Report Guide

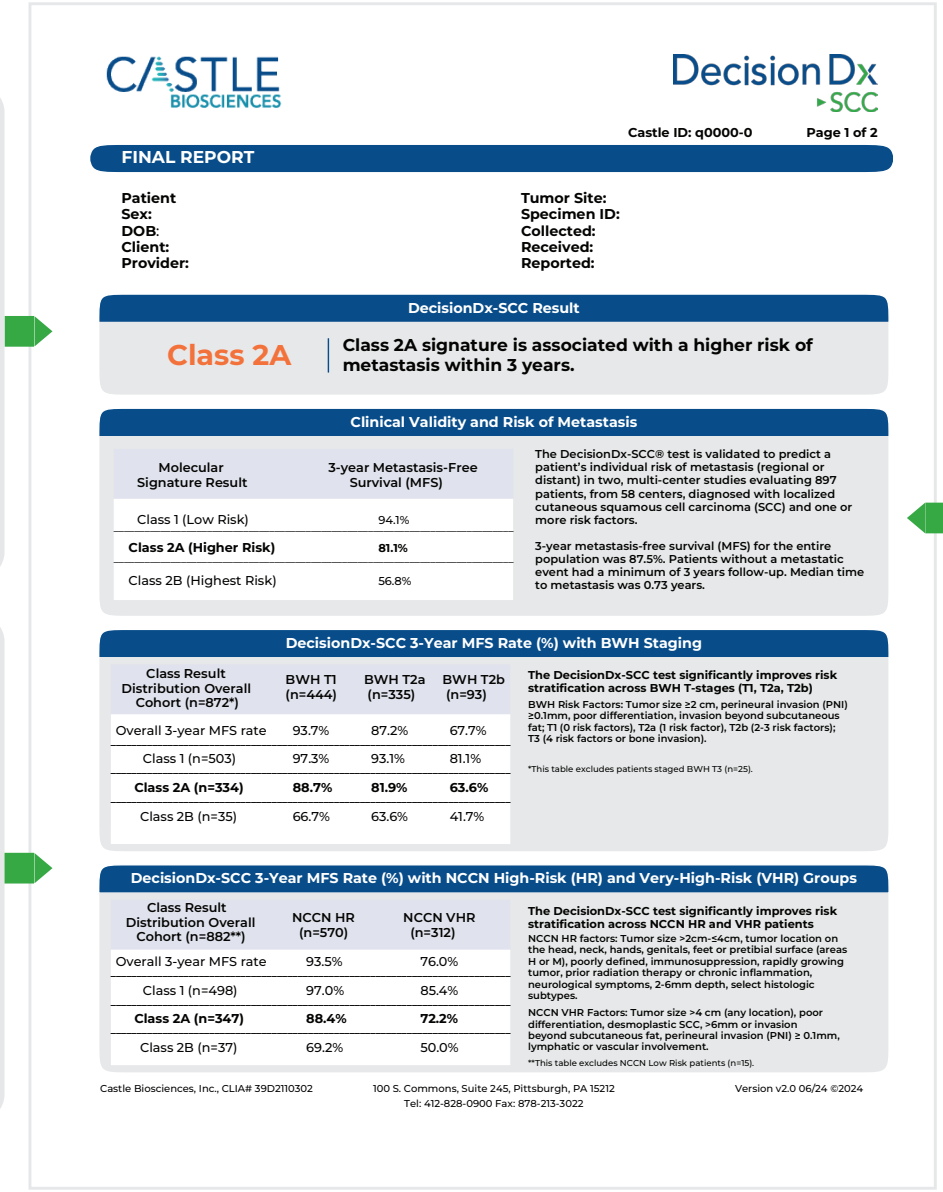
TEST RESULT AND RESULT DESCRIPTION

The test result for DecisionDx-SCC is reported as a classification of the gene expression profile result. Results are reported as:

- **Class 1** - Low risk
  <7% risk of metastasis
- **Class 2A** - Higher risk
  ~20% risk of metastasis
- **Class 2B** - Highest risk
  >45% risk of metastasis

3-YEAR MFS RATE USING DECISIONDX-SCC IN CONJUNCTION WITH BWH STAGING AND NCCN RISK GROUPS

DecisionDx-SCC is an independent predictor of metastatic risk and can be combined with BWH staging or NCCN risk groups. Integration of DecisionDx-SCC with BWH or NCCN significantly improves the accuracy of risk stratification allowing more precise treatment decisions.



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DecisionDx-SCC

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FINAL REPORT

Patient
Sex:
DOB:
Client:
Provider:

Tumor Site:
Specimen ID:
Collected:
Received:
Reported:

DecisionDx-SCC Result

Class 2A | **Class 2A signature is associated with a higher risk of metastasis within 3 years.**

Clinical Validity and Risk of Metastasis

Molecular Signature Result	3-year Metastasis-Free Survival (MFS)
Class 1 (Low Risk)	94.1%
Class 2A (Higher Risk)	**81.1%**
Class 2B (Highest Risk)	56.8%

The DecisionDx-SCC® test is validated to predict a patient's individual risk of metastasis (regional or distant) in two, multi-center studies evaluating 897 patients, from 58 centers, diagnosed with localized cutaneous squamous cell carcinoma (SCC) and one or more risk factors.

3-year metastasis-free survival (MFS) for the entire population was 87.5%. Patients without a metastatic event had a minimum of 3 years follow-up. Median time to metastasis was 0.73 years.

