Prospective multicenter evaluation (MERLIN_001 trial) of a clinicopathologic and gene expression profile test to predict sentinel node status in T1-T3 cN0 melanoma

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Introduction

Guidelines recommend staging melanoma patients (pts) with sentinel lymph node biopsy (SLNB) for a predicted risk of SLN metastasis ≥10% and considering SLNB for 5-10% risk. A gene expression profile (GEP)-based test that accurately identifies pts with a low risk of SLN metastasis would help refine pt selection for SLNB, but current guidelines advise against using GEP for SLN risk prediction absent prospective trial data. This blinded prospective multicenter study evaluated the performance of a test combining clinicopathologic factors (age, Breslow thickness) with an 8-gene GEP (CP-GEP test) for predicting SLN status in pT1-T3 cN0M0 cutaneous melanoma pts undergoing clinically indicated SLN biopsy.

Methods

The CP-GEP was performed on formalin-fixed, paraffin-embedded tissue from the primary tumor biopsy and results recorded in binary fashion as Low or High Risk. The primary endpoint was negative predictive value (NPV) in Low Risk pts. Preplanned analyses included NPV assessment by T substage and age.

Results

The GEP was successfully performed in 97.4% of samples. 1,686 pts with a successful GEP underwent SLNB (17.6% SLN-positive); 37% were classified as Low Risk by CP-GEP. Among all pts classified as Low Risk, the SLN was positive in 7.1% for an NPV of 92.9% (95% CI 90.6-94.8%). High Risk pts were SLN positive in 23.8%. Most T1b pts (66.6%) were Low Risk, with an NPV of 94.9% (95% CI 91.8%-97.0%); fewer T2a pts were Low Risk (37.6%), with an NPV of 92.7% (95% CI 87.9-95.2%). Test performance was consistent across age subgroups.

Conclusion

In the first prospective multicenter blinded trial of a GEP prediction tool for SLN status, the CP-GEP test reliably identified pts with <10% risk of SLN metastasis, suggesting its potential to more precisely estimate individual pt risk of a SLN metastasis and inform shared decision-making for SLNB.