

Supplementary data

Efficacy and Safety of PD-1/PD-L1 Checkpoint Inhibitors versus Anti-PD-1/PD-L1 Combined with Other Therapies for Tumors: A Systematic Review

Table S1 Search strategy

#1 ("Programmed Cell Death 1 Receptor"[Mesh]) OR (((((((((((PD-1 Protein[Title/Abstract]) OR (PD 1 Protein[Title/Abstract])) OR (PD-1 Receptor[Title/Abstract])) OR (PD 1 Receptor[Title/Abstract])) OR (Receptor, PD-1[Title/Abstract])) OR (Antigens, CD279[Title/Abstract])) OR (CD279 Antigens[Title/Abstract])) OR (CD279 Antigen[Title/Abstract])) OR (Antigen, CD279[Title/Abstract])) OR (PD1 Receptor[Title/Abstract])) OR (Receptor, PD1[Title/Abstract])) OR (Programmed Cell Death Protein 1[Title/Abstract])) OR (Programmed Cell Death 1 Protein[Title/Abstract]))

#2 ("Immune Checkpoint Inhibitors"[Mesh]) OR (((((((((((((((((((((((Checkpoint Inhibitors, Immune[Title/Abstract]) OR (Immune Checkpoint Inhibitor[Title/Abstract])) OR (Checkpoint Inhibitor, Immune[Title/Abstract])) OR (Immune Checkpoint Blockers[Title/Abstract])) OR (Checkpoint Blockers, Immune[Title/Abstract])) OR (Immune Checkpoint Blockade[Title/Abstract])) OR (Checkpoint Blockade, Immune[Title/Abstract])) OR (Immune Checkpoint Inhibition[Title/Abstract])) OR (Checkpoint Inhibition, Immune[Title/Abstract])) OR (PD-L1 Inhibitors[Title/Abstract])) OR (PD L1 Inhibitors[Title/Abstract])) OR (PD-L1 Inhibitor[Title/Abstract])) OR (PD L1 Inhibitor[Title/Abstract])) OR (Programmed Death-Ligand 1 Inhibitors[Title/Abstract])) OR (Programmed Death Ligand 1 Inhibitors[Title/Abstract])) OR (PD-1-PD-L1 Blockade[Title/Abstract])) OR (Blockade, PD-1-PD-L1[Title/Abstract])) OR (PD 1 PD L1 Blockade[Title/Abstract])) OR (CTLA-4 Inhibitors[Title/Abstract])) OR (CTLA 4 Inhibitors[Title/Abstract])) OR (CTLA-4 Inhibitor[Title/Abstract])) OR (CTLA 4 Inhibitor[Title/Abstract])) OR (Cytotoxic T-Lymphocyte-Associated Protein 4 Inhibitors[Title/Abstract])) OR (Cytotoxic T Lymphocyte Associated Protein 4 Inhibitors[Title/Abstract])) OR (Cytotoxic T-Lymphocyte-Associated Protein 4 Inhibitor[Title/Abstract])) OR (Cytotoxic T Lymphocyte Associated Protein 4 Inhibitor[Title/Abstract])) OR (PD-1 Inhibitors[Title/Abstract])) OR (PD 1 Inhibitors[Title/Abstract])) OR (PD-1 Inhibitor[Title/Abstract])) OR (Inhibitor, PD-1[Title/Abstract])) OR (PD 1

Inhibitor[Title/Abstract])) OR (Programmed Cell Death Protein 1
 Inhibitor[Title/Abstract])) OR (Programmed Cell Death Protein 1
 Inhibitors[Title/Abstract]))

#3 (((((((Nivolumab[Title/Abstract]) OR (Pembrolizumab[Title/Abstract])) OR
 (Cemiplimab[Title/Abstract])) OR (Toripalimab[Title/Abstract])) OR
 (Cindilimab[Title/Abstract])) OR (Camrelizumab[Title/Abstract])) OR
 (Atezolizumab[Title/Abstract])) OR (Avelumab[Title/Abstract])) OR
 (Durvalumab[Title/Abstract]))

#4 #1 OR #2 OR #3

#5 ("Neoplasms"[Mesh]) OR (((((((((((Tumor[Title/Abstract]) OR
 (Neoplasm[Title/Abstract])) OR (Tumors[Title/Abstract])) OR
 (Neoplasia[Title/Abstract])) OR (Neoplasias[Title/Abstract])) OR
 (Cancer[Title/Abstract])) OR (Cancers[Title/Abstract])) OR (Malignant
 Neoplasm[Title/Abstract])) OR (Malignancy[Title/Abstract])) OR
 (Malignancies[Title/Abstract])) OR (Malignant Neoplasms[Title/Abstract])) OR
 (Neoplasm, Malignant[Title/Abstract])) OR (Neoplasms, Malignant[Title/Abstract]))
 OR (Benign Neoplasms[Title/Abstract])) OR (Benign Neoplasm[Title/Abstract])) OR
 (Neoplasms, Benign[Title/Abstract])) OR (Neoplasm, Benign[Title/Abstract]))

#6 #4 AND #5 filters: from 1000/1/1 - 2022/2/16

Table S2 Baseline demographics and clinical characteristics

Author	Study type	Region	Male : Female	Median follow-up, months		Median age (range), years		ECAEs	RECT
				experimental : control	total	experimental : control	total		
Boyer 2021 ¹⁵	Randomized, double-blind	24 countries	393 : 175	NR	20.6	64(35-85) : 65(35-85)	NR	NCI-CTCAE v.4.0	RECIST v.1.1
D'Angelo 2018 ¹⁶	Open-label, non-comparative, randomised	USA	41 : 44	14.2 : 13.6	NR	57.0 (27.0–81.0) : 56.0 (21.0–76.0)	NR	NCI-CTCAE v.4.0	RECIST v.1.1
Ferrarotto 2020 ¹⁷	Randomized	USA	28 : 1	NR	15.79	NR	NR	NCI-CTCAE v.4.03	RECIST v.1.1
Ferris 2020 ¹⁸	Randomized, open-label	NR	411 : 76	6.3 : 7.6	NR	61.0 (23–81) : 59.0 (24–84)	NR	NCI-CTCAE v.4.03	RECIST v.1.1
Gettinger 2021 ¹⁹	Randomized, multicenter, open-label	NR	169 : 83	NR	29.5	67.5 (41.8-83.4) : 68.1 (48.6-90.3)	67.5 (41.8-90.3)	NCI-CTCAE v.4.03	RECIST v.1.1
Janjigian 2018 ²⁰	Open-label, two-stage, multicohort	USA and Europe	90 : 21	22 : 24	NR	58(19-81) : 60(29-80)	NR	NCI-CTCAE v.4.0	RECIST v.1.1

Kaseb 2022 ²¹	Single-centre, randomised, open-label	USA	19 : 8	NR	24.6	62 (53–72) : 64 (56–68)	64 (53–69)	NCI-CTCAE v.4.0	RECIST v.1.1
Kelley 2021 ²²	Randomized, open-label	9 countries	157 : 22	NR	NR	66(26-86) : 64.5(32-89)	NR	NCI-CTCAE v.4.03	RECIST v.1.1
Kelly 2019 ²³	Randomized, multicenter, open-label	6 countries	39 : 12	9.2 : 3.5	NR	64.0 (27–78) : 60.0 (29–79)	NR	NCI-CTCAE v.4.0	RECIST v.1.1
Long 2018 ²⁴	Multicentre, open-label, randomised	Australia	48 : 12	14:17	17	59 (53–68) : 63 (52–74)	NR	NCI-CTCAE v.4.0	RECIST v.1.1
Long 2019 ²⁵	International, randomised, placebo-controlled, double-blind, parallel-group	23 countries	423 : 283	NR	12.4	64 (52–72) : 63 (53.5–72)	64 (53–72)	NR	RECIST v.1.1
Omuro 2017 ²⁶	Exploratory cohorts	USA	11 : 9	NR	NR	57 (37–68) : 58.5 (42–73)	NR	NCI-CTCAE v.4.0	RANO
O'Reilly 2019 ²⁷	Multicenter, randomized, open-label	6 countries	34 : 31	NR	3.2	60.0 (37-81) : 62.0 (40-78)	61 (37-81)	NCI-CTCAE v.4.03	RECIST v.1.1

