

Table S1. Immune related adverse events (irAEs) in select clinical trials.

Clinical Trials	Details	Number of patients, type of Immune Checkpoint Inhibitor and dose.	Adverse events		
			Organ system / event	All grade	Grade ≥ 3
Anti- cytotoxic T-lymphocyte –associated protein 4 (CTLA 4)					
Eggermont et al.¹⁹ 2016 Ipilimumab	Phase 3 stage III melanoma	471 patients on ipilimumab at dose of 10ml/kg every 3 weeks for 4 doses then every 3 monthly for up to 3 years (reported after median follow up of 5.3 years)	Any irAEs	426 (90.4)	201 (42.7)
			Dermatological	298(63.3)	20(4.2)
			Rash	161(34.2)	5(1.1)
			Gastrointestinal	217(46)	70(16.1)
			Diarrhea	194(41)	46(9.8)
			Colitis	73(15.5)	39(8.2)
			Endocrine	178(37.8)	37(7.9)
			Hypophysitis	77(16.3)	21(4.4)
			Hepatic	115(24.2)	51(10.8)
			↑ Liver enzymes	83(17.6)	20(4.3)
Neurologic	21(4.5)	9(1.9)			
Eggermont et al.²⁰ 2015 Ipilimumab	Phase 3 Stage III melanoma	471 patients on ipilimumab at dose of 10mg/kg every 3 weeks for 4 doses then every 3 monthly for up to 3 years (reported after median follow up of 2.7 years)	Any irAEs	226(48)	200(43)
			Dermatologic	277(59)	21(4)
			Pruritus	176(37)	2(11)
			Rash	156(33)	6(17)
			Gastrointestinal	142(30)	75(16)
			Diarrhea	150(32)	45(10)
			Colitis	39(8)	36(8)
			Endocrine	137(29)	40(9)
			Hypophysitis	62(13)	24(6)
			Hypothyroidism	41(9)	1(<1)
Hepatic	68(14)	50(11)			
↑ Liver enzymes	68(14)	25(5)			
Neurologic	12(3)	9(2)			
Hodi et al.¹ 2010 Ipilimumab	Phase 3 Unresectable stage III / IV melanoma	137 patients on ipilimumab alone at dose of 3mg/kg every 3 weeks up to 4 doses.	Any irAEs	80(61.1)	19(14.5)
			Dermatologic	57(43.5)	2(1.5)
			Pruritus	32(2.4)	0 (0)
			Rash	25(19.1)	1(<1)
			Gastrointestinal	38(29)	10(7.6)
			Diarrhea	36(27.5)	6(4.6)
			Colitis	10(7.6)	7(5.3)
			Endocrine	10(7.6)	5(3.8)
			Hypothyroidism	2(1.5)	0 (0)
			Hypophysitis	3(2.3)	2(1.6)
Adrenal insufficiency	2(1.5)	2(1.5)			
Hepatic	5(3.8)	0 (0)			

