South Beach Symposium
medical + aesthetic dermatology
CELEBRATING 20 YEARS
OF PREMIER MEDICAL & AESTHETIC DERMATOLOGY EDUCATION

REIMAGINING
MEDICAL AND
AESTHETIC
DERMATOLOGY

Genetic Approaches to the Prognosis of Melanoma

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Gene Expression Profile Overview

GEP provides an objective view of the tumor biology for each lesion tested by providing . . .

- RNA gene expression vs. DNA or protein
- Insight regarding abnormalities in the regulation and function of genes

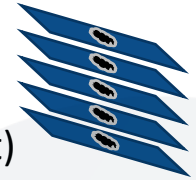
DNA
FISH, CGH, SNP, NGS
Detects chromosomal and DNA sequence abnormalities

RNA
Gene Expression
captures abnormalities in the function of the genes

Protein
Immunohistochemistry
detects cellular protein expression

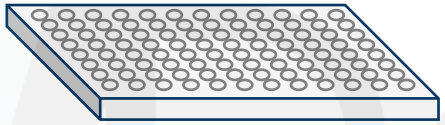
Melanoma GEP test workflow

Primary CM tumor tissue
(≥ 40% tumor content)



RNA isolation

cDNA generation and amplification (14X)



Open Array PCR gene card
28 discriminant gene targets and 3 control genes

Analysis of gene expression profile with a proprietary algorithm to determine class and metastatic risk

Class 1
low metastatic risk

Class 1A **Class 1B**

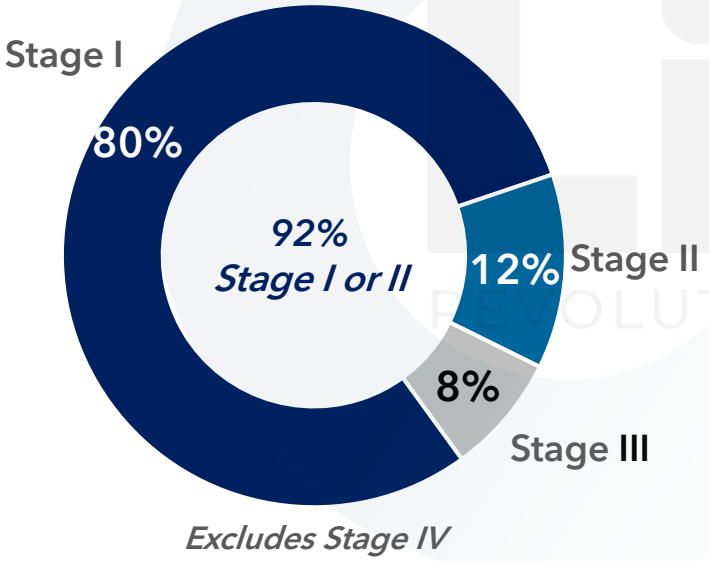
Class 2
high metastatic risk

Class 2A **Class 2B**

This approach misses patients with aggressive tumor biology

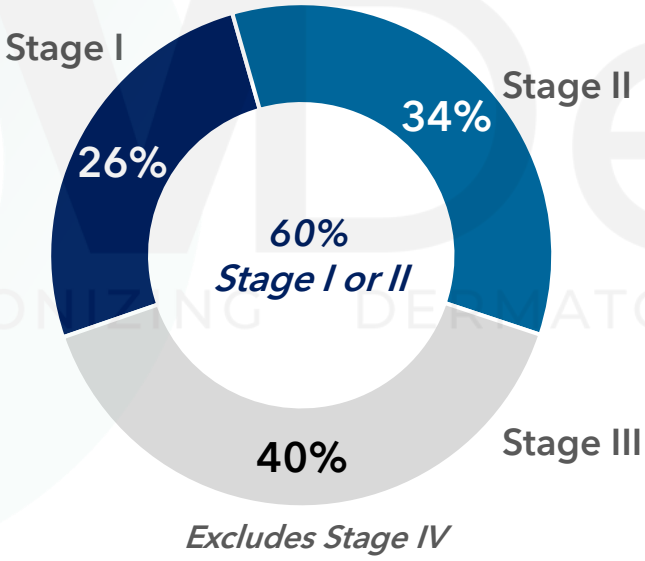
AJCC stage, based mostly on histopathology, is inadequate for predicting clinical outcome

Stage at Diagnosis



Excludes Stage IV

Melanoma Deaths by Stage at Diagnosis

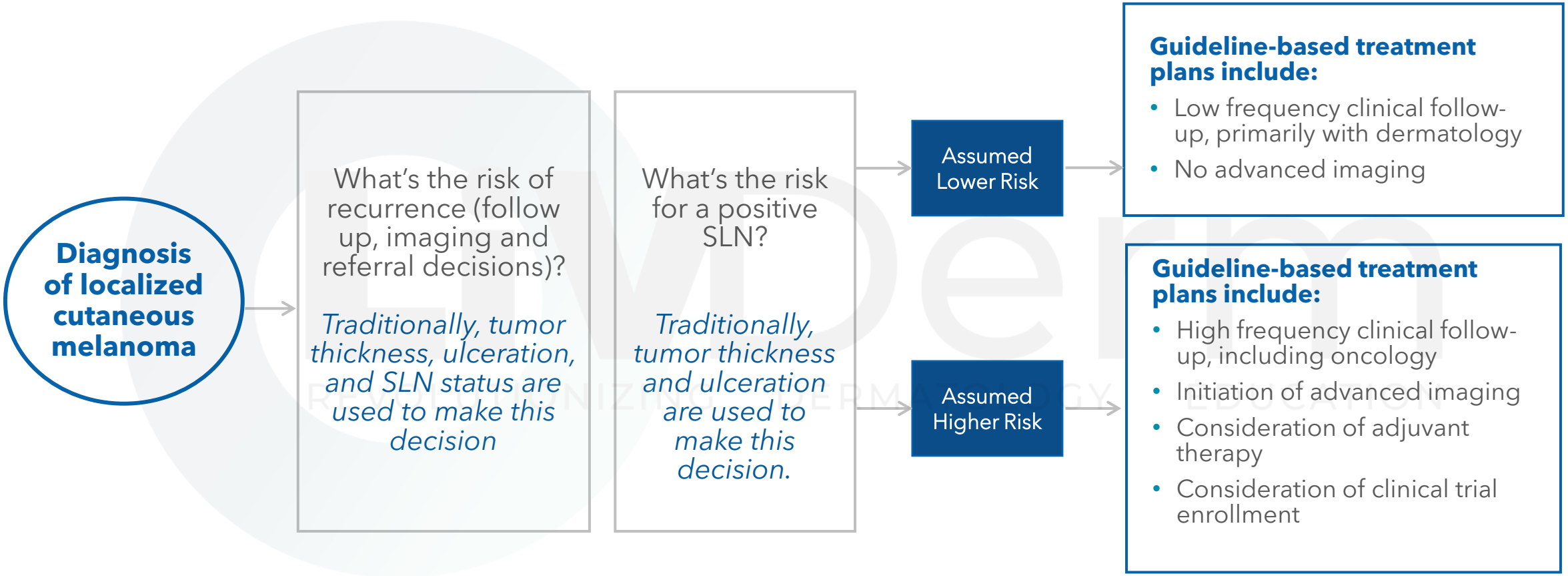


Excludes Stage IV

- Many high-risk tumors are being **misidentified** as low-risk at time of diagnosis
- **Prognostic accuracy** may be improved to inform patient management decisions
- Patients **twice as likely to survive** if they had asymptomatic detected recurrence than symptomatic recurrence

1. AJCCv7 J Clin Oncol 2009. 2. SEER data release 2017. 3. Whiteman D et al. J Invest Derm 2015. 4. Shaikh W et al. J Natl Cancer Inst 2016.

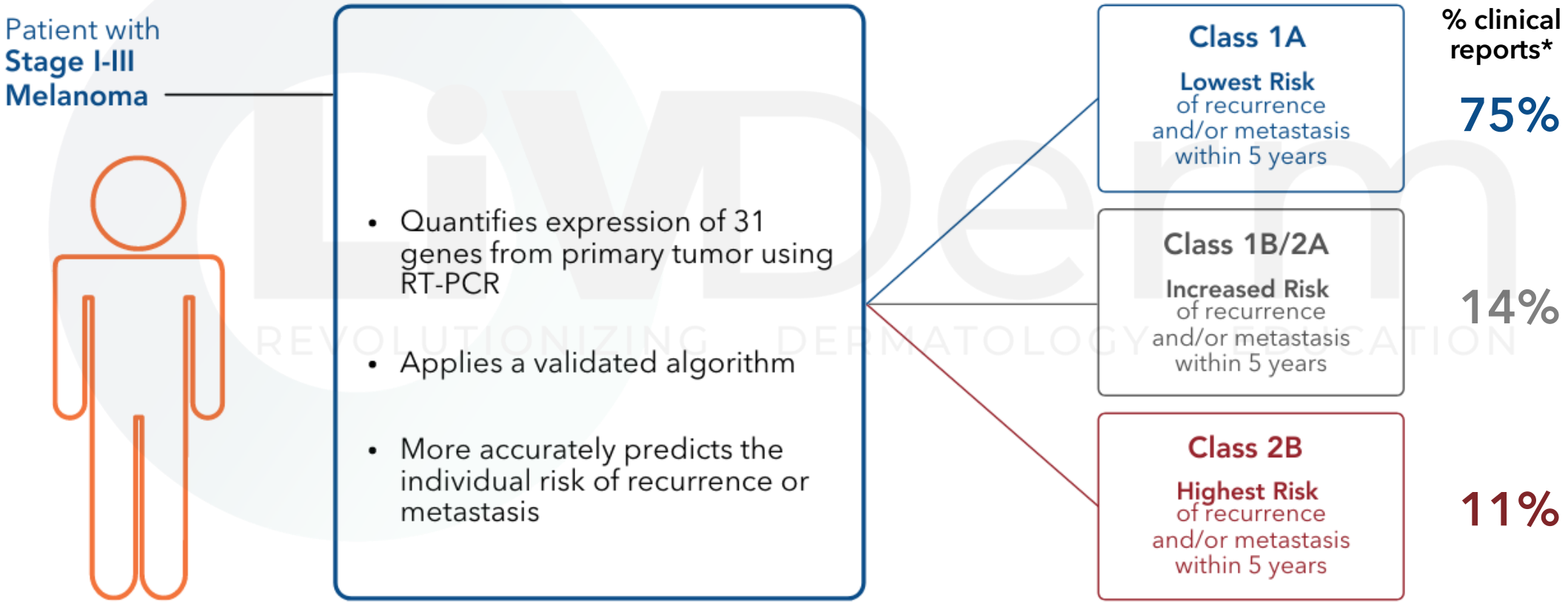
Traditionally, staging and clinicopathology factors answer two key treatment questions following diagnosis of cutaneous melanoma



