The Oncologist
The official journal of the Society for Translational Oncology

Supplemental Tables for:
Immune checkpoint inhibitors associated primary adrenal insufficiency - WHO VigiBase report analysis
Virginie Grouthier et al.

Supplemental data

Table S1: MedDRA terms used to discriminate definite versus possible PAI

Table S2: Clinical characteristics of patients with ICI associated definite (n=45) versus possible (n=406) PAI collected from VigiBase (last accessed: 10/2018).

Table S3: Drugs involved in and outcomes of ICI therapies inducing definite (n=45) versus possible PAI (n=406).

Table S1: MedDRA terms used to discriminate definite versus **possible** PAI

Definite PAI (n=45)	**Possible PAI (n=406)**
After exclusion of "secondary adrenocortical insufficiency", "adrenocorticotropic hormone deficiency", "hypophysitis", "blood corticotrophin decreased", "hypopituitarism", "hypothalamo-pituitary disorder" and their combination.	
• **Addison's disease** • **Adrenalitis** • **Adrenocortical insufficiency acute** • **Adrenal insufficiency + hyponatremia + hyperkalemia**	• **Adrenal insufficiency + hyponatremie + hypotension** • **Adrenal insufficiency + dehydration + electrolyte imbalance (hyponatremia or hyperkalemia)** • **Adrenal insufficiency + hyponatremia + digestive symptoms** • **Adrenal insufficiency**

Table S2: Clinical characteristics of patients with ICI associated definite (n:46) versus possible (n:406) PAI collected from VigiBase (last accessed: 10/2018).

	Definite PAI n=45	Possible PAI n=406	p
Reporting region (n (%))			
Americas	**15 (33.3%)**	**195 (48.1%)**	**<0.0001**
Europe	**25 (55.6%)**	**91 (22.4%)**	
Australia	**1 (2.2%)**	**7 (1.7%)**	
Asia	**4 (8.9%)**	**113 (27.8%)**	
Reporters (n (%))			
Health-care professional	**39 (86.7%)**	**325 (80.0%)**	**0.57**
Non health-care professional	**4 (8.9%)**	**55 (13.6%)**	
Unspecified	**2 (4.4%)**	**26 (6.4%)**	
Reporting year (n (%))			
2018	**14 (31.0%)**	**155 (38.2%)**	**0.19**
2017	**19 (42.2%)**	**128 (31.5%)**	
2016	**3 (6.7%)**	**50 (12.3%)**	
2015	**3 (6.7%)**	**48 (11.8%)**	
2014	**3 (6.7%)**	**10 (2.5%)**	
≤ 2013	**3 (6.7%)**	**15 (3.7%)**	
Sex (n (%))			
Female	**17 (37.8%)**	**144 (35.5%)**	**0.5**
Male	**27 (60%)**	**235 (57.9%)**	
Unspecified	**1 (2.2%)**	**27 (6.6%)**	
Age at onset, years. median (range max) (n=369)	**64 (33-87) n=36**	**66 (30-95) n=336**	**0.28**

Indication of ICI (n (%))			
Skin cancer	**18 (40.0%)**	**168 (41.3%)**	**0.44**
Lung cancer	**9 (20.0%)**	**120 (29.6%)**	
Renal cancer	**5 (11.1%)**	**26 (6.4%)**	
Gastrointestinal cancer	**0 (0.0%)**	**6 (1.4%)**	
Ovarian cancer	**1 (2.2%)**	**1 (0.25%)**	
Bladder cancer	**1 (2.2%)**	**2 (0.5%)**	
Pancreatic carcinoma	**0 (0.0%)**	**2 (0.5%)**	
Breast cancer	**0 (0.0%)**	**3 (0.75%)**	
Endometrial cancer	**0 (0.0%)**	**3 (0.75%)**	
Myeloma	**1 (2.2%)**	**2 (0.5%)**	
Glioblastoma	**0 (0.0%)**	**2 (0.5%)**	
Hepatocellular cancer	**0 (0.0%)**	**1 (0.25%)**	
Pleural cancer	**0 (0.0%)**	**3 (0.75%)**	
Vulvar cancer	**0 (0.0%)**	**2 (0.5%)**	
Prostate cancer	**0 (0.0%)**	**1 (0.25%)**	
Testis cancer	**0 (0.0%)**	**1 (0.25%)**	
Hodgkin’s disease	**0 (0.0%)**	**1 (0.25%)**	
Neoplasm of unknown sites	**5 (11.1%)**	**14 (3.5%)**	
Data unspecified	**5 (11.1%)**	**48 (11.8%)**	

Table S3: Drugs involved in and outcomes of ICI therapies inducing definite (n=45) versus possible PAI (n=406).

	Definite PAI n=45	Possible PAI n=406	p
Suspected drugs (n(%))			
Only ICI	44 (97.8%)	353 (86.9%)	0.1
ICI plus one other drug	1 (2.2%)	43 (10.6%)	
ICI plus two or more other drugs	0 (0.0%)	10 (2.5%)	
Drugs (n(%))			
Monotherapy anti-PD1 or anti-PD-L1	26 (57.8%)	238 (58.6%)	0.54
Nivolumab	18 (40.0%)	182 (44.9%)	
Pembrolizumab	8 (17.8%)	45 (11.1%)	
Atezolizumab	0 (0%)	7 (1.7%)	
Durvalumab	0 (0%)	3 (0.7%)	
Avelumab	0 (0%)	1 (0.2%)	
Monotherapy anti-CTL4 (ipilimumab)	13 (28.9%)	93 (22.9%)	
Combination therapy	6 (13.3%)	75 (18.5%)	
Nivolumab + ipilimumab	6 (13.3%)	69 (17.0%)	
Pembrolizumab + ipilimumab	0 (0%)	5 (1.3%)	
Tremelimumab + Durvalumab	0 (0%)	1 (0.2%)	
Time to irAE onset, days. median (range max) (n=119)	120 (6-506) n=11	120,5 (6-576) n=108	0.54
Drug dosing (n(%))			
Nivolumab			
1–2 mg/kg	3/16 (18.7%)	51/181 (28.2%)	0.41
≥3 mg/kg	13/16 (81.3%)	130/181 (71.8%)	
Pembrolizumab			
≤2 mg/kg	1/6 (16.7%)	11/25 (44.0%)	0.22
>2 mg/kg	5/6 (83.3%)	14/25 (56.0%)	
Ipilimumab			
<5 mg/kg	8/11 (72.7%)	84/88 (95.5%)	0.006
>5 mg/kg	3/11 (27.3%)	4/88 (4.5%)	
Severe adverse event (n(%))	45 (100%)	365 (89.9%)	0.03
Death (n(%))	5 (11.1%)	28 (6.9%)	0.3