

Supplemental Tables for:
 Endocrine Adverse Events of Immune Checkpoint Inhibitors: Review and Management
 Delvys Rodriguez-Abreu et al.

Table S1: Endocrine Adverse Events in studies with anti-CTLA4 antibodies.

Agent	First Author N	Phase	Tumor type (% of total if available)	Pretreatment	Schedule	Endocrine AE, any grade (%)		Endocrine AE, grade 3-4 (%)	
Ipilimumab	Hodi et al. ^[1] N= 676	III	mMM	Pretreated	3mg/kg Q3W alone or plus gp100	Any endocrine AE	4.9	Any endocrine AE	1.8
						Ipilimumab only	3.9	Ipilimumab only	1.1
						+ gp100	7.6	+ gp100	3.8
						Hypothyroidism	1.6	Hypothyroidism	0.2
						Ipilimumab only	1.6	Ipilimumab only	0.3
						+ gp100	1.5	+ gp100	0
						Hypopituitarism	1.2	Hypopituitarism	0.8
						Ipilimumab only	0.8	Ipilimumab only	0.5
						+ gp100	2.3	+ gp100	1.5
						Hypophysitis	0.8	Hypophysitis	0.8
						Ipilimumab only	0.5	Ipilimumab only	0.5
						+ gp100	1.5	+ gp100	1.5
						Adrenal insufficiency	1.0	Adrenal insufficiency	0.4
						Ipilimumab only	0.8	Ipilimumab only	0.5
						+ gp100	1.5	+ gp100	0
						Decrease in ACTH	0.4	Decrease in ACTH	0.2
						Ipilimumab only	0	Ipilimumab only	0
						+ gp100	1.5	+ gp100	0.8
	Eggermont et al. ^[2] N=951	III	Stage III MM as adjuvant after complete resection	Naïve	3mg/kg Q3W (N=475) vs Placebo	Any endocrine AE	29	Any endocrine AE	5.5
						Hypothyroidism	9.0	Hypothyroidism	0.2
						Hypophysitis	13.0	Hypophysitis	5.1

Kwon et al. ^[3] N=799	III	Castration resistant prostate cancer	Radiotherapy	3mg/kg Q3W (N=399)	Any endocrine AE 5.3 Hypothyroidism 2.3 Hypopituitarism 0.8 Hypophysitis 1.0 Adrenal insufficiency 1.5	Any endocrine AE 1.5 Hypothyroidism 0.5 Hypopituitarism 0.8 Hypophysitis 0.3 Adrenal insufficiency 0.5
Chiaroni Sileni et al. ^[4] N=188	III	mMM	Pretreated	3mg/kg Q3W	No endocrine AEs reported	
Chiaroni Sileni et al. ^[5] N=51		mMM	Ipilimumab	3mg/kg Q3W (retreated)	Hypothyroidism 2.0	Hypothyroidism 0
Altomonte et al. ^[6] N=74	IV	mMM	Pretreated	10mg/kg Q3W	Any endocrine AE 5.4 Hypothyroidism 2.7 Hyperthyroidism 2.7	Any endocrine AE 0
Weber et al. ^[7] N=59	I	mMM	Naïve	10mg/kg Q3W	No endocrine AEs reported	
Slovin et al. ^[8] N=71	I/II	Castration-resistant prostate cancer	Pretreated	3-10mg/kg Q3W	Any endocrine AE 12.7 * Hypothyroidism 2.8 Hyperthyroidism 2.8 Hypophysitis 1.4 Adrenal insufficiency 1.4	Any endocrine AE 0
Margolin et al. ^[9] N=72 irAE occurring in >15% reported	II	mMM with brain metastasis	Pretreated	10mg/kg Q3W	No endocrine AEs reported	
Di Giacomo et al. ^[10] N= 27	II	mMM	Pretreated	10mg/kg Q3W	Hypothyroidism 7.4	Hypothyroidism 0

