

Supplementary materials

Real-world treatment patterns and clinical outcomes in *EGFR*-mutant locally advanced lung adenocarcinoma: a multi-center cohort study

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Supplementary Table 1

The distribution of patients in the hospitals participating in this study.

| Hospital | N | CRT | TKI+RT | TKI |
|----------|-----|-----|--------|-----|
| 1 | 129 | 46 | 35 | 48 |
| 2 | 89 | 14 | 7 | 68 |
| 3 | 49 | 26 | 12 | 11 |
| 4 | 34 | 2 | 9 | 23 |
| 5 | 32 | 3 | 29 | 0 |
| 6 | 31 | 8 | 1 | 22 |
| 7 | 26 | 0 | 0 | 26 |
| 8 | 22 | 0 | 2 | 20 |
| 9 | 14 | 1 | 5 | 8 |
| 10 | 9 | 3 | 5 | 1 |
| 11 | 4 | 0 | 0 | 4 |
| 12 | 1 | 1 | 0 | 0 |
| Overall | 440 | 104 | 105 | 231 |

Abbreviations: CRT, chemoradiation therapy; RT, radiation therapy; TKI, tyrosine kinase inhibitor.

Supplementary Table 2

Baseline variables for different groups with standardized differences before inverse-probability of treatment weighting analysis.

| | Unweighted | | | | | |
|----------------------|---------------------|----------|------------------|----------|---------------------|----------|
| | EGFR-TKI+RT vs. CRT | | EGFR-TKI vs. CRT | | EGFR-TKI+RT vs. TKI | |
| | SMD | <i>P</i> | SMD | <i>P</i> | SMD | <i>P</i> |
| Age | | | | | | |
| ≥ 60 | 0.387 | 0.0011 | 0.302 | 0.011 | 0.085 | 0.537 |
| < 60 | 0.387 | 0.0011 | 0.302 | 0.011 | 0.085 | 0.537 |
| Sex | | | | | | |
| Female | 0.113 | 0.339 | 0.260 | 0.030 | 0.147 | 0.302 |
| Male | 0.113 | 0.339 | 0.260 | 0.030 | 0.147 | 0.302 |
| Smoking | | | | | | |
| Yes | 0.126 | 0.287 | 0.137 | 0.264 | 0.263 | 0.065 |
| No | 0.126 | 0.287 | 0.137 | 0.264 | 0.263 | 0.065 |
| ECOG PS | | | | | | |
| < 2 | 0.223 | 0.059 | 0.094 | 0.460 | 0.129 | 0.246 |
| ≥ 2 | 0.223 | 0.059 | 0.094 | 0.460 | 0.129 | 0.246 |
| Stage | | | | | | |
| III A | 0.142 | 0.231 | 0.129 | 0.265 | 0.270 | 0.050 |
| III B | 0.142 | 0.231 | 0.129 | 0.265 | 0.270 | 0.050 |
| PET-CT | | | | | | |
| Yes | 0.331 | 0.005 | 0.339 | 0.005 | 0.008 | 0.958 |
| No | 0.331 | 0.005 | 0.339 | 0.005 | 0.008 | 0.958 |
| EGFR mutation | | | | | | |
| 19DEL | 0.049 | 0.733 | 0.058 | 0.236 | 0.010 | 0.735 |
| L858R | 0.082 | 0.733 | 0.152 | 0.236 | 0.070 | 0.735 |
| Uncommon | 0.063 | 0.733 | 0.176 | 0.236 | 0.113 | 0.735 |

Abbreviations: 19DEL, exon 19 deletion; CRT, chemoradiation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; PET-CT, positron emission tomography-computed tomography; RT, radiation therapy; SMD, standardized mean difference; TKI, tyrosine kinase inhibitor.