			↑ ALT ↑ AST Hepatitis	2(1.5) 1(<1) 1(<1)	0 (0) 0 (0) 0 (0)
Wolchok et al. ⁹ 2010 Ipilimumab	Phase 2 Previously treated stage III / IV melanoma	71 patients on ipilimumab at dose of 10mg/kg every 3 weeks for 4 doses followed by maintenance every 3 months.	Any irAEs Dermatological Gastrointestinal Endocrine Hepatic	50 (68) 33(45) 28(38) 3(4) 2(3)	18(25) 3(4) 11(15) 1(1) 2(3)
		71 patients on ipilimumab at dose of 3 mg/kg every 3weeks for 4 doses followed by maintenance every 3 months	Any irAEs Dermatological Gastrointestinal Endocrine Hepatic	46(64) 32(44) 23(32) 4(6) 0 (0)	5(7) 1(1) 2(3) 2(3) 0 (0)
		71 patients on ipilimumab at dose of 0.3 mg/kg every 3weeks for 4 doses followed by maintenance every 3 months	Any irAEs Dermatological Gastrointestinal Endocrine Hepatic	19(26) 09(13) 12(17) 0 (0) 0 (0)	0 (0) 0 (0) 0 (0) 0 (0) 0 (0)
Postow et al. ⁸ 2015 Ipilimumab	Phase 2 Unresectable, previously untreated, stage III and IV melanoma	46 patients on ipilimumab at dose of 3 mg/kg.	Dermatological Gastrointestinal Diarrhea Colitis Endocrine Hypothyroidism Hypophysitis Adrenal insufficiency Hepatic ↑ ALT ↑ AST ↑ Lipase Pneumonitis Discontinuation of the therapy	27 (58) 17 (37) 17(37) 6 (13) 8 (17) 7 (15) 3 (7) 2 (4) 2 (4) 2 (4) 2(4) 2(4) 2(4) 2 (4) 8(17)	0 (0) 5 (11) 5(11) 3 (7) 2 (4) 0 (0) 2 (4) 1 (2) 0 (0) 0 (0) 0 (0) 0 (0) 1 (2) 6(13)
Larkin et al. ⁶ 2015 Ipilimumab	Phase 3 Stage III or IV melanoma	311 patients on ipilimumab alone at dose of mg/kg every weeks	Any IrAEs Dermatological Pruritus Rash Vitiligo Gastrointestinal Diarrhea Colitis Endocrine	229 (73.6) 168 (54) 110 (35.4) 65 (20.9) 12 (3.9) 114 (36.7) 103 (33.1) 36 (11.6) 34 (10.9)	58 (18.6) 9 (2.9) 1 (0.3) 5 (1.6) 0 (0) 36 (11.6) 19 (6.1) 27 (8.7) 7 (2.3)

			Hypothyroidism	27 (8.6)	0 (0)
			Hyperthyroidism	13 (4.2)	0 (0)
			Hypophysitis	12 (3.9)	6 (1.9)
			Hepatic	22 (7.1)	5 (1.6)
			↑ ALT	12(3.9)	5(1.6)
			↑ AST	11(3.5)	2 (0.6)
			Pulmonary	6 (1.9)	1 (0.3)
			Pneumonitis	5 (1.6)	1 (0.3)
Ribas et al.³ 2013 Tremelimumab	Phase 3 Stage IIIc/ IV melanoma	325 patients on tremelimumab at dose of 15mg/kg every 90 days	Endocrine	24 (7)	NR
			Thyroid	17 (5)	2(1)
			Hypothalamus and pituitary	6 (2)	4(1)
			Adrenal insufficiency	4(1)	3(1)
			Pancreatitis	3(1)	3(1)
			Hepatitis	2(1)	2(1)
Anti- programmed cell death protein-1/-Ligand1 (PD-1/PD-L1)					
Borghaei et al.⁴⁴ 2015 Nivolumab	Phase 3 IIIb/IV or recurrent nonsquamous NSCLC	292 patients on nivolumab at dose of 3mg/kg every 2 weeks.	Rash	27(9)	1(<1)
			Pruritus	24(8)	0 (0)
			Diarrhea	22(8)	2(1)
			Colitis	2(1)	1(<1)
			Hypothyroidism	19(7)	0 (0)
			Hyperthyroidism	4(1)	0 (0)
			↑ ALT	9(3)	0 (0)
			↑ AST	9(3)	1(<1)
			Pneumonitis	8(3)	3(1)
			ILD	2(1)	1(<1)
			↑ Creatinine	5(2)	0 (0)
			Renal Failure	1(<1)	0 (0)
Topalian et al.¹⁰ 2014 Nivolumab	Phase 1 Advanced melanoma	107 patients on nivolumab at dose of 1mg/kg or 3mg/kg or 10mg/kg once every 2 weeks for up to 96 weeks.	Any irAEs	58 (54.2)	5 (4.7)
			Dermatological	38 (35.5)	0 (0)
			Rash	25(23.4)	0 (0)
			Pruritus	14(3.1)	0 (0)
			Gastrointestinal	19 (17.8)	2 (1.9)
			Diarrhea	19 (17.8)	2 (1.9)
			Colitis	2(2)	1 (0.9)
			Hypothyroidism	6(5.6)	1 (0.9)
			Hyperthyroidism	2(1.9)	0 (0)
			Hepatic	7(6.5)	1 (0.9)
			↑ ALT	5(4.7)	0 (0)
			↑ AST	4(3.7)	0 (0)
			Pneumonitis	2(2)	0 (0)
			Renal Failure	2(2)	0 (0)

