CANCER DIAGNOSIS & PROGNOSIS *5*: 261-267 (2025)
doi: 10.21873/cdp.10438

Comparing Two Gene Expression Profile Tests to Standard of Care for Identifying Patients With Cutaneous Melanoma at Low Risk of Sentinel Lymph Node Positivity

PETER A. PRIETO[1], LAURA K. FERRIS[2] and J. MICHAEL GUENTHER[3]

[1]University of Rochester Medical Center, Rochester, NY, U.S.A.;
[2]Department of Dermatology, University of North Carolina School of Medicine, Chapel Hill, NC, U.S.A.;
[3]St Elizabeth Physicians General & Vascular Surgery, Edgewood, KY, U.S.A.

Abstract

Background/Aim: The National Comprehensive Cancer Network (NCCN) Guidelines for cutaneous melanoma (CM) recommend avoiding sentinel lymph node biopsy (SLNB) when the positivity risk is <5%, considering SLNB when the risk is 5-10%, or offering SLNB when the risk is >10%. Most patients undergoing SLNB have a negative result, showing that reliance upon the American Joint Committee on Cancer (AJCC) T-stage alone results in most patients undergoing an unnecessary, negative, unreliable, invasive procedure.

Materials and Methods: Two gene expression profile (GEP) tests, the CP-GEP and the 31-GEP, have been developed to identify patients at low risk of SLN positivity who may consider avoiding SLNB. We analyzed the accuracy of the CP-GEP and 31-GEP in identifying patients with <5% risk of SLN positivity across the five validation studies of the CP-GEP and four validation studies of the 31-GEP in T1–T2 tumors.

Results: Patients considered low risk by the CP-GEP had an SLN positivity rate of 6.2%, higher than the risk threshold of 5% used by the NCCN to guide SLNB decisions. In contrast, patients considered low risk by the 31-GEP or i31-SLNB had a 2.8% SLN positivity rate, a substantial improvement over AJCC-staging guidance.

Conclusion: Overall, the CP-GEP did not perform as well as AJCC, while the 31-GEP performed better than AJCC.

Keywords: Melanoma, prognosis, gene expression profile, 31-GEP, CP-GEP.

Introduction

The American Joint Committee on Cancer (AJCC) uses staging criteria that include Breslow thickness, tumor ulceration, sentinel lymph node (SLN) status, and the presence and location of tumor metastases to estimate a patient's risk of dying from cutaneous melanoma (CM) (1). SLN biopsy (SLNB) is a prognostic tool for identifying patients with a high risk of dying from their disease. A positive SLN directly affects risk-based management

J. Michael Guenther, MD, St. Elizabeth Physicians General & Vascular Surgery, Edgewood, KY, U.S.A. E-mail: Joseph.Guenther@stelizabeth.com

Received February 24, 2025 | Revised March 6, 2025 | Accepted March 7, 2025

decisions, specifically eligibility for potentially life-saving adjuvant therapies.

The National Comprehensive Cancer Network (NCCN) Guidelines for Cutaneous Melanoma (CM) recommend avoiding SLNB when the sentinel node positivity risk is <5% (T1a tumors with no high-risk factors). Patients should either consider or undergo SLNB when the risk is 5-10% or >10%, respectively (2). The 5% risk threshold means that when avoiding SLNB decision-making using staging criteria alone, one positive SLN would be missed for every 20 patients who avoid SLNB, *i.e.*, a 19:1 true-to-false negative ratio (TN:FN ratio). Patients with T3-T4 tumors have higher rates of SLN positivity, making the decision to undergo SLNB clear. However, over 90% of patients with T1-T2 tumors will have a negative node (3), and in those with thin tumors the likelihood of complications from the procedure exceeds the likelihood of having a positive node (4). Thus, there is a particular unmet need for patients with T1-T2 tumors in predicting which patients are most likely to have a positive node and need to undergo the procedure, and which patients have <5% risk and can safely avoid SLNB. Further, T1-T2 tumors account for most (~75%) newly diagnosed melanoma; thus, this is relevant to most newly diagnosed patients (5). Accurate prognostic tools that clearly meet or exceed well-established thresholds for clinical utility are needed to identify patients who can safely forego SLNB and are at low risk of recurrence after avoiding SLNB to spare patients from unnecessary surgery and complications and significant healthcare costs.

