

### 1 Supplementary Table S1. Characteristics of patients diagnosed with pituitary-irAE

Case	Malignancy	Drug	Age, y	Sex	Days to onset	Symptoms at the onset	Hormone deficiency	MRI findings At the onset
Ipi001	MM	Ipi	69	M	62	HA, fatigue, Hypo Na	C, T, G	Enlarged
Ipi005	MM	Ipi	48	M	26	HA, fatigue, Hypo Na	C, G	Enlarged
Ipi011	MM	Ipi	59	M	79	HA	C, T, G, S	Enlarged
Ipi018	MM	Ipi	69	F	156	HA, fatigue	C	Normal
Ipi008	MM	Ipi	46	M	106	Fatigue	C	Normal
Ipi024	MM	Ipi	71	F	25	Fatigue, Hypo Na	C	Normal
Niv033	MM	Niv	50	F	171	HA, fatigue	C	Normal
Niv060	NSCLC	Niv	72	M	246	Fatigue, Hypo Na	C	Normal
Niv096	MM	Niv	66	M	128	Fatigue	C	Normal
Pem007	MM	Pem	78	F	469	Fatigue, Hypo Na	C	Normal
Pem021	NSCLC	Pem	79	M	216	Fatigue	C	Normal
Pem035	NSCLC	Pem	64	M	114	Fatigue	C	Normal
Pem037	NSCLC	Pem	70	F	149	Fatigue, Hypo Na	C	Normal
Pem092	MM	Pem	78	M	84	Fatigue	C	Normal
Pem098	MM	Pem	62	M	112	Fatigue	C	Normal
Pem110	MM	Pem	60	M	127	Fatigue	C	Normal

2 **Abbreviations:** irAE, immune-related adverse event; MM, malignant melanoma; NSCLC, non-small cell

3 lung carcinoma; Ipi, ipilimumab; Niv, nivolumab; Pem, pembrolizumab; M, male; F, female; HA,

4 headache; Hypo Na, hyponatremia (serum Na < 135); C, corticotroph deficiency; T, thyrotroph

5 deficiency; G, gonadotroph deficiency; S, somatotroph deficiency

6 **Supplementary Table S2. Corticotropin-releasing hormone loading test in patients who developed**7 **pituitary-irAE**

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min.	ACTH (pg/mL)					Cortisol (µg/dL)				
	0	30	60	90	120	0	30	60	90	120
Ipi001	1.3	1.1	1.5	1.6	1.2	1	0.8	0.8	0.6	0.6
Ipi005	1	1.2	1.3	1.3	1.5	0.2	0.2	0.2	0.2	0.2
Ipi011	3.1	3.2	4.3	3.6	2.8	0.5	0.5	0.5	0.5	0.5
Ipi018	1.5	2.7	2.6	2.2	2.6	0.3	0.3	0.3	0.2	0.2
Ipi008	1	1	1	1	1	0.1	0.1	0.1	0.1	0.1
Ipi024	1.1	1.1	1.4	1.3	1.3	5.1	4.4	3.9	3.6	3.2
Niv033	3.1	3.5	3.6	2.4	3.1	0.3	0.3	0.3	0.2	0.3
Niv060	22.8	29	29.3	25.9	24.7	1.6	2.2	2.9	2.3	1.9
Niv096	1.9	2	1.9	1.8	2	0.3	0.2	0.3	0.2	0.2
Pem007	1	2.3	2.8	2.9	3.7	7.5	6.7	6.2	5.9	5.7
Pem021	8.1	10.5	9.5	8.5	9	1.6	1.6	1.6	1.5	1.4
Pem035	2.2	2.8	2.4	2.3	2.6	0.7	0.6	0.5	0.4	0.4
Pem037	2.4	3.8	5.4	4.5	4.2	0.5	0.4	0.4	0.4	0.3
Pem092	9.7	8	8.7	3.8	8.2	1.1	1	0.9	1	0.9
Pem098	7.8	8.9	4	2.4	5.2	0.7	0.8	0.7	0.7	0.7
Pem110	2.4	3.6	3.6	2.7	2.5	0.4	0.6	0.7	0.7	0.6

