

Table SI. Search strategies used to identify articles using the PubMed, Embase and Cochrane Library databases.

Database	Search terms
PubMed	<p>((("2005/01/01"[Date - Publication] : "2023/05/29"[Date - Publication])) AND (((((((("Randomized Controlled Trial"[Title/Abstract]) OR ("RCT"[Title/Abstract])) OR ("Controlled Clinical Trial"[Title/Abstract])) OR (Randomized[Title/Abstract])) OR (Randomly[Title/Abstract])) OR (Trial[Title/Abstract])) AND ("Carcinoma, Non-Small-Cell Lung"[MeSH Terms] OR "NSCLC"[Title/Abstract] OR "Nonsquamous*" OR "Lung Adenocarcinoma"[Title/Abstract] OR "Non-Small Cell Lung Carcinoma"[Title/Abstract])) AND ((((((((((((((((((((((((((((((sintilimab [Supplementary Concept]) OR (tislezumab [Supplementary Concept])) OR ("BGB-A317"[Title/Abstract])) OR (Camrelizumab [Supplementary Concept])) OR (Carrelizumab[Title/Abstract])) OR ("SHR-1210"[Title/Abstract])) OR ("SHR 1210"[Title/Abstract])) OR (Nivolumab[Title/Abstract])) OR (Opdivo[Title/Abstract])) OR (Opdivo[Title/Abstract])) OR ("ONO 4538"[Title/Abstract])) OR ("MDX-1106"[Title/Abstract])) OR ("MDX 1106"[Title/Abstract])) OR ("BMS-936558"[Title/Abstract])) OR ("BMS-936558"[Title/Abstract])) OR (pembrolizumab [Supplementary Concept])) OR ("SCH-900475"[Title/Abstract])) OR ("lambrolizumab"[Title/Abstract])) OR ("MK-3475"[Title/Abstract])) OR ("Keytruda"[Title/Abstract])) OR (atezolizumab [Supplementary Concept])) OR ("Tecentriq"[Title/Abstract])) OR ("RG7446"[Title/Abstract])) OR ("RG7446"[Title/Abstract])) OR (durvalumab [Supplementary Concept])) OR (Imfinzi[Title/Abstract])) OR (Adebrelimab[Title/Abstract])) OR (cemiplimab [Supplementary Concept])) OR</p>

	("REGN2810"[Title/Abstract])) OR ("Programmed Cell Death 1 Receptor"[Title/Abstract])) OR ("programmed cell death-1"[Title/Abstract])) OR ("programmed cell death ligand-1"[Title/Abstract])) OR ("PD-1"[Title/Abstract]) OR ("PD-L1"[Title/Abstract]))
Embase	#1 sintilimab:ti,ab,kw OR tislelizumab:ti,ab,kw OR camrelizumab:ti,ab,kw OR carrelizumab:ti,ab,kw OR nivolumab:ti,ab,kw OR 'nivolumab plus relatlimab':ti,ab,kw OR pembrolizumab:ti,ab,kw OR atezolizumab:ti,ab,kw OR durvalumab:ti,ab,kw OR adebreliumab:ti,ab,kw OR cemiplimab:ti,ab,kw OR 'programmed death 1 receptor':ti,ab,kw OR 'programmed death 1 ligand 1':ti,ab,kw OR 'programmed death 1 ligand 1 inhibitor':ti,ab,kw #2 "Carcinoma, Non-Small-Cell Lung"[MeSH Terms] OR "NSCLC"[Title/Abstract] OR "Nonsquamous*" OR "Lung Adenocarcinoma"[Title/Abstract] OR "Non-Small Cell Lung Carcinoma"[Title/Abstract] #3 (((("Randomized Controlled Trial"[Title/Abstract]) OR ("RCT"[Title/Abstract])) OR ("Controlled Clinical Trial"[Title/Abstract])) OR (Randomized[Title/Abstract])) OR (Randomly[Title/Abstract])) OR (Trial[Title/Abstract]) #4 #1 AND #2 AND #3 AND [01-01-2005]/sd NOT [30-05-2023]/sd
Cochrane library	Comment: ID Search Hits #1 Tislelizumab OR sintilimab OR 'BGB-A317' OR Camrelizumab OR Carrelizumab OR 'SHR-1210' OR Nivolumab OR Opdivo OR 'ONO 4538' OR 'MDX-1106' OR 'BMS-936558' OR pembrolizumab OR 'SCH-900475' OR lambrolizumab OR 'MK-3475' OR 'Keytruda' OR tezolizumab OR 'Tecentriq' OR 'RG7446' OR 'durvalumab' OR

