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Using 31-Gene Expression Profile in Melanoma Risk Prognosis

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Cutaneous melanoma (CM) is one of the most dangerous and fastest growing types of cancer. According to the Center for Disease Control, the incidence of melanoma skin cancer has increased by 2% per year.[1] A majority of CM related deaths are from melanomas initially classified as low-risk subtypes.[2] The prognostic and metastatic risk for CM is therefore underestimated according to current staging criteria.[3]

Current diagnostic recommendations exist based on the American Joint Committee on Cancer's (AJCC) staging system, while current therapeutic recommendations are based on the National Comprehensive Cancer Network (NCCN) guidelines. AJCC staging takes into account several factors like Breslow Depth, ulceration status, nodal involvement, and presence of distant metastasis, which provide important prognostic information and indicate overall and disease-free survival.[4,5] Because the AJCC guidelines are based on pathology alone, there is controversy surrounding this staging and how accurate it is at predicting mortality and morbidity in patients diagnosed with primary CM.[6]

A 31-gene expression profile test has recently been developed to provide further prognostic information in addition to current guidelines. The 31-GEP test (DecisionDx-Melanoma, Castle Biosciences, Inc.) has been developed and validated as an independent prognostic indicator of risk in melanoma, improving overall risk stratification when used in conjunction with AJCC staging. The commercially available GEP test classifies CMs into categories based on risk. The test is validated for use in primary tumor tissue of invasive melanoma Stage I–III, thus excluding cases of melanoma in situ. The 31-GEP test uses formalin-fixed tissue embedded in paraffin from the CM to classify tumor metastasis as low risk (Class 1A/1B) or high risk (Class 2A/2B).[4] After the initial diagnosis, the test provides the expected recurrence-free survival (RFS), distant metastasis-free survival (DMFS), and melanoma specific survival for 5 years after diagnosis[4] and can identify patients who are at higher risk of recurrence and may be eligible for higher intensity surveillance.[7]

There is a robust body of evidence to support the validity of the 31-GEP test in predicting risk in patients with CM independent from traditional clinicopathologic staging. Podlipnik et al showed that the 31-GEP test can identify patients with early stage AJCC CM at risk of relapse and GEP was the only significant predictor of RFS.[7] Gastman et al revealed that the 31-GEP test identified increased risk for metastasis and death independent of node status in patients with head and neck CM.[5] According to Greenhaw et al, the 31-GEP test accurately identified 77% of metastatic CMs as high risk/Class 2.[4] According to this study, Class 2 CMs were 22 times more likely to metastasize compared with Class 1 CMs.[4] Because data supporting the accuracy of the GEP has been demonstrated in over 26 peer reviewed studies, use of the test in clinical practice has been wide-reaching, yet has also been a source of polarization between some working groups.

The addition of this test to current staging guidelines can aid in identifying patients with CM who are at increased risk for distant metastasis and mortality. 31-GEP testing can add prognostic value to the initial work-up of patients after diagnosis. Earlier diagnostic imaging, surveillance, and interventions can be done in the higher risk subset of patients.[7]

From the perspective of a busy dermatology practice that diagnoses 70 malignant melanoma patients annually, we were thrilled to see the 31-GEP test recognized by the NCCN as an important adjunct to AJCC staging for accurate prediction of CM related risk. The addition of this test to our own patient management guidelines has aided in the identification of patients who are at increased risk for metastasis; therefore, patient care was positively impacted by appropriately guiding resource utilization, whether that be surveillance frequency, intensity, or referrals. In accordance with NCCN guidelines and AJCC staging, considerations for earlier diagnostic imaging, surveillance, and interventions in Class 2 patients with a higher recurrence risk are recommended. The literature supports the incorporation of 31-GEP testing into melanoma prognosis determinations. We are confident that guidelines will soon incorporate the 31-GEP test into CM staging criteria.

DISCLOSURES

Authors Vasile G, Ilyas M, Lazzara D, Jacobs D, and Matin T have no relevant conflicts of interest to disclose.
Eduardo Weiss MD is a speaker for Castle Biosciences, Inc.

REFERENCES

1. Centers for Disease Control and Prevention. Melanoma Incidence and Mortality, United States–2012–2016. USCS Data Brief, no. 9. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2019.
2. SEER Data 2017.
3. Hsueh E et al. Interim analysis of survival in a prospective, multi-center registry cohort of cutaneous melanoma tested with a prognostic 31-gene expression profile test. *J Hematol Oncol.* 2017; 10:152. Doi 10.1186/s13045-017-0520-1.
4. Greenhaw BN, Zitelli JA, Broadland DG. Estimation of prognosis in invasive cutaneous melanoma: an independent study of accuracy of gene expression profile test. *Dermatol Surg.* 2018; 44:1494-1500. Doi: 10.1097/DSS. 0000000000001588.
5. Gastman BR et al. Performance of a 31-gene expression profile test in cutaneous melanomas of the head and neck. *Head Neck.* 2019; 41: 871-879. Doi: 10.1002/hed.25473.
6. Keller J et al. Prospective validation of the prognostic 41-gene expression profiling test in primary cutaneous melanoma. *Cancer Med.* 2019; 8: 2205-2212. Doi: 10.1002/cam4.2128.
7. Podlipnik S et al. Early outcome of a 31-gene expression profile test in 86 AJCC stage IB-II melanoma patients. A prospective multicentre cohort study. *JEADV.* 2019; 33: 857-862. Doi: 10.1111/jdv.15454

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