NCCN guidelines recognize that a patient's individual risk of recurrence should drive management decisions and that a patient's individual risk of SLN positivity drives SLN biopsy recommendations

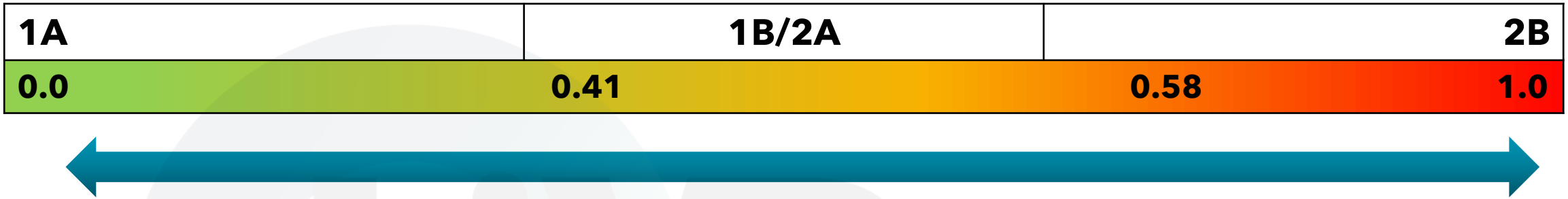
SLN = sentinel lymph node; SLNB = sentinel lymph node biopsy. Source: NCCN Guidelines for Cutaneous Melanoma v3.2022

31-GEP was developed to assess risk of recurrence independent from traditional clinicopathologic factors using tumor biology



Gerami et al. Clin Cancer Res 2015; Gerami et al. JAAD 2015; Zager et al. BMC Cancer 2018; Gastman et al. JAAD 2019
*Percent of clinical reports May 2013- Dec 2021 (n=77,929)

31-GEP: continuous variable and class call



0.00 - 0.41 = *Class 1A*
0.42 - 0.49 = *Class 1B*
0.50 - 0.58 = *Class 2A*
0.59 - 1.00 = *Class 2B*

*[a]NCCN Melanoma Guidelines v3.2020; [b]Vetto et al. *Future Oncol* 2019 and Cook et al. Society of Melanoma Research 2019
Intent to treat population includes SLNB eligible patients (T1b-T2 and T1a with high-risk histologic features) and T1a patients referred to surgical oncology consultation

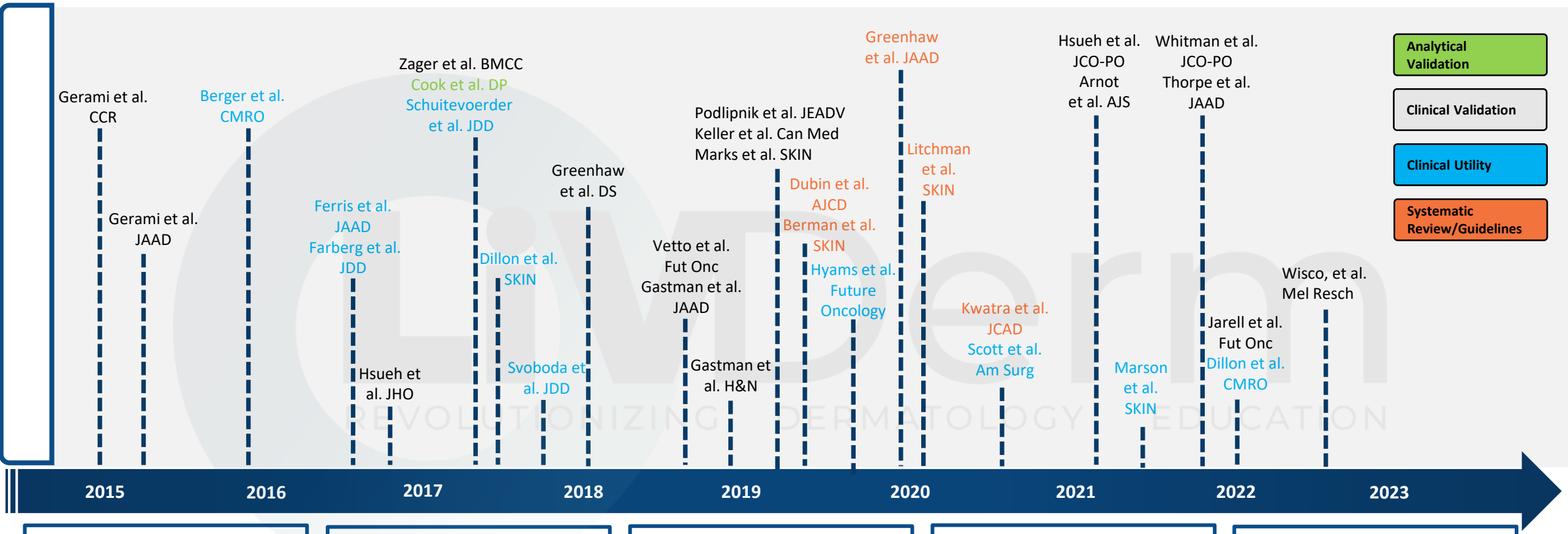
Genes included in the 31-GEP signature

Migration/chemotaxis/ metastasis	CXCL14 SPP1 CLCA2 S100A9 S100A8 BAP-1
Chemokine/secreted molecules	CXCL14 MGP SPP1
Gap junction/cellular adhesion	GJA1 DSC1 PPL
Lymphocytic invasion	LTA4H
Transcription factor	TRIM29
Extracellular functions	KRT6B KRT14

Differentiation/ proliferation	CRABP2 SPRR1B BTG1
Cell surface receptors	TACSTD2 CLCA2 ROBO1
Structural proteins	MGP SPP1 CST6
Angiogenesis regulator	CXCL14
Other	SAP130 ID2 EIF1B ARG1 AQP1 RBM23 TYRP1

Gerami et al. Clin Cancer Res 2015

Extensive scientific validation is critical for adoption into clinical practice



Discovery

- Identification of clinical need
- Review of published literature/ large databases to Identify genes
- Evaluation of candidate genes

Development

- Development of gene signature
- Evaluation of performance in initial cohort

Clinical Validation

- Confirmation of test performance in *independent clinically relevant* cohort
- Multiple studies needed

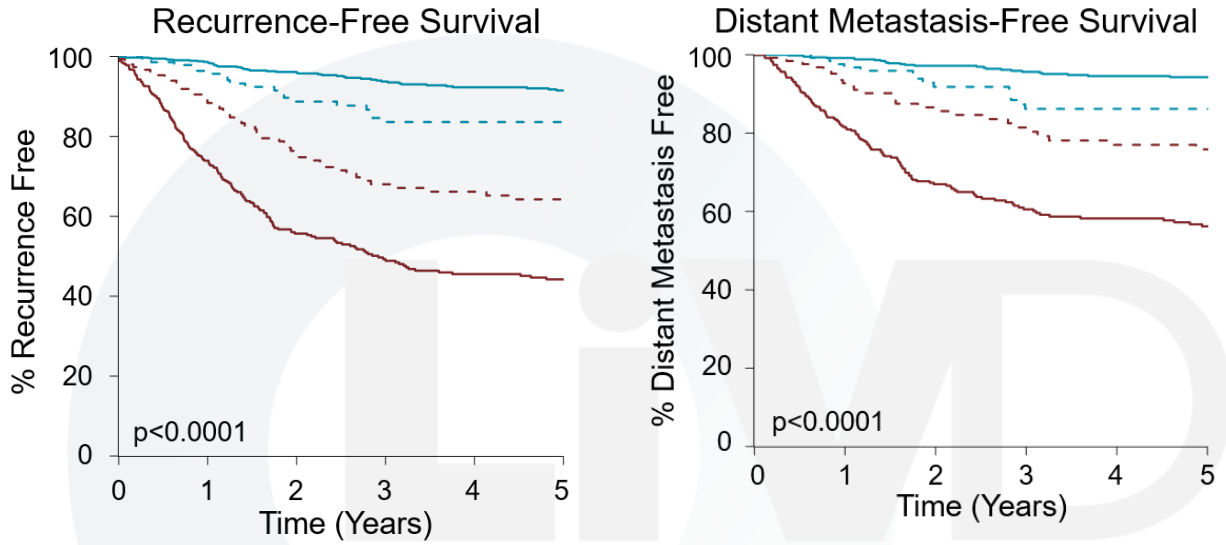
Analytical Validation

- Ensures the test results are accurate and reproducible

Clinical Utility

- Understand test utilization
- Understand what impact the test is making
- Multiple studies needed