'Imfinzi' OR Adebrelimab OR cemiplimab OR 'REGN2810' OR 'Programmed Cell Death 1 Receptor' OR 'programmed cell death-1' OR 'programmed cell death ligand-1' OR 'PD-1' OR 'PD-L1' 9799

#2 'Carcinoma, Non-Small-Cell Lung' OR MeSH descriptor: [Carcinoma, Non-Small-Cell Lung] explode all trees OR NSCLC OR 'non small cell\*' OR 'non-small cell\*' OR nonsquamous\* OR 'lung cancer' OR 'nonsquamous non small cell lung cancer' 38556

#3 'randomized controlled trial' OR RCT OR 'controlled clinical trial' OR randomized OR randomly OR trial 1589313

#4 #1 AND #2 AND #3 with Cochrane Library publication date Between Jan 2005 and May 2023 3188

Table SII. Characteristics of the included literature.

First author, year	Median follow-up, months	Clinical trial	Histology type	Treatment details	Sample size	Median Age, years	% Males	% Smokers	Reported outcomes	(Refs.)
Wang <i>et al</i> , 2023	7.1	CHOICE-01 NCT03856411	NSCLC	Tor+Che	309	63.0	79.9	68.9	OS, PFS, ORR, DCR, grades $\geq 3$ TRAEs, grades $\geq 3$ irAEs	(32)
				Pla+Che	156	61.0	83.3	68.8		
			Squamous	Tor+Che	147	64.0	89.8	81.0	OS, PFS	
				Pla+Che	73	61.0	90.4	80.8		
			Non-squamous	Tor+Che	162	62.0	71.0	58.0	OS, PFS	
				Pla+Che	83	60.0	77.1	57.8		
Makharadze <i>et al</i> , 2023	21.1	EMPOWER-Lung 3 NCT03409614	NSCLC	Cem+Che	312	63.0	85.9	55.4	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(24)
				Pla+Che	154	63.0	79.9	48.7		
			Squamous	Cem+Che	133	NA	NA	NA	OS, PFS	

				Pla+Che	67	NA	NA	NA		
			Non-squamous	Cem+Che	179	NA	NA	NA	OS, PFS	
				Pla+Che	87	NA	NA	NA		
Sezer <i>et al</i> , 2021	14.2	EMPOWER-Lung 1 NCT03088540	NSCLC	Cem	356	63.0	88.0	100.0	OS, PFS, ORR, DCR, grades ≥3 TRAEs, grade ≥3 irAEs	(9)
				Che	354	64.0	83.0	100.0		
			Squamous	Cem	159	NA	NA	NA	OS, PFS	
				Che	152	NA	NA	NA		
			Non-squamous	Cem	197	NA	NA	NA	OS, PFS	
				Che	202	NA	NA	NA		
Spigel <i>et al</i> , 2022	61.6	PACIFIC NCT02125461	NSCLC	Dur	476	NA	57.5	56.4	OS, PFS	(26)
				Pla	237	NA	67.5	64.8		
			Squamous	Dur	224	NA	NA	NA	OS, PFS	
				Pla	102	NA	NA	NA		
			Non-squamous	Dur	252	NA	NA	NA	OS, PFS	
				Pla	135	NA	NA	NA		

Johnson <i>et al</i> , 2023	5.5	POSEIDON NCT03164616	NSCLC	Dur+Che	338	63.0	79.6	79.1	OS, PFS, grade $\geq 3$	(38)				
				Che	337	64.5	74.9	85.6	TRAEs, grade $\geq 3$ irAEs					
			Squamous	Dur+Che	128	NA	NA	NA	OS, PFS					
				Che	122	NA	NA	NA						
			Non-squamous	Dur+Che	209	NA	NA	NA	OS, PFS					
				Che	214	NA	NA	NA						
			Rizvi <i>et al</i> , 2020	16.3	MYSTIC NCT02453282	NSCLC	Dur	163	64.0		69.3	85.2	OS, grade $\geq 3$	(10)
							Che	372	64.5		65.4	74.2	TRAEs, grade $\geq 3$ irAEs	
Zhou <i>et al</i> , 2022	14.3	GEMSTONE-301 NCT03728556	NSCLC	Sug	255	61.0	93.0	84.0	OS, PFS, ORR,	(30)				
				Pla	126	60.0	91.0	87.0	DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs					
			Squamous	Sug	177	NA	NA	NA	PFS					
				Pla	86	NA	NA	NA						
			Non-squamous	Sug	76	NA	NA	NA	PFS					

