

Table S1. Drugs trialed before initiation of dupilumab therapy.

Drug category	Drugs administered before initiation of dupilumab therapy for managing cutaneous immune-related adverse events
Topical treatment	Betamethasone, clobetasol, triamcinolone, fluocinonide, dexamethasone swish and spit, magic mouth wash, nystatin rinse, lidocaine rinse, doxycycline swish and spit, mometasone, clobetasol solution, hydrocortisone, fluocinolone, econazole, calcipotriene, vitamin E, niacinamide, clindamycin gel, mupirocin, topical pimecrolimus, topical tacrolimus, silver sulfadiazine cream, Sarna, Aquaphor, CBD:THC Wonderbalm, camphor/menthol, Curel cream, CeraVe anti-itch cream, Eucerin, Vaseline
Hemorrhagic agents	Pentoxifylline
Oral vitamin	Nicotinamide
Opioid antagonist	Naltrexone
Oral systemic non-steroidal	Methotrexate, apremilast, mycophenolic acid
Anticonvulsants	Gabapentin, pregabalin
Oral antibiotics	Doxycycline, cefalexin, dapsone
Glucocorticoids	Prednisone, oral dexamethasone, intravenous methylprednisolone
Antihistamines	Diphenhydramine, cetirizine, hydroxyzine, fexofenadine, famotidine, loratadine
Biologics	Rituximab, omalizumab
Phototherapy	Narrow band ultraviolet B
Immunoglobulin	Intravenous immunoglobulin
Oral retinoid	Acetretin

Table S2. Time from ICB start to the first cirAE.

ICB to the first cirAE	Case Median [Q1, Q3]	Control 1 Median [Q1, Q3]
Lichenoid dermatitis, maculopapular eruption	9 [9, 9] (one patient)	N/A (no patient)
Maculopapular eruption	14.5 [10.5, 38.5]	21 [12.5, 80]
Eczematous dermatitis	21 [9, 45.5]	98 [18, 199.5]
Rash, NOS	59.5 [50.5, 206.3]	53 [21, 146]
Pruritus	83 [55.3, 129.8]	34 [21, 152.8]
Lichenoid dermatitis	165 [132, 202]	156 [42.5, 215.5]
Bullous pemphigoid	211 [113.8, 496.8]	394 [253, 437.5]
Radiation induced morphea ICB exacerbated	310 [310, 310] (one patient)	N/A
Lichenoid dermatitis, eczematous dermatitis	924 [924, 924] (one patient)	N/A
Psoriasiform eruption	N/A	64.5 [38, 123.3]
Vitiligo	N/A	285 [165.5, 553]

CirAE: Cutaneous immune-related adverse event; NOS: Not otherwise specified; CBC: Complete blood count; Q1: the first quartile; Q3: the third quartile. N/A: not applicable.

Table S3. Response to dupilumab stratified by morphology of cutaneous immune-related adverse events.

	Total (N=53)	Eczematous dermatitis (N=22)	Bullous pemphigoid (N=14)	Lichenoid dermatitis (N=7)	Maculopapular eruption (N=5)
Responder					
Complete	33 (62.3%)	14 (63.6%)	8 (57.1%)	3 (42.9%)	4 (80.0%)
Partial	14 (26.4%)	5 (22.7%)	3 (21.4%)	4 (57.1%)	1 (20.0%)
No	6 (11.3%)	3 (13.6%)	3 (21.4%)	0 (0%)	0 (0%)
	Lichenoid dermatitis, Bullous pemphigoid (N=1)	Lichenoid dermatitis, eczematous dermatitis (N=1)	Lichenoid dermatitis, morbilliform drug eruption (N=1)	Radiation induced morphea ICB exacerbated (N=1)	Sclerodermoid reaction with morphea-profunda (N=1)
Responder					
Complete	1 (100%)	1 (100%)	1 (100%)	0 (0%)	1 (100%)
Partial	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)
No	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table S4. Time-varying Cox proportional hazards models for overall survival with ICB interruption

