Supplemental Files

Supplemental Figures

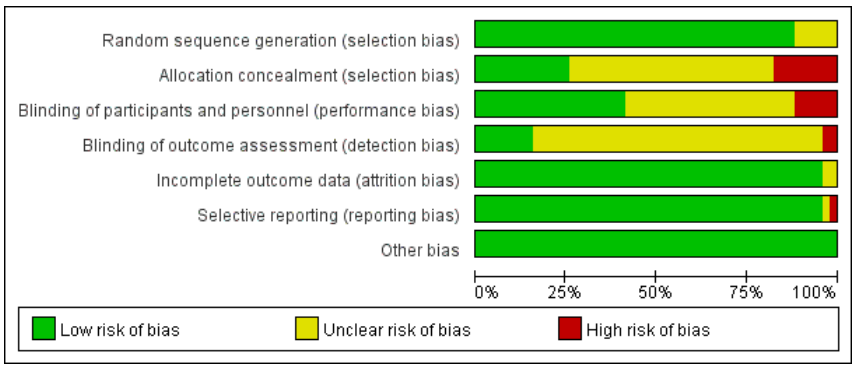

Figure A1. Overall Risk of Bias Assessment of the included studies.

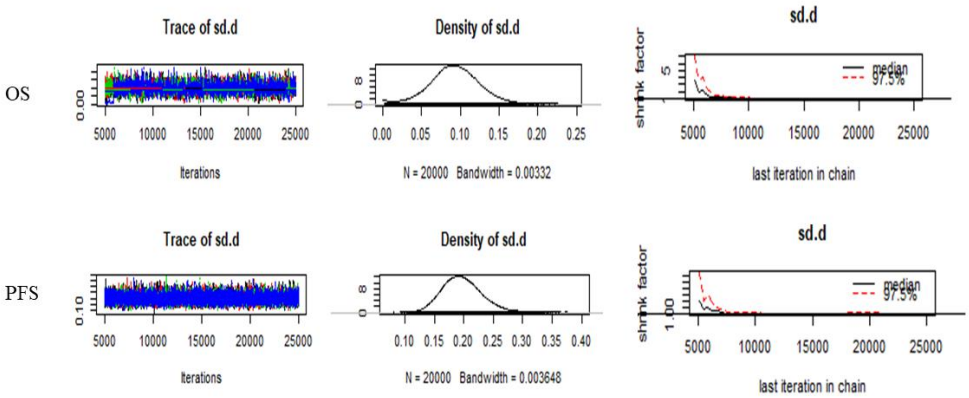

Figure A2. The trace plot, density plot and Brooks-Gelman-Rubin diagnosis plot in OS or PFS analyses. The left picture showed the trace plot: As shown in the figure, each MCMC chain had reached a stable fusion from the beginning, and the overlap area accounts for most of the chain fluctuation range in the subsequent calculations. The middle picture showed the density plot: The graph showed normal distribution, bandwidth=0.00332, 0.003648. The right picture showed the Brooks-Gelman-Rubin diagnosis plot: The median value and the 97.5% value of the shrink factor both approached 1.0 and fit each other. All figures indicated that the model is satisfactory in convergence.

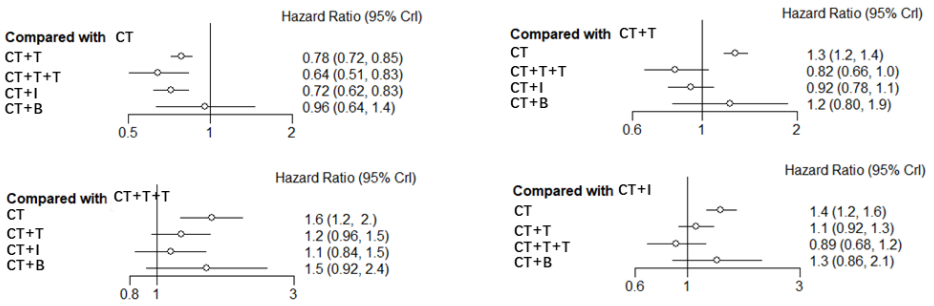

Figure A3. Forest plots for pairwise comparisons in the network of PFS under comparison of different combined treatment strategies. CrI: confidence interval.

