Supplementary

Table S1 Literature search criteria

("non-small-cell lung cancer" [title] OR "non-small cell lung cancer" [title] OR "non small-cell lung cancer" [title] OR "non small cell lung cancer" [title] OR "non-small-cell lung carcinoma" [title] OR "non-small cell lung carcinoma" [title] OR "non small-cell lung carcinoma" [title] OR "non small cell lung carcinoma" [title] OR "nsclc" [title]) AND ("adjuvant"[Title/Abstract] OR "neoadjuvant"[Title/Abstract] OR "postoperative"[Title/Abstract] OR "perioperative"[Title/Abstract] OR "resectable"[Title/Abstract]) AND ("surgery"[Title/Abstract] OR "ipilimumab"[Title/Abstract] OR "tremelimumab"[Title/Abstract] OR "nivolumab"[Title/Abstract] OR "pembrolizumab"[Title/Abstract] OR "atezolizumab"[Title/Abstract] OR "durvalumab"[Title/Abstract] OR "toripalimab"[Title/Abstract] OR "tislelizumab"[Title/Abstract] OR "camrelizumab"[Title/Abstract] OR "sintilimab"[Title/Abstract] OR "sugemalimab"[Title/Abstract] OR "envafolimab"[Title/Abstract] OR "immunotherapy"[Title/Abstract] OR "immune checkpoint inhibitor"[Title/Abstract] OR "programmed cell death protein 1"[Title/Abstract] OR "programmed cell death protein"[Title/Abstract] OR "PD-1"[Title/Abstract] OR "programmed cell death ligand 1"[Title/Abstract] OR "PD-L1"[Title/Abstract] OR "cytotoxic t lymphocyte associated antigen 4"[Title/Abstract] OR "CTLA-4"[Title/Abstract] OR "CTLA4"[Title/Abstract]) AND "chemotherapy"[Title/Abstract] AND ("plus"[Title/Abstract] OR "versus"[Title/Abstract] OR "compare"[Title/Abstract] OR "comparison"[Title/Abstract] OR "comparative"[Title/Abstract] OR "comparing"[Title/Abstract] OR "Trial"[Title/Abstract] OR "phase"[Title/Abstract] OR "randomized controlled trials"[Title/Abstract]) AND ("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type] OR "Randomized"[Title/Abstract] OR "randomised"[Title/Abstract] OR "randomly"[Title/Abstract] OR "Trial"[Title/Abstract] OR "phase"[Title/Abstract]) AND "humans"[MeSH Terms] AND ("0001/01/01"[Date - Publication] : "2024/8/20"[Date - Publication])

NSCLC, non-small-cell lung cancer.

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Table S2 Bayesian ranking results of network meta-analysis

Treatment	Rank of possibility (%)					
	1	2	3	4	5	6
Event-free survival for resectable non-small cell lung cancer						
Peri ChemoIO	84.73*	15.08	0.19	0.00	0.00	0.00
Adj ChemoIO	0.38	28.14	71.46	0.02	0.00	0.00
Neo ChemoIO	14.89	56.78	26.61	1.37	0.32	0.03
Adj Chemo	0.00	0.00	1.69	89.05	9.26	0.00
Neo Chemo	0.00	0.00	0.05	9.57	90.36	0.03
Surgery alone	0.00	0.00	0.00	0.00	0.06	99.94*
Overall survival for resectable non-small cell lung cancer						
Peri ChemoIO	60.43*	37.84	1.65	0.08	0.00	0.00
Adj ChemoIO	1.10	16.15	58.10	13.44	9.18	2.03
Neo ChemoIO	38.46	43.58	9.07	4.08	2.59	2.22
Adj Chemo	0.01	2.11	24.33	60.73	12.79	0.03
Neo Chemo	0.00	0.31	6.84	21.31	68.46	3.07
Surgery alone	0.00	0.00	0.01	0.36	6.97	92.66*
Grade ≥3 treatment-related adverse events for resectable non-small cell lung cancer						
Peri ChemoIO	53.20	43.16	3.55	0.09	0.00	0.00
Adj ChemoIO	45.69	29.39	15.20	9.72	0.00	0.00
Neo ChemoIO	1.11	5.43	14.32	41.14	38.00	0.01
Adj Chemo	0.00	2.59	9.94	27.64	59.77	0.06
Neo Chemo	0.00	19.43	56.99	21.41	2.16	0.00
Surgery alone	0.00	0.00	0.00	0.00	0.06	99.94*

The probability value in each cell indicates the likelihood of each row-defining treatment being ranked at the column-defining position. The values with the highest probability of being ranked first or last are marked with an asterisk (*). Adj Chemo, adjuvant chemotherapy; Adj ChemoIO, adjuvant chemoimmunotherapy; Neo Chemo, neoadjuvant chemotherapy; Neo ChemoIO, neoadjuvant chemoimmunotherapy; Peri ChemoIO, perioperative chemoimmunotherapy.

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Table S3 Characteristics of the other trials comparing chemotherapy with surgery alone

Study (phase, ethnicity)	Participant arm (top: intervention arm; bottom: control arm)	Therapeutic regimen	Sample size (n)	Median age (years)	Male (%)	Clinical stage		Reported outcomes
						I–II (%)	III (%)	
CSLC 0501 2018 (III Multi)	Neo Chemo	Intervention arm: 3 cycles of DC (docetaxel: 75 mg/m^2, carboplatin: AUC =5 on day 1 Q3W) → surgery	97	58	81.4	IB 31.3; IIA 11.5; IIB 27.1	30.2	DFS; OS; grade ≥3 AEs
	Adj Chemo	Surgery → 3 cycles of DC (docetaxel: 75 mg/m^2, carboplatin: AUC =5 on day 1 Q3W)	101	57	79.2	IB 33.7; IIA 12.9; IIB 29.7	23.8	
ANITA 2006 (III Multi)	Adj Chemo	Surgery → 30 mg/m^2 vinorelbine on days 1, 8, 15, and 22 (Q4W) for a maximum of 16 doses; and 100 mg/m^2 cisplatin on days 1, 29, 57, and 85	407	59	85	58	41	DFS; OS; grade ≥3 AEs
	Surgery alone	Surgery → observation	433	59	87	62	37	
IALT 2004 (III Multi)	Adj Chemo	Surgery → each participating center could determine the dose of cisplatin given per cycle, the drug that was combined with cisplatin	932	59	80.7	24.7	39.6	DFS; OS; grade ≥3 AEs
	Surgery alone	Surgery → observation	935	59	80.2	60.9	39.1	
Scagliotti 2003 (III Multi)	Adj Chemo	Surgery → 3 cycles of MVP regimen Q3W	548	61	86	70	29	DFS; OS; grade ≥3 AEs
	Surgery alone	Surgery → observation	540	61	86	72	28	
Timothy 2005 (III North American)	Adj Chemo	Surgery → 4 cycles of cisplatin 50 mg/m^2 on days 1 and 8 every 4 weeks and vinorelbine 25 mg/m^2 weekly for 16 weeks	242	61	65	100	0	DFS; OS; grade ≥3 AEs
	Surgery alone	Surgery → observation	240	61	65	100	0	
Wei 2010 (III single-center)	Adj Chemo	Surgery → 4 cycles of cisplatin 50 mg/m^2 on days 1 and 8 every 4 weeks and vinorelbine 25 mg/m^2 or paclitaxel 175 mg/m^2 weekly for 16 weeks	79	54	56	0	100	DFS; OS; grade ≥3 AEs
	Surgery alone	Surgery → observation	71	59	54	0	100	
Rosell 1999 (III Multi)	Adj Chemo	3 cycles of mitomycin 6 mg/m^2 and ifosfamide 3 g/m^2 intravenously (IV) and cisplatin 50 mg/m^2 → surgery	30	60	54	0	100	DFS; OS; grade ≥3 AEs
	Surgery alone	Surgery → observation	30	60	56	0	100	
NATCH 2010 (III Multi)	Neo Chemo	3 cycles of paclitaxel 200 mg/m^2 followed immediately carboplatin 6.0 mg/mL/min Q3W → surgery	199	65	87.9	97.4	2.5	DFS; OS; grade ≥3 AEs
	Adj Chemo	Surgery → 3 cycles of paclitaxel 200 mg/m^2 followed immediately by carboplatin 6.0 mg/mL/min Q3W	210	64	86.2	99.5	0.5	
	Surgery alone	Surgery → observation	202	64	87.6	98.1	1.9	
CHEST 2011 (III Multi)	Neo Chemo	3 cycles of gemcitabine 1,250 mg/m^2 days 1 and 8 Q3W plus cisplatin 75 mg/m^2 day 1 Q3W → surgery	129	60.6	78	52	5	DFS; OS; grade ≥3 AEs
	Surgery alone	Surgery alone	141	62.7	89	43	2	
Depierre 2002 (III Multi)	Neo Chemo	2 cycles of PCT (mitomycin 6 mg/m^2 on day 1, ifosfamide 1.5 g/m^2 on days 1 to 3, and cisplatin 30 mg/m^2 on days 1 to 3) Q3W → surgery	179	60	93	49	51	DFS; OS; grade ≥3 AEs
	Surgery alone	Primary surgery	176	61	94	57	43	
Gilligan 2007 (III Multi)	Neo Chemo	3 cycles of one of six platinum-based regimens (panel) Q3W → surgery	258	63	72	92	8	DFS; OS
	Surgery alone	Surgery → observation	261	63	72	94	6	
S9900 2010 (III Multi)	Neo Chemo	3 cycles of paclitaxel 225mg/m^2 and carboplatin (area under the curve of 6 given over 30 minutes after paclitaxel) Q3W → surgery	169	65	64	IB/IIA 67; IIB/IIIA 33		DFS; OS; grade ≥3 AEs
	Surgery alone	Surgery → observation	168	64	68	IB/IIA 68; IIB/IIIA 32		

AEs, adverse events; DFS, disease-free survival; EFS, event-free survival; OS, overall survival.

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Table S4 Comparisons of the fit of consistency and inconsistency models using DIC

Analysis group	Outcome/ subgroup	Random, consistency (DIC)	Random, inconsistency (DIC)	Fixed, consistency (DIC)	Fixed, inconsistency (DIC)
Overall analysis	EFS	36.73	36.07	35.10	35.59
	OS	38.99	39.79	36.07	36.92
	Grade ≥3 AEs	40.77	41.24	40.39	40.45
Stage subgroup (EFS)	Stage I–II	20.40	20.40	19.44	20.38
	Stage III	21.87	21.92	20.72	21.93
PD-L1 subgroup (EFS)	TPS <1%	23.07	33.98	21.50	33.95
	TPS 1–49%	29.09	33.95	28.13	34.00
	TPS ≥50%	30.21	33.98	29.23	33.98
ECOG PS subgroup (EFS)	PS =0	13.36	13.31	11.68	11.70
	PS ≥1	15.81	15.74	15.68	15.76

The DIC is a Bayesian model evaluation criterion that measures model fit adjusted with complexity of the model; smaller DIC values correspond to more preferable models. AEs, adverse events; DIC, deviance information criteria; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; OS, overall survival; TPS, tumor proportion score.

