Prospective validation of the i31-GEP for cutaneous melanoma to select patients who may consider foregoing SLNB

J. Michael Guenther, MD
St. Elizabeth Physicians, Edgewood, KY

SSO2024 ANNUAL MEETING

SSO SOCIETY OF SURGICAL ONCOLOGY LEADING. TOGETHER.

#SSO2024
SSO2024.ORG

Disclosures

Speaker’s Bureau: Castle Biosciences, Inc.

Candidates for SLNB in cutaneous melanoma?

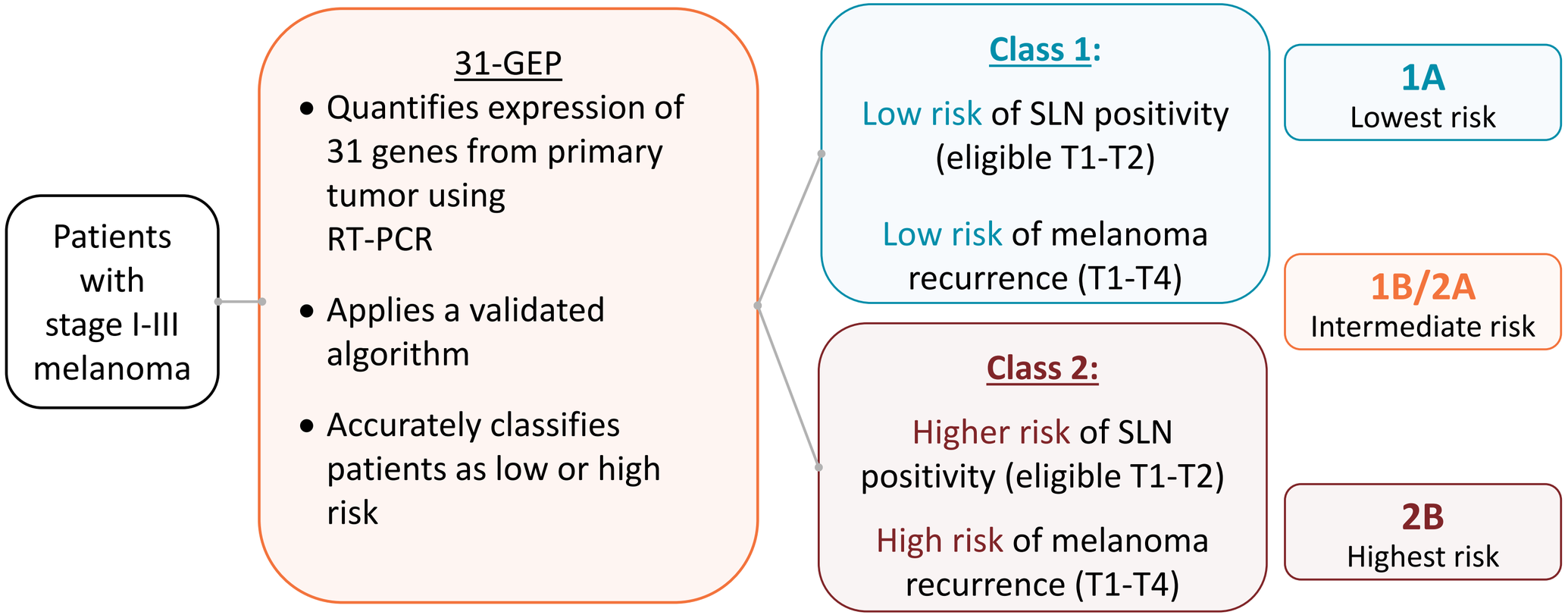
Stage	SLN+ Risk	SLNB Eligibility
T1a	<5%	No
T1a-HR*	5-10%	Yes: Consider
T1b		
T2a	>10%	Yes: Offer
T2b		
T3		
T4		

*HR: High risk features - may include Breslow thickness ≥0.5mm, age ≤42 years, tumor on the H/N, LVI, or MR≥2/mm^{2}[1]

