Universal risk stratification in stage I-III cutaneous melanoma using 31-gene expression profiling: a prospective single-center study

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Abstract

Introduction: Most cutaneous melanoma (CM) recurrences occur in patients diagnosed at early stages. Current guidelines do not recommend gene expression profiling (GEP) in clinical management of CM, and the utility of GEP in risk stratification remains unclear. This study evaluated near-universal DecisionDx 31-GEP testing approach for CM risk stratification in a large, prospective single-center study.

Methods: From 2015–2022, CM patients at a single center were routinely referred for DecisionDx 31-GEP. Patients with prior recurrence or not undergoing excision were excluded. Primary outcomes were recurrence-free (RFS), distant metastasis-free (DMFS), and melanoma-specific survival (MSS). Secondary outcomes included sentinel lymph node biopsy (SLNB) and GEP prognostic performance for recurrence. Kaplan-Meier and Cox proportional hazards models evaluated survival outcomes.

Results: 689 total patients were analyzed: 63% GEP class 1A, 16.1% class 1B/2A, 16.1% class 2B, and 4.8% unclassified. Median age was 65.8 years (IQR 53.5-74.5) and median Breslow depth was 0.9 mm (IQR 0.52-1.9). After staging, 86.6% were stage I/II and 13.4% stage III. Median follow-up was 4.85 years. Median follow-up was 4.85 years. On multivariable analysis, GEP remained significantly predictive of RFS (class 1B/2A HR=4.022; class 2B HR=3.052), DMFS (class 1B/2A HR=4.403; class 2B HR=3.729), and MSS (class 1B/2A HR=6.656; class 2B HR=11.583) ($p<0.05$ for all). Combining GEP with SLNB improved sensitivity for any/distant recurrence to 84.3%/87.1%, with NPV increasing to 92.2%/96.1%, respectively. Older class 1A patients had lower SLNB positivity (2.8% ≥65 years, 0% ≥75 years). We propose a modified pathway for 31-GEP integration to CM care (Figure).

Conclusions: Our data show GEP remains a robust predictor of recurrence and MSS after adjusting for clinicopathologic factors. Patients with T1a lesions not undergoing SLNB may safely forgo GEP testing. Older patients with low-risk GEP may avoid SLNB. High-risk class 2B patients may benefit from adjuvant therapy and intensified surveillance.

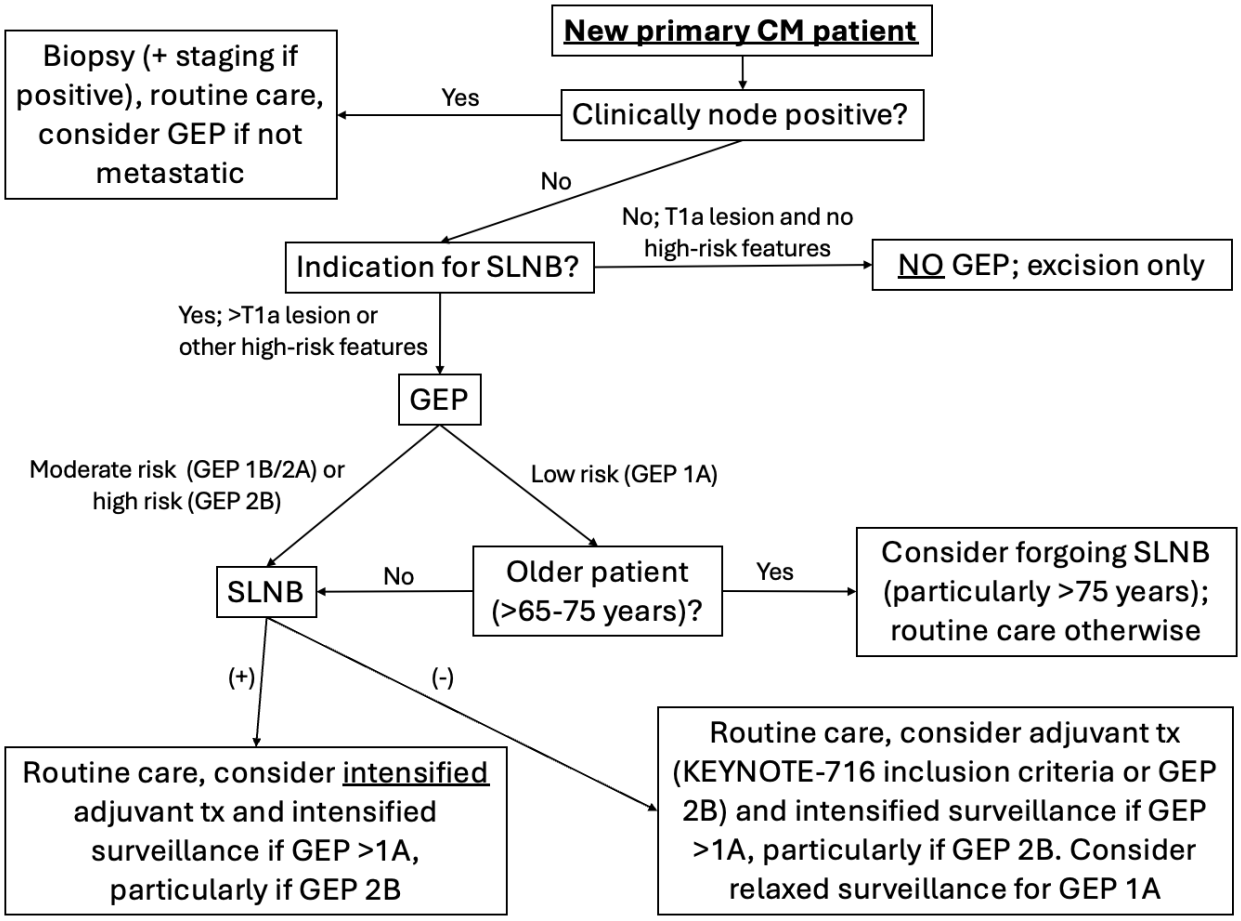

Figure. Proposed care pathway for integrating gene expression profiling (GEP) for patients with cutaneous melanoma (CM) based on results from our prospective, near-universal testing of all CM patients from 2015-2022.