Supplementary Table 1. Associations between baseline characteristics and clinical outcomes in the training cohort (TRIBE)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Progression-Free Survival | | |  | Overall Survival | | |
|  | N | Median, months (95%CI) | HR (95%CI) | *P* value † |  | Median, months (95%CI) | HR (95%CI) | *P* value † |
| Sex |  |  |  | 0.44 |  |  |  | 0.70 |
| Male | 136 | 9.7 (9.0, 11.1) | 1 (Reference) |  |  | 25.8 (21.1, 31.3) | 1 (Reference) |  |
| Female | 87 | 9.5 (8.6, 11.0) | 0.89 (0.65, 1.21) |  |  | 24.0 (20.5, 30.9) | 0.94 (0.69, 1.28) |  |
| Age |  |  |  | 0.50 |  |  |  | **0.004** |
| < 65 | 160 | 9.5 (8.7, 10.8) | 1 (Reference) |  |  | 27.6 (23.0, 33.1) | 1 (Reference) |  |
| ≥ 65 | 63 | 9.7 (9.0, 11.9) | 1.12 (0.81, 1.55) |  |  | 21.1 (18.6, 25.8) | 1.57 (1.14, 2.16) |  |
| Performance status |  |  |  | **0.004** |  |  |  | **< 0.001** |
| ECOG 0 | 183 | 10.5 (9.4, 11.5) | 1 (Reference) |  |  | 28.6 (24.8, 33.0) | 1 (Reference) |  |
| ECOG 1 a | 37 | 8.7 (5.7, 10.3) | 1.71 (1.18, 2.48) |  |  | 14.6 (7.7, 18.4) | 2.35 (1.60, 3.44) |  |
| ECOG 2 a | 2 |  |  |  |  |  |  |  |
| Unknown | 1 | - | - |  |  | - | - |  |
| Primary tumor site |  |  |  | 0.13 |  |  |  | **< 0.001** |
| Right side | 57 | 8.8 (7.6, 10.3) | 1 (Reference) |  |  | 20.0 (14.7, 24.7) | 1 (Reference) |  |
| Left side | 151 | 10.6 (9.4, 11.3) | 0.71 (0.51, 1.01) |  |  | 30.9 (25.1, 35.8) | 0.54 (0.38, 0.76) |  |
| Unknown | 15 | 9.2 (7.9, 13.0) | 0.91 (0.49, 1.69) |  |  | 23.0 (12.7, 27.3) | 1.07 (0.58, 1.95) |  |
| Liver only metastases |  |  |  | 0.60 |  |  |  | 0.24 |
| Yes | 71 | 10.3 (8.3, 11.9) | 1 (Reference) |  |  | 29.1 (22.3, 33.5) | 1 (Reference) |  |
| No | 152 | 9.5 (9.0, 10.8) | 1.09 (0.78, 1.54) |  |  | 24.3 (20.5, 26.8) | 1.21 (0.88, 1.67) |  |
| Number of metastases |  |  |  | 0.60 |  |  |  | **0.040** |
| <2 | 95 | 10.3 (8.8, 11.7) | 1 (Reference) |  |  | 29.8 (24.8, 34.4) | 1 (Reference) |  |
| ≥ 2 | 128 | 9.5 (8.8, 10.8) | 1.09 (0.79, 1.49) |  |  | 22.9 (20.3, 26.3) | 1.37 (1.01, 1.86) |  |
| Time to metastasis |  |  |  | 0.12 |  |  |  | **0.007** |
| Synchronous | 184 | 9.5 (9.0, 10.8) | 1 (Reference) |  |  | 24.9 (20.5, 27.3) | 1 (Reference) |  |
| Metachronous | 39 | 10.8 (8.6, 14.3) | 0.72 (0.47, 1.09) |  |  | 36.7 (21.5, 48.6) | 0.57 (0.37, 0.87) |  |
| Primary tumor resected |  |  |  | **0.003** |  |  |  | **< 0.001** |
| Yes | 142 | 10.8 (9.5, 11.6) | 1 (Reference) |  |  | 29.8 (24.7, 35.8) | 1 (Reference) |  |
| No | 81 | 9.0 (7.9, 9.5) | 1.58 (1.15, 2.16) |  |  | 20.5 (16.4, 25.8) | 1.70 (1.26, 2.31) |  |
| Adjuvant chemotherapy |  |  |  | 0.083 |  |  |  | **0.011** |
| Yes | 27 | 11.3 (8.4, 20.0) | 1 (Reference) |  |  | 39.1 (22.5, 65.3+) | 1 (Reference) |  |
| No | 196 | 9.5 (9.0, 10.5) | 1.55 (0.94, 2.56) |  |  | 24.8 (20.5, 26.8) | 1.88 (1.14, 3.11) |  |
| High LDH |  |  |  | 0.065 |  |  |  | 0.13 |
| Yes | 104 | 9.4 (8.4, 10.4) | 1 (Reference) |  |  | 21.7 (19.0, 26.3) | 1 (Reference) |  |
| No | 87 | 11.7 (9.0, 13.4) | 0.69 (0.50, 0.96) |  |  | 30.9 (24.0, 37.5) | 0.72 (0.52, 1.00) |  |
| Unknown | 32 | 9.7 (8.7, 11.1) | 0.97 (0.61, 1.53) |  |  | 27.1 (15.3, 36.1) | 0.93 (0.60, 1.45) |  |
| *KRAS* status |  |  |  | 0.13 |  |  |  | 0.11 |
| Wildtype | 95 | 11.0 (9.3, 11.6) | 1 (Reference) |  |  | 30.8 (22.7, 36.1) | 1 (Reference) |  |
| Mutant | 90 | 9.5 (8.7, 10.8) | 0.96 (0.68, 1.34) |  |  | 23.9 (19.8, 28.6) | 1.11 (0.80, 1.55) |  |
| Unknown | 38 | 9.3 (7.8, 10.5) | 1.44 (0.94, 2.19) |  |  | 22.6 (16.3, 29.8) | 1.54 (1.01, 2.35) |  |
| *BRAF* status |  |  |  | **0.005** |  |  |  | **0.001** |
| Wildtype | 173 | 10.3 (9.3, 11.2) | 1 (Reference) |  |  | 26.8 (23.0, 32.6) | 1 (Reference) |  |
| Mutant | 12 | 5.4 (1.6, 11.0) | 2.45 (1.31, 4.59) |  |  | 10.7 (3.1, 24.8) | 2.80 (1.50, 5.23) |  |
| Unknown | 38 | 9.3 (7.8, 10.8) | 1.40 (0.95, 2.07) |  |  | 22.6 (16.3, 29.8) | 1.45 (0.98, 2.16) |  |

