Supplementary

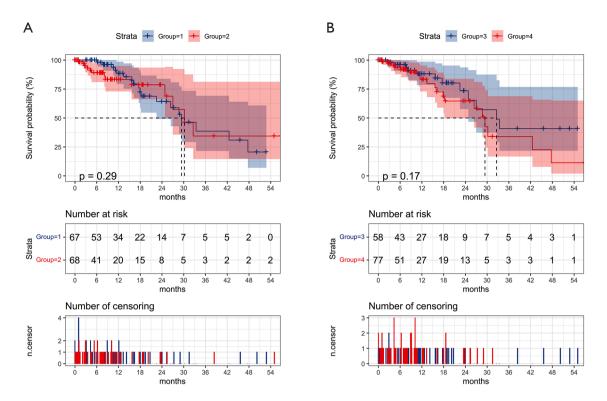


Figure S1 Kaplan-Meier curves for overall survival in advanced NSCLC patients treated with TKIs, stratified by (A) baseline CK level, and (B) CK change during TKI therapy. CK, creatine kinase; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor.

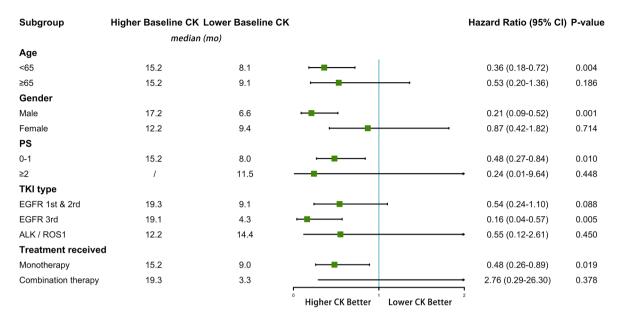


Figure S2 Subgroup analyses of the effect of baseline CK level on TKI efficacy. Progression-free survival and subgroup analyses were estimated by the Kaplan-Meier method and Cox proportional-hazards model. Covariables included age, gender, PS, TKI type, and treatment received. ALK, anaplastic lymphoma kinase; CI, confidence interval; CK, creatine kinase; EGFR, epidermal growth factor receptor; PS, performance status; ROS-1, c-ROS oncogene 1; TKI, tyrosine kinase inhibitor.

Subgroup	Highest/Baseline CK Highest/Baseline CK		к	Hazard Ratio (95% CI) P-value	
	≥2 times	<2 times		Hazard Ratio (95% Ci) P-value
	median	(mo)			
Age					
<65	12.9	10.0		0.49 (0.25-0.96)	0.037
≥65	15.2	9.1	·	0.50 (0.19-1.35)	0.173
Gender					
Male	15.8	14.2	·	0.36 (0.14-0.87)	0.024
Female	14.4	9.1	·	0.55 (0.27-1.13)	0.102
PS					
0-1	14.4	9.7	· · · · · · · · · · · · · · · · · · ·	0.61 (0.35-1.05)	0.076
≥2	1	11.5		→ 0.57 (0.02-21.53)	0.759
TKI type					
EGFR 1st & 2rd	12.9	14.6		→ 1.05 (0.53-2.10)	0.882
EGFR 3rd	8.1	7.1	- -	0.21 (0.06-0.72)	0.013
ALK / ROS1	21.3	6.5	⊢∎	0.19 (0.04-0.89)	0.035
Treatment receive	d				
Monotherapy	14.4	11.5		0.60 (0.33-1.09)	0.094
Combination therapy	19.3	3.3	•	0.04 (0.00-0.65)	0.023
			°≥2 Times Better 1 <2 Times Bet	ter ²	

Figure S3 Subgroup analyses of the effect of CK elevation on TKI efficacy. Progression-free survival and subgroup analyses were estimated by the Kaplan-Meier method and Cox proportional-hazards model. Covariables included age, gender, PS, TKI type, and treatment received. ALK, anaplastic lymphoma kinase; CI, confidence interval; CK, creatine kinase; EGFR, epidermal growth factor receptor; PS, performance status; ROS-1, c-ROS oncogene 1; TKI, tyrosine kinase inhibitor.