Consistent and independent prognostic value of 31-GEP across studies

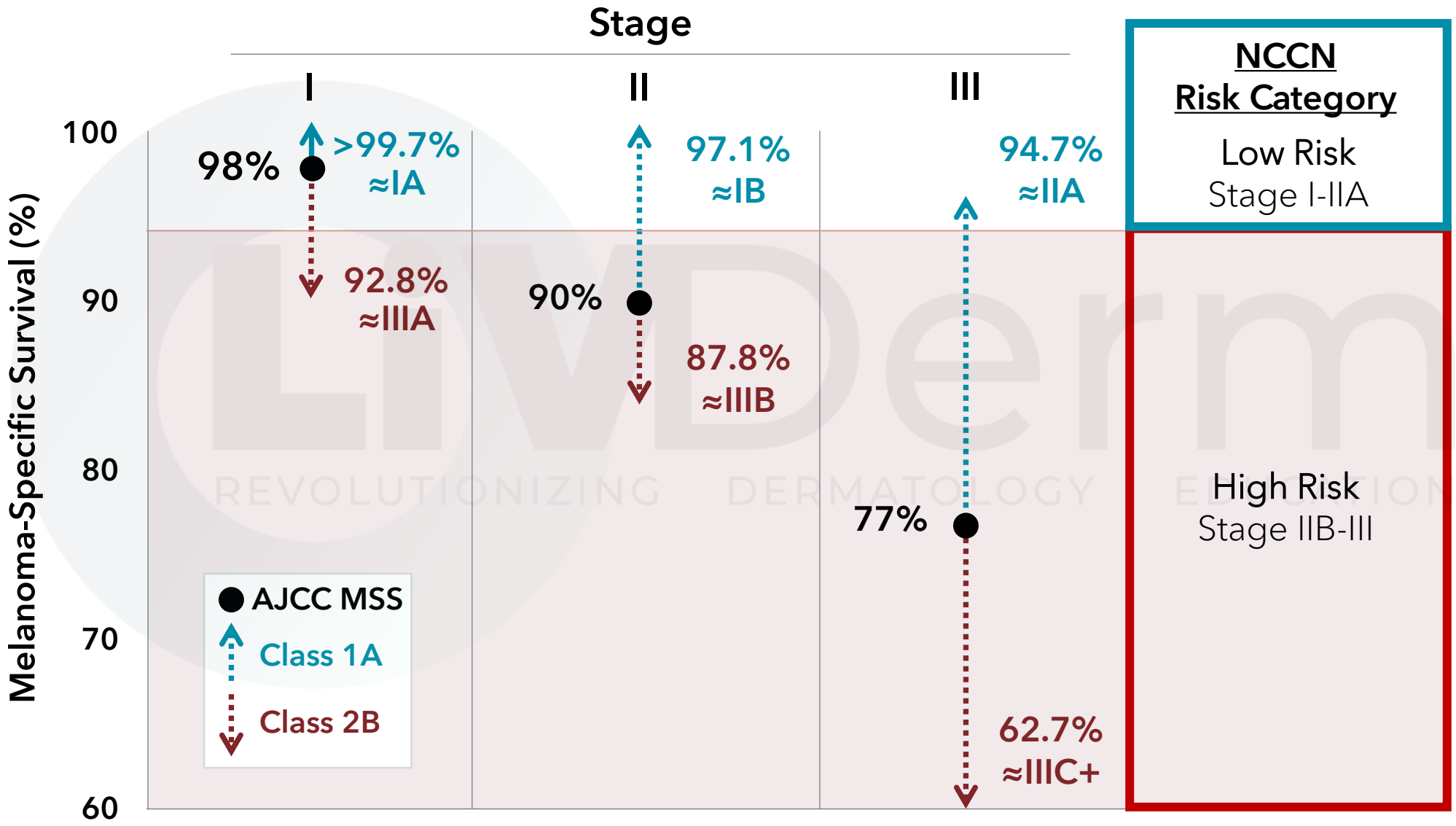


GEP Result	5-year RFS	Recurrence Event Rate	5-year DMFS	Dist Met Event Rate
Class 1A	91.4%	6.7%	94.1%	5.5%
Class 1B	85.1%	14.2%	88.1%	12.2%
Class 2A	64.0%	35.8%	75.9%	24.1%
Class 2B	43.6%	50.1%	55.5%	38.8%

Multivariate Hazard Ratios (HR) for Class 2B[a]	
Publication	**HR**
RFS	
Greenhaw et al[b]	7.96
Hsueh et al[b]	5.60
Gastman et al	2.66
Novel Cohort	2.75
Overall[c]	**2.90**
DMFS	
Hsueh et al[b]	5.79
Gastman et al	2.79
Novel Cohort	2.41
Overall[c]	**2.75**

Greenhaw et al. *JAAD* 2020; [a]Multivariate model included all 31-GEP subclasses, age, Breslow thickness, ulceration, and node status; [b]Prospective study; [c]Same hazard ratio with fixed effect and random effects models

More precise and personalized risk prediction than with AJCC8 alone

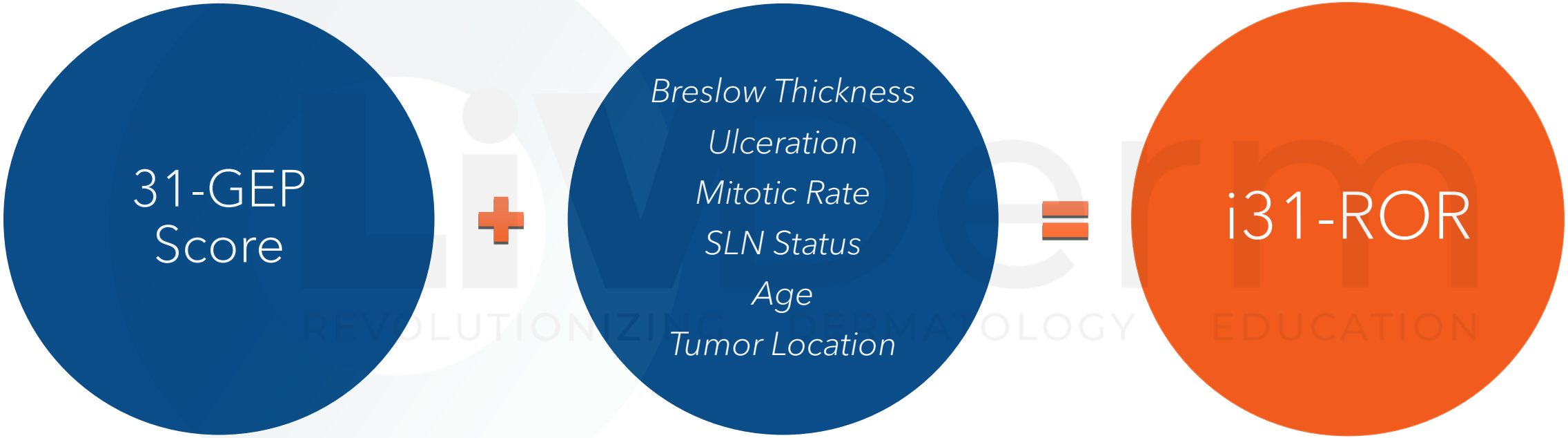


Wisco et al. Melanoma Research 2022

i31-ROR

Precise and Personalized Predictions of Risk of Recurrence, Melanoma-Specific Survival, and Distant Metastasis-Free Survival

Integrating the 31-GEP score with clinicopathologic factors in a validated algorithm for precise, personalized risk and survival outcomes prediction

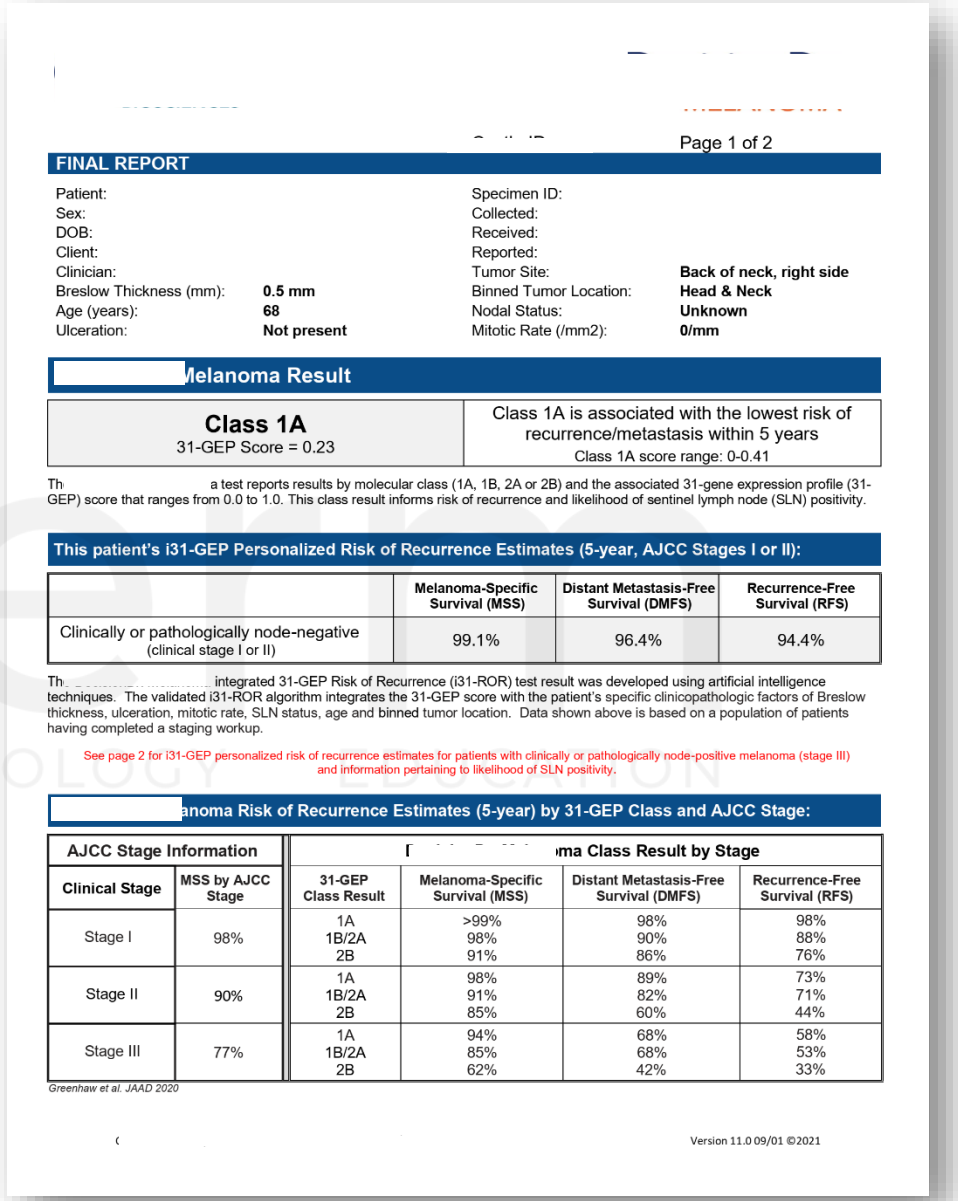


The 31-GEP score was an independent and significant variable in risk of recurrence outcomes

Taylor AAD Summer Meeting 2021 (Oral Presentation);

To further refine a patient's treatment plan, 31-GEP now provides a personalized risk of recurrence for MSS, RFS and DMFS

- Class designation is reported with the 31-GEP score (used in the validated algorithm for the individual risk of recurrence).
- The patient's MSS, DMFS and RFS are reported for patients that are stage I-II.
  - For patients that receive a positive SLNB result while awaiting their result and are staged as a stage III, the MSS, DMFS ad RFS are reported on the 2nd page.
- For comparison, MSS by AJCC stage and population-based MSS, DMFS and RFS from the 1,479-patient meta-analysis, are provided.



