Real-world evidence confirms risk stratification of the 31-GEP and i31-GEP in prospectively tested patients with stage I-III cutaneous melanoma

David Pariser, MD[1], Jeffrey Sussman, MD[2], Brian Martin, PhD[3], Lindsay Ackerman, MD[4], Craig A. Kraffert, MD[5], Abel Jarell, MD[6]

[1]Virginia Clinical Research, Inc. and Eastern Virginia Medical School, Norfolk, VA, [2]University of Cincinnati Medical Center, Cincinnati, OH, [3]Castle Biosciences, Friendswood, TX,[4]Medical Dermatology Specialists, Phoenix, AZ, [5]CK Derm, Redding, CA, [6]SracSkin Research and Consulting, PLLC, Portsmouth, NH

Scan or click here for more info

Background

- Current American Joint Committee on Cancer (AJCC 8th edition) guidelines bin patients with cutaneous melanoma (CM) into risk categories based on the pathological tumor data of Breslow thickness, ulceration status, and sentinel lymph node status.[1] However, this does not consider the heterogenous nature of CM or the tumor's molecular biology.
- The 31-gene expression profile test is prospectively validated to identify patients considered high or low risk by AJCC with low or high-risk tumor biology who may be over- or undertreated by current guidelines and has been shown to have a positive impact on patient outcomes.[2-7]
- To further advance personalized patient care, the 31-GEP result was integrated with clinical and pathological factors (i31-GEP for risk of recurrence, ROR) to provide a more personalized, precise risk of tumor recurrence to guide clinical management of CM.[8]

Objective

- **Validate the 31-GEP and i31-GEP ROR in a prospectively tested, real world cohort of patients with stage I-III CM to demonstrate added value of 31-GEP testing in clinical care.**

Methods

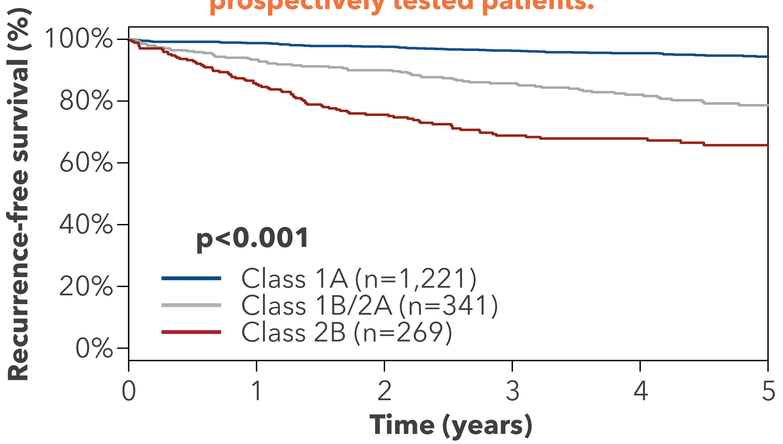
- Patients with stage I-III CM enrolled in the CONNECTION study were prospectively tested with the 31-GEP between 2013 and 2017 (n=1,831). Kaplan-Meier analysis with the log-rank test was used to estimate survival differences between low (Class 1A), intermediate (Class 1B/2A), and high (Class 2) risk groups and the i31-GEP risk groups. The i31-GEP ROR combines Breslow thickness, ulceration, SLN status, mitotic rate, tumor location, age, and the 31-GEP to provide a personalized estimate of recurrence-free survival (RFS).[8] While guidelines have not established an ROR threshold for determining when to escalate or de-escalate care, the NCCN uses stage IIA versus IIB to differentiate management intensity.[9] This cut-point translates to a 5-year RFS rate of 69.8% and was used here. Cox multivariable regression analysis was used to identify predictors of recurrence.

References

1. Gershenwald JE, et al. Ann Surg Oncol. 2018. 2. Greenhaw BN, et al. Dermatol Surg. 2018. 3. Hsueh EC, et al. JCO Precision Oncology. 2021. 4. Vetto JT, et al. Future Oncology. 2019. 5. Podlipnik S, et al. J Eur Acad Dermatol Venereol. 2019. 6. Dillon LD, et al. SKIN J Cutaneous Med. 2018. 7. Berger AC, et al. Curr Med Res Opin. 2016. 8. Jarell A, et al. J Am Acad Dermatol. 2022. 9. Cutaneous Melanoma NCCN panel. Melanoma: Cutaneous, Version 3.2023. 2023.

Results

Figure 1. The 31-GEP stratifies recurrence risk in prospectively tested patients.

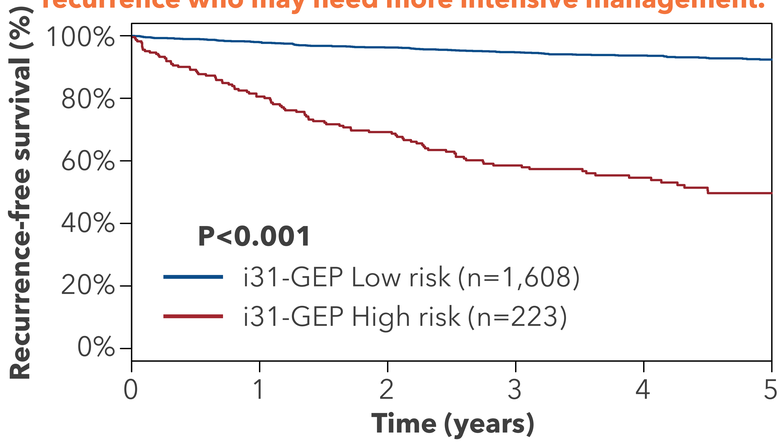


Patients with Class 1A results had higher 5-year RFS (Class 1A: 94.4%; Class 1B/2A: 78.6%; Class 2B: 65.5%, p<0.001).

Table 1. Multivariable analysis demonstrates independent and significant prognostic information

Recurrence-free survival	Multivariable HR	p-value
31-GEP Class 1A	Reference	--
31-GEP Class 1B/2A	2.07	<0.001
31-GEP Class 2B	2.40	<0.001
Age (continuous)	1.02	<0.001
SLN negative	Reference	--
SLN unknown	0.71	0.085
SLN positive	4.54	<0.001
Breslow thickness (continuous)	1.09	0.027
Ulceration absent	Reference	--
Ulceration present	1.57	0.005
Mitotic rate <2/mm^2	Reference	--
Mitotic rate ≥2/mm^2	1.47	0.016

Figure 2. The i31-GEP predicts patients at high risk of recurrence who may need more intensive management.



Patients with a low-risk i31-GEP result had significantly higher 5-year RFS (92.4%) than those considered high risk (49.7%, p<0.001).

Clinical Impact

- Identifying high-risk patients allows for earlier management decisions while patients have a lower tumor burden.
- Baseline high-risk patient detection may promote earlier administration of immunotherapy and potentially better therapeutic outcomes

Conclusions

- This real-world evidence study of prospectively tested patients confirms the independent performance of both the 31-GEP and the i31-GEP in improving treatment pathway decision accuracy.

Acknowledgments & Disclosures

- DP is an investigator for Castle Biosciences, Inc. BM is an employee/shareholder of Castle Biosciences, Inc. AJ is on the speaker's bureau of Castle Biosciences, Inc. JS, LA, and CAK have no conflicts of interest.