Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Search Strategies

Sources	Search strategies
PubMed/MEDLINE	((("advanced melanoma" OR (("Melanoma"[Mesh] OR melanoma) AND (metastatic OR unresectable OR advanced OR Metastasis OR metastasize*))))) AND ((((("Ipilimumab"[Mesh] OR ipilimumab OR "Nivolumab"[Mesh] OR opdivo OR yervoy OR keytruda OR "pembrolizumab" [Supplementary Concept] OR Keytruda OR lambrolizumab OR "immune checkpoint inhibitor" OR "immune checkpoint inhibitors" OR CTLA-4 OR CTLA 4 Antigen OR "Programmed Cell Death 1 Receptor"[Mesh] OR PD-1 Receptor OR "CTLA-4 Antigen"[Mesh]))))
Elsevier EMBASE	('melanoma metastasis'/exp OR 'melanoma metastasis' OR 'metastatic melanoma'/exp OR 'metastatic melanoma' OR 'advanced melanoma'/exp OR 'advanced melanoma' OR 'unresectable melanoma' OR 'metastasized melanoma') AND ('mdx 101' OR 'mdx010' OR 'mdx101' OR 'strentarga' OR 'yervoy' OR 'nivolumab'/exp OR 'bms 936558' OR 'bms936558' OR 'cmab 819' OR 'cmab819' OR 'mdx 1106' OR 'mdx1106' OR 'nivolumab' OR 'ono 4538' OR 'ono4538' OR 'opdivo' OR 'pembrolizumab'/exp OR 'keytruda' OR 'lambrolizumab' OR 'mk 3475' OR 'mk3475' OR 'pembrolizumab' OR 'sch 900475' OR 'sch900475' OR 'cytotoxic t lymphocyte antigen 4'/exp OR 'cd152 antigen' OR 'ctla 4' OR 'ctla 4 antigen' OR 'ctla-4 antigen' OR 'antigen cd152' OR 'ctla4' OR 'cytotoxic t lymphocyte antigen 4' OR 'cytotoxic t lymphocyte associated antigen 4' OR 'programmed death 1 receptor'/exp OR 'cd279 antigen' OR 'pd 1 protein' OR 'pdcd1 protein' OR 'antigen cd279' OR 'programmed cell death 1 protein' OR 'programmed cell death 1 receptor' OR 'programmed cell death protein 1' OR 'programmed death 1 protein' OR 'programmed death 1 receptor' OR 'programmed death protein 1' OR 'protein pd 1' OR 'protein pdcd1' OR 'protein programmed cell death 1' OR 'protein programmed death 1' OR 'immune checkpoint inhibitors')
Thomson Reuters Web of Science	((TS=("Advanced melanoma" OR "Metastatic melanoma" OR "Unresectable melanoma"))) AND ((TS=(ipilimumab OR pembrolizumab OR nivolumab or Yervoy or keytruda or opdivo or “Immune checkpoint inhibitors”))) AND (TS=(controlled trial) OR TS=(prospective stud) OR TI=(random) OR TS=(placebo) OR TS=(double blind) OR TS=(comparative stud))
Elsevier Scopus	(TITLE-ABS-KEY ("advanced melanoma" OR "Metastatic melanoma" OR "Unresectable melanoma")) AND (TITLE-ABS-KEY (ipilimumab OR nivolumab OR pembrolizumab)) AND (TITLE-ABS-KEY ("clinical trials" OR "clinical trials as a topic" OR "randomized controlled trial" OR "Randomized Controlled Trials as Topic" OR "random allocation" OR "Double-Blind Method" OR "Cross-Over Studies" OR "Placebos" OR "multicenter study" OR "double blind procedure" OR "crossover procedure" OR "clinical trial" OR "controlled study" OR "randomization" OR "placebo"))

eTable 2. Characteristics of Included Randomized Controlled Trials (n=9) for Advanced Melanoma Events

Author, year	Country	Intervention (I) (dosage)	Comparator (C) (dosage)	Follow-up months	Patients, n		Age, Median		Female, %	
					I	C	I	C	I	C
Wolchok, 2010[1]	Multiple	IPI (3 mg/kg/q3 wks)	IPI (10 mg/kg/q3 wks)	8.7(I)/10.7(C)	72	72	59	56	33	39
Robert, 2014[2]	Multiple	NIV (3 mg/kg/q2 wks)	DTIC	5.2-16.7	210	208	64	66	42	40
Robert, 2015[3]	NR	PEM (10 mg/kg/q2 wks)	IPI (3 mg/kg/q3 wks)	7.9	279	278	61	62	42	42
		PEM (10 mg/kg/q3 wks)			277	278	63	62	37	42
Weber, 2015[4]	Multiple	NIV (3 mg/kg/q2 wks)	DTIC or PTX + CBP	24	272	133	62	62	35	36
Hodi, 2017[5]	Multiple	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	IPI (3 mg/kg/q3 wks)	24.0(I)/23.0(C)	95	47	64	67	34	32
Ascierto, 2017[6]	Multiple	IPI (10 mg/kg/q3 wks)	IPI (3 mg/kg/q3 wks)	14.5(I)/11.2(C)	365	362	62	62	40	36
Hamid, 2017[7]	Multiple	PEM (10 mg/kg/q3 wks)	DTIC + PTX, PTX, DTIC, or TEM	28.1	181	179	60	63	40	36
		PEM (2 mg/kg/q3 wks)			180	179	62	63	42	36
Weber, 2017[8]	Multiple	NIV (3 mg/kg/q2 wks)	IPI (10 mg/kg/q3 wks)	18	453	453	56	54	43	41
Wolchok, 2017[9]	Multiple	NIV (3 mg/kg/q2 wks)	IPI (3 mg/kg/q3 wks)	35.7(I)/18.6(C)	313	311	59	61	36	36
		NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)		38(I)/18.6(C)	313	311	59	61	34	36

Abbreviations: C: comparator; CBP: carboplatin; DTIC: dacarbazine; I: intervention; IPI: ipilimumab; MN: multination; NIV: nivolumab; NR: not reported; PEM: pembrolizumab; PTX: paclitaxel; TEM: temozolomide; wks: weeks.

eTable 3. Frequencies of Any Immune-Related AEs in the Included Studies (n=9)