Paz-Ares 2021 ²⁷	Randomized, open-label	North America, Europe, Asia and other 10 countries	527 : 265	NR	54.8	64 (26–84) : 64 (27–85)	NR	NR	NR
Planchard 2020 ²⁹	Randomized, open-label, multicenter study	26 countries	188 : 103	NR	NR	62.5 (26–81) : 63.0 (19–83)	NR	NR	RECIST v.1.1
Powles 2020 ³⁰	Open-label, multicentre, randomised, controlled	23 countries	505 : 183	NR	41.2	68 (60–73) : 67 (60–73)	NR	NCI- CTCAE v.4.03	RECIST v.1.1
Ready 2019 ³¹	Randomized, multicenter, open-label	8 countries	147 : 96	NR	NR	65.0 (41–91) : 63.0 (29–83)	NR	NCI- CTCAE v.4.0	RECIST v.1.1
Scherpereel 2019 ³²	Multicentre, open-label, randomised, non- comparative	France	100 : 25	NR	20.1	71.2 (48.1–88.1) : 72.3 (32.5–87.2)	NR	NCI- CTCAE v.4.0	RECIST v.1.0
Schoenfeld 2020 ³³	Open label, randomized	NR	18 : 11	NR	NR	65.2 (32.5-78.4) : 64.4 (39.1-81.0)	NR	NCI- CTCAE v.4.0	RECIST

Sharma 2019 ³⁴	Multicenter, open-label, multiarm	8 countries	135 : 47	NR	NR	64(39-83) : 65.5(31-85)	NR	NCI-CTCAE v.4.0	RECIST v.1.1
Singh 2021 ³⁵	Randomized , noncomparative, parallel group, unblinded	NR	19 : 17	NR	NR	NR	61 (21-80)	NCI-CTCAE v.4.03	RECIST v.1.1
Siu 2018 ³⁶	Randomized, open-label, multicenter, global	North America, Europe and Asia Pacific	167 : 33	6.5 : 6.0	NR	62 (26-81) : 62 (23-82)	NR	NR	RECIST v.1.1
Tawbi 2022 ³⁷	Global, double-blind, randomized	America, Europe, Australia and New Zealand	416 : 298	NR	13.2	63.0 (20–94) : 62.0 (21–90)	63 (20–94)	NCI-CTCAE v.5.0	RECIST v.1.1
Wolchok 2021 ³⁸	Randomized	5 countries	408 : 222	57.5 : 36	NR	61 (18-88) : 60 (25-90)	NR	NCI-CTCAE v.4.0	RECIST v.1.1
Zamarin 2020 ³⁹	Open-label, randomized	USA	all female	NR	NR	62(38-92) : 63(37-87)	NR	NCI-CTCAE v.4.0	RECIST v.1.1
Zimmer 2020 ⁴⁰	Randomised, double-blind, placebo-controlled	Germany	62 : 53	NR	28.4	52 (45–59) : 57 (48–65)	NR	NCI-CTCAE v.4.0	RECIST v.1.1

Eng 2019 ⁴¹	Multicentre, open-label, randomised, controlled	11 countries	166 : 107	NR	7.3	58 (51–67) : 56 (51–64)	NR	NCI- CTCAE v.4.0	RECIST v.1.1
Gogas 2020 ⁴²	International, randomized, open-label	North America, Europe and others	270 : 176	7.1 : 7.2	NR	66 (54-73) : 66 (55-73)	NR	NCI- CTCAE v.4.0	RECIST v.1.1
Lee 2020 ⁴³	Open-label, multicentre, multiarm	7 countries	103 : 16	6.6 : 6.7	12.4	60 (22–82) : 63 (23–85)	NR	NCI- CTCAE v.4.0	RECIST v.1.1
McDermott 2018 ⁴⁴	Randomised	NR	151 : 53	NR	20.7	62 (32-88) : 61 (27-81)	NR	NR	RECIST v.1.1
Nayak 2020 ⁴⁵	Multicenter, open-label, two- cohort	NR	54 : 26	NR	NR	52 (42–59) : 55 (42–62)	53 (42– 60)	NCI- CTCAE v.4.0	RANO
Taylor 2022 ⁴⁶	Multicenter, open-label, randomized	USA	69 : 7	6.4 : 9.2	NR	58.0 (45.0–97.0) : 61.0 (38.0–83.0)	60.5 (38- 97)	NCI- CTCAE v.4.03	RECIST v.1.1
Yarchoan 2021 ⁴⁷	Randomised	USA	29 : 48	NR	NR	NR	NR	NR	RECIST v.1.1
Zhang 2020 ⁴⁸	Randomized, open-label, multicenter	USA	57 : 18	NR	NR	68 (36-83) : 65 (46-96)	NR	NCI- CTCAE v.4.03	RECIST v.1.1

Altorki 2021 ⁴⁹	Single-centre, open-label, randomised, controlled	USA	31 : 29	NR	16.9	70.0 (64.2–74.0) : 71.0 (65.2–75.0)	NR	NCI-CTCAE v.4.0	RECIST v.1.1.13
McBride 2020 ⁵⁰	Single-center, randomized	USA	NR	NR	20.2	66(35-83) : 60.5(29-77)	63 (29-83)	NCI-CTCAE v.4.03	RECIST v.1.1
Papadopoulos 2019 ⁵¹	Open-label, multicenter	NR	NR	NR	4.4	NR	58 (31-79)	NCI-CTCAE v.4.03	RECIST v.1.1
Theelen 2019 ⁵²	Multicenter, randomized	Netherlands	44 : 32	NR	23.6	NR	62 (35-78)	NCI-CTCAE v.4.0	RECIST v.1.1
Burtneess 2019 ⁵³	Randomised, open-label	37 countries	474 : 108	13.0 : 11.5	NR	61.0 (55.0–68.0) : 62.0 (56.0–68.0)	NR	NCI-CTCAE v.4.0	RECIST v.1.1
Fang 2018 ⁵⁴	Two single-arm	China	92 : 24	10.2 : 9.9	NR	44 (34–51) : 45 (38–52)	NR	NCI-CTCAE v.4.03	RECIST v.1.1
Galsky 2020 ⁵⁵	Multicentre, randomised, placebo-controlled	35 countries	618 : 195	NR	11.8	69 (62–75) : 67 (62–74)	NR	NCI-CTCAE v.4.0	RECIST v.1.1

Levy 2019 ⁵⁶	Multicenter, international, randomised, placebo- controlled, double-blind	USA and Europe	57 : 43	11.3 : 12.2	NR	65 (39–82) : 66 (39–82)	65 (39– 82)	NCI- CTCAE v.4.0	RECIST v.1.1
Nie 2019 ⁵⁷	Two-arm, open- label	China	37 : 24	NR	14.9	26(18.3-31.8) : 28(23.5-32)	NR	NCI- CTCAE v.4.0	RRCML
Powles 2021 ⁵⁸	Randomised, open-label	21 countries	500 : 158	NR	31.7	69 (62–75) : 68 (61–74)	NR	NCI- CTCAE v.4.0	RECIST v.1.1
Shitara 2020 ⁵⁹	Randomized, controlled, partially blinded interventional	29 countries	375 : 138	NR	29.4	62.0 (22-83) : 61.0 (20-83)	NR	NCI- CTCAE v.4.0	RECIST v.1.1
Ueno 2019 ⁶⁰	Non- randomised, multicentre, open-label	Janpan	32 : 28	8.2 : 5.1	NR	67.5 (54–75) : 68 (60–71)	NR	NCI- CTCAE v.4.0	RECIST v.1.1
Gutierrez 2020 ⁶¹	Open-label	7 countries	NE*	NR	NR	NR	55-69	NCI- CTCAE v.4.03	RECIST v.1.1
Spigel 2020 ⁶²	Randomised	NR	60 : 41	NR	10	69 (49-82) : 68 (49-83)	NR	NCI- CTCAE v.4.03	RECIST v.1.1

NCI-CTCAE: National Cancer Institute Common Terminology Criteria for Adverse Events. RECIST: Response Evaluation Criteria In Solid Tumors. RANO: Response Assessment in Neuro-Oncology. RRCML: Revised Response Criteria for Malignant Lymphomas (2014 Lugano classification). NR: not reported. NE: not estimate; * The monotherapy group was described together with another group which we are not focused on in the baseline. ECAEs: Evaluation criteria of AEs. RECT: Response evaluation criteria in tumors.

