The clinicopathological and gene expression profile (CP-GEP) is a biomarker for outcome in patients with melanoma who are eligible for sentinel lymph node biopsy.

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Introduction

Currently, sentinel lymph node biopsy (SLNB), is still considered the most appropriate, standard of care, tool to stage melanoma patients, who present with newly diagnosed stage IB-II melanomas. With the developments in systemic therapy, specifically the shift towards earlier stages of disease, the use of the minimally invasive, but nonetheless invasive, SLNB is once again being scrutinized. The aim of the current study was to validate the diagnostic accuracy of the clinicopathological-gene expression profile (CP-GEP) model on an independent cohort from the Netherlands Cancer Institute.

Methods

Patients who presented with newly diagnosed clinical stage I/II melanoma, who presented at the Netherlands Cancer Institute (NKI; Amsterdam, the Netherlands), between 2007 and 2015, were eligible for this current study. Data were prospectively collected in an institutional database and were retrospectively analysed. Data cut-off for follow-up was January 2022. The CP-GEP included

the RNA expression of eight target genes associated with tumor development (i.e. MLANA, GDF15, CXCL8, LOXL4, TGFBR1, ITGB3, PLAT and SERPINE2) and two housekeeping genes in combination with CP variables Breslow thickness and age.

Results

A total of 252 patient's samples and clinical data were submitted. In 9 patients, the CP-GEP was unable to be performed, in n=4 this was due to the lack of being able to identify the housekeeping genes (1.6%) and n=5 due to both a lack of housekeeping and target gene expression (2.0%). The final analysis was performed on the remaining 243 cases. Median age was 57 years old (IGR 46 – 67), 51.4% was female. Breslow thickness was 1.8 mm (IQR 1.3-2.95) and 53 patients demonstrated involvement of the SLNB (21.8%). Over half of the patients were diagnosed with pT2 tumour of which 44.9% pT2a. Median follow-up was 83 months. CP-GEP identified 68 (28%) patients as CP-GEP Low Risk and 175 (72%) as High Risk. The sensitivity of CP-GEP was 92.5%, specificity was 33.7%, PPV was 28.0% and NPV was 94.1% for all comers (T1-T4). The CP-GEP had the best performance in T1 with a NPV 95.2% and SLNB reduction rate (RR) of 80.8%, and in the pT1b-pT2a melanomas with a NPV of 93.3% and a SLNB RR of 45.5%. In terms of long-term survival, the 5-year RFS of CP-GEP low-risk was 89.6% (95% CI: 79.5-94.9) vs. 76.8% (95% CI: 69.8-82.4) for CP-GEP high-risk patients.

Conclusion

This CP-GEP model demonstrated good prognostic performance in an independent validation cohort, particularly for pT1b-pT2a melanoma patients and thus should be considered added value to current standard of care practice.

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