Gene expression profile (GEP) tests use gene expression levels to calculate a tumor's molecular risk level for outcomes such as sentinel node, distant metastases, or disease mortality. GEP tests have the potential to add valuable additional risk information when used with current staging systems. A useful GEP test should provide clinical utility in guiding SLNB decisions, and it must provide independent and accurate risk assessment. Patients who forego the procedure due to the GEP result must not have poor outcomes. The 31-GEP test has been previously validated to provide significant risk stratification of recurrence, metastasis, and melanoma-specific mortality (6). Studies have shown the 31-GEP consistently provides significant prognostic prediction independent of clinical and pathological factors in univariate and multivariable analyses (6-9). Additionally, studies have found that adding 31-GEP results to AJCC staging improved prognostic accuracy compared to using AJCC staging alone (10). More recently, distinct algorithms incorporating the 31-GEP result with clinical and pathological features have been validated to provide a precise risk of SLNB positivity (i31-SLNB) and risk of recurrence (i31-ROR) (11, 12). The i31-SLNB and i31-ROR algorithms were developed using different computational methods (a neural network algorithm and a Cox regression model, respectively), and the clinicopathological factors that contributed to the algorithms differed (Breslow thickness, mitotic rate, and age for i31-SLNB and age, Breslow thickness, mitotic rate, N-category, ulceration, and tumor location for the i31-ROR) (11, 12). In the present analysis, we identified four studies focused on validating the performance of 31-GEP/i31-SLNB risk prediction to calculate false-negative rates in the T1-T2 population, where SLNB decision-making is most difficult and where additional prognostic information regarding SLN positivity can provide the most value (13-15).

The CP-GEP test combines clinicopathological (CP) factors (Breslow thickness and age) with GEP of 8 genes to predict a patient's risk of SLN positivity as high or low (16). Recent data have explored whether the CP-GEP can predict a patient's prognosis for recurrence; however, the test was not developed to assess recurrence risk prediction (17). We identified five studies that focused on validating the performance of CP-GEP for SLNB risk prediction and enabled calculation of false-negative rates in the T1-T2 population (16, 18-21). However, previous independent analyses indicated that the CP-GEP test did not perform better or add value beyond using CP factors alone (22, 23). In this analysis, we compared the performance of the CP-GEP and 31-GEP/i31-SLNB tests to the NCCN standard of 19:1 TN:FN ratio (*i.e.*, 5% false-negative rate) for the accurate identification of patients who can safely avoid SLNB.

Table I. P*erformance of the CP-GEP and 31-GEP tests to identify true negative sentinel lymph node biopsies in patients with T1-T2 tumors classified as low risk by GEP testing.*

GEP test	TN:FN ratio[a]	FN rate	Reference
CP-GEP			
T1-T2	**12:1**	7.9%	Mulder *et al.*, 2020 (18)
T1-T2	27:1	3.5%	Johansson *et al.*, 2021 (19)
T1-T2	**15:1**	6.3%	Yousaf *et al.*, 2021 (20)
T1-T2	27:1	3.5%	Stassen *et al.*, 2023 (21)
T1-T2	**14:1**	6.8%	Sondak *et al.*, SMR 2024 (34)
CP-GEP T1-T2 Overall	**15:1**	6.2%	
31-GEP/i31-SLNB			
T1-T2 (31-GEP)	34:1	3.0%	Yamamoto *et al.*, 2023 (13)
T1-T2 (i31-SLNB)[b]	25:1	3.9%	Whitman *et al.*, 2021 (11)
T1-T2 (i31-SLNB)	30:0	0%	Kriza *et al.*, 2024 (14)
T1-T2a (i31-SLNB)	58:0	0%	Beard *et al.*, ECDO 2024 (24)
31-GEP/i31-SLNB T1-T2 Overall	34:1	2.8%	

