

Characteristics and Outcomes of Patients with Early or Late Uveal Melanoma Recurrence: Analysis from the Ocular Melanoma Natural History (OMNi) Study

Joseph J. Sacco^{1,2}, Marcus O. Butler³, Shaheer Khan⁴, Marlana Orloff⁵, Sapna P. Patel⁶, Alexander Shoushtari⁻, Ryan Sullivan⁶, Jemma Proudfoot-Jones¹,², Li-Anne Lim⁶, Mark Shackleton¹⁰, Heather Shaw¹¹, Krishna Garadi¹², Eric Schulz¹³, Leah Young¹³, Femida H. Gwadry-Sridhar¹³, Anthony M. Joshua¹⁴, Richard D. Carvajal⁴

¹University of Liverpool, Liverpool, Liverpool, UK; ²Clatterbridge Cancer Centre, Liverpool, UK; ³Princess Margaret Hospital, Toronto, Canada; ⁴Northwell Health, Lake Success, NY; ⁵Thomas Jefferson University, Philadelphia, PA; ⁶University of Colorado, Aurora, CO; ⁷Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Thomas Jefferson University, Philadelphia, PA; ⁶University of Colorado, Aurora, CO; ⁷Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Thomas Jefferson University, Philadelphia, PA; ⁶University of Colorado, Aurora, CO; ⁷Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Thomas Jefferson University, Philadelphia, PA; ⁶University of Colorado, Aurora, CO; ⁷Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Thomas Jefferson University of Colorado, Aurora, CO; ⁷Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Thomas Jefferson University of Colorado, Aurora, CO; ⁷Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Thomas Jefferson University of Colorado, Aurora, CO; ⁷Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Thomas Jefferson University of Colorado, Aurora, CO; ⁷Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Thomas Jefferson University of Colorado, Aurora, CO; ⁸Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Thomas Jefferson University of Colorado, Aurora, CO; ⁸Memorial Sloan Kettering Cancer Center, New York, NY; ⁸Memorial Sloan Kettering Cancer Center, NY; ⁸Memorial Sloan Kettering Can

Background

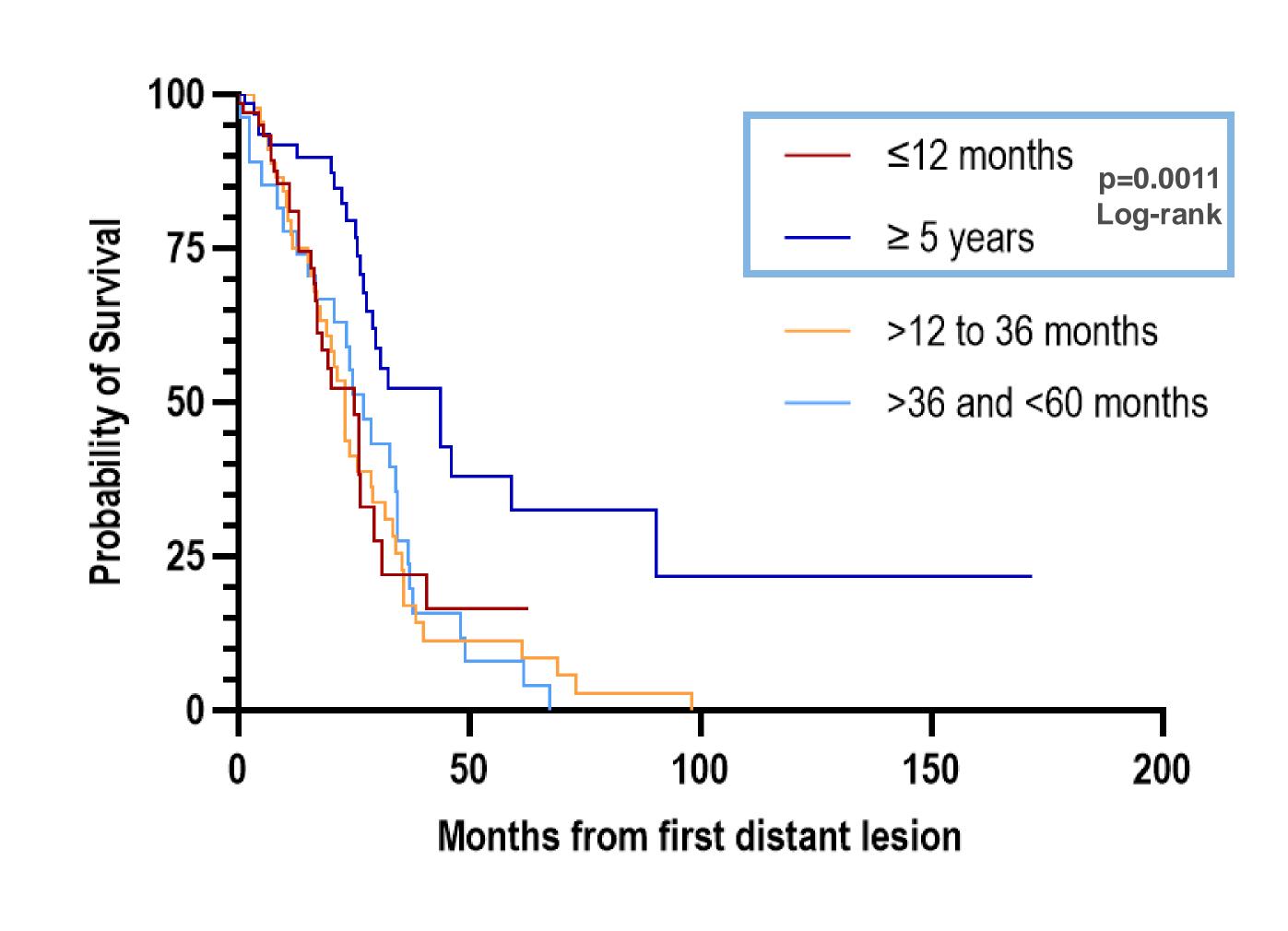
- Despite definitive therapy of the primary tumor, up to 50% of patients with uveal melanoma will experience disease recurrence.
- The estimated 5-year metastasis-free-survival is over 98% for those with low-risk disease as defined by the NCCN.
- The estimated 5-year metastasis-free-survival is less than 85% for those with intermediate- to high-risk disease.
- Although most recurrences occur within 3-5 years of primary diagnosis, late recurrences are observed.

