Figure S1 Progression-free survival curves (A,C) and overall survival curves (B,D) for NSCLC patients in subset stratified according to the absence or presence of baseline CNS metastases. PFS, progression-free survival; OS, overall survival; NSCLC, non-small cell lung cancer; CNS, central nervous system; TKI, tyrosine kinase inhibitor.

Figure S2 Progression-free survival curves (A,C) and overall survival curves (B,D) for NSCLC patients in subset stratified according to the status of baseline CNS metastases. PFS, progression-free survival; OS, overall survival; NSCLC, non-small cell lung cancer; CNS, central nervous system; TKI, tyrosine kinase inhibitor.
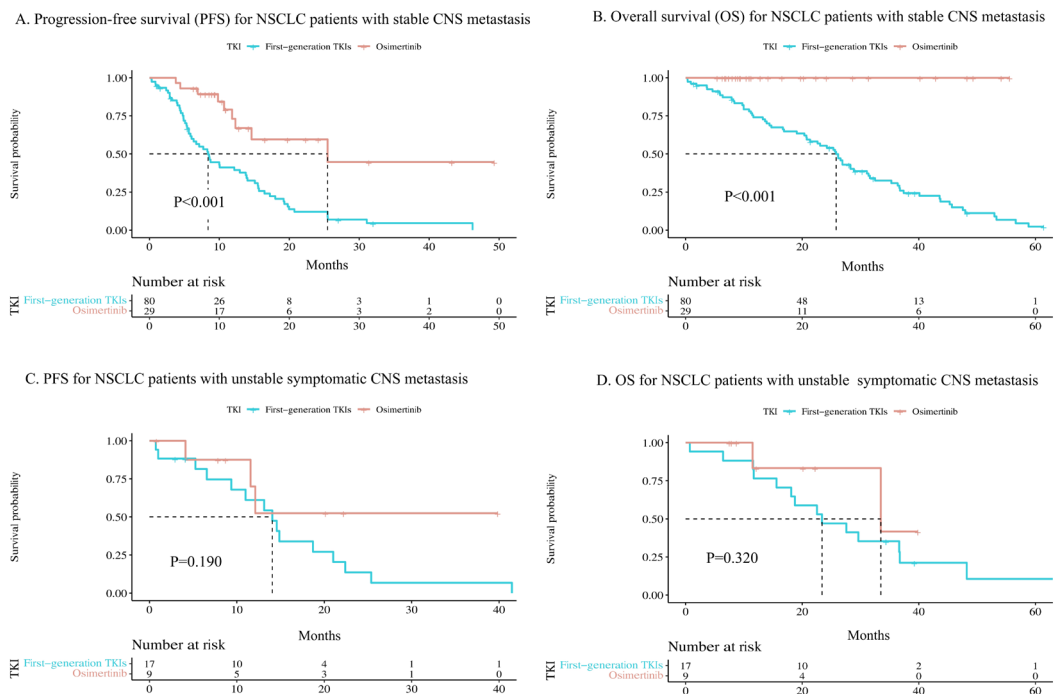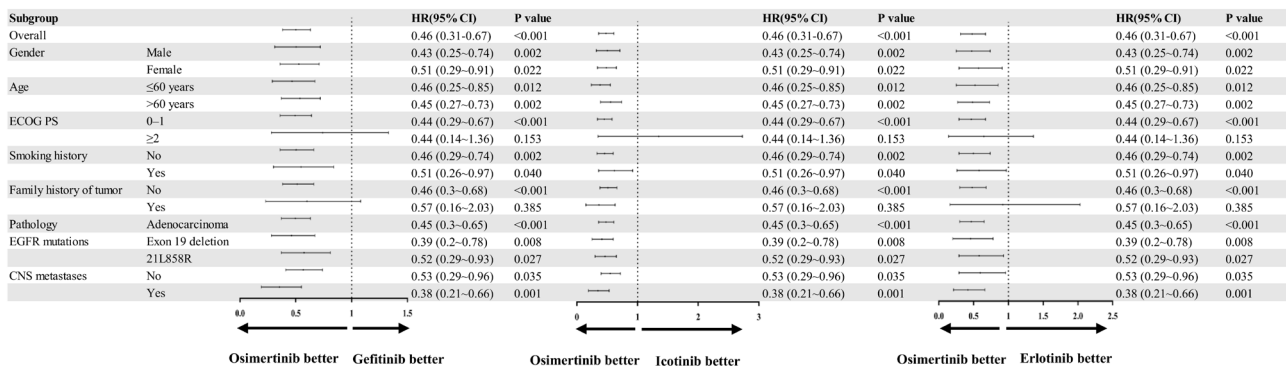
Figure S3