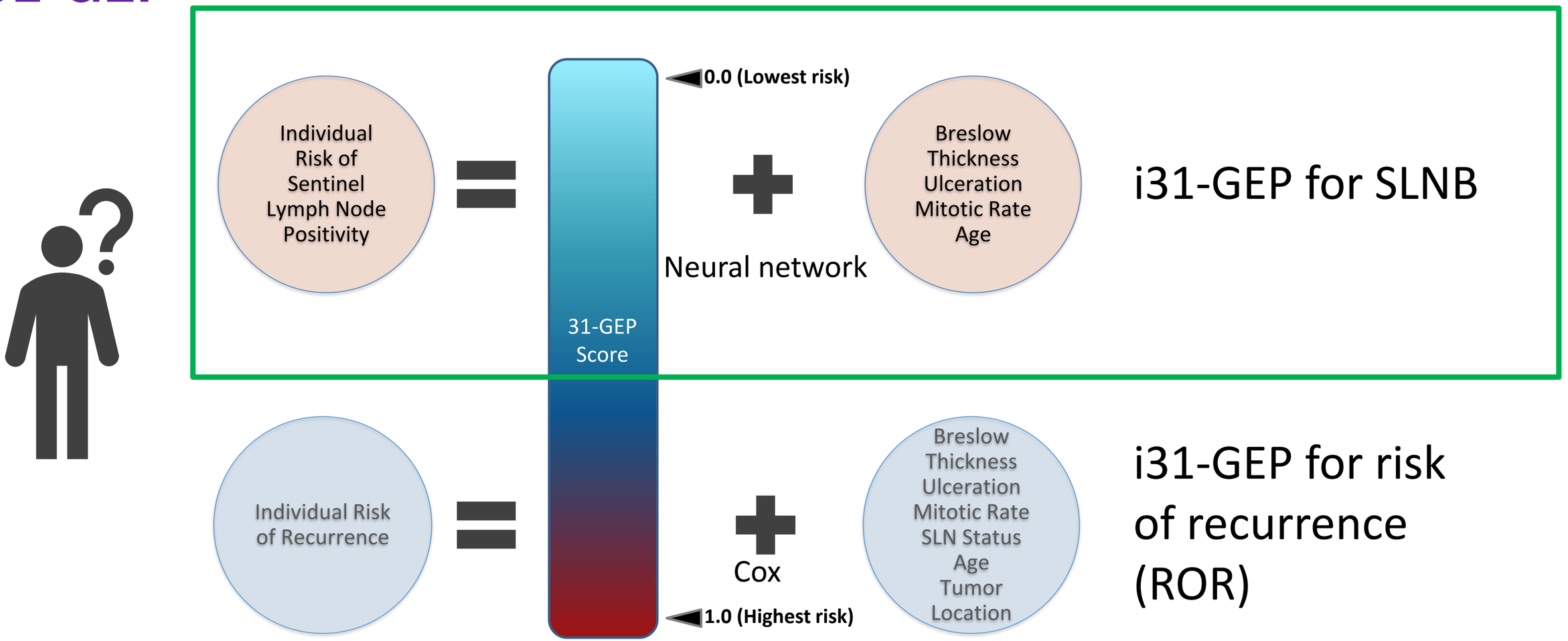
[1]NCCN Melanoma Guidelines, 2023.v3

- 88% negative SLNB
- Only 12% have potential benefit

What is the 31-Gene Expression Profile?



Clinical and pathologic factors have been integrated with the 31-GEP



Initial development (n=1,398) and validation (n=1,674) of the i31-GEP for SLNB positivity[1]

Accuracy Metric	T1-T4
NPV	98.1%
False-negative rate	1.9%
Potential SLNB reduction rate	23.0%
Sensitivity	95.1%

What does performance look like in a prospective study?

[1]Whitman et al. JCO PO 2021

Study Design: Decision Dx Melanoma Impact on Sentinel Lymph Node Biopsy Decisions and Clinical Outcomes (DECIDE)

Study Visit 1:
Informed Consent
- Melanoma Dx within 2 months
- Age ≥18 years
- Considering SLNB
- Ordering 31-GEP to guide SLNB decision

