How Mohs surgeons utilize prognostic testing for high-risk cutaneous squamous cell carcinoma (SCC): a clinical impact study

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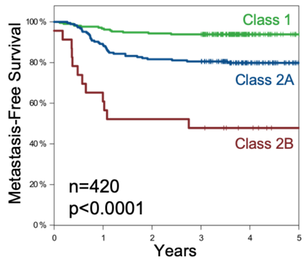
Synopsis

- Of the 1.8 million annually diagnosed SCC cases, more than 95% are cured by surgery; however, an average of 5% progress to metastasis, with up to 2.1% dying from the disease.[1-3]
- A SCC patient's likelihood for poor outcomes governs management decisions regarding a multitude of treatment modalities.
- The 40-gene expression profile (40-GEP) test has been validated to stratify primary SCC patients having one or more clinicopathologic risk factors into three biological risk groups (Low = Class 1; Moderate = Class 2A; High = Class 2B) based on risk for regional, nodal, or distant metastasis (Figure 1). [4,5]
- Clinical validity studies have shown an improvement to risk stratification of high-risk SCC patients when compared to staging systems. [4,5]
- When 40-GEP test results are incorporated into a clinician's initial risk assessment, clinical utility studies have demonstrated the ability of the test to personalize patient management plans in a risk-aligned manner. [5-9]

Figure 1. Performance of the 40-GEP to Stratify Patients by Risk of Regional or Distant Metastasis from SCC



40-GEP Risk Class	Overall Cohort 3-year MFS (95% CI)	Overall Event Rate
Class 1	93.9% (90.7-97.2%)	6.6%
Class 2A	80.5% (75.0-86.5%)	20.0%
Class 2B	47.8% (31.2-73.3%)	52.2%
Without 40-GEP	85.5% (82.2-88.9%)	15.0%

Objective

- As Mohs surgeons are a clinical specialty likely to see high-risk SCC patients frequently, a clinical impact study was performed to determine how patient management decisions are impacted by their use of the 40-GEP test.

Methods

- An anonymous survey was distributed to current American College of Mohs Surgery (ACMS) members. The study consisted of demographic questions, familiarity with and use of NCCN guidelines, AJCC-8 staging, BWH staging, and the 40-GEP.
- Participants (n=39) were provided with background on the validation of the 40-GEP test, then evaluated the use of risk factors for the assessment of SCC patients within their practice and which were concerning enough to warrant the use of the 40-GEP.
- Participants were presented with a high-risk SCC patient vignette and asked for their risk assessment and treatment approaches pre- and post-40-GEP results.

Results

- Demographics of the n=39 Mohs surgeons who participated in the study are shown in **Table 1**. The distribution of study participants usage of National Comprehensive Cancer Network (NCCN) guidelines and staging systems for risk assessment, along with their familiarity with GEP testing for SCC are shown in **Figure 2**.

Results

- **Table 2** displays the highest-ranking risk factors (on a scale of 1-5) most likely to cause metastasis as decided on by study participants. Factors that participants rank as most concerning are also the factors they feel would most likely benefit from the prognostic information provided by the 40-GEP.
- Study participants were presented with a high-risk SCC patient vignette (**Figure 3**). Responses to treatment modalities demonstrated increases in elevation of management when Class results indicated an increased risk of metastasis.
- Overall confidence in decision making increased when integrating 40-GEP test results (**Figure 4**)

Table 1. Demographics of study participants

Years in practice	(%)
1-10 years	46
11-20 years	38
21-30 years	8
>30 years	8

Institution	(%)
Academic center	33
Multi-specialty group	25
Other private practice	36
Hospital based	5
other	0

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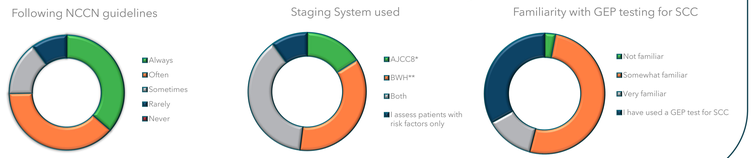
Figure 2. Summary of study participants preferred methods of risk assessment and familiarity with GEP



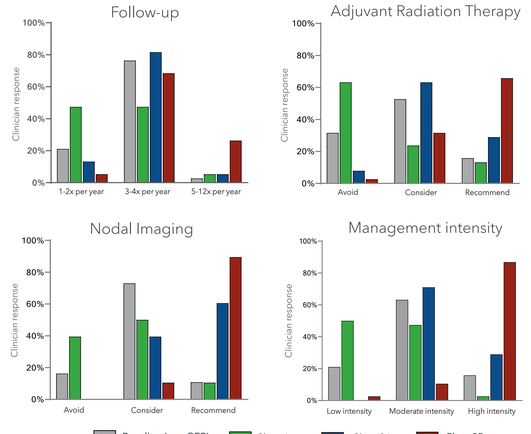
* American Joint Committee on Cancer Staging Manual, 8th edition; **Brigham and Women's Hospital staging system

Table 2. Utilization of the 40-GEP by study participants aligns with NCCN very and high-risk factors

Ranking	Clinicopathologic risk factor	Utilize 40-GEP
5	Depth >6mm or invasion beyond subcutaneous fat*	79%
5	Perineural involvement (Tumor cells within the nerve sheath of a nerve lying deeper than the dermis or ≥0.1mm)*	72%
5	Lymphatic or vascular involvement*	67%
5	Neurologic symptoms	56%
4	Poor differentiation*	69%
4	Immunosuppression	64%
4	Tumor diameter >4cm any location*	59%
4	Desmoplastic SCC*	31%
3	Tumor at site of prior radiation therapy	36%
3	Histologic features (acantholytic, adenosquamous or metasplastic)	46%
3	Rapidly growing tumor	26%
3	Recurrent	26%
3	Perineural involvement (Tumor cells within the nerve sheath of a nerve ≤0.1mm)	23%
3	Tumor diameter ≥2cm - <4cm on the trunk, extremities	15%

* Indicates NCCN defined very high-risk factor

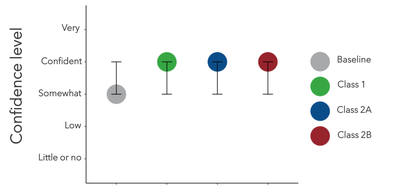
Figure 3. Risk aligned treatment decision are made when 40-GEP test results are integrated into patient management



Patient Vignette

- 68-year-old male
- 2.6 diameter lesion on left temple
- Biopsy confirmed SCC
- Infiltrating subtype
- Poor differentiation

Figure 4. Confidence in patient management decisions increased with use of 40-GEP



42% of Mohs surgeons reported increased confidence in management decisions with 40-GEP testing

Conclusions

- 97% of Mohs surgeons in this study are familiar with or use the 40-GEP test for high-risk SCC patients.
- Study results determined that clinicopathologic risk factors most likely to cause metastasis are also ones that would prompt usage of the personalized molecular information provided by the 40-GEP.
- 40-GEP results guide Mohs surgeons to make risk-aligned management plans and increase their confidence in these decisions.
- Overall, the 40-GEP can focus treatment options in the most risk-appropriate manner, allowing for an optimization of healthcare resources and improved patient outcomes.

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Disclosures

- JJS, SJK, ALF, AP, BR are employees and shareholders of Castle Biosciences, Inc.
- STA is a consultant for Castle Biosciences, Inc.

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