

# The 31-Gene Expression Profile Stratifies Recurrence and Metastasis Risk in Patients with Cutaneous Melanoma

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## Background

›The 31-gene expression profile (31-GEP) test assesses gene expression measurements from primary cutaneous melanoma (CM) tumor tissue to predict risk of tumor recurrence or metastasis and has been validated to stratify risk as: low risk (Class 1A), intermediate risk (Class 1B/2A), or high risk (Class 2B) in multiple prospective and retrospective studies<sup>1-7</sup>.

›Sentinel lymph node biopsy (SLNB) is a prognostic indicator of CM recurrence.

## Objective

›Validate the ability of the 31-GEP test to stratify risk in patients with stage I-III CM

›Evaluate whether 31-GEP test results combined with SLNB results better predict risk of recurrence than SLNB alone.

## Methods

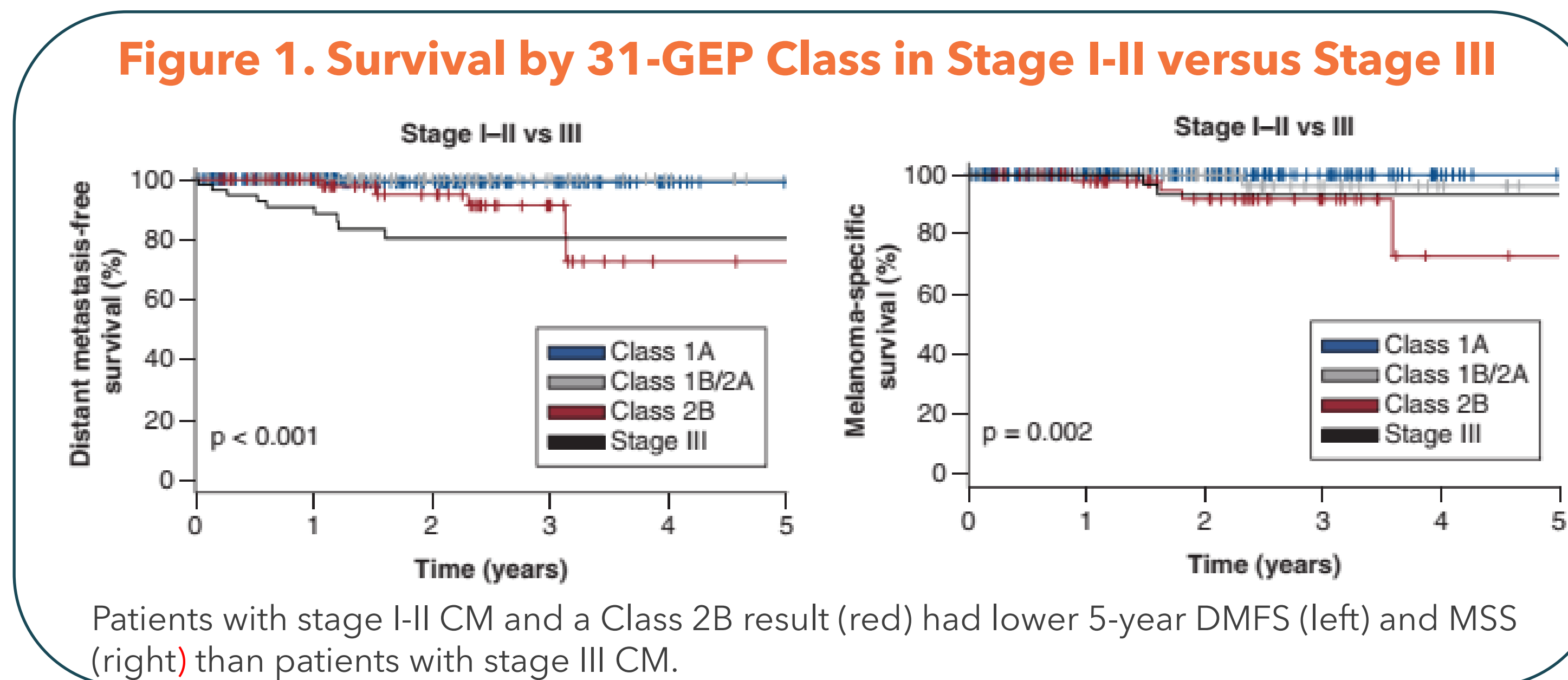
›Kaplan-Meier, Cox regression, and accuracy metrics were retrospectively analyzed for 438 patients with stage I-III melanoma from two surgical oncology and one dermatology center, consecutively tested with the 31-GEP test. Patients were stratified by 31-GEP class.

