Clinical impact of a 31-gene expression profile test on physician recommendations for management of melanoma patients in a prospectively tested cohort

Martin Fleming, MD[1], Clare Johnson, RN[2], Kyle Covington, PhD[2], Joseph Gadzia, MD[3], Larry Dillon, MD[4], Federico A. Monzon, MD[2]

[1]The University of Tennessee Health Science Center, Memphis, TN; [2]Castle Biosciences, Inc., Friendswood, TX; [3]Kansas Medical Clinic, Topeka, KS; [4]Dr. Larry Dillon, Colorado Springs, CO

Background

- A 31-gene expression profile (GEP) test which identifies cutaneous melanoma tumors as low risk (Class 1) or high risk (Class 2) of metastasis has been clinically validated.[1-3]
- The test has been shown to influence physicians to direct clinical management of cutaneous melanoma patients in several clinical use studies (Table 1).[4-6]
- To further assess the clinical impact of the GEP test, we undertook a study to evaluate and compare clinical management plans prospectively, including initial workup, follow-up intervals, and referral patterns, established by physicians prior to and after GEP testing.
- Here we present preliminary results of this multicenter, prospective clinical utility study to determine the clinical impact of the GEP test on patient management plans.

Table 1. Management changes in three clinical use studies

Study	Result
Berger (2016)[4] Prospective, multicenter n patients = 163	53% changed mgmt after inclusion of GEP result
Farberg (2017)[5] Dermatologist survey n physicians = 169	47-50% changed mgmt after inclusion of GEP result
Schuitevoerder (2017)[6] Prospective, single center n patients = 91	52% of mgmt decision based on GEP result using decision tree model

Methods

- Of 269 patients enrolled in the study, 247 patients from 16 dermatology, medical oncology and surgical oncology centers had complete data at time of censoring (September 30, 2017).
- The RT-PCR-based GEP test was performed using primary melanoma tumor tissue from FFPE samples. The test provides a binary classification for risk of metastasis, Class 1 (low risk) or Class 2 (high-risk), using a proprietary predictive modeling algorithm.
- At initial evaluation, prior to GEP testing, each patient's pre-test management recommendations were collected, including laboratory tests (labs), imaging, clinical visits, adjuvant treatment discussion, and referral to surgical or medical oncology.
- Post-test management recommendations were collected at the subsequent visit following receipt of GEP test result.
- Pre- and post-test management plans were compared and changes were categorized as increase, decrease, or inconclusive.

Results

Table 2. Cohort demographics

Clinical Characteristics	Overall n=247
Median age (range), years	63 (19-94)
T stage	
T1	115 (47%)
T2	66 (27%)
T3	33 (13%)
T4	18 (7%)
Not assessed	12 (6%)
Breslow thickness	
Median (range), mm	1.1 (0.1-18.0)
≤1 mm	121 (49%)
>1 mm	126 (51%)
Mitotic index	
<1/mm^2	87 (35%)
≥1/mm^2	160 (65%)
Ulceration	
Absent	204 (83%)
Present	43 (17%)
Site	
Trunk	77 (31%)
Extremity	124 (50%)
Head and neck	43 (17%)
GEP result	
Class 1	181 (73%)
Class 2	66 (27%)

Table 3. Clinical and molecular features across treatment groups

Feature	Dermatology n=74	Surgical Oncology n=166	Medical Oncology n=7
Breslow[a]	0.6 (0.1-10.3)	1.3 (0.1-8.0)	1.1 (0.2-18.0)
Ulceration[b]			
Absent	65 (88%)	133 (80%)	6 (86%)
Present	9 (12%)	33 (20%)	1 (14%)
Mitosis[b]			
<1/mm^2	38 (51%)	45 (27%)	4 (57%)
≥1/mm^2	36 (49%)	121 (73%)	3 (43%)
GEP Class[b]*			
Class 1	60 (81%)	114 (69%)	7 (100%)
Class 2	14 (19%)	52 (31%)	0 (0%)

[a]Median (range), [b]Count (percent), *p<0.05, Fisher's exact test

Figure 1. Number of cases with a documented change in management

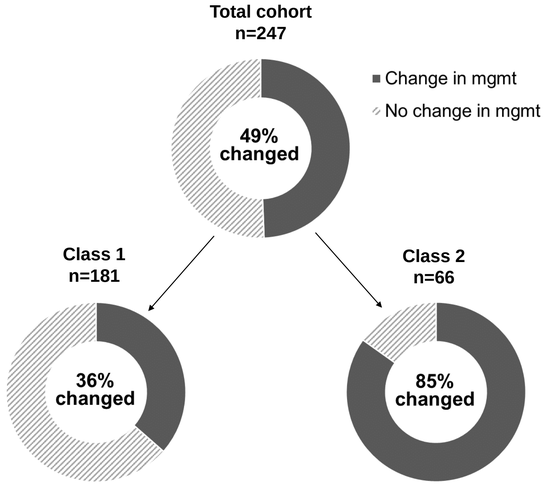
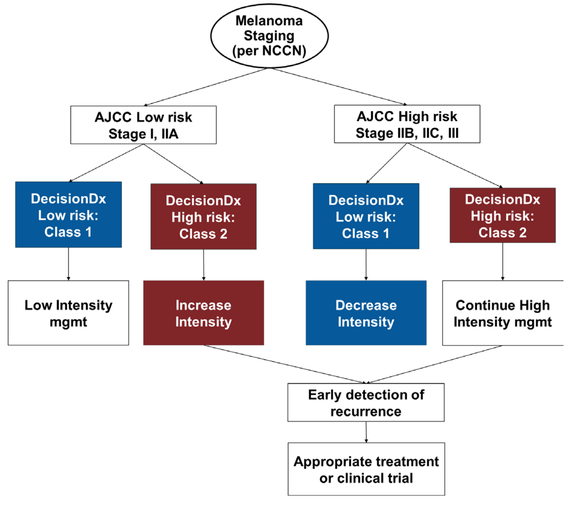


Table 4. Frequency of each modality of change in Class 2 patients with decreases or increases in intensity of clinical management

	Class 2	
	Decrease	Increase
Labs	3	22
Imaging	4	41
Visits	1	27
Referral	3	13

Figure 3. Schematic representation of risk stratification using AJCC stage with GEP test result to guide patients' clinical management



Conclusions

- Overall, 49% of tested patients had a change in clinical management.
- The majority of reported management changes were in a risk-appropriate direction, with 91% of decreases in care provided to low-risk Class 1 patients and 72% of increases in care provided to high-risk Class 2 patients.
- Physicians used GEP results to individualize management based on biological risk, as determined by the test, while still remaining within the context of established practice guidelines.
- Results of this prospective study show that the accurate identification of risk provided by the GEP informs appropriate clinical management and patient care. The proportion of patients in which the test informs change in management is similar to that reported in three additional clinical utility studies.[4-6]

References

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Disclosures

CJ, KC and FAM are employees and stockholders of Castle Biosciences, Inc.
The proprietary GEP test is clinically available through Castle Biosciences as the DecisionDx®-Melanoma test (www.SkinMelanoma.com).