Recurrence prediction in cutaneous melanoma with 31-gene expression profiling and sentinel lymph node biopsy

Graham Litchman DO[1], MS, Hillary Caruso PhD[2], Kyle Covington PhD[2], Robert Cook PhD[2], Darrell Rigel MD, MS[3]
1. National Center for Cutaneous Melanoma 2. Castle Biosciences, Inc. 3. New York University School of Medicine

BACKGROUND

- The prognostic 31-GEP test is an accurate predictor of metastatic risk for patients with cutaneous melanoma, stratifying patients into low (Class 1A), intermediate (Class 1B/2A), and high-risk (Class 2B) [1-2].
- Previous prospective and retrospective studies have validated the 31-GEP as a strong predictor of risk of recurrence and distant metastasis, independent of other clinical and pathological features [2-7].
- The test has demonstrated clinical utility in guiding patient management, including frequency of follow-up, use of imaging for surveillance, and referral for interdisciplinary care [8-12].
- Use of the 31-GEP to guide sentinel lymph node biopsy (SLNB) decisions has recently been validated, such that patients with T1-T2 melanoma over the age of 55 with a GEP Class 1A result have a very low probability of SLN positivity and favorable outcomes[11].

OBJECTIVE

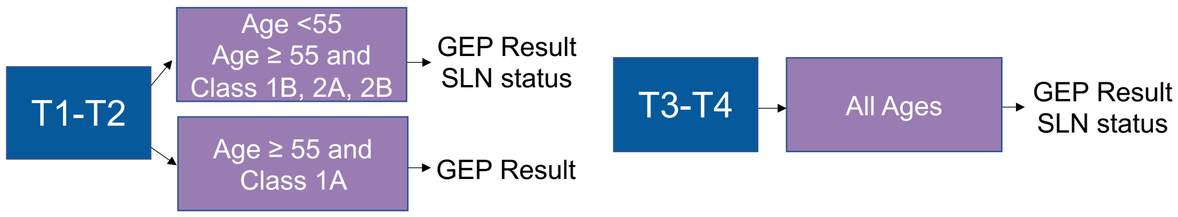
To perform a comparative evaluation of the prognostic accuracy of the 31-GEP and sentinel lymph node biopsy.

METHODS

- We evaluated the prognostic accuracy of the 31-GEP and SLNB in a cohort of 1479 patients comprised of 3 previously described cohorts[4-6] and a novel cohort of stage I-III cutaneous melanoma cases collected from 7 institutions under an IRB-approved protocol.

Study	Design	n
Novel cohort	Archival, multi-center	211
Gastman et al.[4]	Archival, multi-center	690
Greenhaw et al.[6]	Prospective, single center	256
Hsueh et al.[5]	Prospective, multi-center	322

- We also compared the sensitivity and NPV of 31-GEP and SLNB in a model which assumed use of the 31-GEP to triage patients for SLNB.



RESULTS

Table 1. Demographics of the 1479 patients in study

Variable	All Cases (n=342)
Age, median (range)	61 (18-94)
Breslow thickness, mm median (range)	1.2 (0.1-29)
Ulceration present	346 (23.4%)
AJCC stage	
I	852 (57.6%)
II	313 (21.1%)
III	312 (21.1%)

Table 2. Accuracy metrics of GEP and SLN

	GEP	SLN	GEP and SLN
RFS	*n=1479*	*n=867*	*n=1479*
Sensitivity	76% (71-80%)	57% (51-63%)	86% (82-90%)
Specificity	76% (73-78%)	74% (70-77%)	69% (66-72%)
PPV	46% (42-50%)	50% (44-56%)	43% (41-45%)
NPV	92% (90-94%)	79% (75-82%)	95% (93-96%)
DMFS	*n=1223*	*n=867*	*n=1223*
Sensitivity	76% (70-82%)	61% (55-68%)	88% (83-92%)
Specificity	69% (66-72%)	72% (68-75%)	60% (57-63%)
PPV	35% (31-39%)	39% (34-44%)	32% (30-34%)
NPV	93% (91-95%)	86% (83-89%)	96% (94-97%)
MSS	*n=1157*	*n=630*	*n=1157*
Sensitivity	86% (77-92%)	72% (60-80%)	94% (87-98%)
Specificity	65% (62-68%)	67% (64-70%)	57% (54-60%)
PPV	17% (13-20%)	16% (13-21%)	15% (14-16%)
NPV	98% (97-99%)	96% (95-98%)	99% (98-100%)

Only patients with reported end points were included in analysis. Patients from Greenhaw, et. al. did not have DMFS or SLN status reported. Patients from Hsueh, et. al. did not have MSS reported. Accuracy metrics of combined tests determined for patients who had positive SLN OR GEP Class 2 result.

Table 2. Sensitivity and NPV of 31-GEP and SLNB in a model assuming use of 31-GEP to guide SLNB decisions

	GEP	SLN	GEP and SLN
RFS	*n=1479*	*n=842*	*n=1479*
Sensitivity	76% (71-80%)	56% (50-62%)	84% (79-88%)
NPV	92% (90-94%)	79% (75-82%)	94% (93-95%)
DMFS	*n=1223*	*n=842*	*n=1223*
Sensitivity	76% (70-82%)	61% (53-68%)	86% (80-90%)
NPV	93% (91-95%)	86% (83-89%)	95% (94-97%)
MSS	*n=1157*	*n=609*	*n=1157*
Sensitivity	86% (77-92%)	72% (60-82%)	94% (97-98%)
NPV	98% (97-99%)	96% (95-98%)	99% (98-100%)

CONCLUSIONS AND SIGNIFICANCE

- These results show that the 31-GEP detects more patients with high-risk melanoma than SLNB and combining both achieves best sensitivity.
- The high NPV of the 31-GEP test assures that patients with low-risk results have low probability of metastasis or death from melanoma.
- Use of 31-GEP to guide SLNB decisions does not alter the sensitivity of combined 31-GEP and SLN status on prognosis.

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