Supplementary Table 1. Demographic data and patient characteristics (TCVGH cohort)

|  |  |
| --- | --- |
| Patient characteristics | N = 466 |
| Age (yr), median (range) | 64 (31-94) |
| Gender, n (%) Male Female | 182 (39.1)284 (60.9) |
| Smoking status, n (%) Non-smokers Current/former smokers | 351 (75.3)115 (24.7) |
| Stage, n (%) Unresectable stage III Stage IV | 24 (5.2)442 (94.8) |
| ECOG PS, n (%) 0-1 2 or more | 378 (81.1)88 (18.9) |
| *EGFR* mutation type, n (%) Exon 19 deletion Exon 21 L858R Othersa | 215 (46.1)218 (46.8)33 (7.1) |
| First-line EGFR-TKI regimen, n (%) Gefitinib Erlotinib Afatinib | 284 (60.9)163 (35.0)19 (4.1) |
| Post-primary tumor resection, n (%) Yes* Post-operative recurrent disease
* Diagnostic purposeb

 No | 76 (16.3)* 59
* 17

390 (83.7) |

ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor.

aInclude complex mutations involving 19Del or L858R; among them, 6 with 19Del+L858R complex mutation.

bIn addition to primary tumor resection, 11 with pleura, 1 with pericardium, 2 with another lung nodule(s), 2 with bone, and 1 with mediastinal lymph node resection/biopsy.

Supplementary Table 2. Association of survival time with performance status, metastatic burden, and M stage

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Comparison | PFS | Pa  | OS | Pa  |
| ECOG PS | 0-1 (378) | 11.6 (10.0-13.3) | 0.002 | 37.1 (33.2-41.0) | <0.001 |
|  | 2 or more (88) | 8.6(7.6-9.5) |  | 21.5 (17.8-25.1) |  |
| Metastatic burden | Oligo-M (105) | 15.1 (10.9-19.3) | <0.001 | 46.1 (38.4-53.9) | <0.001 |
|  | Non-Oligo-M (361) | 10.5 (9.3-11.6) |  | 30.9 (26.8-34.9) |  |
| M stage | Non-M1c (211) | 14.3 (12.1-16.6) | <0.001 | 46.4 (40.3-52.5) | <0.001 |
|  | M1c (255) | 8.9 (8.1-9.6) |  | 25.6 (21.8-29.4) |  |

PFS, progression-free survival; OS, overall survival; ECOG PS, Eastern Cooperative Oncology Group performance status; Oligo-M, oligometastasis (defined as extra-nodal metastatic sites ≤ 5).

aBy log-rank test.

Supplementary Table 3. Comparison of the survival time between patients with resection of primary tumor and subgroup patients within non-resection group

|  |  |  |
| --- | --- | --- |
|  | Progression-free survival (95% CI) | Overall survival (95% CI) |
| Post-resection of primary tumor (n = 76) | 25.1 (16.6-33.7) | 56.8 (36.3-77.2) |
| Non-resection (ECOG PS 0-1) (n = 305) | 10.0 (8.9-11.1) | 33.1 (29.2-37.0) |
| Non-resection (oligometastasis) (n = 72) | 10.9 (9.2-12.7) | 42.7 (34.3-51.1) |
| Non-resection (non-M1c) (n = 155) | 11.8 (10.0-13.7) | 38.2 (31.5-45.0) |

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status.

Supplmentary Table 4. Characteristics and outcome of patients receiving concurrent radiotherapy during EGFR-TKI treatment

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No. | Pt.a | Smokingb | PSc | TNM staged | Metastasis site | *EGFR*-m | EGFR-TKI | RT, cGy (site)e | Time to RTf | PFS | OS |
| 1 | 67/F | N | 0 | T2aN2M1b | Pleura, brain x1 | 19Del | Afatinib | 6000 (L/M) | 8.2m | 26.4m | 35.2m\* |
| 2 | 43/F | N | 0 | T4N0M1b | Lung(s), brain x1 | 19Del | Gefitinib | 6000 (L) | 18.2m | 28.9m | 86.3m\* |
| 3 | 60/M | Y | 1 | T2aN3M1c | Brain(s), bone(s) | L858R | Gefitinib | 3800 (L) | 30.7m | 38.6m\* | 38.6m\* |
| 4 | 74/F | N | 1 | T4N2M0 | N/A | L858R+S768I | Erlotinib | 6000 (L) | 9.3m | 51.9m\* | 51.9m\* |
| 5 | 41/F | N | 1 | T3N3M0 | N/A | L858R | Gefitinib | 7000 (L/M) | 6.2m | 13.4m | 23.1m |
| 6 | 85/M | Y | 1 | T1bN0M1b | Neck LN x1 | G719A | Afatinib | 4400 (L) | 11.8m | 39.7m\* | 39.7m\* |
| 7 | 66/F | N | 1 | T1aN3M1b | Neck LN x1 | 19Del | Gefitinib | 6000 (L) | 2.8m | 86.1m\* | 86.1m\* |
| 8 | 63/F | N | 1 | T2bN0M1b | Neck LN x1 | L858R | Gefitinib | 5000 (L/M) | 5.3m | 10.6m | 34.2m\* |
| 9 | 53/F | N | 1 | T4N2M1a | Lung(s) | L858R | Erlotinib | 6000 (L/M) | 10.6m | 23.1m | 36.0m\* |
| 10 | 78/M | Y | 1 | T1aN1M1c | Bone(s) | 19Del | Erlotinib | 5600 (L) | 6.1m | 34.0m\* | 34.0m\* |
| 11 | 72/M | Y | 1 | T2aN0M1a | Pleura | 19Del | Erlotinib | 5000 (L) | 24.2m | 31.5m | 39.2m\* |

aPatients’ age (year)/gender (F: female; M: male).

bSmoking status (N: non-smokers; Y: smokers)

cPS, performance status by Eastern Cooperative Oncology Group classification.

dTNM staging, AJCC TNM staging 8th edition.

eRT, radiotherapy (denote the dose to primary lung tumor); site (L: primary lung tumor; M: mediastinal lymph node).

fDenote the time between start of EGFR-TKI and start of radiotherapy.

\*Denote not yet progression for progression-free survival (PFS) and still alive for overall survival (OS).