The i31-GEP for sentinel lymph node (SLN) biopsy outperforms the MSKCC nomogram in predicting the risk of having a positive SLN in patients with cutaneous melanoma

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Background

- National Comprehensive Cancer Network (NCCN) guidelines recommend foregoing sentinel lymph node biopsy (SLNB) if the population-based point-estimate risk of positivity is <5% (T1a with no high-risk features), discuss and consider SLNB if the risk is 5-10% (T1a with high-risk feature(s), T1b), and recommend SLNB if the risk is >10% (T2-T4).[1]
- With the current SLNB positivity rate at approximately 12%,[2,3] better tools are needed to refine patient selection for the procedure to avoid potential complications and additional healthcare costs. Such methods that improve patient selection of those who will have a positive SLNB, while identifying the correct patients with low enough risk (<5% positivity risk by current guidelines) that they can safely forego SLNB could reduce the number of unnecessary surgical procedures, lower healthcare costs, and improve patient care.
- Two tools, the i31-gene expression profile test for SLNB (i31-GEP for SLNB)[4] and the nomogram developed at the Memorial Sloan Kettering Cancer Center (MSKCC)[5,6] predict the risk of SLN positivity in patients with cutaneous melanoma (CM) by combining a tumor's molecular risk profile, clinical and pathological factors (i31-GEP test) clinical and pathological factors only (MSKCC).
- We compared the performance of the i31-GEP for SLNB result prediction to that of the MSKCC nomogram.

Table 1: Variables included in i31-GEP test or MSKCC Model

Prediction Variables	Included in i31-GEP Test	Included in MSKCC Model
31-GEP continuous score	√	
Breslow thickness	√	√
Mitotic Rate	√	
Ulceration	√	√
Age	√	√
Clark Level		√
Tumor location		√

31-GEP score, Breslow thickness, mitotic rate, age, and Clark level were continuous variables. Ulceration was present or absent, and tumor location was entered as trunk, extremity, or head/neck. Tumor location was evaluated in development of the i31-GEP but was not significant for prediction; Clark level was not evaluated because most providers use Breslow thickness instead.

Methods

Patients with T1–T2 tumors from previously published multicenter cohort studies who had undergone the SLNB procedure were analyzed by both the i31-GEP and the MSKCC nomogram (n=465).[6] Accuracy metrics were compared using <5% predicted risk as a negative result and ≥5% as a positive result.

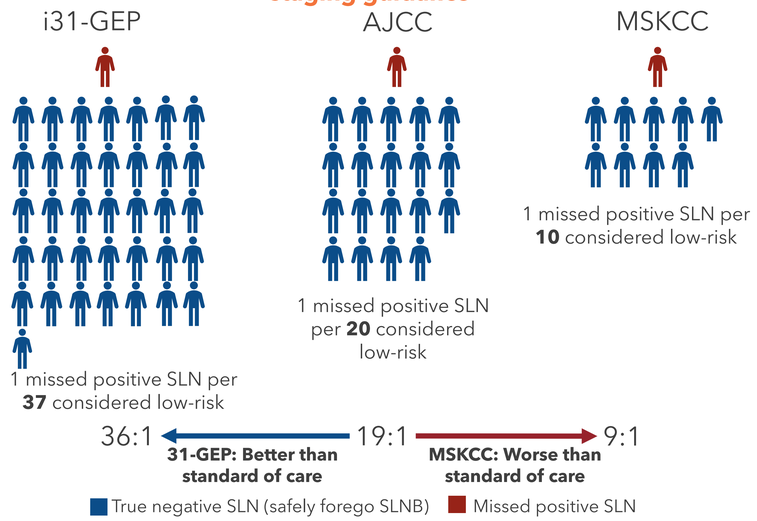
References

1. National Comprehensive Cancer Guidelines, v2, 2022. 2. Joyce KM, et al. Ir J Med Sci 186:847–853, 2017. 3. Chen et al. Oncotarget 7:45671-45677. 4. Whitman ED, et al. JCO Precision Oncology 1466-1479, 2021. 5. Wong SL, et al. Ann Surg Oncol 12:282–288, 2005. 6. Pasquali S, et al. Eur J Surg Oncol 37:675–80, 2011.

Clinical Impact

- Using only clinical and pathologic features to predict SLN status limits the ability to identify tumors with spread to the SLN (e.g., 12% positivity rate). Integrating clinical and pathological factors with molecular tumor biology assessed by the prospectively validated gene expression risk profile (31-GEP) improves risk stratification to guide personalized patient care.
- Beyond the utility for SLNB guidance, the integrated 31-GEP (i31-GEP) also provides a precise risk for recurrence, metastasis, and disease-specific mortality for an individual patient.

Figure 1. i31-GEP SLNB guidance results in fewer missed positive SLNs than the MSKCC nomogram or standard staging guidance



- The i31-GEP had a significantly lower false negative rate (3/111; 2.7%) than the MSKCC nomogram (11/110; 10.0%) (p=0.026).
- The i31-GEP also had a lower false negative rate than using AJCC staging, which does not recommend SLNB if the risk is 5% or less.

Table 2. The i31-GEP for SLNB has higher accuracy than MSKCC for predicting SLN positivity in patients with T1-T2 tumors

Test	Sensitivity	Specificity	Negative predictive value	Positive predictive value
i31-GEP	94.8%	26.5%	97.3%	15.5%
MSKCC	81.0%	24.3%	90.0%	13.2%

Table 3. Reclassification of risk in patients with 5-10% risk (NCCN/AJCC T1b tumors) for whom guidance is not definitive

Test	Predicted <5% risk	Positivity rate in <5% group	Predicted >10% risk	Positivity rate in >10% group	Total reclassified
i31-GEP	36.2% (46/127)	2.2% (1/46)	15.7% (20/127)	15% (3/20)	52.0% (66/127)
MSKCC	29.9% (38/127)	7.9% (3/38)	2.4% (3/127)	0% (0/3)	32.3% (41/127)

All results are % (n/N).

Conclusions

- The MSKCC nomogram using clinical and pathological factors alone had a 10% miss rate in patients it predicted to have <5% risk of SLN positivity—worse than AJCC staging alone.
- The i31-GEP for SLNB missed 2.7%, significantly lower than MSKCC—better than both MSKCC and AJCC staging.
- The i31-GEP for SLNB showed an 89% increase in the number of patients who could forego SLNB compared with current guidelines (36:1 vs. 19:1 true to false negative ratio) compared with a 53% decrease if using MSKCC.
- The i31-GEP for SLNB ~~has~~ demonstrated clinical utility to guide SLNB decisions in patients with T1-T2 tumors as well as guiding subsequent treatment plans with risk-of-recurrence.

Acknowledgments & Disclosures

- Funding provided by Castle Biosciences.
- DZ and NB have no conflicts of interest. SKM is an employee and stock/options holder at Castle Biosciences.

Presented at the 2023 Winter Clinical-Miami Dermatology Conference.