GEP: Gene expression profile; TN:FN ratio: true negative to false negative ratio; FN rate: false-negative rate; 31-GEP: 31-gene expression profile; i31-SLNB: integrated 31-GEP test for sentinel lymph node biopsy prediction; SMR: Society for Melanoma Research; ECDO: European Congress on Dermato-Oncology. [a]Bold indicates that the TN:FN ratio was the same or worse than using standard clinicopathologic features (19:1). For calculations, negative was defined as "low risk" by CP-GEP, Class 1A for 31-GEP, and <5% risk of SLN positivity by i31-SLNB. [b]The current analysis includes only data from the original development and validation of the i31-SLNB (Whitman *et al.*, 2021) for patients who underwent SLNB (11).

Materials and Methods

We calculated the TN:FN ratios for patients with T1 and T2 tumors included in five reported validation cohorts using the CP-GEP, one cohort using the 31-GEP, and three cohorts using the i31-SLNB (Table I). For the CP-GEP, Mulder *et al.* included a cohort of 210 patients (T1-T2=105), Johansson *et al.* included 421 patients (T1-T2=240), Yousaf *et al.* included 208 patients (T1-T2=153), Stassen included 260 patients (T1-T2=186), and Sondak *et al.* included 1,686 patients (T1-T2=1,345). For the 31-GEP, Yamamoto *et al.* included a cohort of 193 patients (T1-T2=193). For the i31-SLNB, Whitman *et al.* included a cohort of 1,258 patients (896 T1-T2), Kriza *et al.* included a cohort of 156 patients (T1-T2=91), and Beard *et al.* included a cohort of 471 patients (T1-T2a=471) (11, 13, 14, 24).

We compared the TN:FN ratio and false negative rates calculated for patients considered low risk by the CP-GEP or 31-GEP/i31-SLNB tests to that based on staging (*i.e.*, 5% false negative rate or 19:1 TN:FN ratio) (18-21). A ratio less than 19:1 or false negative rate ≥5% indicated the test performed worse than current staging, and a test with a ratio greater than 19:1 or false negative rate <5% indicated it performed better than staging at identifying patients who could safely avoid SLNB. A Chi-squared test was used to test for significant difference in the false negative rates, with $p<0.05$ as statistically significant.

Results

In T1-T2 tumors, the calculated TN:FN ratio for the CP-GEP test was 12:1 (7.9% false-negative rate) in Mulder *et al.*, 27:1 (3.5% false-negative rate) in Johansson *et al.*, 15:1 (6.3% false-negative rate) in Yousaf *et al.*, and 27:1 (3.5% false-negative rate) in Stassen *et al.* (Table I) (18-21). The most recent data from a large, multi-center U.S.-based prospective study (MERLIN_001) found a 14:1 ratio (6.8% false-negative rate) among the T1-T2 patients. Calculating the overall weighted-average performance from these studies resulted in an overall ratio of 15:1 (6.2% false-negative rate) for the CP-GEP test in this population, which is inferior to AJCC staging to rule-out an SLNB.

Next, we analyzed the ratio for the 31-GEP/i31-SLNB test in T1-T2 tumors. The calculated TN:FN ratio was 34:1

(3.0% false-negative rate; 31-GEP) in Yamamoto *et al.* (13), 25:1 (3.9% false-negative rate, i31-SLNB) in Whitman *et al.* (11), and 30:0 (0% false-negative rate; i31-SLNB) in Kriza *et al.* (14). The most recent data from a large multi-center U.S.-based prospective study found a 58:0 ratio (0% false-negative rate; i31-SLNB) (24). Calculating the overall weighted-average performance from these studies resulted in an overall ratio of 34:1 (2.8% false-negative rate) for the 31-GEP/i31-SLNB test in this population, which is superior to standard of care AJCC staging. Chi-squared analysis comparing the false negative rates of CP-GEP to the 31-GEP/i31-SLNB found that the 31-GEP/i31-SLNB had a significantly lower false negative rate than CP-GEP (p=0.012).

