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

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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.[1-4]
- The test has been shown to influence physicians to direct clinical management of cutaneous melanoma patients in several clinical use studies (Table 1).[5-7]
- 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)[5] Prospective, multicenter n patients = 163	53% changed mgmt after inclusion of GEP result
Farberg (2017)[6] Dermatologist survey n physicians = 169	47-50% changed mgmt after inclusion of GEP result
Schuitevoerder (2017)[7] Prospective, single center n patients = 91	52% of mgmt decision based on GEP result using decision tree model

Methods

- Of 204 patients enrolled in the study, 127 patients from 15 dermatology, medical oncology and surgical oncology centers completed study participation at time of censoring (June 30, 2017).

Methods

- The RT-PCR-based GEP test was performed using primary tumor tissue. Metastatic risk class was determined using a proprietary predictive modeling algorithm which provides a binary classification of Class 1 (low risk) or Class 2 (high-risk).
- At initial evaluation, prior to GEP testing, each patient's baseline data was assessed. Physicians' pre-test recommendations for follow-up were collected and categorized as laboratory tests (labs), imaging, clinical visits, adjuvant treatment discussion, and referral to surgical or medical oncology.
- At the subsequent visit following receipt of GEP test result, follow-up recommendations were again collected to capture any changes in management.
- Changes were categorized as increases, decreases or no change based on comparison of management plans pre- and post-receipt of GEP test result.

Results

Table 2. Cohort demographics

Clinical Characteristics	Overall n=127
Median age (range), years	63 (28-95)
T stage	
T1	61 (48%)
T2	32 (25%)
T3	17 (13%)
T4	8 (6%)
Not reported	9 (7%)
Breslow thickness	
Median (range), mm	1.0 (0.1-18.0)
≤1 mm	66 (52%)
>1 mm	61 (48%)
Mitotic index	
<1/mm^2	78 (61%)
≥1/mm^2	49 (31%)
Ulceration	
Absent	103 (81%)
Present	20 (16%)
Growth pattern	
Superficial spreading	30 (24%)
Nodular	16 (13%)
Desmoplastic	6 (5%)
Lentigo maligna	3 (2%)
Other/not assessed	72 (56%)
Site	
Trunk	43 (34%)
Extremity	66 (52%)
Head and neck	18 (14%)
GEP result	
Class 1	96 (76%)
Class 2	31 (24%)

Table 3. Clinical and molecular features across treatment groups

Feature	Dermatology n=41	Surgical Oncology n=82	Medical Oncology n=4
Breslow[a]*	0.5 (0.1-4.9)	1.2 (0.0-7.5)	1.7 (0.2-18.0)
Ulceration[b]			
Absent	88% (36)	78% (64)	75% (3)
Present	12% (5)	17% (14)	25% (1)
Mitosis[b]			
<1/mm^2	68% (28)	60% (49)	25% (1)
≥1/mm^2	32% (13)	40% (33)	75% (3)
GEP Class[b]			
Class 1	83% (34)	71% (58)	100% (4)
Class 2	17% (7)	29% (24)	0% (0)

[a]Median (range), [b]Percent (count), *p<0.001

Figure 1. Number of cases increasing or decreasing intensity of management by GEP Class

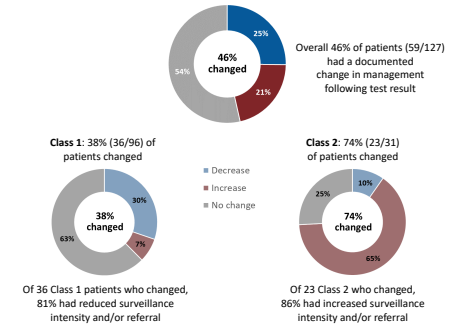
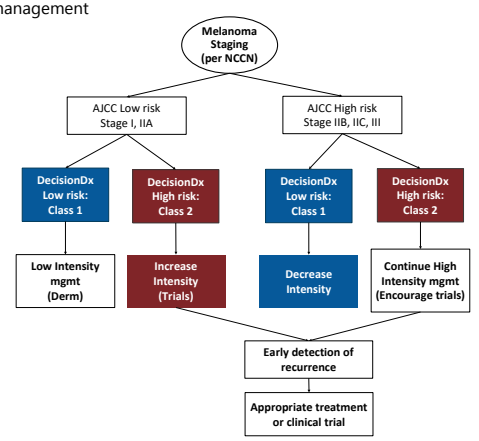


Table 4. Frequency of each modality of change in patients with decreases or increases in intensity of clinical management

	Class 1		Class 2	
	Decrease	Increase	Decrease	Increase
Labs*	3	0	1	7
Imaging*	4	0	2	14
Adjuvant	0	0	0	1
Visits*	14	4	0	10
Referral*	13	2	3	6

*p≤0.005, Fisher's exact test

Figure 2. Schematic representation of risk stratification using AJCC stage with GEP test result to guide patients' clinical management



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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).

Conclusions

- Overall, 46% of tested patients had a change in clinical management
- The majority of reported management changes were in a risk-appropriate direction, with 81% of decreases in care provided to low-risk Class 1 patients and 87% 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 change in management is similar to three additional clinical utility studies.