NEWS RELEASE

Meta-Analysis Showing DecisionDx-Melanoma Test as Independent, Significant Predictor of Recurrence and Metastatic Risk Presented during Late-Breaking Research Session at the 2019 AAD Annual Meeting

3/4/2019

PDF Version

Additional data presented at AAD demonstrate value of the DecisionDx-Melanoma test in identifying high-risk patients with Stage IB-IIA cutaneous melanoma and provide update on cSCC test development

Friendswood, TX – March 4, 2019 – Castle Biosciences, Inc., a skin cancer diagnostics company providing personalized genomic information to improve cancer management decisions, today announced three presentations at the 2019 American Academy of Dermatology (AAD) Annual Meeting held in Washington, DC from March 1-5.

A meta-analysis of four DecisionDx®-Melanoma studies including 1,479 patients titled, "Meta-Analysis of the Prognostic 31-Gene Expression Profile Test in 1479 Melanoma Cases," was presented during the Late-Breaking Research: Basic Science/Cutaneous Oncology/Pathology session. The study demonstrates that the DecisionDx-Melanoma test is an independent, significant predictor of recurrence and metastatic risk in a meta-analysis of four study cohorts.

DecisionDx-Melanoma Meta-Analysis

Multiple published archival and prospective studies have described the prognostic capability, performance and clinical utility of the DecisionDx-Melanoma test to assess recurrence risk and inform patient management decisions

on sentinel lymph node recommendations, follow up, surveillance imaging, and referrals for patients with cutaneous melanoma.

This meta-analysis was performed to evaluate the cumulative prognostic effect of the test across multiple cohorts with a focus on differences in recurrence and distant metastasis between patients with a Class 1A (lowest risk) and Class 2B (highest risk) test result. Three published studies and one newly reported cohort including a total of 1,479 non-overlapping patients with Stage I-III melanoma were included in the analysis.

Key Study Findings:

- The meta-analysis demonstrates that the DecisionDx-Melanoma test accurately identifies cutaneous melanoma patients who are at greater risk of metastasis with an effect that is consistent across multiple studies reaching the highest Strength of Recommendation Taxonomy (SORT) level for a prognostic biomarker (Level 1A evidence).
- The DecisionDx-Melanoma test was found to be a consistent, independent and significant predictor of recurrence and metastatic risk in a meta-analysis of four study cohorts.
- The DecisionDx-Melanoma risk assessment is independent from other clinical factors (age, Breslow tumor thickness, ulceration and node status)
- Patients with Class 2B tumors are 2.83 times more likely to experience a recurrence than patients with Class 1A tumors ($p<0.0001$). Likewise, patients with Class 2B tumors are 2.75 times more likely to experience a distant metastasis than patients with Class 1A tumors ($p<0.0001$).
- Despite differences in populations and study design, heterogeneity among the four studies was not significant.

“This study is important because it demonstrates the strong and consistent effect of the DecisionDx-Melanoma test as a significant, independent predictor of recurrence and metastasis in patients with Stage I-III melanoma,” said lead author Bradley Greenhaw, M.D., Dermatology Center of North Mississippi, Tupelo, Mississippi. “Across these four unique study cohorts, this meta-analysis shows that the highest level of evidence supports the use of the DecisionDx-Melanoma gene expression profile test to inform patient management decisions.”

The SORT system is used by the AAD and other organizations to evaluate the quality, quantity and consistency of evidence supporting tests such as DecisionDx-Melanoma. The SORT scale evaluates both the quality of the evidence (Level 1, 2 or 3) and strength of the recommendation (A, B or C). Using SORT ranking, a systematic review or meta-analysis of good quality studies or a prospective study with good follow-up represents the highest level of evidence (Level 1), and recommendations based on consistent, good quality evidence are deemed strongest (Strength of Recommendation: A).

Additional Castle Biosciences Data

DecisionDx-Melanoma Value in Stage IB-IIA Melanoma

A second study titled, “Improved Risk Assessment through Incorporation of a Prognostic 31-gene Expression Profile Test for AJCC Stage IB-IIA Cutaneous Melanoma,” (Abstract 10597), which highlights the test’s accuracy in patients with Stage IB-IIA melanoma was presented as a poster at the AAD 2019 Annual Meeting.

Risk assessment is critical for guiding patient care decisions and treatment of cutaneous melanoma, especially for patients with Stage IB-IIA cutaneous melanoma who are considered for sentinel lymph node biopsy and adjuvant clinical trials. This study of 214 patients with Stage IB-IIA cutaneous melanoma from a previously published multicenter cohort with long-term outcomes assessed the use of AJCC staging combined with results from the DecisionDx-Melanoma test to improve recurrence risk prediction.

