Improvement of risk assessment in cutaneous melanoma (CM) by a prognostic 31-gene expression profile (31-GEP) test over AJCC-based staging alone

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BACKGROUND

• A substantial number of melanoma-related deaths occur in patients originally diagnosed with early American Joint Committee on Cancer (AJCC) stage disease, suggesting aggressive tumor biology despite having clinicopathologic features associated with low-risk disease.

• A 31-gene expression profile (31-GEP) test has been developed and validated in retrospective and prospective studies2,3 to predict 5-year metastatic risk from primary cutaneous melanoma (CM) tumor tissue with a high degree of technical reliability.9

• The 31-GEP test classifies melanoma as Class 1A (lowest risk), Class 1B (low risk), Class 2A (increased risk), or Class 2B (highest risk).

• This prognostic information is used to inform patient management decisions, including frequency of follow-up and surveillance imaging, referrals, sentinel lymph node biopsy guidance, and consideration of adjuvant therapy.10-15

OBJECTIVE

To determine the impact on risk prediction when results from the 31-GEP test are used with AJCC 8th edition staging.

METHODS

• Archival formalin-fixed paraffin-embedded CM tumor samples from 18 U.S. centers (n=690, Stage I-III) along with clinical, pathological, and outcomes data for each case were collected under an IRB-approved protocol1-4. Stage I-II cases were restaged according to AJCC 8th edition criteria.

• The 31-GEP test was performed in a CAP-accredited/CLIA-certified laboratory using high-throughput RT-PCR assays as previously described1-5.

• The Kaplan-Meier method was used to estimate 5-year recurrence-free (RFS; time to either a regional or distant metastatic event), distant metastasis-free (DMFS; time to any metastatic event beyond the regional nodal basin), and melanoma-specific survival (MSS; time from diagnosis to death documented as from melanoma) rates with significance determined by log-rank test. All non-recurrent cases had at least 5 years of follow-up.

• Class 1A- and 2B-predicted MSS outcomes for each stage were compared to rates associated with AJCC 8th edition staging16.

• Based on National Comprehensive Cancer Network (NCCN) guidelines for surveillance and follow-up, AJCC binary low and high-risk groups are defined as Stage I-IIA and Stage IIB-IIV, respectively. Cox multivariate regression analysis for MSS was performed comparing AJCC binary risk and 31-GEP test results.

RESULTS

Figure 1. Stage-specific survival rates for the 31-GEP cohort align with the AJCC 8th edition database survival rates

Figure 2. 31-GEP results identify significantly different risk groups

Table: 31-GEP cohort with 8th ed. staging

Table: AJCC 8th ed. cohort16

Table: 5-year MSS (95% CI) Event Rate

Table: Cox multivariate regression analysis

Figure 3. Addition of 31-GEP test results improves risk obtained by AJCC 8th edition staging alone

CONCLUSIONS

• In the study cohort of Stage I-III melanoma cases1,4 with similar survival outcomes to the 8th edition AJCC cohort, the 31-GEP test result was able to add information to further stratify patients with lower and higher risks than predicted by clinicopathologic staging alone. Multivariate analysis demonstrated that a 31-GEP Class 2B result was an independent predictor of MSS with a greater hazard ratio than AJCC binary risk.

• As accurate risk assessment is important for patient management decisions, use of the 31-GEP test can help guide these choices, including follow-up, sentinel lymph node biopsy guidance, surveillance and possible adjuvant therapy, as has been previously published10-15.

REFERENCES


ACKNOWLEDGEMENTS

The authors wish to acknowledge the following collaborating physicians and institutions for their contributions to this study: Drs. Nancy Leachman and John Vello, Oregon Health and Science University; Drs. Pamela Gerami and Jeff Wyman, Northwestern University; Drs. Jane Messina and Jonathan Zager, Moffitt Cancer Center; Dr. Rene Gonzales, University of Colorado Cancer Center; Drs. David Lawson, Keith Dietlein, and Marie Russell, Emory University; Dr. Stephen Lyle, University of Massachusetts Medical School; Dr. Gilbert Jackel, Keck-Sanford Clinic, Dr. Anthony Gmahgee, Kelsey-Reed Foundation, Dr. Lene Cramer, University of Arizona Cancer Center, Dr. T. Christopher Winstead, Florida Hospital Memorial Medical Center; Dr. Lemme Krintzes, Dermatology North Palm Beach, Dr. Martin Fleming, University of Tennessee Health Science Center; Drs. Laura Perin and Jonathan Ho, University of Pittsburgh Medical Center; Dr. Alexander Miller, START Center for Cancer Care; Dr. Sarah Espada, Affiliated Dermatology, Dr. Jason Robbins, Pathology Associates, Dr. David Fantus, Partner Dermatology Specialists, Dr. Brian Gastner, Cleveland Clinic, and Dr. Daniel Rosen, Baylor College of Medicine.

FUNDING & DISCLOSURES

This study was sponsored by Castle Biosciences, Inc., which provided funding to contributing centers for tissue and clinical data retrieval. RWC, KRC, & FAM are employees and options holders of Castle Biosciences, Inc. GP is a fellow with the National Society for Cutaneous Medicine which receives funding from Castle Biosciences, Inc. OR is a consultant for Castle Biosciences, Inc.