Discussion

The *post-hoc* analysis showed that the CP-GEP performance provides less accurate predictions of sentinel node positivity than T-stage alone for identifying patients with T1-T2 melanoma with a <5% risk of having a positive SLNB. By contrast, the 31-GEP/i31-SLNB test outperforms T staging alone. The low-risk CP-GEP group in the studies had a mean 6.2% false-negative rate. In contrast, the 31-GEP had a false-negative rate of 3% and the i31-SLNB had a false-negative rate of 0% in two studies. These data show that the CP-GEP does not add additional prognostic information to help identify patients at low risk of SLN positivity, while the 31-GEP and i31-SLNB allow for risk stratification that exceeds that of AJCC staging alone.

SLN positivity risk-based decisions have traditionally been determined using only clinicopathologic factors, including Breslow thickness, ulceration, mitotic rate, tumor location, lympho-vascular invasion, and age (2). In addition to AJCC staging, several nomograms based on different clinicopathologic factors have been developed to try to improve SLN prediction, but these tools have not been assessed in prospective studies and have not demonstrated a benefit over standard AJCC staging for predicting SLN positivity (25-27). Furthermore, several different GEP tools have been developed to predict if a patient is likely to have a positive SLN or is at low risk and can safely avoid SLNB. In the present analysis, we found that one test, the CP-GEP, did not outperform staging in identifying patients with a low risk of SLN positivity. This is perhaps unsurprising given that no studies have found that the gene expression data included in the CP-GEP test provide additional independent prognostic information to the clinicopathologic factors; therefore, it is unknown if the gene expression data included in the algorithm provide any improvement over AJCC staging in SLNB prediction accuracy. In contrast, the 31-GEP/i31-SLNB, did perform better than AJCC staging. These findings are consistent with previous studies that show the 31-GEP and i31-SLNB improve SLNB and risk prediction accuracy compared with AJCC staging and that they more accurately predict SLN positivity than nomograms that only include clinicopathologic factors (*i.e.*, MSKCC and MIA SLNB prediction nomograms) (10-12).

A recent study sought to assess an additional utility for the CP-GEP test in predicting the risk of recurrence. Patients with high-risk CP-GEP results had lower recurrence-free survival (RFS) rates than those classified as low risk by the test; although, an online nomogram using CP factors alone provided better risk stratification (17). The study authors concluded that the current CP-GEP test did not provide precise and accurate enough information to be introduced into clinical practice as a risk stratification tool for recurrence (17). Furthermore, Eggermont *et al.* published a report showing that in patients with a low-risk CP-GEP result who had a positive SLN (*i.e.*, false negative), 5-year recurrence-free survival was 68%, suggesting that had CP-GEP been used to guide care, these patients would have been considered low risk when they were actually at high risk of recurrence (28).

In contrast, the 31-GEP and i31-SLNB consistently provided improved SLNB risk prediction compared with AJCC staging alone. The combined 31-GEP/i31-SLNB TN:FN ratio was 34:1 (2.8% false-negative rate), an improvement over AJCC staging. Further, a follow-up study of low-risk (Class 1A) patients who avoided SLNB found no recurrences with a median follow-up of 2 years (29). In

addition, multiple prospective studies have demonstrated that the 31-GEP stratifies risk of recurrence, metastasis, and death (30-32), and two studies have shown that patients who received the 31-GEP test as part of their clinical care had higher survival rates than patients who did not receive 31-GEP testing 9,33. Thus, the current analysis adds to the evidence that the 31-GEP provides personalized risk information, allowing clinicians and patients to make risk-appropriate management and treatment decisions, associated with improved patient outcomes. This analysis also shows that the 31-GEP/i31-SLNB is superior to the performance of the CP-GEP. Limitations of this analysis include the relatively small number of patients in the different study subsets and the challenges of comparing results across different studies.