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Table S5 Results of network meta-regression analysis assessing potential effect modifiers

Outcome	Covariate	Coefficient	Std_Error	Z_value	P_value	ci_lb	ci_ub
Event-free survival	2 cycles	0.153902054	0.20164836	0.763219965	0.45	−0.24132147	0.549125577
	3 cycles	0.119924857	0.108964873	1.100582727	0.27	−0.09364237	0.333492083
	3–4 cycles	−0.11099997	0.120006221	−0.9249518	0.35	−0.34620784	0.124207901
	4 cycles	−0.05615449	0.112064684	−0.50108996	0.62	−0.27579723	0.163488257
	Stage III percentage*	−0.00420296	0.001299784	−3.23358051	0.001*	−0.00675048	−0.00165543
	Median age	−0.00420832	0.012392428	−0.33958794	0.73	−0.02849703	0.020080393
	Male percentage	0.000864339	0.00350946	0.246288258	0.81	−0.00601408	0.007742753
	Sample size*	0.000410978	0.000173097	2.374268883	0.02*	0.0000072	0.000750241
Overall survival	2 cycles	−0.00904	0.235148	−0.03843	0.97	−0.46992	0.451845
	3 cycles	−0.00566	0.138358	−0.04089	0.97	−0.27683	0.265519
	3–4 cycles	−0.2519	0.146714	−1.71698	0.09	−0.53946	0.035649
	4 cycles	−0.12738	0.146005	−0.87242	0.38	−0.41354	0.158787
	Stage III percentage	−0.00244	0.001504	−1.62319	0.10	−0.00539	0.000506
	Median age	0.009044	0.015883	0.569453	0.57	−0.02209	0.040174
	Male percentage	0.002568	0.004006	0.641104	0.52	−0.00528	0.01042
	Sample size*	0.000469	0.000209	2.247292	0.02*	0.00006	0.000878
Grade >3 AEs	3 cycles	0.283395493	2.067276543	0.137086397	0.89	−3.76839208	4.335183065
	3–4 cycles	−0.98964057	1.507608553	−0.65643072	0.51	−3.94449903	1.965217902
	4 cycles	−0.61014253	1.103950878	−0.55268993	0.58	−2.77384649	1.553561433
	Stage III percentage	−0.00225651	0.013423194	−0.16810509	0.87	−0.02856548	0.024052469
	Median age	0.149138744	0.157517521	0.946807335	0.34	−0.15958992	0.457867413
	Male percentage	0.033741097	0.045939882	0.73446198	0.46	−0.05629942	0.12378161
	Sample size	−0.00021822	0.004444177	−0.04910302	0.96	−0.00892865	0.008492203

Results of the network meta-regression analysis assessing potential effect modifiers are presented as the beta coefficient, along with the corresponding 95% credible interval lower bound (ci_lb) and upper bound (ci_ub), standard error (SE), Z-value, and P value. These values were calculated using a random-effects network meta-regression model. The SE represents the precision of the estimated coefficient, with a smaller SE indicating greater precision. The Z-value is the ratio of the coefficient to the SE, used to assess the statistical significance of each covariate. A P value <0.05 indicates statistical significance. Covariates with 95% credible intervals including 0 are considered to have nonsignificant effects. The statistically significant covariates are marked with an asterisk (*).

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Table S6 Bayesian ranking results of network meta-analysis in subgroup analyses by disease stage, PD-L1 expression level and ECOG PS score

Treatment	Rank of possibility (%)					
	1	2	3	4	5	6
Event-free survival for resectable non-small cell lung cancer of stage IB–IIB						
Peri ChemoIO	33.24	41.40	18.54	5.15	1.16	0.52
Adj ChemoIO	51.79*	35.03	11.60	1.19	0.28	0.10
Neo ChemoIO	14.79	14.81	21.09	14.71	9.91	24.69
Adj Chemo	0.13	7.90	40.90	38.76	11.30	1.00
Neo Chemo	0.03	0.70	6.52	30.34	48.56	13.85
Surgery alone	0.02	0.17	1.34	9.85	28.79	59.83*
Event-free survival for resectable non-small cell lung cancer of stage IIIA–IIIB						
Peri ChemoIO	48.56	51.39	0.04	0.00	0.00	0.00
Adj ChemoIO	0.04	0.18	5.65	86.75	6.54	0.84
Neo ChemoIO	51.40*	48.33	0.23	0.04	0.01	0.00
Adj Chemo	0.00	0.01	0.17	8.31	87.11	4.40
Neo Chemo	0.00	0.10	93.90	4.10	1.58	0.33
Surgery alone	0.00	0.00	0.00	0.79	4.78	94.43*
Event-free survival for resectable non-small cell lung cancer of PD-L1 TPS <1%						
Peri ChemoIO	56.56*	32.44	9.94	0.94	0.12	0.00
Adj ChemoIO	18.40	41.74	32.10	4.60	3.01	0.16
Neo ChemoIO	24.98	22.16	20.58	9.11	13.06	10.10
Adj Chemo	0.06	3.15	31.96	53.80	11.03	0.00
Neo Chemo	0.00	0.51	5.42	31.51	62.51	0.05
Surgery alone	0.00	0.00	0.00	0.04	10.28	89.68*
Event-free survival for resectable non-small cell lung cancer of PD-L1 TPS 1–49%						
Peri ChemoIO	49.32*	44.89	5.79	0.00	0.00	0.00
Adj ChemoIO	4.60	28.89	65.38	0.72	0.39	0.02
Neo ChemoIO	46.07	26.14	20.18	2.43	2.89	2.29
Adj Chemo	0.00	0.07	7.63	77.92	14.38	0.00
Neo Chemo	0.00	0.01	1.03	18.92	79.96	0.07
Surgery alone	0.00	0.00	0.00	0.01	2.38	97.62*
Event-free survival for resectable non-small cell lung cancer of PD-L1 TPS ≥50%						
Peri ChemoIO	9.84	84.23	5.93	0.00	0.00	0.00
Adj ChemoIO	0.46	8.20	91.20	0.08	0.05	0.00
Neo ChemoIO	89.70*	7.56	2.58	0.06	0.06	0.04
Adj Chemo	0.00	0.00	0.23	84.57	15.20	0.00
Neo Chemo	0.00	0.00	0.07	15.28	84.56	0.10
Surgery alone	0.00	0.00	0.00	0.00	0.14	99.86*

Table S6 (*continued*)

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Table S6 (*continued*)

Treatment	Rank of possibility (%)					
	1	2	3	4	5	6
Event-free survival for resectable non-small cell lung cancer of ECOG PS =0						
Peri ChemoIO	53.17	40.15	6.36	0.32	0.00	0.00
Adj ChemoIO	6.96	18.05	64.36	8.35	2.26	0.03
Neo ChemoIO	39.87	41.54	15.39	2.69	0.37	0.14
Adj Chemo	0.00	0.17	2.98	41.15	31.60	24.10
Neo Chemo	0.00	0.09	10.49	43.17	42.27	3.99
Surgery alone	0.00	0.01	0.42	4.33	23.51	71.74
Event-free survival for resectable non-small cell lung cancer of ECOG PS ≥1						
Peri ChemoIO	76.96	21.66	1.29	0.09	0.00	0.00
Adj ChemoIO	2.34	25.20	47.80	10.52	12.07	2.07
Neo ChemoIO	20.69	49.81	14.50	6.07	3.34	5.59
Adj Chemo	0.01	0.40	9.22	29.67	19.98	40.72
Neo Chemo	0.00	1.87	19.15	33.22	34.04	11.73
Surgery alone	0.00	1.07	8.05	20.42	30.58	39.89

The values with the highest probability of being ranked first or last are marked with an asterisk (*). Adj Chemo, adjuvant chemotherapy; Adj ChemoIO, adjuvant chemoimmunotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; Neo Chemo, neoadjuvant chemotherapy; Neo ChemoIO, neoadjuvant chemoimmunotherapy; Peri ChemoIO, perioperative chemoimmunotherapy; TPS, tumor proportion score.

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Table S7 Comparisons of the fit of consistency and inconsistency models using DIC in the sensitivity analysis

	Outcome/subgroup	Model	First sensitivity analysis	Second sensitivity analysis
Overall analysis	Event-free survival	Random, consistency	29.92*	23.17
		Random, inconsistency	30.62	21.95
		Fixed, consistency	31.67	21.46*
		Fixed, inconsistency	29.95	21.92
	Overall survival	Random, consistency	28.51*	27.64
		Random, inconsistency	29.19	28.68
		Fixed, consistency	31.25	27.47*
		Fixed, inconsistency	29.18	28.71
	Grade ≥3 adverse events	Random, consistency	40.77	38.00*
		Random, inconsistency	41.24	38.51
		Fixed, consistency	40.39*	37.98
		Fixed, inconsistency	40.45	38.04
Stage subgroup (event-free survival)	Stage I–II	Random, consistency	17.13	20.40
		Random, inconsistency	16.97	20.40
		Fixed, consistency	15.60*	19.44*
		Fixed, inconsistency	16.92	20.38
	Stage III	Random, consistency	19.63	17.44
		Random, inconsistency	19.70	17.40
		Fixed, consistency	18.05*	15.91*
		Fixed, inconsistency	19.69	17.44
PD-L1 subgroup (event-free survival)	TPS <1%	Random, consistency	19.26	21.50
		Random, inconsistency	25.98	33.95
		Fixed, consistency	17.82*	21.37*
		Fixed, inconsistency	25.95	32.02
	TPS 1–49%	Random, consistency	24.59	24.65
		Random, inconsistency	25.96	31.98
		Fixed, consistency	24.39*	23.26*
		Fixed, inconsistency	25.98	32.03
	TPS ≥50%	Random, consistency	24.72*	28.87
		Random, inconsistency	26.01	31.96
		Fixed, consistency	25.54	28.04*
		Fixed, inconsistency	26.02	32.03

The DIC is a Bayesian model evaluation criterion that measures model fit adjusted with complexity of the model; smaller DIC values correspond to more preferable models. *, statistically significant. DIC, deviance information criteria; TPS, tumor proportion score.

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Table S8 Bayesian ranking results of network meta-analysis in the first sensitivity analysis

Treatment	Rank of possibility (%) (the first sensitivity analysis)					
	1	2	3	4	5	6
Event-free survival for resectable non-small cell lung cancer						
Peri ChemoIO	84.21*	15.47	0.32	0.00	0.00	0.00
Adj ChemoIO	0.82	26.97	72.02	0.18	0.00	0.00
Neo ChemoIO	14.97	57.56	25.32	1.83	0.28	0.03
Adj Chemo	0.00	0.00	2.08	75.56	22.36	0.00
Neo Chemo	0.00	0.00	0.25	22.42	75.93	1.40
Surgery alone	0.00	0.00	0.00	0.00	1.43	98.57*
Overall survival for resectable non-small cell lung cancer						
Peri ChemoIO	60.84*	38.45	0.68	0.03	0.00	0.00
Adj ChemoIO	0.46	9.62	49.26	21.92	16.34	2.40
Neo ChemoIO	38.70	49.38	6.13	2.39	2.23	1.17
Adj Chemo	0.00	0.87	11.40	41.95	45.68	0.11
Neo Chemo	0.00	1.68	32.53	33.44	30.55	1.79
Surgery alone	0.00	0.00	0.01	0.25	5.21	94.53*
Grade ≥3 treatment-related adverse events for resectable non-small cell lung cancer						
Peri ChemoIO	53.20*	43.16	3.55	0.09	0.00	0.00
Adj ChemoIO	45.69	29.39	15.20	9.72	0.00	0.00
Neo ChemoIO	1.11	5.43	14.32	41.14	38.00	0.01
Adj Chemo	0.00	2.59	9.94	27.64	59.77	0.06
Neo Chemo	0.00	19.43	56.99	21.41	2.16	0.00
Surgery alone	0.00	0.00	0.00	0.00	0.06	99.94*

The values with the highest probability of being ranked first or last are marked with an asterisk (*). Adj Chemo, adjuvant chemotherapy; Adj ChemoIO, adjuvant chemoimmunotherapy; Neo Chemo, neoadjuvant chemotherapy; Neo ChemoIO, neoadjuvant chemoimmunotherapy; Peri ChemoIO, perioperative chemoimmunotherapy.

