

Additional Table S1. Characteristics of included trials.

	Author, year	Phase	Cancer type	Stage	Intervention	NO. of patients	Fatal adverse events
1	Hiroyuki, 2020	III	urothelial cancer	metastatic	pembrolizumab	30	0
2	Shin, 2020	II	ovarian cancer	metastatic	pembrolizumab	21	0
3	Neal, 2019	I/ II	lung cancer	metastatic	nivolumab	109	1
4	Lillian, 2019	II	head and neck squamous cell carcinoma	metastatic	durvalumab	65	0
					tremelimumab	65	0
					durvalumab+ tremelimumab	133	1
5	Yung, 2019	II	gastric/gastroesophageal junction adenocarcinoma	metastatic	pembrolizumab	31	0
					pembrolizumab + chemotherapy	25	0
6	Leisha, 2019	I	triple-negative breast cancer	metastatic	atezolizumab	116	0
7	Ken, 2019	III	gastric/gastroesophageal junction adenocarcinoma	metastatic	nivolumab	152	0
8	Adams, 2019	II	triple-negative breast cancer	metastatic	pembrolizumab	170	0
9	Paolo, 2019	III	melanoma	metastatic	nivolumab	206	0
10	Yutaka, 2019	I	gastric/gastroesophageal junction adenocarcinoma	metastatic	durvalumab	22	0
11	Manish, 2019	II	esophageal cancer	metastatic	pembrolizumab	121	1
12	Stephen, 2019	II	B-cell lymphoma	non-metastatic	nivolumab	121	0
13	Makoto, 2019	I	lung cancer	metastatic	pembrolizumab	38	1
14	Robert, 2019	II	hodgkin lymphoma	non-metastatic	pembrolizumab	210	0
15	Janice, 2019	I	thyroid cancer	metastatic	pembrolizumab	22	0
16	Adams, 2019	II	triple-negative breast cancer	metastatic	pembrolizumab	84	0
17	Kenji, 2019	II	uterine cervical cancer	metastatic	nivolumab	64	0
18	Paul, 2019	II	merkel cell carcinoma	metastatic	pembrolizumab	50	1

19	Ahmad, 2019	II	melanoma	metastatic	ipilimumab	44	0
					ipilimumab+ interferon- α 2b	39	0
20	Melissa, 2019	I	melanoma	metastatic	pembrolizumab	40	0
21	Ulrich, 2019	I	melanoma	metastatic	avelumab	51	0
22	Hellmann, 2018	III	lung cancer	metastatic	nivolumab	391	2
					nivolumab+ ipilimumab	576	7
23	Yelena, 2018	I/ II	esophagogastric cancer	metastatic	nivolumab	59	0
					nivolumab+ ipilimumab	101	1
24	Sandra, 2018	II	sarcoma	metastatic	nivolumab	42	0
					nivolumab+ ipilimumab	42	6
25	Alexand, 2018	III	melanoma	metastatic	pembrolizumab	509	1
26	David, 2018	II	renal cell carcinoma	metastatic	atezolizumab	103	0
27	Robert, 2018	III	head and neck squamous cell carcinoma	metastatic	nivolumab	236	2
28	Antonio, 2018	I	glioblastoma	non-metastatic	nivolumab	10	0
					nivolumab+ ipilimumab	30	2
29	Matteo, 2018	III	melanoma	metastatic	pembrolizumab	368	1
					ipilimumab	168	0
30	Migden, 2018	II	cutaneous squamous- cell carcinoma	metastatic	cemiplimab	59	3
31	Charles, 2018	II	gastric/gastroesophageal junction adenocarcinoma	metastatic	pembrolizumab	259	0
32	Brigitte, 2018	II	nasopharyngeal carcinoma	metastatic	nivolumab	45	1
33	Ranee, 2018	I	head and neck squamous cell carcinoma	metastatic	pembrolizumab	192	0
34	Richard, 2018	II	melanoma	metastatic	ipilimumab	6	0
35	James, 2018	III	melanoma	metastatic	nivolumab	268	0
36	Daniel, 2018	I	urothelial cancer	metastatic	atezolizumab	95	0
37	Toyoaki, 2018	III	lung cancer	metastatic	atezolizumab	56	0