Author, year/Treatment regimens	Wolchok, 2010[1]	Robert, 2014[2]	Robert, 2015[3]	Weber, 2015[4]	Hodi, 2017[5]	Ascierto, 2017[6]	Hamid, 2017[7]	Weber, 2017[8]	Wolchok, 2017[9]	Total
Threshold* (AE reporting rate)	5%	10%	NR	1%	NR	NR	5%	10%	5%	N/A
IPI (3 mg/kg/q3 wks)	46	N/A	187	N/A	43	197	N/A	N/A	268	741
IPI (10 mg/kg/q3 wks)	50	N/A	N/A	N/A	N/A	269	N/A	434	N/A	753
NIV (3 mg/kg/q2 wks)	N/A	153	N/A	181	N/A	N/A	N/A	385	270	989
NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	N/A	N/A	N/A	N/A	86	N/A	N/A	N/A	300	386
PEM (2 mg/kg/q3 wks)	N/A	N/A	N/A	N/A	N/A	N/A	125	N/A	N/A	125
PEM (10 mg/kg/q2 wks)	N/A	N/A	221	N/A	N/A	N/A	N/A	N/A	N/A	221
PEM (10 mg/kg/q3 wks)	N/A	N/A	202	N/A	N/A	N/A	136	N/A	N/A	338
Chemotherapy[a]	N/A	155	N/A	81	N/A	N/A	168	N/A	N/A	404

Abbreviations: **IPI**: ipilimumab; **NIV**: nivolumab; **PEM**: pembrolizumab. **N/A**: not applicable. **NR**: not reported.
*Threshold: The percentage of AEs the authors established as needing to reach to report AEs.
[a] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eTable 4. Probability Ranking of Being the Best Treatment Regimen With the Lowest Risk of Severe Immune-Related Adverse Events

Treatment regimens	**Median rank**[b]	**95% CrI**[c]
NIV (3 mg/kg/q2 wks)	1	1-5
PEM (10 mg/kg/q3 wks)	2	1-5
PEM (2 mg/kg/q3 wks)	3	1-7
PEM (10 mg/kg/q2 wks)	4	1-6
IPI (3 mg/kg/q3 wks)	5	2-6
Chemotherapy[d]	6	3-7
IPI (10 mg/kg/q3 wks)	7	5-8
NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	7	6-8

Abbreviations: CrI: credible interval; **IPI**: ipilimumab; **NIV**: nivolumab; **PEM**: pembrolizumab.
[a] We ranked the probability of being the best treatment regimen with the lowest risk of immune-related AEs by estimating the median and the 95% credible intervals of the posterior distribution for the rank of each treatment regimen. The lowest rank means the best treatment regimen (lowest risk of immune-related AEs).
[b] Median rank refers to median of the posterior distribution for the rank of each treatment.
[c] 95% CrI refers to 95% CrI of the posterior distribution for the rank of each treatment.
[d] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eTable 5. Probability Ranking of Being the Best Treatment Regimen With the Lowest Risk of Individual Severe Immune-Related Adverse Events

Treatment regimens	Median rank[b]	95% CrI[c]	Median rank[b]	95% CrI[c]	Median rank[b]	95% CrI[c]
Dermatologic AEs	**Pruritus**		**Rash**		**Vitiligo**	
Chemotherapy[d]	5	1-8	3	1-7	6	1-8
IPI (3 mg/kg/q3 wks)	5	2-7	7	4-8	4	1-8
IPI (10 mg/kg/q3 wks)	6	3-8	5	2-7	4	1-8
PEM (10 mg/kg/q2 wks)	2	1-7	3	1-8	4	1-8
NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	7	3-8	8	5-8	4	1-8
NIV (3 mg/kg/q2 wks)	3	1-6	3	1-6	5	1-8
PEM (10 mg/kg/q3 wks)	3	1-7	3	1-7	4	1-8
PEM (2 mg/kg/q3 wks)	4	1-8	2	1-8	5	1-8
Gastrointestinal AEs	**Diarrhea**		**Colitis**			
Chemotherapy[d]	4	2-7	2	2-8		
IPI (3 mg/kg/q3 wks)	6	3-7	6	4-8		
IPI (10 mg/kg/q3 wks)	8	5-8	7	4-8		
PEM (10 mg/kg/q2 wks)	5	1-8	4	2-7		
NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	7	2-8	8	4-8		
NIV (3 mg/kg/q2 wks)	3	1-6	3	2-6		
PEM (10 mg/kg/q3 wks)	3	1-7	5	2-8		
PEM (2 mg/kg/q3 wks)	1	1-5	N/A	N/A		
Endocrine AEs	**Hypothyroidism**		**Hypophysis**			
Chemotherapy[d]	5	1-8	N/A	N/A		
IPI (3 mg/kg/q3 wks)	4	1-7	5	3-6		
IPI (10 mg/kg/q3 wks)	5	1-8	6	2-6		
PEM (10 mg/kg/q2 wks)	6	1-8	2	1-6		
NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	4	1-8	4	1-6		
NIV (3 mg/kg/q2 wks)	3	1-7	2	1-5		
PEM (10 mg/kg/q3 wks)	4	1-8	2	1-6		
PEM (2 mg/kg/q3 wks)	5	1-8	N/A	N/A		

eTable 5 (Continued).

Treatment regimens	Median rank[b]	95% CrI[c]	Median rank[b]	95% CrI[c]	Median rank[b]	95% CrI[c]
Liver AEs	**ALT increased**		**AST increased**		**Hepatitis**	
Chemotherapy[d]	1	1-5	1	1-5	N/A	N/A
IPI (3 mg/kg/q3 wks)	2	1-3	2	1-3	1	1-3
IPI (10 mg/kg/q3 wks)	4	3-5	5	3-5	2	1-4
PEM (10 mg/kg/q2 wks)	N/A	N/A	N/A	N/A	3	1-4
NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	5	3-5	4	3-5	N/A	N/A
NIV (3 mg/kg/q2 wks)	2	1-4	2	1-4	N/A	N/A
PEM (10 mg/kg/q3 wks)	N/A	N/A	N/A	N/A	3	1-4
PEM (2 mg/kg/q3 wks)	N/A	N/A	N/A	N/A	N/A	N/A
Pulmonary AEs	**Pneumonitis**					
Chemotherapy[d]	5	1-7				
IPI (3 mg/kg/q3 wks)	3	1-6				
IPI (10 mg/kg/q3 wks)	7	2-7				
PEM (10 mg/kg/q2 wks)	2	1-7				
NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	5	1-7				
NIV (3 mg/kg/q2 wks)	3	1-6				
PEM (10 mg/kg/q3 wks)	3	1-7				
PEM (2 mg/kg/q3 wks)	N/A	N/A				

Abbreviations: AEs: adverse events; **ALT**: alanine aminotransferase; **AST**: aspartate aminotransferase; **CrI**: credible interval; **IPI**: ipilimumab; **NIV**: nivolumab; **N/A**: not applicable. No specific individual immune-related AE was reported in that treatment regimen in the included studies, so the indirect evidence cannot be generated. (For example, pneumonitis was not reported in any included studies comparing PEM (2 mg/kg/q3 wks) with other treatments, so we cannot generate the indirect evidence of pneumonitis from PEM (2 mg/kg/q3 wks) by linking that with other treatments); **PEM**: pembrolizumab.

[a] We ranked the probability of being the best treatment regimen with the lowest risk of immune-related AEs by estimating the median and the 95% credible intervals of the posterior distribution for the rank of each treatment regimen. The lowest rank means the best treatment regimen (lowest risk of immune-related AEs).