In summary, the analyses reported here indicate that the CP-GEP does not perform better than AJCC staging for identifying patients at low risk of SLN positivity and should not be used to guide patient management. In contrast, the 31-GEP and i31-SLNB improve SLNB decision-making in patients with T1-T2 tumors over AJCC staging and can help provide better risk-aligned patient management decisions.

Conflicts of Interest

JMG is on the Speaker's Bureau for Castle Biosciences, Inc. PAP is a consultant for Castle Biosciences, Inc. LKF has no conflicts to declare.

Authors' Contributions

PAP, LKF, and JMG approved the study design and analysis. PAP, LKF, and JMG edited, reviewed, and approved the final version of the manuscript.

Acknowledgements

Writing assistance was provided by Castle Biosciences, Inc. Data analysis assistance was provided by Castle Biosciences, Inc.

Funding

This study was funded by Castle Biosciences, Inc.

References

1 Gershenwald JE, Scolyer RA, Hess KR, Thompson JF, Long GV, Ross MI, Amin MB, Edge S, Greene F, Byrd DR, Brookland RK: 8th Edition AJCC Melanoma Staging System. In: AJCC Cancer Staging Manual. Cham, Switzerland, Springer, pp. 563-589, 2017.

2 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Melanoma: Cutaneous V.2.2023. © National Comprehensive Cancer Network, Inc., 2023.

3 Le ELH, Lamping E, Helmkamp L, Bone J, McCarter M, Kounalakis N, Stewart C: Analysis of time between skin lesion and lymph node biopsies and lymph node metastasis in patients with melanoma. JAMA Netw Open 6(5): e2311472, 2023. DOI: 10.1001/jamanetworkopen.2023.11472

4 Moody JA, Ali RF, Carbone AC, Singh S, Hardwicke JT: Complications of sentinel lymph node biopsy for melanoma – A systematic review of the literature. Eur J Surg Oncol 43(2): 270-277, 2017. DOI: 10.1016/j.ejso.2016.06.407

5 Chen ML, de Vere Hunt IJ, John EM, Weinstock MA, Swetter SM, Linos E: Differences in thickness-specific incidence and factors associated with cutaneous melanoma in the US from 2010 to 2018. JAMA Oncol 8(5): 755-759, 2022. DOI: 10.1001/jamaoncol.2022.0134

6 Durgham RA, Nassar SI, Gun R, Nguyen SA, Asarkar AA, Nathan CO: The prognostic value of the 31-gene expression profile test in cutaneous melanoma: a systematic review and meta-analysis. Cancers (Basel) 16(21): 3714, 2024. DOI: 10.3390/cancers16213714

7 Gerami P, Cook RW, Wilkinson J, Russell MC, Dhillon N, Amaria RN, Gonzalez R, Lyle S, Johnson CE, Oelschlager KM, Jackson GL, Greisinger AJ, Maetzold D, Delman KA, Lawson DH, Stone JF: Development of a prognostic genetic signature to predict the metastatic risk associated with cutaneous melanoma. Clin Cancer Res 21(1): 175-183, 2015. DOI: 10.1158/1078-0432.CCR-13-3316

8 Gerami P, Cook RW, Russell MC, Wilkinson J, Amaria RN, Gonzalez R, Lyle S, Jackson GL, Greisinger AJ, Johnson CE, Oelschlager KM, Stone JF, Maetzold DJ, Ferris LK, Wayne JD, Cooper C, Obregon R, Delman KA, Lawson D: Gene expression profiling for molecular staging of cutaneous melanoma in patients undergoing sentinel lymph node biopsy. J Am Acad Dermatol 72(5): 780-785.e3, 2015. DOI: 10.1016/j.jaad.2015.01.009