9 **Abbreviations:** irAE, immune-related adverse event; ACTH, adrenocorticotropic hormone; Ipi,

10 ipilimumab; Niv, nivolumab; Pem, pembrolizumab

11 **Supplementary Table S3. Median OS in NSCLC and MM patients who did and did not develop**12 **irAEs**

	NSCLC ( <i>n</i> = 108)			MM ( <i>n</i> = 52)		
	With irAE	Without irAE	<i>P</i> value	With irAE	Without irAE	<i>P</i> value
All irAEs	Not reached	378 (220 - 536)	0.004	534 (245 - 823)	189 (52 - 326)	0.035
Endocrine-irAE	Not reached	401 (240 - 562)	0.004	649 (367 - 931)	342 (131 - 553)	0.107
Pituitary-irAE	Not reached	441 (NC)	0.036	885 (434 - 1336)	298 (84 - 512)	0.038
Thyroid-irAE	Not reached	441 (317 - 565)	0.048	427 (0 - 871)	393 (219 - 567)	0.875
Non-Endo-irAE	585 (321 - 849)	441 (297 - 585)	0.247	534 (268 - 800)	241 (0 - 523)	0.268
Lung-irAE	488 (167 - 809)	474 (334 - 614)	0.710	1259 (0 - 2655)	393 (237 - 549)	0.202
Skin-irAE	669 (438 - 900)	441 (310 - 572)	0.550	649 (NC)	379 (252 - 506)	0.560
GI-irAE	Not reached	481 (351 - 597)	0.731	491 (152 - 830)	393 (174 - 612)	0.581

13 Data are reported as median (95% CI, days). NC = not calculated (too few patients to calculate reliably).

14 **Abbreviations:** OS, overall survival; NSCLC, non-small cell lung carcinoma; MM, malignant

15 melanoma; irAEs, immune related adverse events; Non-Endo-irAE, any irAE other than endocrine-irAE;

16 GI-irAE, gastrointestinal irAE

17 **Supplementary Table S4. Clinical characteristics of NSCLC patients included in the Kaplan-Meier**18 **analysis according to development of pituitary-irAE**

Characteristics		Total <i>n</i> = 108	With pituitary-irAE <i>n</i> = 4	Without pituitary-irAE <i>n</i> = 104	<i>P</i> value
Age, y		67 ± 10	71 ± 6	67 ± 11	0.396
Sex	Female	29 (26.9)	1 (25.0)	28 (26.9)	1.000
	Male	79 (73.1)	3 (75.0)	76 (73.1)	
Drugs	Niv	57 (52.8)	1 (25.0)	56 (53.8)	0.342
	Pem	51 (47.2)	3 (75.0)	48 (46.2)	0.342
	Ate	9 (8.3)	1 (25.0)	8 (7.7)	0.298
History of prior ICI use		0	0	0	1.000
Treatment lines	First line	32 (29.6)	1 (25.0)	31 (29.8)	1.000
	≥ Second line	76 (70.4)	3 (75.0)	73 (70.2)	

19 Data are mean ± SD or *n* (%).20 **Abbreviations:** NSCLC, non-small cell lung carcinoma; irAE, immune-related adverse event; Niv,

21 nivolumab; Pem, pembrolizumab; Ate, atezolizumab; ICIs, immune checkpoint inhibitors

22 **Supplementary Table S5. Clinical characteristics of MM patients included in the Kaplan-Meier**  
 23 **analysis according to development of pituitary-irAE**

