

Supplementary

Table S1 Multiple Cox regression analysis for PFS in patients with EGFR mutation

Parameter		Parameter estimation	Standard error	P value	HR (95% CI)
Group	Anlotinib	-1.703	0.252	<.0001	0.18 (0.11-0.30)
Number of metastases	≤ 3	-0.394	0.220	0.074	0.68 (0.44-1.04)
Gender	Female	-0.410	0.219	0.061	0.66 (0.43-1.02)
Age (years)	61-69	-0.263	0.235	0.264	0.77 (0.49-1.22)
Age (years)	≥70	-1.557	0.749	0.038	0.21 (0.05-0.92)
Histological type	Others	1.470	0.746	0.049	4.35 (1.01-18.77)
Histological type	Squamous	0.310	0.411	0.451	1.36 (0.61-3.05)
Clinical Stage	IV	-0.798	0.558	0.153	0.45 (0.15-1.34)
Lines of prior chemotherapy	1	-0.033	0.769	0.966	0.97 (0.21-4.37)
Lines of prior chemotherapy	3	-0.254	0.232	0.274	0.78 (0.49-1.22)
Prior target therapy	Yes	-0.583	0.583	0.318	0.56 (0.18-1.75)
Prior radiotherapy	Yes	0.269	0.227	0.235	1.31 (0.84-2.04)
Smoking status	None-smoker	-0.829	0.769	0.281	0.44 (0.10-1.97)
ECOG PS score	1	-0.206	0.277	0.457	0.81 (0.47-1.40)

ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; PFS, progression free survival

Table S2 Multiple Cox regression analysis for OS in patients with EGFR mutation

Parameter		Parameter estimation	Standard error	P value	HR (95% CI)
Group	Anlotinib	-0.638	0.259	0.014	0.53 (0.32-0.88)
Number of metastases	≤3	-1.095	0.258	<.0001	0.33 (0.20-0.56)
Gender	Female	-0.634	0.243	0.009	0.53 (0.33-0.85)
Age (years)	61-69	-0.041	0.261	0.874	0.96 (0.58-1.60)
Age (years)	≥70	-1.287	0.626	0.040	0.27 (0.08-0.94)
Histological type	Others	1.231	0.756	0.104	3.43 (0.78-15.08)
Histological type	Squamous	-0.948	0.616	0.124	0.39 (0.12-1.30)
Clinical Stage	IV	-1.143	0.707	0.106	0.32 (0.08-1.28)
Lines of prior chemotherapy	1	0.445	0.756	0.555	1.56 (0.36-6.86)
Lines of prior chemotherapy	3	-0.387	0.257	0.131	0.68 (0.41-1.12)
Prior targeted therapy	Yes	0.730	0.701	0.298	2.08 (0.53-8.20)
Prior radiotherapy	Yes	0.218	0.237	0.357	1.24 (0.78-1.98)
Smoking status	None-smoker	-1.057	0.649	0.103	0.35 (0.10-1.24)
ECOG PS score	1	0.302	0.315	0.338	1.35 (0.73-2.51)

ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; OS, overall survival.

Table S3 Multiple Cox regression analysis for PFS in patients without EGFR mutation

Parameter		Parameter estimation	Standard error	P value	HR (95% CI)
Group	Anlotinib	-1.371	0.161	<.0001	0.25 (0.19-0.35)
Number of metastases	≤3	-0.506	0.143	0.0004	0.60 (0.46-0.80)
Gender	Female	-0.186	0.172	0.279	0.83 (0.59-1.16)
Age (years)	61-69	-0.479	0.150	0.001	0.62 (0.46-0.83)
Age (years)	≥70	-1.093	0.300	0.0003	0.34 (0.19-0.60)
Histological type	Others	-0.134	0.356	0.706	0.87 (0.44-1.76)
Histological type	Squamous	-0.030	0.174	0.860	0.97 (0.69-1.36)
Clinical Stage	IV	-0.0007	0.301	0.998	1.00 (0.55-1.80)
Clinical Stage	Others	-13.078	407.326	0.974	0.00 (0.00-0.00)
Lines of prior chemotherapy	3	-0.034	0.147	0.817	0.98 (0.72-1.29)
Prior targeted therapy	Yes	0.036	0.161	0.822	1.04 (0.76-1.42)
Prior radiotherapy	Yes	-0.214	0.148	0.148	0.81 (0.60-1.08)
Smoking status	None-smoker	-0.090	0.273	0.741	0.91 (0.54-1.56)
ECOG PS score	1	0.249	0.188	0.186	1.28 (0.89-1.85)
ECOG PS score	2	1.647	0.756	0.029	5.19 (1.18-22.85)

ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; PFS, progression free survival.

