**Supplementary Table S3.** Association between GC and VDR SNPs and clinical outcomes in the validation cohort 1 (TRIBE FOLFIRI/bevacizumab arm)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | 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\* |
| GCrs4588 |  |  |  | 0.20 |  |  |  | 0.62 |  | 0.16 |  |  |  | 0.46 |  | 0.052 |
|  C/C | 124 | 73(61%) | 47(39%) |  |  | 10.3(8.8,11.1) | 1 (Reference) |  | 1 (Reference) |  |  | 26.2(22.4,32.9) | 1 (Reference) |  | 1 (Reference) |  |
|  C/A | 87 | 50(58%) | 36(42%) |  |  | 9.6(8.8,11.1) | 0.94(0.68,1.29) |  | 0.90(0.65,1.25) |  |  | 26.1(20.5,30.8) | 1.12(0.82,1.54) |  | 1.24(0.89,1.71) |  |
|  A/A | 16 | 5(36%) | 9(64%) |  |  | 7.5(3.6,14.1) | 1.24(0.71,2.14) |  | 1.66(0.90,3.05) |  |  | 18.1(5.5,36.7) | 1.39(0.79,2.43) |  | 2.01(1.12,3.62) |  |
|  |  |  |  | 0.38 |  |  |  | 0.90 |  | 0.88 |  |  |  | 0.32 |  | 0.081 |
|  C/C | 124 | 73(61%) | 47(39%) |  |  | 10.3(8.8,11.1) | 1 (Reference) |  | 1 (Reference) |  |  | 26.2(22.4,32.9) | 1 (Reference) |  | 1 (Reference) |  |
|  Any A | 103 | 55(55%) | 45(45%) |  |  | 9.5(8.7,10.8) | 0.98(0.73,1.32) |  | 0.98(0.71,1.33) |  |  | 25.4(20.5,29.8) | 1.16(0.86,1.56) |  | 1.32(0.97,1.79) |  |
|  |  |  |  | 0.078 |  |  |  | 0.37 |  | 0.070 |  |  |  | 0.31 |  | **0.037** |
|  Any C | 211 | 123(60%) | 83(40%) |  |  | 9.7(9.3,10.8) | 1 (Reference) |  | 1 (Reference) |  |  | 26.2(22.7,30.8) | 1 (Reference) |  | 1 (Reference) |  |
|  A/A | 16 | 5(36%) | 9(64%) |  |  | 7.5(3.6,14.1) | 1.27(0.75,2.16) |  | 1.73(0.96,3.14) |  |  | 18.1(5.5,36.7) | 1.32(0.76,2.29) |  | 1.83(1.04,3.23) |  |
| VDRrs731236 |  |  |  | 0.61 |  |  |  | 0.77 |  | 0.80 |  |  |  | 0.38 |  | 0.10 |
|  A/A | 74 | 39(53%) | 34(47%) |  |  | 9.5(8.3,11.1) | 1 (Reference) |  | 1 (Reference) |  |  | 27.9(22.0,32.6) | 1 (Reference) |  | 1 (Reference) |  |
|  A/G | 103 | 59(60%) | 40(40%) |  |  | 9.6(8.8,11.5) | 1.03(0.73,1.46) |  | 1.10(0.77,1.57) |  |  | 23.0(19.1,30.8) | 1.18(0.84,1.67) |  | 1.31(0.92,1.86) |  |
|  G/G | 49 | 29(62%) | 18(38%) |  |  | 9.7(8.6,11.1) | 1.16(0.75,1.80) |  | 1.16(0.73,1.86) |  |  | 26.3(22.5,36.1) | 0.92(0.61,1.41) |  | 0.87(0.55,1.37) |  |
|  |  |  |  | 0.33 |  |  |  | 0.70 |  | 0.53 |  |  |  | 0.58 |  | 0.38 |
|  A/A | 74 | 39(53%) | 34(47%) |  |  | 9.5(8.3,11.1) | 1 (Reference) |  | 1 (Reference) |  |  | 27.9(22.0,32.6) | 1 (Reference) |  | 1 (Reference) |  |
|  Any G | 152 | 88(60%) | 58(40%) |  |  | 9.7(9.0,11.0) | 1.07(0.77,1.48) |  | 1.11(0.79,1.57) |  |  | 25.0(20.8,29.8) | 1.09(0.79,1.50) |  | 1.16(0.83,1.62) |  |
|  |  |  |  | 0.56 |  |  |  | 0.48 |  | 0.67 |  |  |  | 0.34 |  | 0.14 |
|  Any A | 177 | 98(57%) | 74(43%) |  |  | 9.5(9.0,10.8) | 1 (Reference) |  | 1 (Reference) |  |  | 25.2(20.8,29.1) | 1 (Reference) |  | 1 (Reference) |  |
|  G/G | 49 | 29(62%) | 18(38%) |  |  | 9.7(8.6,11.1) | 1.14(0.78,1.67) |  | 1.09(0.73,1.64) |  |  | 26.3(22.5,36.1) | 0.84(0.58,1.21) |  | 0.74(0.50,1.11) |  |

\* *P*-value was based on Chi-square test or Fisher’s exact test for tumor response, whenever appropriate, log-rank test for PFS and OS in the univariable analysis (†), and Wald test in the multivariable Cox proportional hazards regression model (‡) adjusting for sex, age, ECOG performance status, primary tumor site, resection of the primary tumor, BRAF status, and prior adjuvant chemotherapy. PR=partial response; CR=complete response; SD=stable disease; PD=progressive disease. *P*-values <0.050 are shown in bold.