Table S3 Median survival ratio of OS based on tumor types

subgroup and Author (Year)	ES	[95% Conf. Interval]		% Weight
NSCLC				
Planchard 2020 ²⁹	1.150	1.025	1.290	3.55
Paz-Ares 2021 ²⁸	1.089	1.016	1.168	3.66
Boyer 2021 ¹⁵	0.977	0.900	1.061	3.63
Gettinger 2021 ¹⁹	0.909	0.804	1.029	3.53
Theelen 2019 ⁵²	2.092	1.671	2.620	3.16
Subgroup, DL	1.151	0.978	1.355	17.52
SCLC				
Ready 2019 ³¹	0.825	0.727	0.935	3.52
Subgroup, DL	0.825	0.727	0.935	3.52
HNSCC				
Burtness 2019 ⁵³	0.872	0.804	0.946	3.63
Siu 2018 ³⁶	1.267	1.100	1.458	3.48
Taylor 2022 ⁴⁶	1.010	0.807	1.265	3.16
Ferris 2020 ¹⁸	0.855	0.783	0.935	3.62
McBride 2020 ⁵⁰	0.979	0.760	1.261	3.03
Subgroup, DL	0.978	0.844	1.135	16.91
genitourinary system				
Zamarin 2020 ³⁹	1.289	1.060	1.568	3.27
Galsky 2020 ⁵⁵	1.019	0.951	1.092	3.66
Sharma 2019 ³⁴	0.747	0.646	0.864	3.46
Powles 2020 ³⁰	1.144	1.062	1.233	3.65
Powles 2021 ⁵⁸	1.090	1.010	1.176	3.64
Zhang 2020 ⁴⁸	0.553	0.441	0.693	3.15
Subgroup, DL	0.955	0.821	1.110	20.83
digestive system				

Singh 2021 ³⁵	0.327	0.235	0.456	2.68
Eng 2019 ⁴¹	1.249	1.110	1.407	3.54
O'Reilly 2019 ²⁷	0.861	0.675	1.098	3.08
Shitara 2020 ⁵⁹	1.179	1.081	1.286	3.62
Ueno 2019 ⁶⁰	2.962	2.299	3.814	3.03
Kelley 2021 ²²	1.238	1.070	1.434	3.46
Kelly 2019 ²³	2.706	2.056	3.560	2.94
Janjigian 2018 ²⁰	0.774	0.643	0.932	3.31
Subgroup, DL	1.164	0.868	1.561	25.66
recurrent				
glioblastoma				
Omuro 2017 ²⁶	0.885	0.564	1.387	2.17
Nayak 2020 ⁴⁵	0.854	0.686	1.064	3.18
Subgroup, DL	0.860	0.706	1.047	5.35
relapsed malignant				
pleural mesothelioma				
Scherpereel 2019 ³²	1.336	1.121	1.592	3.35
Subgroup, DL	1.336	1.121	1.592	3.35
melanoma				
Wolchok 2021 ³⁸	1.954	1.807	2.113	3.64
Subgroup, DL	1.954	1.807	2.113	3.64
metastatic sarcoma				
D'Angelo 2018 ¹⁶	1.336	1.081	1.653	3.21
Subgroup, DL	1.336	1.081	1.653	3.21
Overall, DL	1.086	0.980	1.203	100.00

Tests of subgroup effect size = 1; Cochran's Q statistics for heterogeneity

NSCLC: $z = 1.688$, $P = 0.091$, $I^2 = 91.5\%$; SCLC: $z = -3.007$, $P = 0.003$; HNSCC: $z = -0.288$, $P = 0.773$, $I^2 = 84.0\%$; Genitourinary system: $z = -0.603$, $P = 0.546$, $I^2 = 92.0\%$; Digestive system: $z = 1.014$, $P = 0.311$, $I^2 = 95.9\%$; Recurrent glioblastoma: $z = -1.500$, $P = 0.134$, $I^2 = 0.0\%$; Relapsed malignant pleural me: $z = 3.240$, $P = 0.001$; Melanoma: $z = 16.813$, $P = 0.000$; Metastatic sarcoma: $z = 2.674$, $P = 0.007$; Overall: $z = 1.568$, $P = 0.117$, $I^2 = 95.2\%$; Between: $P = 0.000$

Table S4 Median survival ratio of PFS based on tumor types

subgroup and Author (Year)	ES	[95% Conf. Interval]		% Weight
NSCLC				
Levy 2019 ⁵⁶	0.725	0.596	0.882	2.70
Planchard 2020 ²⁹	1.129	1.006	1.266	2.80
Spigel 2020 ⁶²	1.033	0.850	1.255	2.70
Paz-Ares 2021 ²⁸	1.214	1.133	1.302	2.84
Boyer 2021 ¹⁵	0.976	0.899	1.060	2.83
Gettinger 2021 ¹⁹	1.310	1.158	1.483	2.80
Theelen 2019 ⁵²	3.474	2.774	4.349	2.66
Subgroup, DL	1.231	0.992	1.527	19.34
SCLC				
Ready 2019 ³¹	1.071	0.945	1.215	2.79
Subgroup, DL	1.071	0.945	1.215	2.79
HNSCC				
Burtness 2019 ⁵³	2.130	1.964	2.311	2.83
Siu 2018 ³⁶	1.053	0.914	1.212	2.78
Taylor 2022 ⁴⁶	1.588	1.268	1.989	2.66
McBride 2020 ⁵⁰	1.368	1.063	1.762	2.61
Subgroup, DL	1.490	1.006	2.205	10.87
genitourinary system				
Zamarin 2020 ³⁹	1.950	1.603	2.372	2.70
McDermott 2018 ⁴⁴	1.918	1.672	2.200	2.78
Sharma 2019 ³⁴	0.929	0.803	1.074	2.77
Powles 2020 ³⁰	1.609	1.493	1.734	2.84
Zhang 2020 ⁴⁸	1.375	1.097	1.724	2.65
Subgroup, DL	1.503	1.169	1.933	13.75
digestive system				

Kaseb 2022 ²¹	2.078	1.425	3.030	2.35
Singh 2021 ³⁵	0.710	0.510	0.989	2.45
Eng 2019 ⁴¹	0.985	0.874	1.109	2.80
O'Reilly 2019 ²⁷	1.000	0.784	1.275	2.62
Shitara 2020 ⁵⁹	3.450	3.164	3.762	2.83
Ueno 2019 ⁶⁰	3.000	2.329	3.864	2.61
Yarchoan 2021 ⁴⁷	1.952	1.533	2.484	2.63
Lee 2020 ⁴³	1.647	1.376	1.971	2.73
Kelley 2021 ²²	1.048	0.905	1.214	2.77
Kelly 2019 ²³	1.125	0.855	1.480	2.56
Janjigian 2018 ²⁰	1.143	0.949	1.377	2.72
Subgroup, DL melanoma	1.464	1.011	2.119	29.06
Long 2019 ²⁵	0.959	0.891	1.033	2.84
Long 2018 ²⁴	5.308	4.121	6.836	2.61
Gogas 2020 ⁴²	0.965	0.876	1.063	2.82
Tawbi 2022 ³⁷	2.196	2.040	2.363	2.84
Wolchok 2021 ³⁸	1.667	1.541	1.802	2.84
Subgroup, DL recurrent glioblastoma	1.758	1.158	2.669	13.94
Omuro 2017 ²⁶	0.789	0.504	1.238	2.18
Nayak 2020 ⁴⁵	2.867	2.303	3.570	2.66
Subgroup, DL relapsed malignant pleural mesothelioma	1.528	0.432	5.406	4.85
Scherpereel 2019 ³²	1.400	1.175	1.668	2.73
Subgroup, DL metastatic sarcoma	1.400	1.175	1.668	2.73

