Prospective multicenter evaluation (MERLIN_001 trial, NCT04759781) 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 sentinel lymph node biopsy (SLNB) for cN0 melanoma patients (pts) with a predicted risk of SLN metastasis ≥10% and considering SLNB for a 5-10% risk. A gene expression profile (GEP)-based test that accurately identifies pts with a low risk of SLN metastasis could refine pt selection for SLNB, but current guidelines advise against using GEP for SLN risk prediction absent prospective trial data. This blinded prospective study across nine US centers evaluated the performance of the CP-GEP test, combining clinicopathologic factors (age, Breslow thickness) with gene expression (GEP) of 8 genes for predicting SLN status in pT1-T3 cN0M0 cutaneous melanoma pts undergoing clinically indicated SLNB.

Methods

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

Results

GEP was performed successfully in 97.4% of samples. 1,686 T1-T3 pts with a successful CP-GEP test underwent SLNB (17.6% SLN-positive [SLN+]); 37% were classified as Low Risk by CP-GEP. Among all pts classified as Low Risk, 7.1% were SLN+ for an NPV of 92.9% (95% CI 90.6-94.8%). High Risk classification carried a 23.8% SLN+ rate. Most T1b pts (66.6%) were Low Risk, with a SLN+ rate of 5.1% (95% CI 3.0-9.2%) whereas High Risk T1b patients had a SLN+ rate 17.3% (11.7-24.2%). Fewer T2a pts were Low Risk (37.6%), with a SLN+ rate of 7.9% (95% CI 4.8-12.1%). In the pre-specified clinical stage IB subgroup (T1b-T2a), the SLN+ rate in Low Risk patients was 6.4% (95% CI 4.5-8.7%) and 18.7% (15.6-22.2%) for High Risk patients (Table). Model performance was consistent across age subgroups, with the SLN+ rate in Low Risk patients being 0% (95% CI 0-13.7%) for age <40 (n=145), 8.2% (95% CI 5.6-12.9%) for age 40-64 (n=744), and 6.2% (95% CI 3.9-9.4%) for age >64 (n=797).

Conclusion

In the first prospective multicenter blinded trial of a GEP prediction tool for SLN status, the CP-GEP test reliably identified pts with a <10% risk of SLN metastasis. For Stage IB patients the SLN+ rate was 3-fold greater for a High Risk vs Low Risk CP-GEP test. This approach has potential to more precisely estimate individual pt risk of harboring a SLN metastasis than by clinical stage alone, and thus inform shared surgeon-patient decision-making for SLNB.

Clinical Group	% SLN-Positive	% SLN-Positive in Low Risk (95% CIs)	% SLN-Positive in High Risk (95% CIs)	Percent Low Risk by CP-GEP
All Patients T1-T3 (n=1,686)	17.6%	7.1% (5.2-9.4)	23.8% (21.3-26.5)	37.0%
T1a (n=29)	3.4%	0 (0-14.8)	16.7% (0.4-64.1)	79.3%
T1b (n = 467)	9.2%	5.1% (3.0-8.2)	17.3% (11.7-24.2)	66.6%
T2a (n = 639)	15.0%	7.9% (4.8-12.1)	19.3% (15.5-23.5)	37.6%
Stage IB Subgroup (T1b-T2a) (n = 1,106)	12.6%	6.4% (4.5-8.7)	18.7% (15.6-22.2)	49.8%
T2b (n=177)	18.6%	18.2% (7.0-35.5%)	18.8% (12.7-26.1%)	18.6%
T3a (n=187)	34.8%	14.3% (0.4-57.1%)	35.6% (28.6-43.0%)	3.7%
T3b (n=150)	36.7%	50.0% (1.3-98.7%)	36.5% (28.7-44.8%)	1.3%