

Supplementary

Development of a Metastatic Uveal Melanoma Prognostic Score (MUMPS) for use in Patients Receiving Immune Checkpoint Inhibitors

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Table S1. Treatment duration and discontinuation in the entire study cohort by treatment groups.

	Anti-PD1 (<i>n</i> = 54)	Anti-PD1+anti-CTLA4 (<i>n</i> = 21)	<i>p</i> -value
Total # cycles Anti-PD1+anti-CTLA4			-
1	-	1 (5%)	
2	-	6 (29%)	
3	-	7 (33%)	
4	-	7 (33%)	
Maintenance/Monotherapy			
Anti-PD1	52 (96%)	9 (43%)	<i>p</i> < 0.0001
Anti-PDL1	2 (4%)	0 (0%)	
No maintenance/monotherapy	-	12 (57%)	
# cycles containing standard dose anti-PD1			<i>p</i> = 0.0079
Average	7.2	3.5	
Median	4	2	
Range	1–38	0–29	
Reason for discontinuation			<i>p</i> = 0.21
Progression	46 (85%)	15 (71%)	
Toxicity	5 (9%)	4 (19%)	
On-going treatment	1 (2%)	2 (9%)	
Lost to follow-up	2 (4%)	0 (0%)	

Table S2. Treatment and dosing schedule of combination anti-PD-1 + anti-CTLA4.

Combinations	Number of Patients <i>n</i> = 21 (%)
anti-CTLA4 3 mg/kg + anti-PD1 1 mg/kg Q3W, followed by anti-PD1 3 mg/kg Q2W	17 (81%)
Anti-CTLA4 1 mg/kg + anti-PD1 2mg/kg or 200 mg Q3W, followed by anti-PD1 2 mg/kg Q3W	2 (9.5%)
anti-CTLA4 1 mg/kg + anti-PD1 3 mg/kg Q3W, followed by anti-PD1 3 mg/kg Q2W	2 (9.5%)

Abbreviations: Q2W = every 2 weeks; Q3W = every 3 weeks.

Table S3. Genomic analyses of mUM tumor specimens.

	Entire cohort (n = 75)	Anti-PD1 (n = 54)	Anti-PD1 +anti-CTLA4 (n = 21)	p-value
Impact Genetics				0.128
Yes	16 (21%)	9 (17%)	7 (33%)	
No	59 (79%)	45 (63%)	14 (67%)	
NGS				0.032
Yes	50 (67%)	32 (59%)	18 (86%)	
No	25 (33%)	22 (41%)	3 (14%)	
Impact Genetics				
Chromosome 1				0.163
1p disomy	9 (12%)	5 (9%)	4 (19%)	
1p borderline loss	3 (4%)	1 (2%)	2 (10%)	
1p loss	3 (4%)	2 (4%)	1 (5%)	
Not tested/insufficient	60 (80%)	46 (85%)	14 (67%)	
Chromosome 3				0.170
Monosomy 3	15 (20%)	8 (15%)	7 (33%)	
Partial Monosomy	1 (1%)	1 (2%)	0 (0%)	
Not tested/insufficient	59 (79%)	45 (83%)	14 (67%)	
Chromosome 6p				0.049
6p disomy	12 (16%)	5 (9%)	7 (33%)	
6p gain/borderline gain	3 (4%)	3 (6%)	0 (0%)	
Not tested/insufficient	60 (80%)	46 (85%)	14 (67%)	
Chromosome 6q				0.212
6q disomy	7 (9%)	4 (7%)	3 (14%)	
6q borderline loss	2 (3%)	1 (2%)	1 (5%)	
6q loss	6 (8%)	3 (6%)	3 (14%)	
Not tested/insufficient	60 (80%)	46 (85%)	14 (67%)	
Chromosome 8p				0.130
8p disomy	8 (11%)	6 (11%)	2 (10%)	
8p borderline loss	3 (4%)	1 (2%)	2 (10%)	
8p loss	5 (7%)	2 (4%)	3 (14%)	
Not tested/insufficient	59 (79%)	45 (83%)	14 (67%)	
Chromosome 8q				0.164
8q gain	14 (19%)	7 (13%)	7 (33%)	

