Development and validation of a nomogram incorporating the 31-GEP test and clinicopathologic factors for accurate prediction of recurrence risk in patients with cutaneous melanoma

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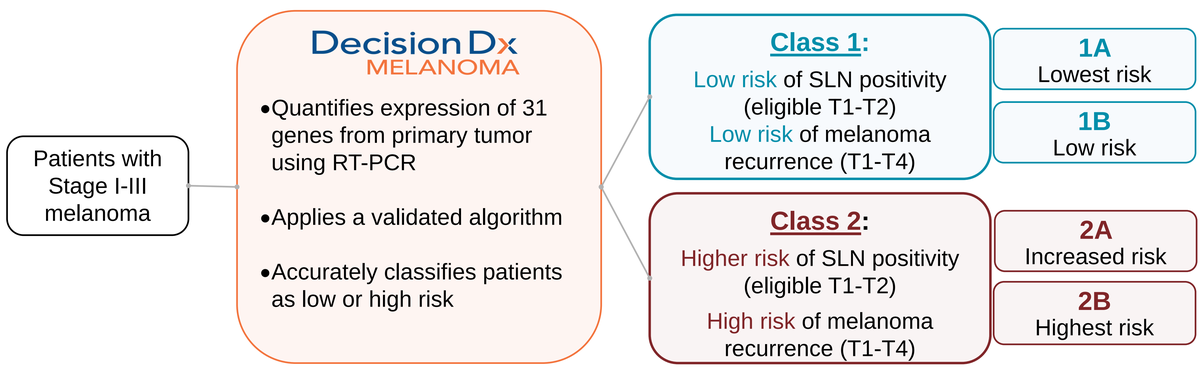
BACKGROUND

- Patients with cutaneous melanoma (CM) have an individual recurrence risk determined by clinical, pathological, and genetic features.
- The 31-gene expression profile (31-GEP) test is an independent significant predictor of 5-year risk of recurrence and distant metastasis.[1-7]
- 31-GEP results classify tumor biology as lowest-risk (Class 1A), low-risk (Class 1B), high-risk (Class 2A), and highest-risk (Class 2B):



OBJECTIVE: To develop a nomogram tool combining 31-GEP class and clinicopathologic risk features for predicting CM recurrence.

METHODS: NOMOGRAM DEVELOPMENT

- A prospective cohort of 685 patients from 9 dermatology centers with minimum 1yr follow-up or a recurrence event at any time was included in nomogram development.
- A logistic regression model was fitted on clinical and pathological data to determine relative predictive value for recurrence risk. Covariate inclusion for the model was selected by lowest Bayesian information criteria (BIC) value with fewest clinical features.
- The nomogram was validated on a retrospective cohort of 901 Stage I-III CM patients with ≥ 5 years follow-up or a recurrence event, and goodness of fit was determined by linear regression.

RESULTS

Table 1. Patient clinical and pathologic features per 31-GEP Class

	All patients n=685	Class 1A n=557	Class 1B n=41	Class 2A n=33	Class 2B n=54
Age median (range), years	67 (22-90)	65 (22-90)	71 (33-90)	71 (52-91)	74 (26-90)
Breslow thickness (range), mm	0.5 (0.1-13)	0.5 (0.1-5)	0.8 (0.2-6)	1.2 (0.2-7.5)	2.6 (0.2-13)
Male	60% (411/685)	59% (330/557)	51% (21/41)	79% (26/33)	63% (34/54)
Ulceration present	7% (50/685)	3% (17/557)	7% (3/41)	6% (2/33)	52% (28/54)
Mitotic rate ≥ 2 mm^2	18% (121/685)	9% (52/557)	32% (13/41)	52% (17/33)	72% (39/54)

REFERENCES

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DISCLOSURES

Castle Biosciences, Inc (CBI) provided statistical analysis support for nomogram development. KRC and HGC are employees and option holders of CBI. Prospective cohort registry is independently managed by the Cutaneous Oncology Research Consortium (CORC). RT, DB, JZ have no relevant disclosures.

