

Clinical use of the 31-gene expression profile for informing sentinel lymph node biopsies: a prospective, multicenter study

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Background

- › A positive sentinel lymph node (SLN) is an indicator of poor outcomes in cutaneous melanoma (CM); however, using clinicopathologic factors to select patients results in up to 88% of all patients having a negative SLNB.¹
- › SLN biopsies (SLNBs) cost up to \$15,223 and are associated with complications in 11.3% of cases.²⁻³ In order to have a positive impact on survival, 142 SLNBs are needed to find one patient who will die from their disease.⁴
- › The 31-gene expression profile (GEP) test stratifies patient risk for recurrence, metastasis, and melanoma death as Class 1A (low-risk), Class 1B/2A (intermediate risk), and Class 2B (high-risk).
- › The 31-GEP is validated to identify patients who have <5% risk of positive SLNB and good outcomes, indicating that these patients could safely forego the procedure.⁵⁻⁶

Clinical Implications

- › Most patients have a negative SLNB
- › Identifying patients at low risk of having a positive SLNB can:
 - › Reduce the number of unnecessary SLNBs
 - › Reduce SLNB-associated complications
 - › Reduce healthcare costs

Study Design



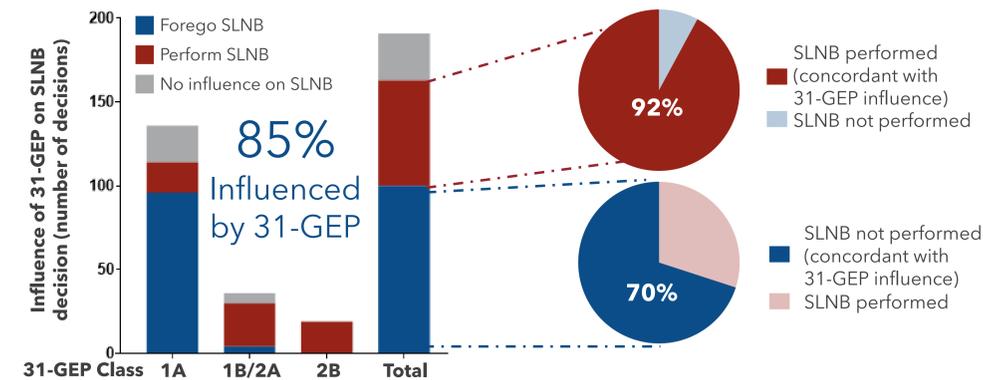
Results

Table 1. Demographic data (n=193)

Descriptor	Class 1A (n=138)	Class 1B (n=23)	Class 2A (n=13)	Class 2B (n=19)	All Pts (n=193)	P-value
Age, median (range)	65 (25-87)	70 (39-90)	65 (22-84)	69 (50-88)	65 (22-90)	0.118
Breslow thickness, median (range)	0.9 (0.2-1.9)	0.8 (0.6-1.85)	1.5 (0.9-1.9)	1.1 (0.4-2)	0.9 (0.2-2)	<0.001
Ulceration						<0.001
Absent	132 (95.7%)	20 (87.0%)	7 (53.9%)	9 (47.4%)	168 (87.1%)	
Present	4 (2.9%)	2 (8.7%)	6 (46.2%)	10 (52.6%)	22 (11.4%)	
Unknown	2 (1.5%)	1 (4.4%)	0 (0%)	0 (0%)	3 (1.6%)	
Mitotic rate (1/mm²)						0.003
<2	99 (78.0%)	14 (63.6%)	4 (33.3%)	10 (55.6%)	127 (70.9%)	
≥2	28 (22.1%)	8 (36.4%)	8 (66.7%)	8 (44.4%)	52 (29.1%)	
Physician Specialty						0.037
Surgical Oncologist	125 (90.6%)	17 (73.9%)	13 (100%)	17 (89.5%)	172 (89.1%)	
Dermatologist	10 (7.3%)	5 (21.7%)	0 (0%)	0 (0%)	15 (7.8%)	
Medical Oncologist	3 (2.2%)	1 (4.4%)	0 (0%)	2 (10.5%)	6 (3.1%)	