[b] Median rank refers to median of the posterior distribution for the rank of each treatment.

[c] 95% CrI refers to 95% CrI of the posterior distribution for the rank of each treatment[d] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eTable 6. Secondary Outcomes of Individual Skin-Related Immune-Related Adverse Events by Severity

Treatments	Comparators	Pruritus		Rash		Vitiligo	
		OR (95%CrI)		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3
PEM (2 mg/kg/q3 wks)	Chemotherapy[a]	6.78 (1.38-44.50)*	NR	3.32 (0.64-16.57)	0.78 (0.002-96.33)	NR	NR
	IPI (3 mg/kg/q3 wks)	1.11 (0.13-9.81)	NR	0.73 (0.10-5.30)	0.08 (0.0001-11.94)	3.09 (0.06-86.02)	NR
	IPI (10 mg/kg/q3 wks)	1.03 (0.10-9.15)	0.19 (0.0003-68.43)	0.92 (0.11-7.42)	0.19 (0.0002-31.94)	NR	NR
	PEM (10 mg/kg/q2 wks)	1.05 (0.07-15.67)	NR	0.73 (0.06-8.52)	NR	0.56 (0.004-27.54)	NR
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	1.00 (0.08-11.61)	0.1 (0.0001-47.11)	0.46 (0.05-4.29)	0.03 (0.00004-50.67)	NR	NR
	NIV (3 mg/kg/q2 wks)	2.14 (0.28-16.47)	NR	0.98 (0.14-6.26)	0.56 (0.001-83.31)	1.01 (0.02-20.78)	NR
	PEM (10 mg/kg/q3 wks)	0.99 (0.12-8.07)	NR	0.90 (0.13-6.22)	NR	0.62 (0.02-13.01)	NR
PEM (10 mg/kg/q3 wks)	Chemotherapy[a]	6.88 (1.90-32.58)*	0.34 (0.003-13.45)	3.70 (0.97-13.64)	1.17 (0.02-49.24)	NR	0.52 (0.003-51.62)
	IPI (3 mg/kg/q3 wks)	1.12 (0.29-4.41)	0.24 (0.01-4.9)	0.81 (0.23-2.88)	0.12 (0.002-2.36)	5.04 (0.45-45.98)	NR
	IPI (10 mg/kg/q3 wks)	1.04 (0.21-4.98)	0.13 (0.002-4.24)	1.03 (0.23-4.49)	0.28 (0.004-8.62)	NR	NR
	PEM (10 mg/kg/q2 wks)	1.06 (0.14-8.82)	NR	0.81 (0.12-5.41)	NR	0.92 (0.02-19.19)	NR
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	1.01 (0.16-5.91)	0.06 (0.001-2.61)	0.52 (0.09-2.67)	0.05 (0.001-1.37)	2.64 (0.07-73.98)	NR
	NIV (3 mg/kg/q2 wks)	2.18 (0.49-9.61)	1.06 (0.02-42.52)	1.09 (0.27-4.21)	0.82 (0.01-22.75)	1.67 (0.09-17.85)	0.58 (0.002-87.66)

eTable 6 (Continued).

Treatments	Comparators	Pruritus		Rash		Vitiligo	
		OR (95%CrI)		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3
NIV (3 mg/kg/q2 wks)	Chemotherapy[a]	3.15 (1.17-11.29)*	0.33 (0.01-4.68)	3.41 (1.15-10.11)*	1.53 (0.10-26.1)	NR	0.84 (0.02-35.02)
	IPI (3 mg/kg/q3 wks)	0.52 (0.17-1.58)	0.23 (0.01-2.66)	0.74 (0.27-2.15)	0.14 (0.02-0.87)	2.93 (0.39-33.23)	NR
	IPI (10 mg/kg/q3 wks)	0.48 (0.14-1.49)	0.12 (0.01-1.26)	0.94 (0.32-2.85)	0.35 (0.07-1.76)	2.87 (0.12-98.34)	NR
	PEM (10 mg/kg/q2 wks)	0.49 (0.07-3.64)	NR	0.74 (0.12-4.79)	NR	0.52 (0.02-16.02)	NR
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	0.47 (0.09-2.28)	0.06 (0.002-1.18)	0.47 (0.1-2.08)	0.06 (0.004-0.49)*	1.46 (0.07-53.11)	NR
NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	6.73 (1.29-50.07)*	NR	7.20 (1.31-38.56)*	NR	NR	NR
	IPI (3 mg/kg/q3 wks)	1.11 (0.36-3.64)	3.52 (0.42-43.73)	1.56 (0.54-4.81)	2.42 (0.57-15.03)	1.95 (0.15-23.95)	NR
	IPI (10 mg/kg/q3 wks)	1.03 (0.22-4.69)	1.95 (0.10-37.14)	1.97 (0.48-8.70)	6.04 (0.74-72.79)	1.94 (0.06-62.34)	NR
	PEM (10 mg/kg/q2 wks)	1.05 (0.15-8.38)	NR	1.55 (0.25-10.10)	NR	0.34 (0.01-11.23)	NR
PEM (10 mg/kg/q2 wks)	Chemotherapy[a]	6.44 (0.86-60.21)	0.16 (0.0002-24.99)	4.59 (0.63-32.49)	NR	NR	NR
	IPI (3 mg/kg/q3 wks)	1.05 (0.20-5.19)	0.13 (0.0003-4.46)	1.01 (0.22-4.54)	0.12(0.0002-4.01)	5.77 (0.46-92.17)	NR
	IPI (10 mg/kg/q3 wks)	0.98 (0.13-6.07)	0.06 (0.0001-3.63)	1.27 (0.21-7.44)	0.28 (0.0004-15.26)	NR	NR

eTable 6 (Continued).

Treatments	Comparators	Pruritus		Rash		Vitiligo	
		OR (95%CrI)		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3
IPI (10 mg/kg/q3 wks)	Chemotherapy[a]	6.62 (1.73-36.71)*	2.68 (0.07-92.85)	3.65 (0.85-14.98)	4.39 (0.20-97.3)	NR	NR
	IPI (3 mg/kg/q3 wks)	1.08 (0.41-3.13)	1.86 (0.29-14.38)	0.79 (0.31-2.05)	0.41 (0.10-2.04)	1.01(0.08-11.72)	1.09 (0.04-25.98)
IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	6.09 (1.70-29.16)*	1.42 (0.04-46.21)	4.59 (1.18-16.88)*	NR	4.51 (0.34-61.74)	0.38 (0.002-51.1)

