Clinical usage data demonstrates appropriate utilization of the prognostic 40-gene expression profile (40-GEP) test for cutaneous squamous cell carcinoma with one or more risk factors

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Background

- The metastatic rate for cutaneous squamous cell carcinoma (cSCC) is low; however, the overall incidence is high (~1-2.5 million cases/year), and patients presenting with high-risk factors have shown rates of regional or distant metastasis of up to 47%.[1]
- The clinically available 40-gene expression profile (40-GEP) test was developed and independently validated to accurately classify risk for regional or distant metastasis as low (Class 1), moderate (Class 2A), or high (Class 2B) in patients with primary cSCC and one or more high-risk factors.[2] (**Figure 1**)
- **Figure 2** demonstrates the ability of the 40-GEP test to classify patients based on risk of metastasis.[3] The 40-GEP test has also shown significant metastatic risk stratification independent of clinicopathologic factors and staging systems using these factors.[2,3]

Figure 1. Clinical use of the 40-GEP test

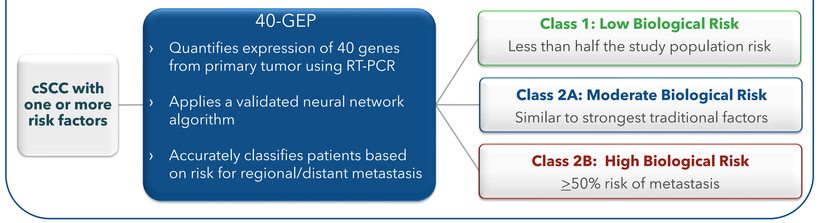
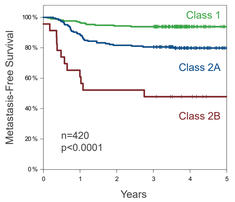


Figure 2. The 40-GEP test classifies patients based on risk for metastasis[2,3]



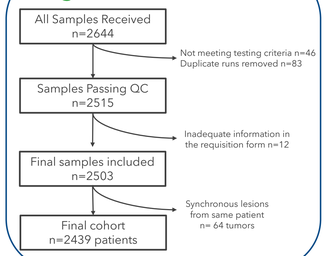
40-GEP Risk Class	Overall Cohort	
	3-year MFS (95% CI)	Overall Event Rate
Class 1	93.9% (90.7-97.2%)	6.6%
Class 2A	80.5% (75.0-86.5%)	20.0%
Class 2B	47.8% (31.2-73.3%)	52.2%
Without 40-GEP	85.5% (82.2-88.9%)	15.0%

All cases were ≥high risk by NCCN guidelines for localized cSCC or met Mohs micrographic surgery appropriate use criteria.[3]

Methods

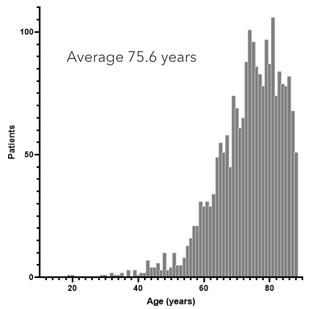
- Summary metrics on the 2503 samples from n=2439 patients received during the first year of clinical ordering (August 31, 2020–August 31, 2021) that met clinical testing criteria, including 40% tumor content and sufficient RNA, were generated (**Figure 3**).
- The 40-GEP Class call and patient risk 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.

Figure 3. Tested Cohort



Results

Figure 4. Age of Patients in Tested Cohort



The average age of the patient cohort was 75.6 years old. >89 years old (304 patients [12%]) were categorized as a single group, as ≥90 is considered protected health information and not available for detailed analysis.

Table 1. Distribution of Clinicopathological Risk Factors

Risk Factor	% of Patients
Located on H or M*	79.5%
Size ≥2 cm	41.8%
Rapidly growing tumor	38.2%
Borders poorly defined	28.0%
Poorly differentiated	19.2%
Invasion beyond subcutaneous fat	17.6%
Specific high-risk subtype	13.5%
Perineural invasion	10.3%
Clarks Level IV or >2mm depth	9.6%
Patient immunosuppression	8.7%
Neurological symptoms in tumor region	4.8%
History and Physical-Other Factor	3.8%
Prior radiation/Chronic Inflammation	1.9%
Lymphovascular involvement	1.2%

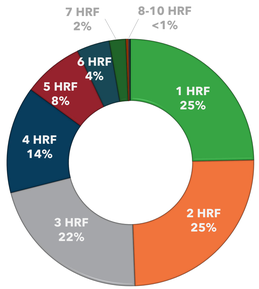
Tumor and patient characteristics of patients tested with the 40-GEP test (n=2503 samples). *mask areas of face, genitalia, hands, feet, cheeks, forehead, scalp, neck and pretibia

Table 2. Cohort aligns with a high-risk cSCC population

Clinicopathologic Risk*		% of Patients
NCCN[4]:	Very High Risk	39.3%
	High Risk	60.5%
	Low Risk**	0.2%
AJCC-8[5]:	T1	48.6%
	T2/T3	51.4%
BWH T-stage[6]:	T1	38.5%
	T2a	39.4%
	T2b	21.5%
	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.

Figure 5. Most tested patients have ≥2 high-risk factors (HRF)



>75% of test ordered had >2 risk factors, with an average of 2.8

Figure 6. Molecular risk profile of patients tested during first year of clinical availability of 40-GEP

Test Result	% of Tests	# of Tests n=2455*	1-2 Risk Factors (99% CI)	3-4 Risk Factors (99% CI)	>5 Risk Factors (99% CI)
Class 1	68.8%	1,687	54.4% (51.2-57.5%)	33.2% (30.2-36.2%)	12.4% (10.40-14.62%)
Class 2A	28.3%	696	38.7% (33.8-43.5%)	41.8% (37.1-46.7%)	19.5% (15.9-23.5%)
Class 2B	2.9%	72	37.5% (22.5-53.0%)	40.3% (25.0-55.3%)	22.2% (10.53-35.8%)

*48 multi-gene failure (MGF) samples were excluded for Class call distribution assessment from n=2503 samples. Bootstrap (x10,000); confidence interval (CI); reject Ho = 0%; p<0.01 for all

Conclusions

- The intended use population aligns with the cases submitted for clinical testing, demonstrating physician consideration of appropriate use criteria for the 40-GEP test.
- Due to the presentation of one or more risk factors, these cSCC patients are at a higher risk of poor outcomes when compared to the general cSCC population, yet nearly 70% received a Class 1 test result, signifying that they are at biologically lower risk for metastasis.
- The information provided by the 40-GEP test can improve stratification of high-risk cSCC patients and if incorporated into clinical assessments with any number of traditional clinicopathologic risk factors, could assist physicians in guiding more risk-appropriate surveillance and treatment decisions.

References

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2. Wysong *et al.* JAAD 2021
3. Ibrahim *et al.* Future Oncology 2021
4. NCCN Guidelines Version 2.2021
5. Amin *et al.* AJCC8 2017
6. Ruiz *et al.* JAMA Derm 2019

Disclosures

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- ASF is an investigator and speaker for CBI and receives research funding and honoraria. ALF, JJS, SJK, MSG and RWC are employees and options holders of CBI.

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