			Infusion Reactions	6(5.6)	0 (0)
Rizvi et al. ⁴⁶ 2015 Nivolumab	Phase2 squamous NSCLC	117 patients on nivolumab at dose of 3mg/kg every 2 weeks	Dermatological Rash Diarrhea Endocrine Hypothyroidism Hyperthyroidism Pneumonitis Renal Failure ↑ ALT	18(15) 13(11) 12(10) 7(6) 3(3) 1(1) 6(5) 1(1) 1(1)	2(2) 1(1) 3(3) 1(1) 0 (0) 0 (0) 4(3) 0 (0) 0 (0)
Larkin et al. ⁶ 2015 Nivolumab	Phase 3 Stage III or IV melanoma	313 patients on nivolumab at dose of 3mg/kg every 2 weeks	Any irAEs Dermatological Pruritus Rash Vitiligo Gastrointestinal Diarrhea Colitis Endocrine Hypothyroidism Hyperthyroidism Hypophysitis Hepatic ↑ ALT ↑ AST Pulmonary Pneumonitis	194 (62) 131 (41.9) 59(18.8) 81(25.9) 23 (7.3) 61 (19.5) 60 (19.2) 4 (1.3) 45 (14.4) 27(8.6) 4(1.3) 2(0.6) 20 (6.4) 12(3.8) 12(3.8) 5 (1.6) 4 (1.3)	24 (7.7) 5 (1.6) 0 (0) 2(0.6) 1 (0.3) 7 (2.2) 7(2.2) 2 (0.6) 2 (0.6) 0 (0) 2 (0.6) 1 (0.3) 8 (2.6) 4(1.3) 3(1) 1 (1.3) 1 (0.3)
Robert et al. ⁵ 2016 Nivolumab	Phase 3 recurrent squamous cell carcinoma of head and neck	240 patients on nivolumab at dose of 3mg/kg every 2 weeks	Dermatological Rash pruritus Gastrointestinal Diarrhea Endocrine Hypothyroidism Hyperthyroidism Hepatic ↑ ALT ↑ AST Pneumonitis Renal Failure	37(15.7) 18(7.6) 17(7.2) 16(6.8) 16(6.8) 18 (7.6) 9(3.8) 2 (0.8) 5 (2.1) 2 (0.8) 2 (0.8) 5(2.1) 1(0.4)	0(0) 0(0) 0(0) 0(0) 1(<1) 0(0) 0(0) 2 (0.8) 1 (0.4) 1 (0.4) 2(0.8) 0(0)
Martin et al. ¹¹ 2016	Stage IV NSCLC	154 patients on pembrolizumab at dose of	Any irAEs Sever skin rash	45(29.2) 6(3.9)	15(9.7) 6(3.9)