Supplementary Table 3

Baseline variables for different groups with standardized difference after inverse-probability of treatment weighting analysis.

| | Unweighted | | | | | |
|----------------------|----------------------------|----------|--------------------|----------|----------------------------|----------|
| | EGFR-TKI+RT vs. CRT | | TKI vs. CRT | | EGFR-TKI+RT vs. TKI | |
| | SMD | P | SMD | P | SMD | P |
| Age | | | | | | |
| ≥ 60 | 0.017 | 0.914 | 0.618 | 0.618 | 0.048 | 0.711 |
| < 60 | 0.017 | 0.914 | 0.618 | 0.618 | 0.048 | 0.711 |
| Sex | | | | | | |
| Female | 0.008 | 0.960 | 0.999 | 0.999 | 0.007 | 0.955 |
| Male | 0.008 | 0.960 | 0.999 | 0.999 | 0.007 | 0.955 |
| Smoking | | | | | | |
| Yes | 0.063 | 0.682 | 0.959 | 0.959 | 0.069 | 0.611 |
| No | 0.063 | 0.682 | 0.959 | 0.959 | 0.069 | 0.611 |
| ECOG PS | | | | | | |
| < 2 | 0.078 | 0.600 | 0.953 | 0.953 | 0.085 | 0.533 |
| ≥ 2 | 0.078 | 0.600 | 0.953 | 0.953 | 0.085 | 0.533 |
| Stage | | | | | | |
| III A | 0.026 | 0.866 | 0.754 | 0.754 | 0.016 | 0.896 |
| III B | 0.026 | 0.866 | 0.754 | 0.754 | 0.016 | 0.896 |
| PET-CT | | | | | | |
| Yes | 0.015 | 0.922 | 0.818 | 0.818 | 0.016 | 0.902 |
| No | 0.015 | 0.922 | 0.818 | 0.818 | 0.016 | 0.902 |
| EGFR mutation | | | | | | |
| 19DEL | 0.001 | 0.861 | 0.829 | 0.829 | 0.013 | 0.994 |
| L858R | 0.042 | 0.861 | 0.829 | 0.829 | 0.013 | 0.994 |
| Uncommon | 0.081 | 0.861 | 0.829 | 0.829 | 0.000* | 0.994 |

Abbreviations: 19DEL, exon 19 deletion; CRT, chemoradiation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; PET-CT, positron emission tomography-computed tomography; RT, radiation therapy; SMD, standardized mean difference; TKI, tyrosine kinase inhibitor.

Supplementary Table 4

The univariate and multivariable analysis of PFS.

| | Univariate analysis | | | Multivariable analysis | | |
|----------------------|---------------------|-----------|---------|------------------------|-----------|----------|
| | HR | 95% CI | P | HR | 95% CI | P |
| Age | | | 0.253 | | | |
| ≥ 60 vs. < 60 | 1.13 | 0.92-1.40 | | | | |
| Sex | | | 0.873 | | | |
| Female vs. male | 1.02 | 0.82-1.26 | | | | |
| Smoking | | | 0.062 | | | 0.384 |
| Yes vs. No | 1.24 | 0.99-1.56 | | 1.11 | 0.88-1.40 | |
| ECOG PS | | | 0.282 | | | |
| ≥ 2 vs. < 2 | 0.78 | 0.49-1.23 | | | | |
| Stage | | | < 0.001 | | | < 0.0001 |
| IIIA vs. IIIB | 0.60 | 0.47-0.76 | | 0.59 | 0.47-0.75 | |
| PET-CT | | | 0.131 | | | |
| Yes vs. No | 1.17 | 0.93-1.46 | | | | |
| EGFR mutation | | | 0.018 | | | 0.022 |
| L858R vs. 19DEL | 0.99 | 0.79-1.23 | 0.882 | 0.96 | 0.77-1.20 | 0.729 |
| Treatment | | | < 0.001 | | | < 0.001 |
| EGFR-TKI vs. CRT | 0.69 | 0.54-0.89 | 0.005 | 0.75 | 0.58-0.97 | 0.030 |
| EGFR-TKI+RT vs. CRT | 0.43 | 0.32-0.59 | < 0.001 | 0.46 | 0.34-0.63 | < 0.001 |

Abbreviations: 19DEL, exon 19 deletion; CI, confidence interval; CRT, chemoradiation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HR, hazard ratio; PET-CT, positron emission tomography-computed tomography; PFS, progression-free survival; RT, radiation therapy; TKI, tyrosine kinase inhibitor.

