**Supplementary Table 1** Associations of combinations of genetic polymorphisms (allele carriers) with incidence of

glucocorticoid-induced grade 4 osteonecrosis

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **Full cohort**  **(N=189)** | **Intermediate/high risk arm only (N=88)** |
|  |  | ***P* Valuea** | ***P* Valuea** |
| *ACP1 (rs12714403)* | *GG vs. GA+AA* | 1.000 | 0.450 |
| *SH3YL1 (rs4241316)* | *TT vs. TC+CC* | 1.000 | 0.450 |
| *GRIK1 (rs2154490)* | *GG vs. GA+AA* | 0.768 | 1.000 |
| *GRIN3A (rs10989692)* | *GG vs. GA+AA* | 0.480 | 0.239 |

a*P* Values were computed by Fisher exact test

**Supplementary Table 2** Odds ratios (95% CI) of glucocorticoid-induced grade 4 osteonecrosis by genotype in intermediate/high risk arm only

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **OR (95%CI)** | ***P* Valuea** |
| *ACP1 (rs12714403)* | *GG vs.GA vs. AA* | 2.21 (0.21-23.20) | 0.508 |
|  |  |  |  |
|  | *GG vs. GA+AA* | 2.21 (0.21-23.20) | 0.508 |
|  |  |  |  |
| *SH3YL1(rs4241316)* | *TT vs. TC vs. CC* | 2.21 (0.21-23.20) | 0.508 |
|  |  |  |  |
|  | *TT vs. TC+CC* | 2.21 (0.21-23.20) | 0.508 |
|  |  |  |  |
| *GRIK1 (rs2154490)* | *GG vs.GA vs. AA* | 0.92 (0.29-2.89) | 0.897 |
|  |  |  |  |
|  | *GG vs. GA+AA* | 1.08 (0.29-3.95) | 0.904 |
|  |  |  |  |
| *GRIN3A (rs10989692)* | *GG vs.GA vs. AA* | 2.32 (0.78-6.86) | 0.128 |
|  |  |  |  |
|  | *GG vs. GA+AA* | 2.38 (0.62-9.11) | 0.204 |
|  |  |  |  |

OR= Odds Ratio CI=Confidence Interval

a*P* Values were computed by univariate logistic regression

**Supplementary Table 3**Time (in weeks) to occurrence of glucocorticoid-induced grade 4 osteonecrosis by genotype in intermediate/high risk arm only

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **N** | **Mean** | **95% CI** | ***P* Valuea** |
| *ACP1 (rs12714403)* | *GG vs.GA* | GG | 84 | 84.06 | 79.54 -88.57 |  |
|  |  | *GA* | 4 | 82.50 | 66.89-98.10 | 0.318 |
| *SH3YL1(rs4241316) (rs4241316) (rs4241316)* | *TT vs. TC* | TT | 84 | 84.06 | 79.54 -88.57 |  |
|  |  | *TC* | 4 | 82.50 | 66.89-98.10 | 0.318 |
| *GRIK1 (rs2154490)* | *GG vs.GA vs. AA* | GG | 60 | 82.18 | 76.68-87.68 |  |
|  |  | GA | 25 | 86.400 | 78.89-93.90 |  |
|  |  | AA | 3 | 100.00 | 100.00-100.00 | 0.306 |
|  | *GG vs. (GA+AA)* | *GA+AA* | 28 | 87.85 | 80.98-94.72 | 0.328 |
| *GRIN3A (rs10989692) (rs10989692)(rs10989692) (rs10989692) (rs10989692)(rs10989692) (rs10989692)* | *GG vs.GA vs. AA* | GG | 70 | 85.90 | 81.22-90.58 |  |
|  |  | GA | 15 | 76.60 | 66.46-86.73 |  |
|  |  | AA | 2 | 64.50 | 0.00-134.08 | 0.152 |
|  | *GG vs. (GA+AA)* | *GA+AA* | 17 | 75.17 | 64.28-86.06 | **0.054** |

CI=Confidence Interval

a*P* Values were computed by Log-rank test

**Supplementary Table 4** Dexamethasone (mg/m2) cumulative dose to glucocorticoid-induced grade 4 osteonecrosis by genotype in intermediate/high risk arm only