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FINAL REPORT

Patient:		Specimen ID:	
Sex:		Collected:	
DOB:		Received:	
Client:		Reported:	
Clinician:		Tumor Site:	**Back of neck, right side**
Breslow Thickness (mm):	**0.5 mm**	Binned Tumor Location:	**Head & Neck**
Age (years):	**68**	Nodal Status:	**Unknown**
Ulceration:	**Not present**	Mitotic Rate (/mm2):	**0/mm**

[redacted]elanoma Result

Class 1A 31-GEP Score = 0.23	Class 1A is associated with the lowest risk of recurrence/metastasis within 5 years Class 1A score range: 0-0.41

Th[redacted] a test reports results by molecular class (1A, 1B, 2A or 2B) and the associated 31-gene expression profile (31-GEP) score that ranges from 0.0 to 1.0. This class result informs risk of recurrence and likelihood of sentinel lymph node (SLN) positivity.

This patient's i31-GEP Personalized Risk of Recurrence Estimates (5-year, AJCC Stages I or II):

	Melanoma-Specific Survival (MSS)	Distant Metastasis-Free Survival (DMFS)	Recurrence-Free Survival (RFS)
Clinically or pathologically node-negative (clinical stage I or II)	99.1%	96.4%	94.4%

Th[redacted] integrated 31-GEP Risk of Recurrence (i31-ROR) test result was developed using artificial intelligence techniques. The validated i31-ROR algorithm integrates the 31-GEP score with the patient's specific clinicopathologic factors of Breslow thickness, ulceration, mitotic rate, SLN status, age and binned tumor location. Data shown above is based on a population of patients having completed a staging workup.

See page 2 for i31-GEP personalized risk of recurrence estimates for patients with clinically or pathologically node-positive melanoma (stage III) and information pertaining to likelihood of SLN positivity.

[redacted]anoma Risk of Recurrence Estimates (5-year) by 31-GEP Class and AJCC Stage:

AJCC Stage Information		[redacted]ma Class Result by Stage			
Clinical Stage	**MSS by AJCC Stage**	**31-GEP Class Result**	**Melanoma-Specific Survival (MSS)**	**Distant Metastasis-Free Survival (DMFS)**	**Recurrence-Free Survival (RFS)**
Stage I	98%	1A 1B/2A 2B	>99% 98% 91%	98% 90% 86%	98% 88% 76%
Stage II	90%	1A 1B/2A 2B	98% 91% 85%	89% 82% 60%	73% 71% 44%
Stage III	77%	1A 1B/2A 2B	94% 85% 62%	68% 68% 42%	58% 53% 33%

Greenhaw et al. JAAD 2020

Version 11.0 09/01 ©2021

This patient's i31-GEP Personalized Risk of Recurrence Estimates (5-year, AJCC Stages I or II):

[redacted]a Risk of Recurrence Estimates (5-year) by 31-GEP Class and AJCC Stage:

AJCC Stage Information		Melanoma Class Result by Stage			
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Stage III	77%	1B/2A	85%	66%	55%
		2B	62%	42%	33%

Greenhaw et al. JAAD 2020

[redacted]-Melanoma Result

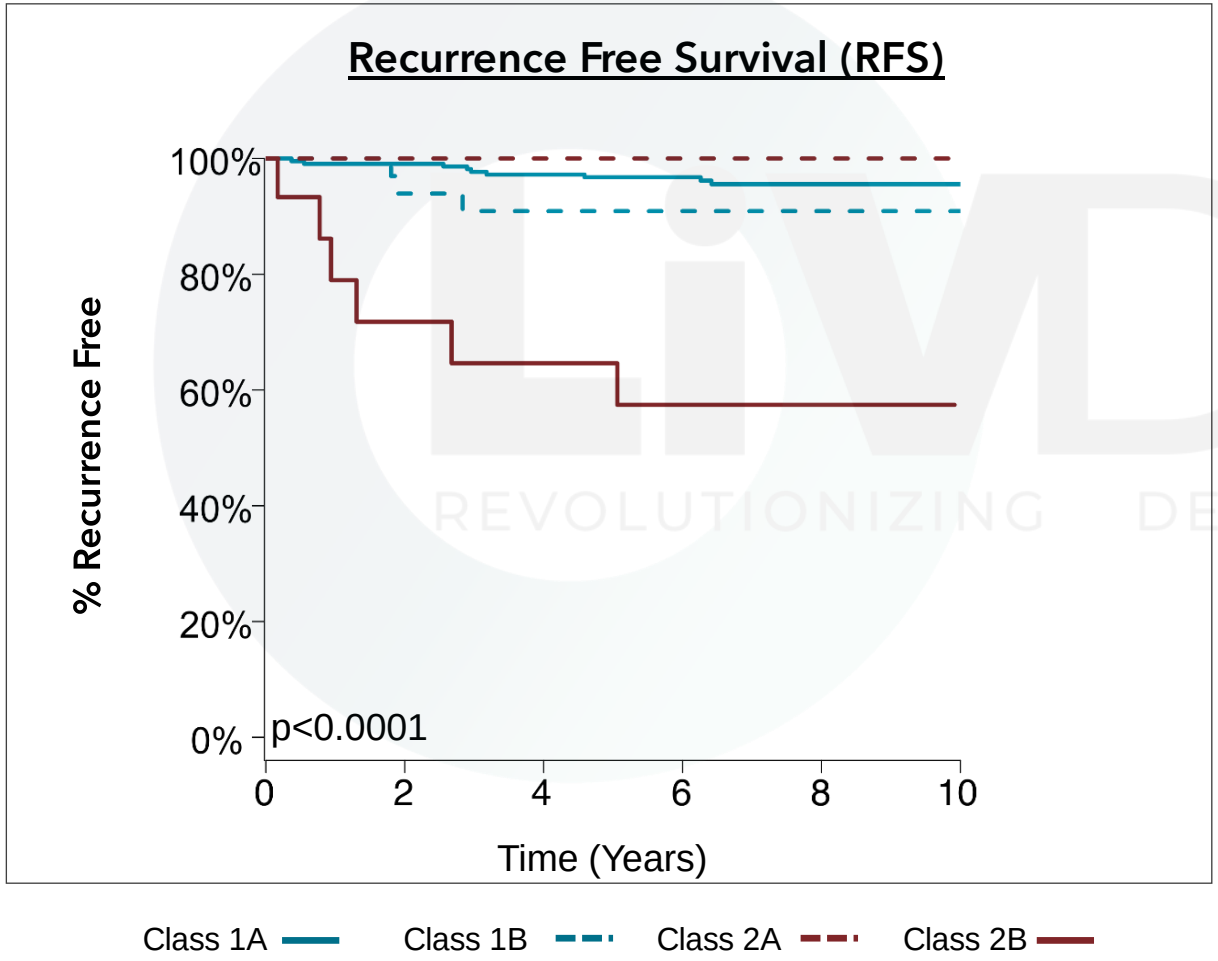
Class 1A 31-GEP Score = 0.23	Class 1A is associated with the lowest risk of recurrence/metastasis within 5 years Class 1A score range: 0-0.41

The [redacted]oma test reports results by molecular class (1A, 1B, 2A or 2B) and the associated 31-gene expression profile (31-GEP) score that ranges from 0.0 to 1.0. This class result informs risk of recurrence and likelihood of sentinel lymph node (SLN) positivity.

Thin Tumors

How does 31-GEP perform in thin tumors?

31-GEP identifies patients at high risk of recurrence and distant metastasis in patients with thin (≤1mm) tumors

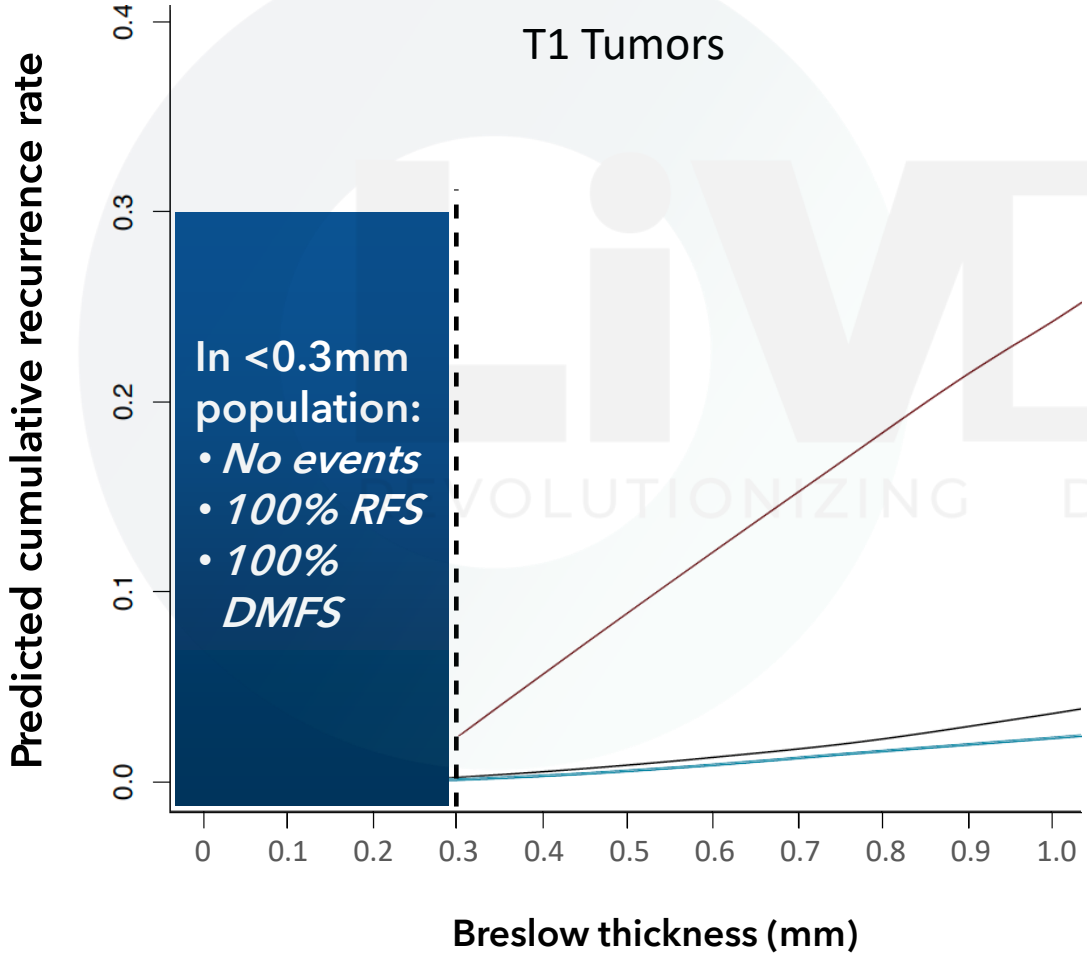


GEP Class	5-year RFS	Event Rate (n)
1A (n=217)	97%	4% (9)
1B (n=34)	91%	9% (3)
2A (n=15)	>99%	0% (0)
2B (n=15)	65%	40% (6)

Cox Multivariate Analysis	RFS	
	HR	P-value
Breslow depth	0.6	0.80
Mitotic rate	1.03	0.83
Ulceration	2.26	0.35
Positive node	4.16	0.09
GEP Class 1B	0.52	0.58
GEP Class 2A	0	1.0
GEP Class 2B	9.34	0.004

Gastman et al. JAAD 2019

Cumulative rate of recurrence and 5-year outcomes shows separation between 31-GEP classes in thin tumors



In 0.3-1.0 mm tumors:		
31-GEP Class	**RFS**	**DMFS**
Class 2B	**75.5%**	**82.1%**
Class 2A	90.9%	90.0%
Class 1B	91.0%	90.6%
Class 1A	**96.8%**	**97.5%**

All T1 Tumors
Class 1A
Class 2B

n=669, 31-GEP: 31-gene expression profile; RFS: recurrence-free survival; DMFS: distant metastasis-free survival
Marks et al SKIN J Cutaneous Med 2019

Stage IA (T1a) Melanoma: Thin tumor – low risk?