Supplementary Table 5

The univariate and multivariable analysis of OS.

| | Univariate analysis | | | Multivariable analysis | | |
|----------------------|---------------------|-----------|-------|------------------------|-------------|-------|
| | HR | 95% CI | P | HR | 95% CI | P |
| Age | | | 0.071 | | | 0.108 |
| ≥ 60 vs. < 60 | 1.33 | 0.98-1.81 | | 1.30 | 0.944-1.784 | |
| Sex | | | 0.123 | | | |
| Female vs. male | 1.29 | 0.93-1.77 | | | | |
| Smoking | | | 0.431 | | | |
| Yes vs. No | 1.15 | 0.82-1.60 | | | | |
| ECOG PS | | | 0.405 | | | |
| ≥ 2 vs. < 2 | 0.76 | 0.40-1.45 | | | | |
| Stage | | | 0.033 | | | 0.024 |
| IIIA vs. IIIB | 0.69 | 0.49-0.97 | | 0.67 | 0.48-0.95 | |
| PET-CT | | | 0.018 | | | 0.014 |
| Yes vs. No | 0.63 | 0.44-0.89 | | 0.64 | 0.44-0.91 | |
| EGFR mutation | | | 0.046 | | | 0.050 |
| L858R vs. 19DEL | 1.40 | 1.01-1.94 | 0.042 | 1.29 | 0.93-1.80 | 0.176 |
| Treatment | | | 0.037 | | | 0.075 |
| EGFR-TKI vs. CRT | 1.04 | 0.73-1.48 | 0.875 | 1.04 | 0.73-1.48 | 0.828 |
| EGFR-TKI+RT vs. CRT | 0.62 | 0.40-0.96 | 0.035 | 0.65 | 0.41-1.02 | 0.059 |

Abbreviations: 19DEL, exon 19 deletion; CI, confidence interval; CRT, chemoradiation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HR, hazard ratio; OS, overall survival; PET-CT, positron emission tomography-computed tomography; RT, radiation therapy; TKI, tyrosine kinase inhibitor.

Supplementary Table 6

The univariate and multivariate analysis of competing risk factors of locoregional recurrence.

| | Univariate analysis | | | Multivariable analysis | | |
|----------------------|---------------------|-------------|----------|------------------------|-------------|----------|
| | SHR | 95% CI | <i>P</i> | SHR | 95% CI | <i>P</i> |
| Age | | | 0.364 | | | |
| ≥ 60 vs. < 60 | 0.88 | 0.676-1.155 | | | | |
| Sex | | | 0.727 | | | |
| Female vs. male | 0.95 | 0.727-1.249 | | | | |
| Smoking | | | 0.220 | | | |
| Yes vs. No | 1.20 | 0.897-1.564 | | | | |
| ECOG PS | | | 0.664 | | | |
| ≥ 2 vs. < 2 | 1.14 | 0.622-2.108 | | | | |
| Stage | | | 0.001 | | | 0.001 |
| IIIA vs. IIIB | 1.68 | 1.243-2.264 | | 1.69 | 1.245-2.288 | |
| PET-CT | | | 0.293 | | | |
| Yes vs. No | 1.05 | 0.876-1.553 | | | | |
| EGFR mutation | | | | | | |
| L858R vs. 19DEL | 0.84 | 0.631-1.117 | 0.231 | 0.80 | 0.596-1.065 | 0.124 |
| Treatment | | | | | | |
| EGFR-TKI vs. CRT | 0.46 | 0.299-0.703 | <0.001 | 0.50 | 0.326-0.775 | 0.002 |
| EGFR-TKI+RT vs. CRT | 1.26 | 0.917-1.730 | 0.155 | 1.45 | 1.034-2.034 | 0.031 |