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Table S9 Bayesian ranking results of network meta-analysis in subgroup analyses by disease stage and PD-L1 status (the first sensitivity analysis)

Treatment	Rank of possibility (%) (the first sensitivity analysis)					
	1	2	3	4	5	6
Event-free survival for resectable non-small cell lung cancer of stage IB–IIB						
Peri ChemoIO	15.19	32.03	31.73	16.62	4.28	0.16
Adj ChemoIO	78.13*	16.24	5.06	0.56	0.00	0.00
Neo ChemoIO	6.67	11.33	16.39	20.41	19.23	25.98
Adj Chemo	0.01	40.15	33.83	18.97	7.03	0.00
Neo Chemo	0.00	0.26	3.11	15.91	40.76	39.97*
Surgery alone	0.00	0.00	9.88	27.53	28.70	33.89
Event-free survival for resectable non-small cell lung cancer of stage III						
Peri ChemoIO	49.93*	49.61	0.31	0.12	0.03	0.00
Adj ChemoIO	0.37	0.70	5.32	69.56	16.44	7.60
Neo ChemoIO	49.63	48.30	1.48	0.33	0.17	0.09
Adj Chemo	0.05	0.21	0.69	9.99	58.12	30.95
Neo Chemo	0.00	1.14	91.96	4.24	2.02	0.64
Surgery alone	0.01	0.04	0.23	15.77	23.22	60.72*
Event-free survival for resectable non-small cell lung cancer of PD-L1 TPS <1%						
Peri ChemoIO	53.62*	33.23	11.11	1.92	0.11	0.02
Adj ChemoIO	22.11	39.63	29.81	5.45	2.77	0.23
Neo ChemoIO	24.10	21.66	19.09	12.31	10.46	12.39
Adj Chemo	0.17	4.53	32.71	47.57	15.02	0.00
Neo Chemo	0.00	0.95	7.27	31.01	56.27	4.50
Surgery alone	0.00	0.00	0.02	1.75	15.36	82.87*
Event-free survival for resectable non-small cell lung cancer of PD-L1 TPS 1–49%						
Peri ChemoIO	48.28*	44.45	7.26	0.01	0.00	0.00
Adj ChemoIO	6.22	30.12	62.22	1.05	0.38	0.02
Neo ChemoIO	45.50	25.31	20.55	3.54	2.31	2.80
Adj Chemo	0.00	0.09	8.35	72.33	19.22	0.00
Neo Chemo	0.00	0.04	1.62	22.70	69.97	5.67
Surgery alone	0.00	0.00	0.00	0.37	8.12	91.51*
Event-free survival for resectable non-small cell lung cancer of PD-L1 TPS >50%						
Peri ChemoIO	11.93	71.94	15.63	0.45	0.05	0.01
Adj ChemoIO	3.61	17.89	75.58	1.87	0.65	0.41
Neo ChemoIO	84.46*	9.99	4.60	0.58	0.17	0.21
Adj Chemo	0.01	0.15	2.25	71.78	22.18	3.64
Neo Chemo	0.00	0.02	1.65	23.22	60.45	14.66
Surgery alone	0.00	0.02	0.29	2.10	16.51	81.08*

The values with the highest probability of being ranked first or last are marked with an asterisk (*). Adj Chemo, adjuvant chemotherapy; Adj ChemoIO, adjuvant chemoimmunotherapy; Neo Chemo, neoadjuvant chemotherapy; Neo ChemoIO, neoadjuvant chemoimmunotherapy; Peri ChemoIO, perioperative chemoimmunotherapy; TPS, tumor proportion score.

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Table S10 Bayesian ranking results of network meta-analysis in the second sensitivity analysis

Treatment	Rank of possibility (%) (the second sensitivity analysis)					
	1	2	3	4	5	6
Event-free survival for resectable non-small cell lung cancer						
Peri ChemoIO	75.27*	23.89	0.84	0.00	0.00	0.00
Adj ChemoIO	1.08	25.12	73.76	0.03	0.00	0.00
Neo ChemoIO	23.65	50.99	23.99	1.03	0.30	0.04
Adj Chemo	0.00	0.00	1.33	83.56	15.11	0.00
Neo Chemo	0.00	0.00	0.08	15.38	84.45	0.10
Surgery alone	0.00	0.00	0.00	0.00	0.14	99.86*
Overall survival for resectable non-small cell lung cancer						
Peri ChemoIO	57.80*	39.49	2.50	0.20	0.01	0.00
Adj ChemoIO	1.56	16.52	57.29	13.43	9.23	1.97
Neo ChemoIO	40.62	41.57	9.01	4.03	2.58	2.19
Adj Chemo	0.01	2.10	24.42	60.71	12.73	0.03
Neo Chemo	0.00	0.33	6.78	21.29	68.57	3.04
Surgery alone	0.00	0.00	0.01	0.32	6.89	92.78*
Grade ≥3 treatment-related adverse events for resectable non-small cell lung cancer						
Peri ChemoIO	50.57*	44.82	4.44	0.17	0.01	0.00
Adj ChemoIO	48.02	26.91	15.28	9.79	0.00	0.00
Neo ChemoIO	1.37	5.47	14.05	41.28	37.82	0.01
Adj Chemo	0.00	3.12	9.34	27.54	59.94	0.06
Neo Chemo	0.04	19.69	56.88	21.22	2.17	0.00
Surgery alone	0.00	0.00	0.00	0.00	0.06	99.94*

The values with the highest probability of being ranked first or last are marked with an asterisk (*). Adj Chemo, adjuvant chemotherapy; Adj ChemoIO, adjuvant chemoimmunotherapy; Neo Chemo, neoadjuvant chemotherapy; Neo ChemoIO, neoadjuvant chemoimmunotherapy; Peri ChemoIO, perioperative chemoimmunotherapy.

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Table S11 Bayesian ranking results of network meta-analysis in subgroup analyses by disease stage and PD-L1 status (the second sensitivity analysis)

Treatment	Rank of possibility (%) (the second sensitivity analysis)					
	1	2	3	4	5	6
Event-free survival for resectable non-small cell lung cancer of stage IB–IIB						
Peri ChemoIO	33.24	41.40	18.54	5.15	1.16	0.52
Adj ChemoIO	51.79*	35.03	11.60	1.19	0.28	0.10
Neo ChemoIO	14.79	14.81	21.09	14.71	9.91	24.69
Adj Chemo	0.13	7.90	40.90	38.76	11.30	1.00
Neo Chemo	0.03	0.70	6.52	30.34	48.56	13.85
Surgery alone	0.02	0.17	1.34	9.85	28.79	59.83*
Event-free survival for resectable non-small cell lung cancer of stage III						
Peri ChemoIO	36.43	63.47	0.09	0.02	0.00	0.00
Adj ChemoIO	0.06	0.20	5.58	86.71	6.55	0.89
Neo ChemoIO	63.51*	36.23	0.22	0.03	0.00	0.00
Adj Chemo	0.00	0.01	0.18	8.32	86.94	4.55
Neo Chemo	0.00	0.09	93.93	4.13	1.55	0.32
Surgery alone	0.00	0.00	0.01	0.80	4.96	94.24*
Event-free survival for resectable non-small cell lung cancer of PD-L1 TPS <1%						
Peri ChemoIO	53.34*	33.48	11.48	1.41	0.29	0.01
Adj ChemoIO	20.13	41.13	31.00	4.60	2.97	0.17
Neo ChemoIO	26.43	21.39	20.04	9.07	12.97	10.10
Adj Chemo	0.10	3.49	32.06	53.14	11.21	0.00
Neo Chemo	0.00	0.51	5.43	31.75	62.25	0.07
Surgery alone	0.00	0.00	0.00	0.04	10.30	89.65*
Event-free survival for resectable non-small cell lung cancer of PD-L1 TPS 1–49%						
Peri ChemoIO	34.86	48.76	16.32	0.06	0.01	0.00
Adj ChemoIO	9.84	32.58	56.41	0.75	0.40	0.02
Neo ChemoIO	55.30*	18.57	18.54	2.47	2.90	2.23
Adj Chemo	0.00	0.08	7.64	78.14	14.14	0.00
Neo Chemo	0.00	0.02	1.09	18.58	80.22	0.09
Surgery alone	0.00	0.00	0.00	0.00	2.33	97.66*
Event-free survival for resectable non-small cell lung cancer of PD-L1 TPS >50%						
Peri ChemoIO	7.77	81.15	11.09	0.00	0.00	0.00
Adj ChemoIO	0.70	12.98	86.19	0.09	0.04	0.00
Neo ChemoIO	91.53*	5.88	2.43	0.06	0.06	0.04
Adj Chemo	0.00	0.00	0.25	84.70	15.05	0.00
Neo Chemo	0.00	0.00	0.05	15.14	84.72	0.09
Surgery alone	0.00	0.00	0.00	0.00	0.13	99.87*

The values with the highest probability of being ranked first or last are marked with an asterisk (*). Adj Chemo, adjuvant chemotherapy; Adj ChemoIO, adjuvant chemoimmunotherapy; Neo Chemo, neoadjuvant chemotherapy; Neo ChemoIO, neoadjuvant chemoimmunotherapy; Peri ChemoIO, perioperative chemoimmunotherapy; TPS, tumor proportion score.

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Table S12 Adjuvant immunochemotherapy termination rate and distribution

Trials	Total	Ongoing Adj ChemoIO	Complete Adj ChemoIO	Reasons for discontinuation			
				Adverse events	Progressive disease	Patient decision	Other
KEYNOTE091 2022	580	0	300	131	72	46	31
IMpower010 2022	495	0	323	92	55	22	3
NEOTORCH 2024	202	26	89	21	26	30	10
KEYNOTE671 2023	290	42	160	37	35	8	8
AEGEAN 2023	264	85	105	22	39	9	4
CheckMate77T 2024	142	8	85	17	16	16	0
Overall	1,973 (100%)	161 (8.16%)	1,062 (53.8%)	320 (16.2%)	243 (12.3%)	131 (6.64%)	56 (2.84%)

Table S13 The neoadjuvant immunochemotherapy phase led to a decline in the rate of surgery

Study	Group	Neoadjuvant phase		Surgery phase	
		Receive	Complete	Definitive surgery	R0 resection
CheckMate816 2024	Nivolumab+ chemo	176	165	149	124
	Chemotherapy	176	149	135	105
Neotorch 2024	Toripalimab + chemo	202	176	166	159
	Placebo + chemo	202	185	148	137
KEYNOTE671 2023	Pembrolizumab	396	295	325	Not available
	Placebo	399	297	317	Not available
AEGEAN 2023	Durvalumab	366	318	284	269
	Placebo	371	331	287	262
RATIONALE315 2024	TIS + CT	226	211	190	Not available
	PBO + CT	226	210	173	Not available
CheckMate77T 2024	NIVO + chemo/NIVO	228	194	178	159
	Chemo/PBO	230	205	178	161
NADIM II 2023	Nivolumab + Chemo	57	57	53	50
	Chemo	29	29	20	17
Overall		1,651 (100%)	1,359 (82.3%)	1,345 (81.5%)	761 (74.0%)

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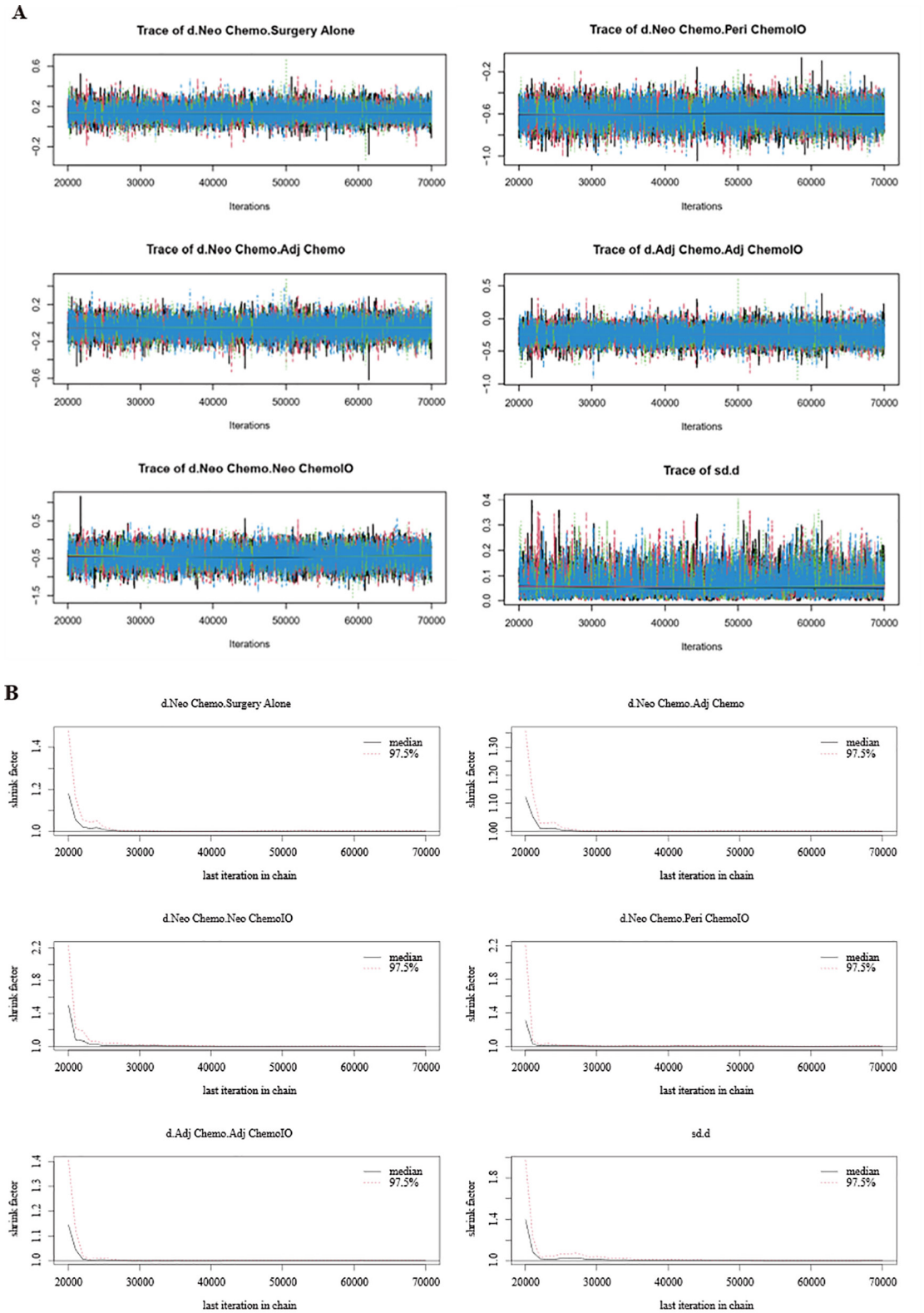

