Using a clinicopathologic and gene expression model to predict prognosis in stage I-II primary cutaneous melanoma: a multicenter Danish cohort study

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Background: Melanoma patients without sentinel node metastasis (stage I-II) constitute a remarkably heterogeneous group regarding recurrence and survival. While adjuvant immunotherapy for stage IIB-C melanoma has gained approval from FDA and EMA, its use can lead to severe adverse effects and financial strain on healthcare systems. There is a need for new diagnostic approaches to more precisely identify early-stage melanoma patients at high risk of recurrence who could benefit from adjuvant treatment and intensified surveillance. The clinicopathological and gene expression profile model (CP-GEP), initially developed to predict sentinel node metastasis, has demonstrated promise in stratifying stage I-II melanoma patients into high and low risk of recurrence. This study aimed to validate the prognostic utility of the CP-GEP in an independent multicentre Danish cohort of stage I-II melanoma patients.

Methods: The study included 438 patients with T1-T3 cutaneous melanoma and negative sentinel node biopsies (stage I-II) performed between 2010 and 2015 at two university clinics in Denmark. Archived formalin-fixed paraffin embedded primary melanoma tissue was collected, and CP-GEP was applied to each case. CP-GEP combines Breslow thickness and patient age with the expression of eight genes in the primary tumor, stratifying patients into high or low risk of recurrence. Data regarding recurrence was obtained from the Danish Melanoma Database. The primary outcome was 5-year recurrence-free survival (RFS), with 5-year overall survival (OS) as secondary outcome.

Results: CP-GEP stratified 199 patients as low-risk and 239 as high-risk. Preliminary results reveals that the CP-GEP low-risk group demonstrated a 5-year RFS of 92.0% (95% CI: 87.2-95.0) compared to 82.8% (95% CI: 77.4- 87.1) in the high-risk group, with a hazard ratio (HR) of 1.75 (95% CI: 1.13-2.72), p=0.011). The 5-year OS was 92.5% (95% CI: 87.8-95.4) for the CP-GEP low-risk group vs. 86.6% (95% CI: 81.6-90.3) for the CPGEP high-risk group (HR 1.65 (95% CI: 1.05-2.59), p=0.030).

Conclusions: CP-GEP can stratify stage I-II melanoma patients into high and low-risk for recurrence, suggesting its potential value in treatment decision-making and surveillance strategies for stage I-II melanoma.

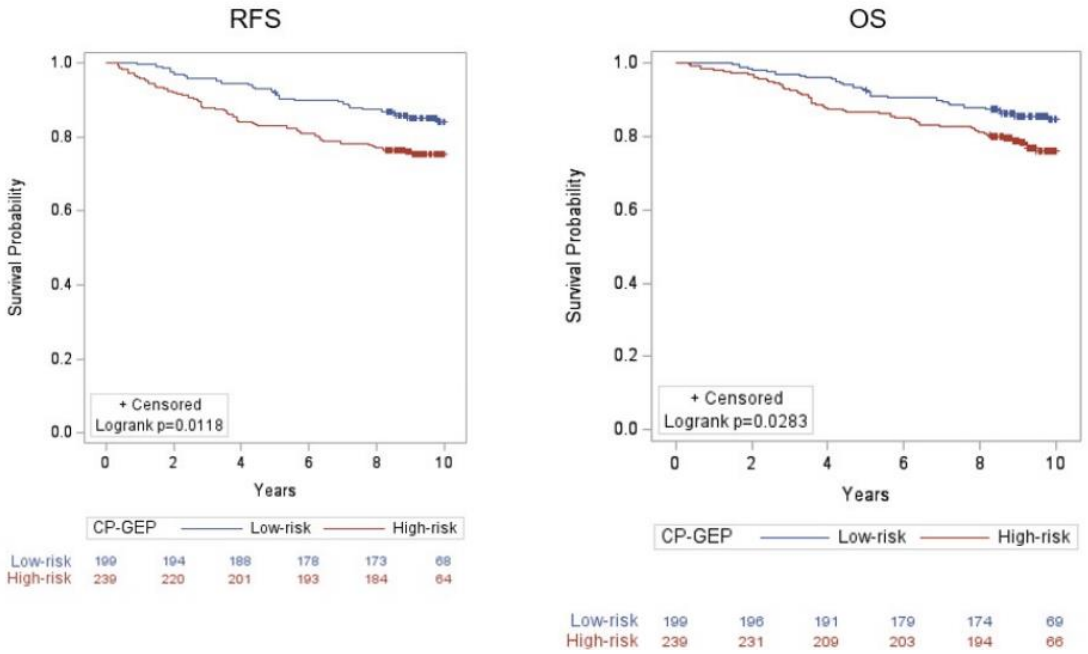

Figure 1. Kaplan–Meier survival curves (RFS, OS) for stage I-II melanoma patients, stratified by CP-GEP classification. Primary endpoint is 5-year RFS. CP-GEP, clinicopathologic and gene expression profile model; DMFS, OS, overall survival; RFS, recurrence-free survival