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| Supplementary Table 1. Association between genotype and toxicity ≥ G3 |
| TS |
|  | N&V | Diarrhoea | Stomatitis | Granulocytes | Haemaglobin | Neuro |
| TS | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes |
| 2R/2R  | 30 | 7 | 36 | 1 | 36 | 1 | 22 | 14 | 37 | 0 | 36 | 1 |
|  | 81.1%64.8-92.0 | 18.9%8.0-35.1 | 97.3%85.8-99.9 | 2.7%0.07-14.16 | 97.3%85.84-99.93 | 2.7%0.06-14.16 | 61.1%43.5-76.9 | 38.9%23.1-56.5 | 100%90.5-100 | 0%0.0-9.5 | 97.3%85.8-99.9 | 2.7%0.07-14.2 |
| 2R/3R | 39 | 9 | 46 | 3 | 44 | 4 | 32 | 15 | 47 | 2 | 42 | 6 |
|  | 81.3%67.4-91.1 | 18.8%8.9-32.6 | 93.9%83.1-98.7 | 6.1%1.28-16.87 | 91.7%80.02-97.68 | 8.3%2.32-19.98 | 68.1%52.9-80.9 | 31.9%19.1-47.1 | 95.9%86.0-99.5 | 4.1%0.5—14.0 | 87.5%74.8-95.3 | 12.5%4.7-25.2 |
| 3R/3R | 32 | 3 | 34 | 1 | 35 | 0 | 19 | 13 | 32 | 3 | 34 | 1 |
|  | 91.4%76.9-98.2 | 8.6%1.8-23.1 | 97.1%85.1-99.9 | 2.9%0.07-14.92 | 100%90.0-100.0 | 0%0-0.1 | 59.4%40.6-76.3 | 40.6%23.7-59.4 | 91.4%76.9-98.2 | 8.6%1.8-23.1 | 97.1%85.1-99.9 | 2.90.07-14.9 |
|  | p=0.377 | p = 0.732 | p = 0.186 | p = 0.711 | p = 0.185 | p = 0.188 |
| 2R/2R | 30 | 7 | 36 | 1 | 36 | 1 | 22 | 14 | 37 | 0 | 36 | 1 |
|  | 81.1%64.8-92.0 | 18.9%8.0-35.1 | 97.3%85.8-99.9 | 2.7%0.07-14.16 | 97.3%85.84-99.93 | 2.7%0.06-14.16 | 61.1%43.5-76.9 | 38.9%23.1-56.5 | 100.0%90.5-100 | 0.0%0-9.5 | 97.3%85.8-99.9 | 2.7%0.06-14.2 |
| 2R/3R/3R/3R | 71 | 12 | 80 | 4 | 79 | 4 | 51 | 28 | 79 | 5 | 76 | 7 |
|  | 85.5%76.1-92.3 | 14.5%7.7-23.9 | 95.2%88.3-98.7 | 4.8%1.3-11.7 | 95.2%88.1-98.7 | 4.8%1.3-11.9 | 64.6%53.0-75.0 | 35.4%23.1-56.5 | 94.0%86.7-98.0 | 6.0%2.0-13.3 | 91.6%83.4-96.5 | 8.4%3.5-16.6 |
|  | p= 0.592 | p = 1.0 | p = 1.0 | p = 0.835 | p = 0.322 | p = 0.432 |
| GSTP1 rs1695 |
|  | N&V | Diarrhoea | Stomatitis | Granulocytes | Haemaglobin | Neuro |
|  | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | yes |
| A  | 59 | 13 | 69 | 3 | 70 | 2 | 44 | 22 | 69 | 3 | 67 | 5 |