Characteristics		Total <i>n</i> = 52	With pituitary-irAE <i>n</i> = 9	Without pituitary-irAE <i>n</i> = 43	<i>P</i> value
Age, y		70 ± 12	62 ± 11	72 ± 11	0.011
Sex	Female	20 (38.5)	4 (44.4)	16 (37.2)	0.719
	Male	32 (61.5)	5 (55.6)	27 (62.8)	
Drugs	Ipi	24 (46.2)	8 (88.9)	16 (37.2)	0.008
	Niv	26 (50.0)	7 (77.8)	19 (44.2)	0.140
	Pem	23 (44.2)	5 (55.6)	18 (41.9)	0.486
	Ipi + Niv	1 (1.9)	0	1 (2.3)	1.000
History of prior ICI use		12 (23.1)	2 (22.2)	10 (23.3)	1.000
Treatment lines	First line	33 (63.5)	7 (77.8)	26 (60.5)	0.458
	≥ Second				
	line				
		19 (36.5)	2 (22.2)	17 (39.5)	

24 Data are mean ± SD or *n* (%).

25 **Abbreviations:** MM, malignant melanoma; irAE, immune-related adverse event; Ipi, ipilimumab; Niv,

26 nivolumab; Pem, pembrolizumab; ICIs, immune checkpoint inhibitors

27 **Supplementary Table S6. Number of patients and median OS in NSCLC and MM patients treated**  
 28 **with a single ICI.**

Malignancy	Drugs	Number of patients (OS)			P value
		Total	With pituitary-irAE	Without pituitary-irAE	
NSCLC	Niv	<i>n</i> = 48	<i>n</i> = 0 (NC)	<i>n</i> = 48 (297, 199 - 395)	NC
	Pem	<i>n</i> = 51	<i>n</i> = 3 (NR)	<i>n</i> = 48 (441, 266 - 616)	0.089
MM	Ipi	<i>n</i> = 6	<i>n</i> = 0 (NC)	<i>n</i> = 6 (156, 85 - 227)	NC
	Niv	<i>n</i> = 10	<i>n</i> = 0 (NC)	<i>n</i> = 10 (179, 80 - 278)	NC
	Pem	<i>n</i> = 15	<i>n</i> = 1 (NR)	<i>n</i> = 14 (NR)	0.424

29 Data are *n* or median (95% CI)

30 **Abbreviations:** OS, overall survival; NSCLC, non-small cell lung carcinoma; MM, malignant

31 melanoma; ICI, immune checkpoint inhibitor; Niv, nivolumab; Pem, pembrolizumab; Ate, atezolizumab;

32 Ipi, ipilimumab; irAE, immune-related adverse event; NC, not calculated (too few patients to calculate

33 reliably); NR, not reached

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36 **Supplementary Table S7. Number of cycles for each drug and follow-up time for NSCLC patients**  
 37 **included in the Kaplan-Meier analysis according to pituitary-irAE development**

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		Total	With pituitary-irAE	Without pituitary-irAE	<i>P</i> value
Number of cycles	Niv	9.3 ± 12.1	15 ( <i>n</i> = 1)	9.2 ± 12.2 ( <i>n</i> = 56)	NC
	Pem	6.7 ± 6.6	10.0 ± 4.0 ( <i>n</i> = 3)	6.5 ± 6.7 ( <i>n</i> = 48)	0.382
	Ate	4.6 ± 8.2	3 ( <i>n</i> = 1)	4.5 ± 7.8 ( <i>n</i> = 8)	NC
Follow-up days	304 (141 - 589, <i>n</i> = 108)	698 (599 - 882, <i>n</i> = 4)	293 (137 - 521, <i>n</i> = 104)	0.013	

39 Data for number of cycles are mean ± SD (*n*). Data for follow-up time are median (IQR, *n*).

40 **Abbreviations:** NSCLC, non-small cell lung carcinoma; irAE, immune-related adverse event; Niv,

41 nivolumab; Pem, pembrolizumab; Ate, atezolizumab; NC, not calculated



42 **Supplementary Table S8. Number of cycles for each drug and follow-up time for MM patients**  
 43 **included in the Kaplan-Meier analysis according to pituitary-irAE development**

