Background

While the majority of cSCC tumors are curable by excision, approximately 20% of patients present with clinical or pathologic features that are associated with disease progression. Since early detection of metastasis can lead to better outcomes through prompt and appropriate intervention, accurate identification of patients at high risk for metastasis is critical.

The 40-GEP test has been validated to improve upon current metastasis risk prediction methods, providing a more precise risk stratification for patients with high-risk cSCC. Clinical utility studies have demonstrated the ability of 40-GEP test results to guide per-risk aligned patient management decisions.

This test stratifies primary cSCC patients having one or more clinicopathologic risk factors into three biologic risk groups based on risk for regional, nodal, or distant metastasis. Low = Class 1; Moderate = Class 2A; High = Class 2B.

Objective

To confirm the performance of the 40-GEP test in an independent, multi-center cohort study of high-risk cSCC patients to augment prognostication of metastasis when compared to clinicopathologic information alone.

Methods

Under an IRB-approved protocol, centralized pathology review and sample analysis were performed in a CAP-accredited, CLIA-certified laboratory using formalin-fixed paraffin-embedded archival primary cSCC tumor specimens (n=552). Clinicopathologic and outcomes data were collected from the 35 contributing centers. Clinicopathologic risk factors were comprehensively assessed, including review of original biopsy reports, definitive surgical reports, and independent review by a board-certified dermatopathologist. Kaplan-Meier analysis for metastasis-free survival (MFS) with log rank test and Cox regression analyses were performed.

Results

The overall cohort had a metastatic rate of 10.9%, indicative of a high-risk cSCC cohort. Significant differences were observed between metastatic and non-metastatic groups among various parameters, including, tumor diameter and thickness, PNI, lymphovascular invasion, and invasion beyond the subcutaneous fat (Table 1).

The 40-GEP demonstrated statistically significant risk stratification as demonstrated by Kaplan-Meier analysis (p<0.0001) (Figure 1). Univariate Cox regression analysis in this independent performance cohort was significant for Class 2A and Class 2B with a hazard ratio (HR) of 5.09 and 11.26, respectively (p<0.001) (Table 2). High-risk clinicopathologic factors (e.g. poor differentiation) and Brigham and Women’s Hospital (BWH) staging were significantly associated with metastatic risk. Importantly, when combined into multivariate Cox models, the 40-GEP significantly contributed to risk stratification with the inclusion of either high-risk factors (p<0.01 for 2A and 2B) or BWH T-stage (p<0.001 for 2A and 2B) (Table 2).

The addition of interaction terms to the multivariate analysis between the 40-GEP test and BWH revealed no significant interactions (p>0.05), demonstrating that the 40-GEP test provides independent prognostic information over BWH staging. Patients with Class 2B results had the highest risk of metastasis and a worse prognosis (Table 2).

Conclusions

This second independent, multi-center cohort study confirms the performance of the 40-GEP test to classify risk for metastasis in cSCC patients with one or more risk factors. The independent contribution of the 40-GEP in risk stratification when compared to high-risk factors or clinical staging systems suggests that incorporating the 40-GEP test results into treatment decisions will guide patient care in a more risk-aligned manner and improve patient outcomes.

References


Disclosures

1. MSG, SUK, JVS, AP, ALF are employees and shareholders of Castle Biosciences, Inc.