31-gene expression profiling improves risk stratification in patients with T1 cutaneous melanoma

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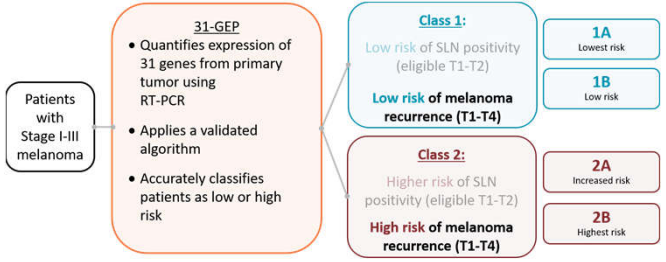
BACKGROUND

- The incidence of melanoma is increasing in the United States while mortality rates remain stable, likely due to increased diagnosis of melanoma of tumors ≤1.0 mm thick (T1 tumors).[1]
- Nearly 70% of tumors are diagnosed as T1,[1] and recurrence-free survival (RFS) is generally good among these patients. However, 27-30% of melanoma related deaths occur in patients originally diagnosed with a T1 tumor,[1,2] suggesting better identification of T1 patients at high risk of recurrence or metastasis is needed.
- The 31-gene expression profile (31-GEP) prognostic test for cutaneous melanoma uses the expression of 28 discriminant genes and 3 control genes from the primary tumor to classify a patient's recurrence risk as low (Class 1: Class 1A lowest) or high (Class 2: Class 2B highest) (**Figure 1**) and has been validated in multiple prospective and retrospective studies.[3-15]
- We hypothesized that the 31-GEP could accurately identify patients with T1 tumors as low and high risk for recurrence.

Figure 1. **31-GEP stratifies patients by recurrence risk.**



METHODS

- Data from patients with T1 tumors (N=669) who had 31-GEP test results and long-term follow-up were analyzed as an overall T1 cohort and split into T-subcategories T1a and T1b for further analysis.
- Kaplan-Meier and Cox regression analyses were used to assess 5-year recurrence-free survival (RFS).
- Prognostic accuracy was assessed by comparing outcomes for Class 1A to Class 2B.

Results

Figure 2. **Five-year RFS in patients with T1 tumors.** Patients with a 31-GEP Class 1A result have significantly higher RFS than patients with a Class 2B result.

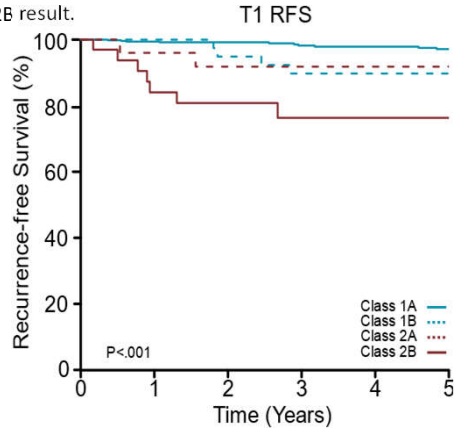


Table 1. **5-year recurrence-free survival (RFS) for patients with T1 melanoma by 31-GEP Class.**

Population	5-yr RFS (95% CI)	*P*-value*
Class 1A (n=556)	97% (95-99%)	
Class 1B (n=53)	90% (81-100%)	<.001
Class 2A (n=27)	92% (82-100%)	
Class 2B (n=33)	76% (62-94%)	

*Log-rank test.

Results

Table 2. **Multivariable Cox regression analysis for 5-year RFS.**

RFS (5-yr)	Univariate		Multivariable	
Feature	HR (95% CI)	P-value	HR (95% CI)	P-value
Mitotic Rate	1.2 (1.0-1.4)	.01	1.1 (0.9-1.3)	.451
SLN positive	6.1 (2.6-14.2)	<.001	3.4 (1.3-8.5)	.009
Ulceration	10.5 (4.7-23.5)	<.001	3.0 (1.2-7.2)	.017
GEP Class 2B	11.1 (4.6-26.8)	<.001	3.1 (1.1-8.5)	.031

Table 3. **Accuracy metrics for the 31-GEP.**

Metric	T1 (95% CI)	Likelihood Ratios
Sensitivity	51.8% (32.3-70.8%)	Positive (95% CI)
Specificity	84.6% 81.5-87.2%)	3.4 (95% CI 2.2-5.0)
PPV	12.4% (7.2-20.2%)	Negative (95% CI)
NPV	97.7% (95.9-98.7%)	0.6 (95% CI 0.4-0.8)

Class 1A was used as a negative result and non-Class 1A as a positive result. PPV: positive predictive value; NPV: negative predictive value.

CONCLUSIONS

- The 31-GEP test can stratify recurrence risk for patients with thin tumors (T1) into low (Class 1A) and high (Class 2B) risk categories.
- Univariate analysis shows the 31-GEP to be a stronger predictor of RFS than SLN status and multivariable analysis shows the 31-GEP to be a strong, independent predictor of RFS.
- With Class 2B RFS status similar to SLN status, Class 2B patients warrant follow-up strategies similar to SLN positive patients.

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