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **N** | **Mean** | **95% CI** | ***P* Valuea** |
| *ACP1 (rs12714403)* | *GG vs.GA* | GG | 84 | 1305.31 | 1232.74-1377.87 |  |
|  |  | *GA* | 4 | 1211.50 | 804.328-1618.672 | 0.276 |
| *SH3YL1(rs4241316) (rs4241316) (rs4241316)* | *TT vs. TC* | TT | 84 | 1305.31 | 1232.74-1377.87 |  |
|  |  | *TC* | 4 | 1211.50 | 804.328-1618.672 | 0.276 |
| *GRIK1 (rs2154490)* | *GG vs.GA vs. AA* | GG | 60 | 1279.16 | 1192.04-1366.29 |  |
|  |  | GA | 25 | 1317.20 | 1183.27-1451.13 |  |
|  |  | AA | 3 | 1604.00 | 1604.00-1604.00 | 0.310 |
|  | *GG vs. (GA+AA)* | *GA+AA* | 28 | 1347.92 | 1224.01-1471.84 | 0.485 |
| *GRIN3A (rs10989692) (rs10989692)(rs10989692) (rs10989692) (rs10989692)(rs10989692) (rs10989692)* | *GG vs.GA vs. AA* | GG | 70 | 1341.14 | 1264.17-1418.11 |  |
|  |  | GA | 15 | 1129.33 | 979.98-1278.68 |  |
|  |  | AA | 2 | 1034.00 | 0.00-2151.20 | **0.039** |
|  | *GG vs. (GA+AA)* | *GA+AA* | 17 | 1118.11 | 954.94-1281.29 | **0.011** |

CI=Confidence Interval

a*P* Values were computed by Log-rank test

**Supplementary Table 5** Hazard Ratios (95% CI) of time (weeks) and Dexamethasone (mg/m2) cumulative dose to occurrence of glucocorticoid-induced grade 4 osteonecrosis by genotype in intermediate/high risk arm only

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Time (weeks) to osteonecrosis** | | **Dexamethasone cumulative dose (mg/m2) to osteonecrosis** | |
|  |  | **Risk** | **HR (95% CI)** | ***P* Value** | **HR (95% CI)** | ***P* Valuea** |
| *ACP1 (rs12714403)* | *GG (REF) vs.GA* | *GA* | 0.70 (0.25-1.92) | 0.492 | 0.66 (0.24-1.80) | 0.417 |
| *SH3YL1(rs4241316) (rs4241316) (rs4241316)* | *TT (REF) vs. TC* | *TC* | 0.70 (0.25-1.92) | 0.492 | 0.66 (0.24-1.80) | 0.417 |
| *GRIK1 (rs2154490)* | *GG (REF) vs.GA vs. AA* | GA | 1.54 (0.48-4.94) | 0.460 | 1.71 (0.53-5.46) | 0.365 |
|  |  | AA | 1.42 (0.43-4.73) | 0.560 | 1.64 (0.49-5.45) | 0.416 |
|  | *GG (REF) vs. (GA+AA)* | *GA+AA* | 1.13(0.72-1.77) | 0.583 | 1.11 (0.70-1.74) | 0.645 |
| *GRIN3A (rs10989692) (rs10989692)(rs10989692) (rs10989692) (rs10989692)(rs10989692) (rs10989692)* | *GG (REF) vs.GA vs. AA* | GA | 0.72 (0.17-2.94) | 0.651 | 0.77 (0.19-3.16) | 0.722 |
|  |  | AA | 0.99 (0.22-4.37) | 0.998 | 1.34 (0.30-5.92) | 0.694 |
|  | *GG (REF) vs. (GA+AA)* | *GA+AA* | 0.72 (0.42-1.23) | 0.235 | 0.60 (0.35-1.02) | **0.061** |

CI=Confidence Interval

a*P* Values were computed by cox regression

**Supplementary Figure 1** Cumulative incidence of glucocorticoid-induced grade 4 osteonecrosis in subjects treated with the intermediate/high risk arm by *GRIN3A* genotype with cumulative dexamethasone dose (*P*=0.039 by Log-rank test)