Abbreviations: CrI: credible interval; **IPI**: ipilimumab; **NIV**: nivolumab; **NR**: not reportable due to small sample sizes; N/A: not applicable. No specific individual immune-related AE was reported in that treatment regimen in the included studies, so the indirect evidence cannot be generated. (For example, pneumonitis was not reported in any included studies comparing PEM (2 mg/kg/q3 wks) with other treatments, so we cannot generate the indirect evidence of pneumonitis from PEM (2 mg/kg/q3 wks) by linking that with other treatments); OR: odds ratio; PEM: pembrolizumab.
*indicates statistical significant.
[a] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eTable 7. Secondary Outcomes of Individual Gastrointestinal Tract-Related Immune-Related Adverse Events by Severity

Treatments	Comparators	Diarrhea		Colitis	
		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3
				N/A	N/A
PEM (2 mg/kg/q3 wks)	Chemotherapy[a]	1.14 (0.47-2.77)	0.06 (0.0001-1.73)		
	IPI (3 mg/kg/q3 wks)	0.57 (0.2-1.64)	0.03 (0.0001-1.33)		
	IPI (10 mg/kg/q3 wks)	0.46 (0.15-1.33)	0.01 (0.00002-0.44)*		
	PEM (10 mg/kg/q2 wks)	0.80 (0.24-2.84)	0.03 (0.0001-2.58)		
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	0.35 (0.11-1.1)	0.02 (0.00004-1.28)		
	NIV (3 mg/kg/q2 wks)	1.17 (0.43-3.25)	0.07 (0.0001-2.98)		
	PEM (10 mg/kg/q3 wks)	0.89 (0.33-2.37)	0.07 (0.0001-2.47)		
PEM (10 mg/kg/q3 wks)	Chemotherapy[a]	1.29 (0.66-2.53)	0.89 (0.13-6.16)	NR	NR
	IPI (3 mg/kg/q3 wks)	0.64 (0.35-1.19)	0.43 (0.07-2.76)	0.42 (0.05-3.3)	0.33 (0.02-4.11)
	IPI (10 mg/kg/q3 wks)	0.52 (0.25-1.04)	0.12 (0.01-1.14)	0.44(0.03-5.68)	0.25 (0.01-5.85)
	PEM (10 mg/kg/q2 wks)	0.90 (0.39-2.21)	0.54 (0.04-7.55)	2.21(0.11-42.8)	1.86 (0.05-74.74)
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	0.39 (0.18-0.87)*	0.31 (0.03-3.44)	0.26 (0.02-2.73)	0.17 (0.01-3.09)
	NIV (3 mg/kg/q2 wks)	1.33 (0.70-2.62)	1.02 (0.14-8.07)	2.33 (0.12-44.96)	NR
NIV (3 mg/kg/q2 wks)	Chemotherapy[a]	0.98 (0.57-1.60)	0.85 (0.14-5.10)	NR	NR
	IPI (3 mg/kg/q3 wks)	0.48 (0.30-0.78)*	0.42 (0.10-1.72)	0.18 (0.02-1.46)	0.11 (0.01-1.64)
	IPI (10 mg/kg/q3 wks)	0.39 (0.23-0.61)*	0.12 (0.02-0.54)*	0.19 (0.01-2.54)	0.08 (0.003-2.12)
	PEM (10 mg/kg/q2 wks)	0.68 (0.30-1.60)	0.52 (0.04-6.01)	0.95 (0.04-20.41)	0.63 (0.02-29.38)
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	0.30 (0.15-0.58)*	0.31 (0.04-2.40)	0.11 (0.01-1.23)	0.06 (0.002-1.13)

eTable 7 (Continued).

Treatments	Comparators	Diarrhea		Colitis	
		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3
NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	3.27 (1.46-7.22)*	2.77 (0.23-29.58)	NR	NR
	IPI (3 mg/kg/q3 wks)	1.62 (0.98-2.78)	1.36 (0.31-5.13)	1.60 (0.42-8.95)	1.92 (0.39-17.66)
	IPI (10 mg/kg/q3 wks)	1.32 (0.65-2.52)	0.40 (0.05-2.71)	1.69 (0.23-17.86)	1.46 (0.10-28.21)
	PEM (10 mg/kg/q2 wks)	2.27 (0.97-5.59)	1.69 (0.13-18.85)	NR	NR
PEM (10 mg/kg/q2 wks)	Chemotherapy[a]	1.44 (0.55-3.51)	1.68 (0.10-26.39)	NR	NR
	IPI (3 mg/kg/q3 wks)	0.71 (0.35-1.42)	0.81 (0.10-6.19)	0.19 (0.02-1.66)	0.18 (0.01-2.26)
	IPI (10 mg/kg/q3 wks)	0.57 (0.24-1.27)	0.23 (0.02-2.82)	0.20 (0.01-2.79)	0.13 (0.004-3.15)
IPI (10 mg/kg/q3 wks)	Chemotherapy[a]	2.49 (1.29-4.94)*	7.14 (0.79-67.23)	NR	NR
	IPI (3 mg/kg/q3 wks)	1.23 (0.82-2.02)	3.44 (0.83-15.2)	0.95 (0.21-4.44)	1.34 (0.19-11.72)
IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	2.02 (1.05-3.71)*	2.06 (0.27-14.91)	NR	NR

Abbreviations: CrI: credible interval; **IPI**: ipilimumab; **NIV**: nivolumab; **NR**: not reportable due to small sample sizes; **N/A**: not applicable. Nospecific individual immune-related AE was reported in that treatment regimen in the included studies, so the indirect evidence cannot be generated. (For example, pneumonitis was not reported in any included studies comparing PEM (2 mg/kg/q3 wks) with other treatments, so we cannot generate the indirect evidence of pneumonitis from PEM (2 mg/kg/q3 wks) by linking that with other treatments); OR: odds ratio; **PEM**: pembrolizumab.
*indicates statistical significant.
[a] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eTable 8. Secondary Outcomes of Individual Endocrine-Related Immune-Related Adverse Events by Severity