CASE STUDY

Clinicopathologic Factors	
Dx: **Invasive malignant melanoma**	
Breslow Depth	**0.6 mm**
Clark Level	**III**
Ulceration	**None**
TILs	**N/A**
Mitosis	**0**
Satelitosis	**None**
AJCC8	**Stage IA (T1a)**

Treatment Plan Recommendation

Based on AJCC staging and NCCN guidelines, this patient would have been followed with a H&P every 6-12 months for 5 years, then annually.

Contributed by a health care provider from Topeka, KS

Stage IA (T1a) Melanoma: Thin tumor – low risk?

CASE STUDY

DecisionDx-Melanoma Result

Class 2B 31-GEP Score = 0.73	Class 2B is associated with the highest risk of recurrence/metastasis within 5 years Class 2B score range: 0.59-1.00

The DecisionDx®-Melanoma test reports results by molecular class (1A, 1B, 2A or 2B) and the associated 31-gene expression profile (31-GEP) score that ranges from 0.0 to 1.0. This class result informs risk of recurrence and likelihood of sentinel lymph node (SLN) positivity.

DecisionDx-Melanoma Risk of Recurrence Estimates (5-year) by 31-GEP Class and AJCC Stage:

AJCC Stage Information		DecisionDx-Melanoma Class Result by Stage			
Clinical Stage	**MSS by AJCC Stage**	**31-GEP Class Result**	**Melanoma-Specific Survival (MSS)**	**Distant Metastasis-Free Survival (DMFS)**	**Recurrence-Free Survival (RFS)**
Stage I	98%	1A 1B/2A 2B	>99% 98% 91%	98% 90% 86%	98% 88% 76%
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Stage III	77%	1A 1B/2A 2B	94% 85% 62%	68% 68% 42%	58% 53% 33%

Greenhaw et al. JAAD 2020

- With Class 2B result, referred to medical oncologist for high-intensity surveillance
- Initial CT scan – clear
- CT scan six months later: biopsy proven oligomet to the lung, BRAF negative
- Radiotherapy to lung metastasis
- Started on combination ipilimumab/nivolumab
- Doing well (clear scans) after 5 years

i31-SLNB

Precise and Personalized Prediction of Positive Sentinel Lymph Node

How are patients currently selected for the SLNB surgical procedure?

Stage	SLN+Risk	SLNB Eligibility
T1a	<5%	No
T1a-HR*	5-10%	Yes: Consider
T1b		
T2a	>10%	Yes: Offer
T2b		
T3		
T4		

*T1a with High-Risk Features

- Use of this 5% threshold was based upon the **5% false negative rate for nodal recurrence** as reported in just one study: MSLT-I[1]
- **This results an overall rate of SLN positivity of ~12%[2-4]**

~88% of patients who undergo the SLNB surgical procedure will have a negative result

Guidelines† recommend that the SLNB procedure can be considered for patients (T1-T4) with an expected risk of being SLN positive above 5% based on Breslow thickness and ulceration status

†NCCN Guidelines for Melanoma v3.2022, ASCO/SSO Guidelines for Sentinel Lymph Node Biopsy 2017, AAD Guidelines for Melanoma 2018; 1Morton NEJM 2014; 2Ellis Am J Surg 2010; 3Bamboat Ann Surg Oncol 2014; 4Joyce Ir J Med Sci 2017

Why improve patient selection for SLNB?

Reduce exposure to anesthesia risks and surgical complications
(rate = 11%)[5]

False negative rate for nodal recurrence = 5-21%
(median = 18%)[4]

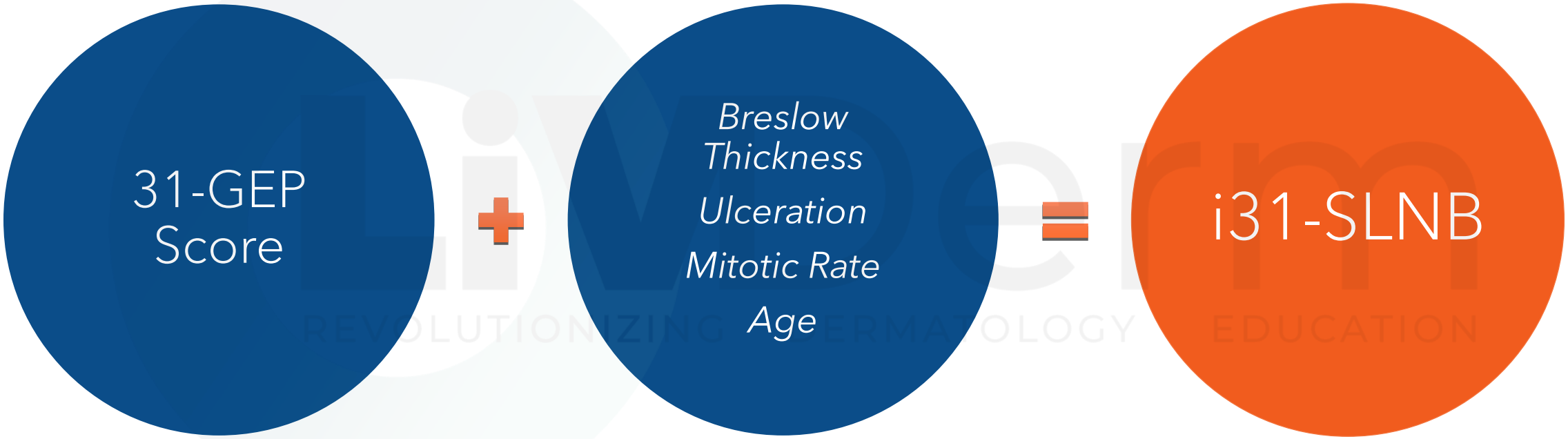
MSLT-I demonstrated *no survival benefit* and *low sensitivity*
(2/3 of melanoma deaths in SLN negative group)[3]

Majority of patients (~88%) subjected to a SLNB are negative and derive little to no benefit[1-2]

Using genetic profiling to better understand who is at higher risk to have a positive sentinel lymph node provides more precise and personalized patient management as well as effective resource management.

1 Ellis et al. AM J Surg 2010; 2 Bamboat et al. Ann Surg Onc 2014; 3 Morton et al. NEJM 2014; 4 Sondak et al. Ann Surg Onc 2009; 5 Moody et al. Eur J Surg Onc 2017

Integrating the 31-GEP score with clinicopathologic factors in a validated algorithm for precise, personalized positive sentinel lymph node prediction



The 31-GEP score was most significant variable in predicting SLN positivity

Whitman JCO PO, 2021

This patient's i31-GEP Personalized Likelihood of Sentinel Lymph Node Positivity

Likelihood of SLNB positivity (i31-SLNB): **11.3%**
For those with risk less than 5%, SLNB is generally not recommended. For those with risk between 5% and 10%, SLNB is sometimes considered. Typically, SLNB is recommended for patients with risk of positivity greater than 10%.

SLNB positivity estimates using histopathologic factors alone:
Breslow thickness of <0.8mm without ulceration or other adverse features* has an estimated likelihood of SLNB positivity of **less than 5%**
Breslow thickness of ≥0.8 – 1.0mm with or without ulceration or thickness <0.8mm with ulceration and/or other adverse features* has an estimated likelihood of SLNB positivity **between 5% and 10%**
Breslow thickness of >1.0mm with or without ulceration has an estimated likelihood of SLNB positivity **greater than 10%**

Whitman et al. JCO-PO 2021

The ma i31-GEP Likelihood of SLN Positivity (i31-SLNB) test result was developed using artificial intelligence techniques. The validated i31-SLNB algorithm integrates the 31-GEP score (0.0 – 1.0) with the patient's specific clinicopathologic factors of Breslow thickness, ulceration, mitotic rate, and age.

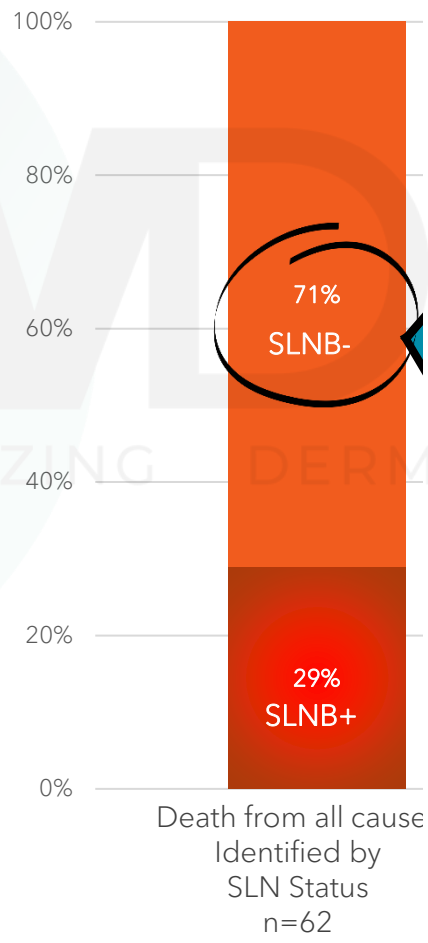
**Adverse features can include uncertainty about the adequacy of micro-staging (positive deep margin), mitotic index ≥2/mm² (particularly in the setting of young age), lymphovascular invasion or a combination of these factors.*

SLNB Negative

31-GEP identifies patients at high-risk for recurrence even after a negative SLNB