Table S4 Multiple Cox regression analysis for OS in patients without EGFR mutation

Parameter		Parameter estimation	Standard error	P value	HR (95% CI)
Group	Anlotinib	-0.370	0.149	0.013	0.69 (0.52-0.93)
Number of metastases	≤3	-0.574	0.144	<.0001	0.56 (0.43-0.75)
Gender	Female	-0.337	0.177	0.056	0.71 (0.51-1.01)
Age (years)	61-69	0.134	0.151	0.377	1.14 (0.85-1.54)
Age (years)	≥70	-0.309	0.312	0.322	0.73 (0.40-1.35)
Histological type	Others	0.059	0.333	0.860	1.06 (0.55-2.04)
Histological type	Squamous	-0.020	0.177	0.912	0.98 (0.69-1.39)
Clinical Stage	IV	0.234	0.333	0.482	1.26 (0.66-2.43)
Clinical Stage	Others	-3.094	1.297	0.017	0.05 (0.004-0.58)
Lines of prior chemotherapy	3	-0.340	0.147	0.020	0.71 (0.53-0.95)
Prior targeted therapy	Yes	0.097	0.164	0.552	1.10 (0.80-1.52)
Prior radiotherapy	Yes	0.010	0.148	0.948	1.01 (0.76-1.35)
Smoking status	None-smoker	-0.186	0.268	0.486	0.83 (0.49-1.40)
ECOG PS score	1	0.644	0.216	0.003	1.91 (1.25-2.91)
ECOG PS score	2	3.902	0.777	<.0001	49.50 (10.80-226.98)

ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; OS, overall survival.

