NEWS RELEASE

Study Demonstrates Use of DecisionDx®-Melanoma to Guide Treatment Decisions Resulted in Earlier Detection of Melanoma with Decreased Metastatic Tumor Burden Compared to Patients Without Surveillance Imaging Studies

5/3/2023

New independent, multi-center study found that patients who received high-risk DecisionDx-Melanoma test results received routine imaging, which led to earlier detection of recurrences, when the tumor burden was lower, which could result in better clinical outcomes

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced the publication of an independent, multi-center study in the Archives of Dermatological Research providing a direct chain of evidence that use of DecisionDx®-Melanoma test results to guide radiological surveillance could lead to improved patient outcomes.[1] The study, authored by Dhillon et al., can be found **here**.

“Published clinical use data, coupled with improved responses with immunotherapy when the metastatic tumor burden is lower, has previously shown an indirect chain of evidence between the clinical use of our DecisionDx-Melanoma test and improved outcomes due to early detection of metastasis and therefore early treatment intervention,” said Derek Maetzold, president and chief executive officer of Castle Biosciences. “We believe this study is significant in that it provides a direct chain of evidence between the use of DecisionDx-Melanoma to guide treatment plan decisions, which could result in improved survival compared to patients from the same institution who did not have their treatment plans informed by our test.”

DecisionDx-Melanoma has been validated to inform two clinical decisions in the management of patients with cutaneous melanoma (CM) that are made in the acute post-diagnosis time period:

1) Use of a sentinel lymph node biopsy (SLNB) surgical procedure,[2] and
2) The subsequent risk-guided follow-up and management plans that are differentiated between patients who have a high versus a low likelihood of metastasis.[3]

"In melanoma, as in all cancers, treatment plan decisions are guided by the risk of disease recurrence and metastasis," continued Maetzold. "In this study, the authors controlled for SLNB (all patients underwent the procedure and were negative) and evaluated the impact of implementing risk-guided metastatic surveillance treatment plans for patients with a high-risk DecisionDx-Melanoma test result versus standard of care under the current guidelines. The direct improvement in melanoma-specific survival is what we would expect based upon indirect chain of evidence analyses."

The Dhillon et al. study, conducted at three National Cancer Institute-designated cancer centers, included patients with Stage I or II CM who had a negative SLNB. The experimental group was comprised of patients who had received high-risk DecisionDx-Melanoma test results and thus received routine imaging every six to twelve months. Patients in the control group did not receive DecisionDx-Melanoma testing and had imaging studies driven only by clinical symptoms or physical exam findings.

Key findings of the study include:

- Patients in the experimental group who received DecisionDx-Melanoma testing and surveillance imaging had melanoma recurrences detected approximately ten months earlier than patients in the control group (p=0.049).
- The average tumor burden detected at patients' melanoma recurrence was significantly lower in the experimental group compared to the control group (27.6 mm vs. 73.1 mm; p=0.027). Note: recent studies cited in the paper suggest a survival benefit when metastatic melanoma is treated at a lower tumor burden.
- Of the patients with a recurrence, 82% in the experimental group and 71% in the control group started immunotherapy.
- At patients' last follow up, 76% of the patients with melanoma recurrence in the experimental group were alive (average follow-up time=45.6 months), compared to 50% of recurrent melanoma patients in the control group (average follow-up time=63.3 months) (p=0.027).

Overall, the study found that using DecisionDx-Melanoma to risk-stratify patients to guide care resulted in earlier detection of melanoma recurrence while the tumor burden was lower, which could lead to improved patient outcomes.

About DecisionDx®-Melanoma

DecisionDx-Melanoma is a gene expression profile risk stratification test. It is designed to inform two clinical questions in the management of cutaneous melanoma: a patient's individual risk of sentinel lymph node (SLN) positivity and a patient's personal risk of melanoma recurrence and/or metastasis. By integrating tumor biology with clinical and pathologic factors using a validated proprietary algorithm, DecisionDx-Melanoma is designed to provide a comprehensive and clinically actionable result to guide risk-aligned patient care. DecisionDx-Melanoma has been shown to be associated with improved patient survival and has been studied in more than 10,000 patient samples. DecisionDx-Melanoma's clinical value is supported by more than 40 peer-reviewed and published studies, providing confidence in disease management plans that incorporate the test's results. Through Dec. 31, 2022, DecisionDx-Melanoma has been ordered 120,287 times for patients diagnosed with cutaneous melanoma. More information about the test and disease can be found at **www.CastleTestInfo.com.**

About Castle Biosciences

Castle Biosciences (Nasdaq: CSTL) is a leading diagnostics company improving health through innovative tests that guide patient care. The Company aims to transform disease management by keeping people first: patients, clinicians, employees and investors.

Castle's current portfolio consists of tests for skin cancers, uveal melanoma, Barrett's esophagus and mental health conditions. Additionally, the Company has active research and development programs for tests in other diseases with high clinical need, including its test in development to predict systemic therapy response in patients with moderate-to-severe psoriasis, atopic dermatitis and related conditions. To learn more, please visit **www.CastleBiosciences.com** and connect with us on **LinkedIn**, **Facebook**, **Twitter** and **Instagram**.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. These forward-looking statements include, but are not limited to, statements concerning the potential of DecisionDx-Melanoma to improve patient outcomes, including improved survival, as a result of treatment plans being informed by the DecisionDx-Melanoma test result. The words "can," "potential" and similar expressions are intended to identify forward-looking statements, although not all forward-

looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. These forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from those in the forward-looking statements, including, without limitation: subsequent study or trial results and findings may contradict earlier study or trial results and findings or may not support the recommendations and guidelines presented in this report, including with respect to the discussion of DecisionDx-Melanoma in this press release; actual application of our tests may not provide the aforementioned benefits to patients; the design of the study referenced in this press release is subject to certain limitations, including the retrospective nature of the study, limited sample size of patients, lack of uniform imaging protocols among the three sites (including the type of imaging study recommended), differences in surveillance intervals, and differences in patient follow-up lengths for patients with recurrence; and the risks set forth under the heading "Risk Factors" in our Annual Report on Form 10-K for the twelve months ended December 31, 2022, and in our other filings with the SEC. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements, except as may be required by law.

1. Dhillon S, Duarte-Bateman D, Fowler G, et al. Routine imaging guided by a 31-gene expression profile assay results in earlier detection of melanoma with decreased metastatic tumor burden compared to patients without surveillance imaging studies. Arch Dermatol Res. 2023. **https://doi.org/10.1007/s00403-023-02613-6**. Accessed April 10, 2023.
2. Whitman E, Koshenkov V, Gastman B, et al. Integrating 31-Gene Expression Profiling with Clinicopathologic Features to Optimize Cutaneous Melanoma Sentinel Lymph Node Metastasis Prediction. JCO Precis Oncol. 2021;(5):1466-1479. doi:10.1200/PO.21.00162
3. Jarell A, Gastman B, Dillon L, et al. Optimizing treatment approaches for patients with cutaneous melanoma by integrating clinical and pathologic features with the 31-gene expression profile test. J Am Acad Dermatol. 2022. doi: **https://doi.org/10.1016/j.jaad.2022.06.1202**

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Source: Castle Biosciences, Inc.