	Comparison 1			Comparison 2		
	HR	95% CI	p-value	HR	95% CI	p-value
Dupilumab	0.69	0.32, 1.49	0.3	0.73	0.34, 1.58	0.4
Systemic glucocorticoid	2.02	1.02, 3.98	0.043	1.68	0.93, 3.04	0.085
Age at ICB initiation	1.03	1, 1.07	0.066	1.01	0.98, 1.04	0.5
CCS	1.1	0.96, 1.27	0.2	1.19	1.07, 1.32	0.002
Cancer stage at ICB						
IV	—	—		—	—	
III and other	0.73	0.35, 1.53	0.4	0.78	0.4, 1.53	0.5
Cancer type						
Melanoma	—	—		—	—	
Genitourinary	2.5	1.1, 5.66	0.028	1.26	0.53, 2.99	0.6
Head and neck	1.94	0.68, 5.51	0.2	2.97	1.22, 7.24	0.017
Thoracic	1.57	0.59, 4.16	0.4	2.04	0.81, 5.15	0.13
Other	2.46	0.72, 8.45	0.2	2.9	1.15, 7.29	0.023
ICB type						
Combination	—	—		—	—	
PD-1/PD-L1	0.98	0.47, 2.07	>0.9	0.74	0.41, 1.32	0.3
ICB interruption ^c						
Continuation	—	—		—	—	
Discontinuation	1.61	0.63, 4.16	0.3	2.24	1.25, 4	0.006
Pause	0.32	0.07, 1.5	0.15	0.39	0.05, 3.01	0.4
Race						
White	—	—		—	—	
Other	1.46	0.57, 3.73	0.4	1.78	0.7, 4.5	0.2
Sex						
Female	—	—		—	—	
Male	0.59	0.31, 1.11	0.1	1.18	0.65, 2.15	0.6

^a Comparison 1: comparison between the dupilumab group and the control 1 group.
^b Comparison 2: comparison between the dupilumab group and the control 2 group.
^c ICB interruption: "discontinuation" if a patient received less than 3 cycles of treatment, "pause" if a patient missed or delayed at least two cycles (two instances of more than 42 days in between successive cycles) within one year after ICB initiation, and "continuation" otherwise.

HR: Hazard Ratio; CI: Confidence Interval; CCS: Charlson Comorbidity Score; PD-1: Programmed Death-1; PD-L1: Programmed Death-Ligand 1

Table S5. Time-varying Cox proportional hazards models for overall survival with ICB duration.

	Comparison 1				Comparison 2		
	HR	95% CI	p-value		HR	95% CI	p-value
Dupilumab	0.65	0.3, 1.38	0.3		0.57	0.26, 1.24	0.2
Systemic glucocorticoid	1.82	0.94, 3.53	0.074		1.37	0.81, 2.31	0.2
ICB duration status	0.02	0, 0.18	<0.001		0.01	0, 0.08	<0.001
Age at ICB initiation	1.02	0.99, 1.06	0.13		1.01	0.98, 1.04	0.6
CCS	1.24	1.07, 1.44	0.004		1.17	1.05, 1.31	0.004
Cancer stage at ICB							
IV	—	—			—	—	
III and other	0.55	0.26, 1.16	0.12		0.7	0.36, 1.35	0.3
Cancer type							
Melanoma	—	—			—	—	
Genitourinary	1.57	0.69, 3.55	0.3		1.17	0.5, 2.76	0.7
Head and neck	2.69	0.93, 7.81	0.069		3.49	1.41, 8.64	0.007
Thoracic	1.89	0.74, 4.81	0.2		1.94	0.78, 4.88	0.2
Other	2.28	0.68, 7.63	0.2		2.96	1.23, 7.15	0.016
ICB type							
Combination	—	—			—	—	
PD-1/PD-L1	1.11	0.54, 2.29	0.8		0.78	0.44, 1.33	0.4
Race							
White	—	—			—	—	
Other	2.08	0.86, 5.02	0.1		2	0.8, 5	0.14
Sex							
Female	—	—			—	—	
Male	0.62	0.33, 1.15	0.13		1.34	0.73, 2.43	0.3

^a Comparison 1: comparison between the dupilumab group and the control 1 group.
^b Comparison 2: comparison between the dupilumab group and the control 2 group.
^c ICB duration status is a time-varying variable: "1" during the ICB treatment and "0" between ICB end to the date of death or the last follow-up.

HR: Hazard Ratio; CI: Confidence Interval; CCS: Charlson Comorbidity Score; PD-1: Programmed Death-1; PD-L1: Programmed Death-Ligand 1

Table S6. List of other irAEs treated with systemic immunosuppression.

	Dupilumab (10)	Control 1 (42)	Control 2 (28)
Colitis	2	11	5
Pneumonitis	1	5	2
Arthritis	0	8	10
Hepatitis	0	4	2
Pancreatitis	2	0	1
Adrenal insufficiency	3	0	0
Hypophysitis	0	3	0
Nephritis	0	1	2
Encephalitis	0	0	2
Myocarditis	0	1	1
Uveitis	1	0	0
Thyroiditis	0	1	0
Hepatitis/Myositis/Myocarditis	1	0	0
Enteritis	0	1	0
Proctitis	0	1	0
Gastritis	0	1	0
Pancytopenia	0	0	1
ICB Induced flare of prior Polymyalgia rheumatica	0	1	0
ICB Induced Flare of Prior Ulcerative colitis	0	1	0
Pneumonitis/Colitis	0	1	0
Encephalitis/Hypophysitis	0	1	0
Pneumonitis/Nephritis	0	1	0
Colitis/Gastritis	0	0	1
Hepatitis/Pancreatitis	0	0	1