D'Angelo 2018 ¹⁶	2.412	1.950	2.983	2.68
Subgroup, DL	2.412	1.950	2.983	2.68
Overall, DL	1.473	1.285	1.688	100.00

Tests of subgroup effect size = 1; Cochran's Q statistics for heterogeneity

NSCLC: $z = 1.887$, $P = 0.059$, $I^2 = 95.6\%$; SCLC: $z = 1.075$, $P = 0.282$; HNSCC: $z = 1.992$, $P = 0.046$, $I^2 = 96.1\%$; Genitourinary system: $z = 3.176$, $P = 0.001$, $I^2 = 93.8\%$; Digestive system: $z = 2.018$, $P = 0.044$, $I^2 = 97.9\%$; Melanoma: $z = 2.650$, $P = 0.008$, $I^2 = 99.1\%$; Recurrent glioblastoma: $z = 0.658$, $P = 0.511$, $I^2 = 96.1\%$; Relapsed malignant pleural me: $z = 3.762$, $P = 0.000$; Metastatic sarcoma: $z = 8.117$, $P = 0.000$; Overall: $z = 5.564$, $P = 0.000$, $I^2 = 97.5\%$; Between: $P = 0.000$

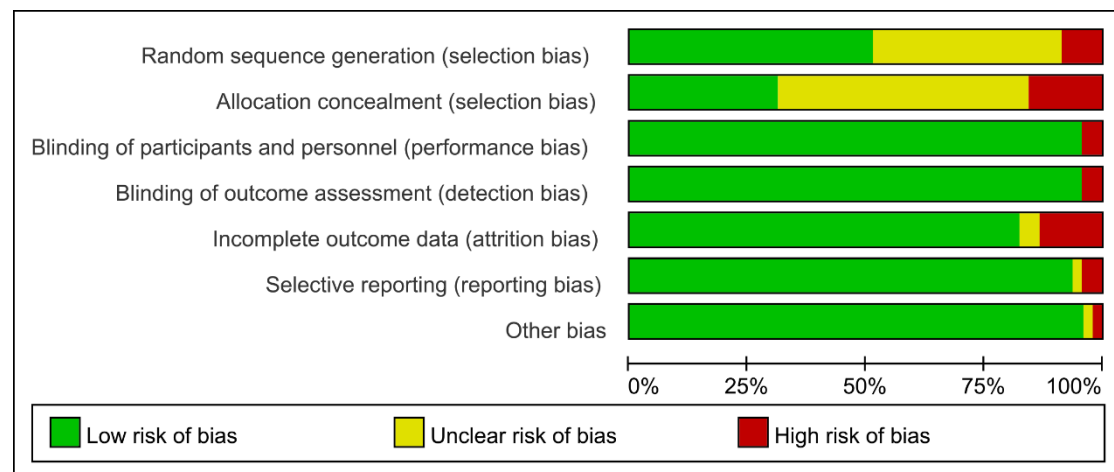


Figure S1 Risk of bias graph: covers 45 studies on the risk of bias judgments.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Altorki 2021	+	?	+	+	+	+	+
Boyer 2021	?	?	+	+	+	+	+
Burtneiss 2019	+	+	+	+	+	+	+
Eng 2019	+	+	+	+	+	+	+
Ferrarotto 2020	+	+	+	+	+	+	+
Ferris 2020	+	+	+	+	?	+	+
Galsky 2020	+	+	+	+	+	+	+
Gettinger 2021	+	+	+	+	+	+	+
Gogas 2020	+	+	+	+	+	+	+
Gutierrez 2020	+	+	+	+	+	+	+
Janjigian 2018	+	+	+	+	+	+	+
Kaseb 2022	+	+	+	+	+	+	+
Kelley 2021	?	?	+	+	+	+	+
Kelly 2019	?	?	+	+	+	+	+
Lee 2020	+	+	+	+	+	+	+
Levy 2019	+	+	+	+	+	+	+
Long 2018	+	+	+	+	+	+	+
Long 2019	+	+	+	+	+	+	+
McBride 2020	?	?	+	+	+	+	+
McDermott 2018	?	?	+	+	+	+	+
Nayak 2020	?	?	+	+	+	+	+
Nie 2019	+	?	+	+	+	+	+
O'Reilly 2019	?	?	+	+	+	+	+
Omuro 2017	?	?	+	+	+	+	+
Papadopoulos 2019	?	?	+	+	+	+	+
Paz-Ares 2021	?	?	+	+	+	+	+
Planchard 2020	?	?	+	+	+	+	+
Powles 2020	+	+	+	+	+	+	+
Powles 2021	+	+	+	+	+	+	+
Ready 2019	+	?	+	+	+	+	+
Scherpereel 2019	+	+	+	+	+	+	+
Schoenfeld 2020	?	?	+	+	?	+	+
Sharma 2019	?	?	+	+	+	+	+
Shitara 2020	+	+	+	+	+	+	+
Singh 2021	?	?	+	+	+	+	+
Siu 2018	+	+	+	+	+	+	+
Spigel 2020	?	?	+	+	+	+	+
Tawbi 2022	+	?	+	+	+	+	+
Taylor 2022	?	?	+	+	+	+	?
Theelen 2019	+	?	+	+	+	+	+
Wolchok 2021	?	?	+	+	+	+	+
Yarchoan 2021	+	+	+	+	+	+	+
Zamarin 2020	+	?	+	+	+	+	+
Zhang 2020	?	?	+	+	+	+	+
Zimmer 2020	+	+	+	+	?	+	+

Figure S2 Risk of bias summary: covers 45 studies on the risk of bias judgments.

