Title: Determination of sentinel lymph node biopsy eligibility using a 31-gene expression profile test in melanoma patients

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Purpose: Sentinel lymph node biopsy (SLNB) is recommended as standard of care to assess the extent of disease in melanoma patients. Decisions to perform SLNB are typically guided by high-risk features recognized by the American Joint Committee on Cancer staging system, including Breslow thickness and ulceration, and the procedure is not recommended in the population of patients in which the SLN positivity rate is <5%. We sought to use molecular features of the primary melanoma tumor, in combination with clinical features, to identify those populations who would most benefit from the addition of SLNB and those who might be spared the procedure. In particular, we evaluated the Medicare population (65 and older), because the majority of patients who die from melanoma are in this group, and their rate of SLN positivity has been observed to be lower.

Summary:
Integration of a 31-gene expression profile (GEP) test result into predictive modeling approaches, alone or in combination with traditional staging factors, identified populations with different positive SLNB rates. Validation of the algorithm was performed in a contemporary, multi-center, prospective study cohort (n=584). Patients in the validation cohort with a high risk (Class 2) tumor profile had lower rates of SLN positivity compared to patients with a low risk (Class 1) profile. The group of patients 65 and older with T1/T2 tumors and Class 1 outcomes had a SLN positive rate of 4% (NPV=96%). SLN positive outcomes were enriched from 12% using current SLNB criteria to 20% if this group of patients was spared the procedure. When analysis was expanded to include all age groups, the algorithm achieved a similar NPV and an increase in the SLN positivity rate from 14% to 22%. The 5-year melanoma specific survival rate for T1/T2 Class 1 patients was 99% with overall survival of 97% and distant metastasis free survival of 93%.

Design: To identify a population with a positive SLN biopsy (SLNB) rate below 5%, predictive modeling was performed on a cohort of 782 retrospectively analyzed primary tumor specimens, wherein traditional staging information, as well as results of a 31-GEP test were known. This clinically available GEP test determines a cutaneous melanoma patient’s risk for metastatic disease, classifying patients into low (Class 1) or high (Class 2) risk groups. Once the model was identified, validation of the algorithm was performed in a contemporary, multi-center, prospective study cohort (n=584). Outcome data were derived from the retrospective cohort.

Conclusions:
The GEP test results can be useful in identifying a patient population with <5% likelihood of a positive SLN and thus has potential utility in guiding SLNB decisions in patients ≥65 years-old.