

# Long-term survival of melanoma patients stratified by a clinicopathologic and gene expression profile (CP-GEP model): A multi-center United States cohort study

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## Introduction

- >97,000 newly cutaneous melanoma (CM) cases diagnosed in 2023 makes it the 5<sup>th</sup> most common cancer in the US<sup>1</sup>.
- Sentinel lymph node biopsy (SLNB) is the gold standard for staging intermediate and thick melanomas<sup>2</sup> but new stratification tools are being developed.
- The CP-GEP model has been developed and validated to predict SLNB status, and recently long-term survival outcomes were evaluated in European cohorts<sup>3-7</sup>.
- Aim:** In this US multi-center study we investigate the long-term survival of CM patients stratified by CP-GEP.

## Methods

- CM patients included from six U.S. institutions.
- CP-GEP model performed on archived primary tissue samples.
- CP-GEP model includes Breslow thickness, patient's age and expression of 8 genes and has a binary outcome: High Risk vs Low Risk<sup>3</sup>.
- 5-year Relapse-Free Survival (RFS), Distant Metastasis-Free Survival (DMFS), and Melanoma-Specific Survival (MSS) were assessed.
- 11 patients were excluded for the survival analysis due to missing survival data.

## Study cohort represents real-world CM population

Table 1 Patient demographics and clinicopathologic characteristics

Variable	Level	US validation N=594
Gender	Female	263 (44.3%)
	Male	331 (55.7%)
Age (years)	Median [1QR, 3QR]	62 (51, 71)
Breslow thickness (mm)	Median [1QR-3QR]	1.40 (1.00, 2.50)
	Absent	452 (76.1%)
Ulceration	Present	137 (23.1%)
	Unknown	5 (0.8%)
SLNB outcome	Negative	485 (81.6%)
	Positive	109 (18.4%)
CP-GEP	Low Risk	198 (33.3%)
	High Risk	396 (66.7%)
Clark level	II	2 (0.3%)
	III	43 (7.2%)
	IV	307 (51.7%)
	V	19 (3.2%)
	Unknown	223 (37.5%)
Primary tumor location	Head/Neck	108 (18.2%)
	Trunk	213 (35.9%)
	Upper Extremities	109 (18.4%)
	Lower Extremities	129 (21.7%)
Histologic type	Other	35 (5.9%)
	Superficial spreading	280 (47.1%)
	Nodular	118 (19.9%)
	Other	196 (33.0%)
Angiolymphatic Invasion	Absent	284 (47.8%)
	Present	26 (4.4%)
	Unknown	284 (47.8%)

