**Supplementary Table S1**

**Summary of prognostic values from 8 studies**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Observation indexes | Follow-up (years) | HR estimation method | HR of OS |  | P | HR of PFS† | P | ORR to TKIs  (TP53 mutation) | ORR to TKIs  (wild type) |
| Aisner 2018 [[18](#_ENREF_18)] | OS | 3 | extrapolated | 1.84 (0.71 - 4.75) |  | 0.06 |  |  |  |  |
| Bria 2015 [[23](#_ENREF_23)] | OS, PFS, ORR | 2 | reported in text | 2.25 (0.43 - 5.16) |  | 0.34 | 4.66 (1.12 - 19.37) | 0.03 | 50% (3/6) | 73% (8/11) |
| CLCGP 2013 [[25](#_ENREF_25)] | OS, PFS | 5 | calculated from raw data | 2.67 (1.30 - 5.50) |  | 0.01 | 2.36 (0.98 - 5.69) | 0.06 |  |  |
| Labbe 2017 [[21](#_ENREF_21)] | OS, PFS, ORR | over 12 | reported in text | 1.20 (0.69 - 2.08) |  | 0.52 | 1.74 (0.98–3.10)§ | 0.06 | 54% (13/24) | 66% (24/36) |
| Li 2016 [[33](#_ENREF_33)] | OS | 1 | calculated from raw data | 2.03 (0.65 - 6.40) |  | 0.23 |  |  |  |  |
| Molina-Vila 2014 [[24](#_ENREF_24)] | OS, ORR | over 5 | reported in text | 1.79 (1.02 - 3.13)‡ |  | 0.04 |  |  | 50% (25/50) | 52% (75/143) |
| Shepherd 2017 [[20](#_ENREF_20)] | OS | 8 | extrapolated | 1.06 (0.08 - 14.0) |  | 0.83 |  |  |  |  |
| VanderLaan 2017 [[19](#_ENREF_19)] | OS, PFS, ORR | 2 | calculated from raw data | 2.03 (0.39 - 10.69) |  | 0.40 | 3.11 (0.84 - 11.56) | 0.09 | 71% (5/7) | 89% (8/9) |

Note: †PFS on EGFR TKI therapy; ‡Disruptive mutation versus nondisruptive mutation & wild type in training cohort; § the HR for “missense mutation versus wild type” is 1.91 (1.01 - 3.60)，P=0.04

Abbreviations: OS, overall survival; PFS, progression free survival; ORR, objective response rate; HR, hazard ratio; TKIs, tyrosine kinase inhibitors

|  |
| --- |
|  |

**Supplementary Table S2**

**Quality assessment of individual study**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| study | Selection | | | | Comparability | Outcome | | | Score |
| Representativeness of exposed cohort | Selection of non-exposed cohort | Ascertainment of exposure | Outcome not present at start | Assessment of outcome | Follow-up length | Follow-up adequacy |
| Aisner 2018 [[18](#_ENREF_18)] | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** |  | 7 |
| Bria 2015 [[23](#_ENREF_23)] |  | **\*** | **\*** | **\*** | **\*** | **\*** |  | **\*** | 6 |
| CLCGP 2013 [[25](#_ENREF_25)] | **\*** | **\*** | **\*** | **\*** | **\*** |  | **\*** | **\*** | 7 |
| Labbe 2017 [[21](#_ENREF_21)] | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** |  | **\*** | 7 |
| Li 2016 [[33](#_ENREF_33)] | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** |  | **\*** | 7 |
| Molina-Vila 2014 [[24](#_ENREF_24)] | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | 8 |
| Shepherd 2017 [[20](#_ENREF_20)] | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | 8 |
| VanderLaan 2017 [[19](#_ENREF_19)] |  | **\*** | **\*** | **\*** | **\*** | **\*** |  | **\*** | 6 |

**Supplementary Table S3**

**Pooled values in the current meta-analysis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Pooled values | Number of studies | Pooled HR (95%CI) | Heterogeneity | |
| **I2** | **P value** |
| Pooled OS | 7 | 1.725 (1.218 - 2.444) | 0.00% | 0.742 |
| Pooled PFS† | 4 | 2.181 (1.418- 3.357) | 0.00% | 0.574 |
| Pooled ORR to TKIs | 4 | 1.153 (0.922 - 1.440) | 0.00% | 0.852 |
|  | | | | |
| Pooled OS after adding nondisruptive mutation | 8 | 1.743 (1.297 - 2.343) | 0.00% | 0.832 |
| Pooled PFS after adding missense mutation | 4 | 2.346 (1.489 - 3.696) | 0.00% | 0.689 |
|  | | | | |
| Stratified analysis of OS by treatment | | | | |
| Targeted therapy | 4 | 2.289 (1.392 –3.763) | 0.00% | 0.940 |
| Others‡ | 3 | 1.315 (0.807 –2.142) | 0.00% | 0.710 |
| Stratified analysis of OS by tumor stage | | | | |
| Advanced stage or recurrent | 4 | 2.001 (1.110 –3.605) | 0.00% | 0.996 |
| Stage I - IV | 3 | 1.656 (0.893 –3.069) | 0.00% | 0.215 |

Note: † PFS on EGFR TKI therapy; ‡ Including surgery, chemotherapy, immunology, observation

Abbreviations: OS, overall survival; PFS, progression free survival; ORR, objective response rate; HR, hazard ratio; TKIs, tyrosine kinase inhibitors

**Figure Legends**

**Supplementary figure S1** Sensitivity analysis. A. overall survival (TP53 mutation group versus wild-type group); B. overall survival (data of TP53 nondisruptive mutation in the study of Molina-Vila et al. was added); C. progression free survival (data of all TP53 mutations in the study of Labbe et al. was used); D. progression free survival (data of TP53 missense mutation in the study of Labbe et al. was used)