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 patient case. Assessments from the 34 responding clinicians were ordinally scored and compared using Wilcoxon test.
- 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 and pathology report review. Risk factors included lesion on the H or M area, ≥2 cm 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).

**Conclusions**

- 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.
- 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.
- 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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**Disclosures**

- This study was sponsored by Castle Biosciences, Inc.
- All authors contributed to and approved the presentation.
- J.S, B.R, A.F, S.K and R.C are employees and shareholders of Castle Biosciences, Inc.