A prospective clinical utility study demonstrates that physicians use the 40-gene expression profile (40-GEP) to guide clinical management decisions for Medicare-eligible patients with cutaneous squamous cell carcinoma (cSCC)

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Background

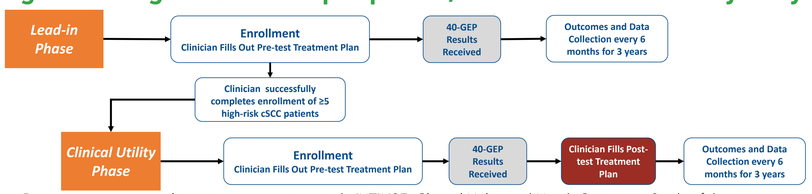
- The 40-GEP has demonstrated both analytical and improved clinical validity for risk stratification when compared to current staging systems, categorizing patients as low (Class 1), moderate (Class 2A), or high (Class 2B) risk for regional or distant metastasis within 3 years of diagnosis. [1-3]
- Previously reported clinical utility studies of the 40-GEP test have demonstrated its use in directing personalized risk-aligned patient management, inclusive of: follow-up, surveillance imaging, sentinel lymph node biopsy, and adjuvant radiation therapy [4-8] (**Table 1**).

Table 1. Previously reported clinical utility studies support personalized risk-aligned changes in overall management plans after 40-GEP testing from clinicians treating high-risk cSCC patients

Study	Design	Cohort (n)	Findings
Teplitz, *et al.* 2019	Prospectively designed study to determine impact of 40-GEP on recommended patient management strategies	402 clinicians (3 patient vignettes)	40-GEP test can significantly impact dermatologist management recommendations while remaining within the context of established guidelines. [4]
Farberg, *et al.* 2020	Retrospectively designed study integrating 40-GEP into NCCN recommendations for patient management	300 patients	Patients were risk-aligned with low, moderate, or high intensity management plans based on 40-GEP Class results. [5]
Litchman, *et al.* 2020	Prospectively designed study to determine impact of 40-GEP on recommended patient management strategies	162 clinicians (2 patient vignettes)	The 40-GEP test results influenced changes in clinical management decisions for high-risk SCC patients in a risk-appropriate manner while remaining within established guidelines. [6]
Au, *et al.* 2021	Case reports of patients retrospectively tested with 40-GEP	2 patients	The utility of the 40-GEP test to provide additional information for guiding patient management decisions and improving outcomes is demonstrated by two cases with identical tumor staging, yet divergent outcomes. [7]
Hooper, *et al.* 2022	Prospectively designed study to determine impact of 40-GEP on recommended patient management strategies	34 real-world clinicians (6 real-world patients)	The incorporation of the 40-GEP Class result had a significant impact on recommended patient management plans in a risk-appropriate manner while adhering to established guidelines. [8]

Methods

Figure 1. Design of UTILISE: a prospective, multi-center clinical utility study



- During an ongoing multi-center, prospective study (UTILISE: Clinical Utility and Heath Outcomes Study of the prognostic 40-GEP test) clinician recommendations for patient management were recorded before and after 40-GEP testing, along with patient clinicopathologic factors, test results, and clinical management.
- Analysis 1 consists of 11 private practice clinicians, comprised of Mohs surgeons (n=7), dermatologists (n=1), and physician assistants (n=3).
- For the lead-in phase, physicians fill out a treatment plan assessment after ordering the 40-GEP test but before receipt of results for 5 patients. Details of patient management and outcomes are then collected at six-month intervals for three years.
- Then, clinicians enroll patients into the clinical utility phase which will include the addition of a second questionnaire to complete after receipt of 40-GEP results. Details of any changes in patient management will be tracked along with patient outcomes, including metastasis-free survival, for all patients every six months for three years.
- This Analysis 1 of the clinical utility phase of Medicare-eligible patients enrolled in the study are reported here (n=59).

Clinical Issue and Objective

Management decisions for cSCC patients are determined by the clinician's evaluation of the risk of disease progression. Contributing to the challenge for implementing risk-appropriate patient management are the limitations of staging systems and treatment guidelines in predicting poor outcomes. A prognostic 40 gene expression profile test (40-GEP) has been validated to accurately stratify risk for metastasis in patients with one or more high risk factors.[1-3]

The objective of this ongoing prospective study is to capture the impact of 40-GEP testing on clinician recommendations and actions for patients for clinical management of their cSCC undergoing testing as part of their clinical care.