CI, confidence interval; HR, hazard ratio; ECOG, Eastern Cooperative Oncology Group; LDH, lactose dehydrogenase.

† *P* value was based on log-rank test for PFS and OS in the univariate analysis.

a Combined together for estimation of HR.

- No events occurred and estimates were not obtained.

+ Estimates not reach.

Supplementary Table 2. Associations between baseline characteristics and clinical outcomes in the validation cohort (FIRE-3)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Progression-Free Survival | | |  | Overall Survival | | |
|  | N | Median, months (95%CI) | HR (95%CI) | *P* value† |  | Median, months (95%CI) | HR (95%CI) | *P* value† |
| Sex |  |  |  | 0.064 |  |  |  | 1.00 |
| Male | 189 | 10.2 (9.3, 11.3) | 1 (Reference) |  |  | 23.7 (20.6, 27.4) | 1 (Reference) |  |
| Female | 99 | 9.7 (8.8, 12.3) | 1.27 (0.98, 1.66) |  |  | 24.8 (21.8, 30.3) | 1.00 (0.75, 1.34) |  |
| Age |  |  |  | 0.94 |  |  |  | 0.26 |
| < 65 | 151 | 9.7 (8.9, 11.7) | 1 (Reference) |  |  | 22.3 (18.7, 27.4) | 1 (Reference) |  |
| ≥ 65 | 137 | 10.3 (9.3, 11.8) | 1.01 (0.78, 1.30) |  |  | 25.4 (23.1, 28.0) | 0.85 (0.64, 1.13) |  |
| Performance status |  |  |  | **0.001** |  |  |  | **< 0.001** |
| ECOG 0 | 159 | 11.5 (10.0, 13.1) | 1 (Reference) |  |  | 28.4 (25.1, 31.5) | 1 (Reference) |  |
| ECOG 1 a | 123 | 9.3 (8.5, 10.1) | 1.51 (1.17, 1.94) |  |  | 20.6 (17.6, 23.1) | 1.67 (1.26, 2.21) |  |
| ECOG 2 a | 6 |  |  |  |  |  |  |  |
| Primary tumor site |  |  |  | 0.078 |  |  |  | **0.023** |
| Right colon | 63 | 9.0 (7.2, 10.9) | 1 (Reference) |  |  | 21.0 (16.5, 23.6) | 1 (Reference) |  |
| Left colon | 173 | 10.7 (9.8, 12.0) | 0.71 (0.51, 0.97) |  |  | 27.4 (23.1, 30.3) | 0.63 (0.44, 0.90) |  |
| Unknown | 52 | 8.9 (8.1, 12.5) | 0.86 (0.58, 1.26) |  |  | 23.1 (16.4, 28.4) | 0.84 (0.55, 1.27) |  |
| Lung metastasis |  |  |  | 0.83 |  |  |  | 0.91 |
| Yes | 91 | 9.8 (8.8, 10.7) | 1 (Reference) |  |  | 25.9 (22.7, 28.1) | 1 (Reference) |  |
| No | 151 | 10.8 (9.7, 12.3) | 1.03 (0.77, 1.38) |  |  | 23.1 (19.5, 28.6) | 0.98 (0.71, 1.36) |  |