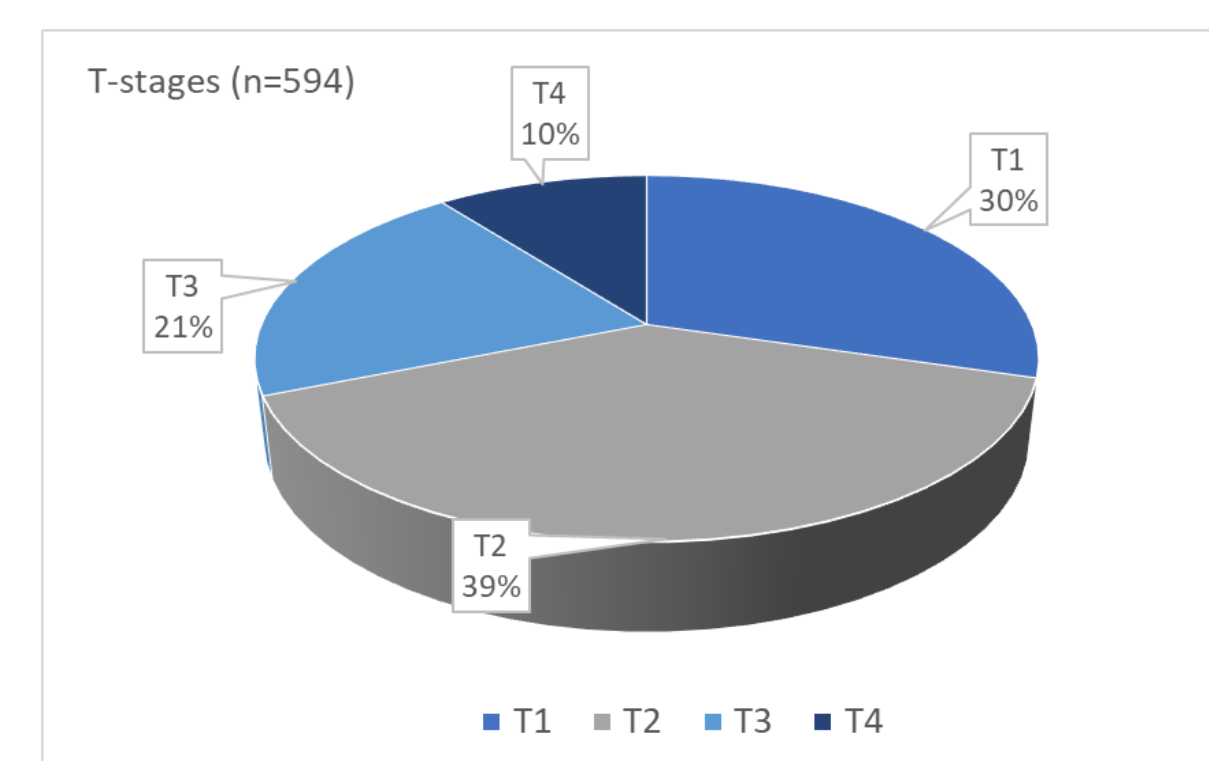
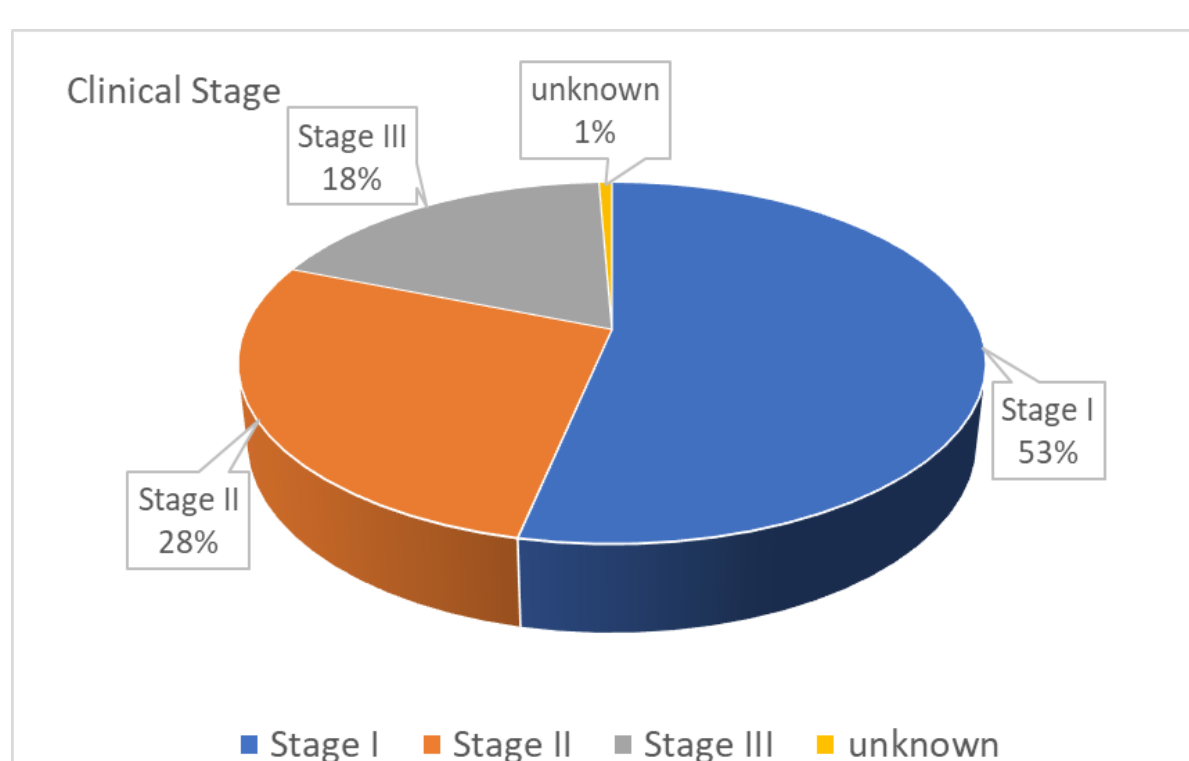
