Supplementary

Table S1 Search strategies

No.	Term
PubMed	
#1	(clinical trial) OR (trial) OR (randomized controlled trial) OR (phase)OR (real word) OR (real-word) OR (retrospective) OR (cohort) OR (case control) OR (case-control)
#2	(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 (NSCLC[Title])
#3	(immune checkpoint inhibitor[Title]) OR (PD-1[Title]) OR (PD-L1[Title]) OR (ICI[Title]) OR (pembrolizumab[Title]) OR (nivolumab[Title]) OR (sintilimab[Title]) OR (toripalimab[Title]) OR (atezolizumab[Title]) OR (tislelizumab[Title]) OR (camrelizumab[Title]) OR (durvalumab[Title]) OR (Tislelizumab[Title])
#4	anlotinib[Title]
#5	#1 AND #2 AND (#3 OR #4)
Web of Science	
#1	TS=(clinical trial) OR TS=(trial) OR TS=(randomized controlled trial) OR TS=(phase) OR TS=(real word) OR TS=(real-word) OR TS=(retrospective) OR TS=(cohort) OR TS=(case control) OR TS=(case-control)
#2	TI=(non-small cell lung cancer) OR TI=(non-small-cell lung cancer) OR TI=(non small-cell lung cancer) OR TI=(non small cell lung carcinoma) OR TI=(NSCLC)
#3	TI=(immune checkpoint inhibitor) OR TI=(PD-1) OR TI=(PD-L1) OR TI=(ICI) OR TI=(pembrolizumab) OR TI=(nivolumab) OR TI=(sintilimab) OR TI=(toripalimab) OR TI=(atezolizumab) OR TI=(tislelizumab) OR TI=(camrelizumab) OR TI=(durvalumab) OR TI=(Tislelizumab)
#4	TI=(anlotinib)
#5	#1 AND #2 AND (#3 OR #4)
ClinicalTrials	
#1	Condition or disease: Non Small Cell Lung Cancer
#2	Intervention/treatment: immune checkpoint inhibitor OR PD-1 OR PD-L1 OR ICI OR pembrolizumab OR nivolumab OR sintilimab OR toripalimab OR atezolizumab OR tislelizumab OR camrelizumab OR durvalumab OR Tislelizumab
#3	Intervention/treatment: anlotinib
#4	Status: Completed
#5	Study Results: With Results
#6	#1 AND #4 AND #5 # AND (#2 OR #3)
Cochrane Central Register of Controlled Trials	
#1	("clinical trial"):ti,ab,kw OR ("trial"):ti,ab,kw OR ("randomized controlled trial"):ti,ab,kw OR ("phase"):ti,ab,kw OR ("real word"):ti,ab,kw OR ("real-word"):ti,ab,kw OR ("retrospective"):ti,ab,kw OR ("cohort"):ti,ab,kw OR ("case control"):ti,ab,kw OR ("case-control"):ti,ab,kw
#2	("non-small cell lung cancer"):ti OR ("non-small-cell lung cancer"):ti OR ("non small-cell lung cancer"):ti OR ("non small cell lung carcinoma"):ti OR ("NSCLC"):ti
#3	("immune checkpoint inhibitor"):ti OR ("PD-1"):ti OR ("PD-L1"):ti OR ("CTLA-4"):ti OR ("pembrolizumab"):ti OR ("nivolumab"):ti OR ("sintilimab"):ti OR ("toripalimab"):ti OR ("atezolizumab"):ti OR ("tislelizumab"):ti OR ("camrelizumab"):ti OR ("durvalumab"):ti OR ("tislelizumab"):ti
#4	("anlotinib"):ti
#5	#1 AND #2 AND (#3 OR #4)

© Translational Cancer Research. All rights reserved.
https://dx.doi.org/10.21037/tcr-23-1483

