Clinical Significance of Gene Expression Profile Testing for Melanoma

Accumulated evidence on GEP Classification suggests that it provides clinically relevant information that can influence patient management for the better.

BY JONATHAN WOLFE, MD

Newer tools, such as gene expression profiling (GEP), are emerging to assist in prognostic assessment of melanoma patients. As discussed in my last column (available at PracticalDermatology.com), more accurate staging may allow the use of targeted treatment regimens with newer therapies, such as ipilimumab. GEP using the DecisionDx assay (Castle Biosciences), which uses reverse transcription polymerase chain reaction (RT-PCR) to assess the expression of 31 genes from primary melanoma tumors, has been shown to be an effective predictor of disease-free, distant metastasis-free, and overall survival in univariate and multivariate regression analysis.[1] A recent analysis further explores the clinical impact of GEP and potential applications for dermatology practice.[2]

ASSESSING GEP'S CLINICAL SIGNIFICANCE

The 31-gene expression profile test is used to predict whether a patient is at low-risk (Class 1) or high-risk (Class 2) for metastasis based on their primary tumor biology. For the current analysis, researchers reviewed medical charts for 156 cutaneous melanoma patients from six institutions (three dermatology and three surgical oncology practices) who consecutively underwent GEP testing.[2]

Based on AJCC stage, 42 percent of patients were Stage I, 47 percent were Stage II, and eight percent were Stage III. Based on GEP analysis, 95 patients (61 percent) were Class 1 and 61 (39 percent) were Class 2. Roughly half of patients (n=82, 53 percent) had documented changes in their management based on GEP classification. The majority of Class 2 patients (77 percent) had management changes—typi-

cally increased intensity of management. For 37 percent of Class 1 patients, there was a reduction in intensity of management.

Researchers stratified GEP Class and AJCC stage, determining that:

- 78 subjects with Stage I or IIA disease had Class 1 GEP status
- 18 subjects with Stage I or IIA disease had Class 2 GEP status
- 17 subjects with Stage IIB, IIC, or III disease had Class 1 GEP status
- 43 subjects with Stage IIB, IIC, or III disease had Class 2 GEP status.

These findings show that biologic characteristics of a melanoma offer additional information and, in fact, a different perspective on risk, compared to AJCC staging.

Among the 156 subjects analyzed for this paper, 112 underwent SLN mapping and biopsy. Within the Class 1 GEP group, five patients were subsequently found to be SLN-positive. None of these subjects had been recommended for an increase in management as a result of their Class 1 GEP results, and two had actually had recommended reductions in management intensity, based on Class 1 GEP status. Four of eight Class 2 GEP subjects who were subsequently found to be SLN-positive had been recommended for intensified management due to GEP classification; management recommendation had been unchanged for the remaining four, based on GEP classification. The authors emphasize that GEP findings may be assessed as *additional* information to SLN status, rather than as a replacement.

TABLE 1. MANAGEMENT "ACTIONS" ASSESSED

- Frequency of clinical visits (H&P)
- Frequency and modality of imaging (chest X-ray, CT, PET-CT, MRI, or ultrasound)
- SLNB procedure recommendation and result (if performed)
- Referral to surgical oncology
- Referral to medical oncology
- Use and frequency of routine bloodwork

TABLE 2. MANAGEMENT CHANGES BASED ON GEP CLASS

GEP Class	n; % of Total Group	Change in Management
1	95; 61%	37%
2	61; 39%	77%

INFORMATION WORTH HAVING

Other technologies are emerging to support diagnosis and assess risk for metastasis through gene expression analysis. A non-invasive adhesive patch biopsy-based LINC/PRAME gene expression test has been shown to improve biopsy specificity from 32.1 percent to 56.9 percent and improve biopsy sensitivity from 95 percent to 98.6 percent, according to a study just published in *JAMA Dermatology* last month (153(7):675-680). In research presented at ASCO 2017 (Hsueh and McMasters) gene testing identified 83 percent of melanoma patients who developed distant metastases as high risk; 50 percent were SLN positive. This further suggests that gene profiling can improve identification of those with high risk melanoma.

As technology expands, physicians are sometimes presented with information of uncertain clinical relevance. GEP appears to be different. The accumulated evidence on GEP Classification suggests that it does, indeed, provide clinically relevant information that can influence patient management for the better. Caution is necessary as GEP Class status must clearly be assessed in light of other data, including validated and accepted standards, including AJCC status. Additionally, the data to date suggest that GEP should not replace SLN biopsy and mapping when these are otherwise indicated. ∎

Jonathan Wolfe, MD is an Associate Professor of Dermatology at the University of Pennsylvania.

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2. Berger AC, Davidson RS, Poitras JK, Chabra I, Hope R, Brackeen A, Johnson CE, Maetzold DJ, Middlebrook B, Oelschlager KM, Cook RW, Monzon FA, Miller AR. Clinical impact of a 31-gene expression profile test for cutaneous melanoma in 156 prospectively and consecutively tested patients. Curr Med Res Opin. 2016 Sep;32(9):1599-604.