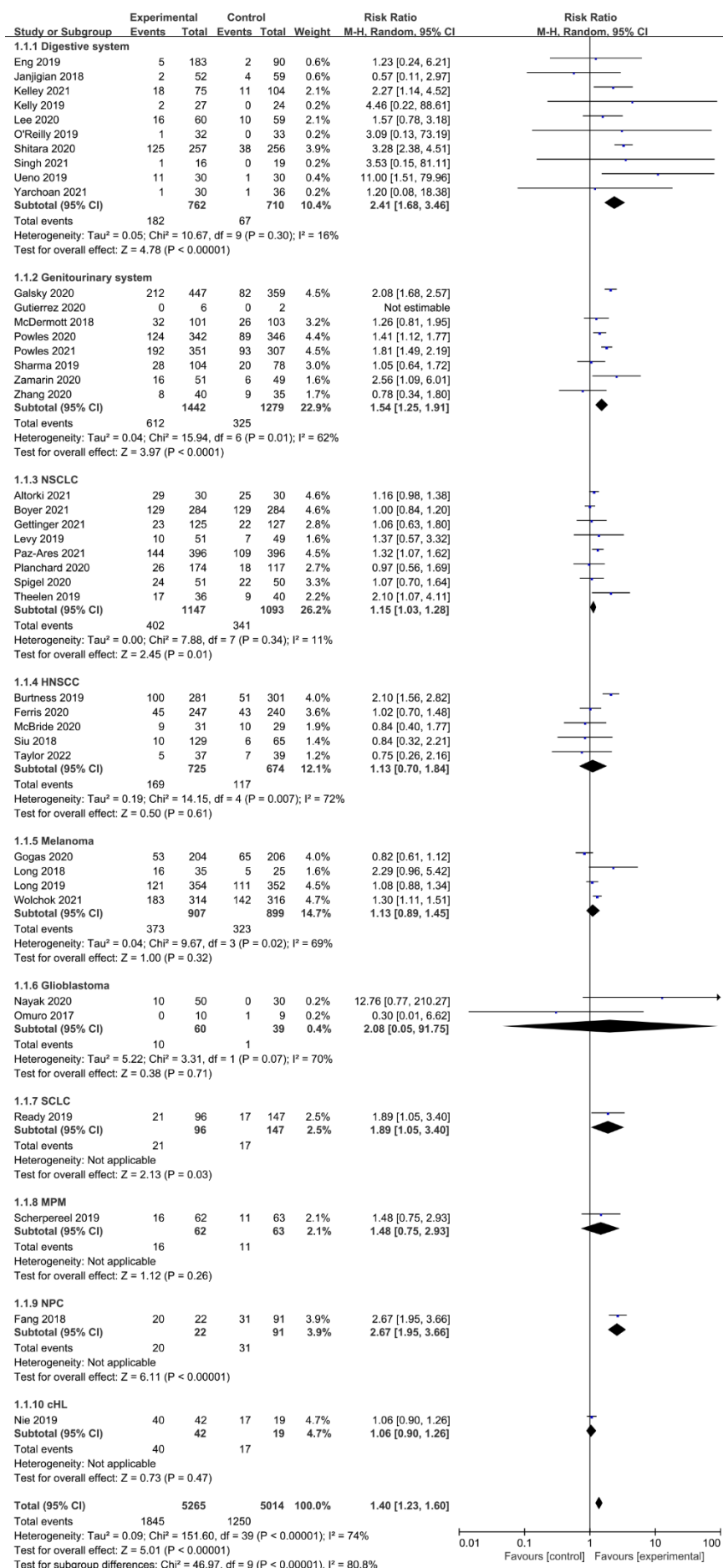


Figure S3 Forest Plot of the Risk ratio of ORR based on tumor types: anti-PD-1/PD-L1 versus combination therapy (digestive system tumors, genitourinary system tumors, non-small cell lung cancer, head and neck squamous cell carcinoma, melanoma, glioblastoma, small cell lung cancer, malignant pleural mesothelioma, nasopharyngeal carcinoma, and classic Hodgkin's lymphoma)

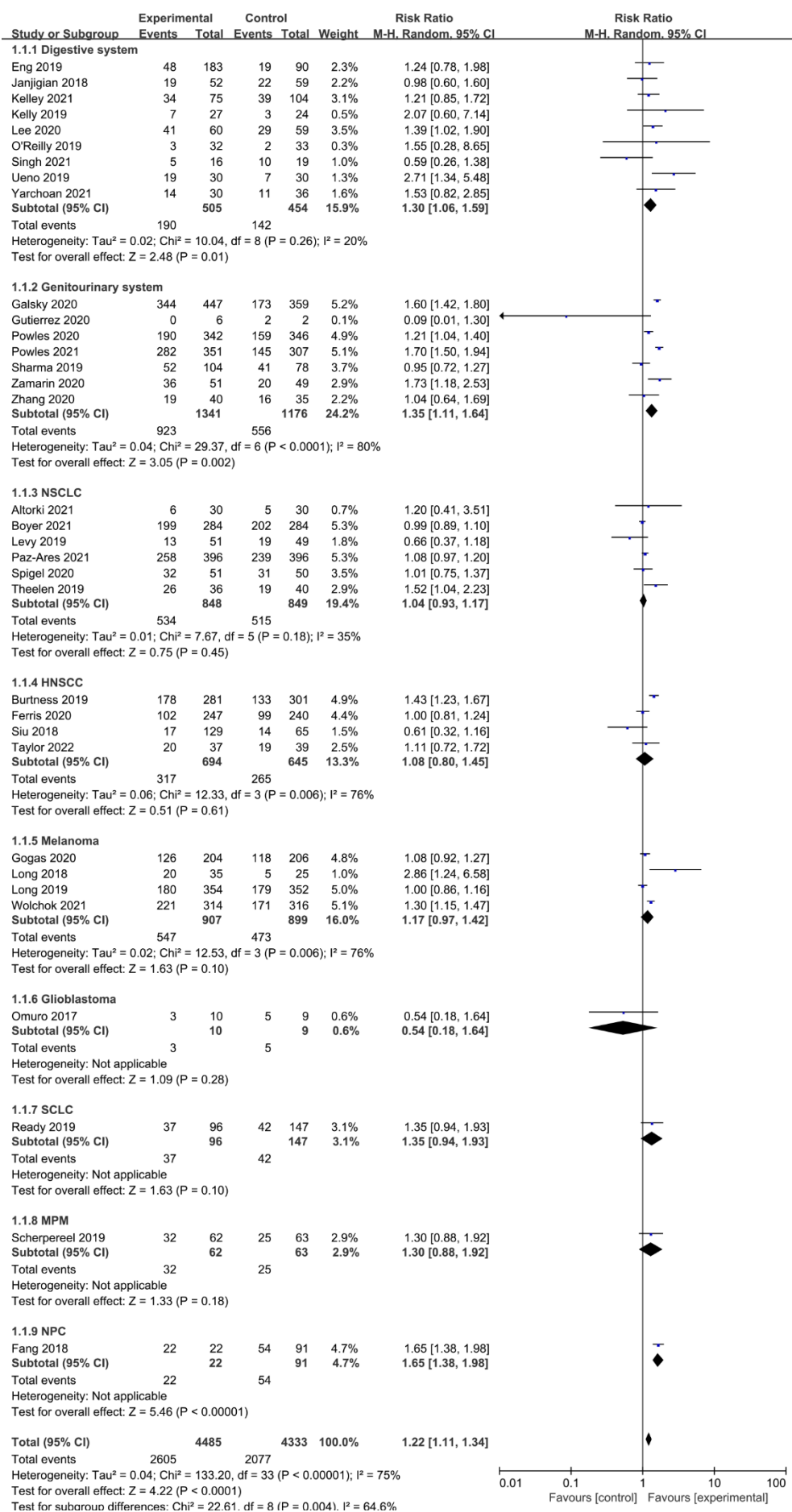


Figure S4 Forest Plot of the Risk ratio of DCR based on tumor types: anti-PD-1/PD-L1 versus combination therapy (digestive system tumors, genitourinary system tumors, non-small cell lung cancer, head and neck squamous cell carcinoma, melanoma, glioblastoma, small cell lung cancer, malignant pleural mesothelioma, and nasopharyngeal carcinoma)

