Appropriate utilization of the prognostic 40-gene expression profile (40-GEP) test for cutaneous squamous cell carcinoma (cSCC) demonstrated by clinical reports and physician evaluation of real-world cases

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Synopsis

- There has been an unprecedented increase in cSCC incidence over the past three decades,[1] along with a continued discordance between available staging systems.[2,3]
- The 40-GEP test was developed and validated to augment traditional assessment approaches with the intention to improve risk-directed patient management for high-risk cSCC patients with one or more risk factors.
- The 40-GEP test has shown significant metastatic risk stratification independent of clinicopathologic factors and staging systems using these factors.[4,5]

Objective

- To evaluate appropriate utilization of the 40-GEP via analysis of a clinician survey, in which real-world cases submitted for clinical testing were presented with or without 40-GEP test results.
- To evaluate demographics of clinicians and usage of the 40-GEP test from one year of clinical orders.

Methods

- Six real-world cases, representing the spectrum of those submitted for clinical testing, were presented to 40-GEP test users (10+ orders/year minimum), first without 40-GEP result (pre-test) and then with 40-GEP results (post-test).
- Clinicians were asked what treatment recommendations they would make for each pre- and post-test patient case. Assessments from the 34 responding clinicians were ordinally scored and compared using Wilcoxon Rank or Kruskal-Wallis.
- Summary metrics on the 2515 samples received during the first year of clinical ordering (August 31, 2020–August 31, 2021) that met clinical testing criteria, including 40% tumor content and sufficient RNA, were generated.
- The 40-GEP Class call and patient risk factors were captured by clinical requisition form review. Risk factors included lesion located on the H or M area, ≥2cm diameter, poorly defined borders, patient immunosuppression, rapidly growing tumor, site of prior RT or chronic inflammation, History & Physical-other factor noted, high-risk subtype, Clark Level IV, >2mm invasion, poorly differentiated, LVI, PNI, invasion beyond the subcutaneous fat.

Results

- Clinicopathologic factors for the 6 real-world cases are shown in **Table 1**. Clinicians were well-aligned in their pre-test risk strategy levels among the real-world cases, despite randomization prior to presentation to clinicians (**Figure 1**).
- Post-testing, clinicians' overall management plan intensity was significantly changed depending on GEP prognostic risk (**Figure 2A**). Recommendations for specific treatment decisions were altered depending on 40-GEP result (**Figure 2B-D**). Asterisks indicate significant change from baseline, corrected for family-wise error, p<0.016).
- 40-GEP testing resulted in 68.8% Class 1, 28.3% Class 2A, 2.9% Class 2B primary SCC lesions (**Figure 3A**). Of the n=2515 samples meeting clinical testing criteria, 98.1% generated successful test results (n=2468 Class call; n= 47 multigene failures) (**Figure 3B**). 75.3% of clinically tested samples have 2 or more high risk factors (median = 3, average = 2.8) (**Figure 3C**). The cases submitted for testing align with the intended use population with almost all cases classifying as NCCN high or very high risk (**Figure 3D**).

Real-World Case Clinical Impact Study

Table 1. Clinicopathologic risk factors for six real-world cases

Case	Age	Sex	Location	Subtype	Differentiation	Additional high-risk factors
High	81	♂	L superior medial forehead	NR	Moderate	Invasion beyond subcutaneous fat, PNI, LVI, ≥2 cm
Moderate High	86	♂	R cheek	Infil	Poor	Invasion >2 mm
Moderate Low	75	♀	R temporal scalp	Infil	Poor	
Low.1	75 IS*	♂	R mid preauricular cheek	Acan	Moderate	
Low.2	69	♀	R inferior postauricular skin	Infil	Moderate	
Lowest	71	♀	R dorsal hand (rapidly growing)	NR	Moderate	

PNI = perineural invasion; LVI = lymphovascular invasion; NR = not reported; Infil = infiltrating; Acan = acantholytic *IS = immunosuppressed