Subgroup		Gefitinib HR (95% CI)	P value	Icotinib HR (95% CI)	P value	Erlotinib HR (95% CI)	P value
Overall		0.46 (0.31~0.67)	<0.001	0.46 (0.31~0.67)	<0.001	0.46 (0.31~0.67)	<0.001
Gender	Male	0.43 (0.25~0.74)	0.002	0.43 (0.25~0.74)	0.002	0.43 (0.25~0.74)	0.002
	Female	0.51 (0.29~0.91)	0.022	0.51 (0.29~0.91)	0.022	0.51 (0.29~0.91)	0.022
Age	≤60 years	0.46 (0.25~0.85)	0.012	0.46 (0.25~0.85)	0.012	0.46 (0.25~0.85)	0.012
	>60 years	0.45 (0.27~0.73)	0.002	0.45 (0.27~0.73)	0.002	0.45 (0.27~0.73)	0.002
ECOG PS	0–1	0.44 (0.29~0.67)	<0.001	0.44 (0.29~0.67)	<0.001	0.44 (0.29~0.67)	<0.001
	≥2	0.44 (0.14~1.36)	0.153	0.44 (0.14~1.36)	0.153	0.44 (0.14~1.36)	0.153
Smoking history	No	0.46 (0.29~0.74)	0.002	0.46 (0.29~0.74)	0.002	0.46 (0.29~0.74)	0.002
	Yes	0.51 (0.26~0.97)	0.040	0.51 (0.26~0.97)	0.040	0.51 (0.26~0.97)	0.040
Family history of tumor	No	0.46 (0.3~0.68)	<0.001	0.46 (0.3~0.68)	<0.001	0.46 (0.3~0.68)	<0.001
	Yes	0.57 (0.16~2.03)	0.385	0.57 (0.16~2.03)	0.385	0.57 (0.16~2.03)	0.385
Pathology	Adenocarcinoma	0.45 (0.3~0.65)	<0.001	0.45 (0.3~0.65)	<0.001	0.45 (0.3~0.65)	<0.001
EGFR mutations	Exon 19 deletion	0.39 (0.2~0.78)	0.008	0.39 (0.2~0.78)	0.008	0.39 (0.2~0.78)	0.008
	21L858R	0.52 (0.29~0.93)	0.027	0.52 (0.29~0.93)	0.027	0.52 (0.29~0.93)	0.027
CNS metastases	No	0.53 (0.29~0.96)	0.035	0.53 (0.29~0.96)	0.035	0.53 (0.29~0.96)	0.035
	Yes	0.38 (0.21~0.66)	0.001	0.38 (0.21~0.66)	0.001	0.38 (0.21~0.66)	0.001

Osimertinib better / Gefitinib better; Osimertinib better / Icotinib better; Osimertinib better / Erlotinib better