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		Total	With pituitary-irAE	Without pituitary-irAE	<i>P</i> value
Number of cycles	Ipi	2.8 ± 1.2	3.3 ± 1.2 ( <i>n</i> = 8)	2.6 ± 1.1 ( <i>n</i> = 16)	0.224
	Niv	8.2 ± 5.6	12.7 ± 2.3 ( <i>n</i> = 7)	6.6 ± 5.6 ( <i>n</i> = 19)	0.010
	Pem	9.3 ± 7.0	13.2 ± 6.9 ( <i>n</i> = 5)	8.2 ± 6.8 ( <i>n</i> = 18)	0.164
	Ipi + Niv	1	NA ( <i>n</i> = 0)	1 ( <i>n</i> = 1)	NC
Follow-up days	353 (132 - 575, <i>n</i> = 53)	699 (556 - 962 <i>n</i> = 9)	213 (105 - 491 <i>n</i> = 43)	0.001	

45 Data for number of cycles are mean ± SD (*n*). Data for follow-up time are median (IQR, *n*)

46 **Abbreviations:** MM, malignant melanoma; Niv, nivolumab; Pem, pembrolizumab; NA, not available;

47 NC, not calculated

48 **Supplementary Table S9. Clinical characteristics of NSCLC patients included in the Kaplan-Meier**  
 49 **analysis according to development of thyroid-irAE**

Characteristics		Total <i>n</i> = 108	With thyroid-irAE <i>n</i> = 8	Without thyroid-irAE <i>n</i> = 100	<i>P</i> value
Age, y		67 ± 10	69 ± 9	67 ± 11	0.562
Sex	Female	29 (26.9)	4 (50.0)	25 (25.0)	0.207
	Male	79 (73.1)	4 (50.0)	75 (75.0)	
Drugs	Niv	57 (52.8)	4 (50.0)	53 (53.0)	1.000
	Pem	51 (47.2)	4 (50.0)	47 (47.0)	1.000
	Ate	9 (8.3)	1 (12.5)	8 (8.0)	0.514
History of prior ICI use		0	0	0	1.000
Treatment lines	First line	32 (29.6)	1 (12.5)	31 (31.0)	0.432
	≥ Second line	76 (70.4)	7 (87.5)	69 (69.0)	

50 Data are mean ± SD or *n* (%).

51 **Abbreviations:** NSCLC, non-small cell lung carcinoma; irAE, immune-related adverse event; Niv,

52 nivolumab; Pem, pembrolizumab; Ate, atezolizumab; ICIs, immune checkpoint inhibitors

53 **Supplementary Table S10. Clinical characteristics of MM patients included in the Kaplan-Meier**  
 54 **analysis according to development of thyroid-irAE**

Characteristics		Total <i>n</i> = 52	With thyroid-irAE <i>n</i> = 7	Without thyroid-irAE <i>n</i> = 45	<i>P</i> value
Age, y		70 ± 12	70 ± 12	71 ± 12	0.864
Sex	Female	20 (38.5)	1 (14.3)	19 (42.2)	0.228
	Male	32 (61.5)	6 (85.7)	26 (57.8)	
Drugs	Ipi	24 (46.2)	4 (57.1)	20 (44.4)	0.690
	Niv	26 (50.0)	4 (57.1)	22 (48.9)	1.000
	Pem	23 (44.2)	4 (57.1)	19 (42.2)	0.686
	Ipi + Niv	1 (1.9)	0	1 (2.2)	1.000
History of prior ICI use		12 (23.1)	0	12 (26.7)	0.181
Treatment lines	First line	33 (63.5)	6 (85.7)	27 (60.0)	0.242
	≥ Second line	19 (36.5)	1 (14.3)	18 (40.0)	

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56 Data are mean ± SD or *n* (%).

57 **Abbreviations:** MM, malignant melanoma; irAE, immune-related adverse event; Ipi, ipilimumab; Niv,

58 nivolumab; Pem, pembrolizumab; ICIs, immune checkpoint inhibitors