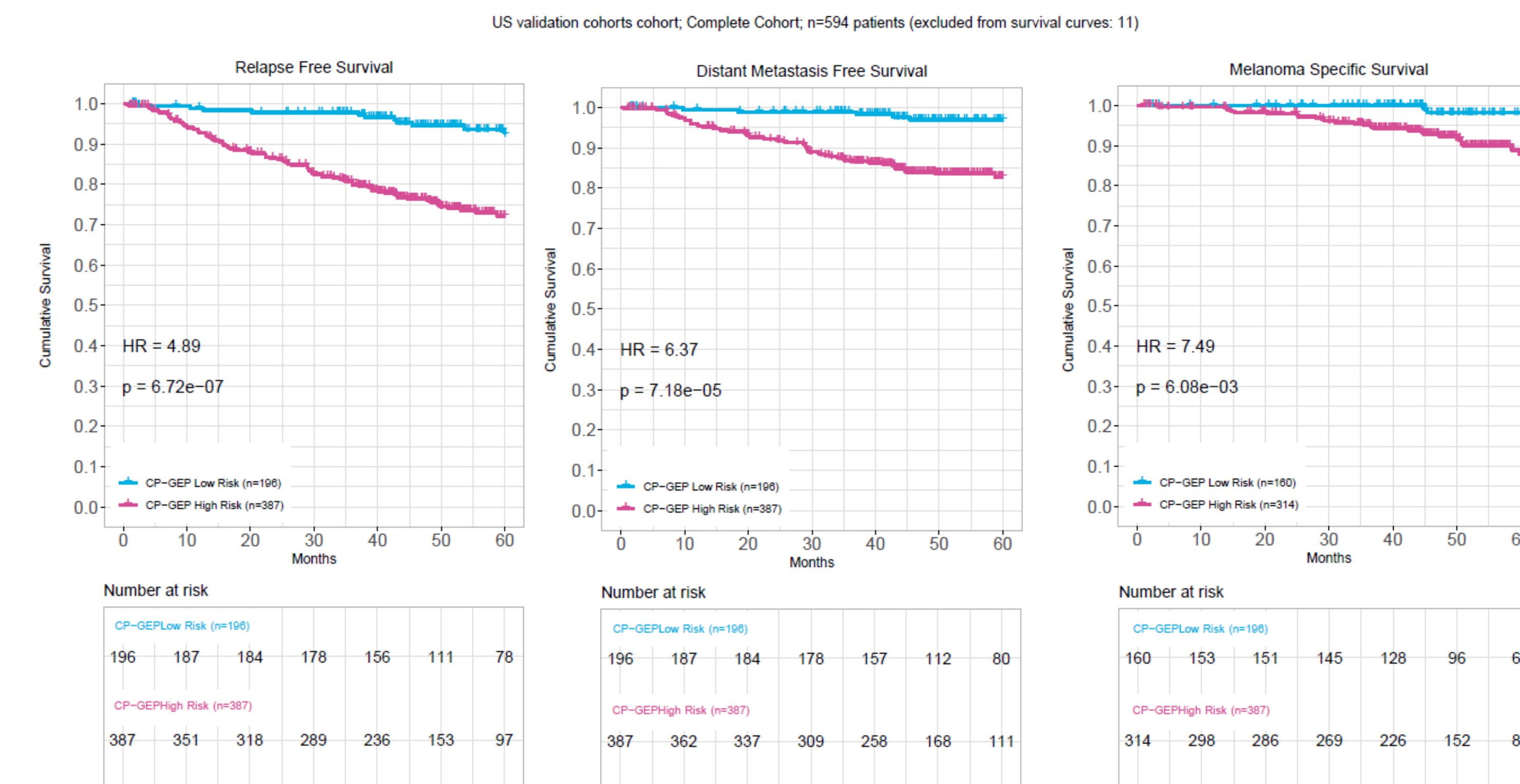