Key Study Findings:

- Using AJCC staging alone, patients with Stage IB melanoma have an estimated 5-year melanoma specific survival (MSS) rate of 97%. Among these patients, those with a Class 1A (lowest risk) DecisionDx-Melanoma test result had an MSS rate of 98.6%, a risk equivalent to AJCC Stage IA. However, patients in this group who had a Class 2B (highest risk) test result had an 87.5% 5-year MSS rate. These risk estimates are lower than AJCC Stage IIIA disease.
- Patients with Stage IIA cutaneous melanoma had an estimated 5-year MSS rate of 94% using AJCC staging alone. Patients in that group who had a Class 1A DecisionDx-Melanoma test result had an MSS rate of >99% (equivalent to Stage IA). Patients with a Class 2B test result had a 5-year MSS rate of 85.7%, similar to risk estimates for AJCC Stage IIIB.
- As a group, Stage IB-IIA patients with a Class 1A result had significantly higher MSS, DMFS and RFS rates of 98.8%, 92.0% and 87.4% than those for patients with a Class 2B result (86.7%, 69.4% and 52%; $p<0.01$).

“Accurate risk assessment is important for clinical decision-making, especially for patients with Stage IB and IIA cutaneous melanoma who may be candidates for sentinel lymph node biopsy and adjuvant therapy clinical trials,” commented study co-author Darrell S. Rigel, M.D., M.S., Clinical Professor at New York University School of Medicine. “These results show that use of the DecisionDx-Melanoma test further stratified patients into lower and higher risk groups following AJCC staging, supporting its value in developing individualized patient management plans and potentially future adjuvant therapy trials.”

Update on cSCC Test Development

An update on the development of a cutaneous squamous cell carcinoma (cSCC) test was also presented at the AAD 2019 meeting as a poster (with oral discussion) titled, “Microarray Analysis to Identify Genes Associated with a High-Risk of Metastasis in Cutaneous Squamous Cell Carcinoma Tumors,” (Abstract 10630). Many patients with cSCC will have a favorable prognosis, but a substantial number of them will experience metastasis or develop recurrences and die from their disease. The goal of this development program is to identify and validate a test that improves upon existing staging systems by identifying patients who have a relatively high risk for recurrence and enable more informed clinical management decisions.

As part of a larger archival development study, microarray analysis was performed on 80 recurrent and non-recurrent cases to identify novel genes associated with disease outcomes. Predictive modeling was performed to select and prioritize genes based on preliminary accuracy metrics for recurrence prediction. A subset of selected genes demonstrated positive correlation between microarray and qPCR analysis, suggesting feasibility in a clinical assay. Gene expression from microarray-identified targets will now be analyzed together with targets previously identified from the literature in order to optimize a prognostic signature.

Collaborative site recruitment and clinical trial activities for the cSCC test development program are actively continuing.

About DecisionDx-Melanoma

DecisionDx-Melanoma is a gene expression profile test that uses an individual patient’s tumor biology to predict individual risk of cutaneous melanoma metastasis or recurrence, as well as sentinel lymph node positivity, independent of traditional staging factors and has been studied in over 2,900 patients. Using tissue from the primary melanoma, the test measures the expression of 31 genes. The test has been validated in three multicenter studies that have included 690 patients and have demonstrated consistent results. Performance has also been confirmed in five prospective studies including over 780 patients. The consistent high performance and accuracy demonstrated in these studies, which combined have included over 1,470 patients, provides confidence in disease management plans that incorporate DecisionDx-Melanoma test results.

Prediction of the likelihood of sentinel lymph node positivity has also been validated in two prospective multicenter studies that included over 1,400 patients. Impact on patient management plans for one of every two patients tested has been demonstrated in multicenter and single-center studies. More information about the test and disease can be found at **www.SkinMelanoma.com**.

About Cutaneous Squamous Cell Carcinoma

Cutaneous squamous cell carcinoma (cSCC), a non-melanoma skin cancer, is one of the most common cancers.

Approximately 200,000 patients are diagnosed with cSCC with high-risk features. Most patients have a favorable prognosis, but a subset of patients will develop metastasis and up to 15,000 patients each year die from their disease. As current staging parameters have a low positive predictive value, many more patients are considered high risk than actually develop metastatic disease. Conversely, many patients that develop metastatic disease are misidentified as low risk. This leads to over and undertreatment of a substantial number of cSCC patients. To address this clinical need, Castle Biosciences is developing a gene expression profile test to improve upon current staging systems and identify patients with cSCC at high risk for metastasis or recurrence, enabling more informed clinical decisions regarding adjuvant therapy and other management options.

About Castle Biosciences

Castle Biosciences is a skin cancer diagnostics company dedicated to helping patients and their physicians make more informed decisions about treatment and follow up care based on the individual molecular signature of the patient's tumor. The Company currently offers tests for patients with cutaneous melanoma (DecisionDx®-Melanoma, DecisionDx®-CMSeq; www.SkinMelanoma.com) and uveal melanoma (DecisionDx®-UM, DecisionDx®-PRAME and DecisionDx®-UMSeq; www.MyUvealMelanoma.com), with programs in development for other underserved cancers, the most advanced of which is focused on patients with cutaneous squamous cell carcinoma. Castle Biosciences is based in Friendswood, Texas (Houston), and has laboratory operations in Phoenix, Arizona. More information can be found at www.CastleBiosciences.com.

Contact

Derek Maetzold, President and CEO

866-788-9007

IR@castlebiosciences.com

PDF Version