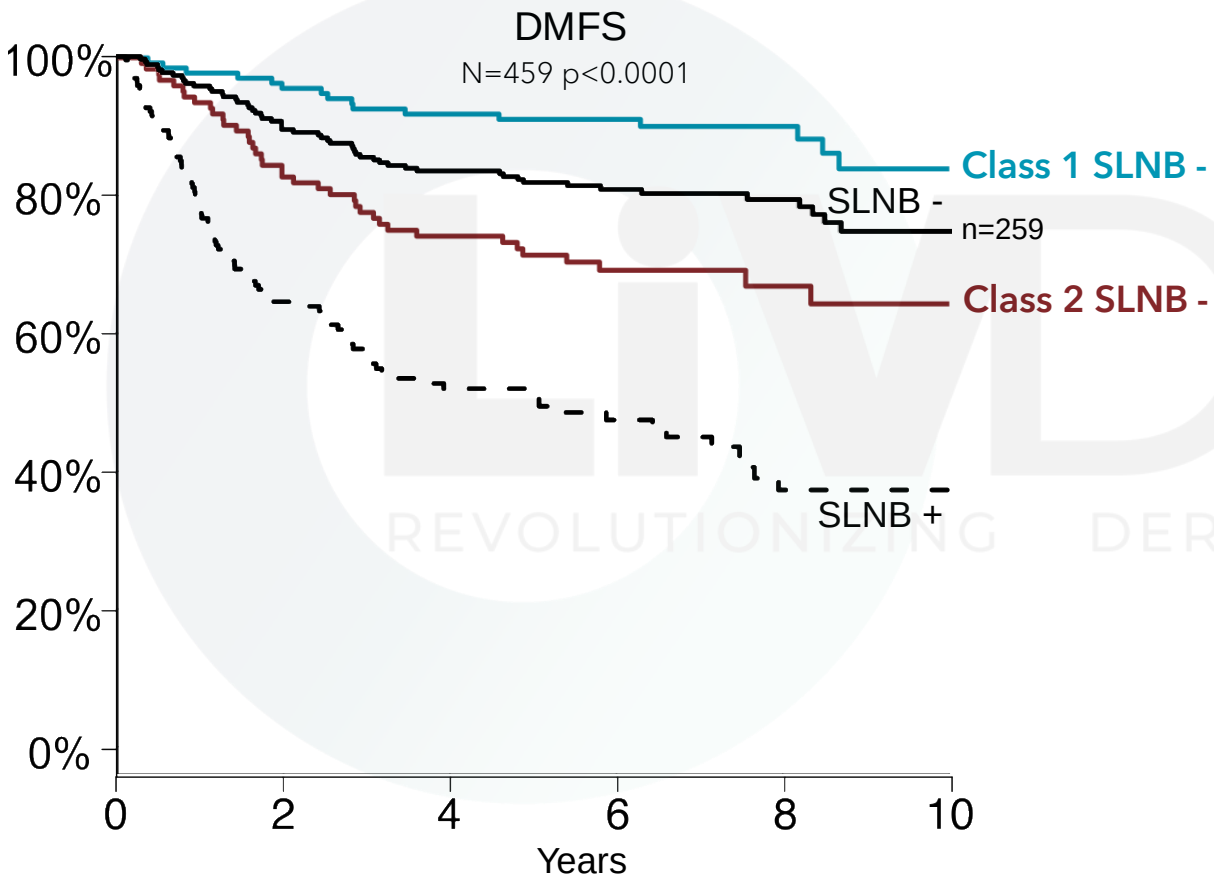
31-GEP outperforms SLNB in identifying the majority of metastatic events from melanoma as high risk

- SLNB identified only 29% of patients that died as SLN positive and 71% of patients that were SLN negative
- Of those that had a negative SLNB, 31-GEP identified 84% of the deaths as high-risk (independent of staging)
- In the full cohort, 31-GEP identified 85% of the events as high-risk outperforming SLNB



Gerami et al, J Am Acad Dermatol 72(5):780-5.e3, 2015

In SLN-negative patients, 31-GEP shows independent prognostic value that complements and adds to information provided by SLNB



	5-year DMFS (95% CI)	Events (%)
SLNB- (n=259)	82% (77-87%)	54 (21%)
SLNB+ (n=200)	51% (44-60%)	94 (47%)

SLNB Negative	5-year DMFS (95% CI)	Events (%)
Class 1 (n=136)	91% (86-96%)	16 (12%)
Class 2 (n=123)	71% (64-80%)	38 (31%)

31-GEP identified **70%** of the events that occurred among SLN-negative patients

Gastman et al. JAAD 2019; Leachman et al. SMR 2017

Clinical Utility

How can 31-GEP be integrated into clinical workflow?

Kwatra et al. Expert Panel publication: Established clinical workflow for 31-GEP testing within AJCC staging and integrated into NCCN guidelines

A Dermatologist's Guide to Implementation of Gene Expression Profiling in the Management of Melanoma

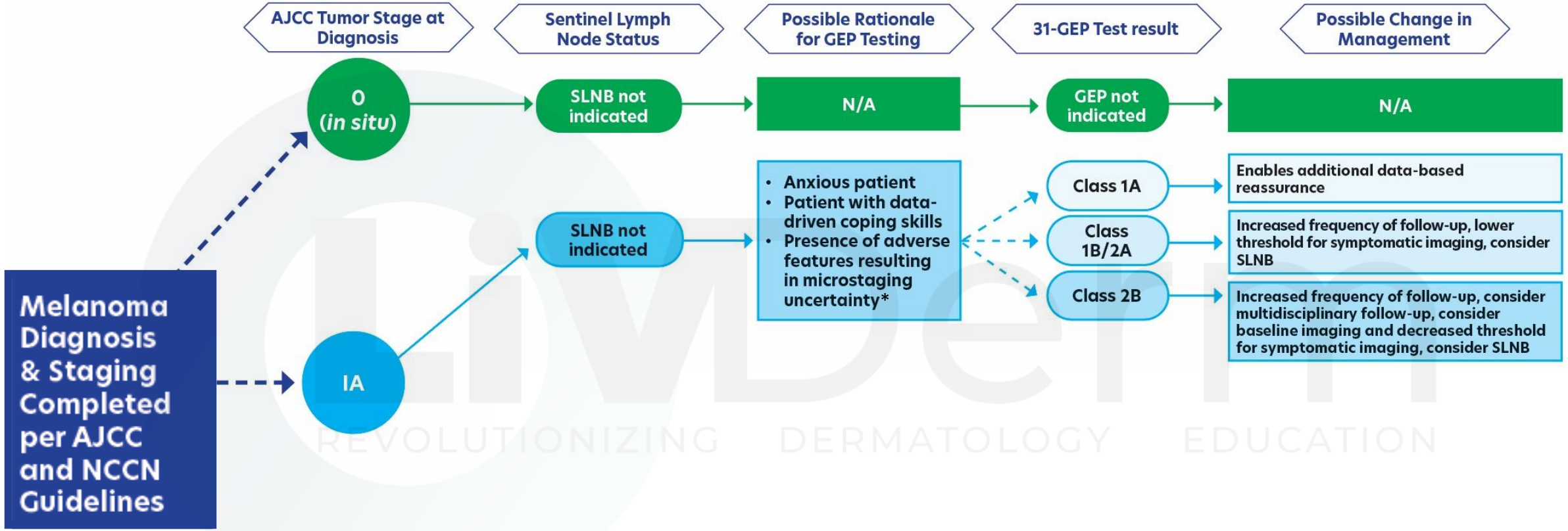
Shawn G. Kwatra, MD[1]; Howard Hines, MD[1]; Yevgeniy R. Semenov, MD[2]; Shannon C. Trotter, DO[3]; Elizabeth Holland, RN, BSN[4]; and Sancy Leachman MD, PhD[5]

[1]Johns Hopkins University School of Medicine, Baltimore MD; [2]Harvard Medical School. Boston MA: [3]Ohio University and Arthur G. James Center, Columbus OH; [illegible], Friendswood, TX; [5]Oregon Health & Science University, Portland, OR

- Five expert dermatologists convened virtually in May 2020
  - Reviewed published literature on prognosis in melanoma
  - Focused on the commercially available GEP test in melanoma
- Established clinical workflow for dermatology to use GEP in melanoma prognosis within AJCC staging and in alignment with NCCN guidelines
- Important to use test in a shared decision-making model
  - Adds objective information to help multidisciplinary care team educate patients and make more informed decisions

Kwatra SG et al. JCAD 2020

Integrating AJCC Staging & Gene Expression Profiling: Stage IA

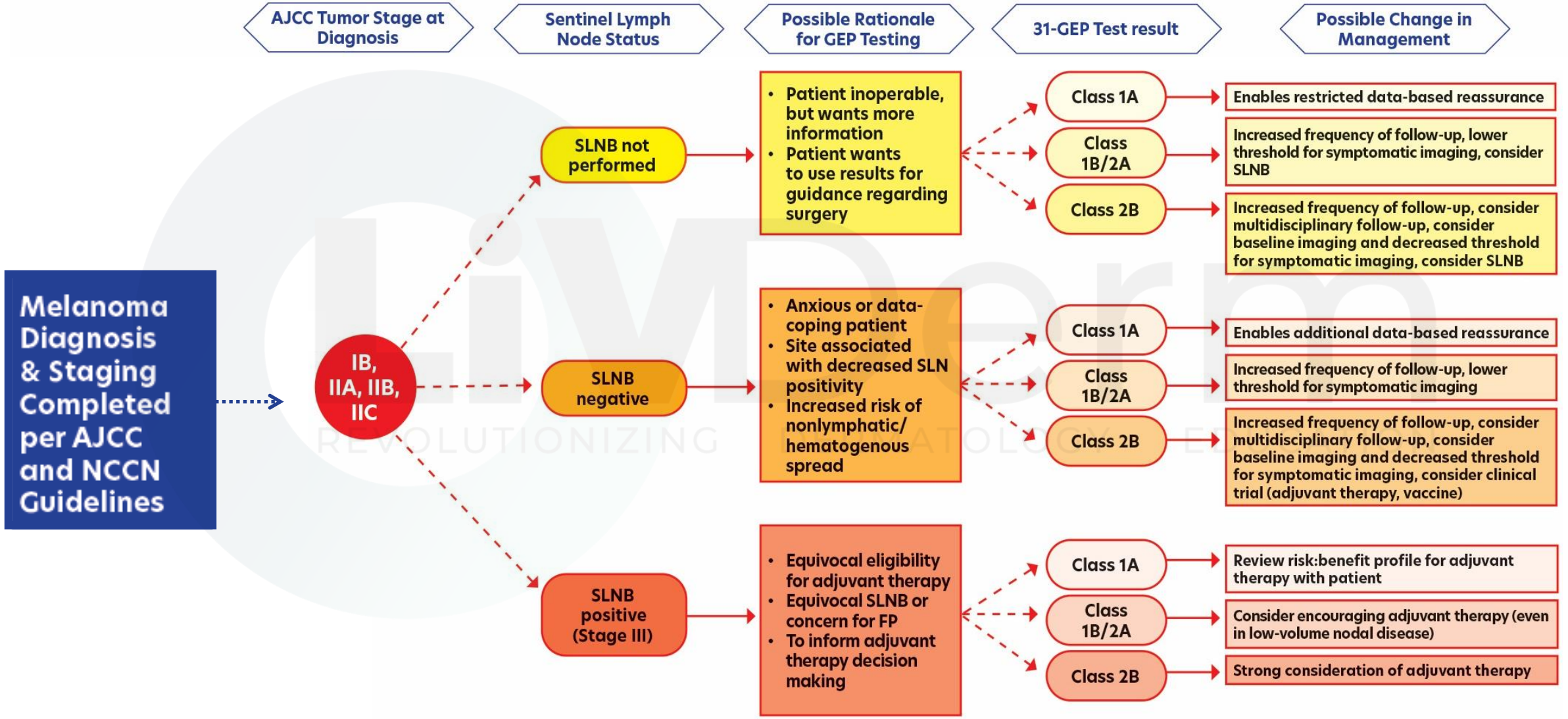


*Adverse features resulting in uncertain microstaging include:

- Biopsies with a transected base
- Mitotic rate >1/mm^2
- Lymphovascular invasion

Kwatra SG et al. JCAD 2020

Integrating AJCC Staging & Gene Expression Profiling: Stages IB-IIC



Kwatra SG et al. JCAD 2020

Collaboration with NCI

Linking 31-GEP clinical testing with patients captured in the NCI-SEER Registry

Castle Biosciences announced a collaboration with the National Cancer Institute (NCI) to link DecisionDx-Melanoma testing data with data from the Surveillance, Epidemiology and End Results (SEER) Program's registries on cutaneous melanoma (CM) cases

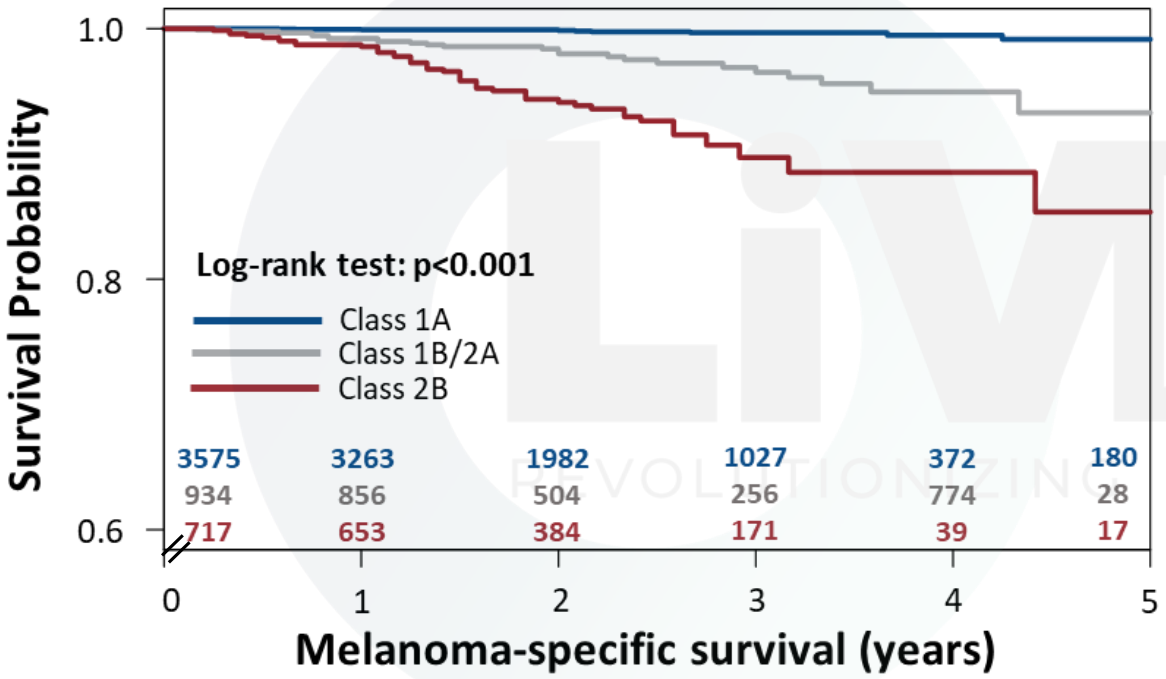
- **Phase 1 Collaboration Objectives:**
- **Validate:** Confirm the performance of 31-GEP
  - Unselected and prospectively tested cohort of patients with CM
  - Provide unbiased real-world data, showing clinical benefit of 31-GEP testing
  - Patients diagnosed from 2013 - 2018
- **Compare:** Does the addition of 31-GEP test results improve outcomes
  - Survival outcomes in patients receiving 31-GEP testing vs. untested patients

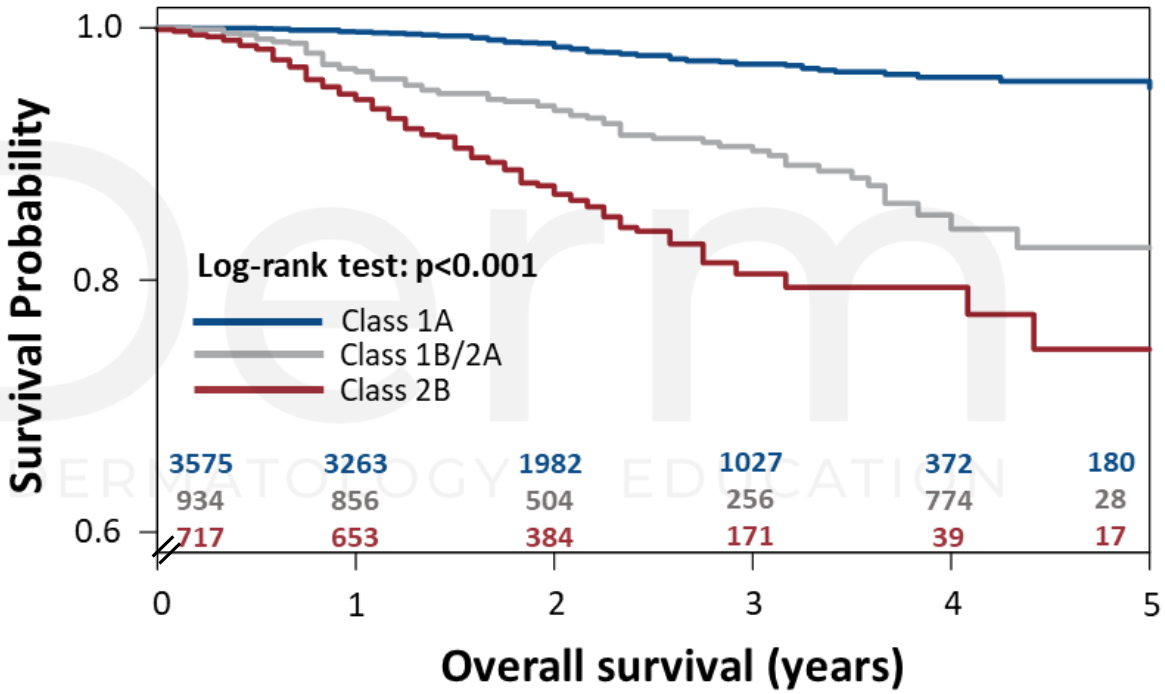
Full Cohort Demographics

- SEER Cancer registry
  - CM cases diagnosed from 2013-2018
  - Stage I-III CM
  - 31-GEP testing results
- Total of 11 covariates analyzed

Descriptor	Characteristics	Full Cohort (N = 5226)
Age	years, median (range)	63 (13-98)
Survival/follow-up	years, median (range)	2.17 (0.6-6.92)
Race	White	4888 (93.5%)
	Not White	338 (6.5%)
Sex	Female	2311 (44.2%)
	Male	2915 (55.8%)
Sentinel Lymph Node Status	Negative	3780 (72.4%)
	Positive	295 (5.6%)
	Unknown	1151 (22.0%)
T-Stage (per AJCC 8th ed.)	T1a	2453 (46.9%)
	T1b	887 (17.0%)
	T2a	880 (16.8%)
	T2b	210 (4.0%)
	T3a	290 (5.6%)
	T3b	214 (4.1%)
	T4a	127 (2.4%)
	T4b	165 (3.2%)

NCI/SEER cohort of unselected prospectively tested patients confirms previously reported risk stratification for patients with Stage I-III cutaneous melanoma (n=5226)





The separation of Class 1A, Class 1B/2A, and Class 2B MSS and OS risk in 31-GEP tested patients within the SEER registry mirrors the risk separation in previously reported studies[1,2]

Kurley et al. Presented at EADO, April 21-23, 2022, 1Gastman et al. JAAD 2019, 2Hsueh et al. JCO Precis Oncol 2021

Matching 31-GEP tested patients to untested patients to isolate the potential effect of 31-GEP testing on outcomes

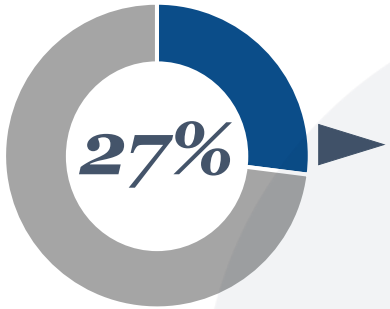
- Patient selection
  - All incident cases of cutaneous melanoma diagnosed between 2013-2018 registered in SEER
  - Cases that were tested with 31-GEP
  - Analysis included all patients within the SEER Database
  - Diagnosed in 2016-2018 to account for potential access to adjuvant therapy
- Matching
  - Patients tested with 31-GEP were matched to untested patients (1:3 ratio)
  - No significant differences between 31-GEP tested and non-tested patients

Successful matching of a cohort of non-31-GEP tested patients to the 31-GEP tested population

Covariates	31-GEP Tested (n=3,621) vs. Non-31-GEP Tested (n=10,863)
Age *(median)*	p=0.607
Follow-up time *(median)*	p=0.474
T-stage	p>0.999
Year of diagnosis (2016-2018)	p=0.327
Sex	p=0.199
Yost index (quintile)	p=0.888
SLN assessment	p=0.813
SLN positivity	p=0.757
Mitotic rate *(median)*	p=0.524
Primary tumor location	p=0.956
Race	p=0.506