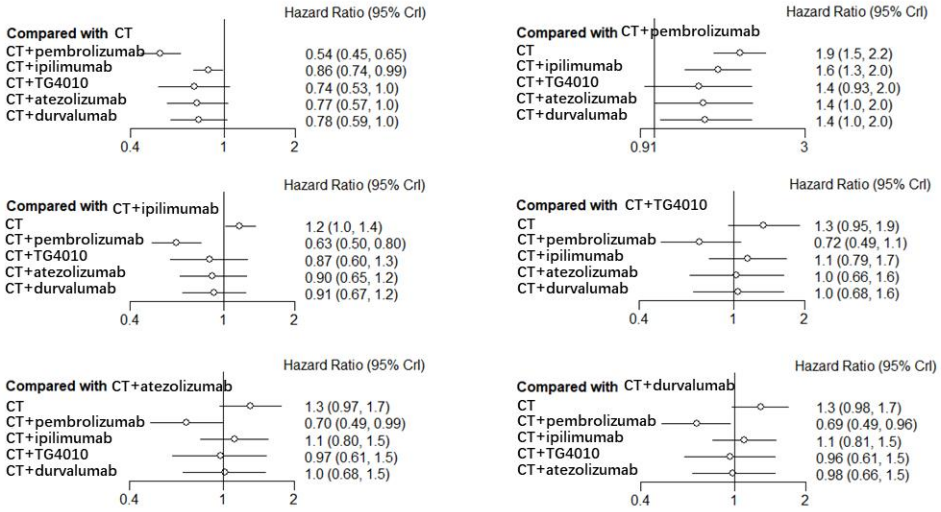

Figure A4. Forest plots for pairwise comparisons in the network of PFS under comparison of different immunotherapeutic drugs. CrI: confidence interval.

Supplemental Tables

Author	study type	Arm	Sample	Hazard ratio of OS (95%CI)	Hazard ratio of PFS (95%CI)	ORR (%)	Adverse (%)
Baggstrom, M. Q 2017							
[1]	Phase III	CT+ sunitinib	100	0.98(0.73,1.31)	0.62(0.47,0.82)	NA	NA
		CT+ placebo	100	1 (Ref)	1 (Ref)	NA	NA
Belani, C. P 2014[2]	Phase II	CT+ axitinib[1]	55	1.05(0.65,1.69)	0.89(0.56,1.42)	45.5	20
		CT+ axitinib[2]	58	1.45(0.92,2.29)	1.02(0.64,1.62)	39.7	17
		CT	57	1 (Ref)	1 (Ref)	26.3	16
Boutsikou, E 2013 [3]	Phase III	CT	61	1 (Ref)	NA	NA	24.6
		CT+ erlotinib	52	0.809(0.39,1.7)	NA	NA	17.3
		CT+ bevacizumab	56	0.768(0.38,1.6)	NA	NA	19.6
		CT+ erlotinib+ bevacizumab	60	0.655(0.27,1.5)	NA	NA	24
Dittrich, C 2014 [4]	Phase II	CT	83	1 (Ref)	1 (Ref)	NA	NA
		CT+ erlotinib	76	0.68(0.46,0.98)	0.63(0.44,0.90)	NA	NA
Doebele, R. C 2015[5]	Phase II	CT	71	1 (Ref)	1 (Ref)	38.0	NA
		CT+ ramucirumab	69	1.03 (90% CI:0.74,1.42)	0.75(90%CI:0.55,1.03)	49.3	NA
Ellis, P. M 2014 [6]	Phase III	CT+ gefitinib/erlotinib+ Dacomitinib	480	1·00(0·83,1·21)	0·66(0·55,0·79)	NA	59
		CT+ gefitinib/erlotinib+ Placebo	240	1 (Ref)	1 (Ref)	NA	NA
Garon, E. B 2014 [7]	Phase III	CT+ ramucirumab	628	0·86(0·75,0·98)	0·76(0·68,0·86)	NA	49
		CT+ Placebo	625	1 (Ref)	1 (Ref)	NA	40
Garon, E. B 2016 [8]	Phase II	CT+ bevacizumab+ CA4P	32	1.06(0.55,2.03)	1.04(0.56,1.91)	NA	50
		CT+ bevacizumab	31	1 (Ref)	1 (Ref)	NA	32
Gerber, D. E 2018 [9]	Phase III	CT+ bavituximab	297	1.06(0.88,1.29)	1.00(0.82,1.22)	NA	21.5
		CT+ Placebo	300	1 (Ref)	1 (Ref)	NA	18.3
Hanna, N. H 2016 [10]	Phase III	CT+ nintedanib	353	1.01(0.85,1.21)	0.83(0.70,0.99)	NA	NA
		CT+ Placebo	360	1 (Ref)	1 (Ref)	NA	NA
Herbst, R. S 2010 [11]	Phase III	CT+ vandetanib	694	0.91(0.78,1.07)	0.79(97.58%CI:0.70,0.90)	NA	NA
		CT+ Placebo	697	1 (Ref)	1 (Ref)	NA	NA
Hirsch, F. R 2008 [12]	Phase III	CT+ Placebo	124	1.38 (1.03,1.86)	NA	29.8	NA
		CT+ erlotinib	121	1 (Ref)	NA	11.6	NA
Johnson, B. E 2013							
[13]	Phase III	CT+ bevacizumab	373	0.92(0.70,1.21)	0.71(0.58,0.86)	NA	NA
		CT+ bevacizumab+ erlotinib	370	1 (Ref)	1 (Ref)	NA	NA
Langer, C. J 2014 [14]	Phase III	CT+ figitumumab	342	1.18(0.99,1.40)	1.10(0.93,1.32)	NA	33
		CT	339	1 (Ref)	1 (Ref)	NA	35
Lu, S 2015[15]	Phase II	CT+ rh-endostatin	69	1.0(0.7,1.5)	0.8(0.6,1.1)	75.4	NA
		CT	69	1 (Ref)	1 (Ref)	66.7	NA
Lynch, T. J 2010 [16]	Phase III	CT+ cetuximab	338	0.890(0.754,1.051)	0.902(0.761,1.069)	25.7	NA
		CT	338	1 (Ref)	1 (Ref)	17.2	NA
Niho, S 2012 [17]	Phase II	CT+ bevacizumab	121	0.99(0.65,1.50)	0.61(0.42,0.89)	60.7	NA
		CT	59	1 (Ref)	1 (Ref)	31.0	NA

