

Supplementary Materials: Medical Needs and Therapeutic Options for Melanoma Patients Resistant to Anti-PD-1 Directed Immune Checkpoint Inhibition

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Table S1. Frequencies of response and resistance in selected neoadjuvant immunotherapy trials in melanoma (ICI monotherapy, or combined ICI).

Trial	Treatment Regimens	Trial Phase	Patients	N	pCR, %	Near pCR, %	pPR, %	pNR, %	MPR %	ORR % RECIST	CR, % RECIST	PR, % RECIST	SD, % RECIST	PD, % RECIST
NeoTrio [Long, ASCO 2022] (NCT02858921)	(i) Pem 200 mg q3w x 2	II	Stage III resect. lymph nodes, no in transit, BRAF V600 mutated	60 (20/arm)										
	(ii) Dab (D) + Tram (T) q1w, Pem 200 mg day 8+22				6 (30%)	2 (10%)	3 (15%)	7 (35%)	40	30	2 (10%)	4 (20%)	5 (25%)	9 (45%)
	(iii) D (150mg bid) + T (2mg qd) + Pem 200mg q3w x 2				3 (15%)	3 (15%)	4 (20%)	10 (50%)	30	45	0	9 (45%)	1 (5%)	10 (50%)
DONIMI [Blank, ESMO 2021] (NCT04133948)	(i) IFNg high: Nivo	Ib	Stage III resectable	40 (10/arm)	7 (70%)	1 (10%)	1 (10%)	1 (10%)	80	50	1 (10%)	4 (40%)	5 (50%)	0
	(ii) IFNg high: Nivo + Domatinostat				5 (50%)	1 (10%)	2 (20%)	2 (20%)	60	70	3 (30%)	4 (40%)	3 (30%)	0
	(iii) IFNg low: Nivo + Domatinostat				1 (10%)	0	2 (20%)	7 (70%)	10	0	0	0	9 (90%)	0
OpACIN [Blank, Nature Med 2018] (NCT02437279)	(iv) IFNg low: Ipi + Nivo + Domatinostat	Ib	Stage III resectable	8	3 (30%)	1 (10%)	0	6 (60%)	40	40	1 (10%)	3 (30%)	1 (10%)	5 (50%)
	(i) Ipi 3mg/kg + Nivo 1mg/kg q3w x2				2 (25%)	3 (37%)	1 (12%)	2 (25%)	62	50	0	4 (50%)	3 (37%)	1 (13%)
	Ipi 3mg/kg + Nivo 1mg/kg													
OpACIN-NEO [Rozeman, ESMO 2018] (NCT02977052)	Ipi 1mg/kg + Nivo 3mg/kg	II	Stage III resectable	(i) 30	14 (47%)	-	7 (23%)	6 (20%)	70	60	2 (7%)	16 (53%)	10 (33%)	2 (7%)
	Ipi 3mg/kg q3w x2, than Nivo 3mg/kg			(ii) 30	17 (57%)	-	2 (7%)	7 (23%)	64	60	3 (10%)	15 (50%)	9 (30%)	2 (7%)
	All three regimen: q3w x2			(iii) 26	6 (23%)	-	15 (17%)	8 (31%)	40	42	1 (4%)	10 (38%)	9 (35%)	6 (23%)
PRADO [Rozeman, ASCO 2020] (NCT02977052)	Ipi 1mg/kg + Nivo 3mg/kg q3w x2	II	Stage III resectable	99	49 (50%)	11 (11%)	10 (10%)	21 (21%)	61	45	14 (14%)	31 (31%)	38 (38%)	13 (13%)
2015-0041 [Amaria ASCO 2021] (NCT02519322)	Rela 160mg+ Nivo 480mg q4w x2	II	Stage III resectable	30	17 (59%)	2 (7%)	2 (7%)	8 (27%)	66	57	0	17 (57%)	10 (33%)	3 (10%)
2015-0041 [Amaria, Nature Med 2018] (NCT02519322)	(i) Nivo 3mg/kg q2w x4	II	Stage III or IV resectable	12	3 (25%)	-	-	-	-	25	0	3 (25%)	5 (42%)	4 (33%)
	(ii) Nivo 1mg/kg + Ipi 3mg/kg q3w x4x			11	5 (45%)	-	-	-	-	73	1 (9%)	7 (64%)	2 (18%)	1 (9%)
UPCC 01615 [Huang, Nature Med 2019] (NCT02434354)	Pem 200mg flat, single-dose	IB	Stage III or IV resectable	27	5 (18%)	3 (11%)	5 (18%)	14 (52%)	29	50	0	3/6 (50%)	1/6 (17%)	2/6 (33%)
SWOG1512 [Kendra, ASCO 2022] (NCT02775851)	Pem 200mg q3w x3	II	Resectable desmoplastic melanoma	29	16 (55%)	-	-	-	-	46	4 (15%)	8 (31%)	12 (46%)	1 (4%)

Abbreviations: Dab, dabrafenib; ICI, immune checkpoint inhibitor; Ipi, ipilimumab; MPR, major pathological response; Nivo, nivolumab; Pem, pembrolizumab; Tram, trametinib; x1 (x2, ...), once (twice, ...).