Impact of a prognostic 40-gene expression profiling test on clinical management decisions for high-risk cutaneous squamous cell carcinoma

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SYNOPSIS

One million cases of cutaneous squamous cell carcinoma (cSCC) are estimated to be diagnosed annually with an mortality rate of 1.5%-2%.[1] A 40-gene expression profile (40-GEP) test that assesses the biology of a primary cSCC tumor was recently validated for determining metastatic potential.[2] The 40-GEP test classifies patients into three risk groups: low (Class 1), high (Class 2A), and highest (Class 2B) risk for developing regional or distant metastasis within 3 years post-diagnosis. To assess the potential utility of the 40-GEP test for guiding cSCC patient management decisions, a clinical impact study was undertaken to determine if more precise risk assessment through 40-GEP testing would alter physicians' management decisions.

OBJECTIVE

To determine how results from the prognostic 40-GEP test would impact clinician management decisions and how their choices would align with a risk-directed management plan for high-risk cSCC, consistent with recommendations from the National Comprehensive Cancer Network (NCCN).

METHODS

Dermatology clinicians (dermatologists, nurse practitioners [NPs] and physician assistants [PAs]) attending a national dermatology conference were presented with 40-GEP test validation data. They were asked to rate clinicopathological features and molecular test results to assess their opinion of how concerning each is to cSCC prognosis (Figure 1). Vignettes describing patients with high-risk features were presented and clinicians were then asked to select a treatment plan using pre-test (no 40-GEP results), then, post-test (40-GEP Class 1, 2A, or 2B results) methodology.

RESULTS

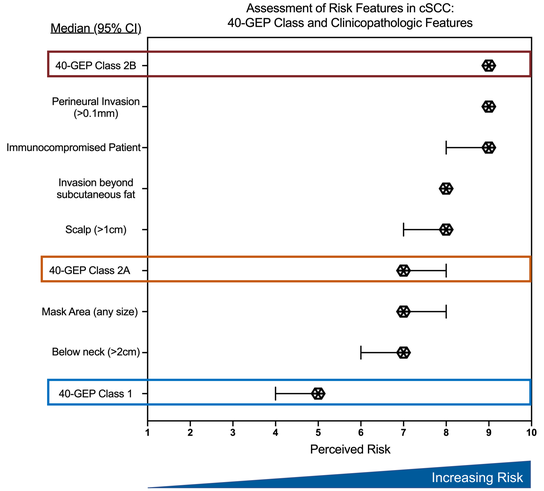
Table 1. Clinician demographics (n=162)

Years in practice	resident	11.7%
	1-10 years	40.7%
	11-20 years	14.2%
	21-30 years	19.8%
	>30 years	13.6%
Specialty	dermatologist	77.2%
	dermatologist/Mohs surgeon	11.1%
	dermatopathologist	1.2%
	dermatology NP/PA	8.6%
	other	1.9%
Newly diagnosed invasive cSCC patients seen in 2019	<50	31.5%
	50-100	34.0%
	100-200	16.7%
	200-400	14.2%
	>400	3.7%
High-risk cSCC patients encountered	≤1%	12.3%
	2-5%	34.0%
	6-10%	30.2%
	11-20%	14.8%
	>20%	8.6%
cSCC staging system used	I do not use any of these methods	30.9%
	I am not aware of these methods	13.0%
	I use a cSCC staging system:	56.1%
	AJCC7	17.6%
	AJCC8	58.2%
	BWH	24.2%

NP/PA = nurse practitioner/physician assistant, AJCC7 or AJCC8 = American Joint Committee on Cancer Staging Manual Edition 7 or 8, BWH = and Brigham and Women's Hospital

RESULTS cont.

Figure 1. Clinician assessment of perceived risk of metastasis with molecular 40-GEP Class and clinicopathologic features in cSCC*



