Enabling access to prognostic gene expression profile (GEP) testing for invasive melanoma by leveraging RNA-based testing in the diagnostic workflow

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Background

- Melanoma diagnoses can be challenging to achieve definitively.[1-3]
- Ancillary testing, typically utilized by the pathologist, can disambiguate problematic lesions and help provide a definitive diagnosis.[4]
- The 23-GEP provides test results of suggestive of benign lesion, suggestive of malignant lesion, or intermediate (cannot exclude malignancy) and is recommended by guideline organizations including the National Comprehensive Cancer Network, American Society of Dermatopathology: Appropriate Use Criteria for Ancillary Diagnostic Testing, the American Academy of Dermatology Guidelines of Care for the Management of Primary Cutaneous Melanoma, and the Skin Cancer Prevention Working group.[4-7]
- The **diagnostic 23-GEP** test has demonstrated accuracy metrics of 90.4 – 94.9% sensitivity and 92.5 – 96.2% specificity including 3 studies with known outcomes.[8-12]
- The **prognostic 31-GEP** test stratifies, independent of clinicopathologic factors, patients with cutaneous melanoma into groups at low, intermediate, or high risk of recurrence, metastasis, or death based on the patient's molecular risk.[13-17]
- Clinicians use the 31-GEP results to make risk-aligned decisions about sentinel lymph node biopsy, surveillance imaging, adjuvant therapy, and follow-up schedule decisions.[18-20]
- Both diagnostic ancillary tests and prognostic tests require tissue to perform, which is a limited resource. Some ancillary testing can take weeks to months to provide results leading to a definite diagnosis.
- The 23-GEP ancillary diagnostic test utilizes the **same base material, RNA**, as the 31-GEP test and is performed in the same laboratory.[21,22]
- **Here, we describe clinical trends that help achieve a definitive diagnosis and provide access to vital prognostic testing utilizing the same tissue.**

Methods

- The study includes clinical cases submitted to Castle Biosciences for 23- and/or 31-GEP testing with results reported between March 1 and July 31, 2023.

References

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Diagnostic 23-GEP clinical orders

Table 1. Patient Characteristics

	Gender (%)	Age (median, (range))
Female (%)	57.4%	49 (4 – 90+)
Male (%)	42.6%	49 (5 – 90+)

Table 2. Biopsy Type

Biopsy Description*	
Shave	88.4%
Punch	7.3%
Excisional	3.6%
Re-excision, WLE	0.1%

*Biopsy percentage was calculated from orders where biopsy type was provided. Biopsy type was provided for 68.1% of orders.

Table 3. 23-GEP Turnaround Time

Turnaround Time*	
Median	4 days

*Turnaround time was calculated as the number of business days (Monday – Friday) from the date the tissue was received until the report date.

› 23-GEP results are returned quickly (43% provided in 3 days or less), avoiding delayed diagnoses for difficult lesions.

Table 4. Clinical result stratification

23-GEP Test Result	Orders (%)
Benign	60.1%
Malignant	19.9%
Intermediate	13.4%
MGF/Fail	6.7%

Table 5. Lesions with resolved ambiguity

Actionable Test Result*	
Resolved ambiguity	79.9%

*23-GEP results of either benign or malignant are considered actionable.

Prognostic 31-GEP Eligibility

› Clinicians can order 23-GEP and 31-GEP on the same tumor tissue specimen for most samples that receive a 23-GEP malignant result.

Table 6. Biopsies eligible for 31-GEP

31-GEP Eligible*	
≥ 40% tumor content	81.5%

*Of patients with 23-GEP malignant results, percentage with ≥ 40% tumor volume (minimum tumor content required for 31-GEP).

Conclusions

- ~80% of cases tested with 23-GEP receive an actionable result in a median of 4 business days.
- ~60% of ambiguous lesions received a benign 23-GEP test result, reducing overdiagnosis and overtreatment for diagnostically challenging lesions.
- ~80% of clinically tested lesions with 23-GEP malignant results have sufficient biopsy tumor content for 31-GEP testing without requesting additional tissue.

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