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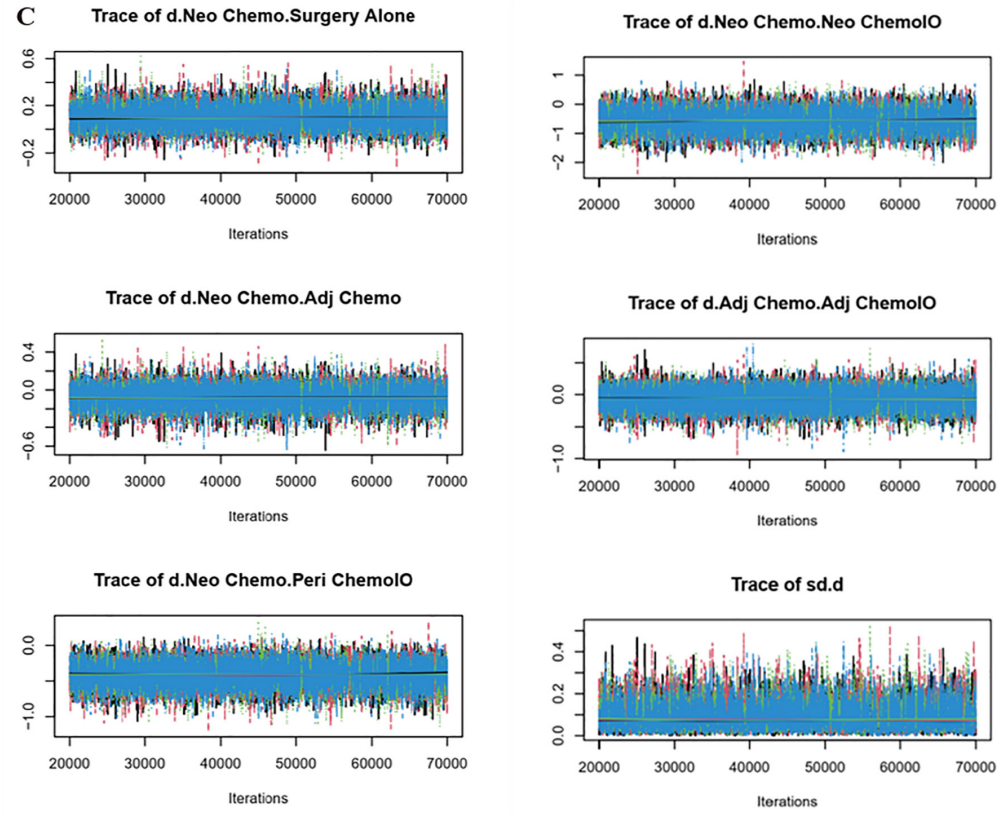

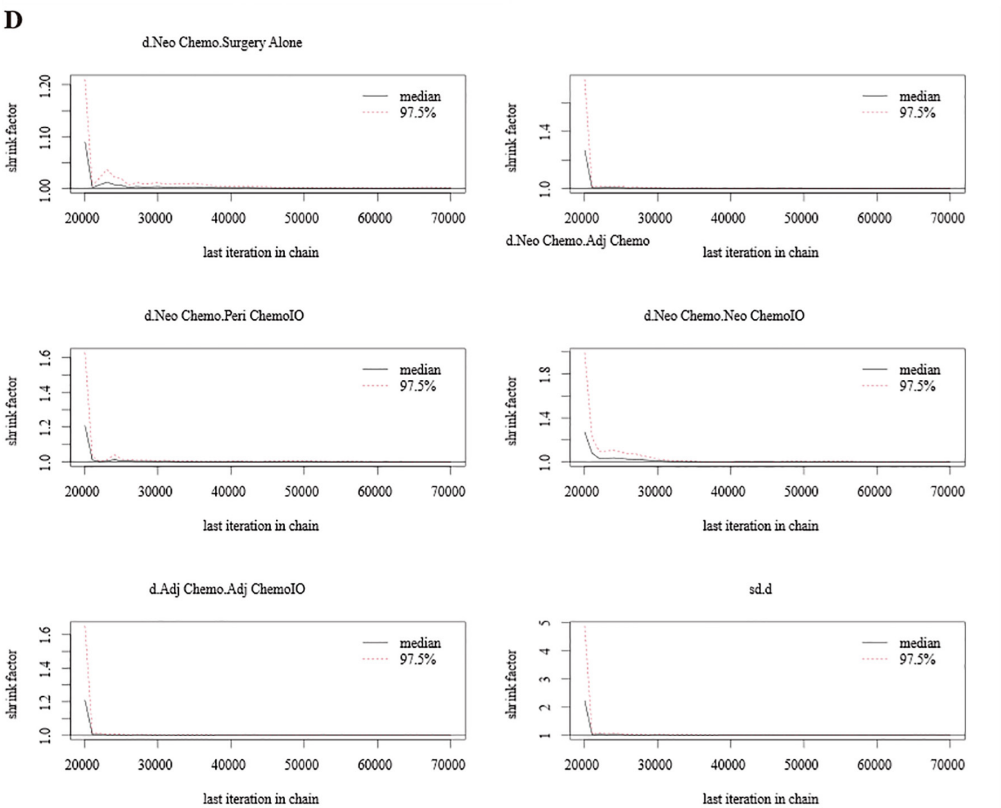

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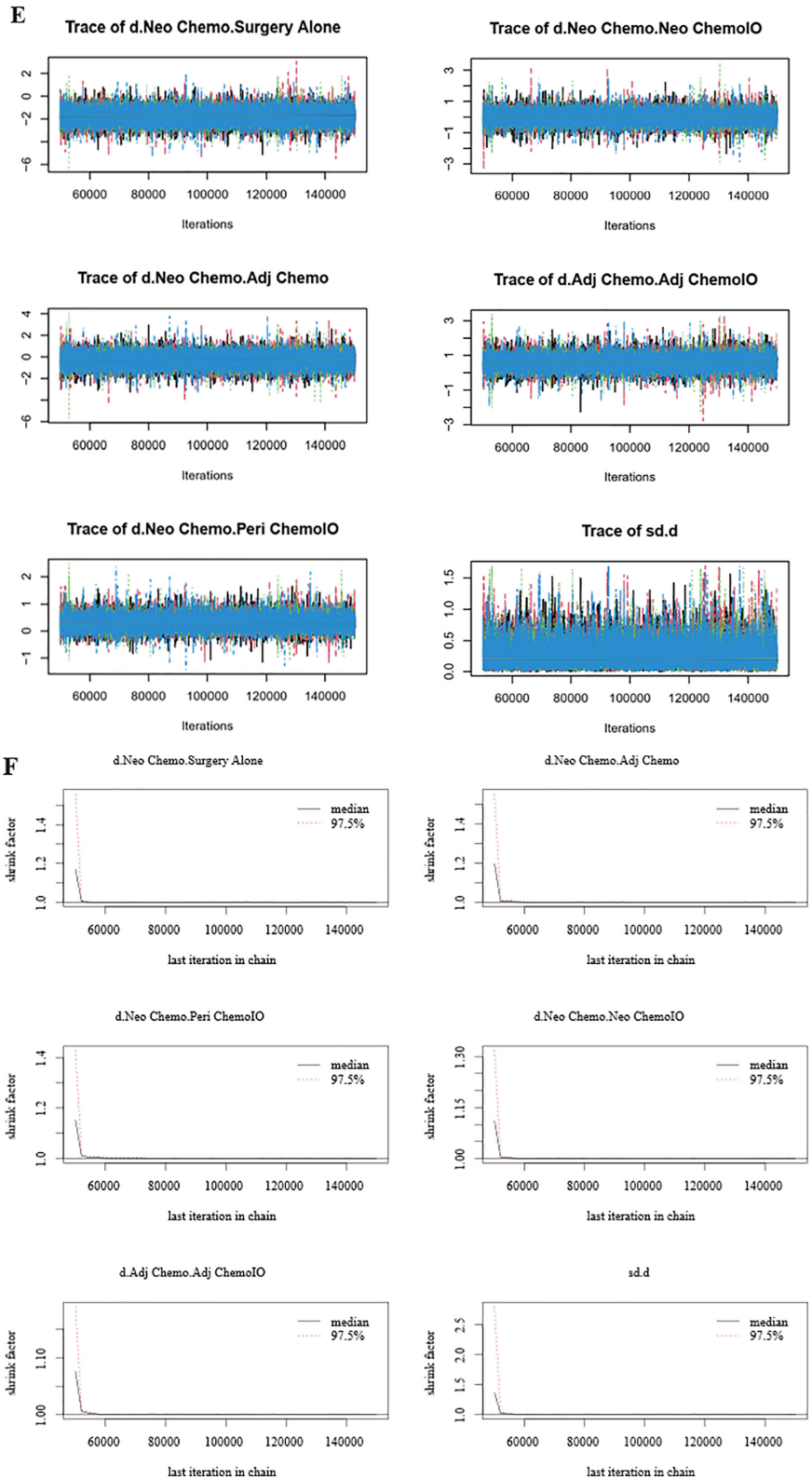

Figure S1 Convergence of the four chains established by inspection of the history feature and the Brooks Gelman-Rubin diagnostic for event-free survival (A,B), overall survival (C,D), and grade ≥3 adverse events (E,F).