Novello, S 2014[18]	Phase III	CT+ motesanib	182	0.89(0.71,1.12)	0.85(0.65,1.11)	NA	NA
		CT+ Placebo	178	1 (Ref)	1 (Ref)	NA	NA
Ouyang, X 2018 [19]	Phase III	CT+ dulanermin	342	0.94(0.74,1.21)	0.4034(0.3181,0.5117)	46.78	NA
		CT+ Placebo	110	1 (Ref)	1 (Ref)	30	NA
Park, K 2016 [20]	Phase III					NA	NA
	cohort 1	CT+ ramucirumab	43	0.762(0.444,1.307)	0.658(0.408,1.060)	25.6	NA
		CT+ Placebo	46	1 (Ref)	1 (Ref)	8.7	NA
	cohort 2	CT+ ramucirumab	585	0.864(0.753,0.991)	0.770(0.681,0.870)	22.7	NA
		CT+ Placebo	579	1 (Ref)	1 (Ref)	14	NA
Paz-Ares, L 2015[21]	Phase III	CT+ necitumumab	315	1.01(0.84,1.21)	0·96(0·80,1·16)	NA	51
		CT	318	1 (Ref)	1 (Ref)	NA	41
Pirker, R 2009 [22]	Phase III	CT+ cetuximab	557	0·871(0·762,0·996)	NA	NA	NA
		CT	568	1 (Ref)	NA	NA	NA
Pujol, J. L 2015 [23]	phase II	CT	37	0.8(0.5,1.3)	1.1(0.7,1.7)	NA	NA
		CT+ bevacizumab	37	1 (Ref)	1 (Ref)	NA	NA
Reck, M 2014 [24]	Phase III	CT+ nintedanib	655	0·75(0·60,0·92)	0·79(0·68,0·92)	NA	6·6
		CT	659	1 (Ref)	1 (Ref)	NA	2·6
Reck, M 2013[25]	Phase II	CT+ tigatuzumab	49	0.95(0.57,1.58)	0.96(0.59,1.57)	NA	20.4
		CT+ Placebo	48	1 (Ref)	1 (Ref)	NA	8.3
Reck, M 2009 [26]	Phase III	CT+ low-dose bevacizumab	345	NA	0.75(0.62,0.91)	34.1	NA
		CT+ high-dose bevacizumab	351	NA	0.82(0.68,0.98)	30.4	NA
		CT+ placebo	347	NA	1 (Ref)	20.1	NA
Sanborn, R. E 2017 [27]	Phase II	CT+ vandetanib	34	0.797(0.443,1.435)	0.982(0.542,1.779)	NA	NA
		CT+ placebo	33	1 (Ref)	1 (Ref)	NA	NA
Soria, J. C 2015 [28]	Phase III	CT+ gefitinib	133	1·62(1·05,2·52)	0·86(0·65,1·13)	NA	8
		CT+ placebo	132	1 (Ref)	1 (Ref)	NA	4
Spigel, D. R 2017 [29]	Phase III	CT+ necitumumab	110	0.83(0.55,1.52)	1.00(0.71,1.42)	48.9	NA
		CT+ Placebo	57	1 (Ref)	1 (Ref)	40.0	NA
Spigel, D. R 2011[30]	Phase II	CT+ bevacizumab	52	1.16(0.66,2.04)	0.53(0.32,0.86)	58	75
		CT+ placebo	50	1 (Ref)	1 (Ref)	48	60
Takeda, K 2010 [31]	Phase III	CT	298	0.86(0.72,1.03)	0.68(0.57,0.80)	NA	NA
		CT+ gefitinib	300	1 (Ref)	1 (Ref)	NA	NA
Thatcher, N 2015 [32]	Phase III	CT+ necitumumab	545	0·84(0·74,0·96)	0·84(0·75,0·95)	NA	72
		CT	548	1 (Ref)	1 (Ref)	NA	62
Wakelee, H 2017 [33]	Phase II					NA	NA
	cohort 1	CT+ Bevacizumab +Onartuzumab	69	1.34;P=0.352	1.25;P=0.333	51.5	68.1
		CT+ Bevacizumab +Placebo	70	1 (Ref)	1 (Ref)	44.8	50.7
	cohort 2	CT+ Onartuzumab	59	1.15;P=0.591	1.23;P=0.329	28.6	60.3
		CT+ placebo	61	1 (Ref)	1 (Ref)	36.1	64.9
Zhou, C 2015[34]	Phase III	CT+ bevacizumab	138	0.68(0.50,0.93)	0.40(0.29,0.54)	54	NA
		CT+ placebo	138	1 (Ref)	1 (Ref)	26	NA
Argiris, A 2017[35]	Phase II	CT+ bevacizumab+ cixutumumab	75	0.99(0.7, 1.41)	0.92(0.65, 1.31)	58.7%	NA

