**Supplementary Figures and Tables**

**Supplementary Figure 1:** Volcano pot showing the overexpressed genes in the clinical benefit vs no clinical benefit cohorts.



**Supplementary Table 1:** Frequency of genomic alterations observed in clinical benefit vs no clinical benefit cohort

|  |  |  |  |
| --- | --- | --- | --- |
| **Genes** | **Clinical Benefit (N=37)** | **No Clinical Benefit (N=16)** | ***p*-value** |
| *PBRM1* | 17 (45.9%) | 8 (50%) | 0.79 |
| *VHL* | 20 (54.1%) | 10 (62.5%) | 0.57 |
| *KDM5C* | 7 (18.9%) | 3 (18.8%) | 0.99 |
| *SETD2* | 7 (18.9%) | 4 (25%) | 0.62 |
| *CDKN2A* | 0 (0%) | 1 (6.2%) | 0.12 |
| *MTAP* | 0 (0%) | 1 (6.2%) | 0.12 |
| *CASP8* | 1 (2.7%) | 0 (0%) | 0.51 |
| *TSC1* | 5 (13.5%) | 1 (6.2%) | 0.44 |
| *BAP1* | 4 (10.8%) | 0 (0%) | 0.17 |
| *ARID1A* | 2 (5.4%) | 1 (6.2%) | 0.90 |
| *TP53* | 2 (5.4%) | 2 (12.5%) | 0.37 |
| *PTEN* | 2 (5.4%) | 2 (12.5%) | 0.37 |
| *STAG2* | 1 (2.7%) | 0 (0%) | 0.51 |
| *MUTYH* | 1 (2.7%) | 0 (0%) | 0.51 |
| *MTOR* | 1 (2.7%) | 0 (0%) | 0.51 |
| *PIK3CA* | 2 (5.4%) | 0 (0%) | 0.34 |
| *TERT* | 4 (10.8%) | 1 (6.2%) | 0.60 |
| *KMT2D* | 0 (0%) | 1 (6.2%) | 0.12 |
| *MYC* | 1 (2.7%) | 0 (0%) | 0.51 |
| *GRM3* | 0 (0%) | 1 (6.2%) | 0.12 |
| *SMARCB1* | 0 (0%) | 1 (6.2%) | 0.12 |
| *SMARCA4* | 0 (0%) | 1 (6.2%) | 0.12 |
| *NOTCH4* | 0 (0%) | 1 (6.2%) | 0.12 |
| *NF2* | 0 (0%) | 1 (6.2%) | 0.12 |
| *IDH1* | 1 (2.7%) | 0 (0%) | 0.51 |
| *MSH2* | 0 (0%) | 1 (6.2%) | 0.12 |
| *TET2* | 0 (0%) | 1 (6.2%) | 0.12 |
| *CXXC4* | 1 (2.7%) | 0 (0%) | 0.51 |
| *MSH3* | 1 (2.7%) | 0 (0%) | 0.51 |
| *PTCH1* | 1 (2.7%) | 0 (0%) | 0.51 |
| *RNF43* | 1 (2.7%) | 0 (0%) | 0.51 |
| *JAK1* | 1 (2.7%) | 0 (0%) | 0.51 |

