

Cutaneous Melanoma Prognostic Algorithmic Tests

- I. Cutaneous melanoma prognostic algorithmic tests with insufficient evidence of clinical validity are considered **investigational** for all indications.

RATIONALE AND REFERENCES

Cutaneous Melanoma Prognostic Algorithmic Tests

Society of Surgical Oncology (SSO)

The SSO, in its 2024 consensus statement “Assessing the Evidence for and Utility of Gene Expression Profiling of Primary Cutaneous Melanoma”, does not recommend the use of gene expression profiling (GEP) in adults with pT1a-pT4b primary cutaneous melanoma for predicting sentinel lymph node (SLN) status, guiding surveillance or follow-up approaches, or informing the use of adjuvant therapy due to insufficient high-level evidence (p. 2). These conclusions were reached through a rigorous process involving 20 experts, who used the PICOT framework to refine clinical questions and systematically reviewed 50 studies selected from over 130 articles. The recommendations were developed through the Modified Delphi process, achieving consensus with at least 80% agreement among a diverse panel of specialists (p. 4-6).

Bartlett EK, O'Donoghue C, Boland G, et al. Society of Surgical Oncology Consensus Statement: Assessing the Evidence for and Utility of Gene Expression Profiling of Primary Cutaneous Melanoma. *Ann Surg Oncol*. 2025;32(3):1429-1442. doi:10.1245/s10434-024-16379-2

ECRI Genetic Test Assessment

A review completed by ECRI (2023) found evidence for the DecisionDx-Melanoma 31-gene profiling (31-GEP) test to be somewhat favorable based on the available data pertaining to clinical validity, and potential clinical utility of the test. Specifically, the available studies demonstrated that they may improve patient outcomes (e.g., overall survival), by informing decisions to escalate surveillance when the test is added to best available care (i.e., tumor staging, SLNB). The review determined that current research does not provide sufficient evidence to conclude whether DecisionDx-Melanoma allows patients to safely skip sentinel lymph node biopsy (SLNB). Additional longitudinal

studies are necessary to assess long-term health outcomes, such as recurrence, in patients who opt out of the biopsy.

ECRI. DecisionDx-Melanoma (Castle Biosciences, Inc.) for Evaluating Prognosis and Guiding Management of Cutaneous Melanoma. Genetic Test Assessment. Published October 2023.

Concert Note

Cutaneous melanoma prognostic testing is addressed by the Local Coverage Determination (LCD), MoIDX: Melanoma Risk Stratification Molecular Testing - L38016, which provides a path to coverage for the DecisionDx-Melanoma and Merlin test assays. However, these recommendations were established prior to the release of the Society of Surgical Oncology (SSO) guidelines, which represent the latest expert consensus in the field. Given the rapidly evolving landscape of precision medicine and the methodological rigor applied in developing these guidelines, we place greater weight on the SSO's recommendations as a more current and comprehensive standard for clinical practice.

Centers for Medicare & Medicaid Services. Medicare Coverage Database: Local Coverage Determination. MoIDX: Melanoma Risk Stratification Molecular Testing (L38016). Revision effective May 15, 2025. <https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=38016&ver=19&>

Bartlett EK, O'Donoghue C, Boland G, et al. Society of Surgical Oncology Consensus Statement: Assessing the Evidence for and Utility of Gene Expression Profiling of Primary Cutaneous Melanoma. Ann Surg Oncol. 2025;32(3):1429-1442. doi:10.1245/s10434-024-16379-2