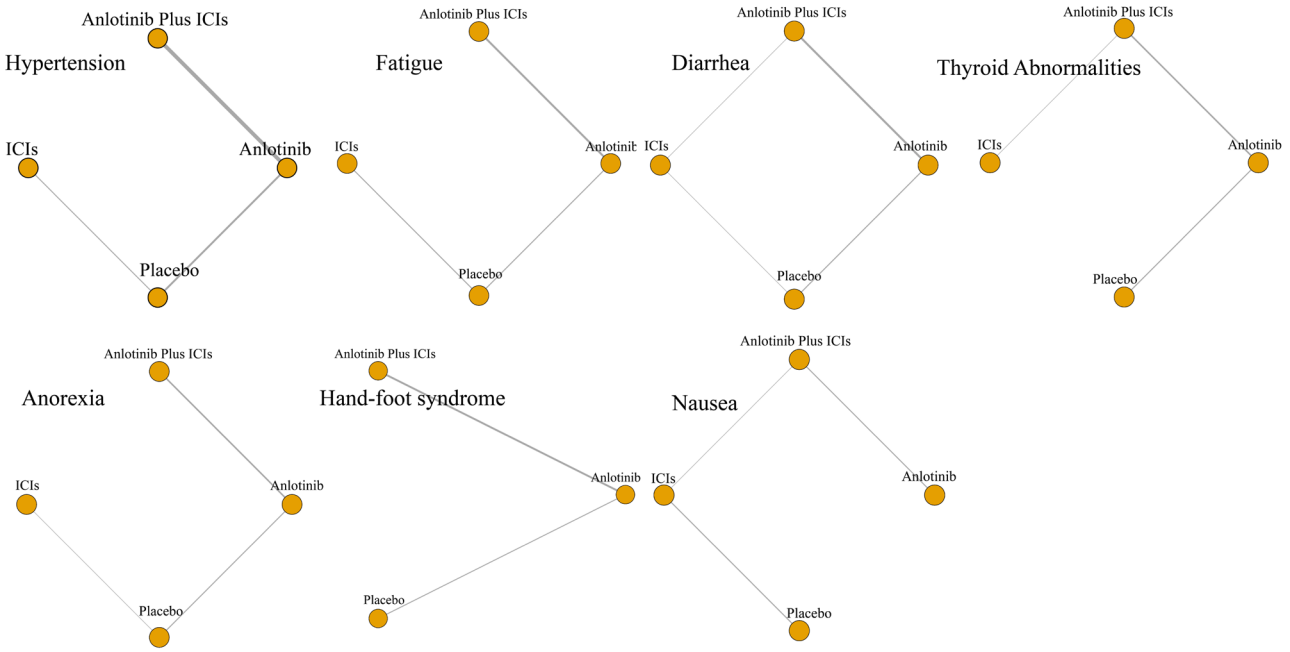

Figure S1 Network plot of common TRAE network meta-analysis. ICIs, immune checkpoint inhibitors; TRAE, treatment-related adverse event.

© Translational Cancer Research. All rights reserved.
https://dx.doi.org/10.21037/tcr-23-1483