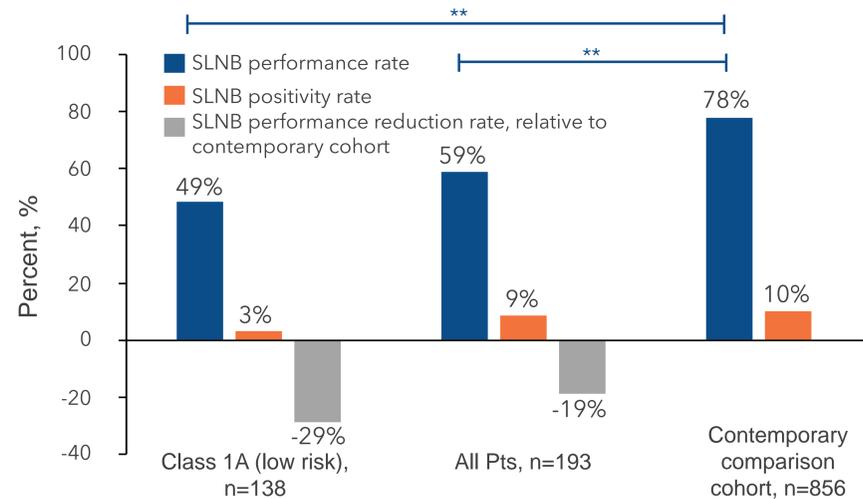
Results

Figure 1. Physicians use 31-GEP results to guide and implement decisions about SLNBs in a risk-aligned manner



The 31-GEP result influenced 85% of SLNB decisions. When the 31-GEP result influenced for SLNB, 92% were performed, and when the 31-GEP result influenced against SLNB, 70% were not performed, indicating that the 31-GEP is used to guide clinical actions. Of the SLNB decisions that were discordant with the 31-GEP result, 83.0% (29/35) were due to patient preference.

Figure 2. SLNB performance rates are significantly reduced when incorporating the 31-GEP result into decision-making



Using the 31-GEP in conjunction with current guidelines reduced the number of SLNBs in the entire population relative to the baseline control (59.1% vs. 78.0%). In Class 1A patients, the reduction in SLNB performance was 29.4%. ** p<0.01

Table 2. Factors associated with decision to perform or forego SLNB.

Decision Factor	Odds Ratio (95% CI)
31-GEP	14.8 (6.1-46.8)*
Patient preference	32.7 (11.5-126.5)*
Tumor-infiltrating lymphocytes	4.7 (1.1-22.5)
Breslow thickness	2.6 (1.2-6.2)
Age	2.1 (0.9-5.1)

Stepwise selection on logistic regression model to identify factors associated with performing an SLNB. *p-values <0.01; Other variables, while contributing to the model, did not reach the statistical significance mark of <0.01 used in this analysis.

Conclusions

- › The 31-GEP result and patient preference play a significant role in SLNB decisions.
- › 85% of SLNB decisions were influenced by the 31-GEP result. 83% of SLNB decisions that were discordant with 31-GEP results were due to patient preference.
- › Using the 31-GEP Class 1A result in conjunction with current guidelines resulted in a 29% decrease in SLNBs compared to not using the 31-GEP to help guide SLNB decisions.

Methods

- › Prospectively enrolled patients (n=191) with T1a tumors and at least one high-risk feature, T1b, or T2 tumors were seen by surgical oncologists (89.1%), dermatologists (7.8%), and medical oncologists (3.1%) from 22 centers.
- › Clinicians received 31-GEP results prior to SLNB decisions and were asked which features influenced their decision whether to perform an SLNB. If the procedure was performed, outcomes were recorded at a subsequent visit.
- › To test the impact of the 31-GEP on SLNB rates, in-study procedure rates were compared to varying baseline rates using the Exact binomial test.⁶
- › The association between clinicopathological features with SLNB performance was studied using stepwise selection on a logistic regression model

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- › CNB, KA, CJ, BM, and SJK are employees and shareholders/option holders of Castle Biosciences, Inc.
- › JMG is on the speakers bureau at Castle Biosciences. MY has no conflicts to disclose.