8q partial gain	2 (3%)	2 (4%)	0	
Not tested/insufficient	59 (79%)	45 (83%)	14 (67%)	
NGS Testing:				
BRAF				0.106
BRAF WT	49 (65%)	32 (59%)	17 (81%)	
BRAF mutated	0	0	0	
Not tested/insufficient	26 (33%)	22 (41%)	4 (19%)	
NRAS				0.119
NRAS WT	46 (61%)	30 (56%)	16 (76%)	
NRAS mutated	0	0	0	
Not tested/insufficient	29 (39%)	24 (44%)	5 (24%)	
GNA11				0.088
GNA11 209	15 (20%)	11 (20%)	4 (19%)	
GNA11 183	2 (3%)	2 (4%)	0	
GNA11 WT	27 (36%)	15 (28%)	12 (57%)	
Not tested/insufficient	31 (41%)	26 (48%)	5 (24%)	
GNAQ				0.024
GNAQ 209	21 (28%)	10 (19%)	11 (52%)	
GNAQ 183	1 (1%)	1 (2%)	0	
GNAQ WT	22 (29%)	17 (31%)	5 (24%)	
Not tested/insufficient	31 (41%)	26 (48%)	5 (24%)	
BAP1				0.003
BAP1 mutated	19 (25%)	8 (15%)	11 (54%)	
BAP1 WT	20 (27%)	15 (28%)	5 (24%)	
Not tested/insufficient	36 (48%)	31 (57%)	5 (24%)	
SF3B1				0.062
SF3B1 mutated	6 (8%)	4 (7%)	2 (10%)	
SF3B1 WT	32 (43%)	19 (35%)	13 (62%)	
Not tested/insufficient	37 (49%)	31 (57%)	6 (28%)	

Table S4. Number of patients who received anti-PD1/L1 monotherapy or anti-PD1/L1 + anti-CTLA4 antibodies.

Treatment	MUMPS good risk (score = 3)	MUMPS intermediate risk (score = 2)	MUMPS poor risk (score = 0 or 1)	<i>p</i> -value
Anti-PD1 monotherapy	17	28	9	<i>p</i> = 0.522
Anti-PD1 + anti-CTLA4	5	10	6	

Table S5. Open Interventional Clinical Trials for the treatment of Metastatic Uveal Melanoma (Current as of 24 January 2021) [1].

Clinical Trial ID	Intervention	Phase	Size ^a	First Posted
NCT04589832	Procaspase-Activating Compound 1 (PAC-1) in combination with Entrectinib (NTRK Inhibitor)	1b/2	38	Oct 2020
NCT04552223	Nivolumab and Relatlimab (LAG-3 Abtibody)	2	27	Sept 2020
NCT04551352	O7293583, A Tyrosinase-Related Protein 1(TYRP 1) - Targeting CD3 T-Cell Engager	1	310	Sept 2020
NCT04335890	Vaccination with Inhibitor Of Nuclear Factor Kappa B Kinase Subunit Beta (IKKb) matured Dendritic Cells	1	12	April 2020
NCT04283890	Percutaneous hepatic perfusion with Ipilimumab and Nivolumab	1/2	88	Feb 2020
NCT04109456	IN10018, a Focal Adhesion Kinase (FAK) Inhibitor +/- Cobimetinib	1b	52	Sept 2019
NCT03947385	IDE196, a PKC inhibitor+/- Binimetinib in patients with solid tumors harboring GNAQ or GNAQ/11 mutations or PRKC fusions	1/2	217	May 2019
NCT03865212	Intravenous Injection of Vesicular Stomatitis Virus Expressing Human Interferon Beta and Tyrosinase Related Protein 1 (VSV-IFN β -TYRP1)	1	71	Mar 2019
NCT03467516	Tumor Infiltrating Lymphocytes	2	59	Mar 2018
NCT03472586	Immunoembolization in combination with ipilimumab and nivolumab	2	35	Mar 2018
NCT03025256	Intrathecal nivolumab in combination with intravenous Nivolumab in treating patients with leptomeningeal disease	1	50	Jan 2017
NCT03068624	Cyclophosphamide, autologous CD8+ SLC45A2-specific T lymphocytes via hepatic arterial infusion and ipilimumab	1b	30	Mar 2017

^a Participant size as stated in registry entry.

