28-4.89)	1.31 (0.18-9.78)
Ulceration present	8.0 (4.88-12.97)	1.59 (0.86-2.94)
Breslow (continuous)	1.42 (1.35-1.52)	1.16 (1.05-1.27)
SLN negative	Reference	Reference
SLNB unknown	0.64 (0.31-1.33)	0.84 (0.40-1.77)
SLN positive	7.37 (4.37-12.44)	2.64 (1.45-4.79)

SLN: sentinel lymph node. SLNB: sentinel lymph node biopsy. HR: Hazard ratio; CI: Confidence interval. Unit increase for each continuous variable: Breslow thickness: 1.0 mm; age: 1 year. N=4,228 after removing 459 observations with missing data for one or more variables.

Conclusions

- In an unselected and prospectively tested cohort of patients with stage I-III CM, the 31-GEP stratified melanoma-specific survival for each risk group classified by current guidelines.
- The 31-GEP Class result was a statistically significant independent predictor of MSS and the most significant predictor of MSS compared to AJCC staging criteria.
- The 31-GEP can identify patients with low risk of death who may potentially forego unnecessary adjuvant therapies.

References

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