Treatments	Comparators	Hypothyroidism		Hypophysitis	
		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3
				N/A	N/A
PEM (2 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR		
	IPI (3 mg/kg/q3 wks)	NR	NR		
	IPI (10 mg/kg/q3 wks)	NR	NR		
	PEM (10 mg/kg/q2 wks)	0.93 (0.03-25.94)	NR		
	NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	1.87 (0.09-48.61)	NR		
	NIV (3 mg/kg/q2 wks)	2.54 (0.12-47.2)	NR		
	PEM (10 mg/kg/q3 wks)	1.09 (0.09-12.44)	NR		
PEM (10 mg/kg/q3 wks)	Chemotherapy[a]	NR	0.57 (0.003-57.87)	N/A	N/A
	IPI (3 mg/kg/q3 wks)	5.01 (0.84-32.08)	NR	0.26 (0.02-2.72)	0.18 (0.002-3.71)
	IPI (10 mg/kg/q3 wks)	3.99 (0.41-39.97)	NR	0.25 (0.01-7.86)	0.06 (0.0002-4.77)
	PEM (10 mg/kg/q2 wks)	0.85 (0.08-9.24)	0.44 (0.002-62.69)	NR	NR
	NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	1.70 (0.21-17.91)	NR	0.12 (0.01-1.86)	0.21 (0.002-8.37)
	NIV (3 mg/kg/q2 wks)	2.29 (0.26-18.72)	NR	1.95 (0.07-53.66)	0.69 (0.004-40.06)
NIV (3 mg/kg/q2 wks)	Chemotherapy[a]	NR	0.35 (0.003-50.98)	N/A	N/A
	IPI (3 mg/kg/q3 wks)	2.16 (0.58-9.98)	0.83 (0.02-24.63)	0.13 (0.01-0.91)*	0.25 (0.02-4.61)
	IPI (10 mg/kg/q3 wks)	1.73 (0.43-7.98)	0.36 (0.01-6.76)	0.13 (0.02-0.74)*	0.10 (0.01-0.92)*
	PEM (10 mg/kg/q2 wks)	0.36 (0.04-4.17)	0.27 (0.001-80.28)	1.16 (0.04-69.06)	NR
	NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	0.71 (0.14-6.10)	0.60 (0.01-39.46)	0.06 (0.01-0.65)*	0.31 (0.01-10.71)

eTable 8 (Continued).

Treatments	Comparators	Hypothyroidism		Hypophysitis	
		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grad ≥3	Grade 1-5	Grade ≥3
NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR	N/A	N/A
	IPI (3 mg/kg/q3 wks)	2.98 (0.71-9.84)	1.27 (0.05-46.99)	2.09 (0.50-9.43)	0.80 (0.11-5.87)
	IPI (10 mg/kg/q3 wks)	2.43 (0.28-15.18)	0.60 (0.01-49.95)	2.06 (0.16-32.96)	0.32 (0.003-9.87)
	PEM (10 mg/kg/q2 wks)	0.49 (0.04-4.39)	NR	NR	NR
PEM (10 mg/kg/q2 wks)	Chemotherapy[a]	NR	NR	N/A	N/A
	IPI (3 mg/kg/q3 wks)	5.98 (0.92-40.69)	NR	0.11 (0.003-1.43)	0.17 (0.003-3.46)
	IPI (10 mg/kg/q3 wks)	4.79 (0.41-51.00)	NR	0.11 (0.002-3.57)	0.06 (0.0002-4.47)
IPI (10 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR	N/A	N/A
	IPI (3 mg/kg/q3 wks)	1.24 (0.28-5.94)	2.19 (0.07-91.41)	1.02 (0.10-9.37)	NR
IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	NR	0.44 (0.003-73.97)	N/A	N/A

Abbreviations: CrI: credible interval; **IPI**: ipilimumab; **NIV**: nivolumab; **NR**: not reportable due to small sample sizes; **N/A**: not applicable. No specific individual immune-related AE was reported in that treatment regimen in the included studies, so the indirect evidence cannot be generated. (For example, pneumonitis was not reported in any included studies comparing PEM (2 mg/kg/q3 wks) with other treatments, so we cannot generate the indirect evidence of pneumonitis from PEM (2 mg/kg/q3 wks) by linking that with other treatments); OR: odds ratio; **PEM**: pembrolizumab.
*****indicates statistical significant.
[a] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eTable 9. Secondary Outcomes of Individual Liver-Related Immune-Related Adverse Events by Severity

Treatments	Comparators	ALT increased		AST increased		Hepatitis	
		OR (95%CrI)		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3
		N/A	N/A			N/A	N/A
PEM (2 mg/kg/q3 wks)	Chemotherapy[a]						
	IPI (3 mg/kg/q3 wks)						
	IPI (10 mg/kg/q3 wks)						
	PEM (10 mg/kg/q2 wks)						
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)						
	NIV (3 mg/kg/q2 wks)						
	PEM (10 mg/kg/q3 wks)						
		N/A	N/A				
PEM (10 mg/kg/q3 wks)	Chemotherapy[a]					N/A	N/A
	IPI (3 mg/kg/q3 wks)					1.68 (0.09-30.1)	NR
	IPI (10 mg/kg/q3 wks)					0.60 (0.01-37.56)	NR
	PEM (10 mg/kg/q2 wks)					1.81 (0.04-84.64)	1.83(0.04-83.96)
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)					N/A	N/A
	NIV (3 mg/kg/q2 wks)					N/A	N/A

eTable 9 (Continued).

Treatments	Comparators	ALT increased		AST increased		Hepatitis	
		OR (95%CrI)		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3
						N/A	**N/A**
NIV (3 mg/kg/q2 wks)	Chemotherapy[a]	NR	NR	NR	NR		
	IPI (3 mg/kg/q3 wks)	1.47 (0.30-8.06)	0.91 (0.15-5.63)	1.59 (0.34-8.11)	1.28 (0.14-12.71)		
	IPI (10 mg/kg/q3 wks)	0.31 (0.05-1.40)	0.16 (0.03-0.86)*	0.30 (0.06-1.25)	0.10 (0.01-0.76)*		
	PEM (10 mg/kg/q2 wks)	N/A	N/A	N/A	N/A		
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	0.26 (0.04-2.67)	0.12 (0.01-1.12)	0.31(0.05-2.61)	0.12(0.01-1.69)		
						N/A	**N/A**
NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR	NR	NR		
	IPI (3 mg/kg/q3 wks)	5.62 (1.19-21.46)*	7.15 (1.57-47.37)*	5.12(1.21-19.11)*	10.42(1.72-92.95)*		
	IPI (10 mg/kg/q3 wks)	1.19 (0.1-8.42)	1.27 (0.12-15.45)	0.98(0.09-6.54)	0.78(0.04-14.62)		
	PEM (10 mg/kg/q2 wks)	N/A	N/A	N/A	N/A		
		N/A	**N/A**	**N/A**	**N/A**		
PEM (10 mg/kg/q2 wks)	Chemotherapy[a]					N/A	N/A
	IPI (3 mg/kg/q3 wks)					0.92 (0.10-18.16)	NR
	IPI (10 mg/kg/q3 wks)					0.32 (0.01-22.14)	NR

eTable 9 (Continued).