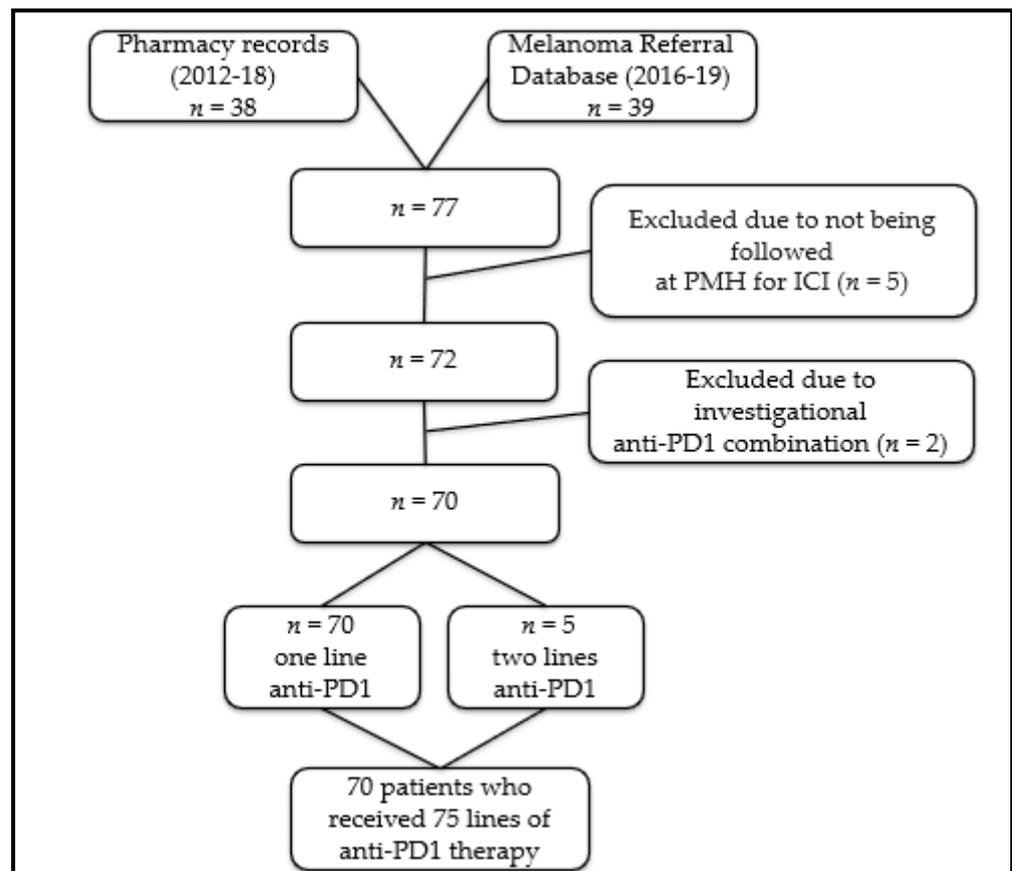


Figure S1. Consort diagram. We identified 77 patients who had received anti-PD1/L1 containing therapy for metastatic uveal melanoma. Two patients were excluded due to non-uveal histology (blue nevus and conjunctival). Two patients were excluded who had received anti-PD1/L1 therapy combined with investigational agents (ie. not anti-CTLA4), Finally, we excluded who were not followed at PM-UHN during their ICI treatment. After exclusion of these patients, the remaining 70 individual patients included 5 patients who had 2 lines of anti-PD1 ICI treatment. We analyzed data from 70 patients who had received a total of 75 lines of anti-PD1 ICI therapy.

References

1. NIH, *Recruiting Studies ; Uveal Melanoma, Metastatic* NIH U.S. National Library of Medicine Clinical Trials.gov URL https://clinicaltrials.gov/ct2/results?cond=Uveal+Melanoma%2C+Metastatic&Search=Apply&recrs=a&age_v=&gndr=&type=&rslt= (Accessed 24 January 2021) 2021.