DecisionDx-SCC 3-Year MFS Rate (%) with BWH Staging

Class Result Distribution Overall Cohort (n=872*)	BWH T1 (n=444)	BWH T2a (n=335)	BWH T2b (n=93)
Overall 3-year MFS rate	93.7%	87.2%	67.7%
Class 1 (n=503)	97.3%	93.1%	81.1%
Class 2A (n=334)	**88.7%**	**81.9%**	**63.6%**
Class 2B (n=35)	66.7%	63.6%	41.7%

The DecisionDx-SCC test significantly improves risk stratification across BWH T-stages (T1, T2a, T2b)

BWH Risk Factors: Tumor size ≥2 cm, perineural invasion (PNI) ≥0.1mm, poor differentiation, invasion beyond subcutaneous fat; T1 (0 risk factors), T2a (1 risk factor), T2b (2-3 risk factors); T3 (4 risk factors or bone invasion).

*This table excludes patients staged BWH T3 (n=25).

DecisionDx-SCC 3-Year MFS Rate (%) with NCCN High-Risk (HR) and Very-High-Risk (VHR) Groups

Class Result Distribution Overall Cohort (n=882**)	NCCN HR (n=570)	NCCN VHR (n=312)
Overall 3-year MFS rate	93.5%	76.0%
Class 1 (n=498)	97.0%	85.4%
Class 2A (n=347)	**88.4%**	**72.2%**
Class 2B (n=37)	69.2%	50.0%

The DecisionDx-SCC test significantly improves risk stratification across NCCN HR and VHR patients

NCCN HR factors: Tumor size >2cm-≤4cm, tumor location on the head, neck, hands, genitals, feet or pretibial surface (areas H or M), poorly defined, immunosuppression, rapidly growing tumor, prior radiation therapy or chronic inflammation, neurological symptoms, 2-6mm depth, select histologic subtypes.

NCCN VHR Factors: Tumor size >4 cm (any location), poor differentiation, desmoplastic SCC, >6mm or invasion beyond subcutaneous fat, perineural invasion (PNI) ≥ 0.1mm, lymphatic or vascular involvement.

**This table excludes NCCN Low Risk patients (n=15).

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VALIDATION AND SUPPORTING DATA

DecisionDx-SCC is validated to predict individual risk of metastasis within 3 years of diagnosis for patients with SCC and one or more risk factors

- Clinically validated in 897 patients in two, independent, multi-center studies with 3-year outcomes
- DecisionDx-SCC is the strongest independent predictor of SCC metastasis
- Test result adds significant information for SCC management

CONTINUED

DecisionDx-SCC

ABOUT THE TEST

- DecisionDx-SCC is a gene expression profile test consisting of 40 genes (34 discriminant and 6 control)
- RT-PCR technology is used to measure gene expression levels of the discriminant genes which are normalized to the control genes

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DecisionDx-SCC

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Multivariate Comparison with Clinicopathologic Risk Factors

Risk Factor	Hazard Ratio (HR) with DecisionDx-SCC	p-Value
Class 1	1.0	-
Class 2A	**2.21**	**<0.001**
Class 2B	4.90	<0.001
Tumor Thickness (>6mm)	2.93	<0.001
Poor Differentiation	2.82	<0.001
Immunosuppression	2.17	<0.001
Invasion beyond subcuaneous fat	1.83	ns
Perineural involvement (>0.1 mm)	0.65	ns
Diameter (2-4 cm)	1.31	ns

This table presents multivariate risk of metastasis for individuals with a specific high-risk factor as hazard ratios (HR). In this analysis, HR represents independent risk added by each variable, and cumulative risk when multiple risk factors are present can be assessed by multiplying the HRs.

For example: A Class 2A result (2.21 HR) with poor differentiation (2.82 HR) would result in a HR of 6.23 (2.21 x 2.82) as these values are multiplicative.

Multivariate analysis demonstrated independence of Class 2A and Class 2B molecular results (HR 2.21 and 4.90, respectively). Tumor thickness (2.93), poor differentiation (2.82) and immunosuppression (2.17) were also statistically significant.

About the Test

The DecisionDx-SCC test is a qRT-PCR assay of 6 control and 34 discriminant genes (40 in total) that uses a neural network algorithm comprised of two gene expression signatures to classify patients into risk categories. The algorithmic score from both signatures is converted to results reflecting risk classification. DecisionDx-SCC is indicated for patients with cutaneous squamous cell carcinoma (SCC) and one or more high-risk factors (see Test Requisition Form). The test predicts individual metastatic risk to help inform risk appropriate management.

The 34 discriminating genes are: ACSBG1, ALOX12, APOBEC3G, ATP6V0E2, BBC3, BHLHB9, CEP76, DUXAP9, GTPBP2, HDDC3, ID2, LCE2B, LIME1, LOC100287896, LOC101927502, MMP10, MRC1, MSANTD4, NFASC, NFIC, PDPN, PI3, PLS3, RCHY1, RNF135, RPP38, RUNX3, SLC1A3, SPP1, TAF6L, TFAP2B, ZNF48, ZNF496 and ZNF839. Six control genes consist of BAG6, FXR1, KMT2C, KMT2D, MDM2, MDM4.

For additional information about the development, validation and clinical use of the DecisionDx-SCC test, including references, scan the QR code below.

<Signature>

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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MULTIVARIATE COMPARISION WITH TRADITIONAL RISK FACTORS

Multivariate analysis shows DecisionDx-SCC provides the strongest independent prognostic information as defined by hazard ratio (HR). HRs are multiplicative in determining risk of metastasis

- Class 2A risk is similar to the strongest established prognostic risk factors (tumor thickness, poor differentiation, immunosuppression)
- Class 2B is the strongest predictor of metastatic risk
- Example: A Class 2A result (2.21 HR) with poor differentiation (2.82 HR) would result in a HR of 6.23 (2.21x2.82) for the patient as these values are multiplicative

Additional information

For additional information about the development and validation of the DecisionDx-SCC test and references, scan the QR code below.

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DDXSCC-007v3-062024