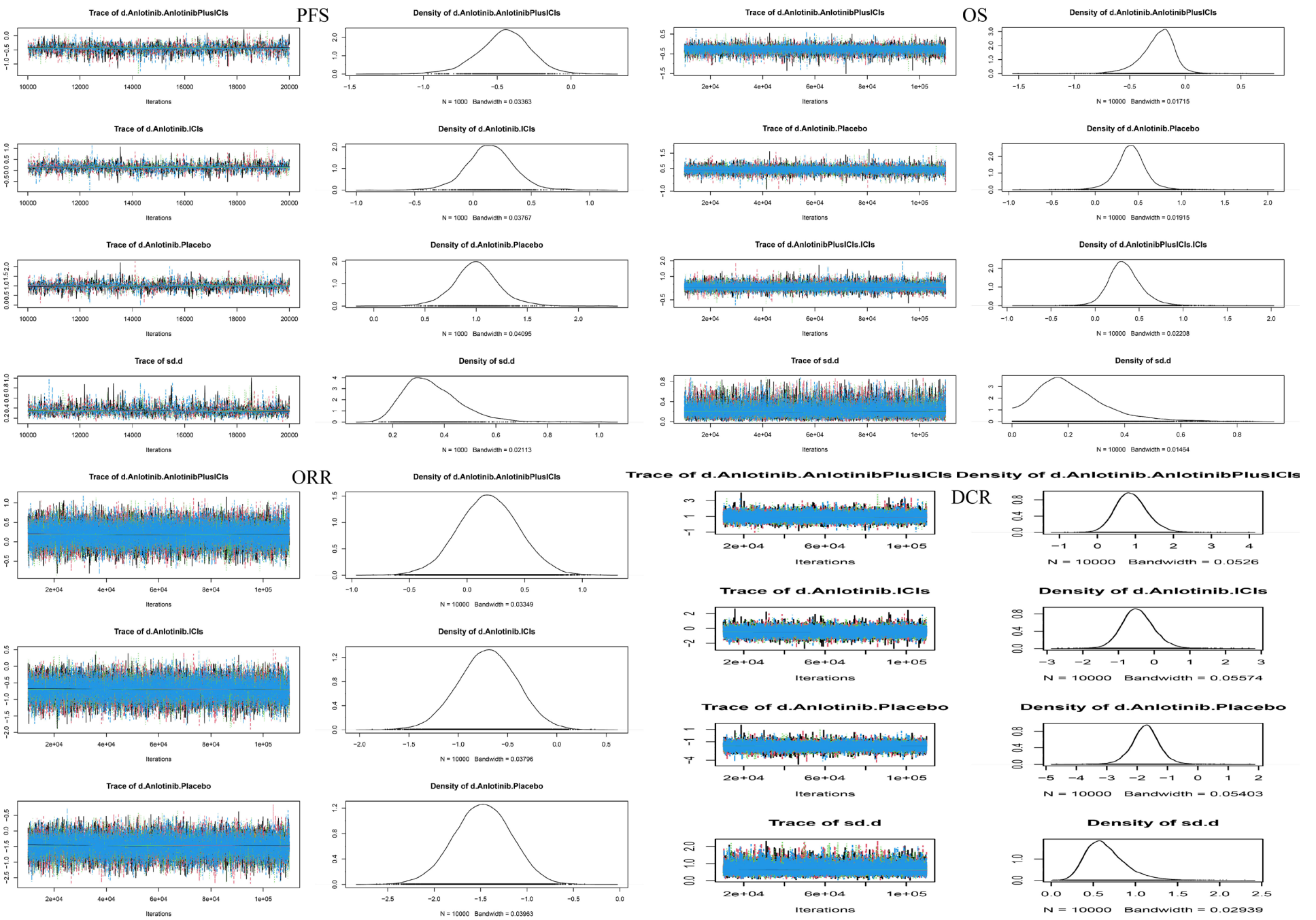

Figure S2 Model trace plot and density plots of efficacy outcomes. ICIs, immune checkpoint inhibitors; PFS, progression-free survival; ORR, objective response rate; OS, overall survival; DCR, disease control rate.

© Translational Cancer Research. All rights reserved.
https://dx.doi.org/10.21037/tcr-23-1483