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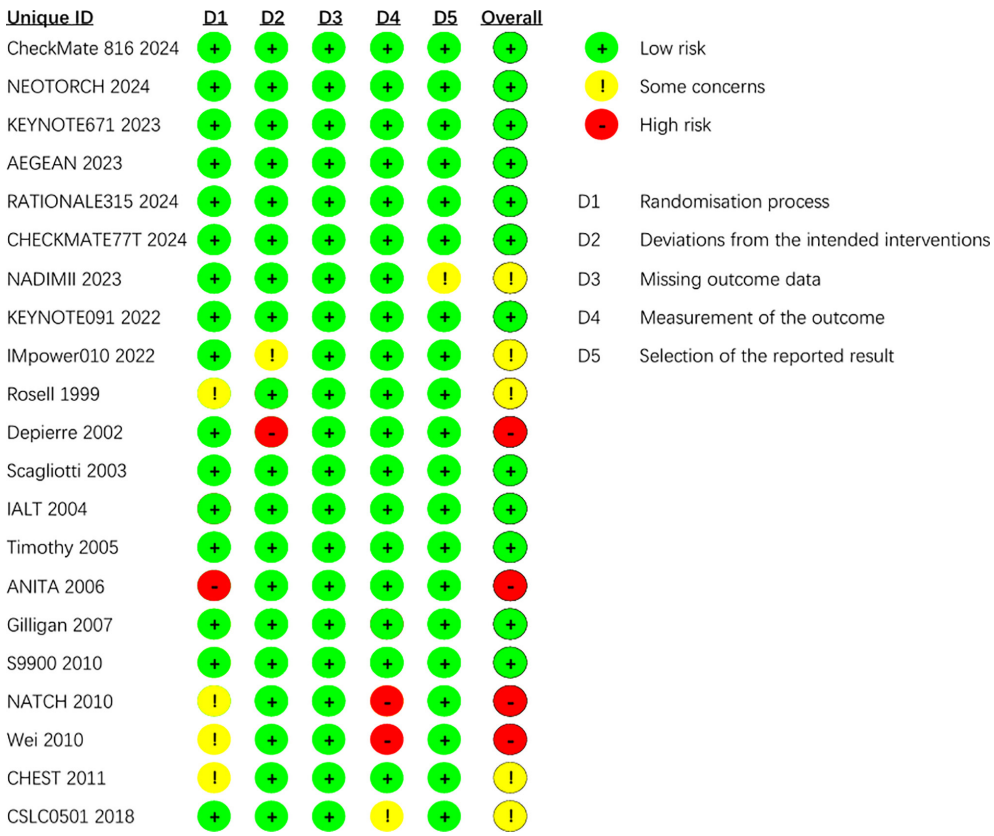

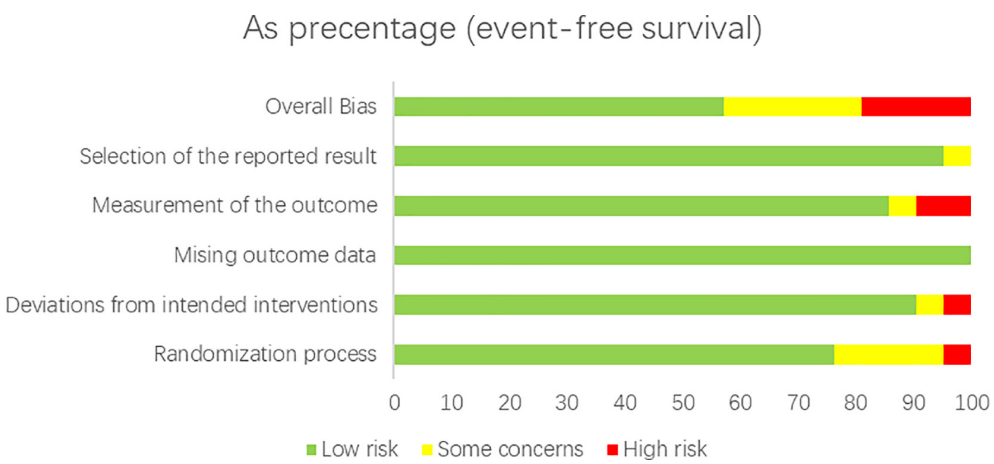

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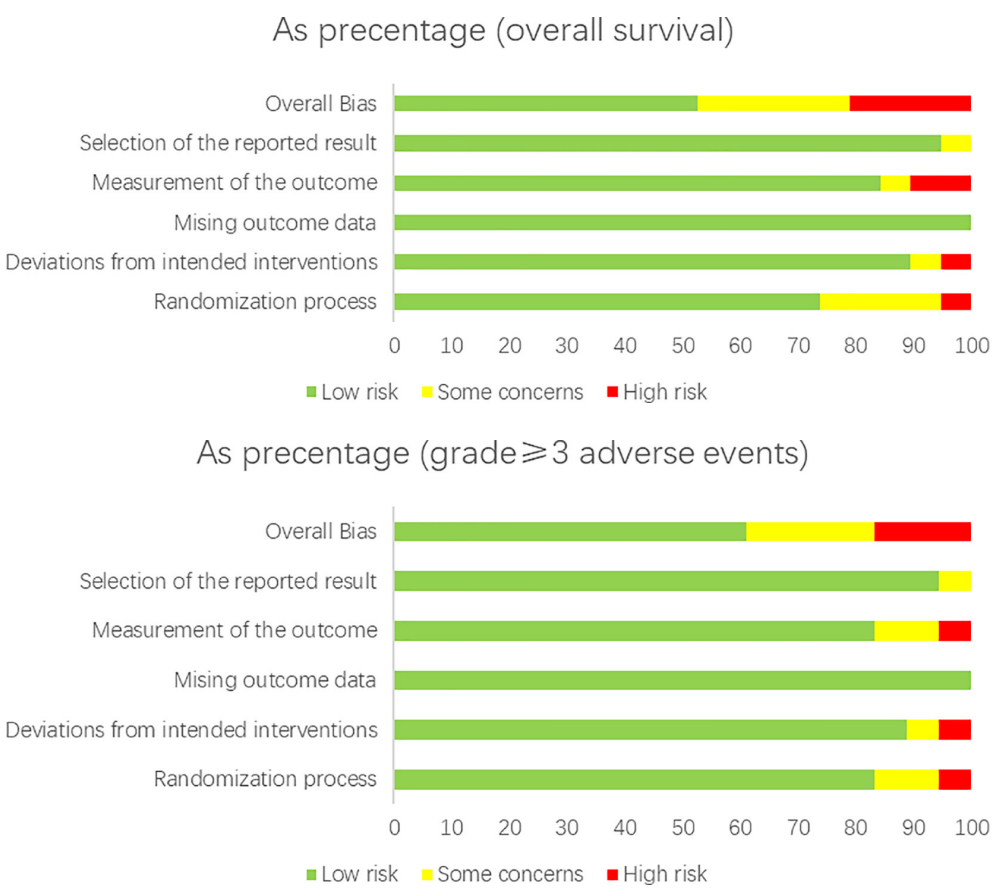

Figure S2 Risk of bias evaluation of the included studies using the Cochrane Risk of Bias tool for randomized trials (RoB2).

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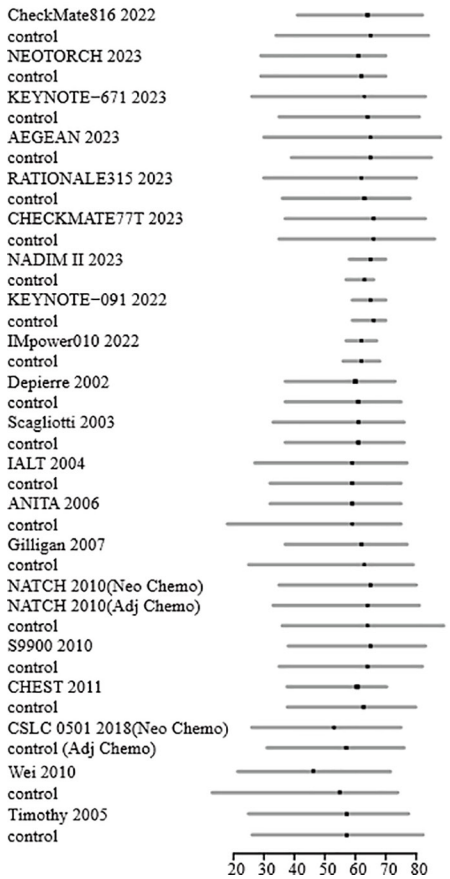

Characteristic	Intervention arm	Control arm
Sample size	0.8498	0.7403
Male ratio	0.2366	0.2012
ECOG 1 Percentage	0.8871	0.6701
Histology Squamous	0.1147	0.0928
Smoking status		
Never	0.9453	0.9453
C urrent or former	0.7263	0.7263
Clinical stage		
IB	0.2936	0.2936
II A-IIB	0.2443	0.2220
IIIA	0.0501	0.0736
IIIB	1.0000	0.8551
PD-L1 expression		
< 1%	0.6875	0.5781
⩾ 1%	0.0935	0.0935
1-49%	0.2012	0.2012
⩾ 50%	0.3613	0.3613

Figure S3 Assessment of transitivity. The above characteristics were assessed in all available trials encompassed within the network. All comparisons exhibited comparable median age (on the left) and other primary characteristics, with a P value exceeding 0.05 (on the right). The smoking status and PD-L1 expression were only assessed in the nine trials containing immune-checkpoint inhibition.

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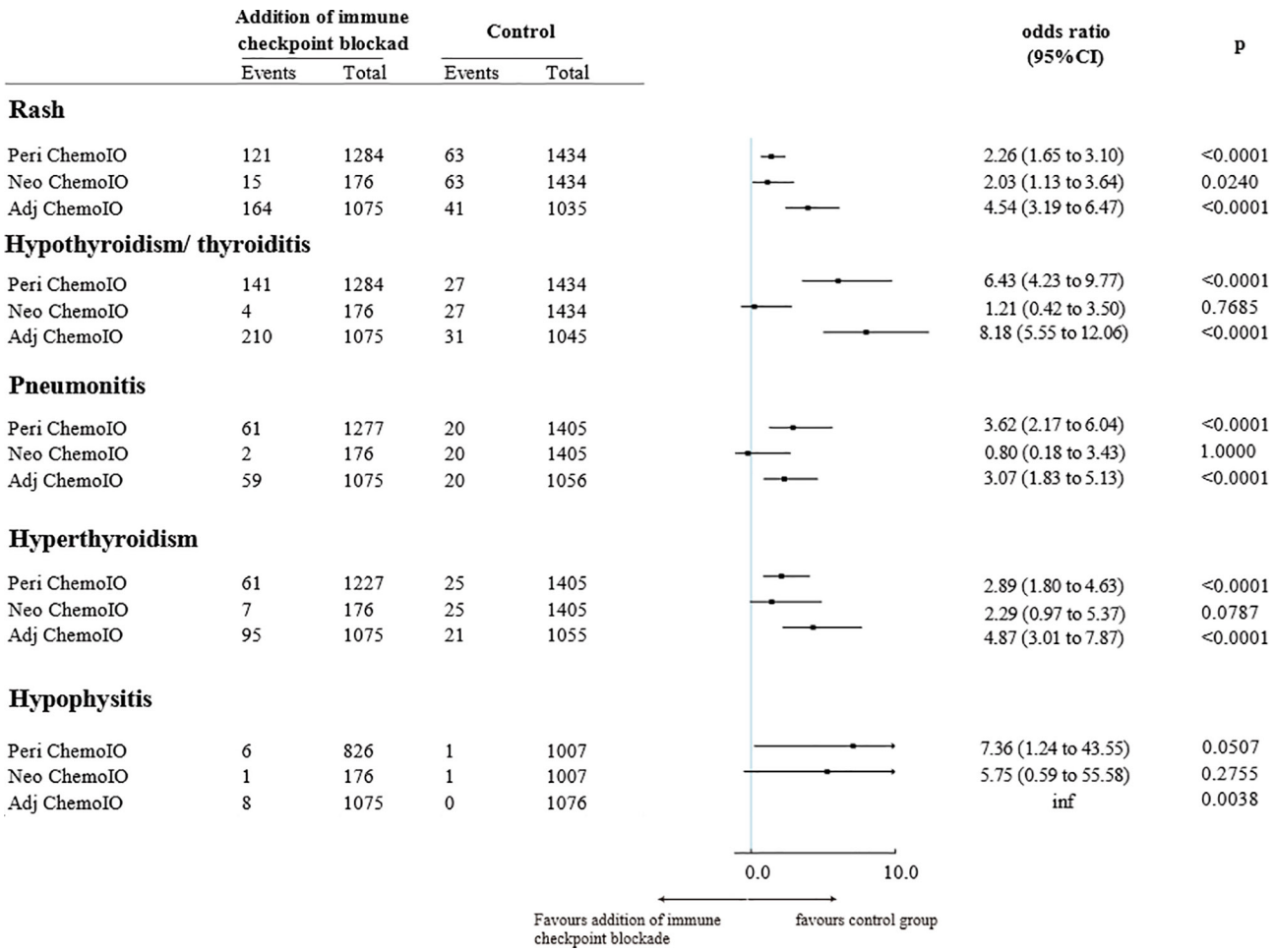

Figure S4 Forest Plot of commonly reported immune-related adverse events of any grade in perioperative, adjuvant and neoadjuvant chemoimmunotherapy.

