# Talk to Your Doctor

If you have been diagnosed with Stage I or II melanoma, it is important to know about a gene test that can provide information about your cancer's risk of spreading, based on your tumor's biology.

The DecisionDx-Melanoma gene expression profile test was discovered and developed by Castle Biosciences, and validated in the largest melanoma biomarker study of its kind. We developed this guide to help you and your doctor decide whether this test is right for you.

MELANOMA DECISIONDx

Fact Sheet

**TEST OVERVIEW**

## What is DecisionDx-Melanoma?

- DecisionDx-Melanoma is a gene expression profile test (GEP) developed to identify high risk Stage I and II patients based on biological information from their tumor tissue. (The assay requires a small sample for lab analysis, obtained from remaining diagnostic biopsy tissue or collected during surgery.)
- The gene test 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 3% chance of spreading within 5 years, or high risk Class 2, with a 69% risk.
- Validated as an accurate, independent predictor of a patient's metastatic risk — irrespective of stage — the DecisionDx-Melanoma test provides additional, personalized information to determine how aggressively to manage the disease.
- A new study analysis presented at the American Academy of Dermatology (AAD) 2014 annual meeting supports the accuracy of the GEP test, showing that the assay can identify the vast majority of primary melanoma tumors that are likely to metastasize in patients who had a negative sentinel lymph node biopsy (SLNB-), historically considered the most accurate prognostic procedure.

**BACKGROUND**

## The Challenge: Identifying High Risk Disease in Stage I or II Melanoma

- A certain percentage of the 60,000 early stage patients diagnosed each year will see their disease progress at some point after the primary tumor is removed.
- While traditional staging provides valuable prognostic information, it does miss many patients. Traditionally a positive sentinel lymph biopsy (SLNB+) result upstages a patient from Stage I or II to Stage III. Stage III is considered the highest risk stage group for disease progression. However, calculations from the AJCC staging guidelines show that two out of three patients that will progress are Stage I or II, including those who had an SLNB with a negative result.

**BACKGROUND** *continued*

- Multi-center studies of the DecisionDx-Melanoma gene test found that there are a number of Stage I and II patients with high risk tumor biology who are missed by staging and SLNB. In fact, patients with Class 2 biology were shown to have a significantly higher metastatic risk than most Stage III patients and it is thought that they should be considered for more aggressive management to avoid under-treatment relative to their risk.
- This, then, is the challenge—identifying the patients staged at low risk of metastasis (by the traditional staging factors and SLNB) who are actually at high risk.
- DecisionDx-Melanoma is designed to address this challenge—using an objective, individualized tool based upon the genomic make-up of the primary tumor for predicting metastatic risk.

**POTENTIAL IMPACT**

## Implications for Managing the Disease

- The information provided by DecisionDx-Melanoma can have significant implications for the management and treatment of early stage disease.
- For example, most Stage II patients solely receive routine skin exams and clinical examination of the lymph nodes, and are not recommended for imaging, such as brain or lung scans, or considered for adjuvant therapy options. Yet, if those Stage II patients were identified as having high risk tumor biology—higher risk than the average Stage III patient, then their doctor might consider further lymph node interrogation, active surveillance, or referral to medical oncology for consideration of systemic drug therapy or clinical trials.
- Similarly, while at a lower overall risk of metastasis, some patients with Stage I melanoma ultimately do metastasize, yet they are treated as low risk patients. If identified, they too could be considered for more aggressive monitoring and treatment.
- While it is not often the urgent focus of oncology management discussions, the impact of receiving a low risk Class 1 designation should not be underestimated.

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**CLINICAL DATA**

## Gene Test Validated as Highly Accurate Predictor of Risk

- The DecisionDx-Melanoma test was analyzed in a prospectively designed, multi-center study using archival specimens in the largest biomarker study of its kind. The study showed that the gene test accurately identified patients who were at high or low risk of metastasis in both the training and validation sets, irrespective of all other traditional staging factors. The study confirmed previous development data.
- Prediction of metastatic risk for the independent validation set resulted in a sensitivity of predicting metastatic disease of 89% and an ROC of 92% (ROC = Receiver Operating Characteristics). Generally speaking, an ROC greater than 80% is considered clinically useful.
- Cox regression analysis for Stage I and II patients showed that Breslow's thickness, AJCC stage and the DecisionDx-Melanoma test are each important predictors of metastatic disease.
- Multivariate analyses found the DecisionDx-Melanoma test to be an independent predictor of metastatic disease to Breslow's thickness, ulceration status, mitotic index, and AJCC stage (Stage I, IIA vs. IIB, IIC).
- New study data presented at AAD 2014 further support the accuracy of the GEP test. Researchers compared GEP and SLNB test results in archival tumor tissue of 134 patients, and results show the GEP assay can identify the vast majority of SLNB- patients who ultimately progressed over the subsequent 5-year period. The rate of 5-year metastasis free survival (MFS) was 55% for SLNB- patients compared to 37% for SLNB+ patients ($p=0.003$). The GEP test results showed improved prognostic accuracy in these same patients with an MFS of 87% for the low risk (Class 1) patients and 31% for the high risk (Class 2) patients ($p<0.0001$).
- For additional data results, please see Clinical Validation and New GEP/SLNB Study pages in the Healthcare Professionals section of SkinMelanoma.com. Additional data from the validation studies will be posted upon publication in medical journals.

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**MORE INFORMATION**

## How to Order

- DecisionDx-Melanoma was discovered and developed by Castle Biosciences. The test is available as a CAP-accredited, CLIA-certified laboratory service and can only be ordered by a licensed physician or other appropriate healthcare provider through direction submission of a requisition to Castle.
- New customers: Call customer service line (866-788-9007) to review the ordering/shipping process before placing your order. Alternately, you may email us at contact@castlebiosciences.com.
- All customers must fill out and fax the requisition form, which can be found in the Healthcare Professionals section of SkinMelanoma.com. Turnaround time is generally less than two to three weeks following receipt of the tumor tissue 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.

## To Learn More

- SkinMelanoma.com was created to provide information to Stage I and II melanoma patients, doctors and insurers about cutaneous melanoma and the value of the DecisionDx-Melanoma prognostic test.

CASTLE BIOSCIENCES INCORPORATED

**MORE INFORMATION**
*continued*

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**MORE INFORMATION**
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