Pembrolizumab		200mg every 3 weeks	Colitis Hypothyroidism Hyperthyroidism Thyroiditis Hypophysitis Myositis Nephritis Pneumonitis Infusion reaction Pancreatitis T1DM	3(1.9) 14(9.1) 12(7.8) 4(2.6) 1(6.6) 3(1.9) 1(0.6) 9(5.8) 7(4.5) 1(0.6) 1(0.6)	2(1.3) 0 (0) 0 (0) 0 (0) 1(6.6) 0 (0) 1(0.6) 4(2.6) 0 (0) 1(0.6) 1(0.6)
Seiwert et al. ⁴⁷ 2016 Pembrolizumab	Phase 1b Recurrent or metastatic squamous cell carcinoma of the head and neck	60 patients on pembrolizumab at dose of 10mg/kg every 2 weeks	Any irAEs Hypothyroidism Adrenal insufficiency Hyperthyroidism Rash Grade 2 myositis	9 (15) 4 (7) 2 (3) 1 (1.5) 1 (1.5) 1 (1.5)	0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0)
Herbst et al. ¹⁸ 2016 Pembrolizumab	Phase 2/3 Advanced NSCLC	345 patients on pembrolizumab at dose of 2mg/kg	Severe skin reactions Colitis Hypothyroidism Hyperthyroidism Hypophysitis Hepatitis Pancreatitis Pneumonitis	4 (1) 4 (1) 28(8) 12 (4) 1(<1) 1(<1) 3 (1) 16(5)	3(1) 3 (1) 0 (0) 0 (0) 1(<1) 1(<1) 2 (1) 7(2)
		346 patients on pembrolizumab at dose of 10 mg/kg every 2 weeks	Severe skin reactions Colitis Hypothyroidism Hyperthyroidism Hypophysitis Hepatitis Pneumonitis	7 (2) 4 (1) 28(8) 20 (6) 2 (1) 2(1) 15(4)	6 (2) 3 (1) 0 (0) 1 (<1) 1 (<1) 0 (0) 0(0)
Garon et al. ⁴⁸ 2015 Pembrolizumab	Phase 1 Advanced or metastatic NSCLC	495 patients on pembrolizumab at dose of 2 mg/kg or 10 mg/kg every 3 weeks or 10 mg/kg every 2 weeks	Pruritus Rash Dry skin Diarrhea Hypothyroidism ↑ ALT ↑ AST Pneumonitis	53(10.7) 48(9.7) 18(3.6) 40 (8.1) 34 (3.6) 15(6.9) 11(3) 18(3.6)	0 (0) 1(0.2) 0(0) 3 (0.6) 1 (0.2) 9(1.8) 3(0.6) 9(1.8)

Rosenberg et al.⁵⁰ 2016 Atezolizumab	Phase 2 Locally advanced or metastatic urothelial carcinoma	310 patients on atezolizumab at dose of 1200mg every 3 weeks	Any irAEs Rash ↑ALT ↑AST Pneumonitis	23(7) 2(1) 2(1) 2(1) 2(1)	15(5) 1(<1) 1(<1) 1(<1) 2(1)
Fehrenbacher et al.¹³ 2016 Atezolizumab	Phase 2 Advanced or metastatic NSCLC	142 patients on atezolizumab at dose of 1200 mg every 3 weeks	Colitis ↑ALT ↑AST Hepatitis Pneumonitis	2 (1) 6 (4) 6 (4) 1 (<1) 4 (3)	1 (<1) 3 (2) 3 (2) 0 (0) 1 (<1)
Rittmeyer et al.¹⁴ 2016 Atezolizumab	Phase 3 Stage IIIB/ IV NSCLC	Safety analysis reported for 609 patients on atezolizumab 1200 mg every 3 weeks	Colitis Hepatitis Pneumonitis	2 (<1) 2 (<1) 6 (1)	0 (0) 2 (<1) 0 (0)
Massard et al.¹² 2016 Durvalumab	Phase 1/2 Inoperable/ metastatic transitional-cell urothelial carcinoma	61 patients on Durvalumab at dose of 10mg/kg every 2 weeks up to 12 months.	Any irAEs [§] Pruritus Diarrhea Colitis Pneumonitis	14 (23) 2 (3.3) 6 (9.8) 0 (0) 0 (0)	3 (4.9) 0 (0) 0 (0) 0 (0) 0 (0)

The cumulative numbers for the specific events may be greater than the number reported for organ category because patients with more than one event were counted separately for each event but only once for organ category.

§ Not all immune related adverse events were captured due to limited follow up.

@NSCLC non –small cell lung cancer.