Validation of a ClinicoPathological and Gene Expression Profile (CP-GEP) model for sentinel lymph node metastasis in primary cutaneous melanoma

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Objective

To validate the CP-GEP model for primary cutaneous melanoma to predict lymph node metastasis. This risk model combines Breslow thickness, age, and gene expression variables from primary melanoma (Sominidi-Damodaran *et al*, EADO 2019).

Introduction

- As patients with primary cutaneous melanoma and a positive sentinel lymph node (SLN, stage III) are candidates for adjuvant systemic therapy, a SLN biopsy (SLNB) is indicated in more patients.
- However, SLNB is an invasive procedure, and is negative in approximately 80% of patients.
- There is a need for a non-invasive test to accurately identify patients with primary cutaneous melanoma without nodal metastases.

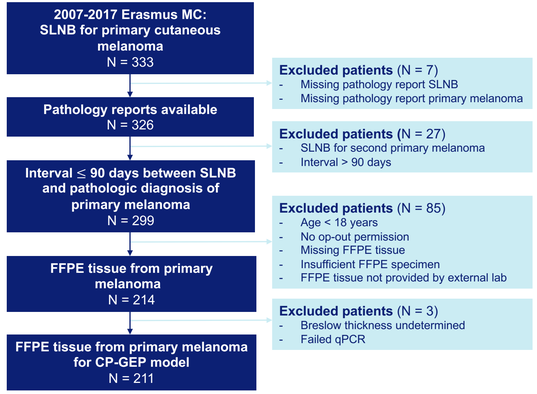
Methods

Patient selection
- >18 years
- SLNB at Erasmus Medical Center (January 2007-December 2017)
- SLNB within 90 days after diagnosis of primary cutaneous melanoma

Tissue analyses
- Total RNA was extracted from formalin-fixed paraffin-embedded (FFPE) primary cutaneous melanomas and reversed transcribed into cDNA.
- Expression of 8 target genes involved in melanoma metastasis (ITGB3, PLAT, SERPINE2, GDF15, TGFBR1, LOXL4, IL8, MLANA) were analyzed using an optimized qPCR protocol.

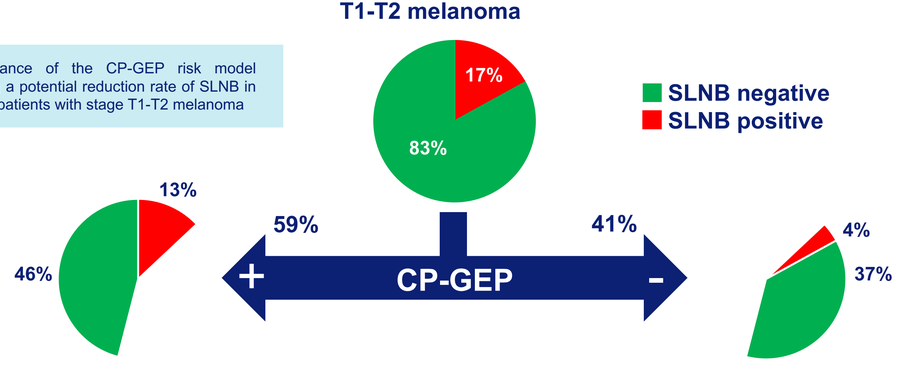
Statistics
- Using the pathology result of SLNB as gold standard, sensitivity (sens), specificity (spec), positive (PPV) and negative predictive value (NPV) of the CP-GEP model were calculated.

Results



Characteristic	SLNB Negative (-) N = 153	SLNB Positive (+) N = 58
Male gender, N (%)	79 (52.9%)	32 (55.2%)
Mean age at SLNB, years (SD)	55 (15)	55 (13)
Biopsy location		
Head & neck	1 (0.7)	0 (0)
Trunk	78 (51.0)	32 (55.2)
Upper extremity	26 (17.0)	7 (12.1)
Lower extremity	47 (30.7)	18 (31.0)
Unknown	1 (0.7)	1 (1.7)
Breslow depth (mm), N (%)		
0.50-1.00	10 (6.5)	1 (1.7)
1.01-2.00	77 (50.3)	17 (29.3)
2.01-4.00	40 (26.1)	30 (51.7)
> 4.00	26 (17.0)	10 (15.8)
Ulceration, N (%)	32/147 (21.8)	22/57 (38.6)

Performance of the CP-GEP risk model showing a potential reduction rate of SLNB in 41% of patients with stage T1-T2 melanoma



T stage	N	Prevalence	SENS	SPEC	NPV	PPV	SLNB reduction rate
All	211	27.5%	91.4%	27.5%	89.4%	32.3%	22.3%
T1	11	9.1%	N/A	100%	90.9%	N/A	100%
T2	94	18.1%	88.4%	37.7%	90.6%	22.6%	34.0%
T3	70	42.9%	96.7%	7.5%	75.0%	43.9%	5.7%
T4	36	27.8%	100%	0.0%	0.0%	27.8	0.0%
T1-T2	105	17.1%	77.8%	44.8%	90.7%	22.6%	41.0%

Conclusions

- **The CP-GEP model is a non-invasive and validated tool that is able to predict nodal metastasis in an independent Dutch population.**
- **This risk model is able to accurately identify patients with primary cutaneous melanoma that can safely forego SLNB.**
- **The CP-GEP model is a promising tool for patient care, preventing unnecessary surgery in the majority of patients.**

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Conflicts of interest

BMS (AvdV, DG), Ipsen (AvdV), Merck (AvdV), MSD (AvdV), Novartis (AvdV, DG), Pfizer (AvdV), Pierre Fabre (AvdV), Roche (AvdV), Sanofi (AvdV), Amgen (DG)