Sarnaik et al. ^[11] N=75	II	mMM, adjuvant		3 (33%) or 10mg/kg (66%) Q3W	Any endocrine AE 16.0 Hypothyroidism 1.3 Hypophysitis 14.7	Any endocrine AE 8.0 Hypothyroidism 0 Hypophysitis 8.0
Royal et al. ^[12] N=27	II	Pancreatic cancer	Pretreated	Ipilimumab 3mg/kg Q3W	Hypophysitis 3.7	Hypophysitis 3.7
O'Day et al. ^[13] N=155	II	mMM	Pretreated	10mg/kg Q3W	Any endocrine AE 5.8	Any endocrine AE 1.3
Hersh et al. ^[14] N=76	II	mMM	Naïve	Ipilimumab 3mg/kg Q3W (n=37) vs Ipilimumab + Dacarbazine (n=35)	Adrenal insufficiency 1.4 (in Ipilimumab+DTIC arm)	
Wolchok et al. ^[15] N=217	II	mMM	Pretreated	0.3/3/10 mg/kg Q3W	Any endocrine AE 4.9	Any endocrine AE 2.1
Weber et al. ^[16] N=115	II	mMM	Pretreated and naïve	10mg/kg Q3W +/- budesonide	Any endocrine AE 9.6	Any endocrine AE 5.2
Yang et al. ^[17] N=61	II	mRCC	Pretreated and naïve	Cohort 1: 1mg/kg Cohort 2: 3mg/kg	Any endocrine AE 4.9 Hypophysitis 3.3 Adrenal insufficiency 1.6	
Weber et al. ^[18] N=88	I/II	mMM	Pretreated	2.8, 3 or 5mg/kg x3	Adrenal insufficiency 1.1	Adrenal insufficiency 1.1
Attia et al. ^[19] N=56	I	mMM	Pretreated	10mg/kg Q3W + gp100	Hypophysitis 1.8	Hypophysitis 1.8

	Maker et al. ^[20] N=46	I/II	mMM	Pretreated	Escalation doses 3-9 mg/kg	Any endocrine AE 21.7 Hypothyroidism 2.2 Hypophysitis 17.4 5mg/kg 2.2 9mg/kg 15.2	Any endocrine AE 17.4 Hypophysitis 17.4
	Phan et al. ^[21] N=14	II	mMM	Pretreated	3mg/kg Q3W + gp100	Hypophysitis 7.1	Hypophysitis 7.1
	Ansell et al. ^[22] N= 18	I	B-cell NHL	Pretreated	Escalation doses 1 to 3mg/kg Q4W	Hypophysitis 6.0	Hypophysitis 0
	Ku et al. ^[23] N=53	EAP	mMM	Pretreated	10mg/kg Q3W	Any endocrine AE 5.7 Hypothyroidism 1.9 Hypophysitis 3.8	Any endocrine AE 3.8 Hypothyroidism 0 Hypophysitis 3.8
	Small et al. ^[24] N=14	I	M Prostate cancer	Pretreated	3mg/kg single dose	No endocrine AEs reported	
Tremelimumab	Camacho et al. ^[25] N= 28 (Ph I) N= 89 (Ph II)	I/II	mMM	Pretreated	Ph I: 3, 6, or 10 mg/kg Ph II: 10 mg/kg monthly or 15 mg/kg Q3M	Any endocrine AE 4.0 Ph I: Thyroiditis (10mg/kg) 3.6 Ph II: Hyperthyroidism (10mg/kg) 1.1	Ph II: Hyperthyroidism (10mg/kg) 1.1
	Kirkwood et al. ^[26] N= 251	II	mMM	Pretreated	15mg/kg Q3M	Any endocrine AE 4.0 Thyroid disorders 3.2 Hypophysitis 0.4	

Ralph et al. ^[27] N= 18	II	Metastatic Gastric and Esophageal ADC	Pretreated	15mg/kg Q3M	No endocrine AR reported	
Chung et al. ^[28] N=47	II	mCRC	Pretreated	15mg/kg Q3M	Thyroiditis 2.1	
Ribas et al. ^[29] N=39	I	mMM, RCC, colon	Pretreated	0.01-15mg/kg, Q3M	Any endocrine AE 7.7 Hypothyroidism 2.6 Hyperthyroidism 2.6 Hypophysitis 2.6	Any endocrine AE 0
Ribas et al. ^[30] N=44 irAE occurring in >10% reported	I	mMM	-	15mg/kg Q3M	No endocrine AR reported	
Aglietta et al. ^[31] N=34	Ib	Pancreatic	Naive	Escalating doses 6,10, or 15 mg/kg on day 1 of each 84-day cycle max x4 + Gemcitabine 1000 mg/m days 1, 8, and 15 of each 28-day	Hyperthyroidism 2.9	Hyperthyroidism 0
Calabró et al. ^[32] N=29	II	Mesothelioma	Pretreated	15mg/kg Q3M	No endocrine AR reported	
Sangro et al. ^[33] N=21	II	HCC + Chronic Hepatitis C	Pretreated	15mg/kg Q3M	Hypothyroidism 5.0	Hypothyroidism 0