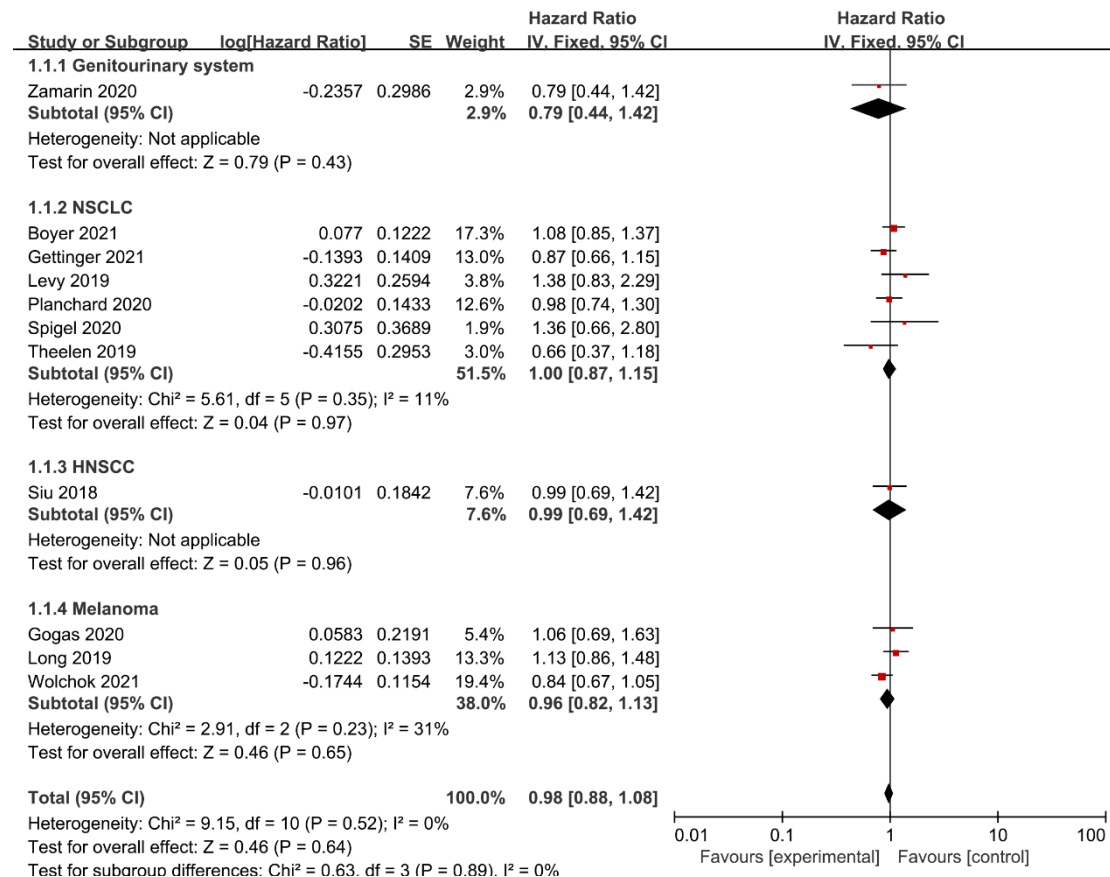


Figure S5 Forest Plot of the Hazard ratio of OS based on tumor types: anti-PD-1/PD-L1 versus combination therapy (genitourinary system tumors, non-small cell lung cancer, head and neck squamous cell carcinoma, and melanoma)

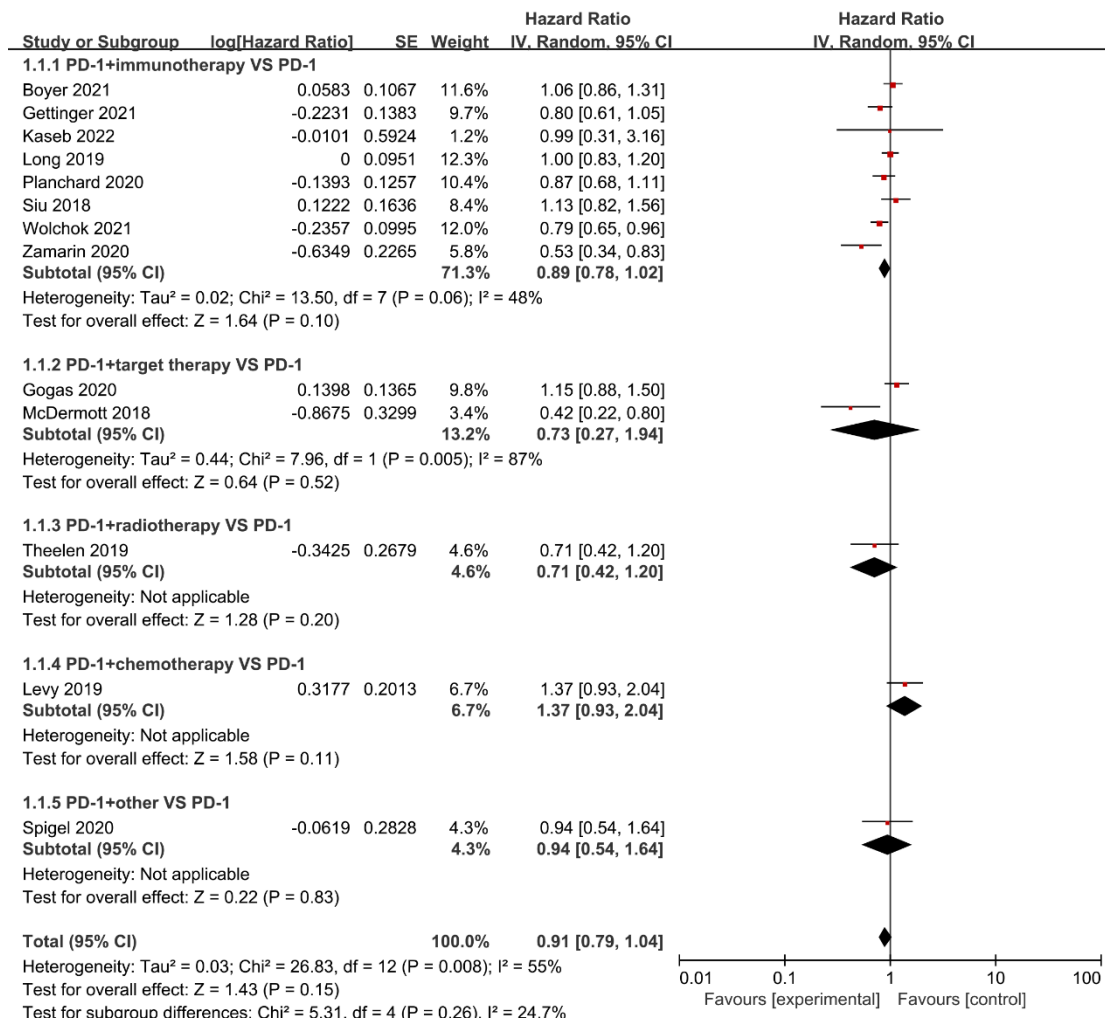


Figure S6 Forest Plot of the Hazard ratio of PFS based on therapeutic schedules: anti-PD-1/PD-L1 versus combination therapy (immunotherapy, targeted therapy, radiotherapy, chemotherapy, and other drugs)