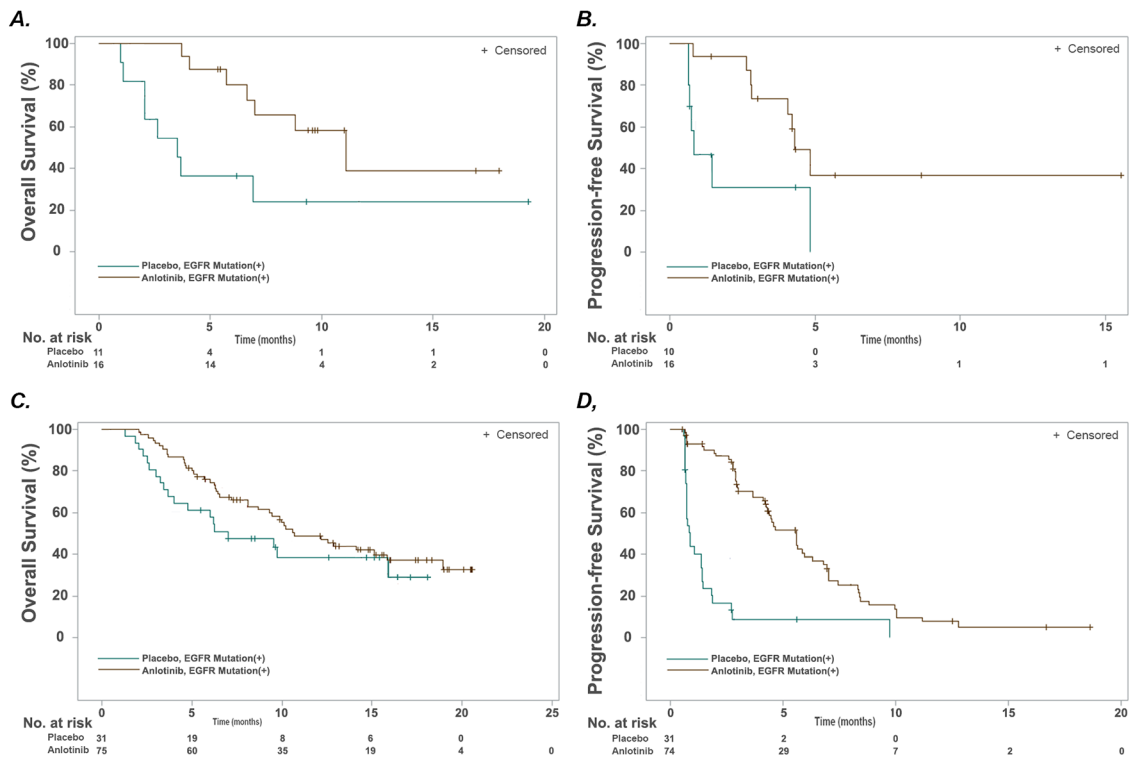


Figure S1 Overall survival and progression-free survival in patients with EGFR mutation who received EGFR TKIs as first- or second-line therapy. (A) Overall survival in patients with EGFR mutation who received EGFR TKIs as first-line therapy; (B) progression-free survival in patients with EGFR mutation who received EGFR TKIs as first-line therapy; (C) overall survival in patients with EGFR mutation who received EGFR TKIs as second-line therapy; (D) progression-free survival in patients with EGFR mutation who received EGFR TKIs as second-line therapy. EGFR, epidermal growth factor receptor; TKIs, tyrosine kinase inhibitors.

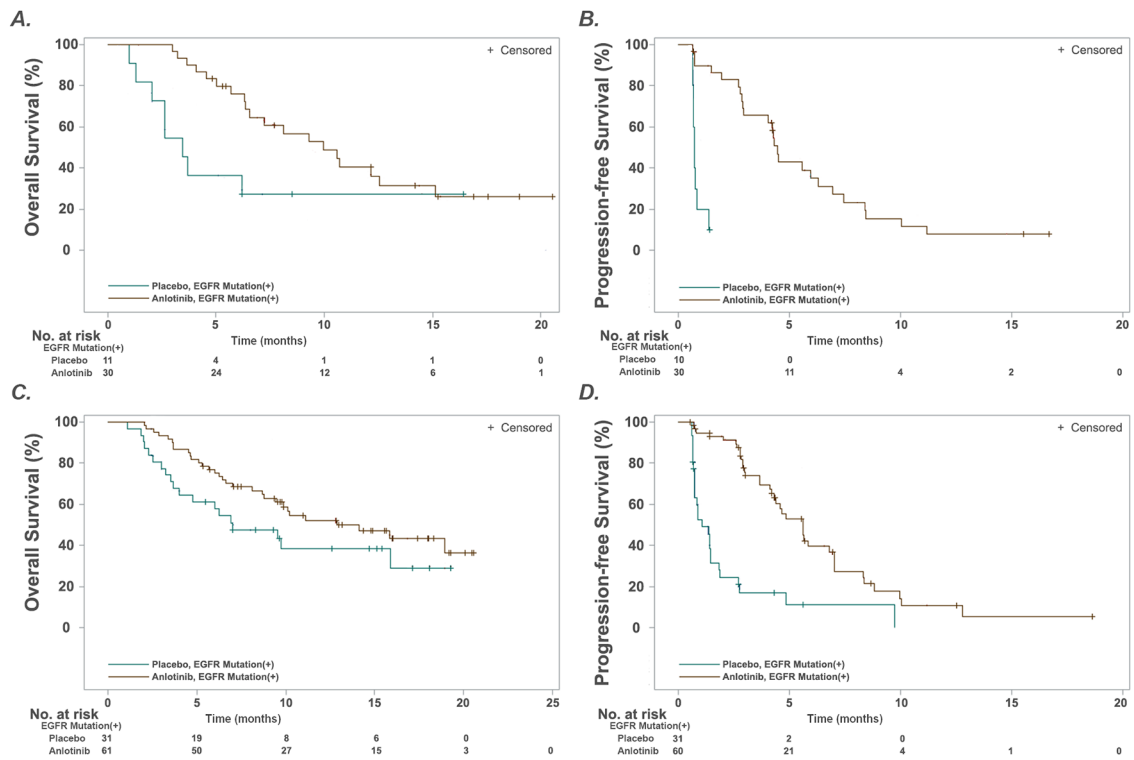


Figure S2 Overall survival and progression-free survival in patients with EGFR mutation who progressed from EGFR TKIs within or exceeding 8 months. (A) Overall survival in patients with EGFR mutation who progressed from EGFR TKIs within 8 months; (B) progression-free survival in patients with EGFR mutation who progressed from EGFR TKIs within 8 months; (C) overall survival in patients with EGFR mutation who progressed from EGFR TKIs exceeding 8 months; (D) progression-free survival in patients with EGFR mutation who progressed from EGFR TKIs exceeding 8 months. EGFR, epidermal growth factor receptor; TKIs, tyrosine kinase inhibitors.