	Ribas et al. <small>[34]</small>	III	mMM	Naïve	15mg/kg Q3M (N=325) vs QMT	Any endocrine AE 8.3 Thyroid disorder 5.0 Hypothalamus/ Pituitary disorder 2.0 Adrenal insufficiency 1.0	Any endocrine AE 3.0 Thyroid disorder 1.0 Hypothalamus/ Pituitary disorder 1.0 Adrenal insufficiency 1.0
	N=655						

* The subtypes listed do not add up to the total because not all the subtypes are provided by the authors.

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Supplement Table 2: Endocrine Adverse Events in studies with anti-PD1 antibodies.

Agent	First Author N	Phase	Tumor type (% of total if available)	Pretreatment	Schedule	Endocrine AE, any grade (%)		Endocrine AE, grade 3-4 (%)	
Pembrolizumab	Hamid et al. ¹ N= 135	I/II	mMM	Ipilimumab (36%), naïve (64%)	10mg/kg Q2W (n=57) or Q3W (n=56) or 2mg/kg Q3W (n=22)	Any Endocrine AE	8.1	Any Endocrine AE	0.7
						Hypothyroidism	8.1	Hypothyroidism	0.7
						10mg/kg Q2W:	15.8	10mg/kg Q2W:	1.8
						10mg/kg Q3W:	1.8	10mg/kg Q3W:	0
						2mg/kg Q3W:	4.5	2mg/kg Q3W:	0
						Hypophysitis	0	Hypophysitis	0
	Robert C et al. ² N= 834	III	mMM	Naïve (66%), Pretreated (33%)	10mg/kg Q2W (n=278) or Q3W (n=277)	Any Endocrine AE	15.1	Any Endocrine AE	0.9
						Hypothyroidism	9.4*	Hypothyroidism	0.1
						10mg/kg Q2W:	10.1	10mg/kg Q2W:	0.4
						10mg/kg Q3W:	8.7	10mg/kg Q3W:	0
						Hyperthyroidism	4.9*	Hyperthyroidism	0
						10mg/kg Q2W:	6.5		
						10mg/kg Q3W:	3.2		
						Hypophysitis	0.5	Hypophysitis	0.3
						10mg/kg Q2W:	0.4	10mg/kg Q2W:	0.4
						10mg/kg Q3W:	0.7	10mg/kg Q3W:	0.4
						Diabetes Mellitus	0.4	Diabetes Mellitus	0.4
						10mg/kg Q2W:	0.4	10mg/kg Q2W:	0.4
						10mg/kg Q3W:	0.4	10mg/kg Q3W:	0.4

					Ipilimumab 3mg/kg Q3W (n=256)	Hypothyroidism 0.8 Hyperthyroidism 2.3 Hypophysitis 1.6	Hypothyroidism 0 Hyperthyroidism 0.8 Hypophysitis 0.8
	Garon EB et al. ³ N = 495	III	NSCLC		10mg/kg Q2W (n=202) or Q3W (n=287) or 2mg/kg Q3W (n=6)	Any Endocrine AE 8.7 Hypothyroidism 6.9 10mg/kg Q2W: 9.4 10mg/kg Q3W: 4.9 2mg/kg Q3W: 16.7 Hyperthyroidism 1.8 10mg/kg Q2W: 1.5 10mg/kg Q3W: 2.1 2mg/kg Q3W: 0	Any Endocrine AE 0.2 Hypothyroidism 0.2
	Robert C et al. ⁴ N=173	I	mMM	Ipilimumab	10mg/kg (n=84) or 2mg/kg (n=89) Q3W	Any Endocrine AE 6.9 Hypothyroidism 4.0 10mg/kg Q3W: 2.4 2mg/kg Q3W: 5.6 Hyperthyroidism 1.2 † 10mg/kg Q3W: 2.4 2mg/kg Q3W: 1.1 Hypophysitis 1.2 10mg/kg Q3W: 0 2mg/kg Q3W: 2.2 Adrenal insufficiency 0.6 10mg/kg Q3W: 0 2mg/kg Q3W: 1.1	Any Endocrine AE 0.6 Hypothyroidism 0 Hyperthyroidism 0 Hypophysitis 0.6 10mg/kg Q3W: 0 2mg/kg Q3W: 1.1 Adrenal insufficiency 0.6 10mg/kg Q3W: 0 2mg/kg Q3W: 1.1

