**Supplementary Table 1. TRAEs occurring in ≥10% of patients.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Afatinib 40 mg (n = 64)** | | | |
| **n (%)** | **All grades** | **Grade 3** | **Grade 4** | **Grade 5** |
| Total with TRAE | 64 (100) | 19 (29.7) | 2 (3.1) | 1 (1.6) |
| Diarrhea | 63 (98.4) | 9 (14.1) | 0 | 0 |
| Rash/acnea | 52 (81.3) | 5 (7.8) | 0 | 0 |
| Stomatitisa | 46 (71.9) | 1 (1.6) | 0 | 0 |
| Paronychiaa | 32 (50.0) | 4 (6.3) | 0 | 0 |
| Alanine aminotransferase increased | 19 (29.7) | 0 | 0 | 0 |
| Nasal dryness | 15 (23.4) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | 12 (18.8) | 0 | 0 | 0 |
| Dry skin | 12 (18.8) | 0 | 0 | 0 |
| Hypocalcemia | 11 (17.2) | 0 | 0 | 0 |
| Hypokalemia | 9 (14.1) | 2 (3.1) | 1 (1.6) | 0 |
| Leukopenia | 9 (14.1) | 0 | 0 | 0 |
| Decreased appetite | 8 (12.5) | 0 | 0 | 1 (1.6) |
| Oropharyngeal pain | 8 (12.5) | 0 | 0 | 0 |
| Blood creatinine phosphokinase increased | 7 (10.9) | 0 | 0 | 0 |
| Weight increased | 7 (10.9) | 0 | 0 | 0 |
| White blood cell count decreased | 7 (10.9) | 0 | 0 | 0 |
| aGrouped term.  TRAEs: Treatment-related adverse events. | | | | |

**Supplementary Table 2. Subgroup analysis of TTSP and PFS in biomarker group.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Biomarker analysis group (n = 64)** | | **Overall population (n = 541)** | | **HR (95% CI), p*-*value** |
| **Subgroup at baseline** | **n in subgroup** | **Median TTSP, months (95% CI)** | **n in subgroup** | **Median TTSP, months (95% CI)** |  |
| All | 64 | 13.53 (10.90–18.00) | 541 | 13.99 (12.91–15.93) | 1.09 (0.81–1.45), 0.5832 |
| Age |  |  |  |  |  |
| – <65 years | 50 | 12.51 (10.11–16.55) | 394 | 13.63 (12.22–15.27) | 1.18 (0.86–1.64), 0.3097 |
| – ≥65 years | 14 | 21.87 (10.90–NE) | 147 | 17.01 (13.69–21.71) | 0.76 (0.38–1.51), 0.4280 |
| ECOG PS |  |  |  |  |  |
| – 0 | 48 | 16.19 (10.87–19.21) | 99 | 16.42 (13.04–21.87) | 1.25 (0.83–1.86), 0.2859 |
| – 1 | 14 | 10.95 (6.54–18.16) | 431 | 13.76 (12.22–15.63) | 1.38 (0.78–2.47), 0.2695 |
| – 2 | 2 | 26.88 (25.71–28.05) | 11 | 15.44 (7.29–25.71) | 0.42 (0.09–2.04), 0.2830 |
| *EGFR* mutation type |  |  |  |  |  |
| – Common | 58 | 14.32 (10.94–18.16) | 477 | 14.42 (13.40–16.39) | 1.09 (0.80–1.49), 0.5657 |
| – Uncommon | 6 | 5.50 (3.38–37.83) | 64 | 9.23 (6.01–20.66) | 1.13 (0.43–2.95), 0.8075 |
| **Subgroup at baseline** | **n in subgroup** | **Median PFS, months (95% CI)** | **n in subgroup** | **Median PFS, months (95% CI)** |  |
| All | 64 | 11.03 (10.11–16.55) | 541 | 12.05 (11.03–13.60) | 0.95 (0.71–1.27), 0.7351 |
| Age |  |  |  |  |  |
| – <65 years | 50 | 10.94 (8.14–16.52) | 394 | 11.53 (10.87–13.56) | 1.07 (0.77–1.47), 0.6927 |
| – ≥65 years | 14 | 21.90 (10.77–NE) | 147 | 13.56 (11.07–15.67) | 0.60 (0.29–1.23), 0.1600 |
| ECOG PS |  |  |  |  |  |
| – 0 | 48 | 14.48 (9.23–19.21) | 99 | 14.84 (12.25–19.31) | 1.18 (0.79–1.76), 0.4258 |
| – 1 | 14 | 10.77 (5.55–18.19) | 431 | 11.33 (10.87–13.04) | 1.22 (0.69–2.18), 0.4931 |
| – 2 | 2 | NE (2.69–NE) | 11 | 10.57 (5.68–19.84) | 0.58 (0.07–4.73), 0.6144 |
| *EGFR* mutation type |  |  |  |  |  |
| – Common | 58 | 12.48 (10.77–18.19) | 477 | 12.68 (11.10–13.83) | 0.95 (0.70–1.30), 0.7661 |
| – Uncommon | 6 | 5.47 (3.81–37.83) | 64 | 9.06 (5.58–12.94) | 0.99 (0.39–2.56), 0.9916 |
| CI: Confidence interval; ECOG PS: Eastern Cooperative Oncology Group performance status; *EGFR*: Epidermal growth factor receptor; HR: Hazard ratio; NE: Not estimable; PFS: Progression-free survival; TTSP: Time to symptomatic progression. | | | | | |