31-GEP testing →

Study Visit 2:
31-GEP Result

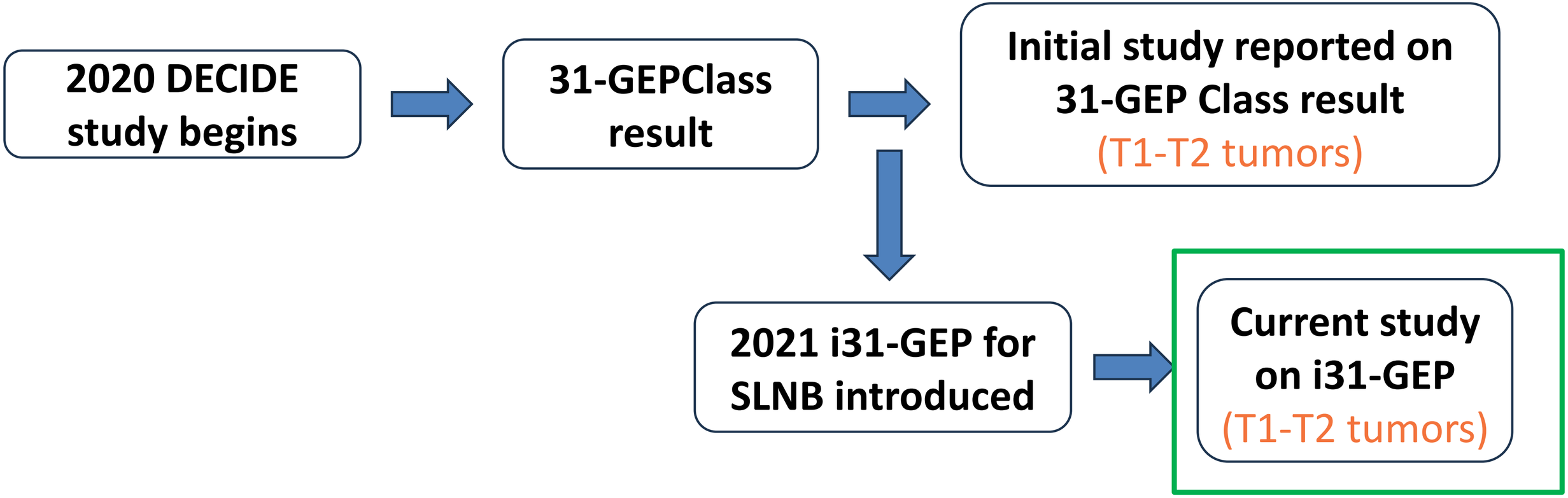
Patient/ Physician Decision →

Study Visit 3:
SLNB Decision
- SLNB
- No SLNB

→ Continue following outcomes: To be reported at a later date.

Three Primary Questions:
1) Are physicians performing fewer SLNBs when utilizing the 31-GEP?
2) Is the false negative rate of the 31-GEP acceptably low?
3) Do patients with a low risk 31-GEP result who do not undergo SLNB have high survival rates?

Study timeline



Patient demographics

	All Patients (n=322)
Age, years, median (range)	63 (20-89)
Sex	
Female	158 (49.1%)
Male	164 (50.9%)