|  | 81.9%71.1-90.0 | 18.1%10.0-28.9 | 95.8%88.3-99.1 | 4.2%0.9-11.7 | 97.2%90.3-99.7 | 2.8%0.3-9.7 | 66.7%54.0-77.8 | 33.3%22.2-46.0 | 95.8%88.3-99.1 | 4.2%0.9-11.7 | 93.1%84.5-97.7 | 6.9%2.3-15.5 |
| AG | 45 | 6 | 50 | 2 | 48 | 3 | 31 | 21 | 48 | 4 | 47 | 4 |
|  | 88.2%76.1-95.6 | 11.8%4.4-23.9 | 96.2%86.8-99.5 | 3.8%0.5-13.2 | 94.1%83.8-98.8 | 5.9%1.2-16.2 | 59.6%45.1-73.0 | 40.4%27.0-55.0 | 92.3%81.5-97.9 | 7.7%2.1-18.5 | 92.2%81.1-97.8 | 7.8%2.2-18.9 |
| G | 5 | 1 | 6 | 0 | 6 | 0 | 79 | 45 | 6 | 0 | 6 | 0 |
|  | 83.3%35.9-99.6 | 16.7%0.4-64.1 | 100.0%54.1-100 | 0.0%0-45.9 | 100.0%54.1-100 | 0.0%0-45.9 | 66.7%22.3-95.7 | 33.3%4.3-77.7 | 100.0%54.1-100.0 | 0.0%0.0-45.9 | 100.0%54.1-100 | 0.0%0.0-45.9 |
|  | p = 0.582 | p = 1.0 | p = 0.724 | p = 0.740 | p = 0.609 | p = 1.0 |
| OPRT |
|  | N&V | Diarrhoea | Stomatitis | Granulocytes | Haemaglobin | Neuro |
|  | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | yes |
| C | 3 | 2 | 4 | 1 | 5 | 0 | 2 | 3 | 5 | 0 | 4 | 1 |
|  | 60%14.7-94.7 | 40%5.3-85.3 | 80%28.4-99.5 | 20%20.00.5-71.6 | 100%47.8-100.0 | 0%0.0-52.18 | 40%5.3-85.3 | 60%14.7-94.7 | 100%47.8-100.0 | 0%0.0-52.18 | 80%28.4-99.5 | 20%0.5-71.6 |
| GC | 30 | 5 | 33 | 2 | 33 | 2 | 24 | 9 | 34 | 1 | 34 | 1 |
|  | 85.7%69.7-95.2 | 14.3%4.8-30.3 | 94.3%80.8-99.3 | 5.70.7-19.2 | 94.3%80.8-99.3 | 5.7%0.7-19.2 | 72.7%54.5-86.7 | 27.3%13.3-45.5 | 97.1%85.1-99.9 | 2.9%0.07-14.92 | 97.1%85.1-99.9 | 2.9%0.1-14.9 |
| G | 76 | 13 | 88 | 2 | 86 | 3 | 53 | 33 | 84 | 6 | 82 | 7 |
|  | 85.4%76.3-92.0 | 14.6%8.0-23.7 | 97.8%92.2—99.7 | 2.2%0.3-7.8 | 96.6%90.5-99.3 | 3.4%0.7-9.5 | 61.6%50.5-71.9 | 38.4%28.1-49.5 | 93.3%86.1-97.5 | 6.7%2.5-13.9 | 92.1%84.5-96.8 | 7.9%3.2-15.5 |
|  | p = 0.283 | p = 0.082 | p = 0.690 | p = 0.303 | p = 0.752 | p = 0.237 |
| DPYD2A IVS14+1G>A |
|  | N&V | Diarrhoea | Stomatitis | Granulocytes | Haemaglobin | Neuro |
|  | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes |
| G | 108 | 19 | 124 | 4 | 122 | 5 | 79 | 41 | 122 | 6 | 118 | 9 |