38	David, 2018	II	lung cancer	metastatic	atezolizumab	137	1
39	Makoto, 2018	I	head and neck squamous cell carcinoma	metastatic	pembrolizumab	26	0
40	Colevas, 2018	I	head and neck squamous cell carcinoma	metastatic	atezolizumab	32	0
41	Dan, 2018	II	lung cancer	metastatic	durvalumab	112	0
42	Adra, 2018	II	germ-cell tumors	metastatic	pembrolizumab	12	0
43	Hope, 2018	I	breast cancer	metastatic	pembrolizumab	25	0
44	Jong, 2018	II	lung cancer	metastatic	nivolumab	100	1
45	Weber, 2017	III	melanoma	metastatic	nivolumab	452	0
					ipilimumab	453	2
46	Arjun, 2017	II	urothelial carcinoma	metastatic	atezolizumab	119	1
47	Achim, 2017	III	lung cancer	metastatic	atezolizumab	609	0
48	Antonia, 2017	III	lung cancer	non-metastatic	durvalumab	475	7
49	Thomas, 2017	I/ II	urothelial carcinoma	metastatic	durvalumab	191	2
50	Van, 2017	II	anal canal carcinoma	metastatic	nivolumab	37	0
51	Michael, 2017	II	colorectal cancer	metastatic	nivolumab	74	0
52	Wolchok, 2017	III	melanoma	metastatic	nivolumab	313	1
					ipilimumab	311	1
					nivolumab+ ipilimumab	313	2
53	Bellmunt, 2017	III	urothelial carcinoma	metastatic	pembrolizumab	266	4
54	Jason, 2017	II	melanoma	metastatic	ipilimumab	95	0
55	Necchi, 2017	II	urothelial carcinoma	metastatic	atezolizumab	137	0
56	Solange, 2017	II	lung cancer	metastatic	atezolizumab	659	1
57	Wei, 2017	II	lymphocytic leukemia	non-metastatic	pembrolizumab	25	0

58	Bert, 2017	I	colorectal carcinoma	metastatic	pembrolizumab	23	0
59	Hui, 2017	I	lung cancer	metastatic	pembrolizumab	101	0
60	Toyoaki, 2017	II	lung cancer	metastatic	nivolumab	35	1
61	Ott, 2017	I	anal carcinoma	metastatic	pembrolizumab	25	0
62	Joshua, 2017	II	head and neck squamous cell carcinoma	metastatic	pembrolizumab	171	1
63	Pier, 2017	I	B-cell lymphoma	non-metastatic	pembrolizumab	18	0
64	Yoshihiko, 2017	III	renal cell carcinoma	non-metastatic	nivolumab	37	0
65	Eytan, 2017	II	uterine leiomyosarcoma	metastatic	nivolumab	12	0
66	Noboru, 2017	I	lung cancer	metastatic	nivolumab	17	0
67	Yung, 2017	II	gastric/gastroesophageal junction adenocarcinoma	metastatic	ipilimumab	57	0
68	Naoya, 2017	I	melanoma	metastatic	pembrolizumab	42	2
69	Keun, 2017	I	lung cancer	metastatic	nivolumab	18	0
70	Naoya, 2017	II	melanoma	metastatic	nivolumab	23	0
71	Tara, 2017	II	melanoma	metastatic	pembrolizumab	947	0
72	Dai, 2017	II	hodgkin lymphoma	non-metastatic	nivolumab	17	0
73	Martin, 2016	III	lung cancer	metastatic	pembrolizumab	154	1
74	Ferris, 2016	III	head and neck squamous cell carcinoma	non-metastatic	nivolumab	236	2
75	Stephen, 2016	II	melanoma	metastatic	ipilimumab	46	0
					nivolumab+ ipilimumab	94	3
76	Rita, 2016	I	triple-negative breast cancer	metastatic	pembrolizumab	32	1
77	Jonathan, 2016	II	urothelial carcinoma	metastatic	atezolizumab	310	0
78	Eggermont 2016	II	melanoma	metastatic	ipilimumab	471	5