RESULTS CONTINUED

Figure 1. Multivariate Cox regression analysis of 31-GEP and clinicopathologic features

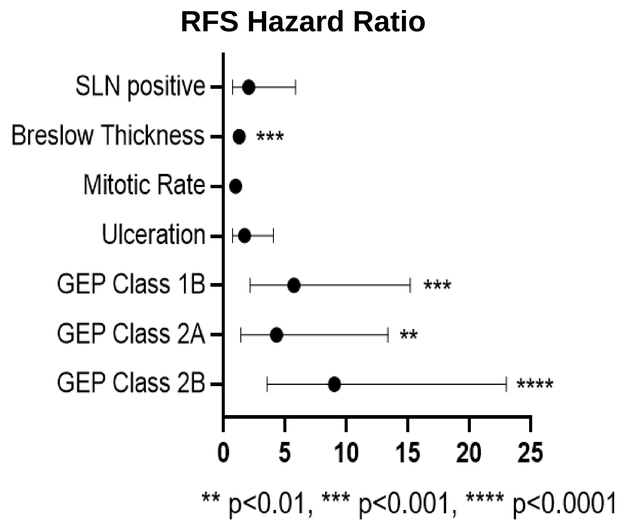
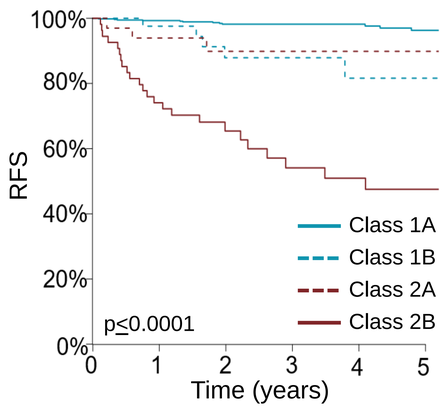


Figure 2. Kaplan-Meier estimation of Recurrence-Free Survival (RFS)



GEP Class	N	Events	1.5-yr RFS
Class 1A	557	14 (2.5%)	98.9% (98.0-99.8%)
Class 1B	41	6 (14.6%)	97.6% (93.0-100%)
Class 2A	33	4 (12.1%)	93.9% (86.1-100%)
Class 2B	54	24 (44.4%)	70.3% (59.1-83.6%)

Figure 3: Optimum Model selected by BIC

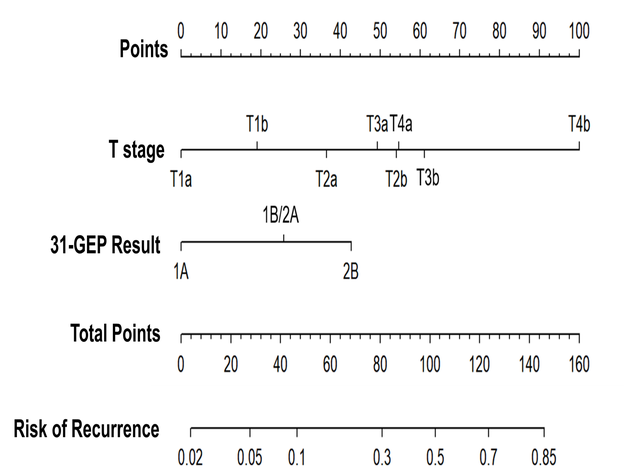
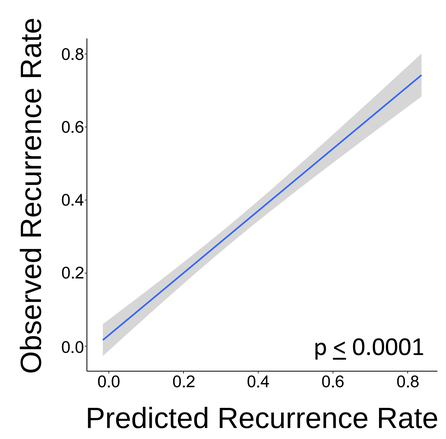


Figure 4. Validation of the nomogram in a retrospective cohort of 901 patients with Stage I-III cutaneous melanoma



CONCLUSIONS

- This nomogram combines the 31-GEP test result with clinical features to create a clinically useful, accurate tool for determining an individual's risk of recurrence to optimize patient care.
- Because Sentinel Lymph Node (SLN) status is not a feature in this nomogram, this tool can be used to provide patient risk of recurrence prior to or in the absence of a SLN biopsy.
- A future aim of this study is to generate a mobile application for conversion of clinical and molecular data to a patient's recurrence risk.

Figure 5. Impact of T stage and 31-GEP on risk of recurrence

	AJCC v8	GEP Class 1A	GEP Class 1B/2A	GEP Class 2B
T1a	1.9%	2%	5%	9%
T1b	6.9%	4%	9%	19%
T2a	12.1%	7%	19%	24%
T2b	25.0%	15%	29%	45%
T3a	25.0%	11%	27%	40%
T3b	45.0%	19%	35%	53%
T4a	37.5%	15%	29%	45%
T4b	85.7%	48%	71%	83%