T stage	
T1a	131 (40.7%)
T1b	131 (40.7%)
T2a	51 (15.8%)
T2b	9 (2.8%)
Tumor Location	
Extremity	155 (48.1%)
Head and Neck	64 (19.9%)
Trunk	103 (32.0%)
Breslow thickness, mm, median (range)	0.8 (0.2-2.0)

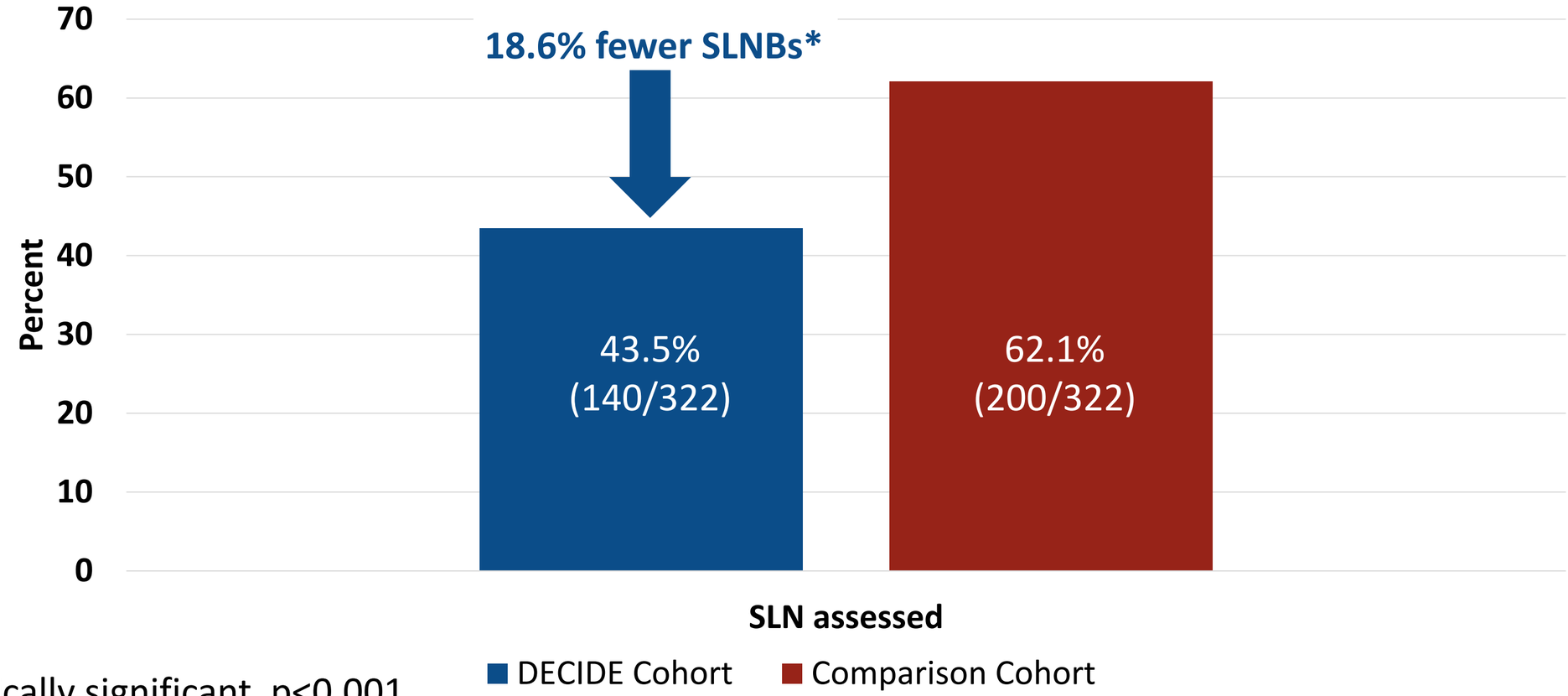
	All Patients (n=322)
Ulceration present	
Yes	25 (7.8%)
No	290 (90.1%)
Unknown	7 (2.2%)
Mitotic rate ($1/mm^2$), median (range)	1 (0-20)
i31-GEP for SLNB	
<5% predicted risk	168 (52.2%)
≥5% predicted risk	154 (47.8%)
Overall sentinel lymph node status	
Negative (of those assessed)	131 (93.6%)
Positive (of those assessed)	9 (6.4%)
Not performed (of whole population)	182 (56.5%)