		CT+ bevacizumab	78	1 (Ref)	1 (Ref)	46.2%	NA
Fukuda, M 2019[36]	Phase II	CT+ bevacizumab	20	0.79(0.4, 1.79)	0.84(0.38, 1.86)	55%	NA
		CT	20	1 (Ref)	1 (Ref)	15%	NA
Owonikoko, T. K 2019[37]	Phase II	CT+ Veliparib	64	0.83(80%CI 0.6, 1.07)	0.63, P = 0.01	71.9%	NA
		CT	64	1 (Ref)	1 (Ref)	65.6%	NA
Reck, M 2019[38]	Phase III	CT+ atezolizumab	399	0.85(0.7, 1.03)	0·81(0.55, 1.21)	NA	NA
		CT+ bevacizumab	394	1 (Ref)	1 (Ref)	NA	NA
Watanabe, S 2019[39]	Phase II	CT+ necitumumab	90	0.66(0.5, 0.93)	0.66(0.47, 0.93)	NA	NA
		CT	91	1 (Ref)	1 (Ref)	NA	NA
Gandhi, L 2018 [40]	Phase III	CT+ pembrolizumab	410	0.49(0.38,0.64)	0.52(0.43,0.64)	NA	67.2
		CT+ Placebo	206	1 (Ref)	1 (Ref)	NA	65.8
Govindan, R 2017 [41]	Phase III	CT+ ipilimumab	388	0.91(0.77,1.07)	0.87(0.75,1.01)	NA	NA
		CT+ Placebo	361	1 (Ref)	1 (Ref)	NA	NA
Langer, C. J 2016 [42]	Phase II	CT+ pembrolizumab	60	0·90(0·42,1·91)	0·53(0·31,0·91)	55	39
		CT	63	1 (Ref)	1 (Ref)	29	26
Lynch, T. J 2012[43]	Phase II	CT+ Placebo	65	1 (Ref)	1 (Ref)	14	6
		CT+ concurrent ipilimumab[3]	71	0.99(0.67,1.46)	0.88(0.61,1.27)	21	20
		CT+ phased ipilimumab[4]	67	0.87(0.59,1.28)	0.69(0.48,1.00)	32	15
Quoix, E 2016 [44]	Phase II	CT+ TG4010	111	0·78(0·57,1·06)	0·74(0·55,0·98)	NA	NA
		CT+ Placebo	111	1 (Ref)	1 (Ref)	NA	NA
Reck, M 2013[45]	Phase II	CT+ placebo	45	1 (Ref)	1 (Ref)	NA	9
		CT+ concurrent ipilimumab[5]	43	0.89(0.57,1.39)	0.93(0.59,1.48)	NA	21
		CT+ phased ipilimumab[6]	42	0.76(0.48,1.19)	0.93(0.59,1.45)	NA	17
Reck, M 2016 [46]	Phase II	CT+ ipilimumab	478	0.94(0.81,1.09)	0.85(0.75,0.97)	NA	NA
		CT+ Placebo	476	1 (Ref)	1 (Ref)	NA	NA
Horn, L 2018[47]	Phase II	CT+ atezolizumab	201	0.7(0.5, 0.91)	0.77(0.62, 0.96)	NA	NA
		CT	202	1 (Ref)	1 (Ref)	NA	NA
Paz-Ares, L 2019[48]	Phase III	CT+ durvalumab	268	0.73(0.6, 0.91)	0.78(0.65, 0.94)	NA	62%
		CT	269	1 (Ref)	1 (Ref)	NA	62%
Paz-Ares, L 2018[49]	Phase III	CT+ pembrolizumab	278	0.64(0.5, 0.85)	0.56(0.45, 0.7)	NA	69.8%
		CT	281	1 (Ref)	1 (Ref)	NA	68.2%
Bradbury, P. A 2018[50]	Phase II	CT+ pelareorep	77	0.98,P=0.90	0.90(0.65,1.25)	NA	83
		CT	75	1 (Ref)	1 (Ref)	NA	58
Chang, J 2015[51]	Phase III	CT+（PAP）	36	1.29(0.73,2.27)	1.08(0.61,1.91)	46.88	NA
		CT	36	1 (Ref)	1 (Ref)	23.53	NA

