Melanoma Gene Test Promising, But More Data Needed

By Lila Abassi — November 4, 2015

Melanoma is a form of skin cancer affecting the cells responsible for producing the pigment in our skin. It ranks fifth and seventh in incidence of cancer in men and women, respectively.

What is most terrifying about the disease is that although it comprises only 4% of all skin cancers, it's associated with the most number of deaths in this category.

Caught early it is far more treatable, and so the American Joint Committee on Cancer (AJCC) divides melanoma into four stages, which takes into account tumor thickness and anatomical level of involvement (localized cutaneous disease) for stages I and II. Stage III involves local regional lymph nodes and stage IV includes distant metastasis (skin, subcutaneous tissue, nodal, visceral, skeletal or CNS).

What guides clinical decision making with regard to melanoma is the risk of metastasis and death. Currently, the AJCC is the standard predictive method utilized to guide clinicians in managing patients. The Individualized Melanoma Patient Outcome Prediction Tool predicts the five-year distant metastasis-free and overall survival of patients.

Sometimes melanoma is treated and comes back, but it has been difficult to know who is most at risk. Castle Biosciences, the makers of a newer test called the Gene Expression Profile (GEP), commercially available as DecisionDx, believe it can accurately identify 80% of Stage I and II patients at high risk of metastatic disease. Additionally, the makers believe they are able to identify those patients as high risk who are node-negative meaning a biopsy of the lymph node did not reveal cancer thereby identifying patients who were previously thought to be in the clear.

The tissue samples studied are categorized according to their metastatic risk based on their molecular signature. Class 1 is low-risk and Class 2 is high risk.

Clearly, the greatest potential benefit is in those patients with intermediate risk melanomas (Stage I and II) as there is no consensus on how to manage them. In a study conducted by Pedram Gerami, MD, Associate Professor in Dermatology, Pathology, and Pediatrics-Dermatology at Northwestern University Feinberg School of Medicine, as compared to having a high-risk AJCC score a Class 2 GEP score has been shown to be 1.5 times more likely to have a poor outcome. This means these patients could receive life-saving preventive therapies.

As promising as this sounds, the data is based on a small sample size (n=217). There are 73,000 melanoma patients per year, so you need almost 400 to have a 95 percent confidence interval and that's without the worry about false positives.

To truly say that a patient previously thought of low risk should proceed with invasive procedures
such as a sentinel lymph node biopsy (SLNB), increased scans or systemic treatments, they need a much larger trial. According to Klaus J. Busam, MD, Director of Dermatopathology Service and the Dermatopathology Fellowship at Memorial Sloan Kettering Cancer Center, The GEP has not yet been adequately tested for outcomes prediction; we have only a few hundred cases of the GEP test; the AJCC has 60,000 cases."

There are three key issues with the DecisionDX test:

(1) A greater number of false positives versus SLNB and that is accompanied by obvious negative sequelae, i.e. demoralizing the patient and unnecessary tests that have not been shown to improve survival;

(2) Increasing the number of scans a patient requires for surveillance per year does not equate to survival benefit;

(3) The GEP test costs up to $7,000 but a sentinel lymph node biopsy is only $12,000 to $15,000. A patient would still need to have both performed, as the GEP test alone is not considered standard of care. The lower cost may be offset by the potential costs related to unnecessary treatment and surveillance associated with false positive test results.

Ideally, there would be a larger prospective study to provide enough robust data to confidently say that GEP testing should be used as the standard prognosticating tool when determining how to manage patients with intermediate risk Stage I/II melanoma.

According to John Vetto, MD, a surgical oncologist at Oregon Health & Science University, These data are early and exciting, but are only on a few hundred patients. We need confirmation in a prospective trial.

Considerable caution should be urged until further more substantial data becomes available.