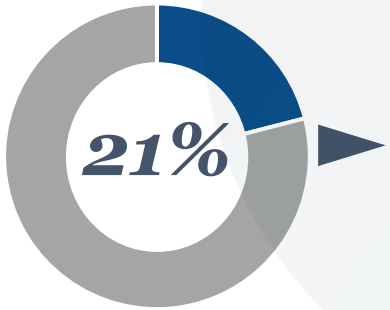
Kurley et al. European Association of Dermato Oncology (EADO) conference in Seville, Spain; April 21-23, 2022

Patients receiving 31-GEP test results had improved melanoma-specific survival and overall survival compared to those not tested, (n=3621)



Benefit in 3-year MSS in patients that were tested over those that were not tested

	3-year MSS (95% CI)	Deaths, % (n/N)
31-GEP Tested	97.7% (97.0-98.4%)	1.6% (58/3621)
Matched Untested	96.6% (96.2-97.1%)	2.2% (238/10863)
Hazard ratio‡	**0.73 (0.54-0.97)**	**P=0.03**



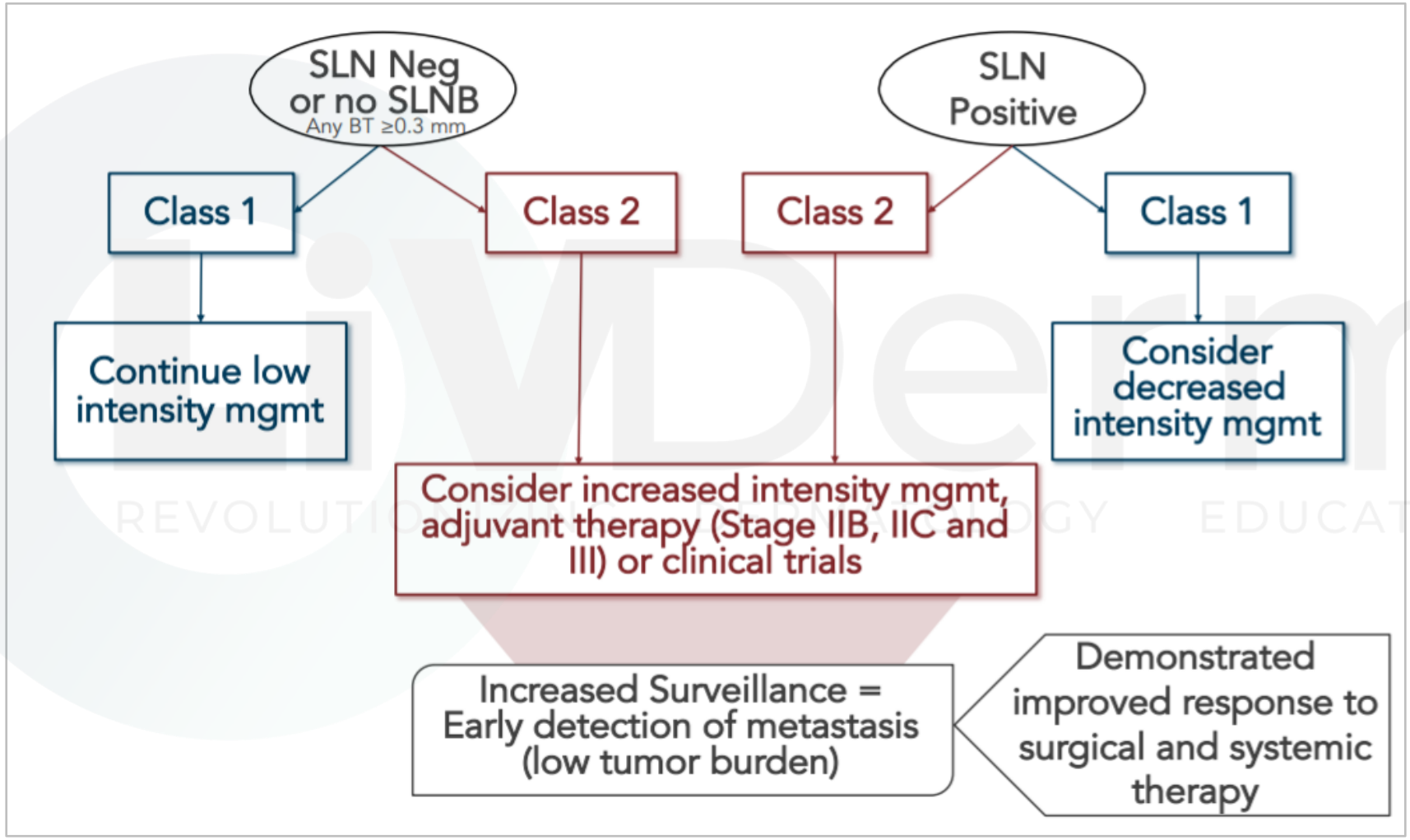
Benefit in 3-year OS in patients that were tested over those that were not tested

	3-year OS (95% CI)	Deaths, % (n/N)
31-GEP Tested	93.1% (92.0-94.2%)	4.8% (174/3621)
Matched Untested	91.2% (90.4-91.9%)	6.1% (658/10863)
Hazard ratio‡	**0.79 (0.67-0.93)**	**P=0.006**

- Study data provide direct evidence that CM patients tested with 31-GEP have better survival rates than untested patients
- Suggests that the testing can aid in risk-aligned treatment plans for improved patient outcomes and survival rates

‡Hazard ratio (HR) was computed using the untested patients as reference for 31-GEP tested cohort. An HR less than 1.0 demonstrates improved survival in 31-GEP tested patients. Diagnosis date 2016 and onward

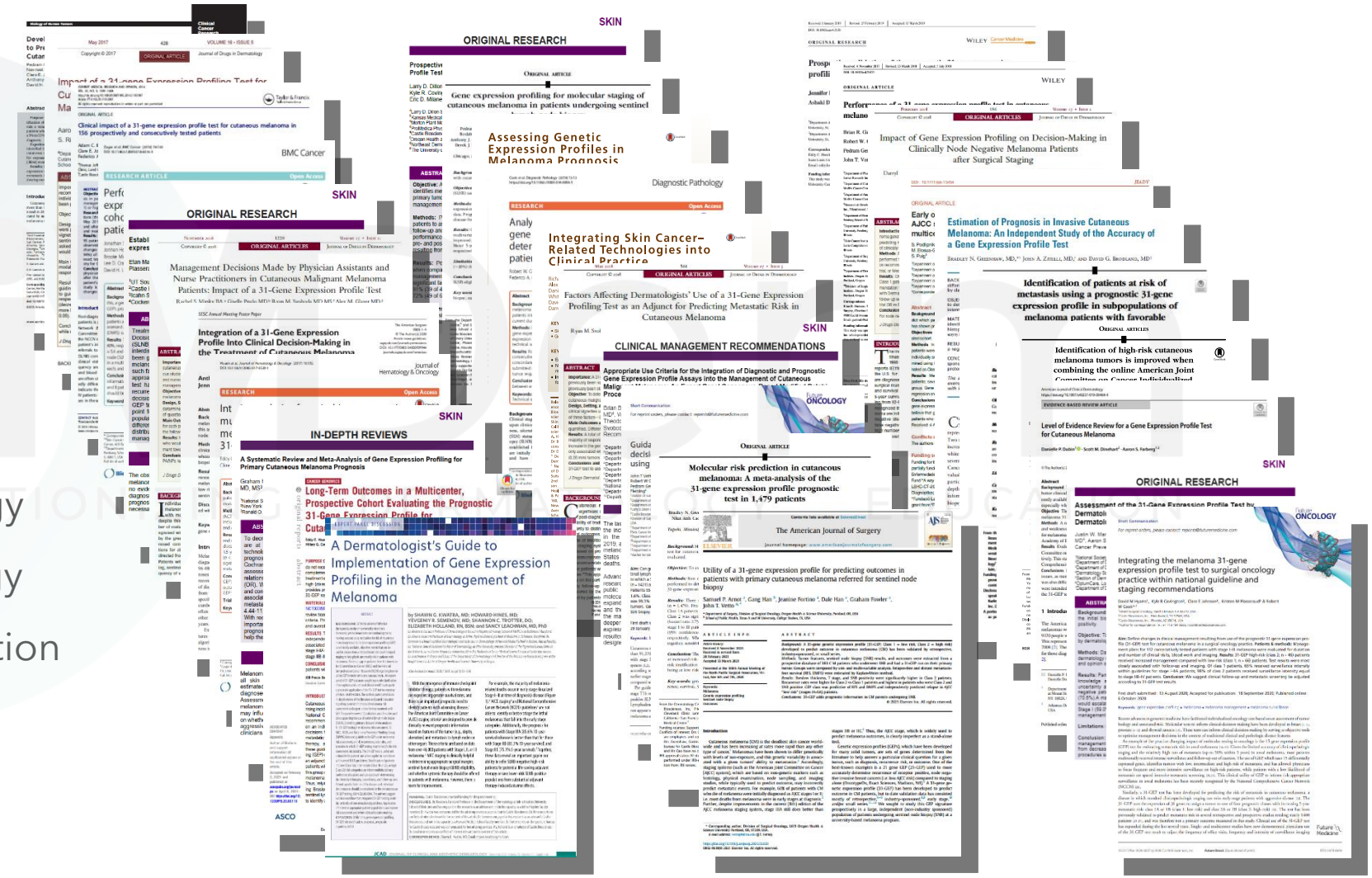
31-GEP Risk-Aligned Management Plans



Bailey et al. Presented at Winter Clinical Dermatology, January 14-19, 2022

31-GEP informs management decisions in stage I-III melanoma

- Frequency of follow-up
- Frequency & modality of surveillance imaging
- Sentinel lymph node biopsy guidance
- Referral to Surgical Oncology
- Referral to Medical Oncology
- Adjuvant therapy consideration



The established leader for melanoma prognostic testing with independent, robust validation AND real-world results

NEW

› i31 Precision

Validated AI-driven algorithms integrating 31-GEP with patient-specific clinicopathologic factors

› 35+

Peer-reviewed, published studies including **prospective studies and 2 meta-analyses**

› >6,300

Patients studied including **independent validation**

› 90,000+

Patients with a clinical **31-GEP** order from ~ **9,300 clinicians**

› 50%

Demonstrated clinical utility providing **change** in management for 1 of 2 patients tested

› Medicare+

Covered by Medicare and multiple private insurers with an **industry-leading** patient assistance program