	Ribas A et al. ⁵ N= 540	II	mMM	Ipilimumab	10mg/kg (33%) or 2mg/kg (33%) Q3W	Any Endocrine AE 10.4 Hypothyroidism 7.3 10mg/kg Q3W: 8.0 2mg/kg Q3W: 6.0 Hyperthyroidism 2.5 10mg/kg Q3W: 1.0 2mg/kg Q3W: 4.0 Hypophysitis 0.6 10mg/kg Q3W: 0.6 2mg/kg Q3W: 0.6	Any Endocrine AE 1.0 Hypothyroidism 0 Hyperthyroidism 0 Hypophysitis 0.3 10mg/kg Q3W: 0 2mg/kg Q3W: 0.6
	Plimack et al. ⁶ N= 33	Ib	mUrothelial cancer	Pretreated	10mg/kg Q2W	No endocrine AEs reported.	
	Goldberg et al. ⁷ N= 16	Ib	NSCLC or MM with brain metastasis	Pretreated	10mg/kg Q2W	No endocrine Aes reported.	
	Doi et al. ⁸ N= 23	Ib	Esophageal carcinoma	Pretreated	10mg/kg Q2W	Any Endocrine AE 13.0 Hypothyroidism 8.7 Adrenal insufficiency 4.3	Any Endocrine AE 0
	Seiwert et al. ⁹ N=132	Ib	Head and Neck Squamous Cell Cancer, recurrent or metastatic	Pretreated	200mg Q3W	Any Endocrine AE 13.0 Hypothyroidism 10.6 Thyroiditis 2.3	Any Endocrine AE 0

	Varga et al. ¹⁰ N=26	Ib	Ovarian, fallopian tube or peritoneal carcinoma	Pretreated	10mg/kg Q2W	Any Endocrine AE Hypothyroidism Hyperthyroidism	19.2 11.5 7.7	Any Endocrine AE	0
	Ott et al. ¹¹ N=20	Ib	SCLC	Pretreated	10mg/kg Q2W	Thyroiditis	5.0	Thyroiditis	0
	Le et al. ¹² N=41	II	Metastatic colorectal carcinoma,	Pretreated	10mg/kg Q2W	Any Endocrine AE Hypothyroidism Hypophysitis Thyroiditis	10 NS NS NS		
Nivolumab	Topalian et al. ¹³ N= 107	I	mMM	Pretreated	Escalating doses 1, 3, 10mg per kg	Any Endocrine AE Hypothyroidism Thyroiditis Hypophysitis	7.4 5.6 0.9 0.9	Hypothyroidism	0.9
	Ansell et al. ¹⁴ N=23	I	Hodgkin's Lymphoma	Pretreated	3mg/kg Q2W	Hypothyroidism	8.7	Hypothyroidism	0
	Brahmer et al. ¹⁵ N=272	III	NSCLC	Pretreated	3mg/kg Q2W (N=135) vs Docetaxel	Any Endocrine AE Hypothyroidism	3.8 3.8	Any Endocrine AE	0
	Robert C et al. ¹⁶ N= 418	III	mMM negative BRAF	Naïve	3mg/kg Q2W (N=206) vs Dacarbazine	Any Endocrine AE Hypothyroidism Hyperthyroidism Hypophysitis Diabetes Mellitus	8.8 4.4 3.4 0.5 0.5	Any Endocrine AE Hypothyroidism Hyperthyroidism Hypophysitis Diabetes Mellitus	0.5 0 0 0.5 0