Treatments	Comparators	ALT increased		AST increased		Hepatitis	
		OR (95%CrI)		OR (95%CrI)		OR (95%CrI)	
		Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3	Grade 1-5	Grade ≥3
IPI (10 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR	NR	NR	N/A	N/A
	IPI (3 mg/kg/q3 wks)	4.79 (1.02-28.17)*	5.75 (0.96-38.82)	5.28(1.21-33.28)*	NR	2.78 (0.15-60.73)	2.76 (0.15-61.00)
IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR	NR	NR	N/A	N/A

Abbreviations: ALT: alanine aminotransferase; **AST**: aspartate aminotransferase; **CrI**: credible interval; **IPI**: ipilimumab; **NIV**: nivolumab; **NR**: not reportable due to small sample sizes; **N/A**: not applicable. No specific individual immune-related AE was reported in that treatment regimen in the included studies, so the indirect evidence cannot be generated. (For example, pneumonitis was not reported in any included studies comparing PEM (2 mg/kg/q3 wks) with other treatments, so we cannot generate the indirect evidence of pneumonitis from PEM (2 mg/kg/q3 wks) by linking that with other treatments); **OR**: odds ratio; **PEM**: pembrolizumab.
*indicates statistical significant.
[a] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eTable 10. Secondary Outcomes of Individual Pulmonary-Related Immune-Related Adverse Events by Severity

Treatments	**Comparators**	**Pneumonitis**	
		OR (95%CrI)	
		Grade 1-5	**Grade ≥3**
		N/A	**N/A**
PEM (2 mg/kg/q3 wks)	Chemotherapy[a]		
	IPI (3 mg/kg/q3 wks)		
	IPI (10 mg/kg/q3 wks)		
	PEM (10 mg/kg/q2 wks)		
	NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)		
	NIV (3 mg/kg/q2 wks)		
	PEM (10 mg/kg/q3 wks)		
PEM (10 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR
	IPI (3 mg/kg/q3 wks)	NR	NR
	IPI (10 mg/kg/q3 wks)	NR	NR
	PEM (10 mg/kg/q2 wks)	NR	NR
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	NR	NR
	NIV (3 mg/kg/q2 wks)	NR	NR
NIV (3 mg/kg/q2 wks)	Chemotherapy[a]	NR	NR
	IPI (3 mg/kg/q3 wks)	1.01 (0.07-15.17)	0.96 (0.01-56.66)
	IPI (10 mg/kg/q3 wks)	0.05 (0.00004-5.37)	0.05 (0.00004-14.13)
	PEM (10 mg/kg/q2 wks)	NR	NR
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	0.20 (0.01-7.31)	0.24 (0.002-14.00)

eTable 10 (Continued).

Treatments	Comparators	Pneumonitis	
		OR (95%CrI)	
		Grade 1-5	Grade ≥3
NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR
	IPI (3 mg/kg/q3 wks)	NR	NR
	IPI (10 mg/kg/q3 wks)	NR	NR
	PEM (10 mg/kg/q2 wks)	NR	NR
PEM (10 mg/kg/q2 wks)	Chemotherapy[a]	NR	NR
	IPI (3 mg/kg/q3 wks)	0.93 (0.02-62.37)	0.29 (0.0003-32.25)
	IPI (10 mg/kg/q3 wks)	0.04 (0.00002-13.1)	0.01 (0.000003-7.07)
IPI (10 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR
	IPI (3 mg/kg/q3 wks)	NR	NR
IPI (3 mg/kg/q3 wks)	Chemotherapy[a]	NR	NR

Abbreviations: CrI: credible interval; **IPI**: ipilimumab; **NIV**: nivolumab; **NR**: not reportable due to small sample sizes; **N/A**: not applicable. No specific individual immune-related AE was reported in that treatment regimen in the included studies, so the indirect evidence cannot be generated. (For example, pneumonitis was not reported in any included studies comparing PEM (2 mg/kg/q3 wks) with other treatments, so we cannot generate the indirect evidence of pneumonitis from PEM (2 mg/kg/q3 wks) by linking that with other treatments); **OR**: odds ratio; **PEM**: pembrolizumab.
*indicates statistical significant.
[a] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eTable 11. Node-Splitting Analysis[a] of the Primary Outcome: Any Immune-Related Adverse Events

Treatments	Comparators	Direct effect		Indirect effect		Inconsistency estimate	
		OR	95% CrI	OR	95% CrI	Ratio of the OR[b]	P-value[c]
PEM (2 mg/kg/q3 wks)	Chemotherapy[d]	0.58	0.15 to 2.17	1.14	NR	0.51	1.00
	IPI (3 mg/kg/q3 wks)	N/A	N/A	0.63	0.15 to 2.70	N/A	1.01
	IPI (10 mg/kg/q3 wks)	N/A	N/A	0.29	0.06 to 1.39	N/A	1.02
	PEM (10 mg/kg/q2 wks)	N/A	N/A	0.46	0.09 to 2.42	N/A	1.01
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	N/A	N/A	0.29	0.05 to 1.56	N/A	1.02
	NIV (3 mg/kg/q2 wks)	N/A	N/A	0.89	0.22 to 3.62	1.23	1.01
	PEM (10 mg/kg/q3 wks)	0.73	0.20 to 2.69	1.93	NR	0.38	0.99
PEM (10 mg/kg/q3 wks)	Chemotherapy[d]	0.75	0.12 to 4.84	1.08	0.08 to 15.05	0.70	0.73
	IPI (3 mg/kg/q3 wks)	0.99	0.17 to 5.81	0.69	0.05 to 9.15	1.44	1.28
	IPI (10 mg/kg/q3 wks)	N/A	N/A	0.41	0.12 to 1.44	N/A	1.01
	PEM (10 mg/kg/q2 wks)	0.69	0.10 to 4.66	0.48	0.02 to 14.12	1.45	1.26
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	N/A	N/A	0.41	0.10 to 1.65	N/A	1.01
	NIV (3 mg/kg/q2 wks)	N/A	N/A	1.26	0.41 to 3.90	N/A	1.00

eTable 11 (Continued).

Treatments	Comparators	Direct effect		Indirect effect		Inconsistency estimate	
		OR	95% CrI	OR	95% CrI	Ratio of the OR[b]	P-value[c]
NIV (3 mg/kg/q2 wks)	Chemotherapy[d]	0.71	0.18 to 2.77	0.48	0.02 to 10.03	1.47	1.28
	IPI (3 mg/kg/q3 wks)	1.04	0.25 to 4.22	0.51	0.15 to 1.67	2.05	1.72
	IPI (10 mg/kg/q3 wks)	0.25	0.04 to 1.37	0.44	0.07 to 2.87	0.56	0.44
	PEM (10 mg/kg/q2 wks)	N/A	N/A	0.52	0.13 to 2.12	N/A	1.01
	NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	0.30	0.05 to 1.92	0.27	0.03 to 2.50	1.10	1.15
NIV (1 mg/kg/q3 wks) + IPI (3 mg/kg/q3 wks)	Chemotherapy[d]	N/A	N/A	2.07	0.54 to 7.89	N/A	1.00
	IPI (3 mg/kg/q3 wks)	2.26	0.76 to 6.74	2.25	NR	1.01	1.00
	IPI (10 mg/kg/q3 wks)	N/A	N/A	1.00	0.30 to 3.42	N/A	1.01
	PEM (10 mg/kg/q2 wks)	N/A	N/A	1.60	0.34 to 7.61	N/A	1.00
PEM (10 mg/kg/q2 wks)	Chemotherapy[d]	N/A	N/A	1.29	0.31 to 5.44	N/A	1.01
	IPI (3 mg/kg/q3 wks)	1.43	0.21 to 9.92	1.01	0.03 to 30.30	1.42	1.24
	IPI (10 mg/kg/q3 wks)	N/A	N/A	0.63	0.15 to 2.62	1.73	1.01
IPI (10 mg/kg/q3 wks)	Chemotherapy[d]	N/A	N/A	2.06	0.63 to 6.80	N/A	1.00
	IPI (3 mg/kg/q3 wks)	1.89	0.57 to 6.30	3.41	0.38 to 30.61	0.55	0.45
IPI (3 mg/kg/q3 wks)	Chemotherapy[d]	N/A	N/A	0.95	0.32 to 2.80	N/A	1.01