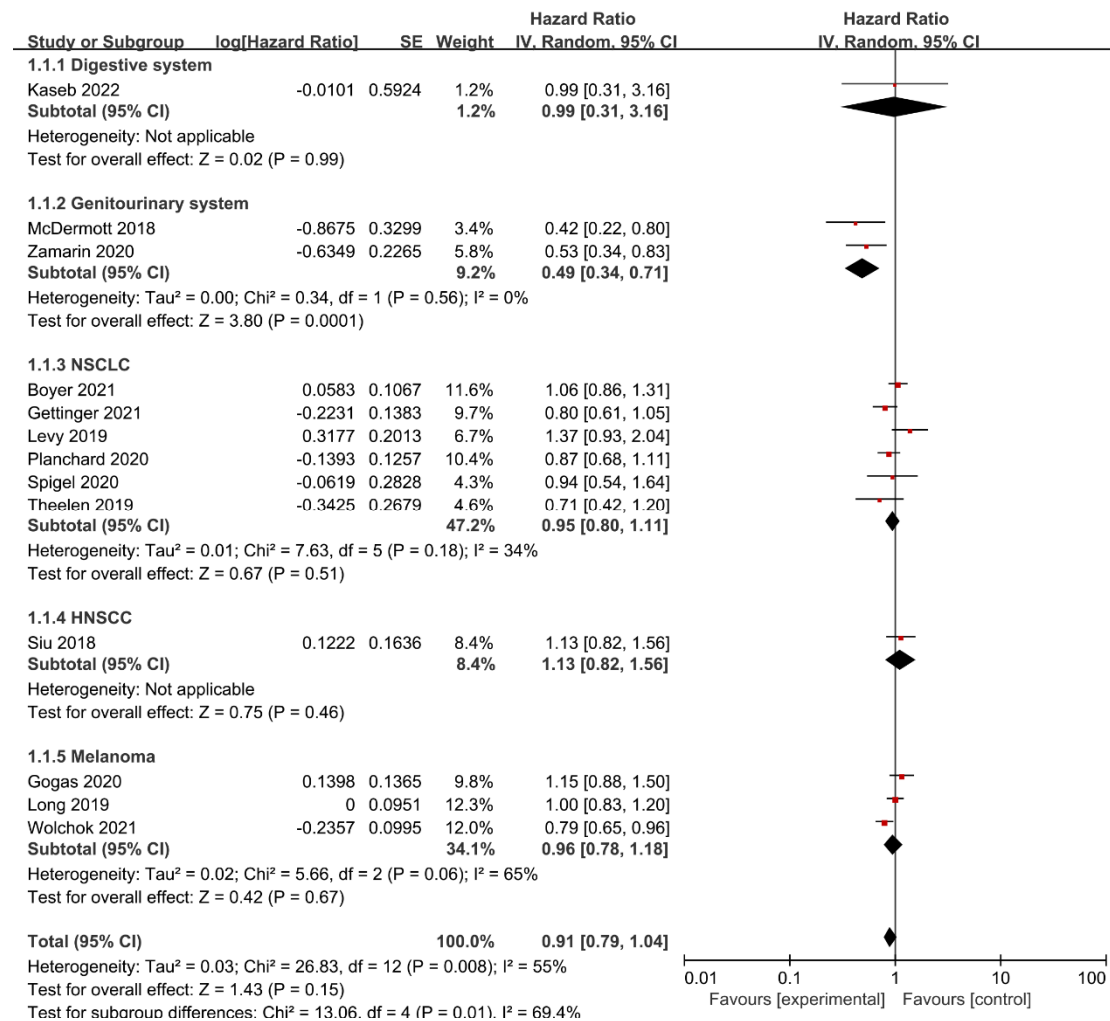


Figure S7 Forest Plot of the Hazard ratio of PFS based on tumor types: anti-PD-1/PD-L1 versus combination therapy (digestive system tumors, genitourinary system tumors, non-small cell lung cancer, head and neck squamous cell carcinoma, and melanoma)

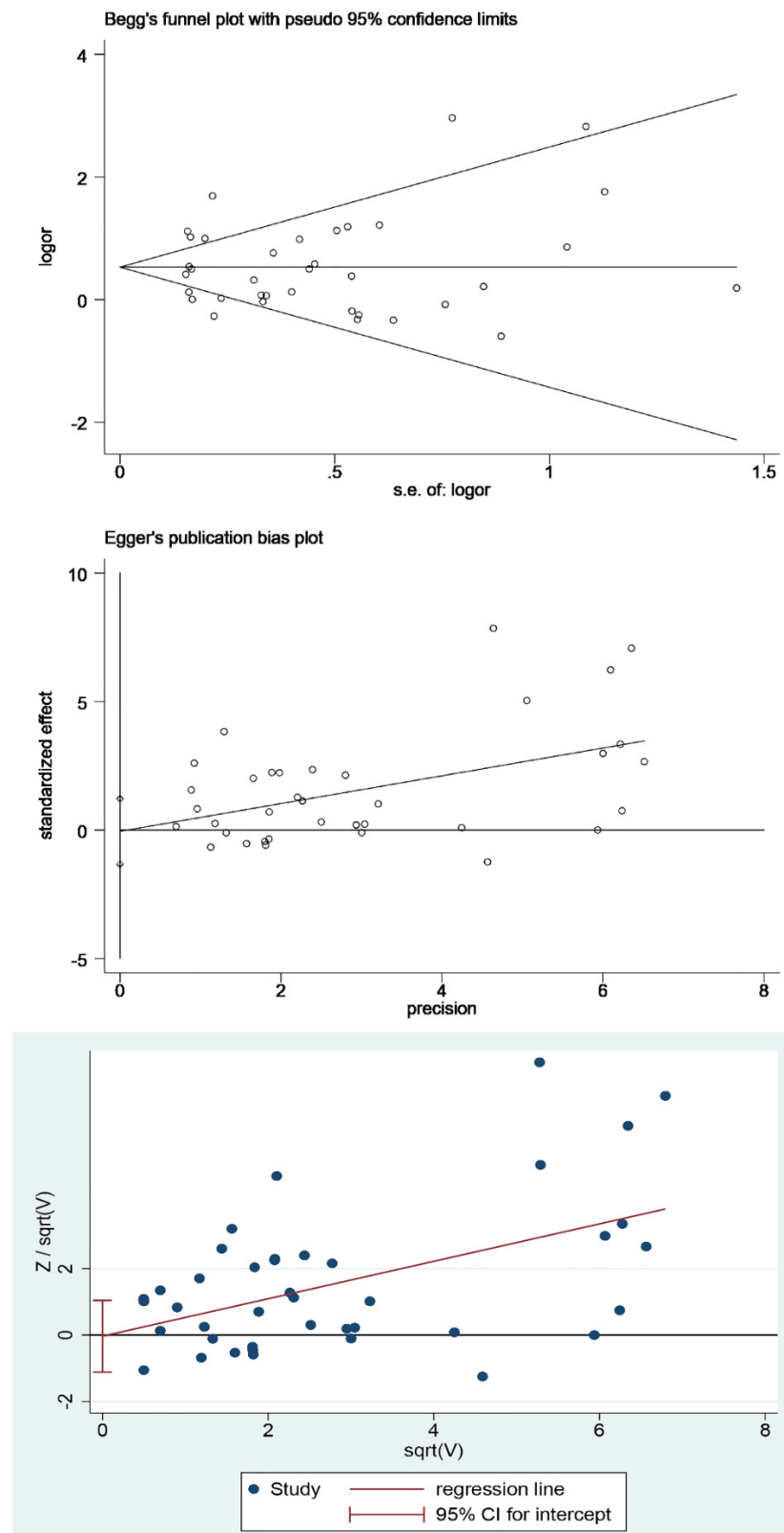


Figure S8 Begg's test ($P=0.406$), Egger's test ($P=0.931$), and Harbord's test ($P=0.952$) showed no significant publication bias in ORR.

