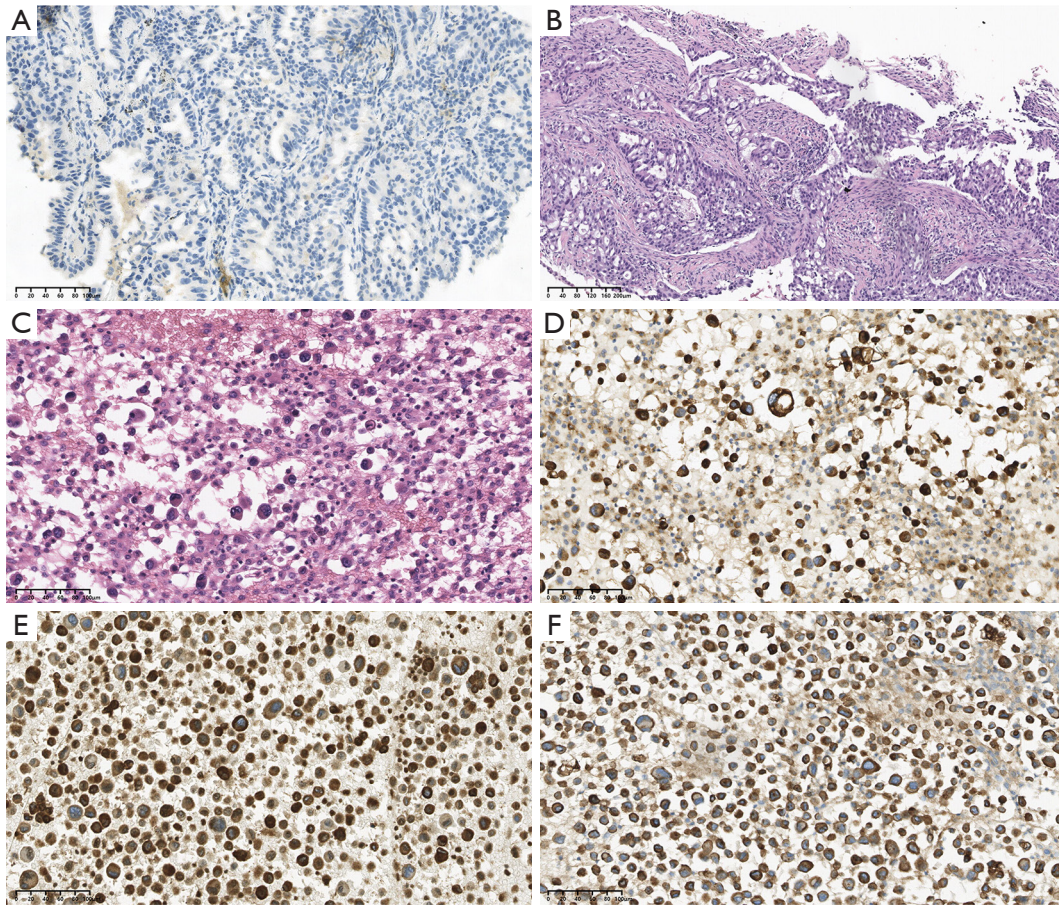


**Figure S1** Flow diagram of the study design. NSCLC, non-small cell lung cancer; EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor.