	Rizvi et al. ¹⁷ N=117	II	NSCLC	Pretreated	3mg/kg Q2W	Any Endocrine AE 6.0 Hypothyroidism 2.6 Thyroiditis 0.9 Adrenal insufficiency 0.9	Any Endocrine AE 0.9 Hypothyroidism 0 Thyroiditis 0 Adrenal insufficiency 0.9
	Weber et al. ¹⁸ N=405	III	mMM	Ipilimumab	3mg/kg Q2W (N=268)	Any Endocrine AE 7.8 Hypothyroidism 5.6 Hyperthyroidism 1.9	Any Endocrine AE 0
	Weber et al. ¹⁹ N=90	I	mMM	Ipilimumab Naïve or Ipilimumab	3mg/kg Q2W	Any Endocrine AE 13.3 Hypothyroidism 10 Thyroiditis 2.2 Hypopituitarism 1.1	Any Endocrine AE 0
	Topalian et al. ²⁰ N=296	I	mMM, NSCLC, mRCC, castration resistant prostate cancer,CRC	Pretreated	Escalating doses 0.1 to 10mg/kg Q2W	Any Endocrine AE 3.4 Hypothyroidism 2.4 Hyperthyroidism 1.0	Any Endocrine AE 0.3
	Brahmer et al. ²¹ N=39	I	mMM, NSCLC, mRCC, Prostate, CRC	Pretreated	Escalating doses 0.3 to10mg/kg Q2W	Hypothyroidism 2.4	Hypothyroidism 0
	Weber et al. ²² N= 92	II	mMM	Ipilimumab	3mg/kg Q2W	Any Endocrine AE 38 Hypothyroidism 12.0 Hyperthyroidism 6.5 Adrenal insufficiency 3.3 Others 16.3	Any Endocrine AE 2.2 Hypothyroidism 0 Hyperthyroidism 0 Adrenal insufficiency 2.2

Hamanishi et al. ²³ N=20	I	Ovarian cancer	Pretreated	1mg/kg (n=10) or 3mg/kg (n=10) Q2W	Hypothyroidism 1 mg/kg 3 mg/kg	40 40 40	Hypothyroidism	0
Nishio et al. ²⁴ N=111	II	Squamous (N=35) and non squamous (N=76) NSCLC	Pretreated	3mg/kg Q2W	Any Endocrine AE Hypothyroidism	13.5 6.3	Any Endocrine AE	0
Bauer et al. ²⁵ N=824	IIIb/IV	NSCLC	Pretreated	3mg/kg Q2W	Any Endocrine AE Hypothyroidism Hyperthyroidism	4.6 3.5 1.0	Any Endocrine AE Hypothyroidism Hyperthyroidism	0.2 0.1 0.1
Gettinger et al. ²⁶ N=52	I	NSCLC	Naïve	3mg/kg Q2W	Any Endocrine AE	14	Any Endocrine AE	0
El-Khoueiry et al. ²⁷ N=47	I	HCC	Pretreated	Escalating doses	No endocrine AEs reported			
Paz-Ares et al. ²⁸ N=582	III	NSCLC	Pretreated	3mg/kg Q2W (N=292) vs Docetaxel	Hypothyroidism	7.0		
Motzer et al. ²⁹ N=168	II	mRCC	Pretreated	0.3mg/kg or 3mg/kg or 10mg/kg Q2W	Any Endocrine AE 0.3mg/kg 3mg/kg or 10mg/kg	9.0 5 11 11	Any Endocrine AE 0.3mg/kg 3mg/kg or 10mg/kg	1.2 0 0 4

Pidilizumab	Armand et al. ³⁰ N= 66	II	Diffuse large B cell lymphoma	Pretreated, autologous hematopoietic stem-cell trans	1.5 mg/kg every 42 days	Hyperglycemia	13.6	
	Atkins et al. ³¹ N=102	II	mMM	Ipilimumab (52%),	1.5 mg/kg or 6 mg/kg	Hyperglycemia	2.0	
	Berger et al. ³² N=17	I	Hematologic malignancies	Pretreated	Escalating doses 1-6 mg/kg	No endocrine AEs		

* Data related to hypothyroidism and hyperthyroidism is different in the tables supplied in the supplementary appendix. We have used the data in the article.

Bibliography of Supplemental Table 2

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Table S3. Endocrine Adverse Events in studies with anti-PDL1 antibodies.