## Results

**Table 1. Participant Demographics**

Descriptor	Class 1A (n=248)	Class 1B/2A (n=94)	Class 2B (n=96)	Combined (n=438)	p-value
Age					0.008
Median (Range)	61 (18-89)	65 (21-93)	64 (26-95)	62 (18-95)	
Sex					0.08
Female	122	39	35	196 (44.8%)	
Male	126	55	61	242 (55.3%)	
AJCC v8					<0.001
Unable to stage	3	1	0	4 (0.91%)	
IA	168	29	5	202 (46.1%)	
IB	52	28	8	88 (20.1%)	
IIA	8	16	20	44 (10.1%)	
IIB	2	5	26	33 (7.5%)	
IIC	0	2	6	8 (1.8%)	
III	15	13	31	59 (13.5%)	
Tumor Location					0.889
Extremity	123	50	44	217 (49.5%)	
Head and Neck	42	16	18	76 (17.4%)	
Trunk	83	28	34	145 (33.1%)	
Breslow Thickness, mm					<0.001
Median (Range)	0.7 (0.2-5.5)	1.1 (0.3-7.0)	2.8 (0.43-10)	0.95 (0.2-10)	
Ulceration present					<0.001
Yes	8	19	55	82 (18.7%)	
No	240	75	41	356 (81.3%)	
Mitotic Rate (1/mm <sup>2</sup> )					<0.001
Median (Range)	1 (0-10)	2 (0-10)	4.25 (0-10)	1 (0-10)	
SLNB status (# performed)	113	70	82	265	<0.001
Positive	13	13	30	56 (12.8%)	

## Results



**Table 2. Cox regression analysis of prognostic ability of 31-GEP and AJCC staging**

RFS	Multivariable HR (95% CI)	Multivariable p-value
31-GEP Class 1A	Reference	--
31-GEP Class 1B/2A	4.12 (1.05-16.14)	.042
31-GEP Class 2B	5.38 (1.40-20.69)	.014
AJCC stage IA-IIA	Reference	--
AJCC stage IIB-III	4.53 (1.70-12.05)	.003

**Table 3. 31-GEP and SLN status in patients that had an SLNB or lymphadenectomy**

31-GEP Class and /or SLN status	Recurrence-free	With recurrence
31-GEP Class		
31-GEP Class 1A	98.2% (111/113)	1.8% (2/113)
31-GEP Class 1B/2A	91.4% (64/70)	8.6% (6/70)
31-GEP Class 2B	80.5% (66/82)	19.5% (16/82)
SLN Status		
SLN Negative	93.8% (196/209)	6.2% (13/209)
SLN Positive	80.4% (45/56)	19.6% (11/56)
Combined SLN Status and 31-GEP Class		
<b>SLN Negative and Class 1A</b>	<b>98.0% (98/100)</b>	<b>2.0% (2/100)</b>
<b>SLN Positive and Class 1A</b>	<b>100% (13/13)</b>	<b>0% (0/13)</b>
SLN Negative and Class 1B/2A	94.7% (54/57)	5.3% (3/57)
SLN Positive and Class 1B/2A	76.9% (10/13)	23.1% (3/13)
<b>SLN Negative and Class 2B</b>	<b>84.6% (44/52)</b>	<b>15.4% (8/52)</b>
<b>SLN Positive and Class 2B</b>	<b>73.3% (22/30)</b>	<b>26.7% (8/30)</b>

›The 31-GEP test stratified patients by risk of recurrence

›The 31-GEP test further stratified SLN-positive patients into those more (Class 2B) and less (Class 1A) likely to experience recurrence.

**Table 4. Accuracy Metrics**

RFS	31-GEP	SLN Status	31-GEP+SLN
Sensitivity	88.9% (63.9-98.1%)	44.4% (22.4-68.7%)	88.9% (63.9-98.1%)
Specificity	62.7% (55.1-69.8%)	80.2% (73.4-85.7%)	55.4% (47.7-62.8%)
PPV	19.5% (11.9-30.0%)	18.6% (8.9-33.9%)	16.8% (10.2-26.2%)
NPV	98.2% (93.1-99.7%)	93.4% (87.9-96.6%)	98.0% (92.3-99.7%)
DMFS	31-GEP	SLN Status	31-GEP+SLN
Sensitivity	92.3% (62.1-99.6%)	46.2% (20.4-73.9%)	92.3% (62.1-99.6%)
Specificity	61.5% (54.0-68.6%)	79.7% (72.9-85.1%)	54.4% (46.9-61.7%)
PPV	14.6% (8.1-24.6%)	14.0% (5.8-28.6%)	12.6% (7.0-21.4%)
NPV	99.1% (94.5-100%)	95.4% (90.4-98.0%)	99.0% (93.8-99.9%)
MSS	31-GEP	SLN Status	31-GEP+SLN
Sensitivity	100% (51.7-100%)	33.3% (6.0-75.9%)	100% (51.7-100%)
Specificity	59.8% (52.4-66.8%)	78.3% (71.6-83.8%)	52.9% (45.5-60.2%)
PPV	7.3% (3.0-15.8%)	4.7% (0.8-17.1%)	6.3% (2.6-13.8%)
NPV	100% (95.9-100%)	97.4% (93.0-99.2%)	100% (95.4-100%)

## Conclusions

- ›The 31-GEP significantly stratified patient risk for RFS (P<.001), DMFS (P<.001), and MSS (P<.001)
- ›31-GEP was a significant independent predictor of metastatic recurrence (Class 2B HR 5.38, P=.014).
- ›Stage I-II patients with a high-risk 31-GEP class result (Class 2B) had lower DMFS and MSS than stage III patients.
- ›Combining the 31-GEP with SLN status identified patients with higher (26.7%; Class 2B/node-positive) or lower (2.0%; Class 1A/node-negative) recurrence risk than if using SLN status alone.

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