| Liver only metastases |  |  |  | 0.40 |  |  |  | **0.018** |
| Yes | 95 | 11.3 (9.3, 13.0) | 1 (Reference) |  |  | 26.7 (21.3, 34.6) | 1 (Reference) |  |
| No | 193 | 9.8 (8.9, 10.7) | 1.12 (0.86, 1.46) |  |  | 23.2 (20.6, 26.1) | 1.43 (1.06, 1.93) |  |
| Number of metastases |  |  |  | 0.12 |  |  |  | **0.013** |
| < 2 | 105 | 11.9 (9.9, 13.0) | 1 (Reference) |  |  | 27.6 (21.3, 36.0) | 1 (Reference) |  |
| ≥ 2 | 137 | 9.7 (8.9, 10.7) | 1.27 (0.96, 1.68) |  |  | 23.2 (20.6, 26.1) | 1.57 (1.14, 2.16) |  |
| Unknown | 46 | 8.8 (7.2, 12.5) | 1.38 (0.96, 1.97) |  |  | 23.1 (16.3, 29.0) | 1.49 (1.01, 2.21) |  |
| Time to metastasis |  |  |  | 0.14 |  |  |  | 0.12 |
| Synchronous | 183 | 10.3 (9.3, 11.8) | 1 (Reference) |  |  | 23.1 (20.6, 25.9) | 1 (Reference) |  |
| Metachronous | 58 | 10.1 (8.9, 12.9) | 0.77 (0.56, 1.07) |  |  | 28.4 (23.7, 42.9) | 0.70 (0.49, 1.02) |  |
| Unknown | 46 | 8.8 (7.2, 12.5) | 1.14 (0.81, 1.59) |  |  | 23.1 (16.3, 29.0) | 1.07 (0.75, 1.53) |  |
| Primary tumor resected |  |  |  | 0.56 |  |  |  | **0.014** |
| Yes | 249 | 10.1 (9.3, 11.3) | 1 (Reference) |  |  | 25.1 (22.3, 28.0) | 1 (Reference) |  |
| No | 39 | 9.7 (7.2, 13.1) | 1.12 (0.76, 1.64) |  |  | 19.5 (11.4, 24.2) | 1.67 (1.09, 2.56) |  |
| Adjuvant chemotherapy |  |  |  | 0.95 |  |  |  | 0.20 |
| Yes | 53 | 9.7 (8.6, 10.8) | 1 (Reference) |  |  | 26.1 (19.5, 37.0) | 1 (Reference) |  |
| No | 235 | 10.4 (9.6, 11.8) | 1.01 (0.74, 1.38) |  |  | 23.7 (21.2, 26.5) | 1.25 (0.88, 1.78) |  |
| High LDH |  |  |  | 0.20 |  |  |  | 0.25 |
| Yes | 71 | 10.5 (9.1, 12.3) | 1 (Reference) |  |  | 23.1 (17.4, 26.1) | 1 (Reference) |  |
| No | 70 | 9.7 (8.6, 12.5) | 0.75 (0.53, 1.08) |  |  | 24.8 (20.1, 31.9) | 0.73 (0.49, 1.08) |  |
| Unknown | 147 | 10.1 (8.9, 11.7) | 0.97 (0.72, 1.31) |  |  | 26.5 (20.6, 29.6) | 0.80 (0.57, 1.12) |  |
| *KRAS* status |  |  |  | 0.23 |  |  |  | 0.36 |
| Wildtype | 242 | 10.2 (9.7, 11.3) | 1 (Reference) |  |  | 24.7 (21.8, 27.4) | 1 (Reference) |  |
| Mutant | 46 | 8.8 (7.2, 12.5) | 1.22 (0.88, 1.68) |  |  | 23.1 (16.3, 29.0) | 1.17 (0.83, 1.66) |  |

