Report Guide

DecisionDx-Melanoma

The DecisionDx®-Melanoma class result and GEP score is combined with clinicopathologic features to provide an individualized risk estimate for risk of recurrence and/or metastasis within five years and likelihood of a positive sentinel lymph node using validated artificial intelligence algorithms.

CLASS RESULT AND GEP SCORE

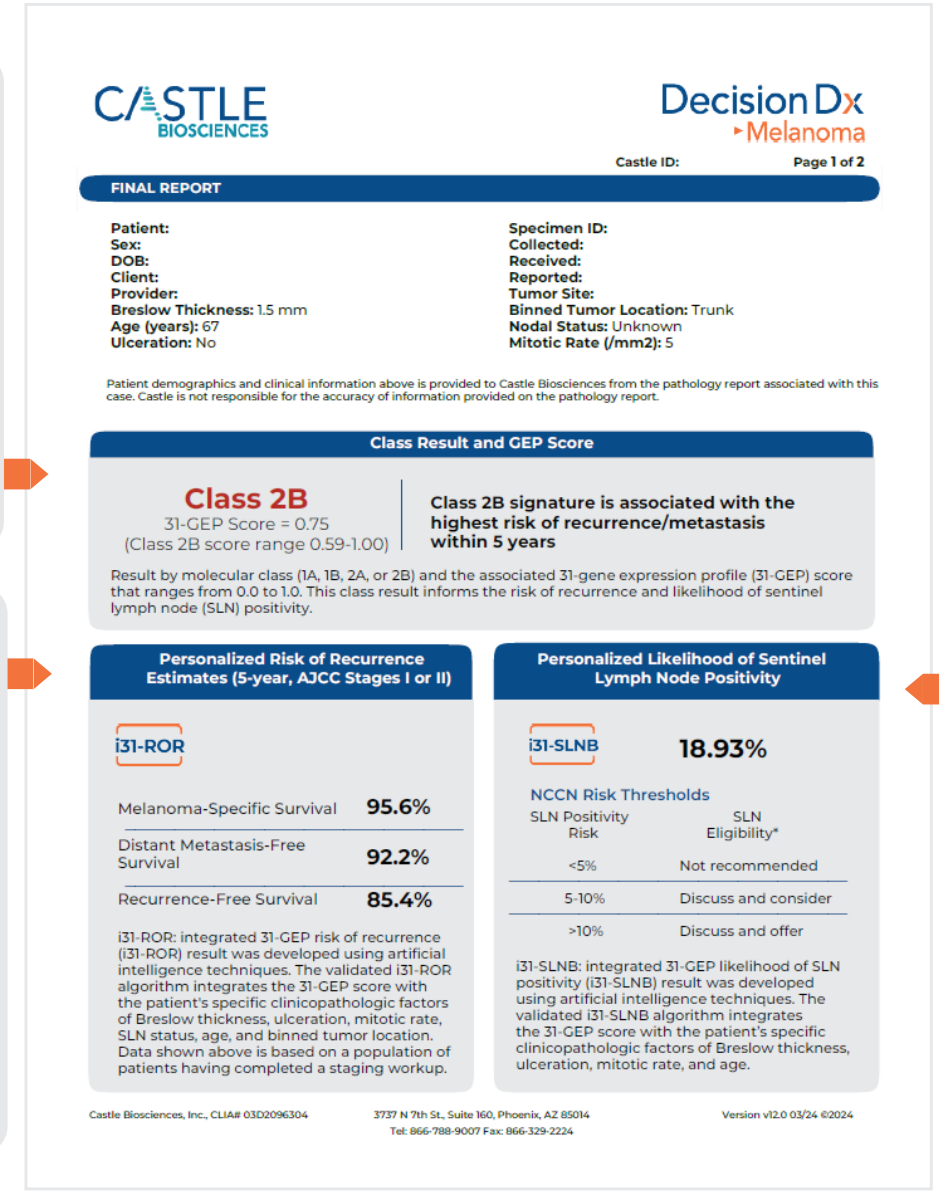
Classification of gene expression profile (GEP) as a class score for risk of recurrence and/or metastasis within five years. Results are reported as:

- **Class 1A** - Lowest risk (0 to 0.41)
- **Class 1B/2A** - Increased risk (>0.41 to <0.59)
- **Class 2B** - Highest risk (0.59 to 1.0)

PERSONALIZED RISK OF RECURRENCE ESTIMATES (5-YEAR, AJCC STAGES I OR II)

The validated i31-ROR algorithm integrates the 31-GEP score with the patient's specific clinicopathologic factors of Breslow thickness, ulceration, mitotic rate, SLN status, age and binned tumor location. Personalized 5-year outcomes for three distinct endpoints are reported:

- Melanoma-Specific Survival (MSS)
- Distant Metastasis-Free Survival (DMFS)
- Recurrence-Free Survival (RFS)



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DecisionDx-Melanoma

Castle ID: Page 1 of 2

FINAL REPORT

Patient:
Sex:
DOB:
Client:
Provider:
Breslow Thickness: 1.5 mm
Age (years): 67
Ulceration: No

Specimen ID:
Collected:
Received:
Reported:
Tumor Site:
Binned Tumor Location: Trunk
Nodal Status: Unknown
Mitotic Rate (/mm2): 5

Patient demographics and clinical information above is provided to Castle Biosciences from the pathology report associated with this case. Castle is not responsible for the accuracy of information provided on the pathology report.

Class Result and GEP Score

Class 2B
31-GEP Score = 0.75
(Class 2B score range 0.59-1.00)

Class 2B signature is associated with the highest risk of recurrence/metastasis within 5 years

Result by molecular class (1A, 1B, 2A, or 2B) and the associated 31-gene expression profile (31-GEP) score that ranges from 0.0 to 1.0. This class result informs the risk of recurrence and likelihood of sentinel lymph node (SLN) positivity.

Personalized Risk of Recurrence Estimates (5-year, AJCC Stages I or II)

i31-ROR

Melanoma-Specific Survival	95.6%
Distant Metastasis-Free Survival	92.2%
Recurrence-Free Survival	85.4%

i31-ROR: integrated 31-GEP risk of recurrence (i31-ROR) result was developed using artificial intelligence techniques. The validated i31-ROR algorithm integrates the 31-GEP score with the patient's specific clinicopathologic factors of Breslow thickness, ulceration, mitotic rate, SLN status, age, and binned tumor location. Data shown above is based on a population of patients having completed a staging workup.

Personalized Likelihood of Sentinel Lymph Node Positivity

i31-SLNB **18.93%**

NCCN Risk Thresholds

SLN Positivity Risk	SLN Eligibility*
<5%	Not recommended
5-10%	Discuss and consider
>10%	Discuss and offer

i31-SLNB: integrated 31-GEP likelihood of SLN positivity (i31-SLNB) result was developed using artificial intelligence techniques. The validated i31-SLNB algorithm integrates the 31-GEP score with the patient's specific clinicopathologic factors of Breslow thickness, ulceration, mitotic rate, and age.

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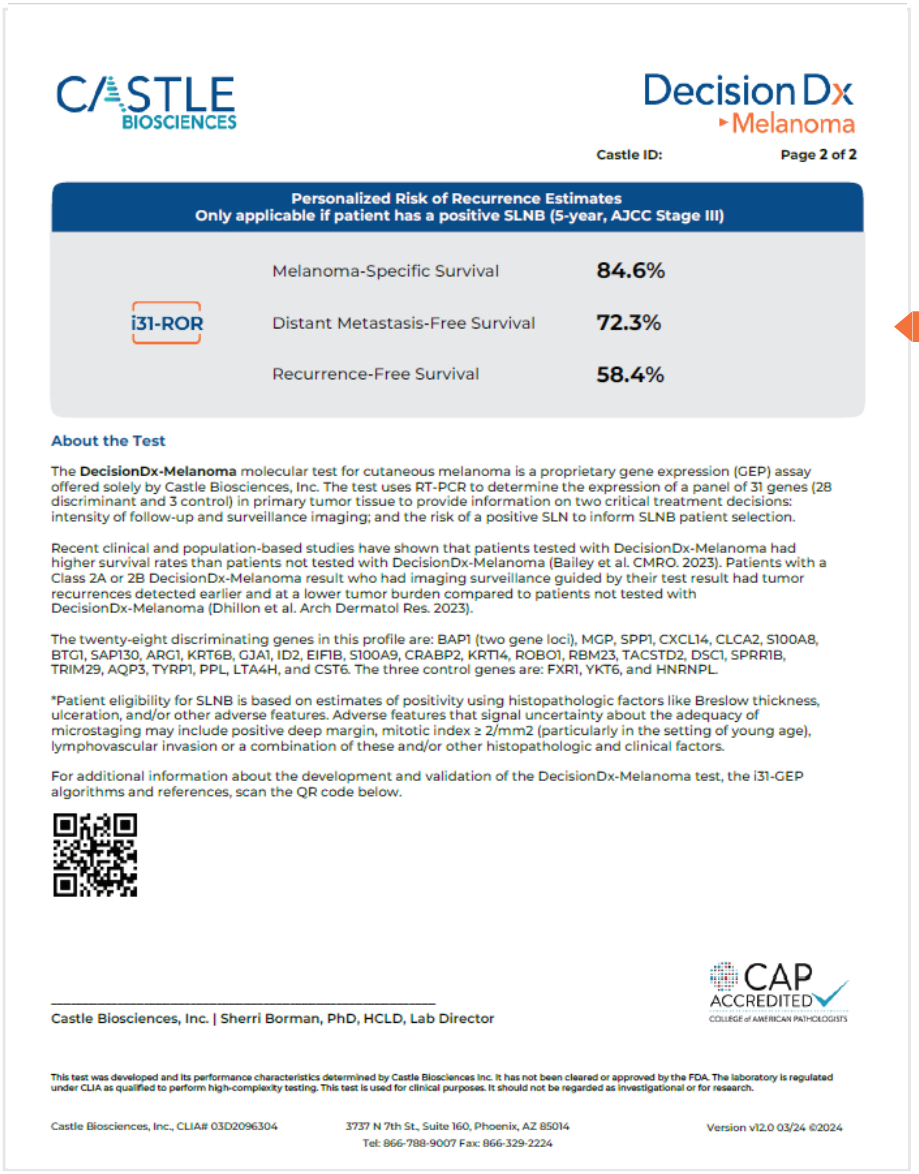
PERSONALIZED LIKELIHOOD OF SENTINEL LYMPH NODE POSITIVITY