				Pla	40	NA	NA	NA		
Zhou <i>et al</i> , 2022	8.6	GEMSTONE-302 NCT03789604	NSCLC	Sug+Che	320	62.0	79.0	73.0	OS, PFS, grade $\geq 3$ irAEs, grade $\geq 3$	(31)
				Pla+Che	159	64.0	81.0	75.0		
			Squamous	Sug+Che	129	NA	NA	NA	PFS	
				Pla+Che	63	NA	NA	NA		
			Non-squamous	Sug+Che	191	NA	NA	NA	PFS	
				Pla+Che	96	NA	NA	NA		
Fehrenbacher <i>et al</i> , 2018	26	OAK NCT02008227	NSCLC	Ate	613	63.0	61.8	81.7	OS, PFS, grade $\geq 3$ irAEs, grade $\geq 3$	(20)
				Che	612	64.0	61.9	84.3		
			Squamous	Ate	161	NA	NA	NA	OS	
				Che	160	NA	NA	NA		
			Non-squamous	Ate	452	NA	NA	NA	OS	
				Che	452	NA	NA	NA		
Reck <i>et al</i> , 2019	13.5	IMpower150 NCT02366143	Non-squamous	Ate+Che	400	63.0	60.0	80.0	OS,PFS, ORR, DCR, grade $\geq 3$ TRAEs	(35)
				Che	400	63.0	60.0	81.0		

Socinski <i>et al</i> , 2021	32.4	IMpower150 NCT02366143	Non-squamous	Ate+Che	400	NA	60.0	79.5	OS, grade $\geq 3$ TRAEs	(6)
				Che	400	NA	59.8	80.8		
West <i>et al</i> , 2019	18.5	IMpower130 NCT02367781	Non-squamous	Ate+Che	483	64.0	57.0	87.0	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs	(34)
				Che	240	65.0	58.0	92.0		
Jotte <i>et al</i> , 2020	14.2	IMpower131 NCT02367794	Squamous	Ate+Che	343	65.0	81.6	90.7	OS,PFS Grades $\geq 3$ TRAEs	(33)
				Che	340	65.0	81.6	92.9		
Jassem <i>et al</i> , 2021	31.3	IMpower110 NCT02409342	NSCLC	Ate	277	64.0	70.8	86.6	OS, PFS, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(21)
				Che	277	65.0	69.7	87.3		
Nishio <i>et al</i> , 2021	14.8	IMpower132 NCT02657434	Non-squamous	Ate+Che	292	64.0	66.8	87.3	OS, PFS, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(36)
				Che	286	63.0	68.1	89.5		
	28.7			Ate+Che	292	64.0	66.8	87.3	OS, PFS	
	Che			286	63.0	68.1	89.5			
Sugawara <i>et al</i> , 2021	13.7	ONO-4538-52/TASUK I-52	Nonsquamous	Niv+Che	275	66.0	74.5	78.8	OS, PFS, ORR, DCR, grade $\geq 3$	(27)
				Pla+Che	275	66.0	74.9	80.3		



		NCT03117049							TRAEs, grade $\geq 3$ irAEs					
Wu <i>et al</i> , 2019	8.8	CheckMate 078 NCT02613507	NSCLC	Niv	338	60.0	78.0	70.0	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs	(16)				
				Che	166	60.0	81.0	71.0						
			Squamous	Niv	133	NA	NA	NA	OS					
				Che	67	NA	NA	NA						
			Non-squamous	Niv	205	NA	NA	NA	OS					
				Che	99	NA	NA	NA						
			Borghae <i>et al</i> , 2015	13.3	CheckMate 057 NCT01673867	NSCLC	Niv	292	61.0		52.0	79.0	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs	(17)
							Che	290	64.0		58.0	78.0		
17.2	Niv	292		61.0		52.0	79.0	OS						
	Che	290		64.0		58.0	78.0							
Brahmer <i>et al</i> , 2015	9.2	CheckMate 017 NCT01642004	NSCLC	Niv	135	62.0	82.0	90.0	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs	(18)				
				Che	137	64.0	71.0	94.0						

