The 31-GEP stratifies risk of death in patients with stage I-IIA cutaneous melanoma: A SEER real-world evidence study

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Background

- Current American Joint Committee on Cancer (AJCC 8th edition) staging stratifies patients with cutaneous melanoma (CM) by their risk of dying from their disease.[1]
- Patients with early-stage I–IIA CM are considered at low risk of poor outcomes; however, recent evidence suggests that many of these patients have a higher risk of death than AJCC suggests.[2]
- Identifying patients who have a higher risk of poor outcomes than suggested by their cancer stage can help clinicians recommend more personalized, risk-appropriate surveillance and treatment management options.[2,3]
- The 31-gene expression profile (31-GEP) is prospectively validated to stratify the risk of death in patients with CM.[4-6]

Objective

Validate 31-GEP MSS and OS risk stratification in patients with stage I-IIA CM in a real-world setting.

Methods

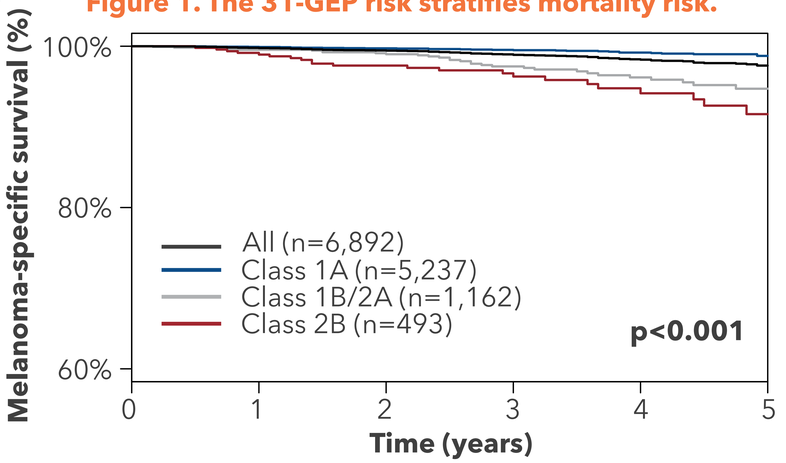
- Registry data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program were linked to data from patients with stage I–IIA CM clinically tested with the 31-GEP (n=6,892). Survival was estimated using Kaplan-Meier analysis, and differences between groups were compared using the log-rank test. Multivariable Cox regression was used to identify predictors of melanoma-specific and all-cause mortality.[4]

Table 1. Patient Demographics

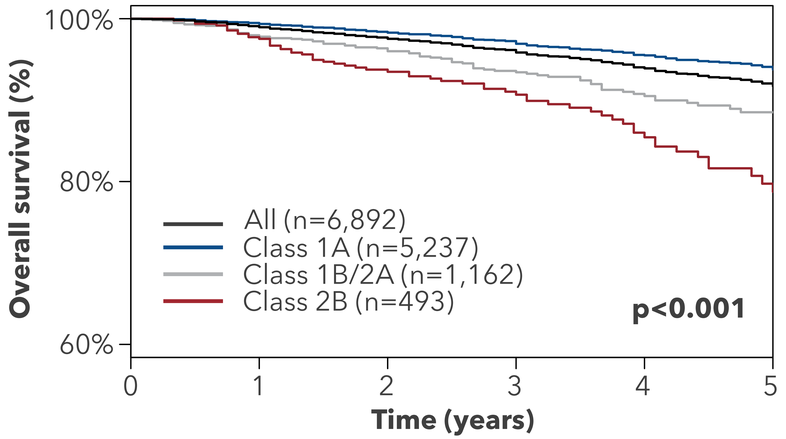
Descriptor	Class 1A (n=5,237)	Class 1B/2A (n=1,162)	Class 2B (n=493)	Combined (n=6,892)
Age				
Median (Range)	60 (18-89+)	65 (18-89+)	67 (22-89+)	62 (18-89+)
Gender				
Female	2448 (46.7%)	465 (40.0%)	185 (37.5%)	3098 (45.0%)
Male	2789 (53.3%)	697 (60.0%)	308 (62.5%)	3794 (55.1%)
AJCCv8 Stage				
Stage IA	4267 (81.5%)	443 (38.1%)	130 (26.4%)	4840 (70.2%)
Stage IB	766 (14.6%)	419 (36.1%)	126 (25.6%)	1311 (19.0%)
Stage IIA	204 (3.9%)	300 (25.8%)	237 (48.1%)	741 (10.8%)
Breslow thickness				
Median (Range)	0.6 (0-4)	1.2 (0.05-4)	1.5 (0.05-4)	0.7 (0-4)
Ulceration				
Absent	4934 (94.2%)	975 (83.9%)	352 (71.4%)	6261 (90.8%)
Unknown	163 (3.1%)	23 (2.0%)	13 (2.6%)	199 (2.9%)
Present	140 (2.7%)	164 (14.1%)	128 (26.0%)	432 (6.3%)

Results

Figure 1. The 31-GEP risk stratifies mortality risk.



Patients with Class 1A results had higher 5-year MSS than patients with Class 1B/2A or Class 2B results (98.8%, 94.7%, vs. 91.6%, p<0.001).



Patients with Class 1A results had higher 5-year OS than patients with Class 1B/2A or Class 2B results (93.8%, 88.5%, vs. 78.7%, p<0.001).

Table 2. Multivariable analysis identifies the 31-GEP as the strongest predictor of melanoma-specific and all-cause mortality

Factor	Melanoma-specific mortality		All-cause mortality	
	Hazard ratio	P-value	Hazard ratio	P-value
Class 1A	Reference	--	Reference	--
Class 1B/2A	**2.81**	**<0.001***	**1.46**	**0.015**
Class 2B	**3.34**	**<0.001***	**1.91**	**<0.001***
Breslow thickness	1.14	0.392	1.13	0.124
Ulceration (absent)*	Reference	--	Reference	--
Ulceration (present)	1.49	0.207	1.05	0.805
Age	**1.05**	**<0.001***	**1.09**	**<0.001***
Mitotic rate	1.06	0.144	1.04	0.174

Bold indicates statistical significance (p<0.05).
*Ulceration unknown HR was ~0 (p>0.99).

Clinical Impact

- In a real-world cohort of patients considered low risk by AJCC staging, the 31-GEP identified patients at higher risk of mortality who may benefit from increased surveillance and management to improve outcomes.

Conclusions

- In a large, real-world cohort of patients with stage I–IIA CM, the 31-GEP stratified MSS and OS.
- The 31-GEP was the strongest predictor of melanoma-specific and all-cause mortality in multivariable analysis.

References

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