Agent	First Author N Comment	Phase	Tumor type (% of total if available)	Pretreatment	Schedule	Endocrine AE, any grade (%)	Endocrine AE, grade 3-4 (%)
Avelumab	Kelly et al. ¹ N= 480	I	Advanced or metastatic solid tumors	Pretreated	10mg Q3W	Hypothyroidism 4.2	
	Yamada et al. ² N= 20	I	Gastric cancer	Pretreated	10mg Q3W	Hyperthyroidism 10	
	Shitara et al. ³ N= 17	I	Advanced solid tumors	Pretreated	Dose scalation 3,10, 20mg Q3W	No endocrine AEs reported	
	Disis et al. ⁴ N=75	Ib	Ovarian Cancer	Pretreated	10mg Q2W	Hypothyroidism 5.3	
	Gulley et al. ⁵ N=184	Ib	NSCLC	Platinum-based QT	10mg Q2W	Hypothyroidism 6.5	
Atezolizumab	Powles et al. ⁶ N=68	I	Metastatic solid tumors or haematological malignancies	Pretreated	15 mg/kg IV Q3W	Hypothyroidism 1.5	
	Kim et al. ⁷ N=85	I	mUBC	Pretreated	15 mg/kg IV Q3W	No endocrine AEs reported	

	Hamid et al. ⁸ N=44 irAE occurring in >15% reported	I	mMM	Pretreated	Escalating doses 0.01-20 mg/kg IV Q3W	Hyperglycemia 9.0	Hyperglycemia 9.0
	Tabernero et al. ⁹ N=20	I	Solid tumors	Pretreated	Escalating doses 0.01-20 mg/kg IV Q3W	No endocrine AEs reported	
	Cho et al. ¹⁰ N= 55 irAE occurring in >16% reported	I	mRCC	Pretreated	Escalating doses 0.01-20 mg/kg IV Q3W	Hyperglycemia 6.0	Hyperglycemia 6.0
	Spigel et al. ¹¹ N=52	I	NSCLC	Pretreated	Escalating doses 0.01-20 mg/kg IV Q3W	Hyperglycemia 4.0	Hyperglycemia 4.0
	Petrylak et al. ¹² N=92	I	UBC	Pretreated	Escalating doses 0.01-20 mg/kg IV Q3W	Hypophysitis 1.0	Hypophysitis 1.0
	Spira et al. ¹³ N=287	II	NSCLC	Pretreated	1200mg IV Q3W Vs Docetaxel	Hypothyroidism 6.0	Hypothyroidism 0
	Herbst et al. ¹⁴ N=171 irAE occurring >17.5% reported	I	mMM (26%), mRCC (32%), NSCLC (30%)	Pretreated	Escalating doses 0.01-20 mg/kg IV Q3W	Hyperglycemia 5.0	Hyperglycemia 5.0

Durvalumab	Segal et al. ¹⁵ N=346	I	NSCLC, SCCHN, MM, Pancreatic, Gastroesophageal, TNBC, HCC	Pretreated	10mg/kg Q2W	Any Endocrine AE 3.8 Hypothyroidism 2.3 Hyperthyroidism 1.2 Hyperglycemia 0.3	Any Endocrine AE 0.6 Hypothyroidism 0.3 Hyperthyroidism 0 Hyperglycemia 0.3
	Lutzky et al. ¹⁶ N=27	I	NSCLC, MM, RCC, CRC	Pretreated	Escalating doses 0.1-10mg/kg Q2W or 15mg/kg Q3W	Hypothyroidism 2.3	
	Iguchi et al. ¹⁷ N= 22	I	Solid tumors	Pretreated	Escalating doses 1-10mg/kg Q2W or 15mg/kg Q3W or 20mg/kg Q4W	Hypothyroidism 4.5	
	Segal et al. ¹⁸ N=62	I	SCCHN	Pretreated	10mg/kg Q2W	Hypothyroidism 4.8	
	Rizvi et al. ¹⁹ N=228	I	NSCLC	Pretreated	10mg/kg q2w	Any Endocrine AE 11.0 Hypothyroidism 3.5 Hyperthyroidism 3.9 Thyroiditis 1.3 Adrenal insufficiency 0.4 Endocrine disorder 1.8	Any Endocrine AE 0.7 Hypothyroidism 0 Hyperthyroidism 0.4 Thyroiditis 0.4 Adrenal insufficiency 0 Endocrine disorder 0.4
BMS-936559	Brahmer JR et al. ²⁰ N= 207	I	NSCLC (36%), mMM (27%), RCC (8%), ovary (8%), CRC (9%), páncreas, (7%), gastric (3%), breast (2%)	Pretreated	BMS-936559	Any Endocrine AE 3.9 Hypothyroidism 2.9 3 mg/kg Q2W: 2 10 mg/kg Q2W: 4 Adrenal insufficiency 1.0 3 mg/kg Q2W: 2 10 mg/kg Q2W: 1 Diabetes Mellitus 0.5	Any Endocrine AE 0.5 Hypothyroidism 0 Adrenal insufficiency 0.5 3 mg/kg Q2W: 2 10 mg/kg Q2W: 0

