

Table S1 The sequence of used primers

| Primer name | Sequence or modification |
|----------------------------|---------------------------------|
| <i>HER2-F</i> | 5'-CTGCGGATTGTGCGAGG-3' |
| <i>HER2-R</i> | 5'-CAGCGGGTCTCCATTGTC-3' |
| <i>HER2-probe</i> | 5'-CCCAGCTCTTTGAGGACAAC-3' |
| <i>HER2-modification</i> | 5'-6-FAM, 3'-MGB |
| <i>EFTUD2-F</i> | 5'-CTCTTCAATATCATGGACACTCCAG-3' |
| <i>EFTUD2-R</i> | 5'-CGCAAAACCAAGACAAGGTTC-3' |
| <i>EFTUD2-probe</i> | 5'-GGACATCCTTTGGCTTTTGA-3' |
| <i>EFTUD2-modification</i> | 5'-VIC, 3'-MGB |

Table S2 The result of univariate Cox regression analysis

| Factors | HR (95% CI) | P value |
|---------------------------------------|-----------------------|---------|
| Age (≥ 60 vs. < 60 years) | 4.621 (1.379, 15.488) | 0.013 |
| Sex (male vs. female) | 0.552 (0.244, 1.249) | 0.154 |
| Smoking (yes vs. no) | 2.598 (1.182, 5.707) | 0.017 |
| NSCLC types (CT: ac-NSCLC) | 2.153 (1.361, 3.405) | 0.001 |
| TNM stage (III vs. IV) | 0.693 (0.273, 1.760) | 0.441 |
| Bone metastasis (yes vs. no) | 0.683 (0.272, 1.712) | 0.416 |
| Pulmonary metastasis (yes vs. no) | 0.594 (0.236, 1.494) | 0.268 |
| Brain metastases (yes vs. no) | 1.023 (0.383, 2.729) | 0.964 |
| Pleura metastases (yes vs. no) | 0.274 (0.082, 0.920) | 0.036 |
| Adrenal gland metastases (yes vs. no) | 1.921 (0.451, 8.185) | 0.377 |
| Liver metastases (yes vs. no) | 0.651 (0.088, 4.824) | 0.674 |
| LN metastases (yes vs. no) | 1.519 (0.348, 6.630) | 0.578 |
| EGFR mutation (uncommon vs. common) | 1.390 (0.439, 4.402) | 0.575 |
| TKI treatment (yes vs. no) | 0.640 (0.231, 1.776) | 0.392 |
| Tissue dPCR (positive vs. negative) | 1.266 (0.568, 2.824) | 0.564 |
| Tissue NGS (positive vs. negative) | 2.614 (1.010, 6.765) | 0.048 |
| Blood dPCR (positive vs. negative) | 3.168 (1.150, 8.725) | 0.026 |
| Blood NGS (positive vs. negative) | 4.481 (0.627, 32.023) | 0.135 |

$P < 0.05$ was considered as significant different. HR, hazard ratio; CI, confidence interval; NSCLC, non-small cell lung cancer; CT, control group; ac-NSCLC, lung adenocarcinoma; TNM, the tumor, node, metastases; LN, Lymph node; EGFR, epidermal growth factor receptor; TKI, Tyrosine kinase inhibitors; dPCR, digital polymerase chain reaction; NGS, next generation sequence.

Table S3 The result of multivariate regression analysis for blood samples

| Factors | HR (95% CI) | P value |
|------------------------------------|-----------------------|---------|
| Age (≥ 60 vs. < 60 years) | 3.749 (1.011, 13.898) | 0.048 |
| Smoking (yes vs. no) | 1.274 (0.464, 3.497) | 0.639 |
| NSCLC types (CT: ac-NSCLC) | 1.480 (0.853, 2.567) | 0.164 |
| Pleura metastases (yes vs. no) | 0.229 (0.052, 1.005) | 0.051 |
| Blood dPCR (positive vs. negative) | 3.874 (1.356, 11.069) | 0.011 |

P<0.05 was considered as significant different. HR, hazard ratio; CI, confidence interval; NSCLC, non-small cell lung cancer; CT, control group; ac-NSCLC, lung adenocarcinoma; dPCR, digital polymerase chain reaction.

Table S4 The result of multivariate regression analysis for tissue samples

| Factors | HR (95% CI) | P value |
|------------------------------------|-----------------------|---------|
| Age (≥ 60 vs. < 60 years) | 4.741 (1.058, 21.250) | 0.042 |
| Smoking (yes vs. no) | 1.446 (0.555, 3.764) | 0.450 |
| NSCLC types (CT: ac-NSCLC) | 1.674 (0.953, 2.940) | 0.073 |
| Pleura metastases (yes vs. no) | 0.369 (0.100, 1.355) | 0.133 |
| Tissue NGS (positive vs. negative) | 1.512 (0.553, 4.136) | 0.421 |

P<0.05 was considered as significant different. HR, hazard ratio; CI, confidence interval; NSCLC, non-small cell lung cancer; CT, control group; ac-NSCLC, lung adenocarcinoma; NGS, next generation sequence.