FINAL REPORT

Patient:
Sex:
DOB:
Client:
Provider:

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

DecisionDx-SCC has been clinically validated in patients diagnosed with localized cutaneous squamous cell carcinoma (SCC) with at least one clinicopathologic risk factor to predict the following: (i) 3-year metastasis-free survival (MFS) (ii) Response to adjuvant radiation therapy (ART) in NCCN (2.2025) High-Risk (HR) or Very High-Risk (VHR) SCC with clear surgical margins; and (iii) local recurrence-free survival (LRFS) in NCCN HR SCC with no residual disease following Mohs surgery. As with all tests, these results should be evaluated within the context of the patient's other risk factors and overall clinical scenario.

DecisionDx-SCC Result

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

The DecisionDx-SCC test is validated to predict a patient's individual risk of metastasis (regional or distant) independent from all clinical or pathological risk factors and staging systems. The test was validated in two multi-center studies evaluating 897 patients, from 58 centers, diagnosed with localized SCC and one or more high-risk factors. **Three-year 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 Metastasis-Free Survival (MFS) Rates With BWH Staging and NCCN Risk Groups

DecisionDx-SCC result significantly improves risk stratification across BWH T-stages (T1, T2a, T2b) and NCCN HR and VHR groups.

DecisionDx-SCC		BWH			NCCN	
CLASS	3-YEAR MFS	T1	T2a	T2b	HR	VHR
Class 1	**94.1%**	**97.3%**	**93.1%**	**81.1%**	**97.0%**	**85.4%**
Class 2A	81.1%	88.7%	81.9%	63.6%	88.4%	72.2%
Class 2B	56.8%	66.7%	63.6%	41.7%	69.2%	50%
Overall	87.5%	93.7%	87.2%	67.7%	93.5%	76.0%

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

NCCN HR Factors: Tumor size >2 cm - ≤ 4 cm on trunk or extremities, any size on the head, neck, hands, feet, pretibial and anogenital area, borders poorly defined, immunosuppression, rapidly growing tumor, site of prior radiation therapy or chronic inflammation, neurological symptoms, 2-6 mm depth and no invasion beyond subcutaneous fat, select histologic subtypes.

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

Response to Adjuvant Radiation Therapy (ART)

Class 1 | **No clinically discernible benefit from ART on metastatic disease progression.**

NCCN (2.2025) recommends consideration of ART in patients with localized NCCN HR or VHR SCC, clear surgical margins and a high risk for regional or distant metastasis. The performance of DecisionDx-SCC in predicting response to ART has been validated in two independent multi-center studies in patients diagnosed with localized invasive SCC and meeting NCCN HR or VHR criteria (Arron et al, Ruiz et al; n=1,320). These studies represent the two largest studies conducted to date evaluating the benefit of ART in patients with high-risk SCC.

For patients with a Class 1 result, both studies report no clinical difference in disease progression rates when comparing Class 1 ART treated and untreated tumors.

Scan the QR code for additional information regarding DecisionDx-SCC ART guidance.

DecisionDx-SCC 3-Year Local Recurrence-Free Survival (LRFS) Rates (%) for Mohs-treated NCCN HR Patients

Class 1 | **Class 1 signature is associated with a low risk of local recurrence over 3 years.**

In a multi-center validation study of 414 patients diagnosed with NCCN HR SCC who underwent definitive Mohs surgery with no residual disease (R0), DecisionDx-SCC was shown to provide risk stratification independent of NCCN and BWH risk systems. This study had an overall local recurrence-free survival (LRFS) rate of 91.8%. A Class 1, Class 2A and Class 2B test result yielded a LRFS rate of 95.3%, 85.5% and 71.4%, respectively. Please refer to page 1 of this report for a full list of NCCN HR factors.

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, response to ART, and risk of local recurrence 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.

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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.