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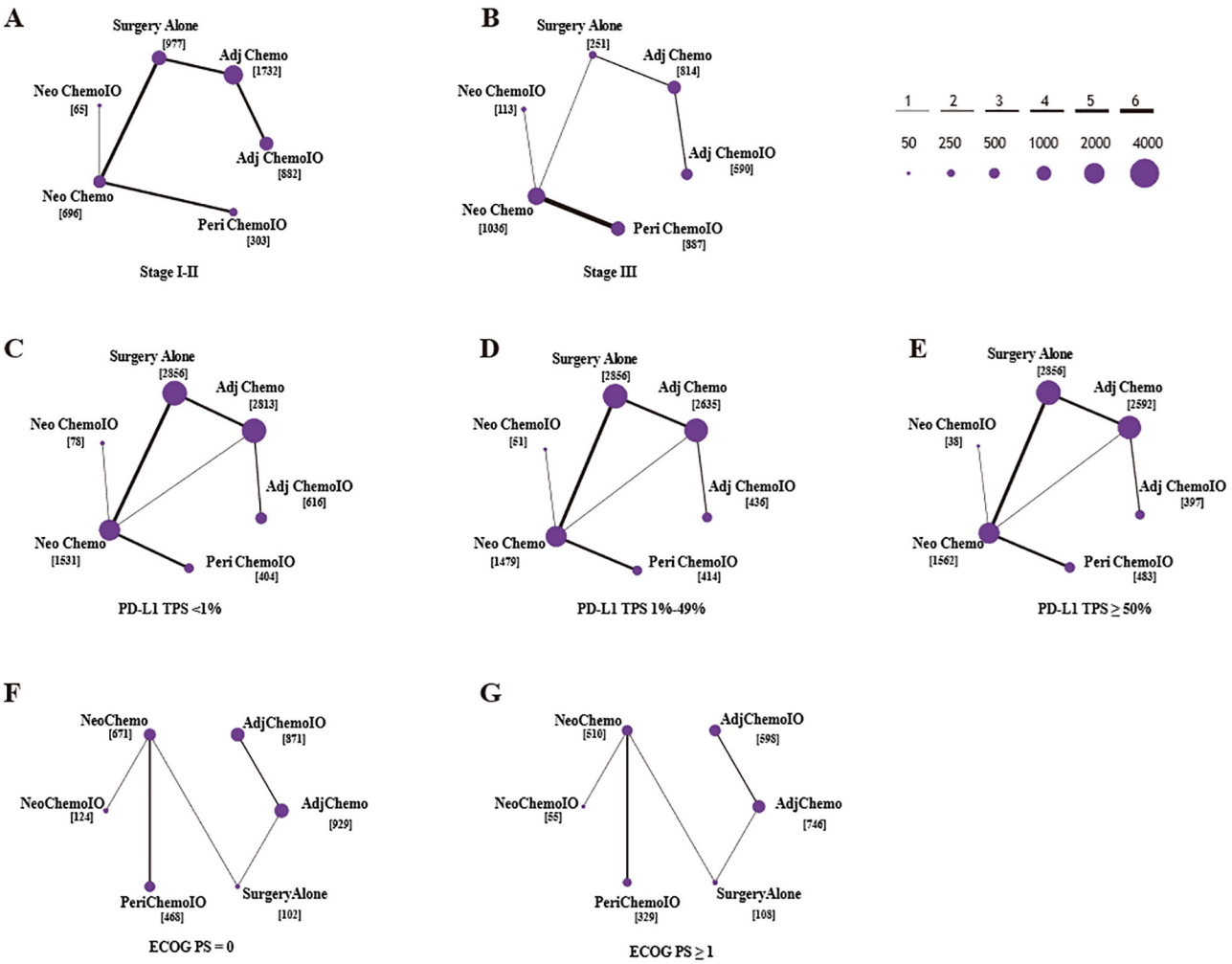

Figure S5 Network diagrams of network meta-analysis in subgroup analyses by disease stage (A,B), PD-L1 expression level (C-E) and ECOG performance status (PS) (F,G). Panel A displays patients with stage I–II tumours, and panel B shows stage III tumours. Panels C, D and E represent subgroups defined by PD-L1 tumour proportion score (TPS < 1 %, TPS 1–49 % and TPS ≥50 %, respectively). Panels F and G represent subgroups defined by ECOG performance status (PS =0 and PS ≥1, respectively). Each purple dot represents an intervention, and its area is proportional to the total number of patients who received that treatment in the corresponding subgroup. Connecting lines indicate head-to-head comparisons, and line width is proportional to the number of trials informing each comparison. ECOG PS, Eastern Cooperative Oncology Group performance status; TPS, Tumour proportion score.

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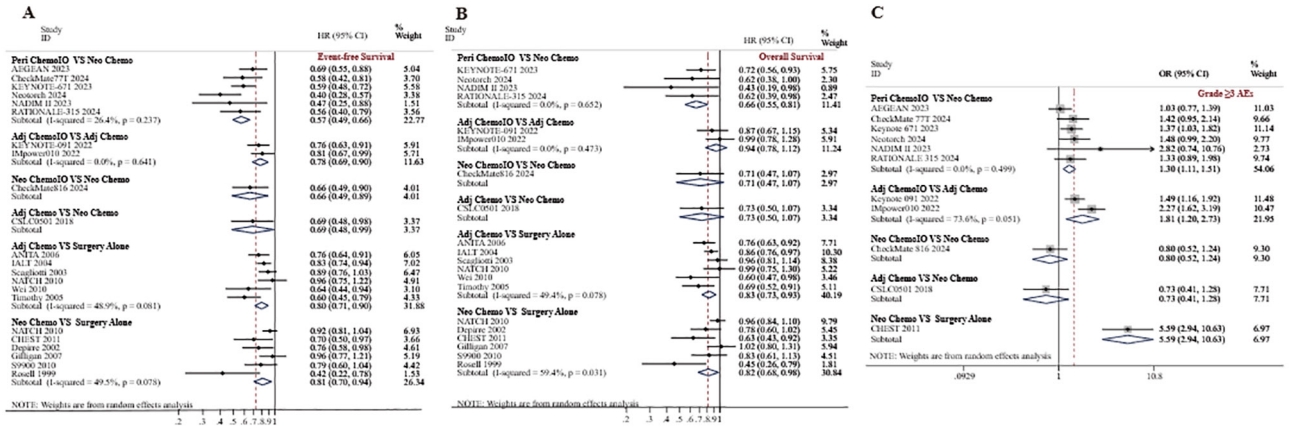

Figure S6 Forest plots depicting results of head-to-head comparisons according to frequentist pairwise meta-analyses on event-free survival (A), overall survival (B) and grade ≥3 adverse events (C).

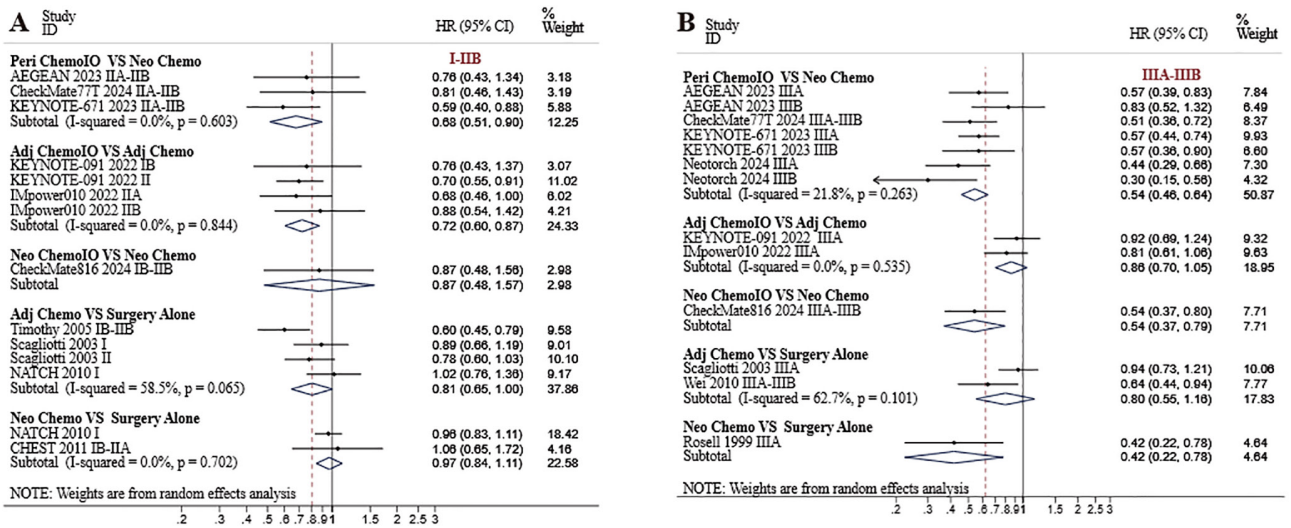

Figure S7 Forest plots depicting event-free survival results of head-to-head comparisons according to frequentist pairwise meta-analyses in patients with stage IB–IIB (A) and IIIA–IIIB (B).

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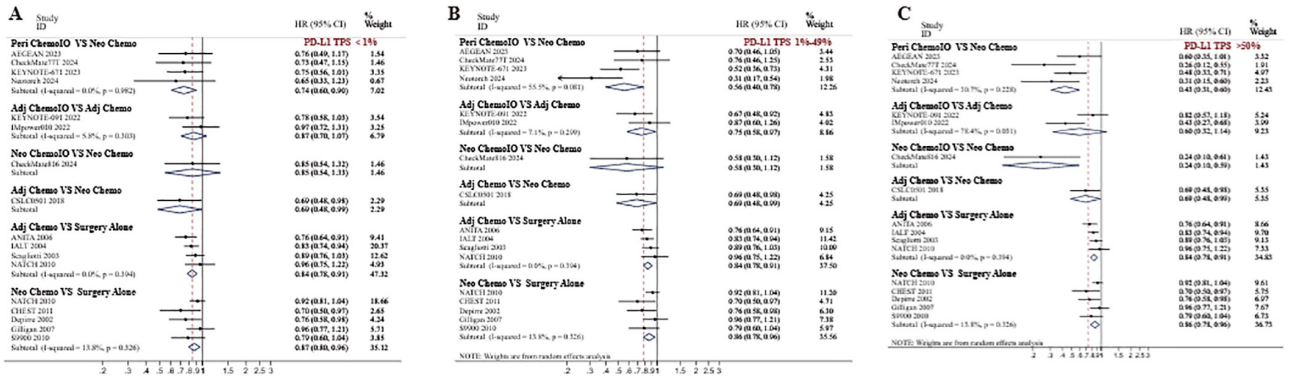

Figure S8 Forest plots depicting event-free survival results of head-to-head comparisons according to frequentist pairwise meta-analyses in patients with PD-L1 TPS<1% (A), PD-L1 TPS 1–49% (B) and PD-L1 TPS ≥50% (C).