9 Bailey CN, Martin BJ, Petkov VI, Schussler NC, Stevens JL, Bentler S, Cress RD, Doherty JA, Durbin EB, Gomez SL, Gonsalves L, Hernandez BY, Liu L, Morawski BM, Schymura MJ, Schwartz SM, Ward KC, Wiggins C, Wu XC, Goldberg MS, Siegel JJ, Cook RW, Covington KR, Kurley SJ: 31-gene

expression profile testing in cutaneous melanoma and survival outcomes in a population-based analysis: a SEER collaboration. JCO Precis Oncol 7: e2300044, 2023. DOI: 10.1200/PO.23.00044

10 Podlipnik S, Martin BJ, Morgan-Linnell SK, Bailey CN, Siegel JJ, Petkov VI, Puig S: The 31-gene expression profile test outperforms AJCC in stratifying risk of recurrence in patients with stage I cutaneous melanoma. Cancers (Basel) 16(2): 287, 2024. DOI: 10.3390/cancers16020287

11 Whitman ED, Koshenkov VP, Gastman BR, Lewis D, Hsueh EC, Pak H, Trezona TP, Davidson RS, McPhee M, Guenther JM, Toomey P, Smith FO, Beitsch PD, Lewis JM, Ward A, Young SE, Shah PK, Quick AP, Martin BJ, Zolochevska O, Covington KR, Monzon FA, Goldberg MS, Cook RW, Fleming MD, Hyams DM, Vetto JT: Integrating 31-gene expression profiling with clinicopathologic features to optimize cutaneous melanoma sentinel lymph node metastasis prediction. JCO Precis Oncol 5: PO.21.00162, 2021. DOI: 10.1200/PO.21.00162

12 Jarell A, Gastman BR, Dillon LD, Hsueh EC, Podlipnik S, Covington KR, Cook RW, Bailey CN, Quick AP, Martin BJ, Kurley SJ, Goldberg MS, Puig S: Optimizing treatment approaches for patients with cutaneous melanoma by integrating clinical and pathologic features with the 31-gene expression profile test. J Am Acad Dermatol 87(6): 1312-1320, 2022. DOI: 10.1016/j.jaad.2022.06.1202

13 Yamamoto M, Sickle-Santanello B, Beard T, Essner R, Martin B, Bailey CN, Guenther JM: The 31-gene expression profile test informs sentinel lymph node biopsy decisions in patients with cutaneous melanoma: results of a prospective, multicenter study. Curr Med Res Opin 39(3): 417-423, 2023. DOI: 10.1080/03007995.2023.2165813

14 Kriza C, Martin B, Bailey CN, Bennett J: Integrating the melanoma 31-gene expression profile test with clinical and pathologic features can provide personalized precision estimates for sentinel lymph node positivity: an independent performance cohort. World J Surg Oncol 22(1): 228, 2024. DOI: 10.1186/s12957-024-03512-4

15 Guenther JM, Ward A, Martin BJ, Cripe M, Sharma R, Leong SP, Clark JI, Hamner J, Beard T: A prospective, multicenter analysis of the integrated 31-gene expression profile test for sentinel lymph node biopsy (i31-GEP for SLNB) test demonstrates reduced number of unnecessary SLNBs in patients with cutaneous melanoma. World J Surg Oncol 23(1): 5, 2025. DOI: 10.1186/s12957-024-03640-x

16 Bellomo D, Arias-Mejias SM, Ramana C, Heim JB, Quattrocchi E, Sominidi-Damodaran S, Bridges AG, Lehman JS, Hieken TJ, Jakub JW, Pittelkow MR, DiCaudo DJ, Pockaj BA, Sluzevich JC, Cappel MA, Bagaria SP, Perniciaro C, Tjien-Fooh FJ, van Vliet MH, Dwarkasing J, Meves A: Model combining tumor molecular and clinicopathologic risk factors predicts sentinel lymph node metastasis in primary cutaneous melanoma. JCO Precis Oncol 4: 319-334, 2020. DOI: 10.1200/po.19.00206