Abbreviations: CrI: credible interval; **IPI**: ipilimumab; **N/A**: not applicable. Nospecific individual immune-related AE was reported in that treatment regimen in the included studies, so the indirect evidence cannot be generated. (For example, pneumonitis was not reported in any included studies comparing PEM (2 mg/kg/q3 wks) with other treatments, so we cannot generate the indirect evidence of pneumonitis from PEM (2 mg/kg/q3 wks) by linking that with other treatments); **NIV**: nivolumab; **NR**: not reportable due to small sample sizes; OR: odds ratio; **PEM**: pembrolizumab; **SD**: standard deviations. [a] We compared posterior means and standard deviations of the log-odds ratios obtained from direct and indirect evidence for each treatment comparison, and then compared

the inconsistency as direct effect minus indirect effect at each treatment comparison. [b] The ratio of the OR indicates ORdirect divied by ORindirect [c] P ≤ 0·05 indicates a significant inconsistency between the direct effect and indirect effects.[d] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eTable 12. Node-Splitting Analysis[a] of the Primary Outcome: Severe Immune-Related Adverse Events

Treatments	Comparators	Direct effect		Indirect effect		Inconsistency estimate	
		OR	95% CrI	OR	95% CrI	Ratio of the OR[b]	P-value[c]
PEM (2 mg/kg/q3 wks)	Chemotherapy[d]	0.42	0.08 to 2.27	0.99	NR	0.43	0.99
	IPI (3 mg/kg/q3 wks)	N/A	N/A	0.47	0.07 to 3.08	N/A	N/A
	IPI (10 mg/kg/q3 wks)	N/A	N/A	0.15	0.02 to 1.17	N/A	N/A
	PEM (10 mg/kg/q2 wks)	N/A	N/A	0.69	0.08 to 6.11	N/A	N/A
	NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	N/A	N/A	0.12	0.01 to 0.95	N/A	N/A
	NIV (3 mg/kg/q2 wks)	N/A	N/A	0.75	0.12 to 4.59	N/A	N/A
	PEM (10 mg/kg/q3 wks)	0.79	0.14 to 4.40	3.34	NR	0.24	1.00
PEM (10 mg/kg/q3 wks)	Chemotherapy[d]	0.56	0.06 to 5.13	0.30	0.01 to 7.11	0.62	1.36
	IPI (3 mg/kg/q3 wks)	0.45	0.05 to 3.98	0.85	0.04 to 19.54	1.90	0.63
	IPI (10 mg/kg/q3 wks)	N/A	N/A	0.18	0.04 to 0.89	N/A	1.01
	PEM (10 mg/kg/q2 wks)	0.72	0.08 to 6.40	1.34	0.03 to 59.88	0.54	0.68
	NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	N/A	N/A	0.14	0.02 to 0.73	N/A	1.01
	NIV (3 mg/kg/q2 wks)	N/A	N/A	0.87	0.21 to 3.71	N/A	1.00
NIV (3 mg/kg/q2 wks)	Chemotherapy[d]	0.47	0.10 to 2.25	0.90	0.03 to 28.23	0.52	0.63
	IPI (3 mg/kg/q3 wks)	0.71	0.07 to 6.72	0.62	0.10 to 3.82	1.14	1.12
	IPI (10 mg/kg/q3 wks)	5.08	0.50 to 52.07	0.21	0.02 to 2.65	-0.05	0.94
	PEM (10 mg/kg/q2 wks)	N/A	N/A	0.93	0.15 to 5.63	N/A	1.00
	NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	0.19	0.02 to 1.71	0.12	0.01 to 1.73	1.60	1.34

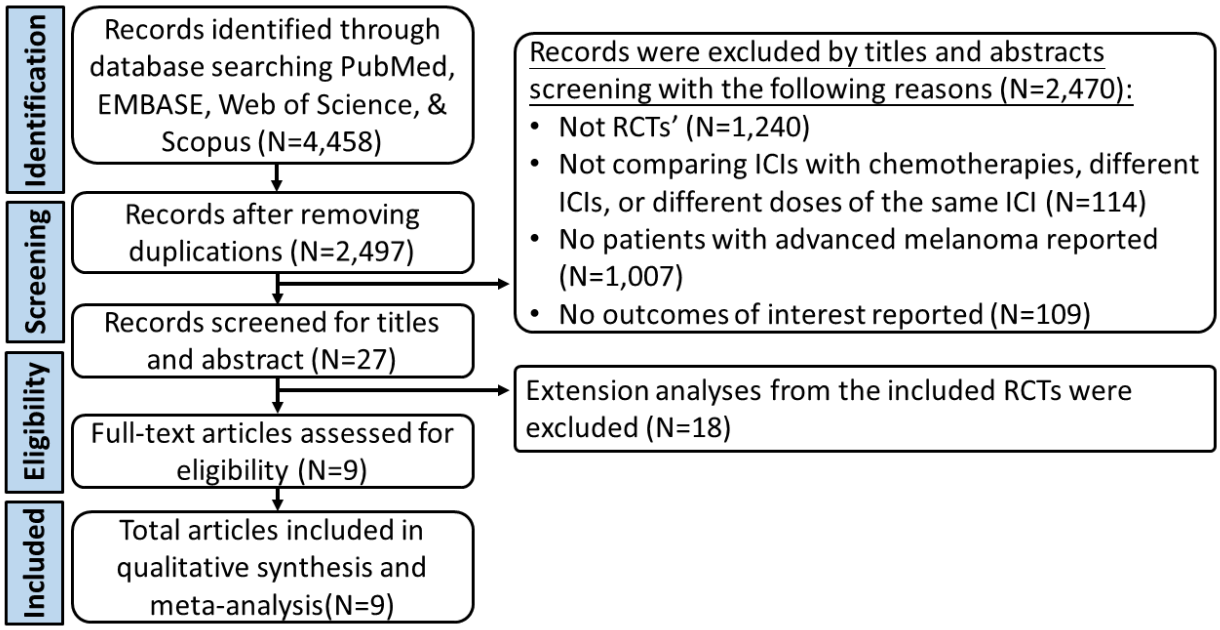
eTable 12 (Continued).