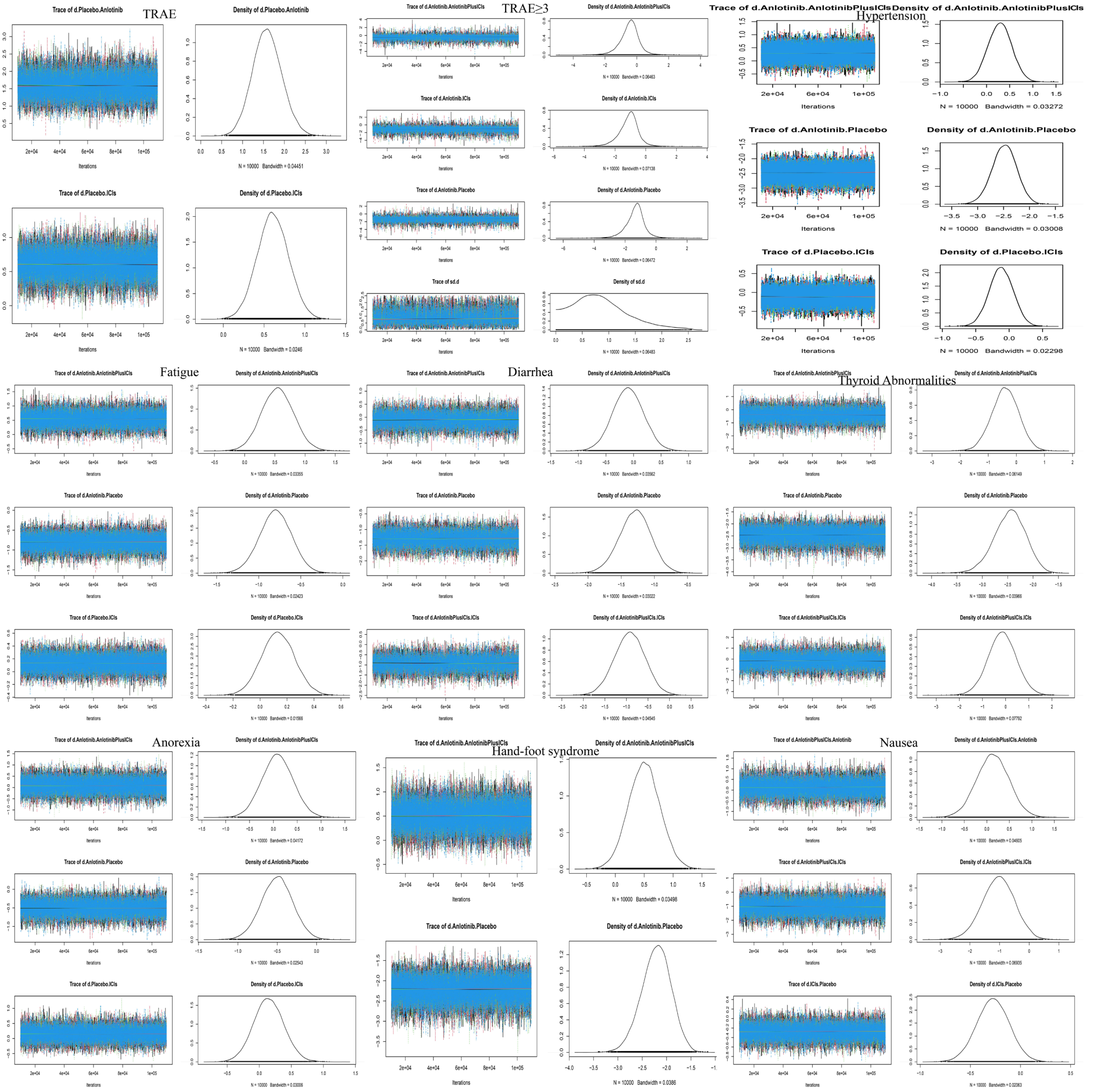

Figure S3 Model trace plot and density plots of safety outcomes. TRAE, treatment-related adverse event; TRAE ≥3, TRAE grade 3 or higher; ICIs, immune checkpoint inhibitors.