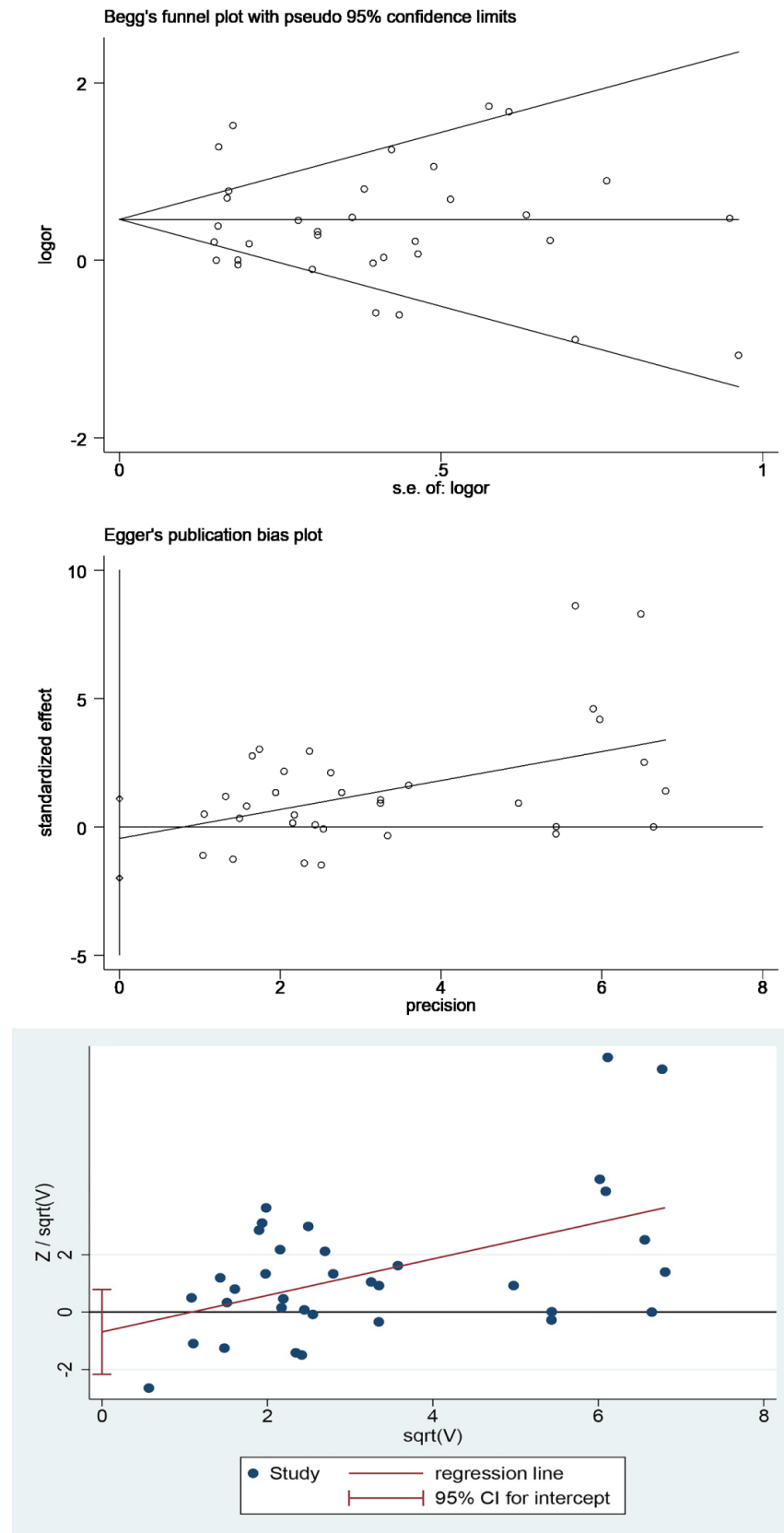


Figure S9 Begg's test ($P=0.448$), Egger's test ($P=0.554$), and Harbord's test ($P=0.348$) showed no significant publication bias in DCR.

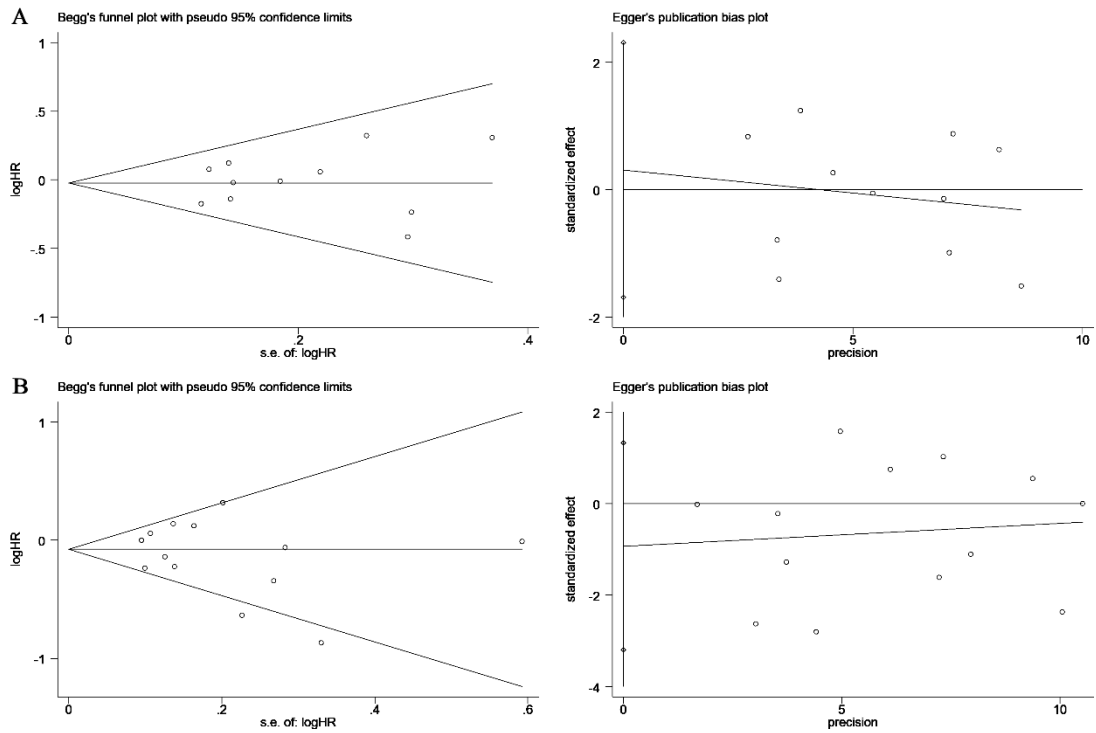


Figure S10 Begg's test and Egger's test

- (A) Begg's test ($P=0.533$) and Egger's test ($P=0.735$) showed no significant publication bias in Hazard ratio of OS.
- (B) Begg's test ($P=0.669$) and Egger's test ($P=0.383$) showed no significant publication bias in Hazard ratio of PFS.

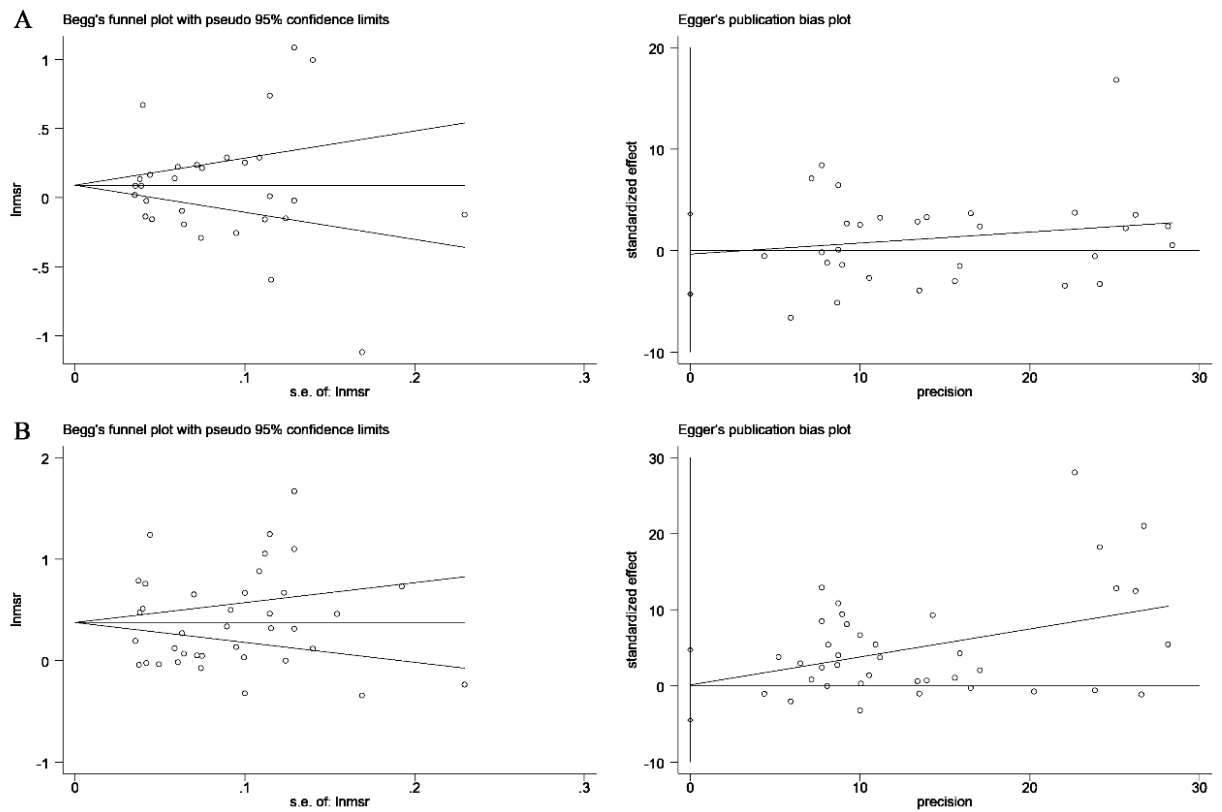


Figure S11 Begg's test and Egger's test

(A) Begg's test ($P=0.803$) and Egger's test ($P=0.860$) showed no significant publication bias in median OS.

(B) Begg's test ($P=0.204$) and Egger's test ($P=0.952$) showed no significant publication bias in median PFS.