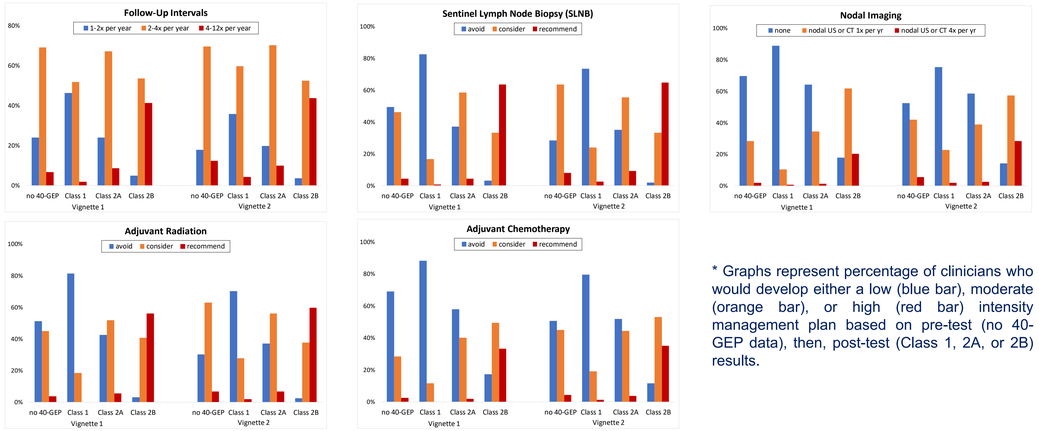
40-GEP Class	p value for comparison to feature		
	<0.0001	<0.05	n.s.
Class 1	All other features	---	---
Class 2A	Perineural invasion, immunosuppressed patient, Class 1 and 2B	Invasion beyond subcutaneous fat	Mask Area, Scalp >1cm, Below neck >2cm
Class 2B	Mask Area, Scalp >1cm, Below neck >2cm, Class 1 and 2A	Invasion beyond subcutaneous fat	Perineural invasion, immunosuppressed patient

*All clinicians surveyed were asked to rate, on a scale of 1-10 (1, lowest; 10, highest), the level of risk for metastasis associated with each of the features presented, independent of each other. Median values are plotted with error bars denoting 95% confidence intervals. P values for comparisons of risk between two features are shown in the table and reflect Friedman tests with a Dunn's correction for multiple comparisons.

Table 2. Clinical characteristics of patient vignettes

Vignette	Age, Sex	Tumor location	Size	Depth of lesion	Margin status	Histological differentiation	AJCC stage
1	67, male	scalp	1.2 cm	1.2mm	well-defined	poor	T1
2	67, male	scalp	1.2 cm	beyond subcutaneous fat	well-defined	well	T3

Figure 2. Effect of 40-GEP test results on clinicians' management decisions



* Graphs represent percentage of clinicians who would develop either a low (blue bar), moderate (orange bar), or high (red bar) intensity management plan based on pre-test (no 40-GEP data), then, post-test (Class 1, 2A, or 2B) results.

40-GEP Class	p value for comparison to 'no 40-GEP'					
	Vignette 1			Vignette 2		
	<.0001	<.05	ns	<.0001	<.05	ns
Class 1	SLNB	F/U, chemo, imaging, RT	----	SLNB, RT	F/U, imaging, chemo	----
Class 2A	----	----	F/U, SLNB, imaging, chemo, RT	----	----	F/U, SLNB, imaging, chemo, RT
Class 2B	F/U, SLNB, imaging, chemo, RT	----	----	F/U, SLNB, imaging, chemo, RT	----	----

SLNB = sentinel lymph node biopsy, F/U = follow-up, chemo = adjuvant chemotherapy, imaging = nodal imaging, RT = adjuvant radiation. Using a Friedman's test with Dunn's multiple comparisons correction, statistical significance was determined for each vignette when all post-test 40-GEP results were compared to pre-test 40-GEP (no 40-GEP)

Table 3. Comparison of changes by management modality

Management Modality*	Vignette 1						Vignette 2					
	Class 1		Class 2A		Class 2B		Class 1		Class 2A		Class 2B	
	Reduce	Increase	Reduce	Increase	Reduce	Increase	Reduce	Increase	Reduce	Increase	Reduce	Increase
Follow-up	47	4	18	22	4	86	43	4	20	15	1	72
Sentinel Lymph Node Biopsy	59	1	11	30	2	133	83	5	25	19	0	118
Nodal Imaging	35	4	12	20	2	103	44	4	26	13	1	89
Adjuvant Radiation	53	1	11	25	1	133	71	2	27	17	2	117
Adjuvant Chemotherapy	34	1	9	26	4	112	53	2	17	15	1	104

*Fisher's exact test with Freeman-Halton extension indicated that each row had statistically significant differences p<0.0001 when comparing Class 1, 2A, and 2B for a given modality.

CONCLUSIONS

- Results from this study support that dermatologists, NPs and PAs understand the prognostic risk associated with each 40-GEP class and can appropriately incorporate 40-GEP test results to assist in management decisions for high-risk cSCC patients.
- Management was altered in a risk-appropriate manner to align with metastatic risk as determined by 40-GEP Class results.
- The findings of this study suggest the possibility of more appropriate management and efficient resource allocation for cSCC patients when the 40-GEP test information is included in prognostic risk assessment.

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REFERENCES

1. Skin Cancer Foundation. https://www.skincancer.org/
2. Wysong, et al. 2020 under review JAAD