Treatments	Comparators	Direct effect		Indirect effect		Inconsistency estimate	
		OR	95% CrI	OR	95% CrI	Ratio of the OR[b]	P-value[c]
NIV (1 mg/kg/q3 wks)+ IPI (3 mg/kg/q3 wks)	Chemotherapy[d]	N/A	N/A	3.38	0.67 to 16.96	0.26	0.99
	IPI (3 mg/kg/q3 wks)	4.28	1.27 to 14.42	0.70	NR	6.15	1.01
	IPI (10 mg/kg/q3 wks)	N/A	N/A	1.32	0.31 to 5.70	N/A	1.00
	PEM (10 mg/kg/q2 wks)	N/A	N/A	5.98	0.89 to 40.34	N/A	0.98
PEM (10 mg/kg/q2 wks)	Chemotherapy[d]	N/A	N/A	0.56	0.09 to 3.65	1.56	1.00
	IPI (3 mg/kg/q3 wks)	0.62	0.07 to 5.69	1.15	0.02 to 56.02	-0.62	0.68
	IPI (10 mg/kg/q3 wks)	N/A	N/A	0.22	0.03 to 1.40	N/A	1.01
IPI (10 mg/kg/q3 wks)	Chemotherapy[d]	N/A	N/A	0.94	0.77	N/A	1.00
	IPI (3 mg/kg/q3 wks)	3.09	0.59 to 16.30	3.25	0.18 to 59.66	0.95	0.94
IPI (3 mg/kg/q3 wks)	Chemotherapy[d]	N/A	N/A	2.56	0.56 to 11.59	N/A	1.00

Abbreviations: CrI: credible interval; **IPI**: ipilimumab; **N/A**: not applicable. Nospecific individual immune-related AE was reported in that treatment regimen in the included studies, so the indirect evidence cannot be generated. (For example, pneumonitis was not reported in any included studies comparing PEM (2 mg/kg/q3 wks) with other treatments, so we cannot generate the indirect evidence of pneumonitis from PEM (2 mg/kg/q3 wks) by linking that with other treatments); **NIV**: nivolumab; **NR**: not reportable due to small sample sizes; OR: odds ratio; **PEM**: pembrolizumab; **SD**: standard deviations.

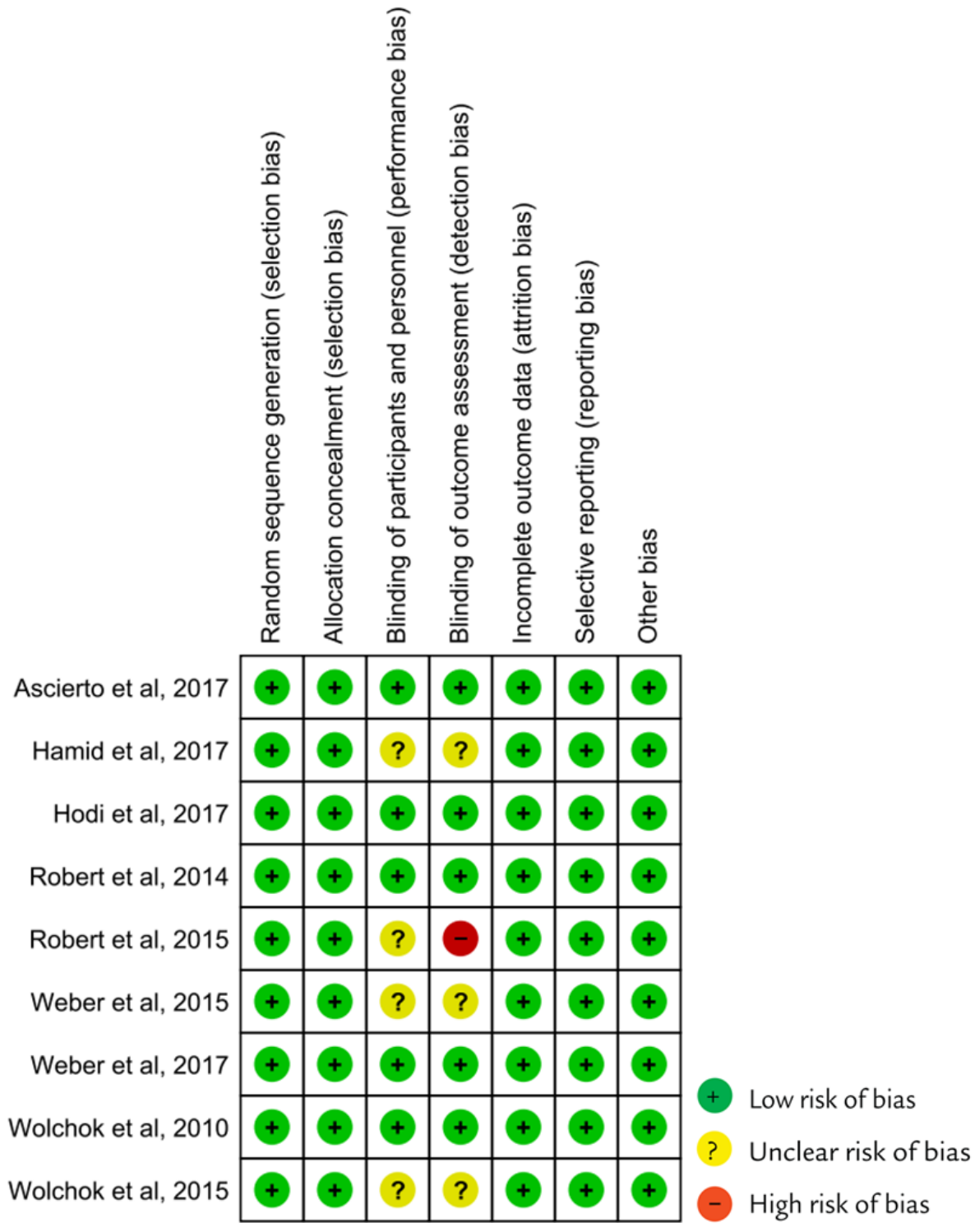
[a] We compared posterior means and standard deviations of the log-odds ratios obtained from direct and indirect evidence for each treatment comparison, and then compared the inconsistency as direct effect minus indirect effect at each treatment comparison. [b] The ratio of the OR indicates ORdirect divied by ORindirect. [c] $P \leq 0{\cdot}05$ indicates a significant inconsistency between the direct effect and indirect effects. [d] Immune-related AEs are defined as AEs caused by ICIs, not chemotherapies (i.e., carboplatin, dacarbazine, and paclitaxel). For chemotherapy users, the AEs we identified are chemotherapy-related AEs.

eFigure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Diagram: Literature Search, Study Identification, Selection, and Exclusion



Abbreviations: ICIs: immune checkpoint inhibitors; RCT: randomized controlled trial.

eFigure 2. Risk of Bias Assessment for the 9 Included Randomized Controlled Trials



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