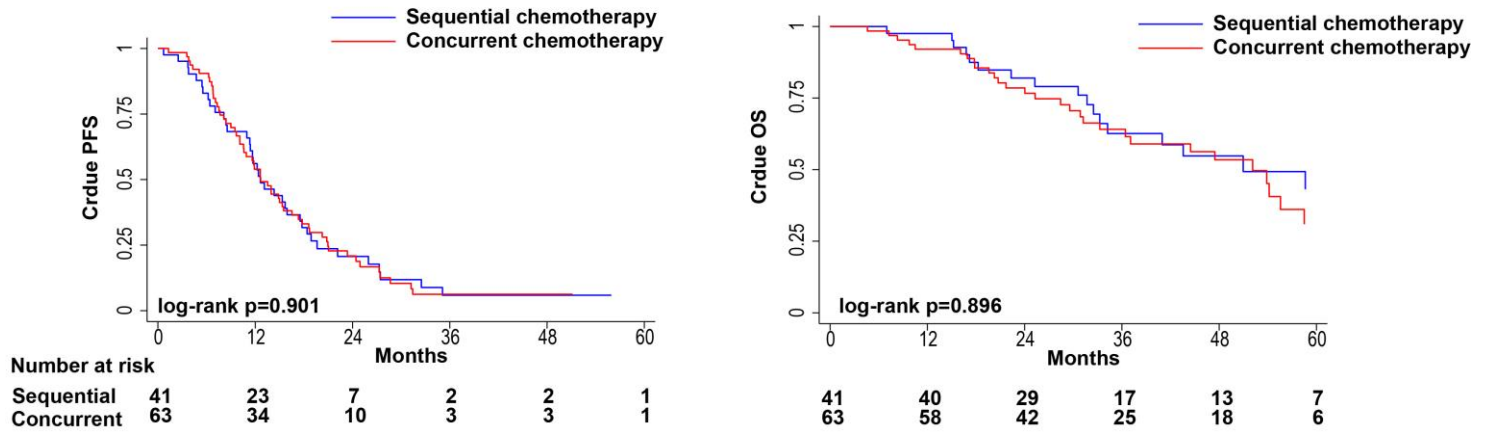
Abbreviations: 19DEL, exon 19 deletion; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; PET-CT, positron emission tomography-computed tomography; SHR, sub-distribution hazard regression.

Supplementary Table 7

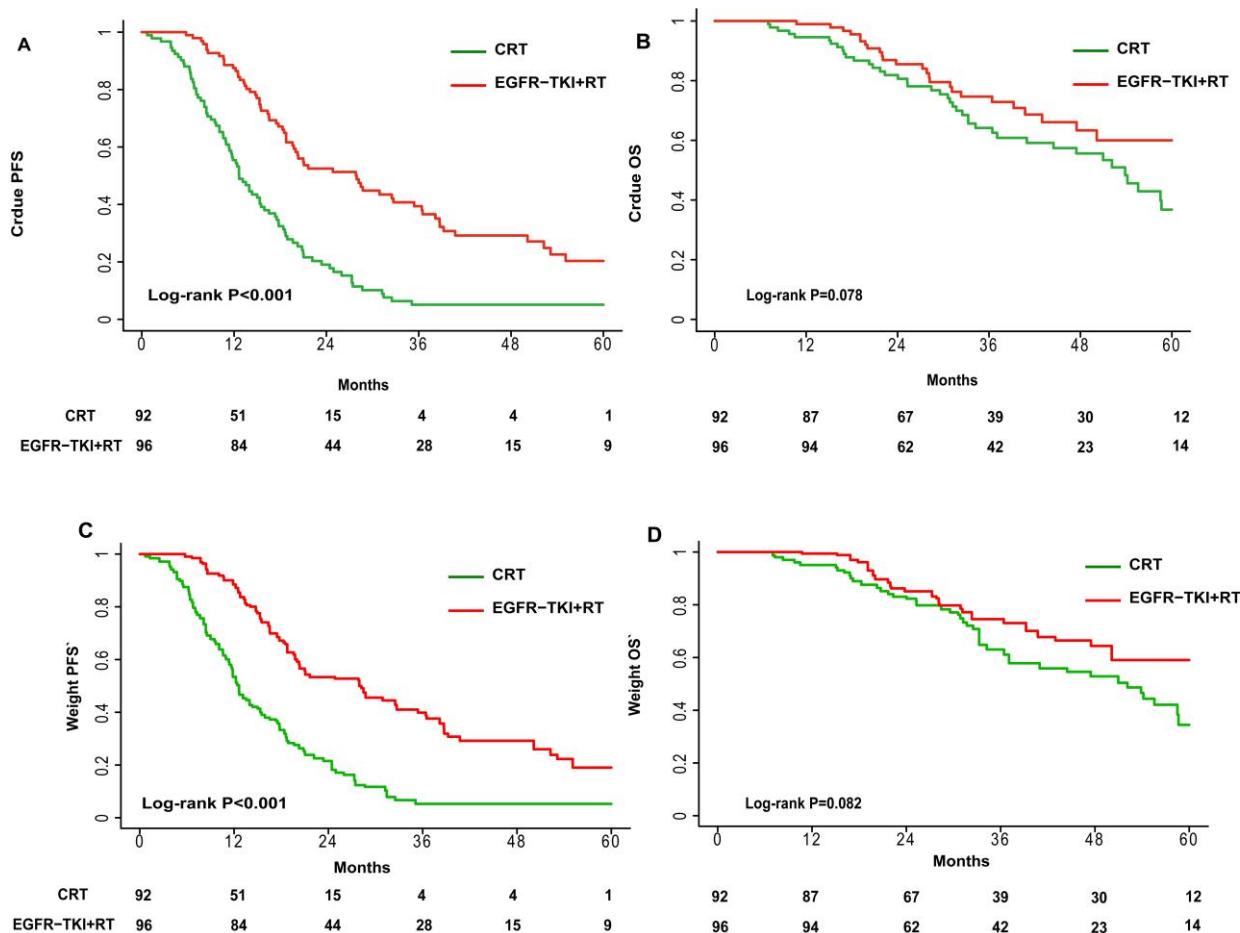
The univariate and multivariable competing risks analysis of distant metastases.