Carbone <i>et al</i> , 2017	4.2	CheckMate 026 NCT02041533	NSCLC	Niv	271	63.0	68.0	88.0	OS, PFS, ORR ,DCR, grade $\geq 3$ TRAEs	(11)				
				Che	270	65.0	55.0	87.0						
			Squamous	Niv	65	NA	NA	NA	OS, PFS					
				Che	64	NA	NA	NA						
			Non-squamous	Niv	206	NA	NA	NA	OS, PFS					
				Che	206	NA	NA	NA						
			Forde <i>et al</i> , 2022	31.6	CheckMate 816 NCT02998528	NSCLC	Niv+Che	179	64.0		71.5	89.4	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(39)
							Che	179	65.0		70.9	88.3		
Squamous	Niv+Che	87				NA	NA	NA	PFS					
	Che	95				NA	NA	NA						
Non-squamous	Niv+Che	92				NA	NA	NA	PFS					
	Che	84				NA	NA	NA						
Lu <i>et al</i> , 2022	9.8	ORIENT-31 NCT03802240				Non-squamous	Siv+Che	145	59.0	41.0	30.0	Grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(40)	
							Che	151	57.0	41.0	30.0			

Yang <i>et al</i> , 2020	8.9	ORIENT-11 NCT03607539	Non-squamous	Sin+Che	266	61.0	76.7	64.3	OS, PFS, ORR, DCR, grade $\geq 3$ irAEs	(25)
				Pla+Che	131	61.0	75.6	66.5		
Yang <i>et al</i> , 2021	22.9	ORIENT-11 NCT03607539	Non-squamous	Sin+Che	266	61.0	76.7	64.3	OS, PFS	(7)
				Pla+Che	131	61.0	75.6	66.4		
Zhang <i>et al</i> , 2022	30.8	ORIENT-11 NCT03607539	Non-squamous	Sin+Che	266	61.0	76.7	64.3	OS	(8)
				Pla+Che	131	61.0	75.6	66.4		
Zhou <i>et al</i> , 2021	12.9	ORIENT-12 NCT03629925	Squamous	Sin+Che	179	64.0	91.1	86.6	OS, PFS, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(22)
				Pla+Che	178	62.0	92.1	82.6		
Wang <i>et al</i> , 2021	8.6	RATIONALE-307 NCT03594747	Squamous	Tis+Che	120	60.0	89.2	80.0	PFS, ORR, DCR, grade $\geq 3$ TRAEs	(42)
				Che	121	62.0	91.7	89.9		
Lu <i>et al</i> , 2021	9.8	RATIONALE 304 NCT03663205	Non-squamous	Tis+Che	223	60.0	75.3	65.9	PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(41)
				Che	111	61.0	71.2	59.4		
Zhou <i>et al</i> , 2023	16	RATIONALE-303 NCT03358875	NSCLC	Tis	535	61.0	71.8	69.7	OS, PFS, ORR, DCR	(19)
				Che	270	61.0	76.3	69.6		
			Squamous	Tis	248	NA	NA	NA	OS	

				Che	122	NA	NA	NA		
			Non-squamous	Tis	287	NA	NA	NA	OS	
				Che	148	NA	NA	NA		
Ren <i>et al</i> , 2022	13.5	CameL-Sq NCT03668496	Squamous	Cam+Che	193	64.0	93.0	89.0	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(23)
				Pla+Che	196	62.0	92.0	88.0		
Zhou <i>et al</i> , 2023	27	CameL NCT03134872	Non-squamous	Cam+Che	205	59.0	71.2	NA	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(37)
				Che	207	61.0	72.0	NA		
Herbst <i>et al</i> , 2021	67.4	KEYNOTE-010 NCT01905657	NSCLC	Pem	690	NA	61.6	81.9	OS, PFS, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(12)
				Che	343	NA	60.9	78.4		
			Squamous	Pem	156	NA	NA	NA	OS	
				Che	66	NA	NA	NA		
			Non-squamous	Pem	486	NA	NA	NA	OS	

				Che	240	NA	NA	NA		
Reck <i>et al</i> , 2021	59.9	KEYNOTE-024 NCT02142738	NSCLC	Pem	154	64.5	59.7	96.8	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(14)
				Che	151	66.0	62.9	87.4		
Garassino <i>et al</i> , 2023	64.6	KEYNOTE-189 NCT02578680	Non-squamous	Pem+Che	410	65.0	62.0	88.3	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(29)
				Pla+Che	206	63.5	52.9	87.9		
Novello <i>et al</i> , 2023	56.9	KEYNOTE-407 NCT02775435	Squamous	Pem+Che	278	65.0	79.1	92.1	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(28)
				Pla+Che	281	65.0	83.6	93.2		
de Castro <i>et al</i> , 2023	61.1	KEYNOTE-042 NCT02220894	NSCLC	Pem	637	63.0	70.6	77.8	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	(13)
				Che	637	63.0	71.0	78.0		