CI, confidence interval; HR, hazard ratio; ECOG, Eastern Cooperative Oncology Group; LDH, lactose dehydrogenase.

† *P* value was based on log-rank test for PFS and OS in the univariate analysis.

a Combined for estimates of HR.

Supplementary Table 3. Associations between baseline characteristics and clinical outcomes in the control cohort (FIRE-3)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Progression-Free Survival | | |  | Overall Survival | | |
|  | N | Median, months (95%CI) | HR (95%CI) | *P* value† |  | Median, months (95%CI) | HR (95%CI) | *P* value† |
| Sex |  |  |  | **0.012** |  |  |  | 0.26 |
| Male | 171 | 10.0 (8.8, 11.1) | 1 (Reference) |  |  | 28.7 (22.5, 37.5) | 1 (Reference) |  |
| Female | 93 | 8.5 (6.3, 9.7) | 1.41 (1.07, 1.84) |  |  | 27.9 (20.2, 34.2) | 1.20 (0.87, 1.65) |  |
| Age |  |  |  | 0.66 |  |  |  | 0.74 |
| < 65 | 140 | 9.9 (8.3, 10.6) | 1 (Reference) |  |  | 28.0 (22.6, 36.6) | 1 (Reference) |  |
| ≥ 65 | 124 | 9.4 (7.4, 10.6) | 1.06 (0.82, 1.37) |  |  | 30.6 (20.4, 38.3) | 1.06 (0.77, 1.45) |  |
| Performance status |  |  |  | 0.45 |  |  |  | 0.073 |
| ECOG 0 | 135 | 10.1 (9.3, 12.1) | 1 (Reference) |  |  | 33.6 (23.7, 38.4) | 1 (Reference) |  |
| ECOG 1 a | 122 | 8.3 (7.3, 10.2) | 1.10 (0.85, 1.43) |  |  | 24.8 (19.9, 30.4) | 1.33 (0.97, 1.82) |  |
| ECOG 2 a | 7 |  |  |  |  |  |  |  |
| Primary tumor site |  |  |  | **0.001** |  |  |  | **< 0.001** |
| Right colon | 38 | 7.3 (5.1, 9.0) | 1 (Reference) |  |  | 18.5 (14.9, 27.9) | 1 (Reference) |  |
| Left colon | 174 | 10.2 (9.2, 11.1) | 0.51 (0.35, 0.75) |  |  | 38.3 (28.7, 45.0) | 0.44 (0.28, 0.68) |  |
| Unknown | 52 | 9.6 (6.2, 10.6) | 0.65 (0.42, 1.00) |  |  | 23.0 (17.1, 28.5) | 0.76 (0.47, 1.24) |  |
| Lung metastasis |  |  |  | 0.16 |  |  |  | **0.047** |
| Yes | 82 | 8.1 (6.8, 10.2) | 1 (Reference) |  |  | 27.9 (17.9, 36.6) | 1 (Reference) |  |
| No | 135 | 10.4 (9.2, 11.5) | 0.81 (0.60, 1.09) |  |  | 37.1 (23.9, 41.2) | 0.69 (0.47, 1.00) |  |