The validated i31-SLNB algorithm integrates the 31-GEP score with the patient's specific clinicopathologic factors of Breslow thickness, ulceration, mitotic rate, and age. It provides a personalized risk assessment for the likelihood of having a positive sentinel lymph node biopsy (SLNB).

- This information will not be reported if a SLNB has already been performed.

CONTINUED

Decision Dx ▸Melanoma



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Castle ID: Page 2 of 2

Personalized Risk of Recurrence Estimates
Only applicable if patient has a positive SLNB (5-year, AJCC Stage III)

i31-ROR

Melanoma-Specific Survival	**84.6%**
Distant Metastasis-Free Survival	**72.3%**
Recurrence-Free Survival	**58.4%**

About the Test

The **DecisionDx-Melanoma** molecular test for cutaneous melanoma is a proprietary gene expression (GEP) assay offered solely by Castle Biosciences, Inc. The test uses RT-PCR to determine the expression of a panel of 31 genes (28 discriminant and 3 control) in primary tumor tissue to provide information on two critical treatment decisions: intensity of follow-up and surveillance imaging; and the risk of a positive SLN to inform SLNB patient selection.

Recent clinical and population-based studies have shown that patients tested with DecisionDx-Melanoma had higher survival rates than patients not tested with DecisionDx-Melanoma (Bailey et al. CMRO. 2023). Patients with a Class 2A or 2B DecisionDx-Melanoma result who had imaging surveillance guided by their test result had tumor recurrences detected earlier and at a lower tumor burden compared to patients not tested with DecisionDx-Melanoma (Dhillon et al. Arch Dermatol Res. 2023).

The twenty-eight discriminating genes in this profile are: BAP1 (two gene loci), MGP, SPP1, CXCL14, CLCA2, S100A8, BTG1, SAP130, ARG1, KRT6B, GJA1, ID2, EIF1B, S100A9, CRABP2, KRT14, ROBO1, RBM23, TACSTD2, DSC1, SPRR1B, TRIM29, AQP3, TYRP1, PPL, LTA4H, and CST6. The three control genes are: FXR1, YKT6, and HNRNPL.

*Patient eligibility for SLNB is based on estimates of positivity using histopathologic factors like Breslow thickness, ulceration, and/or other adverse features. Adverse features that signal uncertainty about the adequacy of microstaging may include positive deep margin, mitotic index ≥ 2/mm2 (particularly in the setting of young age), lymphovascular invasion or a combination of these and/or other histopathologic and clinical factors.

For additional information about the development and validation of the DecisionDx-Melanoma test, the i31-GEP algorithms and references, scan the QR code below.

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

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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.

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PERSONALIZED RISK OF RECURRENCE ESTIMATES (5-YEAR AJCC STAGE III)

DecisionDx-Melanoma testing is commonly performed prior to an SLNB procedure.

If a patient is or becomes clinically or pathologically node-positive (AJCC Stage III) personalized 5-year outcomes are proactively reported, including:

- Melanoma-Specific Survival (MSS)
- Distant Metastasis-Free Survival (DMFS)
- Recurrence-Free Survival (RFS)

Including this information proactively reduces the need for amended reporting.

Additional information

For additional information about the development and validation of the DecisionDx-Melanoma test, the i31-GEP algorithms, and references scan the QR code below.

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