FINAL REPORT

Patient:
Sex:
DOB:
Client:
Clinician:

Tumor Site:
Specimen ID:
Collected:
Received:
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[2]
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.

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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	19.7%
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 and lymphovascular invasion.

COMPARISON WITH CLINICOPATHOLOGIC RISK FACTORS

Risk Factor		Hazard Ratio	p value
DecisionDx-SCC	Class 1	1.00	---
	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

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

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 6.86, respectively). Poor differentiation (HR 2.29) and deep invasion**(HR 2.05) were also statistically significant.

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: 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.

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]

REFERENCE LIST

1. Wysong A, Newman JG, Covington KR, et al. J Am Acad Dermatol 2020.
2. Castle Biosciences. Data on File.
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4. Alam M, Armstrong A, Baum C, et al. J Am Acad Dermatol 2018;78(3):560-578.
5. Farberg AS, Hall MA, Douglas L, et al. Curr Med Res Opin 2020.