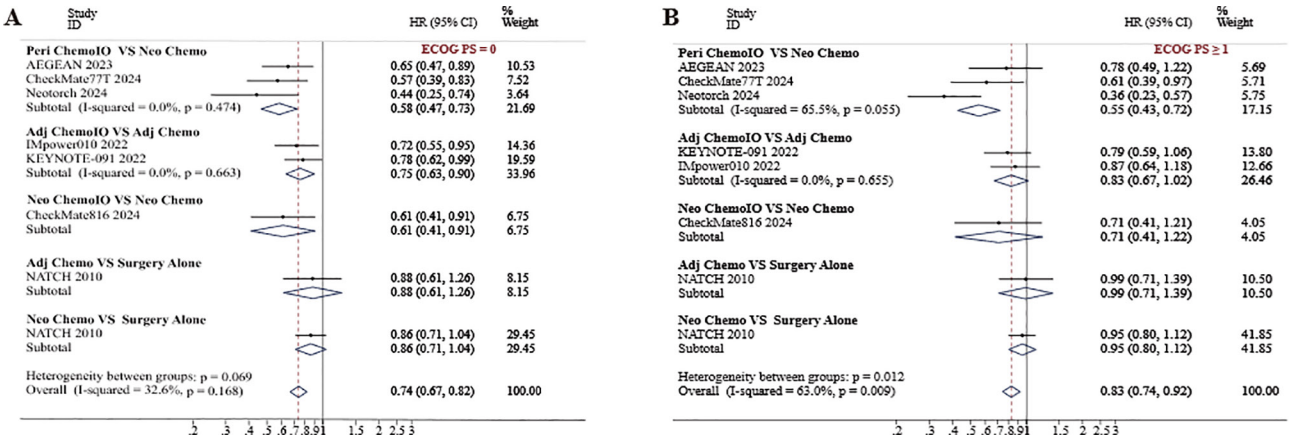

Figure S9 Forest plots depicting event-free survival results of head-to-head comparisons according to frequentist pairwise meta-analyses in patients with ECOG PS =0 (A) and ECOG PS ≥1 (B).

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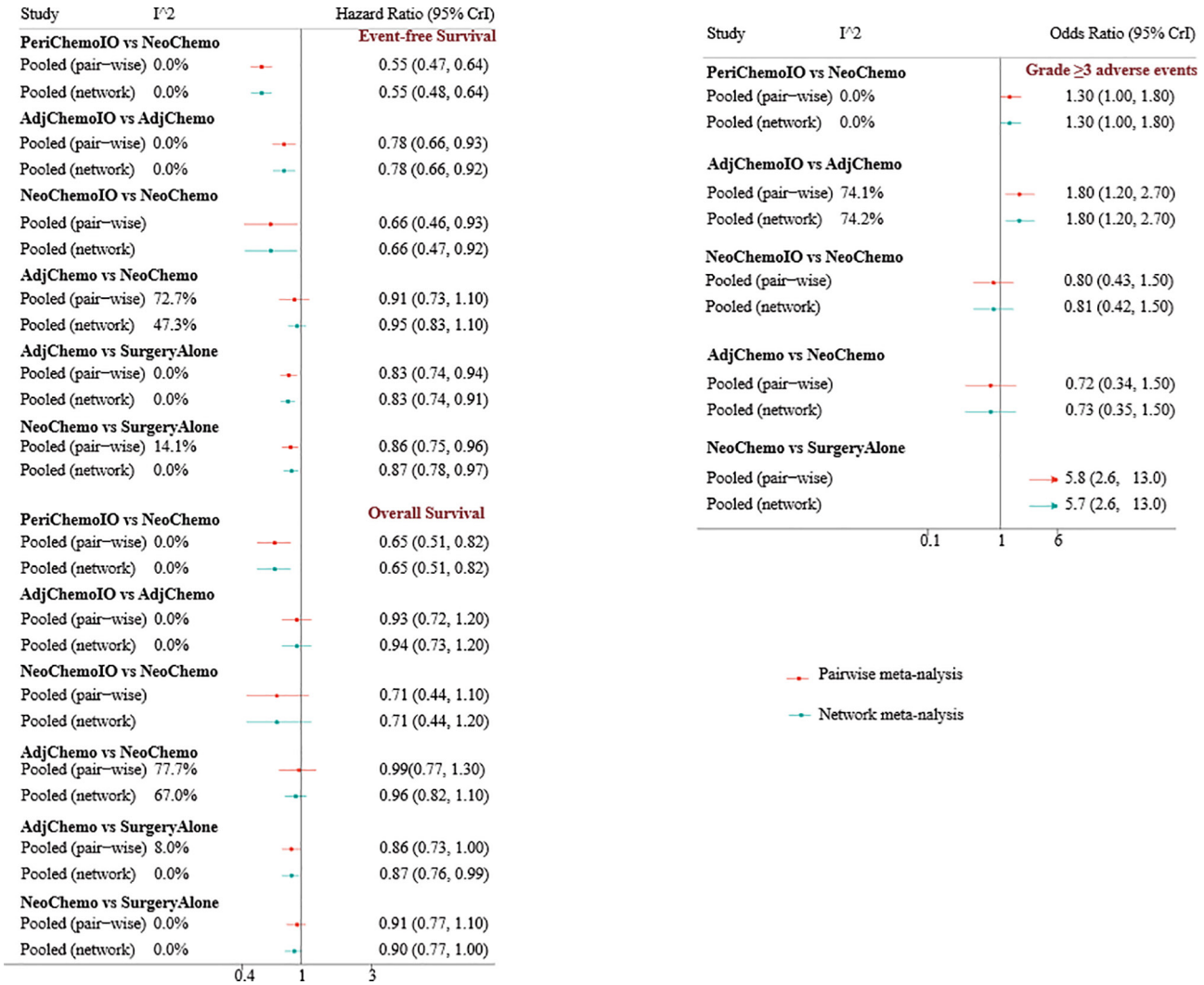

Figure S10 Forest plots depicting results from pairwise and network meta-analyses on event-free survival, overall survival and grade ≥3 adverse events.

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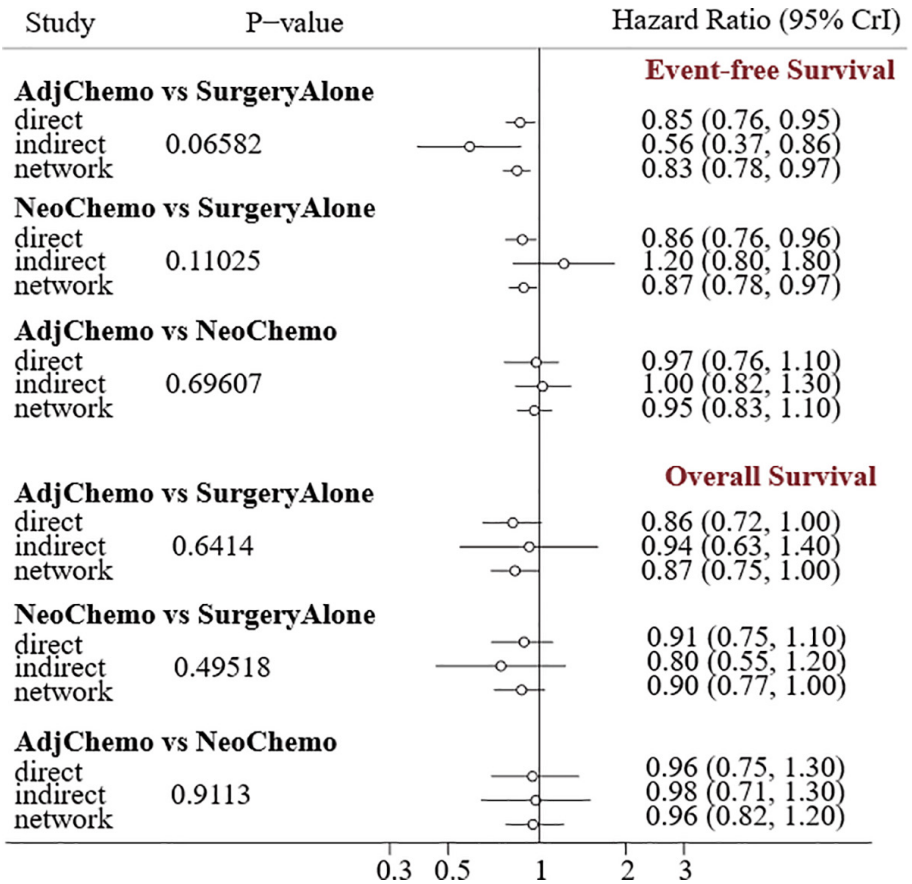

Figure S11 Node-splitting analysis of inconsistency.

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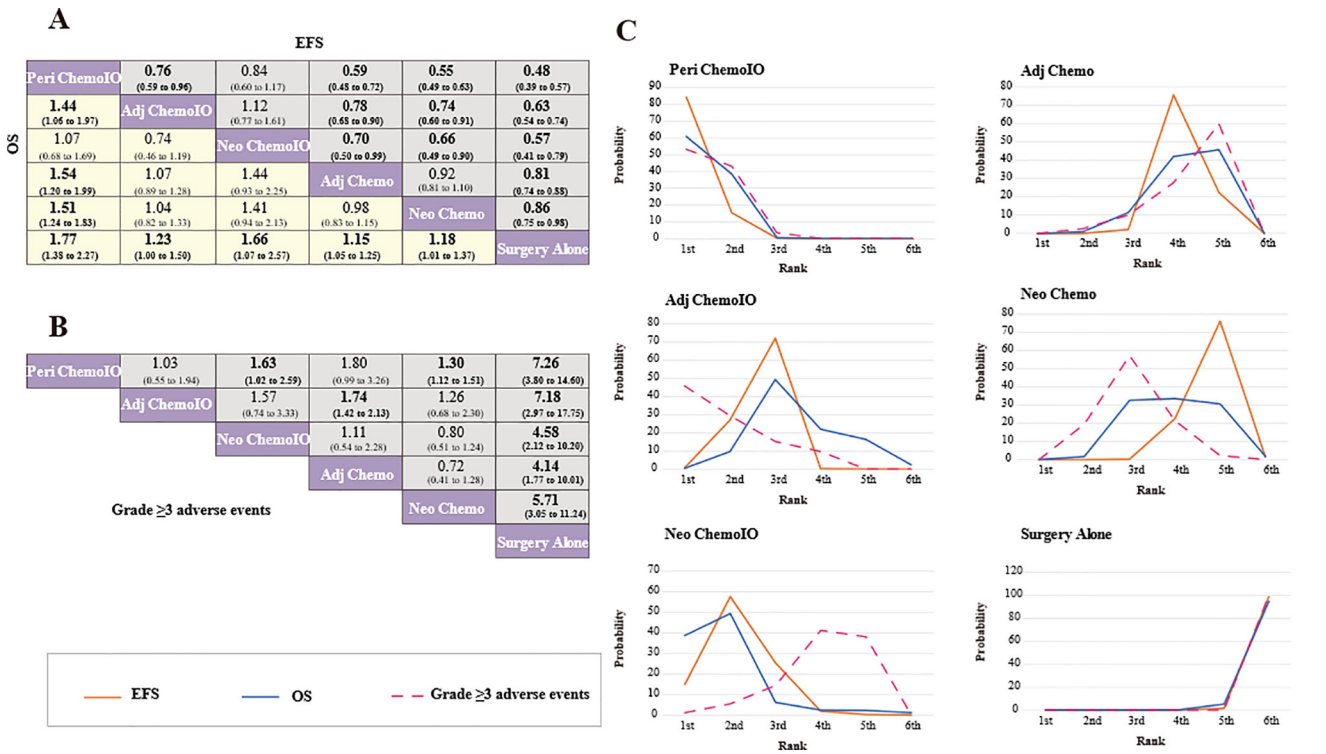

Figure S12 Network meta-analyses for different outcomes of the first sensitivity analysis excluding high-risk studies. (A) Pooled hazard ratios with 95% credible intervals for EFS (upper triangular region) and OS (lower triangular region). (B) Pooled odds ratios with 95% credible intervals for grade ≥3 adverse events. Row-defining treatment is preferred when hazard ratios or odds ratios are less than 1. (C) The ranking curves provide a possibility for every outcome of ranking from the first to sixth. Evaluated outcomes were represented by the blue line for EFS, orange line for OS, and red line for grade ≥3 adverse events. These curves correspond to the Bayesian ranking results presented in *Table S8*.