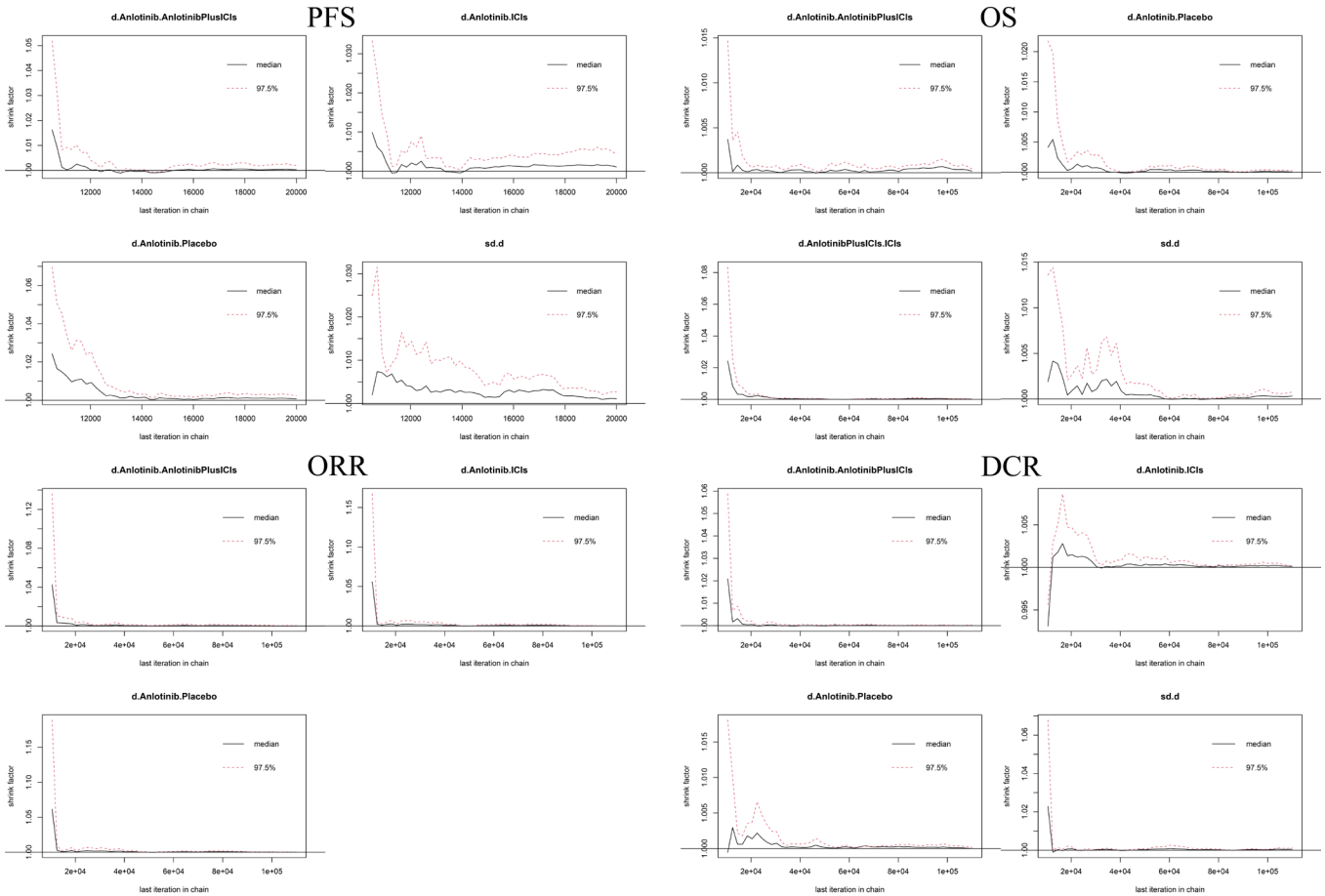

Figure S4 Diagnostic plots of efficacy outcomes. PFS, progression-free survival; OS, overall survival; ORR, objective response rate; DCR, disease control rate; ICIs, immune checkpoint inhibitors.

© Translational Cancer Research. All rights reserved.
https://dx.doi.org/10.21037/tcr-23-1483