Methods

- Data were utilized from 7 centers in the United States, Canada, the UK and Australia as part of the Ocular Melanoma Natural History (OMNi) study.
- We assessed characteristics and clinical outcomes in patients with early and late recurrence.

Overall Survival by Time-to-First Metastasis

Time-to-First Metastasis	n	Median Survival After First Metastasis (range)
≤12 months	66	25.2 months (0.3-62.7 months)
>12-36 months	110	23.1 months (3.4-98.2 months)
>36-60 months	57	27.1 months (0.5-67.5 month)
>60 months	68	43.7 months (1.1-171.8 months)



Systemic Therapies Received by Cohort

	Early Recurrence (n = 66; 0-12 months)	Early Intermediate Recurrence (n = 110; >12 – 36 months)	Late Intermediate Recurrence (n = 57; >36 - 60 months)	Late Recurrence (n = 68; ≥60 months)
Tebentafusp	19 (29%)	12 (11%)	6 (10%)	16 (24%)
Ipilimumab/Nivolumab	13 (20%)	17 (15%)	12 (21%)	9 (13%)
Pembrolizumab	11 (17%)	11 (10%)	5 (9%)	7 (10%)
Nivolumab	6 (9%)	4 (4%)	6 (11%)	9 (13%)
Ipilimumab	1 (2%)	10 (9%)	3 (5%)	2 (3%)
Darovasertib	2 (3%)	1 (1%)	0 (0%)	7 (10%)
Darovasertib/Crizotinib	2 (3%)	0 (0%)	1 (2%)	2 (3%)

Clinical Characteristics of Those with Early vs Late Recurrence

	Early Recurrence (0-12 months)	Late Recurrence (>60 months)	p value
Sex	n = 66	n = 68	
Male	69.7% (46)	35.2% (24)	< 0.001
Female	30.3% (20)	64.7% (44)	< 0.001
Age at Diagnosis, Years	n = 66	n = 68	
Median (range)	68.5 (30.0 - 85.2)	54.3 (19.8 – 86.6)	< 0.001
Primary Tumor Size, mm	n = 58 (ht); 53 (dia)	n = 33 (ht); 35 (dia)	
Median Height (range)	10.4 (2.0 - 20.0)	5.1 (1.2 - 11.5)	< 0.001
Median Diameter (range)	17.6 (11.0 - 30.0)	12.0 (2.2 - 20.0)	< 0.001
Treatment of Primary Tumor	n = 62	n = 60	
Plaque brachytherapy only	48.4% (30)	71.7% (43)	
Surgery only	50.0% (31)	25.0% (15)	0.005
Plaque brachytherapy + Surgery	1.6% (1)	3.3% (2)	
Recurrence Pattern	n = 66	n = 68	
Liver only	48.5% (32)	42.6% (29)	
Liver + other	47.0% (31)	51.1% (35)	0.8
Other only	4.5% (3)	4.4% (4)	

Molecular Characteristics of Those with Early vs Late Recurrence

	Early Recurrence (0-12 months)	Late Recurrence (>60 months)	p value
Cytogenetics	n = 29	n = 9	
Monosomy 3/no gain in 8q	7.4% (2)	11.1% (1)	1.000
Monosomy 3 + gain in 8q	74.1% (20)	33.3% (3)	< 0.001
Other	18.5% (5)	55.6% (7)	0.8
Genetic Mutations			
GNAQ mutation positive	34.5% (8)	65.2% (15)	0.08
GNA11 mutation positive	65.9% (24)	34.1% (14)	0.04
SF3B1 mutation positive	26.7% (4)	73.3% (11)	Not calculated
BAP1 IHC	n = 9	n = 10	
Negative IHC staining	77.8% (7)	20.0% (2)	Not calculated

Conclusions

- The median overall survival in those with recurrence 5 years or more from time of initial therapy is significantly greater than those recurring within 1 year.
- The median overall survival was similar in those who experienced recurrence < 60 months from treatment.
- Early recurrences were observed more frequently in males and those who underwent surgical management of the primary tumor, and was associated with older age and larger tumors.
- Tumors associated with late recurrences were more frequently characterized by the presence of SF3B1 mutations, while tumors with monosomy 3 combined with gains in 8q was more frequent in those experiencing early recurrences.

OMNi Study Consortium Centers



North America

- Columbia University
- Massachusetts General
 Hospital
- MD Anderson Cancer Center
- Memorial Sloan Kettering
 Cancer Center
- Northwell Health
- Princess Margaret Hospital
- Thomas Jefferson University
- University of Miami

United Kingdom

- Clatterbridge Hospital
- Sheffield Teaching Hospitals

Australia

- Adelaide Eye and Retina
 Center
- Chatswood Eye Specialists
- Conway Private Rooms
- Pennington Eye Clinic
- Perth Retina
- Royal Adelaide Hospital
- St Vincent's Hospital





Information about Pulse oncology RWD (lung cancer, melanoma, uveal melanoma, non-melanoma skin cancer), resulting publications, and healthieTM can be found at PulseInfoframe.com linked through the QR.