							Diabetes Mellitus	0.5
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Table S4: Endocrine Adverse Events in studies with combinations of immune checkpoint inhibitors.

Agents	First Author	Phase	Tumor type	Pretreatment	Schedule	Endocrine AE, any grade (%)	Endocrine AE, grade 3-4 (%)
Nivolumab + Ipilimumab	Wolchok et al. ¹ n= 86 irAE occurring ≥3% reported	I	mMM	≥ 3 doses ipilimumab	Nivolumab + Ipilimumab concurrent (n=53)	Any Endocrine AE 16.7	Any Endocrine AE 2.0
					Scalating doses	Hypothyroidism 4.0 Hypophysitis 4.0 Adrenal insufficiency 4.0 Thyroiditis 6.0	Hypothyroidism 0 Hypophysitis 2.0 Adrenal insufficiency 0 Thyroiditis 0
	Ipilimumab, Nivolumab sequential (n=33)	Any Endocrine AE 9.0 Hypothyroidism 3.0 Hypophysitis 3.0 Adrenal insufficiency 3.0	Any Endocrine AE 6.0 Hypothyroidism 0 Hypophysitis 3.0 Adrenal insufficiency 3.0				
	Postow et al. ² N= 142	II	mMM	Naïve	Nivolumab + Ipilimumab N 1mg/kg Q3W + I 3mg/kg Q3W x4, then N 3mg/kg Q2W	Any endocrine AE 38.4* Hypothyroidism 16 Hyperthyroidism 4.3 Hypophysitis 11.7 Adrenal insufficiency 6.4	Any endocrine AE 3.2 Hypothyroidism 0 Hyperthyroidism 0 Hypophysitis 2.1 Adrenal insufficiency 0

							1.1 Decreased TSH	0
					Ipilimumab 3 mg/kg Q3W x4	Hypothyroidism 1.5 Hypopituitarism 2.3 Hypophysitis 1.5 Adrenal insufficiency 1.5	Hypothyroidism 1.5 Hypopituitarism 2.3 Hypophysitis 1.5 Adrenal insufficiency 1.5	
Larkin et al. ³ N= 945 irAE occurring ≥5% reported	III	mMM	Naïve	Nivolumab + Ipilimumab	Any Endocrine AE 32.6*	Any Endocrine AE 2.9		
				N 1mg/kg Q3W + I 3mg/kg Q3W x4, then I 3mg/kg Q2W	Hypothyroidism 15 Hyperthyroidism 9.9 Hypophysitis 7.7	Hypothyroidism 0.3 Hyperthyroidism 1.0 Hypophysitis 1.6		
				Ipilimumab 3 mg/kg Q3W x4	Hypothyroidism 4.2 Hyperthyroidism 1 Hypophysitis 3.9	Hypothyroidism Hyperthyroidism Hypophysitis 1.9	0 0	
				Nivolumab 3mg/kg Q2W	Hypothyroidism 8.6 Hyperthyroidism 4.2 Hypophysitis 0.6	Hypothyroidism Hyperthyroidism Hypophysitis 0.3	0 0	
Sampson et al. ⁴	I	Glioblastoma	Pretreated	Nivolumab + Ipilimumab	Any endocrine AE 50	Any endocrine AE	20	

