100 S. Commons, Suite 245,
Pittsburgh, PA 15212

FINAL REPORT

Patient: Patient Name
Sex: Male
DOB: 04/01/1980
MRN: MRN123
Client: Institution
Clinician: Treating Clinician

Type of Specimen: Fresh Frozen FNAB
Specimen ID: FNAB
Collected: 01/01/2025
Received: 01/02/2025
Reported: 01/03/2025

DecisionDx-UM Result

Class 1
Discriminant Value: 0.52

Class 1 molecular signature is associated with a low risk of near term (within 5 years) clinical metastasis. A discriminant value ≥0.10 is reported with normal confidence.

Test results should be interpreted using the Clinical Experience information below, which is derived from clinical studies involving patient populations with specific clinical features. These results have not been validated in patients with clinical features different from those described. The discriminant value relates to Class 1 vs 2. See page 2 of report for discussion on discriminant value confidence.

Clinical Experience for DecisionDx-UM

The clinical performance of the DecisionDx-UM test has been evaluated in multiple prospective and retrospective studies. The two largest prospective multi-center studies are COOG1 and COOG2.

DecisionDx-UM Performance in the COOG2 Study:
COOG2 is the largest and most contemporary study (censor date of March 9, 2023) and included 1,577 patients with follow-up data available for analysis. Patients were prospectively enrolled between Jan. 2017 and April 2020. The outcomes for metastasis for Class 1 and Class 2 are shown below. In the COOG2 study, the performance of *PRAME* gene expression status was shown to refine the predicted risk of metastasis within Class 1 and Class 2 tumors. *PRAME* status is reported separately on the DecisionDx-PRAME report and can be ordered by selecting the appropriate option on the requisition form. Class 1 tumors were previously divided into sub-classes 1A and 1B based upon the COOG1 study and other studies - see page 2 and (*) below.

Molecular Class	Precentage Metastasis Free (3 years)	Percentage Metastasis Free (5 years)
Class 1*	**96.2%** (95.1%, 97.4%)	**92.3%** (90.2%, 94.4%)
Class 2	**63.9%** (59.6%, 68.5%)	**52.1%** (47.0%, 57.8%)

N=1,577; Log-rank (Mantel-Cox) test; p<0.001

***Subanalysis indicates this tumor is sub-class 1A, which was associated with the lowest metastatic risk, based on data from the prospective COOG1 validation study.**

Digitally signed by Castle Lab Director, PhD, HCLD[R01]

Castle Biosciences, Inc. | Sherri Borman, PhD, HCLD, Lab Director

This test was developed and its performance characteristics determined by Castle Biosciences Inc. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research.

DecisionDx-UM Performance in the COOG1 Study:

The first prospective multi-center study, COOG1, validated the predictive accuracy of DecisionDx-UM. Outcomes were collected and the ability of the molecular signature to predict metastasis was evaluated in tumors obtained from patients between Nov. 1998 and Nov. 2010. The latest censor date was June 9, 2011. Class 1 tumors were further divided into prognostically distinct sub-classes 1A and 1B based on data from this initial validation study (data on file). At five years, the metastasis-free survival rates were 98% for Class 1A (lowest risk of metastasis), 79% for Class 1B (intermediate risk), and 28% for Class 2 (highest risk).

Additional Information

Performance variation between COOG1 and COOG2 cohorts may be attributed to shifts in the baseline demographic differences and clinical management of uveal melanoma patients over time. COOG2 contained substantially more small tumors and less enucleated tumors than COOG1. In addition to COOG1 and COOG2, numerous other prospective and retrospective studies have confirmed that Class 1 and 2 tumors have distinct and significantly different survival outcomes, and that the prognostic accuracy of the DecisionDx-UM test is independent from and exceeds that of clinicopathologic factors, cytogenetics, *PRAME* status, and mutations.

Assay Description

The DecisionDx-UM molecular test for uveal melanoma is a proprietary test that uses RT-PCR to determine the expression of a panel of 12 discriminating genes and 3 control genes in the primary tumor tissue. The twelve genes of interest are: *CDH1, ECM1, EIF1B, FXR1, HTR2B, ID2, LMCD1, LTA4H, MTUS1, RAB31, ROBO1,* and *SATB1*. The three control genes are: *MRPS21, RBM23,* and *SAP130*. The optimized molecular model determines Δ Ct values for each of the twelve genes of interest. The Δ Ct values are imported into a support vector machine learning algorithm (SVM), which analyzes their combined gene expression profile. SVM calculates a predicted classification and a discriminant value. As the absolute value of the discriminant value approaches zero, the probability that the prediction is incorrect increases. Discriminant values from the concordance study conducted on both FNAB and FFPE specimens were analyzed at 97.5% and 95% confidence levels. The 97.5% confidence level equated to a discriminant value of 0.07; the 95% confidence level equated to a discriminant value of 0.06. Based on these findings, a conservative discriminant value cut-point of 0.10 has been set to differentiate between normal and reduced confidence.

For additional information about the data supporting the DecisionDx-UM test, scan the QR code below.