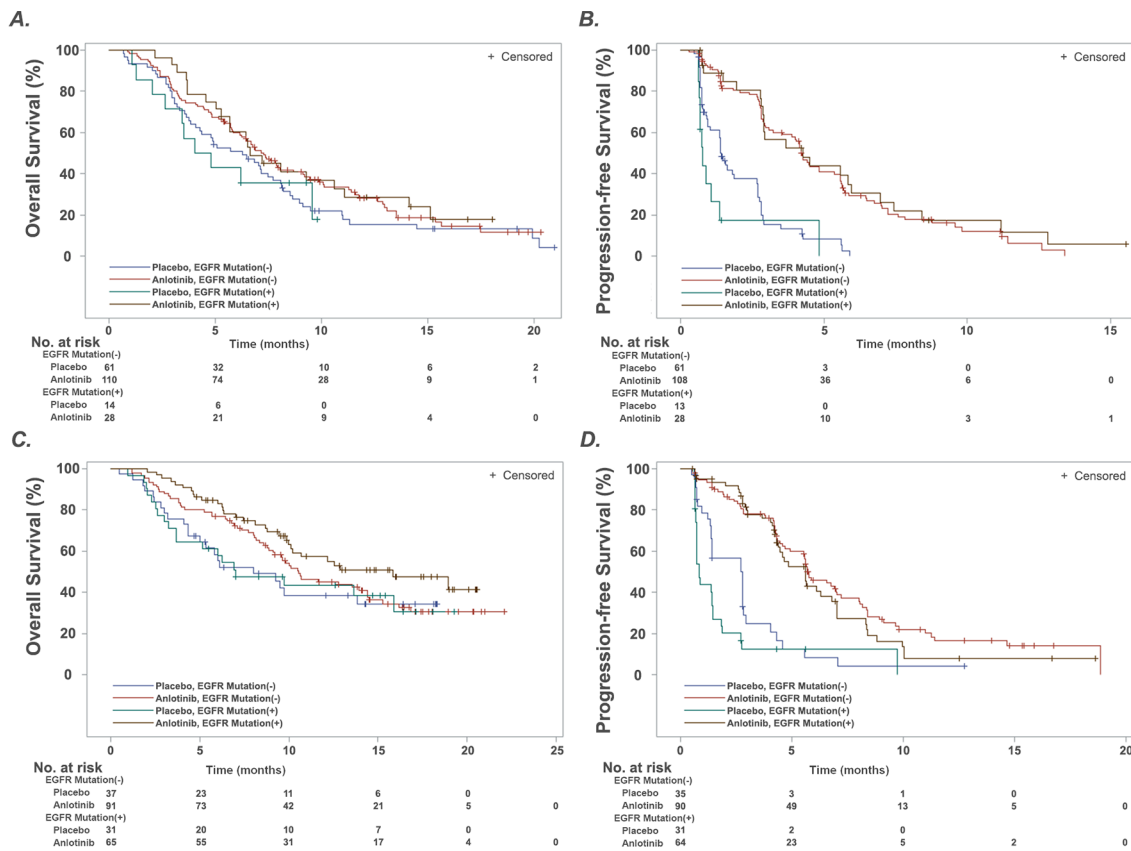


Figure S3 Overall survival and progression-free survival in patients with time since TSPT ≤ 18 or > 18 months according to EGFR mutation status. (A) Overall survival in patients with TSPT ≤ 18 months according to EGFR mutation status; (B) progression-free survival in patients with TSPT ≤ 18 months according to EGFR mutation status; (C) overall survival in patients with TSPT > 18 months according to EGFR mutation status; (D) progression-free survival in patients with TSPT > 18 months according to EGFR mutation status. TSPT, the start of prior therapy; EGFR, epidermal growth factor receptor.