Figure S3 Forest plot for PFS of NSCLC patients in subset stratified according to the first-generation EGFR-TKI types. HR, hazard ratio; PFS, progression-free survival; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; CNS, central nervous system; EGFR-TKIs, epidermal growth factor receptor-tyrosine kinase inhibitors.
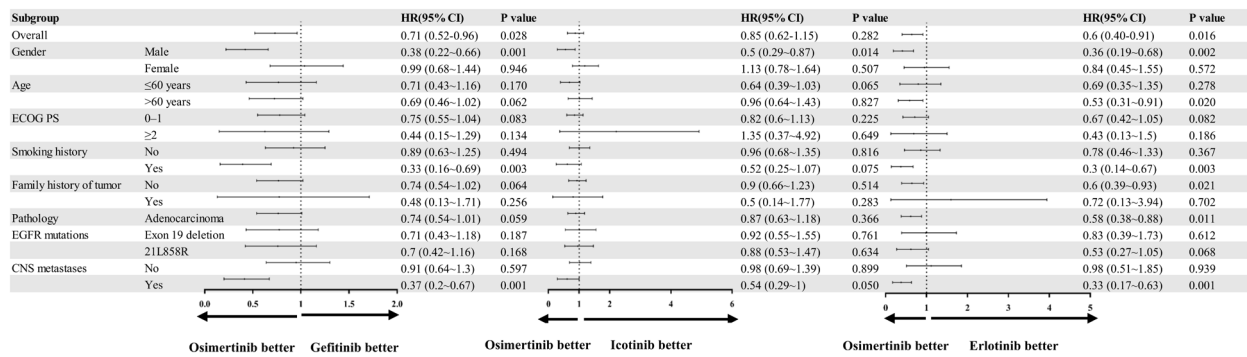
Figure S4

Subgroup		Gefitinib HR (95% CI)	P value	Icotinib HR (95% CI)	P value	Erlotinib HR (95% CI)	P value
Overall		0.71 (0.52-0.96)	0.028	0.85 (0.62-1.15)	0.282	0.6 (0.40-0.91)	0.016
Gender	Male	0.38 (0.22~0.66)	0.001	0.5 (0.29~0.87)	0.014	0.36 (0.19~0.68)	0.002
	Female	0.99 (0.68~1.44)	0.946	1.13 (0.78~1.64)	0.507	0.84 (0.45~1.55)	0.572
Age	≤60 years	0.71 (0.43~1.16)	0.170	0.64 (0.39~1.03)	0.065	0.69 (0.35~1.35)	0.278
	>60 years	0.69 (0.46~1.02)	0.062	0.96 (0.64~1.43)	0.827	0.53 (0.31~0.91)	0.020
ECOG PS	0–1	0.75 (0.55~1.04)	0.083	0.82 (0.6~1.13)	0.225	0.67 (0.42~1.05)	0.082
	≥2	0.44 (0.15~1.29)	0.134	1.35 (0.37~4.92)	0.649	0.43 (0.13~1.5)	0.186
Smoking history	No	0.89 (0.63~1.25)	0.494	0.96 (0.68~1.35)	0.816	0.78 (0.46~1.33)	0.367
	Yes	0.33 (0.16~0.69)	0.003	0.52 (0.25~1.07)	0.075	0.3 (0.14~0.67)	0.003
Family history of tumor	No	0.74 (0.54~1.02)	0.064	0.9 (0.66~1.23)	0.514	0.6 (0.39~0.93)	0.021
	Yes	0.48 (0.13~1.71)	0.256	0.5 (0.14~1.77)	0.283	0.72 (0.13~3.94)	0.702
Pathology	Adenocarcinoma	0.74 (0.54~1.01)	0.059	0.87 (0.63~1.18)	0.366	0.58 (0.38~0.88)	0.011
EGFR mutations	Exon 19 deletion	0.71 (0.43~1.18)	0.187	0.92 (0.55~1.55)	0.761	0.83 (0.39~1.73)	0.612
	21L858R	0.7 (0.42~1.16)	0.168	0.88 (0.53~1.47)	0.634	0.53 (0.27~1.05)	0.068
CNS metastases	No	0.91 (0.64~1.3)	0.597	0.98 (0.69~1.39)	0.899	0.98 (0.51~1.85)	0.939
	Yes	0.37 (0.2~0.67)	0.001	0.54 (0.29~1)	0.050	0.33 (0.17~0.63)	0.001

Osimertinib better / Gefitinib better; Osimertinib better / Icotinib better; Osimertinib better / Erlotinib better

Figure S4 Forest plot for OS of NSCLC patients in subset stratified according to the first-generation EGFR-TKI types. HR, hazard ratio; OS, overall survival; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; CNS, central nervous system; EGFR-TKIs, epidermal growth factor receptor-tyrosine kinase inhibitor.