|  | 85.0%77.6-90.7 | 15.0%9.3-22.4 | 96.9%92.2-99.1 | 3.1% | 96.1%91.1-98.7 | 3.9%1.3-8.9 | 64.8%55.6-73.2 | 35.2%26.8-44.4 | 95.3%90.1-98.3 | 4.7%1.7-9.9 | 92.9%87.0-96.7 | 7.1%3.3-13.0 |
| GA | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 0 |
|  | 0.0%0-97.5 | 100.0%2.5-1.0 | 0.0%0.0-97.5 | 100.0%2.5-100.0 | 100.0%2.5-100.0 | 0.0%0-97.5 | 0.0%0.0-97.5 | 100.0%2.5-100.0 | 100.0%2.5-100.0 | 0.0%0.0-97.5 | 100.0%2.5-100.0 | 0.0%0.0-97.5 |
|  | p = 0.156 | p = 0.039 | p = 1.0 | p = 0.358 | p = 1.0 | p = 1.0 |
| DPYD rs1801159 |
|  | N&V | Diarrhoea | Stomatitis | Granulocytes | Haemaglobin | Neuro |
|  | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes |
| A | 78 | 15 | 90 | 4 | 91 | 2 | 61 | 28 | 90 | 4 | 87 | 6 |
|  | 83.9%74.8-90.7 | 16.1%9.3-25.2 | 95.7%89.5-98.8 | 4.3%1.2-10.5 | 97.8%92.4-99.7 | 2.2%0.3-7.6 | 68.5%57.8-78.0 | 31.5%22.0-42.2 | 95.7%89.5-98.8 | 4.3%1.2-10.5 | 93.5%86.5-97.6 | 6.5%2.4-13.5 |
| AG | 23 | 3 | 25 | 1 | 24 | 2 | 13 | 12 | 25 | 1 | 24 | 2 |
|  | 88.5%69.8-97.6 | 11.5%2.4-30.2 | 96.2%80.4-99.9 | 3.8%0.09-19.6 | 92.3%74.9—99.1 | 7.7%0.9-25.1 | 52.0%31.3-72.2 | 48.0%27.8-68.7 | 96.2%80.4-99.9 | 3.8%0.09-19.6 | 92.3%74.9-99.1 | 7.7%0.9-25.1 |
| G | 7 | 2 | 9 | 0 | 123 | 5 | 5 | 4 | 8 | 1 | 119 | 9 |
|  | 77.8%40.0-97.2 | 22.2%2.8-60.0 | 100.0%66.3-100.0 | 0.0%0.0-33.6 | 96.1%51.8-99.7 | 3.9%0.2-48.2 | 55.6%21.2-86.3 | 44.4%13.7-78.8 | 88.9%51.8-99.7 | 11.1%0.2-48.2 | 88.9%51.8-99.7 | 11.1%0.2-48.2 |
|  | p = 0.698 | p = 1.0 | p = 0.143 | p = 0.264 | p = 0.432 | p = 0.700 |
| ERCC1 rs11615 |
|  | N&V | Diarrhoea | Stomatitis | Granulocytes | Haemaglobin | Neuro |
|  | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes |
| C | 16 | 2 | 18 | 1 | 18 | 0 | 10 | 9 | 16 | 3 | 16 | 2 |
|  | 88.9%65.3-98.6 | 11.1%1.4-34.7 | 94.7%74.0-99.9 | 5.3%0.1-26.0 | 100.0%81.5-100 | 0.0%0.0-18.5 | 52.6%28.9-75.6 | 47.4%24.5-71.1 | 84.2%60.4-96.6 | 15.8%3.4-39.6 | 88.9%65.3-98.6 | 11.1%1.4-43.7 |
| CT | 57 | 12 | 65 | 4 | 67 | 2 | 46 | 19 | 67 | 2 | 65 | 4 |
