**Supplemental Table 1: Comparison of Genomic Features by Treatment Cohort: Results of Multivariable Analysis**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Summary Statistics | | | | Multivariable Analysis | | |
| Dependent Variable | **Overall,**  **N = 487** | **Curative,**  **N = 230** | **Palliative,**  **N = 257** | **p-value1** | **Treatment Coef.3** | **95% CI4** | **p-value2** |
| Fraction of genome altered | 0.45  (0.31, 0.57) | 0.40  (0.23, 0.53) | 0.50  (0.38, 0.58) | <0.001 | 0.06 | 0.03, 0.09 | <0.001 |
| Whole-genome doubling | 176 (38%) | 59 (29%) | 117 (46%) | <0.001 | 1.86 | 1.24, 2.80 | 0.003 |
| Number of Pathways Altered | 3 (2, 4) | 2 (2, 3) | 3 (2, 4) | <0.001 | 0.22 | -0.01, 0.45 | 0.062 |
| Number of Oncogenic Drivers | 2 (1, 3) | 2 (1, 3) | 3 (2, 3) | <0.001 | 0.28 | 0.05, 0.50 | 0.017 |

Statistics are presented as median (IQR).

1 Statistical comparison by Wilcoxon rank sum test.

2 Based on evaluating association of dependent variable with treatment cohort, palliative vs. curative (reference), while controlling for tumor purity and site of tissue sampling.

3 Values > 0 indicate larger greater numbers in palliative cohort.

4 CI = Confidence Interval.

**Supplemental Table 2: Results of Adjusted Univariate Analysis**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Genomic Feature, Alteration, or Pathway | Adjusted for Tumor Mutation Burden | | | | Adjusted for clinicopathologic variables | | | |
| **N** | **HR**1 | **95% CI**1 | **p-value** | **N** | **HR**1 | **95% CI**1 | **p-value** |
| Fraction of genome altered | 434 | 1.40 | 0.69, 2.85 | 0.4 | 433 | 0.55 | 0.27, 1.13 | 0.10 |
| Whole-genome doubling2 | 434 | 1.09 | 0.85, 1.40 | 0.5 | 433 | 0.93 | 0.72, 1.19 | 0.6 |
| Number of pathways altered | 459 | 1.07 | 0.97, 1.18 | 0.15 | 459 | 1.05 | 0.96, 1.15 | 0.3 |
| Number of oncogenic drivers | 459 | 1.12 | 1.02, 1.24 | 0.017 | 459 | 1.11 | 1.01, 1.22 | **0.030** |
| Tumor mutation burden |  |  |  |  | 447 | 0.99 | 0.96, 1.02 | 0.5 |
| *CDKN2A* | 459 | 1.60 | 1.23, 2.09 | <0.001 | 459 | 1.65 | 1.26, 2.16 | **<0.001** |
| *SMAD4* | 459 | 1.48 | 1.05, 2.08 | 0.023 | 459 | 1.60 | 1.14, 2.26 | **0.007** |
| *TP53* | 459 | 1.02 | 0.73, 1.41 | >0.9 | 459 | 1.02 | 0.74, 1.39 | >0.9 |
| *ARID1A* | 459 | 0.90 | 0.60, 1.33 | 0.6 | 459 | 0.88 | 0.59, 1.30 | 0.5 |
| *APC* | 459 | 0.75 | 0.43, 1.32 | 0.3 | 459 | 0.82 | 0.46, 1.49 | 0.5 |
| *PIK3CA* | 459 | 0.62 | 0.34, 1.11 | 0.11 | 459 | 0.83 | 0.46, 1.50 | 0.5 |
| *ERBB2* amplification | 459 | 0.71 | 0.53, 0.95 | 0.022 | 459 | 0.62 | 0.45, 0.85 | **0.003** |
| *KRAS* amplification | 459 | 1.94 | 1.40, 2.69 | <0.001 | 459 | 2.05 | 1.48, 2.85 | **<0.001** |
| *CCNE1* amplification | 459 | 0.84 | 0.56, 1.26 | 0.4 | 459 | 0.82 | 0.53, 1.25 | 0.4 |
| *MYC* amplification | 459 | 1.43 | 0.96, 2.12 | 0.077 | 459 | 1.23 | 0.82, 1.84 | 0.3 |
| *CCND1* amplification | 459 | 1.49 | 1.01, 2.19 | 0.045 | 459 | 1.13 | 0.76, 1.67 | 0.5 |
| *VEGFA* amplification | 415 | 0.93 | 0.56, 1.55 | 0.8 | 415 | 0.81 | 0.48, 1.36 | 0.4 |
| *MDM2* amplification | 459 | 1.31 | 0.84, 2.04 | 0.2 | 459 | 1.45 | 0.93, 2.27 | 0.10 |
| *CCND3* amplification | 459 | 1.02 | 0.60, 1.75 | >0.9 | 459 | 1.11 | 0.64, 1.93 | 0.7 |
| *EGFR* amplification | 459 | 1.38 | 0.88, 2.18 | 0.2 | 459 | 1.30 | 0.81, 2.06 | 0.3 |
| *CDK6* amplification | 459 | 1.18 | 0.72, 1.93 | 0.5 | 459 | 1.14 | 0.70, 1.84 | 0.6 |
| RTK-RAS Pathway | 459 | 0.95 | 0.75, 1.22 | 0.7 | 459 | 0.95 | 0.73, 1.24 | 0.7 |
| WNT Pathway | 459 | 1.07 | 0.74, 1.54 | 0.7 | 459 | 1.26 | 0.87, 1.82 | 0.2 |
| TP53 Pathway | 459 | 1.19 | 0.78, 1.82 | 0.4 | 459 | 1.14 | 0.77, 1.68 | 0.5 |
| Cell Cycle Pathway | 459 | 1.40 | 1.10, 1.78 | 0.007 | 459 | 1.32 | 1.03, 1.68 | **0.029** |
| HIPPO Pathway | 459 | 0.97 | 0.46, 2.01 | >0.9 | 459 | 0.85 | 0.41, 1.73 | 0.6 |
| MYC Pathway | 459 | 1.38 | 0.96, 2.00 | 0.084 | 459 | 1.12 | 0.77, 1.64 | 0.5 |
| NRF2 Pathway | 459 | 0.75 | 0.23, 2.52 | 0.6 | 459 | 0.77 | 0.23, 2.54 | 0.7 |
| TGFβ Pathway | 459 | 1.33 | 0.96, 1.83 | 0.085 | 459 | 1.45 | 1.05, 2.01 | **0.026** |
| PI3K Pathway | 459 | 0.88 | 0.64, 1.21 | 0.4 | 459 | 0.91 | 0.66, 1.24 | 0.5 |
| NOTCH Pathway | 459 | 0.72 | 0.45, 1.15 | 0.2 | 459 | 0.73 | 0.46, 1.17 | 0.2 |
| DDR Pathway | 459 | 0.94 | 0.64, 1.40 | 0.8 | 459 | 0.92 | 0.62, 1.37 | 0.7 |

1 HR = Hazard Ratio, CI = Confidence Interval

2 Treated as a dichotomous variable (yes/no)