NA: not available; Ref=reference group (hence hazard ratio set to 1). MOS: Median overall survival in months; Sample: the number of patients; PFS: Progression-free

survival in months; ORR: objective response rate; CT: chemotherapy; PAP: Pseudomonas aeruginosa preparation

1 CT+ axitinib[1]: pemetrexed and cisplatin+ axitinib.

2 CT+ axitinib[2]: pemetrexed or cisplatin+ axitinib.

3 concurrent ipilimumab[3]: four doses of ipilimumab plus paclitaxel and carboplatin followed by two doses of placebo plus paclitaxel and carboplatin.

4 phased ipilimumab[4]: two doses of placebo plus paclitaxel and carboplatin followed by four doses of ipilimumab plus paclitaxel and carboplatin.

5 concurrent ipilimumab[5]: ipilimumab+ paclitaxel/carboplatin followed by placebo+ paclitaxel/carboplatin.

6 phased ipilimumab[6]: placebo+ paclitaxel/carboplatin followed by ipilimumab+ paclitaxel/carboplatin.

Table A1. Basic information of included studies.

Author	Arms	Sample	Responder	
			ORR	Adverse
Belani, C. P 2014*	CT+T	113	48	21
	CT	57	15	9
Boutsikou, E 2013*	CT	61	NA	15
	CT+T	108	NA	20
	CT+T+T	60	NA	24
Doebele, R. C 2015	CT	71	27	NA
	CT+T	69	34	NA
Garon, E. B 2014	CT+T	628	NA	306
	CT	625	NA	246
Garon, E. B 2016	CT+T+T	32	NA	16
	CT+T	31	NA	10
Gerber, D. E 2018	CT+T	297	NA	64
	CT	300	NA	55
Hirsch, F. R 2008	CT	124	34	NA