17 Mulder EEAP, Johansson I, Grünhagen DJ, Tempel D, Rentroia-Pacheco B, Dwarkasing JT, Verver D, Mooyaart AL, van der Veldt AAM, Wakkee M, Nijsten TEC, Verhoef C, Mattsson J, Ny L, Hollestein LM, Olofsson Bagge R: Using a clinicopathologic and gene expression (CP-GEP) model to identify stage I-II melanoma patients at risk of disease relapse. Cancers (Basel) 14(12): 2854, 2022. DOI: 10.3390/cancers14122854

18 Mulder EEAP, Dwarkasing JT, Tempel D, van der Spek A, Bosman L, Verver D, Mooyaart AL, van der Veldt AAM, Verhoef C, Nijsten TEC, Grunhagen DJ, Hollestein LM: Validation of a clinicopathological and gene expression profile model for sentinel lymph node metastasis in primary cutaneous melanoma. Br J Dermatol 184(5): 944-951, 2021. DOI: 10.1111/bjd.19499

19 Johansson I, Tempel D, Dwarkasing JT, Rentroia-Pacheco B, Mattsson J, Ny L, Olofsson Bagge R: Validation of a clinicopathological and gene expression profile model to identify patients with cutaneous melanoma where sentinel lymph node biopsy is unnecessary. Eur J Surg Oncol 48(2): 320-325, 2022. DOI: 10.1016/j.ejso.2021.11.010

20 Yousaf A, Tjien-Fooh FJ, Rentroia-Pacheco B, Quattrocchi E, Kobic A, Tempel D, Kolodney M, Meves A: Validation of CP-GEP (Merlin Assay) for predicting sentinel lymph node metastasis in primary cutaneous melanoma patients: A U.S. cohort study. Int J Dermatol 60(7): 851-856, 2021. DOI: 10.1111/ijd.15594

21 Stassen RC, Mulder EEAP, Mooyaart AL, Francken AB, van der Hage J, Aarts MJB, van der Veldt AAM, Verhoef C, Grünhagen DJ: Clinical evaluation of the clinicopathologic and gene expression profile (CP-GEP) in patients with melanoma eligible for sentinel lymph node biopsy: A multicenter prospective Dutch study. Eur J Surg Oncol 49(12): 107249, 2023. DOI: 10.1016/j.ejso.2023.107249

22 Bartlett EK, Marchetti MA, Coit DG: Gene expression profile-based risk modeling to select patients with melanoma who can avoid sentinel lymph node biopsy: are we there yet? JCO Precis Oncol 4: 988-989, 2020. DOI: 10.1200/PO.20.00146

23 Glazer A, Tassavor M, Portela D, Soleymani T: The integrated 31-gene expression profile test (i31-GEP) for cutaneous melanoma outperforms the CP-GEP at identifying patients who can forego sentinel lymph node biopsy when applying NCCN guidelines. J Skin 6(6): 474-481, 2022. DOI: 10.25251/skin.6.6.4

24 Beard T, Leong SP, Kulkarni RP, Martin B, Ahmed K, Ward A, Sharma R, Guenther JM, Young S: Abstract: Clinical use of the i31-SLNB for T1-T2a cutaneous melanoma significantly and safely reduces unnecessary procedures. In: The European Congress on Dermato-Oncology, Vienna, Austria, 2024.

25 Maddineni S, Dizon MP, Muralidharan V, Young LA, Sunwoo JB, Baik FM, Swetter SM: Validation of the Melanoma Institute of Australia's Sentinel Lymph Node Biopsy Risk Prediction Tool for Cutaneous Melanoma. Ann Surg Oncol 31(4): 2737-2746, 2024. DOI: 10.1245/s10434-023-14862-w

26 Drebin HM, Hosein S, Kurtansky NR, Nadelmann E, Moy AP, Ariyan CE, Bello DM, Brady MS, Coit DG, Marchetti MA, Bartlett EK: Clinical utility of melanoma sentinel lymph node biopsy nomograms. J Am Coll Surg 238(1): 23-31, 2024. DOI: 10.1097/XCS.0000000000000886