|  | 82.6%71.6-90.7 | 17.4%9.3-28.4 | 94.2%85.8-98.4 | 5.8%1.6-14.2 | 97.1%89.92-99.65 | 2.9%0.4-10.1 | 70.8%58.2-81.4 | 29.2%18.6-41.8 | 97.1%89.9-99.6 | 2.9%0.4-10.0 | 94.2%85.8-98.4 | 5.8%1.6-14.2 |
| T | 36 | 6 | 42 | 0 | 39 | 3 | 23 | 17 | 40 | 2 | 39 | 3 |
|  | 85.7%71.5-94.6 | 14.3%5.4-28.5 | 100.0%91.6-100.0 | 0.0%0-8.4 | 92.9%80.5-98.5 | 7.1%1.5-19.5 | 57.5%40.9-73.0 | 42.5%27.0-59.1 | 95.2%83.8-99.4 | 4.80.6-16.2 | 92.9%80.5-98.5 | 7.1%1.5-19.5 |
|  | p = 0.839 | p = 0.282 | p = 0.428 | p = 0.216 | p = 0.101 | p = 0.711 |
| C  | 16 | 2 | 18 | 1 | 18 | 0 | 10 | 9 | 16 | 3 | 16 | 2 |
|  | 88.9%65.3-98.6 | 11.1%1.4-34.7 | 94.7%74.0-99.9 | 5.3%0.1-26.0 | 100.0%81.5-100 | 0.0%0.0-18.5 | 52.6%28.9-75.6 | 47.4%24.5-71.1 | 84.2%60.4-96.6 | 15.8%3.4-39.6 | 88.9%65.3-98.6 | 11.1%1.4-43.7 |
| CT + T | 93 | 18 | 107 | 4 | 106 | 5 | 69 | 36 | 107 | 4 | 104 | 7 |
|  | 83.8% | 16.2% | 96.4% | 3.6% | 95.5% | 4.5% | 65.7% | 34.3% | 96.4% | 3.6% | 93.7% | 6.3% |
|  | p = 0.737 | p = 0.552 | p = 1.0 | p = 0.306 | p = 0.064 | p = 0.612 |
| ERCC1 rs3212986 |
|  | N&V | Diarrhoea | Stomatitis | Granulocytes | Haemaglobin | Neuro |
| G | 51 | 8 | 59 | 0 | 55 | 4 | 33 | 22 | 57 | 2 | 57 | 2 |
|  | 86.4%75.0-94.0 | 13.6%6.0-25.0 | 100.0%93.9-100 | 0.0%0.0-6.0 | 93.2%83.5-98.1 | 6.8%1.9-16.5 | 60.0%45.9-73.0 | 40.0%27.0-54.1 | 96.6%88.3-99.6 | 3.4%0.4-11.7 | 96.6%88.3-99.6 | 3.4%0.4-11.7 |
| GT | 50 | 12 | 58 | 5 | 61 | 1 | 41 | 20 | 59 | 4 | 56 | 6 |
|  | 80.6%68.6-89.6 | 19.4%10.4-31.4 | 92.1%82.4-97.4 | 7.9%2.6-17.6 | 98.4%91.3-100.0 | 1.6%0.04-8.7 | 67.2%54.0-78.7 | 32.8%21.3-46.0 | 93.7%84.5-98.2 | 6.3%1.8-15.5 | 90.3%80.1-96.4 | 9.7%3.6-19.9 |
| T | 7 | 0 | 7 | 0 | 7 | 0 | 5 | 2 | 7 | 0 | 6 | 1 |
|  | 100.0%59.0-100.0 | 0.0%0.0-41.0 | 100.0%59.0-100.0 | 0.0%0.0-41.0 | 100.0%59.0-100.0 | 0.0%0.0-41.0 | 71.4%29.0-96.3 | 28.6%3.7-71.0 | 100.0%59.0-100.0 | 0.0%0.0-41.0 | 85.7%42.1-99.6 | 14.3%0.4-57.9 |
|  | p = 0.438 | p = 0.094 | p = 0.399 | p = 0.676 | p = 0.773 | p = 0.221 |
