Clinical utility of the 40-gene expression profile (40-GEP) for improved patient management decisions when combined with current clinicopathological risk factors for cutaneous squamous cell carcinoma (cSCC): Case Series

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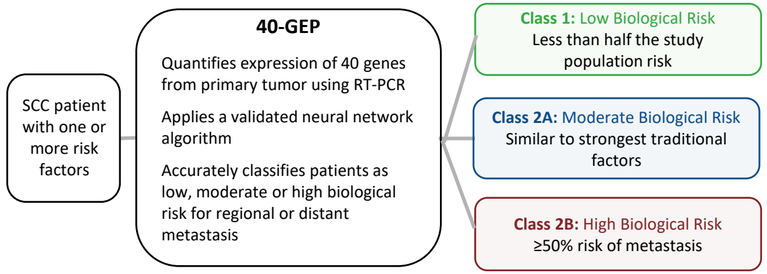
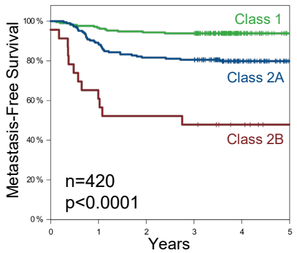
BACKGROUND

- Managing cSCC is a significant clinical issue. Although the fatality rate is low, the incidence of cSCC is high (~1-2.5 million cases/year), and **deaths from this disease are estimated to surpass those from melanoma**.[1,2]
- The National Comprehensive Cancer Network (NCCN)[3] categorizes a patient as high risk for recurrence and/or metastasis by the presence of a single NCCN-defined high-risk factor, resulting in a broad range of downstream management guidelines.
- Current tumor staging systems, such as the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 8th Edition (AJCC8)[4] and Brigham and Women's Hospital (BWH) system,[5] help determine recurrence and metastatic risk by translation of high-risk factors into tumor (T) stages. However, these systems often fail to adequately classify patient risk.
- **Despite attempts to improve risk assessment, a standardized and accurate stratification system remains a clinically unmet need in the care of cSCC patients.**
- A prognostic 40-gene expression profile (40-GEP) test has recently been developed and independently validated to show improved stratification of metastatic risk in high-risk cSCC patients compared to current staging systems.[6]





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%

Figure 1. The 40-GEP test classified patients based on risk for regional and/or distant metastasis. Formalin-fixed paraffin-embedded samples from primary cSCC lesions with corresponding clinicopathologic and outcomes data were collected and assessed by the 40-GEP (n=420). All cases were either high-risk by NCCN guidelines for localized cSCC or met Mohs Micrographic Surgery (MMS) appropriate use criteria (AUC).[7] Kaplan-Meier analysis demonstrated a statistically significant difference between Class results.

REFERENCES

1. Rogers *et al* JAMA Derm 2015
2. Karia *et al* JAAD 2013
3. NCCN Guidelines Version 2.2020
4. Amin *et al* 2017
5. Ruiz *et al* JAMA Derm 2019
6. Wysong *et al* JAAD 2021
7. Ibrahim *et al* Derm Surg. Under review

FUNDING & DISCLOSURES

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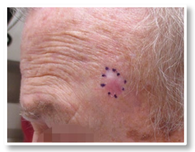
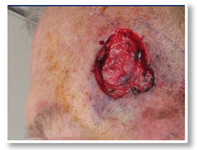
RESULTS

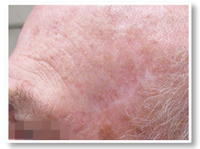
Case #1

- 65 y.o. male
- Liver/Kidney SOTR
- 1.3 cm
- Poorly diff SCC
- **AJCC8 Stage T1**
- **BWH Stage T2a**

- History of renal and liver transplantation and cSCC
- Presented with a papule on left temple, previously treated with cryotherapy
- Mohs micrographic surgery (MMS) was completed in 4 stages
- Subsequent pathology review demonstrated margins positive for cSCC
- The patient declined any further treatments and was recurrence-free for 4 years (death by other causes)
- **Retrospective analysis of the initial biopsy with the 40-GEP test resulted in a Class 1 result**

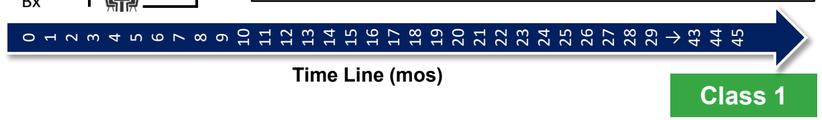






MMS- 4 stages, Marginal Layer D (+) foci of SCC (initially determined to be negative, but on subsequent analysis showed a small foci of cSCC)

Patient notified of false negative results
After Rad/Onc consultation, Patient declined any further treatment

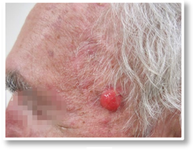


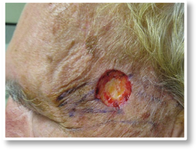
Class 1

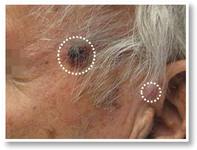
Case #2

- 69 y.o. male
- Liver SOTR
- 1.5 cm
- Poorly diff SCC
- **AJCC8 Stage T1**
- **BWH Stage T2a**

- History of liver transplantation and cSCC
- Presented with a 2-month history of an exophytic growth on left temple
- Mohs micrographic surgery (MMS) was completed in 2 stages
- Metastatic SCC's presented 3 months later
- **Retrospective analysis of the initial biopsy with the 40-GEP test resulted in a Class 2B result**







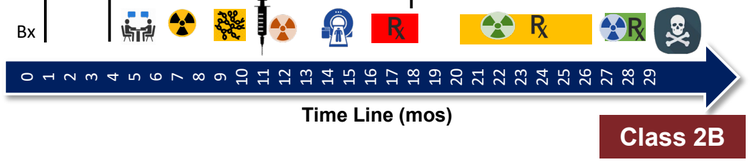
MMS- 2 stages

Recurrence

(+) for metastatic poorly diff. SCC

(+) for mediastinal metastasis

Discontinued due to disease progression



Class 2B

LEGEND

- Onc/Rad Onc Consult
- 52Gy Rad Left scalp/forehead
- 67Gy Radiation Left neck LNs
- 50Gy Right lower lung lobe
- 28Gy Esophageal region
- Left neck/Lymphadenopathy
- U/S guided FNA – Left neck LN
- PET/CT
- Cetuximab
- Carboplatin/Paclitaxel (6 cycles)
- Pembrolizumab
- Palliative Care/Patient Deceased

CONCLUSIONS

- These findings demonstrate the utility of the 40-GEP test as an adjunct to enhance cSCC risk stratification.
- Case #1 highlighted a biologically less aggressive tumor with the same staging as Case #2 that did not metastasize despite incomplete surgical clearance.
- Case #2 highlighted a biologically aggressive tumor despite having a relatively less aggressive BWH staging. Adjuvant treatment might have been appropriate for the patient earlier in the disease course and may have altered his prognosis.
- Integrating novel molecular prognostication with traditional clinicopathological risk factors can improve stratification of high-risk cSCC patients and may inform selection of risk-appropriate treatment and surveillance strategies.