**Table S1** Baseline characteristics of 105 NSCLC patients harboring mutations in *EGFR* exon 18

| Characteristics                    | Overall (N=105)      | G719X or E709X mutations (N=88) | Very rare mutations (N=17) | P value |
|------------------------------------|----------------------|---------------------------------|----------------------------|---------|
| Presence of common mutation, n (%) |                      |                                 |                            | >0.99   |
| Yes                                | 15 (14.3)            | 13 (14.8)                       | 2 (11.8)                   |         |
| No                                 | 90 (85.7)            | 75 (85.2)                       | 15 (88.2)                  |         |
| L858R or 19del, n (%)              |                      |                                 |                            |         |
| L858R                              | 13 (12.4)            | 12 (13.6)                       | 1 (5.9)                    | 0.688   |
| 19del                              | 2 (1.9)              | 1 (1.1)                         | 1 (5.9)                    | 0.299   |
| Age (years), median (range)        | 60.00 (53.00, 68.00) | 60.00 (53.00, 70.50)            | 56.00 (51.00, 65.00)       | 0.377   |
| Age (years), n (%)                 |                      |                                 |                            | 0.510   |
| <60                                | 51 (48.6)            | 41 (46.6)                       | 10 (58.8)                  |         |
| ≥60                                | 54 (51.4)            | 47 (53.4)                       | 7 (41.2)                   |         |
| Gender, n (%)                      |                      |                                 |                            | 0.830   |
| Female                             | 55 (52.4)            | 47 (53.4)                       | 8 (47.1)                   |         |
| Male                               | 50 (47.6)            | 41 (46.6)                       | 9 (52.9)                   |         |
| Smoking, n (%)                     |                      |                                 |                            | 0.854   |
| Current/former smoking             | 20 (19.0)            | 16 (18.2)                       | 4 (23.5)                   |         |
| Never smoking                      | 77 (73.3)            | 65 (73.9)                       | 12 (70.6)                  |         |
| Unknow                             | 8 (7.6)              | 7 (8.0)                         | 1 (5.9)                    |         |
| Smoking index, n (%)               |                      |                                 |                            | 0.708   |
| ≤200                               | 80 (76.2)            | 67 (76.1)                       | 13 (76.5)                  |         |
| >200                               | 14 (13.3)            | 11 (12.5)                       | 3 (17.6)                   |         |
| Unknown                            | 11 (10.5)            | 10 (11.4)                       | 1 (5.9)                    |         |
| ECOG PS, n (%)                     |                      |                                 |                            | 0.998   |
| ≥2                                 | 6 (5.7)              | 5 (5.7)                         | 1 (5.9)                    |         |
| 0–1                                | 80 (76.2)            | 67 (76.1)                       | 13 (76.5)                  |         |
| Unknown                            | 19 (18.1)            | 16 (18.2)                       | 3 (17.6)                   |         |
| Pathology, n (%)                   |                      |                                 |                            | >0.99   |
| Adenocarcinoma                     | 102 (97.1)           | 85 (96.6)                       | 17 (100.0)                 |         |
| Squamous cell carcinoma            | 3 (2.9)              | 3 (3.4)                         | 0 (0.0)                    |         |
| Stage, n (%)                       |                      |                                 |                            | 0.518   |
| I–II                               | 43 (41.0)            | 35 (39.8)                       | 8 (47.1)                   |         |
| III                                | 11 (10.5)            | 9 (10.2)                        | 2 (11.8)                   |         |
| IVA                                | 26 (24.8)            | 21 (23.9)                       | 5 (29.4)                   |         |
| IVB                                | 22 (21.0)            | 21 (23.9)                       | 1 (5.9)                    |         |
| Unknown                            | 3 (2.9)              | 2 (2.3)                         | 1 (5.9)                    |         |
| Metastases, n (%)                  |                      |                                 |                            | 0.356   |
| Multiple organ metastasis          | 20 (19.0)            | 19 (21.6)                       | 1 (5.9)                    |         |
| No organ metastasis                | 57 (54.3)            | 45 (51.1)                       | 12 (70.6)                  |         |
| Single organ metastasis            | 26 (24.8)            | 22 (25.0)                       | 4 (23.5)                   |         |
| Unknown                            | 2 (1.9)              | 2 (2.3)                         | 0 (0.0)                    |         |

EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; ECOG, Eastern Cooperative Oncology Group; PS, performance status; common mutation, *EGFR* 19del and L858R.



**Figure S2** Pathological images of NSCLC patients with very rare mutations. (A-C) Hematoxylin and eosin section of patient 44 (HE staining,  $\times 200$ ), patient 40 (HE staining,  $\times 100$ ), and patient 43 (HE staining,  $\times 200$ ), respectively. And their pathologic types were all adenocarcinoma. (D-F) Immunohistochemistry examinations on NapsinA, CEA, E-C for patient 43, respectively. NapsinA, CEA and E-C were positive for patient 43. NSCLC, non-small cell lung cancer; HE, hematoxylin and eosin.