

Supplementary Tables

Supplementary Table 1: Subanalysis of outcomes based on event of flare or irAE

	No flare or irAE n =10 (%)	irAE alone n = 27 (%)	Flare alone n = 9 (%)	Flare and irAE n = 9 (%)
Baseline immunosuppression	1 (10%)	4 (15%)	4 (44%)	4 (44%)
Steroids	1	2	2	1
SSA [#]	0	1	1	1
Steroids + SSA	0	1	1	2
None	9 (90%)	23 (85%)	5 (56%)	5 (56%)
Management of Events during combination IO				
Steroids	0	19 (70%)	7 (78%)	8 (89%)
SSA+Steroids	0	9	5	7
IVIg/Plasmapheresis	0	8	2	1
	0	2	0	0
Number alive at time of analysis	6 (60%)	19 (70%)	6 (67%)	7 (78%)
Number with ongoing response at time of analysis	2 (20%)	12 (44%)	4 (44%)	4 (44%)

[#] SSA = Steroid sparing agent

Supplementary Table 2: Baseline Characteristics and outcomes of Complete Responders

Demographics	No. (%)	Detail
Gender		
Male	6 (43%)	
Female	8 (57%)	
ECOG 0	14 (100%)	
AJCC Stage		
III	3	
M1a/M1b	2	
M1c	4	
M1d	5	
Mutation Status		
BRAF/NRAS Wild Type	2 (14%)	
BRAF	9 (64%)	
NRAS	3 (21%)	
Drugs received		
Ipilimumab 3mg/kg + Nivolumab 1mg/kg	10 (71%)	
Ipilimumab 1mg/kg + Pembrolizumab 2mg/kg	4 (29%)	
Autoimmune disorder (AD)*		
Rheumatologic	1 (7%)	Polymyalgia – 1,
Gastrointestinal	1 (7%)	Ulcerative colitis – 1
Endocrine	7 (50%)	Grave's disease – 2, Hashimoto's thyroiditis – 4, Type I Diabetes – 1
Dermatologic	3 (21%)	Psoriasis – 3
Haematologic	1 (7%)	ITP – 1
Other	1 (7%)	Sarcoidosis – 1
Activity of AD		
Clinically active	2 (14%)	
Not clinically active	12 (86%)	
Immunosuppression		
Corticosteroids	2 (24%)	
SSA [#]	0 (0%)	
Corticosteroids + SSA [#]	0 (0%)	
No immunosuppression	12 (76%)	
Flare of Autoimmune Disease		
No	11 (79%)	
Yes	3 (21%)	Psoriasis, Polymyalgia, Ulcerative colitis
Immunosuppression for AD flare		
IV steroids	1 (33%)	Ulcerative colitis – 1
Steroids and SSA [#]	2 (67%)	Cyclosporin – 1 for psoriasis, sulfasalazine – 1 for polymyalgia

IO Dosing after flare

Both drugs ceased	1 (33%)	Ulcerative colitis – 1
PD1 alone continued	0	
Both continued	2 (67%)	Psoriasis – 1, Polymyalgia – 1

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Supplementary Table 3: irAE outcomes of Complete Responders

Demographics	No. (%)	Detail
irAE		
No	2 (14%)	
Yes	12 (86%)	
irAE Grade		
G1,2	5 (42%)	Colitis, Hepatitis, Hypophysitis, Thyroiditis, T1 Diabetes
G3	4 (33%)	Colitis – 1, Hepatitis – 2, Colitis + Hepatitis – 1 Pneumonitis – 2, Thyroiditis
G4	3 (42%)	Colitis, Hepatitis, Myasthenia Gravis
Immunosuppression for irAE	9 (64%)	
Oral steroids	1 (8%)	Hepatitis
IV steroids	1 (8%)	Hepatitis
Steroid and SSA [#]	6 (67%)	Colitis – 3, Hepatitis – 2, Colitis + Hepatitis – 1
Plasmapheresis	1 (8%)	Myasthenia Gravis

[#]SSA = Steroid sparing agent

Supplementary Table 4: Outcomes of Endocrine Autoimmune Disorders vs. Non-Endocrine Autoimmune disorders

	Endocrine Autoimmune Disorder* n = 19	Non-endocrine Autoimmune Disorder n = 36
Total flare events	3/19 (16%)	15/36 (42%)
Flare of autoimmune disorder	2/19 (11%)	7/36 (19%)
Both irAE and flare	1/19 (5%)	8/36 (22%)
Neither	8/19 (42%)	5/36 (14%)
Immune related adverse event	8/19 (42%)	16/36 (44%)
Median OS	35 months (95% CI 21.72 – 48.28)	22 months (95% CI 9.32 – 34.68)
Median PFS	36 months (95% CI 28.36 – 57.87)	7 months (95% 1.94 – 12.06)

*Including endocrine only disorders. Not patients that had an additional autoimmune condition that was not affecting the endocrine system