The i31-SLNB identifies patients with cutaneous melanoma who have less than 5% risk of SLN positivity while the CP-GEP does not

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Background

- Sentinel lymph node biopsy (SLNB) is a prognostic procedure that can help guide management pathways for patients with cutaneous melanoma (CM). Up to 88% of SLNBs are negative, indicating that most patients may not require the procedure.[1]
- The National Comprehensive Cancer Network (NCCN) guidelines recommend that patients avoid an SLNB when the risk of positivity is <5%, whereas those with a risk of 5-10% should be considered for an SLNB, and those with a risk of 10% should be offered an SLNB (**Table 1**).[2]
- A clinically useful molecular test to inform SLNB decision making should identify individuals who can safely forgo SLNB by predicting patients who have <5% risk of SLN positivity.
- The i31-SLNB test was specifically developed to achieve the 5% guideline threshold and combines age, Breslow thickness, mitotic rate, and ulceration with the 31-GEP continuous score (**Figure 1**).[3] Optimizing risk of recurrence (RoR) prediction required a different set of clinicopathologic factors.[4]
- The CP-GEP test was specifically developed to achieve the 5% guideline threshold and combines 8 genes with age and Breslow thickness.[5]

Methods

- The i31-SLNB and CP-GEP test's false negative rates were calculated from Whitman et al., 2021 (T1-T4: n=1,258),[3] and Sondak et al. 2024 (T1-T3: n=1,686), respectively.[6]
- GEP false negative rates were calculated as 1-negative predictive value and represents the percentage of patients considered low risk by a GEP test who had a positive SLN (**Table 2**).
- Only patients who had an SLNB were included.

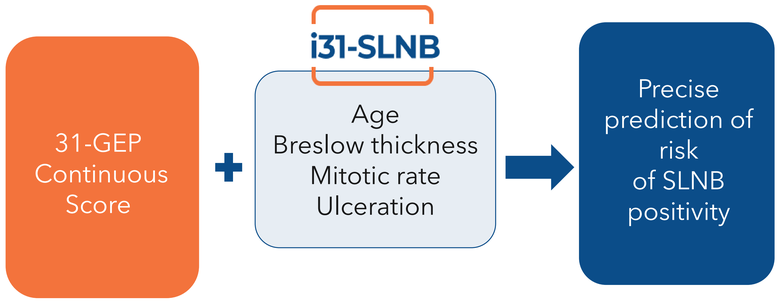
Objective

- **Compare the performance of the i31-SLNB and CP-GEP in predicting patients with low risk (<5%) of SLN positivity**

Table 1. Recommendations from NCCN guidelines for SLNB decisions.

Stage	SLN+ Risk	SLNB Eligibility
T1a-LR	<5%	No
T1a-HR	5-10%	Yes: Consider
T1b		
T2a – T4	>10%	Yes: Offer

Figure 1. The i31-GEP combines the 31-GEP with SLNB specific clinicopathologic factors using a neural network for a personalized risk of SLNB positivity[3]



References

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Acknowledgments & Disclosures

SD is an employee/shareholder of Castle Biosciences, Inc. JMG and JV are both speakers for Castle Biosciences, Inc.

Results

Table 2. The i31-SLNB identifies patients with <5% risk of SLN positivity, achieving the 5% guideline threshold while CP-GEP does not.

Group	i31-SLNB % of patients considered low risk who had a positive SLN	CP-GEP % of patients considered low risk who had a positive SLN
All T-stages	**3.9%**	**7.1%**
T1b	2.8%	5.1%
T2a	4.3%	7.3%

Clinical Impact

- The i31-SLNB achieves the 5% guideline threshold, thereby enabling a reduction in unnecessary SLNB associated morbidity and lower healthcare costs.
- The CP-GEP did not achieve the 5% guideline threshold.

Conclusions

- The i31-SLNB accurately identifies patients with a risk of SLN positivity below the NCCN guideline of a 5% risk threshold for avoiding SLNB, with a GEP false negative rate nearly half that of CP-GEP.
- Patients identified as low risk by CP-GEP had SLN positivity rates over 5% - above the 5% guideline threshold and should therefore be considered insufficient for informing clinical decisions regarding SLNB.