|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 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 | 2.9  0.07-14.9 |
|  | 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%  20.0  0.5-71.6 | 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 | | 5.7  0.7-19.2 | 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 | 4.8  0.6-16.2 | 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 | |