| ERCC2 rs13181 |
|  | N&V | Diarrhoea | Stomatitis | Granulocytes | Haemaglobin | Neuro |
| G | 19 | 4 | 22 | 1 | 22 | 1 | 14 | 8 | 20 | 3 | 23 | 0 |
|  | 82.6%61.2-95.0 | 17.4%5.0-38.8 | 95.7%78.1-99.9 | 4.3%0.1-21.9 | 95.7%78.1-99.9 | 4.3%0.1-21.9 | 63.6%40.7-82.8 | 36.4%17.2-59.3 | 87.0%66.4-97.2 | 13.0%2.8-33.6 | 100.0%85.2-100.0 | 0.0%0.0-14.8 |
| GT | 50 | 8 | 56 | 3 | 56 | 2 | 38 | 17 | 56 | 3 | 53 | 5 |
|  | 86.2%74.6-93.9 | 13.8%6.1-25.4 | 94.9%85.9-98.9 | 5.1%1.1-14.1 | 96.6%88.1-99.6 | 3.4%0.4-11.9 | 69.1%55.2-80.9 | 30.9%19.1-44.8 | 94.9%85.9-98.9 | 5.1%1.1-14.1 | 91.4%81.0-97.1 | 8.6%2.9-19.0 |
| T | 40 | 8 | 47 | 1 | 46 | 2 | 27 | 20 | 47 | 1 | 44 | 4 |
|  | 83.3%69.8-92.5 | 16.7%7.5-30.2 | 97.9%88.9-99.9 | 2.1%0.1-11.1 | 95.8%85.7-99.5 | 4.2%0.5-14.3 | 57.4%42.2-71.7 | 42.6%28.3-57.8 | 97.9%88.9-99.9 | 2.1%0.1-11.1 | 91.7%80.0-97.7 | 8.3%2.3-20.0 |
|  | p = 0.853 | p = 0.717 | p = 1.0 | p = 0.483 | p = 0.155 | p = 0.433 |
| XRCC1 rs25487 |
|  | N&V | Diarrhoea | Stomatitis | Granulocytes | Haemaglobin | Neuro |
|  | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes |
| A | 17 | 1 | 18 | 0 | 18 | 0 | 10 | 8 | 17 | 1 | 17 | 1 |
|  | 94.4%72.7-99.9 | 5.6%0.1-27.3 | 100.0%81.5-100.0 | 0.0%0.0-18.5 | 100.0%81.5-100.0 | 0.0%0.0-18.5 | 55.6%30.8-78.5 | 44.4%21.5-69.2 | 94.4%72.7-99.9 | 5.6%0.1-27.3 | 94.4%72.7-99.9 | 5.6%0.1-27.3 |
| AG | 45 | 10 | 52 | 4 | 51 | 4 | 35 | 19 | 55 | 1 | 49 | 6 |
|  | 81.8%69.1-90.9 | 18.2%9.1-30.9 | 92.9%82.7-98.0 | 7.1%2.0-17.3 | 92.7%82.4-98.0 | 7.3%2.0-17.6 | 64.8%50.6-77.3 | 35.2%22.7-49.4 | 98.2%90.4-100.0 | 1.8%0.0-9.6 | 89.1%77.8-95.9 | 10.9%4.1-22.2 |
| G | 46 | 9 | 54 | 1 | 54 | 1 | 34 | 17 | 51 | 4 | 53 | 2 |
|  | 83.6%71.2-92.2 | 16.4%7.8-28.8 | 98.2%90.3-100.0 | 1.8%0.1-9.7 | 98.2%90.3-100.0 | 1.8%0.05-9.7 | 66.7%52.1-79.2 | 33.3%20.8-47.9 | 92.7%82.4-98.0 | 7.3%2.0-17.6 | 96.4%87.5-99.6 | 3.6%0.3-8.7 |
|  | p = 0.505 | p = 0.358 | p = 0.359 | p = 0.691 | p = 0.300 | p = 0.367 |