27 Hosein S, Drebin HM, Kurtansky NR, Olofsson Bagge R, Coit DG, Bartlett EK, Marchetti MA: Are the MIA and MSKCC nomograms useful in selecting patients with melanoma for sentinel lymph node biopsy? J Surg Oncol 127(7): 1167-1173, 2023. DOI: 10.1002/jso.27231

28 Eggermont AMM, Bellomo D, Arias-Mejias SM, Quattrocchi E, Sominidi-Damodaran S, Bridges AG, Lehman JS, Hieken TJ, Jakub JW, Murphree DH, Pittelkow MR, Sluzevich JC, Cappel MA, Bagaria SP, Perniciaro C, Tjien-Fooh FJ, Rentroia-Pacheco B, Wever R, van Vliet MH, Dwarkasing J, Meves A: Identification of stage I/IIA melanoma patients at high risk for disease relapse using a clinicopathologic and gene expression model. Eur J Cancer 140: 11-18, 2020. DOI: 10.1016/j.ejca.2020.08.029

29 Guenther JM, Ward A, Martin B, Beard T, Sharma R, Leong SP, Yamamoto M, Cook RW: Patients who forego sentinel lymph node biopsy after 31-GEP testing are not harmed: A prospective, multicenter analysis. EJC Skin Cancer 2: 100175, 2024. DOI: 10.1016/j.ejcskn.2024.100175

30 Podlipnik S, Carrera C, Boada A, Richarz NA, López-Estebaranz JL, Pinedo-Moraleda F, Elosua-González M, Martín-González MM, Carrillo-Gijón R, Redondo P, Moreno E, Malvehy J, Puig S: Early outcome of a 31-gene expression profile test in 86 AJCC stage IB-II melanoma patients. A prospective multicentre cohort study. J Eur Acad Dermatol Venereol 33(5): 857-862, 2019. DOI: 10.1111/jdv.15454

31 Hsueh EC, DeBloom JR, Lee JH, Sussman JJ, Covington KR, Caruso HG, Quick AP, Cook RW, Slingluff CL Jr, McMasters KM: Long-term outcomes in a multicenter, prospective cohort evaluating the prognostic 31-gene expression profile for cutaneous melanoma. JCO Precis Oncol 5: PO.20.00119, 2021. DOI: 10.1200/PO.20.00119

32 Keller J, Schwartz TL, Lizalek JM, Chang ES, Patel AD, Hurley MY, Hsueh EC: Prospective validation of the prognostic 31-gene expression profiling test in primary cutaneous melanoma. Cancer Med 8(5): 2205-2212, 2019. DOI: 10.1002/cam4.2128

33 Dhillon S, Duarte-Bateman D, Fowler G, Hagstrom MNE, Lampley N, Olivares S, Fumero-Velázquez MS, Vu K, Wayne JD, Gastman BR, Vetto J, Gerami P: Routine imaging guided by a 31-gene expression profile assay results in earlier detection of melanoma with decreased metastatic tumor burden compared to patients without surveillance imaging studies. Arch Dermatol Res 315(8): 2295-2302, 2023. DOI: 10.1007/s00403-023-02613-6

34 Sondak VK, Egger ME, Angeles CV, Hyngstrom JR, Burke EE, Lowe MC, Beasley GM, Bartlett EK, Bresler SC, Harms KL, Zager JS, Wasif N, Bagaria SP, McMasters KM, Wada D, Pandalai P, Delman K, Lee J, Busam KJ, Hieken TJ: Abstract: Prospective multicenter evaluation (MERLIN_001 trial) of a clinicopathologic and gene expression profile test to predict sentinel node status in T1-T3 cN0 melanoma, 2024. Available at: https://falconprogram.com/files/SMR%202024%20Abstract%20MERLIN_001.pdf [Last accessed on March 7, 2025]