| Liver only metastases |  | 9.2 (6.0, 10.3) | 1.19 (0.85, 1.67) |  |  | 23.0 (17.1, 28.7) | 1.28 (0.89, 1.84) |  |
| Yes | 88 |  |  | 0.10 |  |  |  | **0.004** |
| No | 176 | 10.0 (9.2, 12.6) | 1 (Reference) |  |  | 34.2 (24.4, 40.9) | 1 (Reference) |  |
| Number of metastases |  | 9.2 (7.8, 10.3) | 1.26 (0.95, 1.66) |  |  | 23.9 (20.6, 33.1) | 1.63 (1.16, 2.30) |  |
| < 2 | 92 |  |  | 0.47 |  |  |  | **0.032** |
| ≥ 2 | 125 | 10.0 (9.0, 11.5) | 1 (Reference) |  |  | 37.1 (25.2, 42.8) | 1 (Reference) |  |
| Unknown | 47 | 9.0 (7.8, 10.9) | 1.12 (0.84, 1.51) |  |  | 28.0 (20.6, 38.7) | 1.38 (0.95, 2.01) |  |
| Time to metastasis |  | 9.2 (6.0, 10.3) | 1.25 (0.87, 1.81) |  |  | 23.0 (17.1, 28.7) | 1.72 (1.14, 2.60) |  |
| Synchronous | 163 |  |  | 0.57 |  |  |  | **0.016** |
| Metachronous | 52 | 9.6 (8.1, 10.8) | 1 (Reference) |  |  | 26.5 (20.6, 37.1) | 1 (Reference) |  |
| Unknown | 47 | 9.9 (7.9, 12.2) | 1.07 (0.77, 1.50) |  |  | 38.5 (28.7, 56.2) | 0.61 (0.38, 0.96) |  |
| Primary tumor resected |  |  |  | 0.69 |  |  |  | 0.30 |
| Yes | 219 | 9.6 (8.3, 10.3) | 1 (Reference) |  |  | 28.7 (23.7, 36.4) | 1 (Reference) |  |
| No | 44 | 9.6 (5.7, 13.5) | 0.93 (0.65, 1.34) |  |  | 28.0 (14.1, 50.1) | 1.25 (0.81, 1.92) |  |
| Adjuvant chemotherapy |  |  |  | 0.18 |  |  |  | 0.84 |
| Yes | 56 | 9.6 (7.4, 10.9) | 1 (Reference) |  |  | 30.4 (18.1, 38.5) | 1 (Reference) |  |
| No | 207 | 9.6 (8.2, 10.4) | 0.81 (0.59, 1.11) |  |  | 26.5 (22.4, 34.2) | 0.96 (0.66, 1.40) |  |
| High LDH |  |  |  | 0.20 |  |  |  | **0.034** |
| Yes | 64 | 7.9 (6.5, 9.9) | 1 (Reference) |  |  | 20.3 (16.0, 33.1) | 1 (Reference) |  |
| No | 64 | 10.9 (8.8, 12.9) | 0.72 (0.49, 1.04) |  |  | 37.5 (23.7, 56.2) | 0.55 (0.35, 0.88) |  |
| Unknown | 136 | 9.6 (7.8, 10.5) | 0.85 (0.61, 1.17) |  |  | 27.9 (23.0, 33.6) | 0.79 (0.54, 1.16) |  |
| *KRAS* status |  |  |  | 0.33 |  |  |  | **0.041** |
| Wildtype | 217 | 9.7 (8.5, 10.6) | 1 (Reference) |  |  | 30.6 (23.8, 38.5) | 1 (Reference) |  |
| Mutant | 47 | 9.2 (6.0, 10.3) | 1.17 (0.85, 1.62) |  |  | 23.0 (17.1, 28.7) | 1.44 (1.01, 2.05) |  |