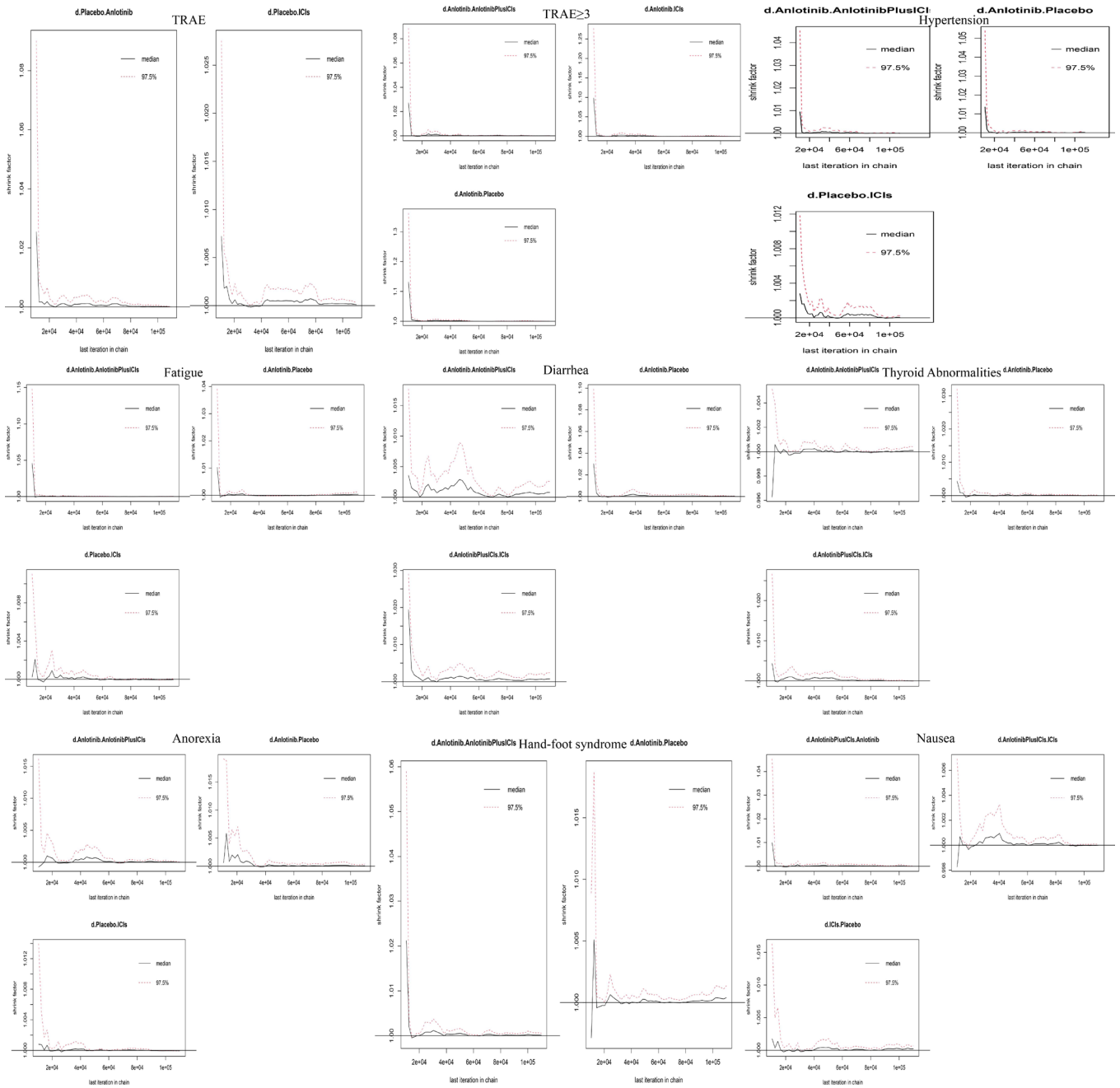

Figure S5 Diagnostic plots of safety outcomes. TRAE, treatment-related adverse event; TRAE ≥3, TRAE grade 3 or higher; ICIs, immune checkpoint inhibitors.

© Translational Cancer Research. All rights reserved.
https://dx.doi.org/10.21037/tcr-23-1483

