

Title Page

Title: Treatment Trends and Survival Outcomes in Clinical Stage III Melanoma: Real-World Analysis of NCDB Data

Running Title: Stage III Melanoma Treatment and Survival

Authors/Degrees: Daniel Park DO^{1,†}, Helena T. Wu^{2,9†}, Dani Ran Castillo MD², Kelly Mahuron MD³, Arya Amini MD⁴, Krupal Patel MD⁵, Badri Modi MD⁶, Ravi Salgia MD², Ed Wang MD², Vijay Trisal MD³, Mengni Guo MD⁷, S. Peter Wu MD^{8*}, Yan Xing MD, PhD^{2,*}

Affiliations:

1. Division of Medical Oncology and Hematology, Harbor-UCLA Medical Center, Torrance, California
 2. Division of Medical Oncology and Hematology, City of Hope Medical Center, Duarte, California
 3. Division of Surgical Oncology, City of Hope Medical Center, Duarte, California
 4. Department of Radiation Oncology, City of Hope Medical Center, Duarte, California
 5. Division of Head and Neck Surgery, City of Hope Medical Center, Duarte, California
 6. Department of Dermatology, City of Hope Medical Center, Duarte, California
 7. Division of Medical Oncology and Hematology, Loma Linda University, Loma Linda, California
 8. Department of Radiation Oncology, Mt. Sinai, New York City, New York
 9. Data Science Institute, The University of Chicago, Chicago, Illinois
- † These authors contributed equally to this work.
* These authors are co-senior authors.

Corresponding Author:

Yan Xing <yxing@coh.org>

Address: 1500 E. Duarte Road, Duarte, CA 91010

Phone Number: (866) 880-6308

Conflicts of Interest: The authors declare no potential conflicts of interest.

Word Count: 4,509

	N	Hazard Ratio		
Characteristic	N = 14,164	HR	95% CI	p-value
Age				
1. <50	3,700	1.00	—	
2. 50-65	4,932	1.25	1.16, 1.34	<0.001
3. > or = 65	5,532	2.06	1.92, 2.21	<0.001
Treatment				
1. Surgery Only	6,889	1.00	—	
2. Resection + ICI	6,057	0.76	0.71, 0.80	<0.001
3. Resection + Targeted Therapy	844	1.21	1.09, 1.34	<0.001
4. Neoadjuvant Immunotherapy	320	0.68	0.54, 0.84	<0.001
5. Neoadjuvant Targeted Therapy	54	0.91	0.60, 1.39	0.7
Sex				
Female	5,079	1.00	—	
Male	9,085	1.16	1.10, 1.22	<0.001
Race				
0. White	13,306	1.00	—	
1. East Asian, South Asian, Pacific Islander	94	0.81	0.60, 1.10	0.2
2. Black	166	1.11	0.89, 1.38	0.4
3. Hispanic	428	0.95	0.81, 1.11	0.5
5. Other	170	0.97	0.76, 1.22	0.8
Lymphovascular Invasion				
Absent	5,612	1.00	—	
Present	1,765	1.36	1.26, 1.47	<0.001
Unknown/Indeterminate	6,787	1.09	1.01, 1.17	0.018
Breslow Depth				
<= 1.0 mm	1,321	1.00	—	

> 1.0 - 2.0 mm	1,419	0.83	0.74, 0.93	0.001
> 2.0 - 4.0 mm	1,864	1.03	0.93, 1.15	0.6
> 4.0 mm	2,755	1.37	1.24, 1.51	<0.001
Unknown	6,805	0.97	0.85, 1.11	0.7
Mitotic Rate				
1. 0 mitoses per square mm	433	1.00	—	
2. 1-5 mitoses per square mm	2,304	1.09	0.92, 1.29	0.3
3. 6-10 mitoses per square mm	989	1.25	1.04, 1.50	0.015
4. 11 or more mitoses per square mm	925	1.20	1.00, 1.44	0.052
Unknown	9,513	1.37	1.15, 1.62	<0.001
Ulceration				
No ulceration present	4,089	1.00	—	
Ulceration present	3,805	1.46	1.36, 1.57	<0.001
Unknown	6,270	1.07	0.96, 1.19	0.2
Clinical N-Category				
N1	8,781	1.00	—	
N2	3,413	1.10	1.04, 1.17	0.002
N3	1,970	1.63	1.52, 1.75	<0.001
LDH				
Range 1: < 1.5x upper limit	510	1.00	—	
Range 2: 1.5 - 10x upper limit	80	1.05	0.75, 1.47	0.8
Range 3: > 10x upper limit	20	1.50	0.84, 2.68	0.2
Unknown	12,205	0.98	0.86, 1.11	0.7
Within normal limits	1,349	1.00	0.86, 1.16	>0.9
Primary Site				
1. Skin of scalp and neck	2,594	1.00	—	
2. Skin of trunk	3,824	1.06	0.98, 1.14	0.14
3. Skin of upper limb and shoulder	2,185	0.92	0.84, 1.00	0.050

4. Skin of lower limb and hip	2,679	1.01	0.93, 1.10	0.8
5. Skin, NOS	2,858	0.69	0.61, 0.78	<0.001
9. Unknown	24	0.89	0.46, 1.72	0.7
Surgical Margins				
Negative	9,715	1.00	—	
Positive Macroscopic	40	1.31	0.86, 2.01	0.2
Positive Microscopic	404	1.47	1.28, 1.68	<0.001
Positive NOS	404	1.28	1.12, 1.47	<0.001
Unknown	3,601	1.10	0.99, 1.21	0.074
CDCC Score				
0	11,600	1.00	—	
1	1,832	1.16	1.08, 1.25	<0.001
2	448	1.43	1.26, 1.62	<0.001
3	284	1.69	1.44, 1.98	<0.001

Supplementary Table 1. Values are hazard ratios (95% CI) from the multivariable Cox proportional hazards model, adjusted for all variables shown. Reference categories are indicated by '1 [Reference]' where applicable.