Question 1) Are physicians performing fewer SLNBs? Patients were matched to a comparison cohort for whom 31-GEP was not used to guide SLNB decisions

Descriptor	DECIDE (n=322)	Comparison Cohort (n=322)
Age		P=0.921
Median (Range)	63 (20-89)	63 (21-89)
T-stage		P>0.999
T1aHR	60 (18.6%)	60 (18.6%)
T1aLR	71 (22.1%)	71 (22.1%)
T1b	131 (40.7%)	131 (40.7%)
T2a	51 (15.8%)	51 (15.8%)
T2b	9 (2.8%)	9 (2.8%)
Mitotic rate (1/mm^2)		P>0.999
<2	244 (75.8%)	244 (75.8%)
≥2	78 (24.2%)	78 (24.2%)

T1aHR: T1a tumors with at least one additional high-risk factor. T1aLR: T1a tumors with no additional high-risk factors.

Fewer SLNBs are performed when incorporating 31-GEP testing



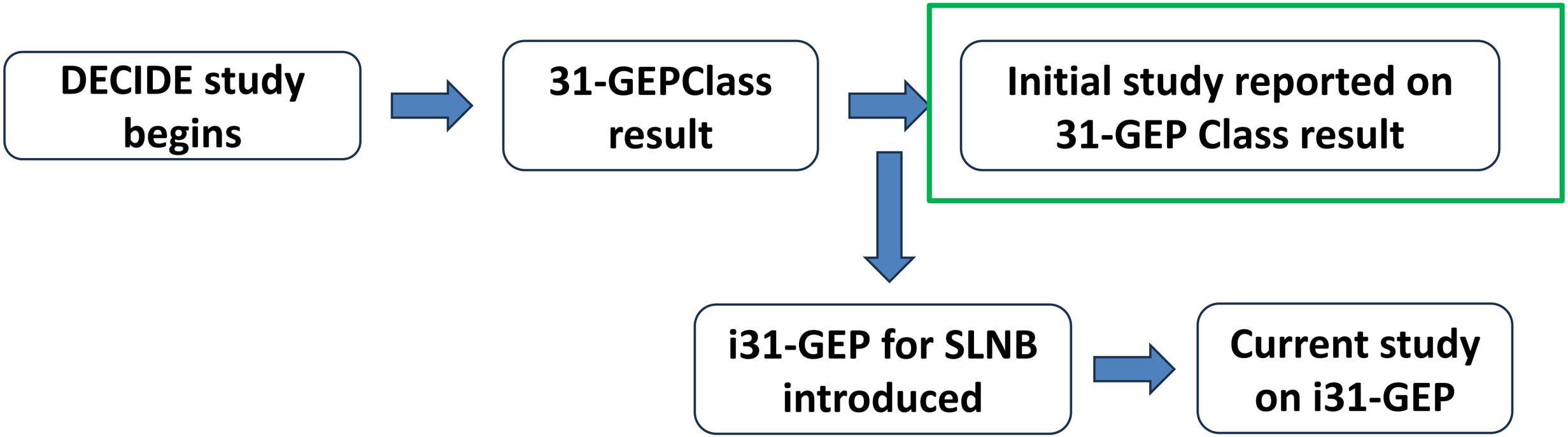
*Statistically significant, p<0.001

Question 2) Is the false-negative rate acceptably low?
No patient with an i31-GEP SLNB predicted risk of <5% had a positive SLN (35 pts, 24.8%)

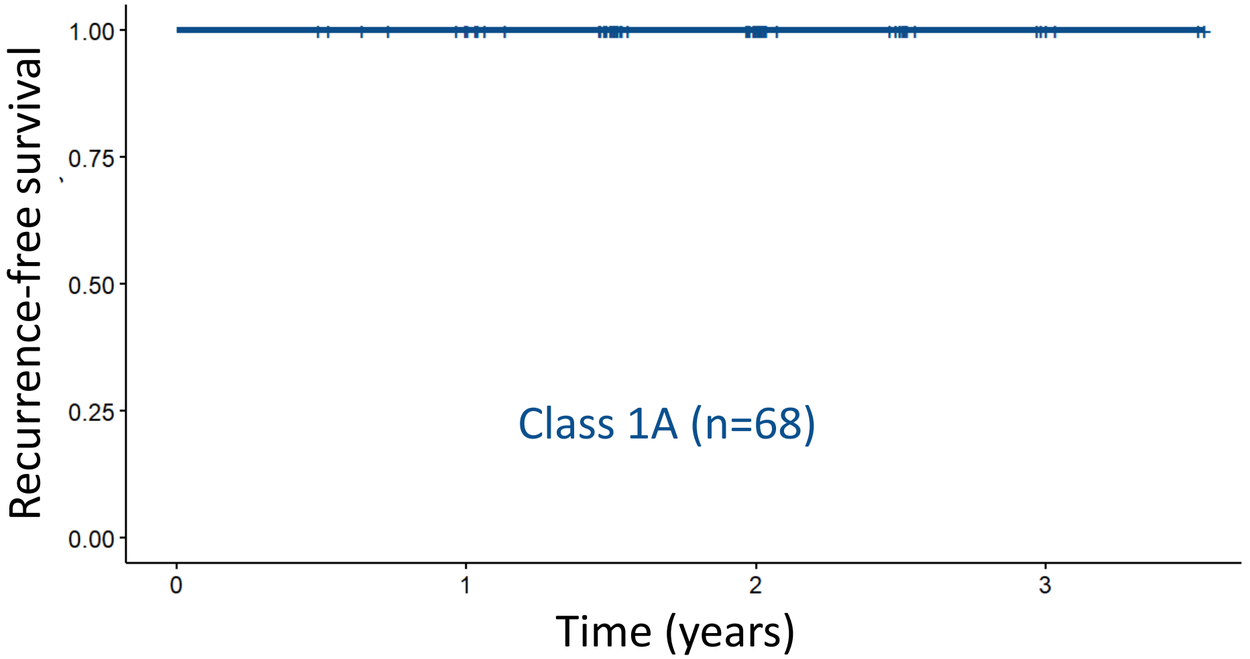
i31 GEP for SLNB	<5% risk			
T stage	T1a	T1b	T2a	T2b
SLN status				
Negative	11	19	4	1
Positive	0	0	0	0
SLN positivity rate	0%	0%	0%	0%

Study timeline

*3-year outcomes reported here for the first time



Question 3) Do low risk patients avoiding SLNB have high survival?
No patient with a Class 1A result has had a recurrence*



*Median follow-up: 2.0 years

Conclusions

- In this prospective study:
  - No patient with an i31-GEP for SLNB predicted risk of <5% had a positive SLN, and
  - RFS was 100% for patients with a Class 1A test result
- If the i31-GEP for SLNB was used to inform management decisions in this study, then the test could have further reduced the number of patients with T1-T2 cutaneous melanoma who could have avoided SLNB by 25%
- The performance data presented here in conjunction with previous validation and performance studies show the i31-GEP as an accurate and precise clinical tool to identify patients who may safely forego SLNB, reducing the number of unnecessary SLNBs performed

THANK YOU

SSO2024
ANNUAL MEETING

SSO
SOCIETY OF SURGICAL ONCOLOGY
LEADING. TOGETHER.

#SSO2024
SSO2024.ORG