79	Christophe 2016	I/ II	bladder cancer	metastatic	durvalumab	61	0
80	Alexander 2016	I	hodgkin lymphoma	non-metastatic	nivolumab	81	1
81	Scott, 2016	I	lung cancer	metastatic	nivolumab	52	0
82	Anas, 2016	II	hodgkin lymphoma	non-metastatic	nivolumab	80	1
83	Paul, 2016	II	merkel-cell carcinoma	metastatic	pembrolizumab	26	0
84	Melinda, 2016	I	melanoma	metastatic	ipilimumab	33	0
85	Padmanee, 2016	I/ II	urothelial carcinoma	metastatic	nivolumab	78	1
86	Philippe, 2016	I	hodgkin lymphoma	non-metastatic	pembrolizumab	31	0
87	Toshio, 2016	I	lung cancer	metastatic	pembrolizumab	10	0
88	James, 2015	III	melanoma	metastatic	nivolumab	313	1
					ipilimumab	311	1
					nivolumab+ ipilimumab	313	0
89	Le, 2015	II	colorectal carcinomas	metastatic	pembrolizumab	41	0
90	Hossein, 2015	III	lung cancer	metastatic	nivolumab	287	1
91	Robert, 2015	III	renal cell carcinoma	metastatic	nivolumab	406	0
92	Julie, 2015	III	lung cancer	metastatic	nivolumab	131	0
93	Caroline, 2015	III	melanoma	metastatic	nivolumab	206	0
94	Edward, 2015	I	lung cancer	metastatic	pembrolizumab	495	1
95	Caroline, 2015	III	melanoma	metastatic	pembrolizumab	550	0
					ipilimumab	256	1
96	Stephen, 2015	I	hodgkin lymphoma	non-metastatic	nivolumab	23	0
97	Michael, 2015	I	melanoma	metastatic	ipilimumab	46	0
					nivolumab+ ipilimumab	94	0
98	Naiyer, 2015	II	lung cancer	metastatic	nivolumab	117	2

99	Robert, 2015	II	renal cell carcinoma	metastatic	nivolumab	167	0
100	Scott, 2015	I	lung cancer	metastatic	nivolumab	129	3
101	David, 2015	I	renal cell carcinoma	metastatic	nivolumab	34	0
102	Lisa, 2015	II	melanoma	metastatic	ipilimumab	103	0
103	Disa, 2015	II	melanoma	metastatic	ipilimumab	53	1
104	Yamazaki, 2015	II	melanoma	metastatic	ipilimumab	20	0
105	Yoshihiko, 2020	III	renal cell carcinoma	non-metastatic	nivolumab+ ipilimumab	38	1
106	Celeste, 2019	III	melanoma	metastatic	nivolumab+ ipilimumab	358	1
107	Michael, 2019	II	melanoma	metastatic	nivolumab+ ipilimumab	124	0
108	Motzer, 2018	III	renal cell carcinoma	metastatic	nivolumab+ ipilimumab	547	8
109	Hussein, 2018	II	melanoma	metastatic	nivolumab+ ipilimumab	94	1
110	Kenjiro, 2018	II	melanoma	metastatic	nivolumab+ ipilimumab	30	0
111	Michael, 2018	I	melanoma	metastatic	ipilimumab+ pembrolizumab	22	0
112	Margaret, 2018	I	melanoma	metastatic	nivolumab+ ipilimumab	94	1
113	Matthew, 2017	I	lung cancer	metastatic	nivolumab+ ipilimumab	77	0
114	Scott, 2016	I	lung cancer	metastatic	durvalumab+ tremelimumab	103	3
115	Jeffrey, 2016	II	melanoma	metastatic	nivolumab+ ipilimumab	138	0
116	Alex, 2020	I/ II	B-cell lymphoma	non-metastatic	durvalumab+ ibrutinib	61	0
117	Erminia, 2019	II	oropharyngeal cancer	non-metastatic	nivolumab+ vaccine	24	0
118	Boku, 2019	II	gastric/gastroesophageal junction adenocarcinoma	metastatic	nivolumab+ chemotherapy	21	0
					nivolumab+ chemotherapy	18	0