	CT+T	121	22	NA
Langer, C. J 2014	CT+T	342	NA	113
	CT	339	NA	119
Lu, S 2015	CT+T	69	52	NA
	CT	69	46	NA
Lynch, T. J 2010	CT+T	338	87	NA
	CT	338	58	NA
Niho, S 2012	CT+T	121	73	NA
	CT	59	18	NA
Ouyang, X 2018	CT+T	342	160	NA
	CT	110	33	NA
Park, K 2016*	CT+T	628	144	NA
	CT	625	85	NA
Paz-Ares, L 2015	CT+T	315	NA	155
	CT	318	NA	127
Reck, M 2014	CT+T	655	NA	43
	CT	659	NA	17
Reck, M 2013	CT+T	49	NA	10
	CT	48	NA	4
Reck, M 2009*	CT+T	351	225	NA
	CT	347	70	NA
Soria, J. C 2015	CT+T	133	NA	11
	CT	132	NA	5
Spigel, D. R 2017	CT+T	110	54	NA
	CT	57	23	NA
Spigel, D. R 2011	CT+T	52	30	39
	CT	50	24	30
Thatcher, N 2015	CT+T	545	NA	388
	CT	548	NA	333
Wakelee, H 2017*	CT+T+T	69	34	47
	CT+T	129	46	70
	CT	61	22	37
Zhou, C 2015	CT+T	138	75	NA
	CT	138	36	NA
Argiris, A 2017	CT+T+T	75	44	NA
	CT+T	78	36	NA
Fukuda, M 2019	CT+T	20	11	NA
	CT	20	3	NA
Owonikoko, T. K 2019	CT+T	64	46	NA
	CT	64	42	NA
Gandhi, L 2018	CT+I	410	NA	275
	CT	206	NA	135
Langer, C. J 2016	CT+I	60	33	23
	CT	63	18	16

Lynch, T. J 2012*	CT	65	9	39
	CT+I	138	36	24
Reck, M 2013*	CT	45	NA	4
	CT+I	43	NA	16
Paz-Ares, L 2019	CT+I	268	NA	166
	CT	269	NA	167
Paz-Ares, L 2018	CT+I	278	NA	37
	CT	281	NA	18
Bradbury, P. A 2018	CT+B	77	NA	63
	CT	75	NA	43
Chang, J 2015	CT+B	36	14	NA
	CT	36	8	NA

NA: not available, *represents the combined data

Table A2. Summary of ORR and Adverse data in randomized controlled trials of patients with advanced lung cancer undergone combined therapy. This table summarizes the number of samples and the number of cases of reaction (ORR) or grade 3-4 adverse events (adverse) in each study.

OS	1	2	3	4	5
CT	0	0.0001875	0.060825	0.6146375	0.32435
CT+T	0.0010875	0.34635	0.5556125	0.0968625	0.0000875
CT+T+T	0.0713125	0.4606125	0.295225	0.126725	0.046125
CT+I	0.8985625	0.0963375	0.004925	0.000175	0
CT+B	0.0290375	0.0965125	0.0834125	0.1616	0.6294375
PFS	1	2	3	4	5
CT	0	0	0.0001875	0.4218125	0.578
CT+T	0.007875	0.162275	0.6877125	0.1421375	0
CT+T+T	0.7529125	0.1807	0.053275	0.012675	0.0004375
CT+I	0.201825	0.5932625	0.1768	0.0280625	0.00005
CT+B	0.0373875	0.0637625	0.082025	0.3953125	0.4215125
ORR	1	2	3	4	5
CT	0	0	0.0000625	0.088425	0.9115125
CT+T	0.000575	0.0318	0.3596	0.608025	0
CT+T+T	0.2531	0.457675	0.2742875	0.0149375	0
CT+I	0.4227	0.3413125	0.1839	0.0518875	0.0002
CT+B	0.323625	0.1692125	0.18215	0.23675	0.0882875
Adverse	1	2	3	4	5
CT	0	0	0.0002875	0.5757125	0.424

CT+T	0.0001875	0.0477125	0.951125	0.000975	0
CT+T+T	0.5967125	0.397325	0.0058625	0.0000875	0.0000125
CT+I	0	0.0000375	0.0018375	0.4224625	0.5756625
CT+B	0.4031	0.554925	0.0408875	0.0007625	0.000325

Table A3. Ranking of treatments in terms of OS, PFS, ORR, Adverse. The table summarizes the ranking results of the network-analysis under the four outcome indicators. The number of rows (1-5) indicates the sequence number, the column corresponds to five treatment strategies, the values in the table indicate the probability percentage that the corresponding treatment strategy ranked in the corresponding serial number.

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