Primary cutaneous melanoma patients stratified by the Merlin assay (CP-GEP): risk of nodal metastasis and long-term survival outcome in a U.S. cohort

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Introduction

- Sentinel lymph node biopsy (SLNB) is used for nodal assessment, even though 80-85% of patients return negative for metastases.[1]
- Also, many patients who relapse or die from melanoma are initially diagnosed as early-stage primary cutaneous melanoma (CM) patients.[2]
- CP-GEP has previously been developed and validated to predict SLNB status[3-7], and recently long-term survival outcomes were evaluated.[8-11]
- Investigate the capability of the CP-GEP to stratify primary cutaneous melanoma patients at risk for nodal metastases and evaluate their long-term survival outcomes.

Methods

- 176 primary CM patients from University Hospitals Cleveland Medical Center - all underwent SLNB between 2007 and 2017, staging according to AJCC 8th edition.
- CP-GEP combines Breslow thickness and patient's age at diagnosis with the expression of eight genes from the primary tumor - Binary output: High Risk or Low Risk.
- 5-year Relapse-Free Survival (RFS), Distant Metastasis-Free Survival (DMFS), and Melanoma-Specific Survival (MSS) were assessed.

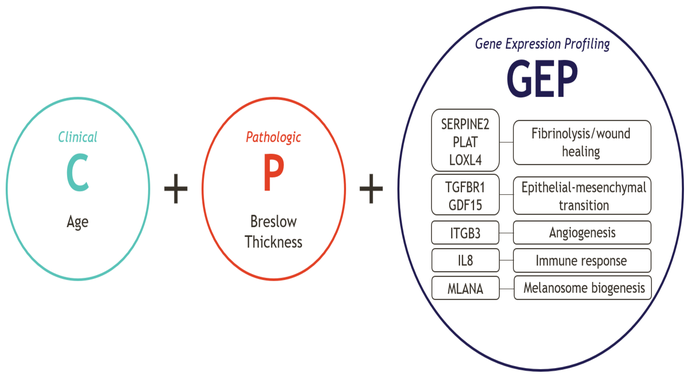


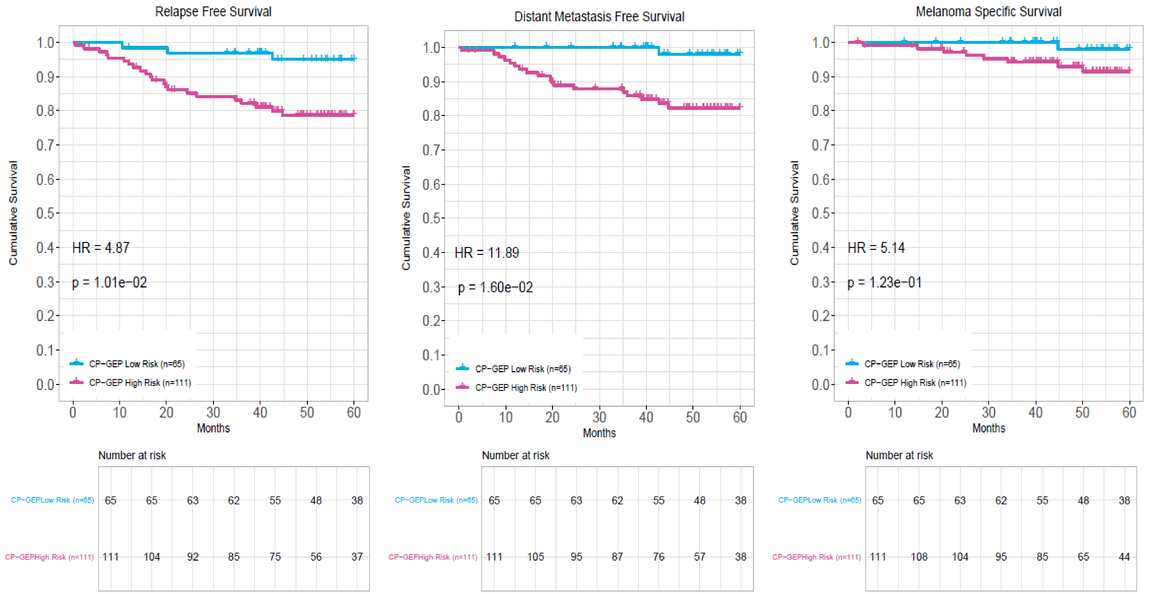
Table 1. Patient Characteristics

Variable	Level	U.S cohort N=176
Gender	Female	75 (42.6%)
	Male	101 (57.4%)
Age (years)	Median [1QR, 3QR]	68 (55, 77)
Breslow thickness (mm)	Median [1QR-3QR]	1.50 (1.08, 2.70)
SLNB outcome	Negative	154 (87.5%)
	Positive	22 (12.5%)
CP-GEP	Low Risk	65 (36.9%)
	High Risk	111 (63.1%)
Stages	IA	41 (23.3%)
	IB	51 (29.0%)
	IIA	30 (17.0%)
	IIB	24 (13.6%)
	IIC	8 (4.5%)
	III	22 (12.5%)
Primary tumor location	Head neck	55 (31.2%)
	Trunk	48 (27.3%)
	Upper extremities	35 (19.9%)
	Lower extremities	30 (17.0%)
	Acral undefined	8 (4.5%)

Results

- Total cohort of 176 patients and SLNB positivity rate of 12.5%. CP-GEP achieved an SLNB reduction rate of 36.9% at a negative predictive value of 93.8%.
- Across all stages, Low Risk patients had better long-term survival outcomes than High Risk patients (Figure 1). 111 patients were categorized as High Risk (63.1%) – capturing 22 out of the total 25 recurrences (88.0%).

CP-GEP stratifies cutaneous melanoma patients as Low Risk and High Risk in long-term survival outcome



	N	Events RFS	5-years RFS, 95% CI		Events DMFS	5-years DMFS, 95% CI		Events MSS	5-years MSS, 95% CI	
Complete Cohort	176	25	84.9	[78.4-89.5]	19	88.2	[82.1-92.4]	9	94.0	[88.7-96.9]