N=20					N 1mg/kg Q3W + I 3mg/kg Q3W x4, then I 3mg/kg Q2W (n=10)	Hypothyroidism 20 Hyperthyroidism 30	Hypothyroidism Hyperthyroidism 10	10
					Ipilimumab 3 mg/kg Q3W x4 (n=10)	Any endocrine AE Hypothyroidism 10 Hyperthyroidism 10	Any endocrine AE	0
Hammers et al. ⁵ N=100	I	mRCC	Pretreated	Cohort 1: N 3mg/kg + I 1 mg/kg Q3W Cohort 2: N 1mg/kg + I 3mg/kg Q3W Cohort 3: N 1mg/kg + I 1mg/kg Q3W	Any endocrine AE 36 Hypothyroidism 27 Hyperthyroidism 14 Adrenal insufficiency 8	Any endocrine AE Hypothyroidism Hyperthyroidism Adrenal insufficiency	1 0 1 0	
Antonia et al. ⁶ N=90	I/II	SCLC	Pretreated	Cohort 1: N 3mg/kg + I 1 mg/kg Q3W Cohort 2: N 1mg/kg + I 3mg/kg Q3W Cohort 3: N 1mg/kg + I 1mg/kg Q3W	Any endocrine AE 28 Hypothyroidism 15 Hyperthyroidism 13	Any endocrine AE	0	
				Nivolumab 3mg/kg Q3W	Any endocrine AE 5	Any endocrine AE	0	

						Hypothyroidism 2.5 Hyperthyroidism 2.5	
Hodi et al. ⁷ N=142	II	mMM	Naïve	N 1mg/kg Q3W + I 3mg/kg Q3W x4, then I 3mg/kg Q2W (N=95)	Any endocrine AE 36.2 Hypothyroidism 17 Thyroid disorder 24.5 Hypophysitis 12.8	Any endocrine AE 5.3 Hypothyroidism 0 Thyroid disorder 1.0 Hypophysitis 2.1	
				Ipilimumab 3 mg/kg Q3W (N=47)	Any endocrine AE 37 Hypothyroidism 32.6 Thyroid disorder 32.6 Hypophysitis 15.2	Any endocrine AE 8.7 Hypothyroidism 0 Thyroid disorder 0 Hypophysitis 8.7	
Antonia et al. ASCO 2014 N=49		NSCLC	Naïve	Cohort 1: N 1mg/kg + I 3 mg/kg Q3W Cohort 2: N 3mg/kg + I 1mg/kg Q3W	Any endocrine AE 22.4 N1 + I3 N1 + I3 NR N3 + I1 NR Adrenal insufficiency 6.0 N1 + I3 8.3 N3 + I1 4.0	Any endocrine AE 6.1 N1 + I3 8.3 N3 + I1 4.0 Adrenal insufficiency 4.0 N1 + I3 4.2 N3 + I1 4.0	

Pembrolizumab + Ipilimumab	Atkins et al. ⁸ N= 22	I	mMM (54%) mRCC (45%)	Pretreated	Pembrolizumab 2 mg/kg + Ipilimumab 1 mg/kg Q3W fx4, then pembrolizumab 2 mg/kg Q3W	Any endocrine AE 27.3 Hypothyroidism 13.6 Hyperthyroidism 4.5 Hypophysitis 9.1	Any endocrine AE 4.5 Hypothyroidism 0 Hyperthyroidism 4.5 Hypophysitis 0
	Patnaik et al. ⁹ N= 18	I	NSCLC	Pretreated	Cohort 1: P 10 mg/kg Q3W + I 3 mg/kg Cohort 2: P 10 mg/kg Q3W + I 1mg/kg Cohort 3: P 2 mg/kg Q3W + I 1 mg/kg	Any endocrine AE 27.8 Hypothyroidism 6.0 Hyperthyroidism 6.0 Thyroiditis 6.0 Autoimmune thyroiditis 6.0 Adrenal insufficiency 6.0	Any endocrine AE 6.0 Hypothyroidism 0 Hyperthyroidism 0 Thyroiditis 0 Autoimmune thyroiditis 0 Adrenal insufficiency 6.0
Durvalumab + Tremelimumab	Antonia et al. ¹⁰ N=102	Ib	NSCLC	Pretreated	Durvalumab 3-20mg/kg Q4W or 10mg/kg Q2W + Tremelimumab 3-10mg/kg Q4W	Hypothyroidism 5.9	Hypothyroidism 1.0

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