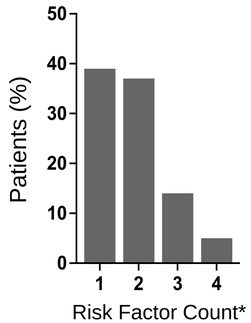
Results

Table 2. Patient demographics (n=59) of the Medicare-eligible cohort

Feature	n (%)
Age (range)	65-90*
Male	38 (64.4)
Location on Head or Neck	43 (72.9)
Patient immunosuppressed	2 (3.4)
Neurologic symptoms at tumor site	1 (1.7)
Chronic inflammation at tumor site	2 (3.4)
Tumor diameter ≥2cm	21 (35.6)
Rapidly growing tumor	6 (10.2)
Poorly defined borders	10 (17.2)
Poor differentiation	1 (1.7)
Depth of Invasion**	
Beyond subcutaneous fat	1 (1.7)
Clark level IV or V	18 (30.5)
Breslow's Thickness ≥2mm	3 (5.1)
Lymphovascular invasion	1 (1.7)
Perineural invasion	2 (3.4)
40-GEP Result***	
Class 1	52 (88.1)
Class 2A	7 (11.9)

*To maintain confidentiality, any age over 89 was reported as 90
**Investigators were allowed to report depth of invasion using various options
***No Class 2B risk scores were observed at the time of analysis

Figure 2. Clinicopathologic risk factor count for cohort



*n=3 cases with missingness and risk factor count of zero. Physician attested to eligibility for testing.

Table 3. Clinicians' perception of metastasis likelihood and overall management intensity changes with 40-GEP results

Class 1 — 40-GEP aligned **decrease** in risk perception and treatment

Class 2A — 40-GEP aligned **increase** in risk perception and treatment

What is the patient's risk of developing nodal or distant metastasis?

Pre-GEP	Post-GEP	n	% of Class 1*
5-10%	<5%	12	23.5%
10-30%	<5%	1	2.0%

Pre-GEP	Post-GEP	n	% of Class 2A
<5%	10-30%	3	42.9%
5-10%	10-30%	2	28.6%

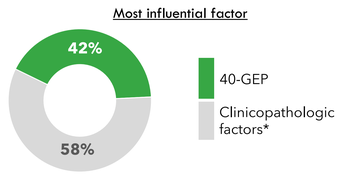
What is the overall management recommendation for this patient?

		n	
Moderate	Low	8	15.7%

		n	
Low	Moderate	3	42.9%
Moderate	High	1	14.3%

*n=1 case with no response

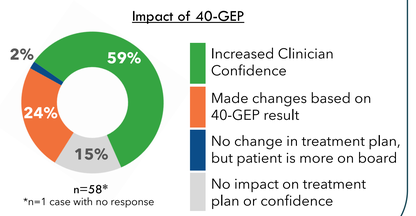
Figure 3. The 40-GEP result is the most influential factor impacting clinicians' management plans for 42% of patients



n=59

*Clinicopathologic factors as choice options: tumor size, location, depth, differentiation status, histological subtypes, perineural or lymphovascular invasion, immune status, patient age, history of cSCC, medical history

Figure 4. The 40-GEP result positively impacted patient management in over 80% of patients



n=58*

*n=1 case with no response

Table 4. Overall management change in patients tested with the 40-GEP compared to commonly used prognostic GEP tests in other cancers

Prognostic GEP test (Cancer)	Intended Use	Overall change in management
40-GEP (cSCC)	To guide treatment decisions in patients with cSCC with one or more high-risk factors	24%
70-GEP (breast)	To guide therapy decisions in patients with early-stage breast cancer[9]	24%
50-GEP (breast)	To guide adjuvant treatment selection in patients with early-stage breast cancer[10]	20%
21-GEP (breast)	To guide adjuvant treatment selection in patients with early-stage breast cancer[11]	44%
22-GEP (prostate)	To guide decisions about adjuvant radiation therapy[12]	18%
17-GEP (prostate)	To guide treatment decisions, including active surveillance, prostatectomy, and radiation therapy[13]	18%
23-GEP (lung)	To guide invasive procedures, including surgery and surveillance in low/intermediate risk of lung malignancy[14]	25%

Conclusions

- In this ongoing, prospective Clinical Utility and Health Outcomes Study (UTILISE), Analysis 1 showed that for more than 80% of patients under study, clinicians reported that the 40-GEP had a positive impact toward managing their high-risk SCC patient (i.e., increased confidence in treatment plan, risk-aligned changes, and patient more on board).
- The 40-GEP impacts physicians' assessment of risk for their patients with cSCC, which, in line with guidelines, is driving risk-aligned changes in treatment plans.
- The clinical actionability rates of the 40-GEP for cSCC are comparable to those of currently covered molecular tests for cancer patients, such as those GEP tests for breast, prostate, and lung cancer.

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Disclosures

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