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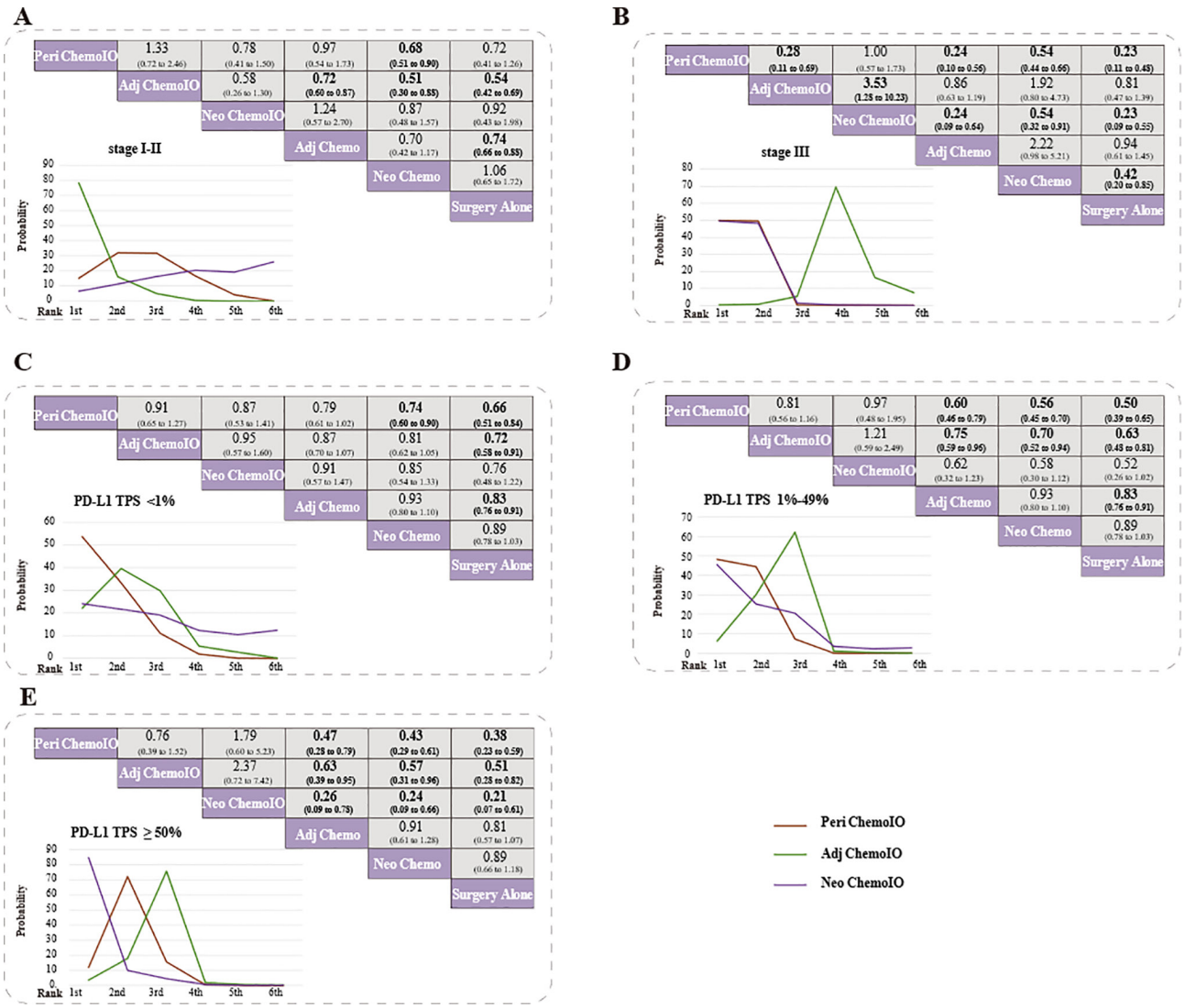

Figure S13 Network meta-analyses in the subgroup of patients with different clinical stage and PD-L1 expression level for the first sensitivity analysis excluding high-risk studies. This figure presents the pooled hazard ratios with 95% credible intervals in subgroup analysis when high-risk studies excluded. Row-defining treatment is preferred when hazard ratios are less than 1. The ranking curves provide a possibility for each method of ranking from the first to sixth. Evaluated EFS were represented by the brown line for Peri ChemoIO, green line for Adj ChemoIO, and purple line for Neo ChemoIO. These curves correspond to the Bayesian ranking results presented in *Table S9*.

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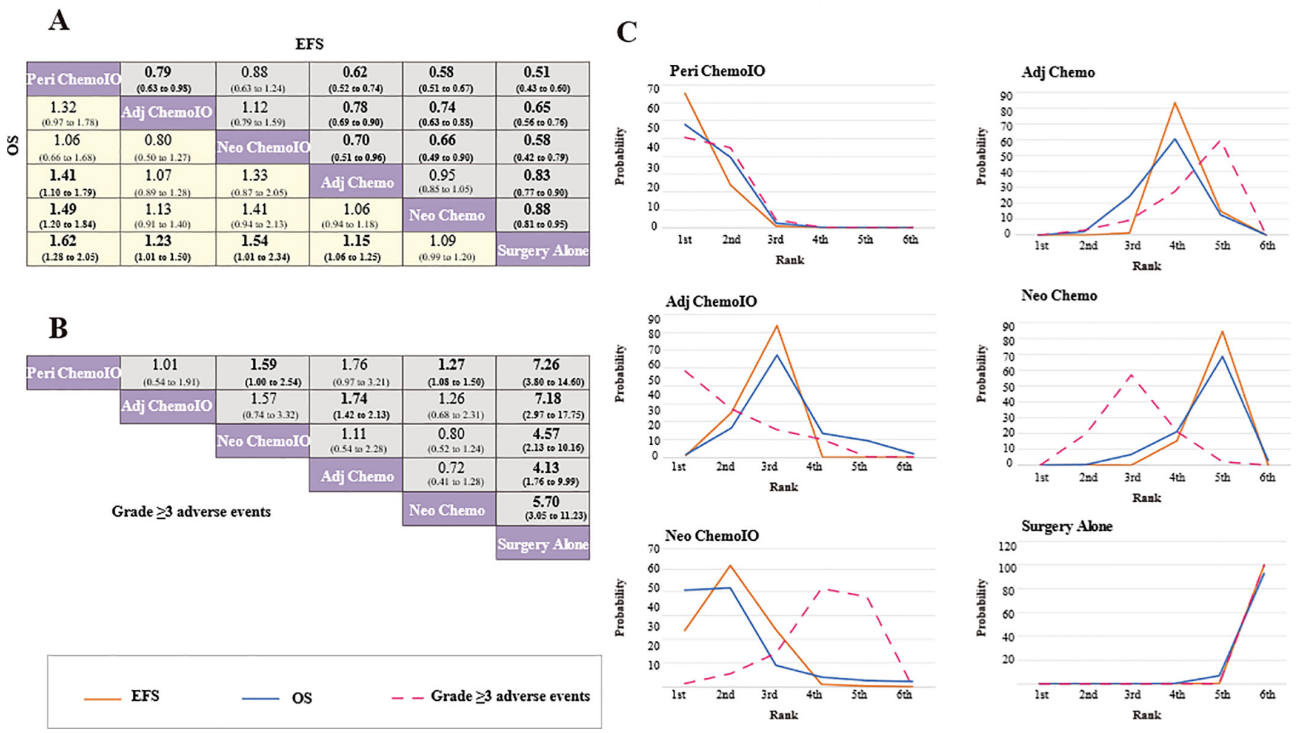

Figure S14 Network meta-analyses for different outcomes of the second sensitivity analysis excluding Neotorch study. (A) Pooled hazard ratios with 95% credible intervals for EFS (upper triangular region) and OS (lower triangular region). (B) Pooled odds ratios with 95% credible intervals for grade ≥3 adverse events. Row-defining treatment is preferred when hazard ratios or odds ratios are less than 1. (C) The ranking curves provide a possibility for every outcome of ranking from the first to sixth. Evaluated outcomes were represented by the blue line for EFS, orange line for OS, and red line for grade ≥3 adverse events. These curves correspond to the Bayesian ranking results presented in *Table S10*.

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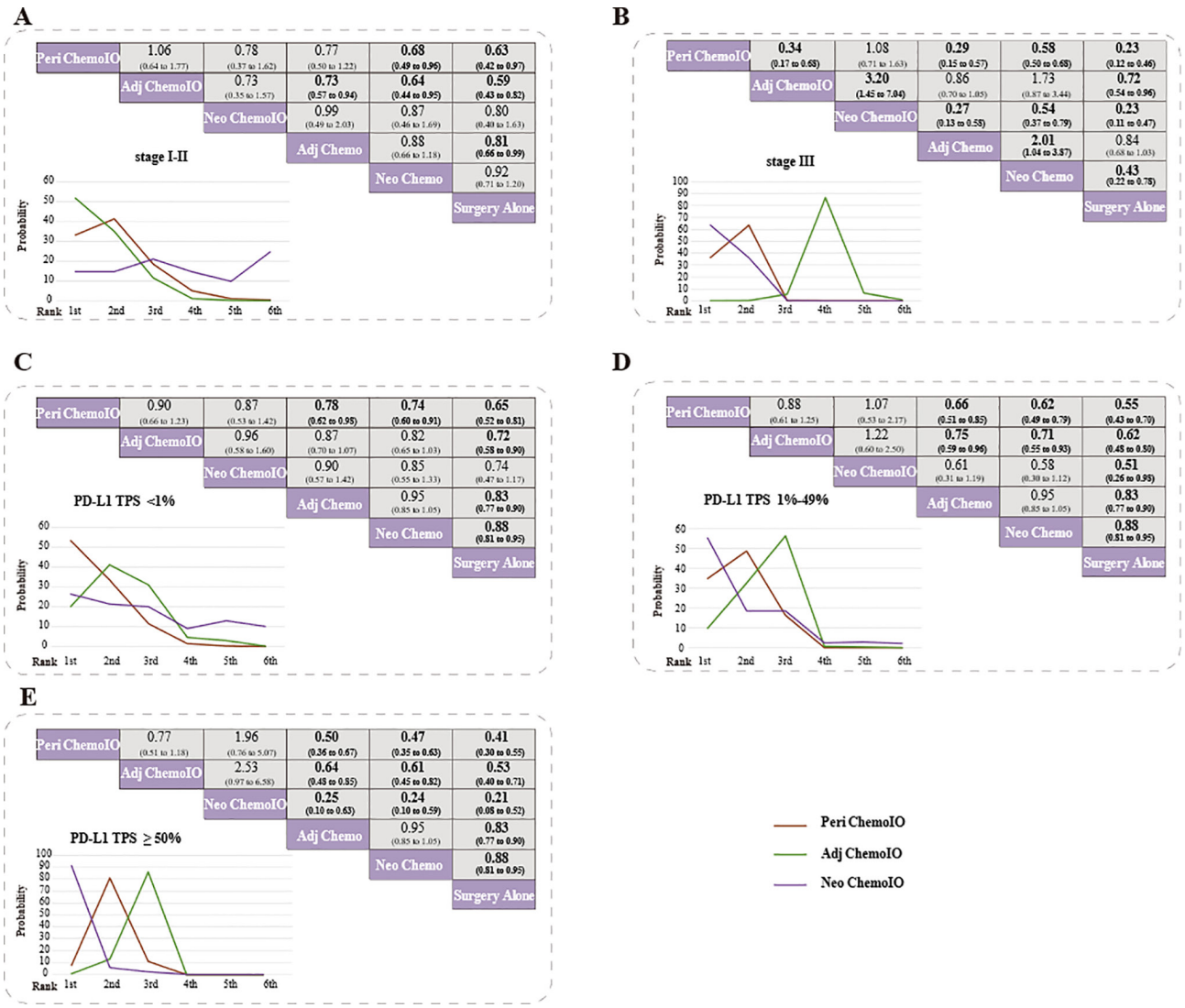

Figure S15 Network meta-analyses in the subgroup of patients with different clinical stage (A,B) and PD-L1 (C-E) expression level for the second sensitivity analysis excluding Neotorch study. This figure presents the pooled hazard ratios with 95% credible intervals in subgroup analysis when Neotorch study was excluded. Row-defining treatment is preferred when hazard ratios are less than 1. The ranking curves provide a possibility for each method of ranking from the first to the sixth. Evaluated EFS were represented by the brown line for Peri ChemoIO, green line for Adj ChemoIO, and purple line for Neo ChemoIO. These curves correspond to the Bayesian ranking results presented in *Table S11*.

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