

DecisionDx®-SCC predicts biological risk of metastasis for SCC patients with one or more risk factors to inform risk-appropriate management.

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: Moderate risk**
20% risk of metastasis
- **Class 2B: High risk**
≥50% risk of metastasis

INTENDED USE

Informs risk appropriate management by predicting individual metastatic risk.

- Indicated for use in patients SCC and one or more high-risk factors.
- Results should be interpreted in the context of all other clinical and histopathological findings.

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FINAL REPORT

Patient:	Tumor Site:
Sex:	Specimen ID:
DOB:	Collected:
Client:	Received:
Clinician:	Reported:

DecisionDx-SCC Result

Class 1

Class 1 signature is associated with a low risk of metastasis within 3 years.

CLINICAL VALIDITY AND RISK OF METASTASIS

Molecular Signature Result	3-year Metastasis Free Survival ^P
Class 1	93.9%
Class 2A	80.5%
Class 2B	47.8%

The DecisionDx®-SCC test was validated to predict a patient's individual risk of metastasis (regional or distant) in a multi-center (33), 420-patient study in patients diagnosed with localized cutaneous squamous cell carcinoma (SCC) and one or more risk factors.^{1,2}

3-year Metastasis Free Survival (MFS) for the entire population was 85.5%. Patients without a metastatic event had a minimum of 3 years follow-up. Median time to metastasis was 0.91 years.^{1,2}

INTENDED USE


Background: Risk-appropriate SCC management is limited by classification systems (NCCN, AJCC, BWH) with low positive predictive value. Guidelines provide a range of management options based on risk, for patients with localized, surgically resectable SCC.^{3,4}

Intended use: DecisionDx-SCC is indicated for patients with cutaneous squamous cell carcinoma (SCC) and one or more high-risk factors (see Test Requisition Form). DecisionDx-SCC predicts individual metastatic risk to inform risk appropriate management.⁵

DecisionDx-SCC has not been evaluated for testing in tissue from locally recurrent tumors.

TEST DESCRIPTION

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 algorithm was trained on a set of patients with known outcomes (n=122). The algorithmic score from both signatures is converted to results reflecting risk classification: Class 1 for low risk, Class 2A for moderate risk, and Class 2B for highest risk of metastasis. This test has not been validated in patients with clinical features different from those described in the Intended Use section above.



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. Patent Pending.
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VALIDATION AND SUPPORTING DATA

DecisionDx-SCC is validated to predict metastatic risk for SCC patients with one or more risk factors.

- Independently validated in a prospectively designed study of 420 SCC patients with 3-year outcomes.
- DecisionDx-SCC is the strongest predictor in univariate and multivariate analyses.
- Test result adds significant information for SCC management.

TEST RESULT AND RISK FACTORS

Metastatic risk is reported two ways: independently and segmented by number of traditional risk factors.

- Incorporation of traditional risk factors with DecisionDx-SCC results provides superior patient classification compared to traditional risk factors alone.
- Number of risk factors (1 or ≥2) further stratifies patient metastatic risk of patients in the independent validation study.

ADDITIONAL INFORMATION

- 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.



Cutaneous Squamous Cell Carcinoma (SCC)

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DECISIONDX-SCC STRATIFICATION IN COMBINATION WITH RISK FACTORS

The table below presents overall rate of metastasis for patients with primary SCC compared to the subgroup that has 1 high-risk factor as well as ≥2 high-risk factors from the 420 patient clinical validation cohort.* A Class 1 result reduced the metastatic rate from 8.2% to 4.0% in patients with 1 high-risk factor. A Class 2B result more than doubled the metastasis rate to ≥50% in both groups.^{1,2}

*Of 63 overall metastases, 60 occurred within 3 years. The remaining 3 occurred greater than 3 years following diagnosis.

Result	Overall		1 Factor		≥2 Factors	
	n	Metastasis Rate	n	Metastasis Rate	n	Metastasis Rate
Overall Cohort	420	15.0%	171	8.2%	249	10.7%
Class 1	212	6.6%	101	4.0%	111	9.0%
Class 2A	185	20.0%	65	10.8%	120	25.0%
Class 2B	23	52.2%	5	60.0%	18	50.0%

Risk factors included in the above table: location and size (areas H, M or any ≥2 cm), immunosuppression, any PNI, tumors with invasion (beyond subcutaneous fat, depth ≥2mm, or Clark level IV/V), poorly differentiated tumor histology, aggressive histologic subtypes^{3,4} and lymphovascular invasion.

COMPARISON WITH CLINICOPATHOLOGIC RISK FACTORS

Risk Factor	Hazard Ratio	p value
Class 1	1.00	---
DecisionDx-SCC Class 2A	3.22	<0.001
Class 2B	11.61	<0.001
Poor differentiation	3.93	<0.001
Perineural invasion	3.28	<0.001
Deep invasion**	3.11	<0.001
Tumor diameter (per cm)	1.15	<0.001
Immunosuppression	1.46	ns

This table presents univariate risk of metastasis for individuals with a specific high-risk feature as hazard ratios. Hazard ratio represents the likelihood of a metastatic event in the group with the risk factor compared to the group without the risk factor (e.g. a Class 2B patient has a risk of metastasis that is 11.6 times greater than a Class 1 patient).

Multivariate analysis demonstrated independence of Class 2A and Class 2B molecular results (HR 2.33 and 6.66, respectively). Poor differentiation (HR 2.29) and deep invasion** (HR 2.05) were also statistically significant.

**Deep invasion: beyond subcutaneous fat, depth >6 mm or Clark level V

ADDITIONAL INFORMATION ABOUT THE TEST

The proprietary DecisionDx-SCC test is an empirically derived multi-analyte algorithmic assay (e.g. MAAA). The 34 discriminating genes are: AOSBG1, ALOX12, APOBEC3G, ATP9VD2, BBO3, BHLHE9, CEP76, DUXAP6, GTFPB72, HDDC3, ID2, LCE2B, LIME1, LOC100287898, LOC101927502, MMP10, MRC1, MSANTD4, NFASC, NFIC, PDPN, P13, PLS3, RCHY1, RNF135, RPP3B, RUNX3, SLC1A3, SPP1, TAF6L, TFAP2B, ZNF48, ZNF496 and ZNF839. Six control genes consist of BAG6, FXR1, KMT2C, KMT2D, MDM2, MDM4.

All data shown in this report were collected and verified under an IRB approved multi-center study to establish and validate the test's prognostic accuracy in primary cutaneous squamous cell carcinoma.^{1,2}

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COMPARISON WITH TRADITIONAL RISK FACTORS

Multivariate analysis shows DecisionDx-SCC provides the strongest independent prognostic information.

- Class 2A risk is similar to the strongest established prognostic risk factors (deep invasion, poor differentiation, perineural invasion).
- Class 2B is the strongest predictor of metastatic risk (11.6x greater risk than Class 1 patient) in univariate analysis.
- Class 2B is a 3x stronger predictor of risk than the strongest traditional prognostic risk factors (deep invasion, poor differentiation, or perineural invasion).