Performance and clinical decision-making using the prognostic 40-gene expression profile (40-GEP) test in 1,018 patients with high-risk cutaneous squamous cell carcinoma (SCC)

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Background

- The 40-gene expression profile (40-GEP) test categorizes patients with a primary SCC who have one or more clinicopathologic risk factors into three biological risk groups based on the likelihood of regional, nodal, or distant metastasis (Low= Class 1; Moderate= Class 2A; High= Class 2B).[6]
- The 40-GEP test has been shown to improve risk assessment and provide more precise, individualized metastatic risk stratification when combined with current risk prediction methods.[6,7]
- Clinical utility studies have demonstrated the ability of 40-GEP test results to guide risk-aligned patient management including changes to follow-up, surveillance imaging, SLNB, and ART following 40-GEP testing (**Table 1**).[8-10]

Table 1. Individualized risk-aligned changes in overall management plans are made post-40-GEP testing

Clinical Impact Studies of 40-GEP[8-10]			
Clinicians	**Patients**	**Specific clinical recommendation changed with 40-GEP**	**Overall change in management plan recommended with 40-GEP**
34 real-world test users	6 real-world cases	F/U, SLNB, baseline nodal imaging, adjuvant radiation (ART), adjuvant chemotherapy, surveillance imaging	Integration of the 40-GEP Class call significantly impacted recommended patient management plans in a risk-appropriate manner while staying within guidelines.
162 dermatologists*	2 patient vignettes	F/U, SLNB, nodal imaging, adjuvant radiation, adjuvant chemotherapy	
402 dermatologists	3 patient vignettes	F/U, SLNB referral, radiation, chemotherapy, immunotherapy	

F/U = follow up schedule; SLNB = sentinel lymph node biopsy; *Majority dermatologists with 8.6% dermatology NP/PA, 1.2% dermatopathologist, 1.9% other

Methods

- The two independent cohorts (n=420, validation[7] n=598, performance[11]) were compared and then combined (n=1,018).
- Overall event (i.e., metastasis) rates, Kaplan-Meier analysis for metastasis-free survival, and univariate Cox regression analysis were performed for both the individual and combined cohorts.
- Clinical utility and management changes in the combined cohort were modeled based on the pre- and post-40-GEP test results of a published clinical impact study of real-world cases.[8]

References

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Disclosures

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Clinical Issue and Objective

SCC is a common skin cancer with overall favorable prognosis. However, due to its high incidence, mortality exceeds that of melanoma.[1,2] Broad guidelines, along with lack of standardized and accurate risk assessment methods complicates treatment planning for SCC patients.[3-5]

This study reports on 40-GEP performance metrics in risk stratification of >1,000 patients and highlight its impact on guiding risk-aligned decisions for patients with SCC

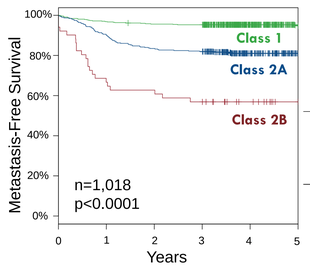
Results

Table 2. 40-GEP accurately and consistently stratifies metastatic risk

	Ibrahim et al.[7] (n=420) Overall event rate = 15.0%	Arron *et al.*[11] (n=598) Overall event rate = 9.9%
	Relative fold change (Class/Overall)	**Relative fold change (Class/Overall)**
Class 1	**0.4x**	**0.4x**
Class 2A	**1.3x**	**1.7x**
Class 2B	**3.5x**	**3.6x**

- Statistically significant 40-GEP-based risk stratification was observed in each of the two independent cohorts (p<0.001, log-rank).

Figure 1. Performance of the 40-GEP to stratify high-risk SCC patients by risk for regional or distant metastasis (n=1,018)



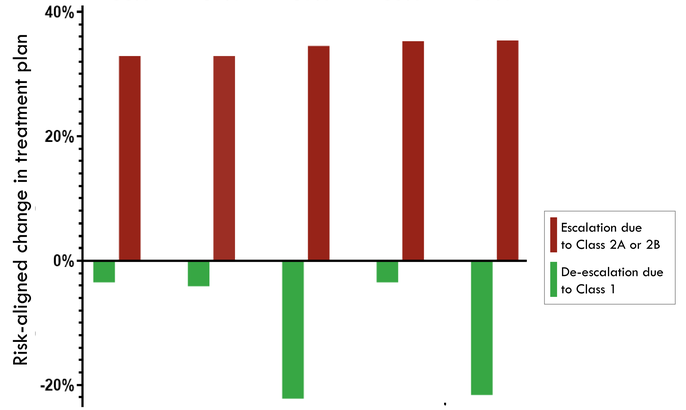
40-GEP Risk Class	Overall Cohort 3-year MFS (95% CI)	Overall Event Rate	Univariate Cox regression analysis (HR)
Class 1	95.3% (93.6-97.0%)	5.1%	1
Class 2A	81.9% (78.2-85.8%)	18.8%	4.0
Class 2B	56.9% (44.8-72.2%)	43.1%	11.4
Without 40-GEP	88.2% (86.3-90.2%)	12.3%	--

p < 0.0001; CI= confidence interval; HR= Hazard Ratio; MFS= metastasis free survival

- Kaplan-Meier survival analysis of the combined cohort (n=1,018) demonstrated statistically significant 3-year metastasis-free survival between all classes. Cox regression analysis established hazard ratios for Class 2A and Class 2B as 4.0 and 11.4, respectively (p<0.0001).

Figure 2. 60% of patients in the combined cohort would have a risk-aligned change in management plans post-40-GEP results

% Patients with change due to 40-GEP	Follow-up Frequency	Adjuvant Radiation Therapy	Nodal Imaging	Surveillance Imaging	Overall Management Change
	36%	37%	57%	39%	57%



- When management changes from Hooper *et al.*[8] were used on the combined cohort to model clinical utility of the 40-GEP, results showed that 60% of high-risk SCC patients would have risk-aligned (i.e., escalation of treatment due to Class 2A or 2B results; de-escalation due to a Class 1 result) alterations in at least one of the following modalities: follow-up frequency, adjuvant radiation therapy, nodal imaging, and surveillance imaging.

Conclusions

- In two independent high-risk SCC cohorts, the 40-GEP consistently demonstrates significant metastatic risk stratification.
- When cohorts are combined, the 40-GEP continues significant performance in identifying metastatic risk, as shown with patients receiving Class 2A and Class 2B results incurring a 4- and 11-fold increase in metastasis, respectively, when compared to those with Class 1 results.
- The impact of the 40-GEP on management decisions modeled across this large cohort represents a substantial improvement in risk-aligned clinical decision-making.

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