Hearing the words “you have skin cancer” is overwhelming and would leave anyone with a lot of questions. If you have been diagnosed with Stage I or II cutaneous melanoma with no apparent spread to the lymph nodes, it is important to know about a new molecular test that can tell you if your cancer is actually at high risk of spreading.

The gene expression profile test, DecisionDx-Melanoma, is available only through Castle Biosciences, a company which focuses on molecular diagnostic and prognostic testing for rare cancers. Castle developed this guide to help you and your doctor decide whether this test is right for you.
The Challenge: Identifying High-Risk Disease in Stage I or II Melanoma

Like other cancers, melanoma can spread through the hematogenous (or blood) system, the lymphatic system, or both. Since there is currently no method to detect metastasis in the blood, physicians have relied solely on histologic features of the tumor and sentinel lymph node biopsy to determine risk of the disease spreading. This may help explain why an estimated 8,500 (14%) of the 60,000 people diagnosed each year with Stage I or II melanoma do metastasize—even though they were thought to be at lower risk. It also indicates the need for additional tools for determining prognosis.

While tumor depth and sentinel node status are the strongest traditional predictors of outcome in patients with cutaneous melanoma, there is wide variability in metastatic rates within, and across stages. As you can see in Table 1, some Stage II patients will have a similar or even higher metastatic risk than some patients in Stage III, yet as a group they are generally treated very differently.

For example, most patients in Stage II solely receive routine skin exams, and are not recommended for imaging, such as brain or lung scans, or considered for adjuvant therapy options. However, those Stage II patients with high-risk tumor biology could potentially benefit from more aggressive monitoring and treatment. Similarly, while at a lower overall risk of metastasis, some patients with Stage I melanoma do metastasize, yet they are treated as low-risk patients.

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<th>Table 1: AJCC Survival by Stage</th>
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<td>Stage I</td>
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Addressing the Unmet Need in Cutaneous Melanoma

Validated as a more accurate predictor of metastatic risk than all other traditional staging factors, the DecisionDx-Melanoma test can help a patient and their physician determine the optimal follow-up and treatment plan by incorporating accurate, personalized information about their tumor biology.

The DecisionDx-Melanoma gene expression profile (GEP) test was developed to provide insight beyond histopathology to help identify the AJCC Stage I or II patients who may be at high risk of metastasis. The test requires a small sample of the tumor for laboratory analysis, which can be taken from remaining diagnostic biopsy tissue, or from tissue collected during subsequent surgery, such as wide excision.

Specifically, DecisionDx-Melanoma quantifies the expression of 31 genes (3 control, 28 discriminating) within the individual tumor using real time polymerase chain reaction technology. A validated algorithm is then applied to stratify patients into low-risk Class 1, with a 4% chance of spreading within 5 years, or high-risk Class 2, with a 72% chance of metastasis within 5 years.

Potential Impact of DecisionDx-Melanoma Test

The GEP test's ability to accurately identify risk could have significant impact on evaluation, treatment, and long-term survival. For instance, patients whose tumor biology has a Class 2 signature could realize several benefits: Referral to surgeon/oncologist for consideration of higher intensity monitoring, sentinel lymph node biopsy (if not originally performed), adjuvant treatment, or clinical trials.
GEP Test Validated as Highly Accurate Predictor of Risk

The accuracy of the DecisionDx-Melanoma test was analyzed in a prospectively designed, multi-center study using archival specimens. The study was the largest melanoma biomarker study of its kind, and showed that DecisionDx-Melanoma provided an accurate identification of patients who were at low risk or high risk of metastasis in both the training and validation sets, irrespective of all other histologic factors. The study confirmed the previous development data which showed that by analyzing the expression of 31 genes within a patient's tumor, DecisionDx-Melanoma can, with a high rate of accuracy, identify 5-year metastatic risk.

Analysis of the training set showed a sensitivity of predicting metastatic disease of 85% with a Reciprocal Operating Characteristic (ROC) of 90%. Prediction of metastatic risk for the independent validation set resulted in a sensitivity of predicting metastatic disease of 89% and an ROC of 92% (Table 2).

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<tr>
<th>Study</th>
<th>Sensitivity in Predicting Metastasis</th>
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<tr>
<td>Training Study</td>
<td>85%</td>
<td>90%</td>
</tr>
<tr>
<td>Test Study</td>
<td>89%</td>
<td>92%</td>
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Independence of the DecisionDx-Melanoma test was evaluated using Cox regression analysis for patients with Stage I or II melanoma. Cox regression analysis was performed using both the individual AJCC staging criteria of Breslow's thickness, ulceration, and mitosis as well as the combined factors of AJCC stage. The analysis showed that Breslow's thickness is an important predictor of metastatic disease as is AJCC stage. The DecisionDx-Melanoma test was also shown to be an important predictor of metastasis.
Fact Sheet

Importantly, multivariate analyses found the DecisionDx-Melanoma test to be superior to and independent of Breslow's thickness, ulceration status and mitotic index in predicting metastatic disease.

Similarly, multivariate analyses found the DecisionDx-Melanoma test to be superior to and independent of AJCC stage (Stage I, IIA versus IIB, IIC) in predicting metastatic disease.

For additional data results, please see the Clinical Validation section of SkinMelanoma.com, an informational website for patients, doctors and managed care professionals. However, note that some data will not be posted until publication in appropriate medical journals.

MORE INFORMATION

How to Order

DecisionDx-Melanoma is now available as a CAP-accredited / CLIA-certified laboratory service, and can only be ordered by a licensed physician.

New customers: Call customer service line (866-788-9007) to review the ordering/shipping process before placing your order. Or, email us at contact@castlebiosciences.com. All customers must fill out and fax the requisition form, which can be found in the Health Care Professionals section of SkinMelanoma.com. Turnaround time is generally less than two to three weeks following receipt of the specimen from the pathology lab.

Reimbursement

Castle Biosciences works with Medicare, commercial insurers, and the physician's institution to secure coverage for DecisionDx-Melanoma on the patient's behalf. The Company accepts assignment for all insurance companies, and also has a Patient Assistance Program.
References