| | Univariate analysis | | | Multivariable analysis | | |
|----------------------|---------------------|-------------|----------|------------------------|-------------|----------|
| | SHR | 95% CI | <i>P</i> | SHR | 95% CI | <i>P</i> |
| Age | | | 0.009 | | | 0.032 |
| ≥ 60 vs. < 60 | 0.71 | 0.550-0.919 | | 0.75 | 0.574-0.975 | |
| Sex | | | 0.684 | | | |
| Female vs. male | 0.95 | 0.734-1.225 | | | | |
| Smoking | | | 0.668 | | | |
| Yes vs. No | 1.06 | 0.805-1.403 | | | | |
| ECOG PS | | | 0.269 | | | |
| ≥ 2 vs. < 2 | 0.69 | 0.363-1.326 | | | | |
| Stage | | | 0.083 | | | 0.199 |
| IIIA vs. IIIB | 1.27 | 0.969-1.675 | | 1.20 | 0.908-1.589 | |
| PET-CT | | | 0.516 | | | |
| Yes vs. No | 1.09 | 0.833-1.438 | | | | |
| EGFR mutation | | | | | | |
| L858R vs. 19DEL | 1.05 | 0.804-1.368 | 0.726 | 1.09 | 0.839-1.435 | 0.615 |
| Treatment | | | | | | |
| EGFR-TKI vs. CRT | 0.62 | 0.438-0.877 | 0.007 | 0.63 | 0.444-0.894 | 0.010 |
| EGFR-TKI+RT vs. CRT | 0.54 | 0.389-0.739 | < 0.0001 | 0.57 | 0.41-0.790 | 0.001 |

Abbreviations: 19DEL, exon 19 deletion; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; PET-CT, positron emission tomography-computed tomography; SHR, sub-distribution hazard regression.



Supplementary Fig. 1. Progression-free survival (PFS) and overall survival (OS) evaluated using the Kaplan–Meier method in epidermal growth factor receptor mutant patients received chemoradiation therapy.



Supplementary Fig. 2. Progression-free survival (PFS) and overall survival (OS) evaluated using the Kaplan–Meier method before (A, B) and after (C, D) inverse-probability of treatment weighting analysis in patients with EGFR common mutation. CRT, chemoradiation therapy; EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor; RT, radiation therapy.