CP-GEP Low Risk	65	3	95.0	[85.3-98.4]	1	98.1	[87.1-99.7]	1	98.0	[86.6-99.7]
CP-GEP High Risk	111	22	78.7	[69.4-85.5]	18	82.3	[73.3-88.5]	8	91.5	[83.6-95.7]

Figure 1. Kaplan-Meier curves showing 5-year RFS, DMFS, and MSS of 176 patients diagnosed with Stage I-III CM stratified by CP-GEP as Low Risk or High Risk.

Conclusions & Take-home messages

- CP-GEP stratifies primary cutaneous melanoma patients according to their risk for nodal metastases, thereby guiding clinical decision-making on deselecting patients for SLNB surgery and improving healthcare resources.
- CP-GEP identifies Low Risk patients who have a better long-term survival outcome compared to the High Risk labeled patients – effectively capturing 88% of relapse events.

References 1. Morton et al. New Engl J Med 2014. Final trial report of sentinel-node biopsy versus nodal observation in melanoma; 2. Whiteman et al. J Invest Dermatol 2015. More people die from thin melanomas (≤1 mm) than from thick melanomas (>4 mm) in Queensland, Australia; 3. Bellomo et al. JCO PO 2020. model combining tumor molecular and clinicopathologic risk factors predicts sentinel lymph node metastasis in primary cutaneous melanoma; 4. Mulder et al. BJD 2020. Validation of a clinicopathological and gene expression profile model for sentinel lymph node metastasis in primary cutaneous melanoma; 5. Johansson et al. EJSO 2022. Validation of a clinicopathological and gene expression profile model to identify patients with cutaneous melanoma where sentinel lymph node biopsy is unnecessary; 6. Yousaf et al. IJD 2021. Validation of CP-GEP (Merlin Assay) for predicting sentinel lymph node metastasis in primary cutaneous melanoma patients: a US cohort study; 7. Stassen et al. EJSO 2023. Clinical evaluation of the clinicopathologic and gene expression profile (CP-GEP) in patients with melanoma eligible for sentinel lymph node biopsy: A multicenter prospective Dutch study; 8 Eggermont et al. EJC 2020. Identification of stage I/IIA melanoma patients at high risk for disease relapse using a clinicopathologic and gene expression model; 9. Mulder et al. Cancers 2022. Using a clinicopathologic and gene expression (CP-GEP) model to identify stage I-II melanoma patients at risk of disease relapse; 10. Amaral et al. EJC 2022. Identification of stage I/II melanoma patients at high risk for recurrence using a model combining clinicopathologic factors with gene expression profiling (CP-GEP); 11. Yu et al. 2023 SMR poster. Long-term survival of melanoma patients stratified by a clinicopathologic and gene expression profile (CP-GEP model): A multi-center United States cohort study