CI, confidence interval; HR, hazard ratio; ECOG, Eastern Cooperative Oncology Group; LDH, lactose dehydrogenase.

† *P* value was based on log-rank test for PFS and OS in the univariate analysis.

a Combined together for estimation of HR.

Supplementary Table 4. Association between *IL-6*, *STAT3* SNPs with clinical outcomes in the training cohort

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Tumor Response | | |  | Progression-Free Survival | | | | |  | Overall Survival | | | | |
|  | N | PR+CR | SD+PD | *P* value\* |  | Median, months (95%CI) | HR (95%CI) † | *P* value\* | HR (95%CI) ‡ | *P* value\* |  | Median, months (95%CI) | HR (95%CI) † | *P* value\* | HR (95%CI) ‡ | *P* value\* |
| *IL6* rs1800795 |  |  |  | 0.36 |  |  |  | 0.95 |  | 0.38 |  |  |  | 0.76 |  | 0.21 |
| G/G | 92 | 51 (57%) | 39 (43%) |  |  | 9.7 (8.6, 11.5) | 1 (Reference) |  | 1 (Reference) |  |  | 25.1 (20.0, 31.6) | 1 (Reference) |  | 1 (Reference) |  |
| G/C | 84 | 48 (59%) | 33 (41%) |  |  | 9.4 (7.9, 11.0) | 0.98 (0.69, 1.39) |  | 0.74 (0.49, 1.13) |  |  | 24.9 (20.3, 33.0) | 0.96 (0.68, 1.35) |  | 0.69 (0.45, 1.04) |  |
| C/C | 11 | 4 (36%) | 7 (64%) |  |  | 10.3 (4.2, 10.8) | 1.09 (0.56, 2.12) |  | 0.92 (0.43, 1.97) |  |  | 26.4 (5.8, 35.8) | 1.23 (0.63, 2.39) |  | 0.85 (0.38, 1.87) |  |
|  |  |  |  | 1.00 |  |  |  | 0.97 |  | 0.19 |  |  |  | 0.94 |  | 0.089 |
| G/G | 92 | 51 (57%) | 39 (43%) |  |  | 9.7 (8.6, 11.5) | 1 (Reference) |  | 1 (Reference) |  |  | 25.1 (20.0, 31.6) | 1 (Reference) |  | 1 (Reference) |  |
| Any C | 95 | 52 (57%) | 40 (43%) |  |  | 9.5 (8.3, 10.5) | 0.99 (0.71, 1.39) |  | 0.77 (0.51, 1.14) |  |  | 25.8 (21.1, 30.9) | 0.99 (0.71, 1.37) |  | 0.70 (0.47, 1.05) |  |
| *STAT3* rs744166 |  |  |  | 0.29 |  |  |  | 0.91 |  | 0.99 |  |  |  | 0.39 |  | 0.74 |
| A/A | 80 | 39 (50%) | 39 (50%) |  |  | 10.3 (8.6, 11.2) | 1 (Reference) |  | 1 (Reference) |  |  | 26.1 (20.8, 35.8) | 1 (Reference) |  | 1 (Reference) |  |
| A/G | 85 | 51 (62%) | 31 (38%) |  |  | 9.4 (8.2, 10.8) | 1.04 (0.73, 1.49) |  | 0.97 (0.64, 1.47) |  |  | 26.4 (19.8, 33.0) | 1.00 (0.71, 1.41) |  | 0.98 (0.65, 1.45) |  |
