The integrated 31-gene expression profile (i31-GEP) test for cutaneous melanoma outperforms CP-GEP at identifying patients who can safely forego sentinel lymph node biopsy.

Abel Jarell, MD,[1] Brian Martin, PhD,[2] Peter Prieto, MD, MPH[3]

[1]Northeast Dermatology Associates, PC, Portsmouth, NH, [2]Castle Biosciences, Inc., Friendswood, TX, [3]University of Rochester Medical Center, Rochester, NY

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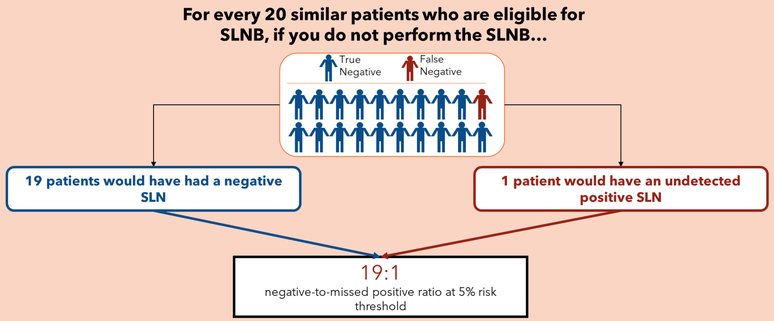
Background

- Management of patients with melanoma involves multiple decision points during clinical care, all of which, in line with guidelines, should be aligned with a patient's risk for poor outcomes. The 31-gene expression profile (GEP) was developed and validated to predict a patient's risk of recurrence and further validated to precisely predict a patient's individualize risk for a positive SLNB.
- An SLNB risk threshold weighs surgical risks against those of missing a positive SLN. Current guidelines recommend a 5% risk threshold for considering SLNB in patients with cutaneous melanoma (T1a with high-risk features, T1a-HR-T4).[1]
- A 5% threshold indicates that, in a group of 20 similar patients foregoing SLNB, 19 would have a negative SLNB, with one missed positive SLN (19:1 negative:positive ratio).[2,3] Any novel test to identify patients who can forego SLNB should increase the ratio of negative-to-missed positive nodes (**Figure 1**).
- A second GEP test was developed to identify patients at low risk of SLN metastasis, CP-GEP, but is not available for survival prognostication.[11-12]

Figure 1. Current guidelines suggest considering SLNB when the risk of a positive biopsy is ≥5% (T1aHR– T4)



Any new test must do better than this when selecting patients to forego SLNB.

Results

Clinical Impact and Objective

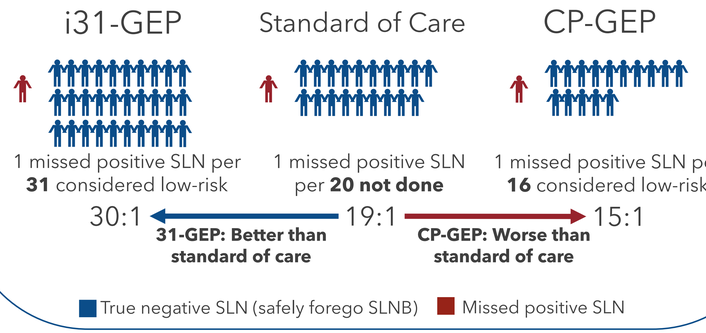
- Patient management decisions, including the decision to undergo SLNB, should be risk-appropriate to the individual being considered for treatment. Currently, national guidelines recommend patients consider SLNB when risk reaches a 5% threshold, broadly identified by T-stage (T1a with high-risk features and greater). Thus, by guidelines, an allowable threshold for true negatives to false negatives when foregoing SLNB is 19:1, and any test use to guide this decision should be superior to this benchmark.
- To compare the utility of the i31-GEP and CP-GEP for SLNB guidance with the current standard of care in T1b-T2 cutaneous melanoma.

Figure 2. Only the i31-GEP performs better than standard of care at identifying those who can safely forgo SLNB (T1b-T2)

Test	TN	FN	Ratio (TN:FN)
i31-GEP	154	5	30:1 (154/5)
Standard	19	1	19:1 (19/1)
CP-GEP	60	4	15:1 (60/4)

i31-GEP results adapted from Whitman et al. *JCO PO* 2021.[4] CP-GEP results obtained from Yousaf et al. *IJD* 2021.[12]
TN: True negative. FN: False negative.

CP-GEP would miss more positive nodes per 100 'low-risk' patients (n~6; 100/15) than using the current standard of 5% (n=5), while i31-GEP would miss less than the standard (n~3; 100/30) and half as much as CP-GEP.



Conclusions

- Standard of care suggests that at a 5% risk threshold, for every 20 patients not getting an SLNB, one positive node will be missed (19:1 true-to-false negative). To be safe and clinically useful, any new test must do better.
- i31-GEP: 30:1 true-to-false negative SLNB ratio is better than using standard of care for identifying patients who may safely forego SLNB.
- CP-GEP: 15:1 true-to-false negative SLNB ratio is worse than using standard of care.
- The i31-GEP is the only test to offer both SLNB risk prediction and risk of recurrence, metastasis, or death prognostication.

Methods

- We compared the performance of two GEP tests, the i31-GEP (n=763)[4] and the CP-GEP (U.S. validation cohort; n=153 [includes three T1a]),[12] in patients with T1b-T2 tumors, with known SLNB results, to determine if either test increased the ratio of negative-to-missed positive nodes.

References

1. National Comprehensive Cancer Guidelines, v2, 2022. 2. Vickers et al. *BMJ* 2015. 3. Vickers et al. *Diagn Progn Res*. 2019. 4. Whitman et al. *JCO PO* 2021. 5. Vetto et al. *Future Oncology*. 2019. 6. Hsueh et al. *JCO PO* 2021. 7. Jarell et al. *JAAD*. 2022. 8. Arnot et al. *AJS*. 2021. 9. Dillon et al. *CMRO*.2022. 10. Ahmed et al. *Cancer Med*. 2022. 11. Bellomo et al. *JCO* PO 2020. 12. Yousaf et al. *IJD* 2021. 13. Mulder et al. *BJD* 2020.

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