Figure 1 Distribution of both clinical stages and T-stages of the combined US cohort, left and right respectively.

## Take home message

- CP-GEP is able to risk stratify CM patients across all clinical stages.
- CP-GEP Low Risk patients have 5-year survival outcome of >90%.

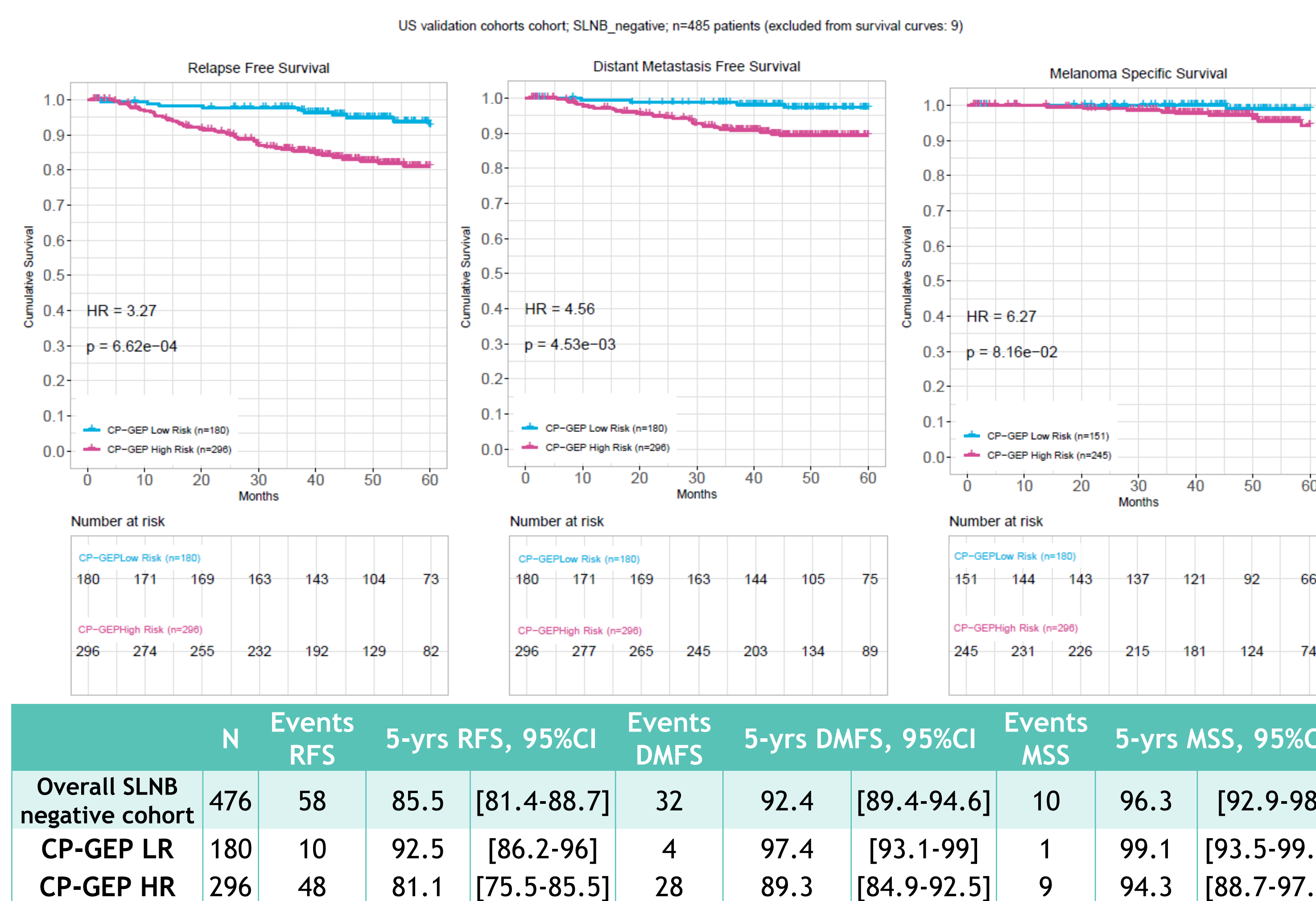
## CP-GEP stratifies CM patients as Low and High Risk in long-term survival outcome