**Supplementary Table 2:** Differentially expressed genes in the Clinical Benefit and no- Clinical Benefit cohort

|  |  |  |  |
| --- | --- | --- | --- |
| **Gene ID** | **Log2 Fold Change** | ***p* value** | ***q* value** |
| **Clinical Benefit**  |
| NACA2 | 23.96 | <0.001 | <0.001 |
| TMEM151A | 6.85 | 0.0001 | 0.07 |
| CTSE | 6.67 | <0.001 | 0.0003 |
| RGS11 | 6.45 | <0.001 | 0.002 |
| OLIG3 | 6.15 | 0.0001 | 0.083 |
| HAND2 | 6.05 | <0.001 | 0.009 |
| PAH | 5.85 | <0.001 | 0.048 |
| TM4SF4 | 5.80 | <0.001 | 0.036 |
| MUC1 | 5.63 | <0.001 | 0.043 |
| KCNG3 | 5.32 | <0.001 | 0.030 |
| ASTN1 | 5.24 | <0.001 | 0.015 |
| SYT14 | 5.12 | <0.001 | 0.009 |
| TTC3 | 4.97 | 0.0001 | 0.075 |
| PTPRT | 4.92 | <0.001 | 0.030 |
| MYLK3 | 4.56 | <0.001 | 0.0003 |
| SYT3 | 4.48 | <0.001 | 0.003 |
| VTN | 4.27 | <0.001 | 0.030 |
| NPC1L1 | 4.11 | <0.001 | 0.047 |
| GPR37 | 3.91 | 0.0001 | 0.085 |
| PROX1 | 3.58 | <0.001 | 0.0002 |
| B3GAT1 | 3.42 | <0.001 | 0.011 |
| KCNH2 | 3.20 | 0.0002 | 0.098 |
| WNT4 | 3.11 | <0.001 | 0.047 |
| MISP | 2.91 | <0.001 | 0.047 |
| LARS2 | 2.85 | <0.001 | 0.011 |
| LRRN2 | 2.72 | <0.001 | 0.051 |
| LDLRAD2 | 2.45 | <0.001 | 0.047 |
| MYO16 | 2.37 | <0.001 | 0.047 |
| CECR2 | 2.19 | 0.0002 | 0.098 |
| CADM4 | 2.18 | <0.001 | 0.011 |
| UNC5C | 2.11 | <0.001 | 0.011 |
| GPR78 | 2.07 | 0.0002 | 0.098 |
| **No-Clinical Benefit**  |
| DHRSX | 0.6390601 | 0.0001 | 0.073 |
| DRAM1 | 0.7176084 | 0.0001 | 0.089 |
| KRTAP5-11 | 1.2809163 | <0.001 | 0.008 |
| SCG5 | 2.1119639 | 0.0001 | 0.075 |
| XPNPEP2 | 3.3636829 | 0.0002 | 0.095 |
| GJB2 | 3.7490521 | <0.001 | 0.009 |
| EDN2 | 4.9833096 | <0.001 | 0.003 |
| WFDC12 | 6.6251082 | <0.001 | 0.044 |

**Supplementary Table 3:** Gene Set Enrichment Analysis showing pathways upregulated in the clinical benefit and the no clinical benefit cohort.

|  |  |  |
| --- | --- | --- |
| **Pathways** | **NES** | ***q*-value** |
| **Clinical Benefit**  |
| Apical surface | 1.67 | 0.009 |
| KRAS*-*downregulated pathways | 1.68 | 0.017 |
| **No Clinical Benefit**  |
| TNF-α Signaling via NFKB  | 2.01 | 0.001 |
| MTORC1 Pathway | 1.89 | 0.002 |
| Glycolysis  | 1.75 | 0.004 |
| Reactive Oxygen Species  | 1.75 | 0.005 |
| Protein Secretion  | 1.65 | 0.013 |
| *P53* Signaling | 1.59 | 0.020 |
| IL6-JAK-STAT3 Signaling | 1.56 | 0.021 |
| TGF-β Signaling  | 1.52 | 0.027 |
| MYC Targets\_V1 Pathway  | 1.51 | 0.028 |
| Interferon-γ Response | 1.49 | 0.030 |
| Inflammatory Response | 1.42 | 0.037 |
| Myogenesis | 1.44 | 0.038 |
| Epithelial-Mesenchymal Transition | 1.43 | 0.039 |
| Interferon-α Response | 1.38 | 0.048 |
| Apoptosis | 1.37 | 0.048 |
| Heme Metabolism | 1.38 | 0.049 |
| Adipogenesis | 1.31 | 0.07 |