Identification of patients at high risk for relapse using the Merlin Assay (CP-GEP) in an independent cohort of 930 patients (pts) with stage I/II melanoma who did not undergo sentinel lymph node biopsy.

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Introduction

Sentinel lymph node biopsy (SLNB) is the gold standard for nodal assessment in staging cutaneous melanoma (CM) according to AJCC v8 guideline. More than 80% of pts are negative for nodal metastasis, but most pts who relapse or die from melanoma are initially diagnosed as 'low risk' early-stage. Previously we showed that the clinicopathological-gene expression profiling (CP-GEP) model can stratify stage I-II pts and pts who did not undergo SLNB in low and high-risk of recurrence (Amaral et al., EJC, 2023). Here we investigate CP-GEP ability to stratify pts who did not undergo SLNB for their risk of recurrence in substantial cohort.

Methods

We analysed formalin-fixed paraffin-embedded primary tumor samples of 930 pts with stage I/II CM diagnosed between 2000-2017, included in the Central Malignant Melanoma Registry, who did not

receive SLNB. Tumors were analysed blinded to clinical outcome. The CP-GEP model used combines the expression of 8 genes (SERPINE2, GDF15, ITGB3, CXCL8, LOXL4, TGFBR1, PLAT and MLANA) by quantitative reverse transcription polymerase chain reaction with age and Breslow thickness to obtain a binary output: CP-GEP Low- or High-Risk. Relapse-free survival (RFS), distant metastasis free survival (DMFS) and Melanoma Specific Survival (MSS) were evaluated using Kaplan-Meier curves.

Results

We included 930 pts (stage IA-IIC). 41% were females, median age was 64-year-old, median Breslow thickness was 0.5 mm, the majority were not ulcerated (94%). For all pts, the 5-year RFS was 90.9%; 5-year DMFS was 96.9 and 5-year MSS was 97.5%. Median follow-up time was 55 months (RFS). CP-GEP identified 879 pts as Low-Risk and 51 pts as High-Risk. The 5-year RFS rate was 94.6% for CP-GEP Low-Risk pts versus 26.6% for CP-GEP High-Risk patients (HR 25.08; $p<0.001$). 5-year DMFS was 98.6% vs 62.1% (HR 35.39; $p<0.001$) for CP-GEP Low-Risk and High-Risk pts, respectively. The 5-year MSS was 99.4% for Low-Risk and 61.7% for High-Risk pts (HR 71.05; $p<0.001$), capturing 12 out of 16 melanoma specific deaths in the CP-GEP High-Risk group.

Conclusion

This comprehensive study shows that CP-GEP has the potential to stratify pts with early-stage melanoma who did not undergo SLNB based on their risk of recurrence. Pts with CP-GEP Low-Risk have a good long-term survival while pts with CP-GEP High-Risk have a high risk of recurrence. CP-GEP may have the potential to stratify pts beyond SLNB.

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