

BRIEF ARTICLE

Risk Stratification for Melanoma Using the 31-Gene Expression Profile Test: A Case Report

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ABSTRACT

Melanoma is the largest contributor to skin cancer related deaths in the United States. Histology and AJCC8 staging have been the primary means for risk stratification until the introduction of the 31-Gene Expression Profile (GEP) testing became available. This test individually stratifies a patient's melanoma risk of recurrence. Without this molecular data, certain early-stage melanoma patients would not receive the more aggressive monitoring needed to minimize their risk. In this case, we discuss a 49-year old female patient with a 0.6mm, non-ulcerated melanoma on her right lateral knee. The 31-GEP results showed a Class 1A, which allowed for standard treatment with wide local excision without needing more aggressive testing or imaging. Since the patient has a past medical history of chronic hepatitis B, there could have been implications if immunotherapy was needed. This patient's results show an ideal scenario for melanoma. The patient was given reassurance regarding her diagnosis having the lowest risk category.

INTRODUCTION

Skin cancer is the most frequently diagnosed cancer in the United States, with melanoma being the largest contributor to skin cancer related deaths.¹ Historically, prognostic factors for melanoma were solely based on histologic evaluation including features such as Breslow depth, ulceration, and mitotic rate. DecisionDX-Melanoma is a 31-Gene Expression Profile (GEP) test that provides individualized risk stratification by categorizing lesions into 4 classes: 1A, 1B, 2A, and 2B, with 2B representing the highest risk. Each class provides information on the

risk of recurrence and the likelihood of sentinel lymph node positivity.² Since the introduction of the 31-GEP test, clinicians have been better able to stratify risk in their melanoma patients when correlating this molecular data with the histological evaluation. The information provided in the 31-GEP test helps guide monitoring and management protocols. According to data collected by Castle Biosciences, 11% in a cohort of over 60,000 patients had a high-risk Class 2B categorization.³ Refer to **Table 1** for percentages associated with each risk class. In another study, 5% of patients with <0.8mm thickness had lymph node positivity.⁴ NCCN guidelines do not recommend sentinel lymph

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node biopsy in T1a (<0.8mm, non-ulcerated) melanomas.⁴ Considering this, a portion of patients with histologically low risk factors could be at greater risk for metastasis due to high-risk gene expression. AJCC8 staging

alone would be inadequate for stratifying risk in these patients. For this reason, the 31-GEP test can be life altering and should be a consideration for all early-stage melanomas.

Table 1. Percentage of Patients Classified as 1A, 1B/2A, or 2B using 31-GEP testing

Class	5 year risk of recurrence/metastasis	% Patients, N=63,765 ^{a,b}
1A	Lowest	74%
1B/2A	Intermediate	15%
2B	Highest	11%

Abbreviations GEP: Gene Expression Profiling

^a May 2013 to December 2020

^b Data on file, Castle Biosciences

CASE REPORT

A 49-year old Caucasian female presented with a clinically suspicious lesion on her right lateral knee. A biopsy was performed and the differential diagnoses considered were melanoma, dysplastic nevus, and melanocytic nevus. The pathology report showed superficial spreading melanoma with 0.6mm thickness and no ulceration, classifying the lesion as a T1a melanoma. Of note, the patient's medical history includes chronic hepatitis B. She has no prior history of cancer and no immediate family with a history of skin cancer. Wide local excision was performed and 31-GEP testing was initiated.

Wide local excision accomplished clear margins. 31-GEP testing showed a Class 1A melanoma, which according to i31-SLNB (sentinel lymph node biopsy) results confers a 4.5% risk of sentinel node positivity. The i31-ROR (risk of recurrence) statistics were as follows: 99.7% melanoma-specific survival, 97.9% distant metastasis-free survival, and 96.1% recurrence-free survival.

DISCUSSION

This patient had the ideal scenario that every clinician hopes for with a melanoma diagnosis. Having resulted in a 31-GEP Class 1A, this patient was able to maintain standard follow up without needing more aggressive testing, imaging, monitoring, or adjuvant therapy. Since the patient has chronic hepatitis B, had this been a more aggressive melanoma or a higher risk classification, there could have been concerns with immunotherapy options. There is a theoretical risk of reactivation of hepatitis B with immune checkpoint inhibitors, including those used in treating melanoma.⁵ Though it is not a contraindication, it should be a consideration when choosing immunotherapy. The 31-GEP test identifies patients at higher risk of recurrence and/or metastasis. These patients may benefit from a prioritized referral to medical and surgical oncology. The most impactful utilization of the 31-GEP test is in identifying high-risk, early-stage melanomas (Class 2B). In those cases, more aggressive monitoring and further testing can be life saving. However, even in this low-risk case, the results are

impactful to the patient. Having this lesion-specific information can help providers give reassurance to patients who are fearful of a diagnosis of melanoma. The psychological implications of a cancer diagnosis with metastatic risk can be burdensome. As clinicians, if we can give personalized prognostic data, we can grant our patients greater peace of mind. In a day and age where technology reigns, the 31-Gene Expression test has the potential to become standard of care for early-stage melanomas.

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