			Squamous	Pem	242	NA	NA	NA	OS	
				Che	249	NA	NA	NA		
			Non-squamous	Pem	395	NA	NA	NA	OS	
				Che	388	NA	NA	NA		
Ren <i>et al</i> , 2023	61.1	KEYNOTE-033 NCT02864394	NSCLC	Pem	213	61.0	73.7	67.1	OS, PFS, ORR, DCR, grade $\geq 3$ TRAEs, grade $\geq 3$ irAEs	
				Che	212	61.0	77.4	69.3		
			Squamous	Pem	81	NA	NA	NA	OS	
				Che	89	NA	NA	NA		
			Non-squamous	Pem	121	NA	NA	NA	OS	
				Che	113	NA	NA	NA		

NSCLC, non-small cell lung cancer; NA, not available; OS, overall survival; PFS, progression-free survival; ORR, objective response rate; DCR, disease control rate; TRAEs, treatment-related adverse events; irAEs, immune-related adverse events; Ate, atezolizumab; Cem, cemiplimab; Cam, camrelizumab; Dur, durvalumab; Tis, tislelizumab; Sug, sugemalimab; Niv, nivolumab; Pem, pembrolizumab; Sin, sintilimab; Tor, toripalimab; Pla, placebo; Che, chemotherapy.

Table SIII. Quality assessment of the included studies using the Cochrane RoB2 tool.

First author, year	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall bias	(Refs.)
Wang <i>et al</i> , 2023	L	L	L	L	L	L	(32)
Makharadze <i>et al</i> , 2023	L	L	L	L	L	L	(24)
Sezer <i>et al</i> , 2021	H	S	L	L	L	H	(9)
Spigel <i>et al</i> , 2022	L	L	L	S	L	S	(26)
Johnson <i>et al</i> , 2023	H	S	L	S	L	H	(38)
Rizvi <i>et al</i> , 2020	H	H	L	L	S	H	(10)
Zhou <i>et al</i> , 2022	L	L	L	L	L	L	(30)
Zhou <i>et al</i> , 2022	L	L	L	L	L	L	(31)
Fehrenbacher <i>et al</i> , 2018	H	S	L	L	L	H	(20)
Reck <i>et al</i> , 2019	H	S	L	L	L	H	(35)
Socinski <i>et al</i> , 2021	H	S	L	L	L	H	(6)
West <i>et al</i> , 2019	H	S	L	L	L	H	(34)
Jotte <i>et al</i> , 2020	H	S	L	L	L	H	(33)
Jassem <i>et al</i> , 2021	H	S	L	L	L	H	(21)

Nishio <i>et al</i> , 2021	H	L	L	L	S	H	(36)
Sugawara <i>et al</i> , 2021	L	L	L	L	L	L	(27)
Wu <i>et al</i> , 2019	H	L	L	L	L	H	(16)
Borghae <i>et al</i> , 2015	H	L	L	L	S	H	(17)
Brahmer <i>et al</i> , 2015	H	L	L	L	L	H	(18)
Carbone <i>et al</i> , 2017	H	L	L	S	S	H	(11)
Forde <i>et al</i> , 2022	H	L	L	L	L	H	(39)
Yang <i>et al</i> , 2020	L	L	L	L	L	L	(25)
Yang <i>et al</i> , 2021	L	L	L	L	L	L	(7)
Zhang <i>et al</i> , 2022	L	L	L	L	L	L	(8)
Zhou <i>et al</i> , 2021	L	L	L	L	L	L	(22)
Zhou <i>et al</i> , 2023	H	L	L	S	L	H	(19)
Ren <i>et al</i> , 2022	L	L	L	L	L	L	(23)
Zhou <i>et al</i> , 2023	H	L	L	L	L	H	(37)
Herbst <i>et al</i> , 2021	H	L	L	L	L	H	(12)
Reck <i>et al</i> , 2021	H	L	L	L	L	H	(14)
Garassino <i>et al</i> , 2023	L	L	L	L	L	L	(29)



Novello <i>et al</i> , 2023	L	L	L	L	L	L	(28)
de Castro <i>et al</i> , 2023	H	L	L	L	L	H	(13)
Ren <i>et al</i> , 2023	H	L	L	L	L	H	(15)
Lu <i>et al</i> , 2022	L	L	L	L	L	L	(40)
Wang <i>et al</i> , 2021	H	L	L	L	L	H	(42)
Lu <i>et al</i> , 2021	H	L	L	L	L	H	(41)

RoB, risk of bias; L, low RoB; R, risk of bias; S, some RoB.