| G/G | 32 | 18 (58%) | 13 (42%) |  |  | 9.5 (8.0, 11.0) | 1.10 (0.70, 1.73) |  | 0.97 (0.55, 1.71) |  |  | 20.3 (16.4, 26.8) | 1.34 (0.84, 2.12) |  | 1.23 (0.68, 2.22) |  |
|  |  |  |  | 0.14 |  |  |  | 0.73 |  | 0.87 |  |  |  | 0.65 |  | 0.90 |
| A/A | 80 | 39 (50%) | 39 (50%) |  |  | 10.3 (8.6, 11.2) | 1 (Reference) |  | 1 (Reference) |  |  | 26.1 (20.8, 35.8) | 1 (Reference) |  | 1 (Reference) |  |
| Any G | 117 | 69 (61%) | 44 (39%) |  |  | 9.4 (8.6, 10.8) | 1.06 (0.76, 1.47) |  | 0.97 (0.66, 1.43) |  |  | 25.0 (19.4, 30.8) | 1.08 (0.78, 1.48) |  | 1.02 (0.70, 1.49) |  |
| *STAT3* rs4796793 |  |  |  | 0.16 |  |  |  | 0.73 |  | 0.95 |  |  |  | 0.90 |  | 0.80 |
| C/C | 114 | 59 (53%) | 52 (47%) |  |  | 10.3 (8.8, 11.1) | 1 (Reference) |  | 1 (Reference) |  |  | 26.1 (22.0, 32.5) | 1 (Reference) |  | 1 (Reference) |  |
| C/G | 78 | 48 (66%) | 25 (34%) |  |  | 9.4 (8.3, 11.5) | 0.95 (0.68, 1.33) |  | 0.94 (0.63, 1.39) |  |  | 24.9 (18.1, 31.6) | 1.01 (0.72, 1.40) |  | 1.07 (0.73, 1.58) |  |
| G/G | 11 | 5 (45%) | 6 (55%) |  |  | 9.5 (6.6, 12.3) | 1.25 (0.63, 2.50) |  | 0.97 (0.39, 2.38) |  |  | 23.0 (7.7, 40.7+) | 1.18 (0.57, 2.44) |  | 0.75 (0.25, 2.31) |  |
|  |  |  |  | 0.19 |  |  |  | 0.90 |  | 0.76 |  |  |  | 0.87 |  | 0.81 |
| C/C | 114 | 59 (53%) | 52 (47%) |  |  | 10.3 (8.8, 11.1) | 1 (Reference) |  | 1 (Reference) |  |  | 26.1 (22.0, 32.5) | 1 (Reference) |  | 1 (Reference) |  |
| Any G | 87 | 53 (63%) | 31 (37%) |  |  | 9.4 (8.3, 11.0) | 0.98 (0.71, 1.35) |  | 0.94 (0.64, 1.38) |  |  | 24.8 (18.4, 30.8) | 1.03 (0.75, 1.41) |  | 1.05 (0.72, 1.54) |  |

CI, confidence interval; HR, hazard ratio

\* P value was based on Fisher’s exact test for tumor response, log-rank test for PFS and OS in the univariable analysis, and Wald test in the multivariable Cox proportional hazards regression model adjusting age, ECOG performance status, primary tumor site, number of metastatic sites, resection of the primary tumors, *BRAF* mutation status, adjuvant chemotherapy.