	N	Events RFS	5-yrs RFS, 95%CI	Events DMFS	5-yrs DMFS, 95%CI	Events MSS	5-yrs MSS, 95%CI
Complete cohort	583	102	79.1 [75.1-82.6]	62	87.7 [84.4-90.3]	28	91.7 [87.9-94.3]
CP-GEP LR	196	11	92.4 [86.4-95.9]	5	96.9 [92.7-98.7]	2	98.2 [93-99.6]
CP-GEP HR	387	91	72.2 [66.7-77]	57	82.9 [78.2-86.6]	26	88 [82.3-91.9]

Figure 2 Kaplan-Meier curves showing 5-year RFS, DMFS, and MSS of patients diagnosed with Stage I-III CM stratified by CP-GEP as Low vs High Risk.

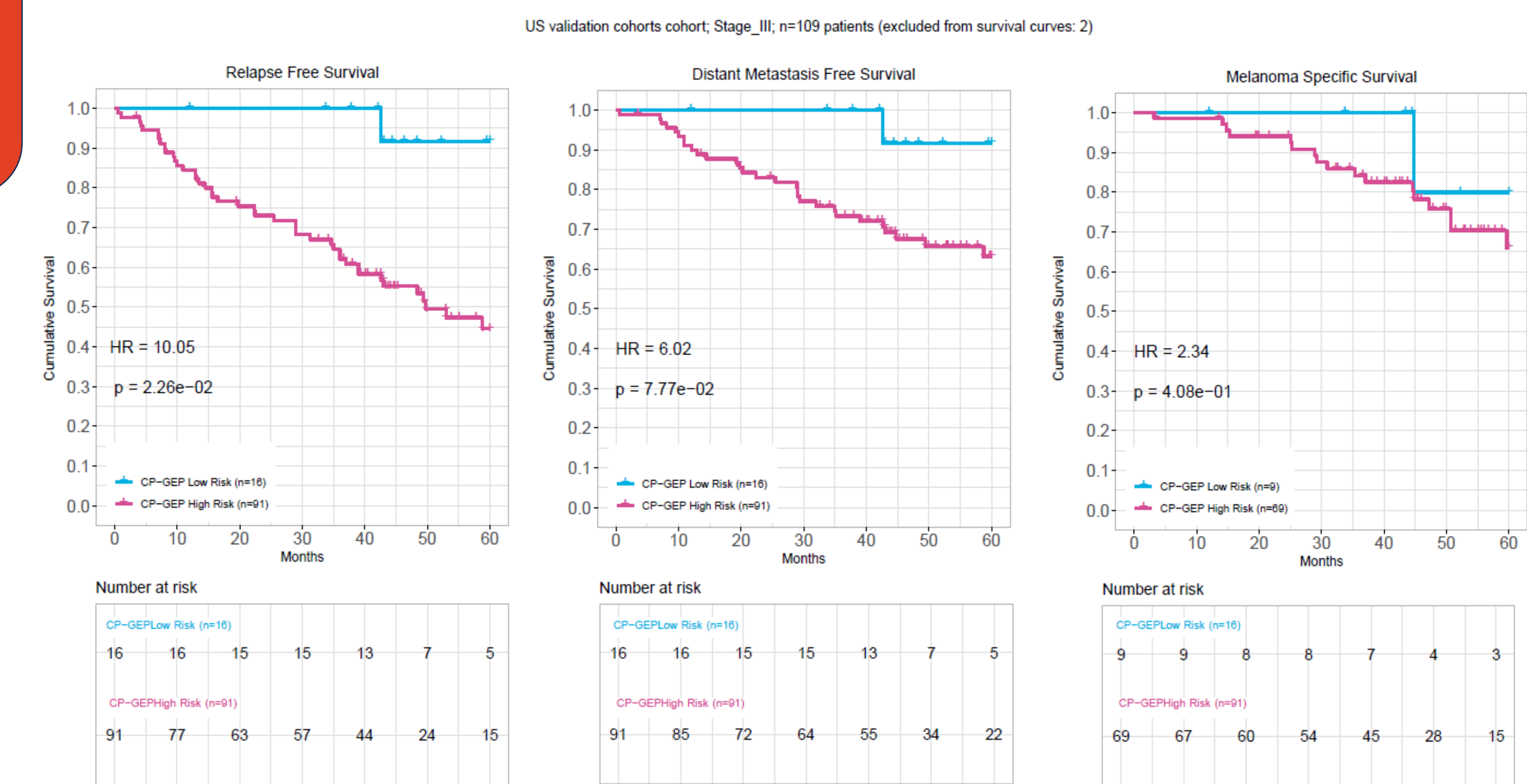
## 5-year survival outcome for Stage I/II patients stratified by CP-GEP



	N	Events RFS	5-yrs RFS, 95%CI	Events DMFS	5-yrs DMFS, 95%CI	Events MSS	5-yrs MSS, 95%CI
Overall SLNB negative cohort	476	58	85.5 [81.4-88.7]	32	92.4 [89.4-94.6]	10	96.3 [92.9-98]
CP-GEP LR	180	10	92.5 [86.2-96]	4	97.4 [93.1-99]	1	99.1 [93.5-99.9]
CP-GEP HR	296	48	81.1 [75.5-85.5]	28	89.3 [84.9-92.5]	9	94.3 [88.7-97.1]

Figure 3 Kaplan-Meier curves showing 5-year RFS, DMFS, and MSS of patients with negative SLNB.

## 5-year survival outcome for Stage III patients stratified by CP-GEP



	N	Events RFS	5-yrs RFS, 95%CI	Events DMFS	5-yrs DMFS, 95%CI	Events MSS	5-yrs MSS, 95%CI
Stage III	107	44	51.4 [39.6-61.9]	30	67.3 [56.1-76.3]	18	67.9 [52.6-79.3]
CP-GEP LR	16	1	91.7 [53.9-98.8]	1	91.7 [53.9-98.8]	1	80 [20.4-96.9]
CP-GEP HR	91	43	44.6 [32.2-56.2]	29	63.1 [50.7-73.2]	17	66 [49.3-78.3]

Figure 4 Kaplan-Meier curves showing 5-year RFS, DMFS, and MSS of patients diagnosed with Stage III CM stratified by CP-GEP.

## Conclusions

- CP-GEP Low Risk patients across all clinical stages show 5-year survival outcome of >90%.
- CP-GEP High Risk categorization identified 83% (48/58) of the stage I/II patients who developed a recurrence.
- CP-GEP is able to identify a subgroup of Low Risk stage III patients who have a better long-term survival outcome compared to the High Risk patients.

## References

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