119	Sylvia, 2019	I	triple-negative breast cancer	metastatic	Atezolizumab+nab-Paclitaxel	33	0
120	James, 2019	I/ II	lung cancer	metastatic	pembrolizumab + erlotinib	12	0
					pembrolizumab + gefitinib	7	0
121	Hiroji, 2019	III	triple-negative breast cancer	metastatic	Atezolizumab+nab-Paclitaxel	34	0
122	Socinski, 2018	III	lung cancer	metastatic	atezolizumab+ bevacizumab	393	11
123	David, 2018	II	renal cell carcinoma	metastatic	atezolizumab+ bevacizumab	101	1
124	Paz-Ares, 2018	III	lung cancer	metastatic	pembrolizumab + chemotherapy	278	10
125	Gandhi, 2018	III	lung cancer	metastatic	pembrolizumab + chemotherapy	405	27
126	Michael, 2018	I	melanoma	metastatic	pembrolizumab + PEG-IFN	17	0
127	Asim, 2018	I	renal cell carcinoma	metastatic	nivolumab+ sunitinib	33	0
					nivolumab+ pazopanib	20	0
128	Michael, 2018	I	renal cell carcinoma	metastatic	pembrolizumab + axitinib	52	0
129	Alex, 2018	I/ II	hodgkin lymphoma	non-metastatic	nivolumab+ brentuximab	61	0
130	Scott, 2018	I	lung cancer	metastatic	nivolumab+ erlotinib	21	0
131	Richard, 2018	II	melanoma	metastatic	ipilimumab+ ATRA	4	0
132	John, 2018	I	lung cancer	metastatic	nivolumab+ interleukin	21	1
133	Hendrik, 2018	I	biliary tract cancer	metastatic	ramucirumab+ pembrolizumab	26	0
134	Mamta, 2018	I	urothelial cancer	metastatic	pembrolizumab + docetaxel	12	0
135	Jason, 2017	II	lung cancer	metastatic	ipilimumab+ talimogene	95	0
136	Anthony, 2017	I	lung cancer	metastatic	pembrolizumab + utomilumab	23	0
137	Chad, 2017	I	lung cancer	metastatic	ipilimumab+ radiation	35	0

138	Sandra, 2017	I	gastrointestinal stromal tumor	metastatic	ipilimumab+ dasatinib	24	0
139	Matthew, 2017	I	melanoma	metastatic	ipilimumab+ imatinib	35	0
140	Corey, 2016	II	lung cancer	metastatic	pembrolizumab + chemotherapy	59	1
141	Naiyer, 2016	I	lung cancer	metastatic	nivolumab+ chemotherapy	56	0
142	Igor, 2016	I	melanoma	metastatic	ipilimumab+ T- VEC	19	0
143	Eburne, 2016	II	lung cancer	metastatic	ipilimumab+ chemotherapy	39	5
144	Yamazaki, 2015	II	melanoma	metastatic	ipilimumab+ dacarbazine	15	0
145	Geoffrey, 2015	II	melanoma	metastatic	nivolumab+ vaccine	33	0

Additional Table S2. Percentages of most common TRAEs

	Cohort1	Cohort2	Cohort3	PD-1	PD-L1	CTLA-4
	n=16295	n=3321	n=2170	n=10407	n=3350	n=2538
Hypothyroidism	0.3	0.3	0.4	0.3	0.5	0.3
Hyperthyroidism	0.1	0.3	0.1	0.0	0.2	0.1
Nausea	0.4	1.5	2.6	0.2	0.8	0.5
Diarrhea	2.1	5.4	4.9	1.0	1.2	7.8
Colitis	1.2	4.0	1.6	0.5	0.4	5.2
ALT increase	1.0	4.5	3.1	0.5	1.3	2.4
AST increase	0.9	3.3	3.0	0.4	1.6	1.8
Arthralgia	0.2	0.1	0.5	0.1	0.4	0.3
Myalgia	0.1	0.0	0.2	0.0	0.1	0.0
Pruritus	0.3	0.7	0.3	0.1	0.6	0.6
Rash	0.7	2.0	2.3	0.4	0.9	1.8
Pneumonitis	0.8	0.5	1.5	0.7	1.3	0.3
Fatigue	1.0	2.8	4.8	0.9	1.3	0.9
Decreased appetite	0.4	0.8	1.8	0.2	0.7	0.4
Hypophysitis	0.3	0.6	0.5	0.1	0.1	1.4

Cohort 1: ICI monotherapy; Cohort 2: combined therapy of two ICIs; Cohort 3: ICI plus other treatments.