Figure 1. Pre-test overall management intensity by case

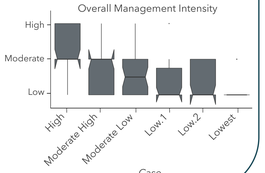
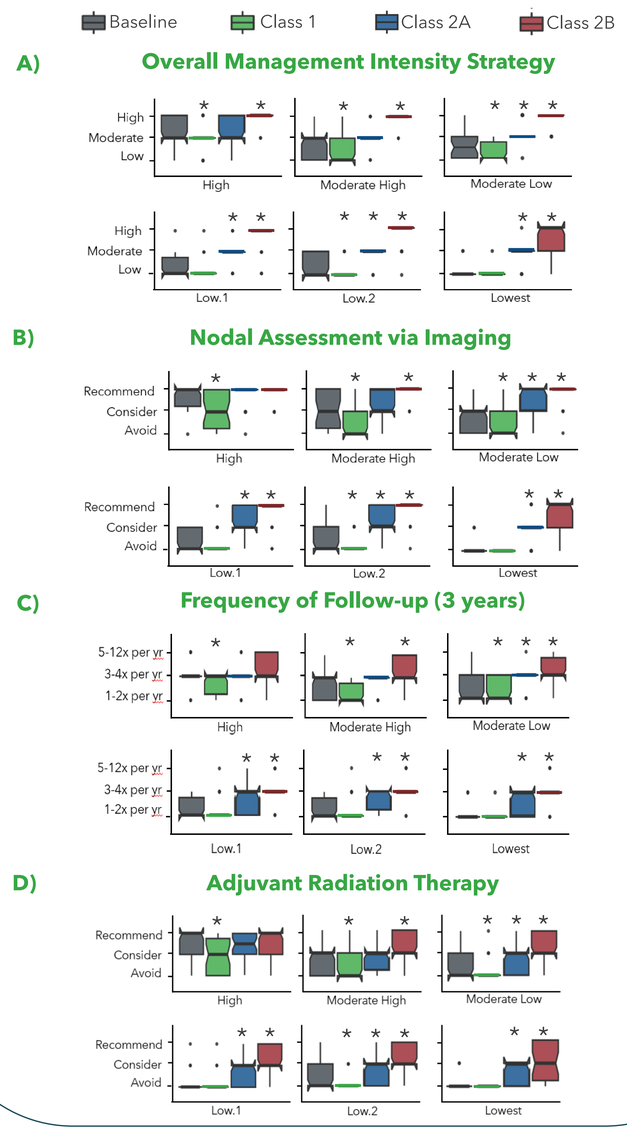


Figure 2. 40-GEP impacts clinician management planning in real-world patient scenarios



Real-World Clinical Testing Experience

Figure 3A. Molecular risk profile of patients tested during first year of clinical availability of 40-GEP

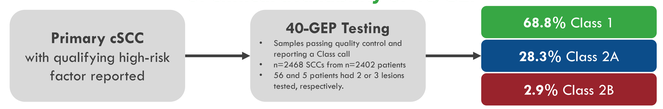


Figure 3B. The 40-GEP test has high technical reliability

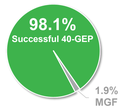


Figure 3C. Most tested patients have 2 or more high risk factors

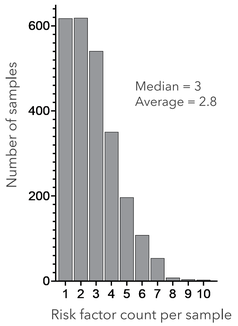


Figure 3D. Clinicopathologic risk group of tested patients

Clinicopathologic Risk*		% of Patients
NCCN:	Very High Risk	39.3%
	High Risk	60.5%
	Low Risk**	0.2%
BWH T-stage:	T1	38.5%
	T2a	39.4%
	T2b	21.6%
	T3	0.6%

*Estimated based on factors reported. All reported PNI was considered an upstaging factor. For patients with >1 lesion tested, the riskiest lesion is reported here. **All patients designated low risk by NCCN presented with infiltrating histopathology.

Conclusions

- Summary metrics from one year of clinical orders of the 40-GEP test demonstrate that clinicians are ordering the test for the intended use population
- Survey findings revealed that when incorporating 40-GEP testing into their decision-making process for high-risk cSCC patients, clinicians do so in a risk-aligned manner
- These results indicate that the additional information provided by the 40-GEP test can appropriately assist in management decisions when included with traditional risk factor assessment.

References

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Acknowledgments & Disclosures

- This study was sponsored by Castle Biosciences, Inc.
- All authors contributed to and approved the presentation.
- JS, BR, AF, SK and RC are employees and shareholders of Castle Biosciences, Inc.

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