Table S2 The results of node-splitting analysis

Outcomes	Comparison	Direct	Indirect	Network	P value
PFS, HR (95% CI)	Anlotinib versus anlotinib plus ICIs	−0.44 (−0.80, −0.18)	0.14 (−0.65, 0.71)	−0.44 (−0.83, −0.11)	0.114625
	Anlotinib versus ICIs	−0.16 (−0.91, 0.59)	0.27 (−0.20, 0.73)	0.15 (−0.24, 0.55)	0.285125
	Anlotinib versus placebo	1.3 (0.78, 1.8)	0.58 (0.0024, 1.2)	1.0 (0.56, 1.5)	0.079075
	Anlotinib plus ICIs versus ICIs	0.49 (0.23, 0.86)	1.2 (0.39, 2.1)	0.59 (0.31, 0.93)	0.10825
	ICIs versus placebo	0.63 (0.17, 1.1)	1.3 (0.65, 1.9)	0.85 (0.42, 1.3)	0.082475
OS, HR (95% CI)	Anlotinib versus anlotinib plus ICIs	−0.20 (−0.62, 0.11)	−0.47 (−1.3, 0.24)	−0.23 (−0.60, 0.0069)	0.450225
	Anlotinib versus placebo	0.34 (−0.14, 0.78)	0.61 (−0.11, 1.4)	0.41 (0.045, 0.76)	0.43625
	Anlotinib plus ICIs versus ICIs	0.44 (−0.031, 1.0)	0.17 (−0.47, 0.90)	0.32 (−0.010, 0.76)	0.4522
	ICIs versus placebo	0.37 (0.014, 0.73)	0.092 (−0.71, 0.85)	0.32 (0.027, 0.61)	0.4381
ORR, OR (95% CI)	Anlotinib versus anlotinib plus ICIs	0.51 (−0.28, 1.4)	−1.9 (−5.4, 0.63)	0.30 (−0.42, 1.2)	0.07035
	Anlotinib versus ICIs	0.042 (−2.2, 2.3)	−1.1 (−2.5, 0.033)	−0.81 (−1.8, 0.093)	0.330175
	Anlotinib versus placebo	−3.5 (−6.8, −1.6)	−1.1 (−2.4, 0.10)	−1.8 (−3.2, −0.82)	0.0432
	Anlotinib plus ICIs versus ICIs	−0.92 (−1.9, −0.32)	−3.3 (−7.2, −0.98)	−1.1 (−2.0, −0.53)	0.065525
	ICIs versus placebo	−0.71 (−1.6, 0.15)	−3.1 (−6.2, −0.89)	−0.93 (−2.1, −0.23)	0.04635
DCR, OR (95% CI)	Anlotinib versus anlotinib plus ICIs	1.2 (0.48, 2.1)	−0.57 (−2.1, 1.0)	0.88 (0.13, 1.8)	0.0425
	Anlotinib versus ICIs	−0.18 (−2.2, 1.8)	−0.60 (−1.6, 0.59)	−0.47 (−1.3, 0.51)	0.699675
	Anlotinib versus placebo	−2.1 (−3.0, −1.3)	−0.48 (−1.9, 0.86)	−1.7 (−2.7, −0.77)	0.04515
	Anlotinib plus ICIs versus ICIs	−1.1 (−1.8, −0.63)	−2.7 (−4.5, −1.1)	−1.3 (−2.0, −0.74)	0.0804
	ICIs versus placebo	−0.52 (−1.6, 0.57)	−2.2 (−3.4, −0.94)	−1.2 (−2.4, −0.26)	0.048475
TRAE ≥3, OR (95% CI)	Anlotinib versus anlotinib plus ICIs	−0.52 (−2.4, 1.2)	−0.36 (−4.6, 3.8)	−0.42 (−1.8, 0.70)	0.930075
	Anlotinib versus ICIs	−2.7 (−4.7, −1.1)	−0.67 (−1.4, 0.056)	−1.1 (−2.7, 0.18)	0.03145
	Anlotinib versus placebo	−1.3 (−3.2, 0.57)	−1.6 (−4.6, 1.1)	−1.3 (−2.8, −0.10)	0.7974
	Anlotinib plus ICIs versus ICIs	−0.47 (−1.3, 0.57)	−1.2 (−2.8, 0.14)	−0.65 (−2.1, 0.72)	0.291275
	ICIs versus placebo	−0.30 (−2.1, 1.5)	0.010 (−2.8, 3.)	−0.25 (−1.5, 1.1)	0.80365
Diarrhea, OR (95% CI)	Anlotinib versus anlotinib plus ICIs	−0.15 (−0.93, 0.64)	0.21 (−2.0, 2.4)	−0.10 (−0.80, 0.55)	0.738775
	Anlotinib versus placebo	−1.3 (−2.4, −0.45)	−1.6 (−3.9, 0.49)	−1.3 (−2.1, −0.66)	0.75915
	Anlotinib plus ICIs versus ICIs	−1.2 (−3., 0.42)	−0.90 (−2.7, 0.72)	−0.96 (−2.1, −0.022)	0.7484
	ICIs versus placebo	−0.28 (−1.4, 0.84)	0.025 (−2.1, 2.1)	−0.26 (−1.0, 0.57)	0.7609

PFS, progression-free survival; OS, overall survival; ORR, objective response rate; DCR, disease control rate; TRAE, treatment-related adverse event; TRAE ≥3, TRAE grade 3 or higher; HR, hazard ratio; CI, confidence interval; OR, odds ratio; ICIs, immune checkpoint inhibitors.

© Translational Cancer Research. All rights reserved.
https://dx.doi.org/10.21037/tcr-23-1483