

# Report Guide

The DecisionDx®-Melanoma class score is now combined with clinicopathologic features to provide an individualized risk estimate for risk of recurrence and/or metastasis within 5 years and likelihood of a positive sentinel lymph node using validated artificial intelligence algorithms.

## CLASS SCORE AND RESULT DESCRIPTION

Classification of gene expression profile as a class score for risk of recurrence and/or metastasis within 5 years. Results are reported as:

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

### FINAL REPORT

<b>Patient:</b>	<b>Specimen ID:</b>
<b>Sex:</b>	<b>Collected:</b>
<b>DOB:</b>	<b>Received:</b>
<b>Client:</b>	<b>Reported:</b>
<b>Provider:</b>	<b>Tumor Site:</b>
<b>Breslow Thickness:</b>	<b>Binned Tumor Location:</b>
<b>Age (years):</b>	<b>Nodal Status:</b>
<b>Ulceration:</b>	<b>Mitotic Rate (/mm2):</b>

### DecisionDx-Melanoma Result

**Class 2B**  
31-GEP Score = 0.61

**Class 2B signature is associated with the highest risk of recurrence/metastasis within 5 years**  
Class 2B score range: 0.59-1.00

The DecisionDx®-Melanoma test reports results 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 risk of recurrence and likelihood of sentinel lymph node (SLN) positivity.

### This patient's i31-GEP Personalized Risk of Recurrence Estimates (5-year, AJCC Stages I or II):

	Melanoma-Specific Survival (MSS)	Distant Metastasis-Free Survival (DMFS)	Recurrence-Free Survival (RFS)
Clinically or pathologically node-negative (clinical stage I or II)	82.6%	53.8%	26.9%

The DecisionDx-Melanoma integrated 31-GEP Risk of Recurrence (i31-ROR) test 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.

See page 2 for i31-GEP personalized risk of recurrence estimates for patients with clinically or pathologically node-positive melanoma (stage III) and information pertaining to likelihood of SLN positivity.

### DecisionDx-Melanoma Risk of Recurrence Estimates (5-year) by 31-GEP Class and AJCC Stage:

AJCC Stage Information		DecisionDx-Melanoma Class Result by Stage			
Clinical Stage	MSS by AJCC Stage	31-GEP Class Result	Melanoma-Specific Survival (MSS)	Distant Metastasis-Free Survival (DMFS)	Recurrence-Free Survival (RFS)
Stage I	98%	1A	>99%	98%	98%
		1B/2A	98%	90%	88%
		2B	91%	86%	76%
Stage II	90%	1A	98%	89%	73%
		1B/2A	91%	82%	71%
		2B	85%	60%	44%
Stage III	77%	1A	94%	68%	58%
		1B/2A	85%	68%	53%
		2B	62%	42%	33%

Greenhaw et al. JAAD 2020

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. Patent Pending.

## PERSONALIZED RISK OF RECURRENCE ESTIMATES FOR STAGE I-II PATIENTS

Personalized 5-year outcomes for three distinct endpoints are reported:

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



## REFINED RISK ESTIMATES

DecisionDx-Melanoma has been shown to provide refined risk estimates beyond AJCC staging alone. Reference table outlines the impact of the 31-GEP class score to three distinct endpoints.

**PERSONALIZED LIKELIHOOD OF SENTINEL LYMPH NODE POSITIVITY**

Personalized risk assessment for the likelihood of having a positive sentinel lymph node biopsy (SLNB).

- Includes reference to current AJCC staging guidelines for comparison
- This information will not be reported if a SLNB has already been performed.

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**This patient's i31-GEP Personalized Likelihood of Sentinel Lymph Node Positivity**

<p style="text-align: center;"><b>Likelihood of SLNB positivity (i31-SLNB):</b></p> <p style="text-align: center; font-size: 1.2em;"><b>28.1%</b></p> <p style="font-size: 0.8em;">For those with risk less than 5%, SLNB is generally not recommended.</p> <p style="font-size: 0.8em;">For those with risk between 5% and 10%, SLNB is sometimes considered.</p> <p style="font-size: 0.8em;">Typically, SLNB is recommended for patients with risk of positivity greater than 10%.</p>	<p><b>SLNB positivity estimates using histopathologic factors alone:</b></p> <p style="font-size: 0.8em;">Breslow thickness of &lt;0.8mm without ulceration or other adverse features* has an estimated likelihood of SLNB positivity of <b>less than 5%</b></p> <p style="font-size: 0.8em;">Breslow thickness of ≥0.8 – 1.0mm with or without ulceration or thickness &lt;0.8mm with ulceration and/or other adverse features* has an estimated likelihood of SLNB positivity <b>between 5% and 10%</b></p> <p style="font-size: 0.8em;">Breslow thickness of &gt;1.0mm with or without ulceration has an estimated likelihood of SLNB positivity <b>greater than 10%</b></p>
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*Whitman et al. JCO-PO 2021*

The DecisionDx-Melanoma i31-GEP Likelihood of SLN Positivity (i31-SLNB) test result was developed using artificial intelligence techniques. The validated i31-SLNB algorithm integrates the 31-GEP score (0.0 – 1.0) with the patient's specific clinicopathologic factors of Breslow thickness, ulceration, mitotic rate, and age.

\*Adverse features that signal uncertainty about the adequacy of microstaging may include positive deep margin, mitotic index ≥ 2/mm<sup>2</sup> (particularly in the setting of young age), lymphovascular invasion or a combination of these and/or other histopathologic and clinical factors.


**This patient's i31-GEP Personalized Risk of Recurrence Estimates (5-year, AJCC Stage III):**

Clinical or pathologically node-positive (clinical stage III)	Melanoma-Specific Survival (MSS)	Distant Metastasis-Free Survival (DMFS)	Recurrence-Free Survival (RFS)
Clinically or pathologically node-positive (clinical stage III)	69.1%	29.5%	7.9%


**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. 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.

For additional information about the development and validation of the DecisionDx-Melanoma test, the i31-GEP algorithms and references, visit [www.castletestinfo.com/decisiondx-melanoma](http://www.castletestinfo.com/decisiondx-melanoma).



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

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Castle Biosciences, Inc., CLIA#03D2096304      3737 N. 7th Street, Suite 160, Phoenix, AZ 85014      Version 11.2.12/22 ©2022

**RISK OF RECURRENCE ESTIMATES FOR STAGE III PATIENTS**

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.