*HLA-B\*38:02:01* Predicts Carbimazole/Methimazole-Induced Agranulocytosis

Table and Figures

Table 1. Association of rs185386680/ HLA-B\*380201 with ATD-induced agranulocytosis.

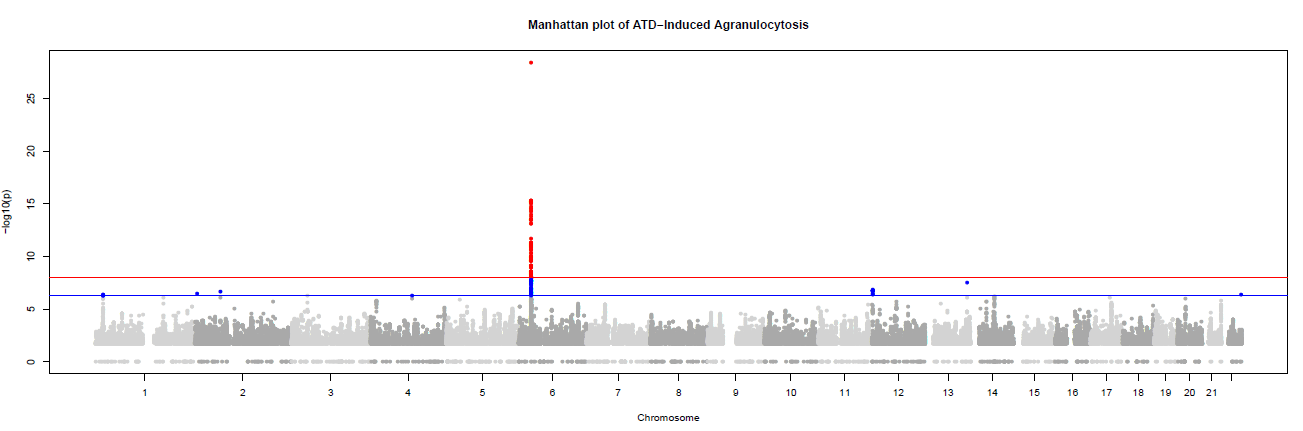
|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Marker |  | Sample size | | MAF | | OR | 95% CI | P-value |
|  | Case | Control | Case | Control |
| ATD-induced agranulocytosis | rs185386680 | Discovery\* | 20 | 775 | 37.50% | 3.80% | 36.4 | 12.8-103.7 | 1.3x10-24 |
| rs185386680 | Replication\* | 4 | 387 | 37.50% | 3.70% | 37 | 3.7-367.4 | 9.6x10-7 |
| rs185386680/ HLA-B\*380201 | Validation\*\* | 24 | 75 | 37.50% | 2.70% | 53.2 | 13.6-208.9 | 9.0x10-13 |
| CMZ/MMI-induced agranulocytosis | rs185386680/ HLA-B\*380201 | Validation\*\* | 19 | 59 | 47.40% | 3.20% | 265.5 | 27.87-2528.0 | 2.5x10-14 |
| PTU-induced agranulocytosis | rs185386680/ HLA-B\*380201 | Validation\*\* | 5 | 16 | 0% | 0% | NA | NA | NA |

\*versus healthy control

\*\*versus ATD-tolerant control

Abbreviation: ATD, anti-thyroid drug; CMZ, carbimazole; MMI, methimazole; PTU, propylthiouracil; MAF: minor allele frequency; OR: odds ratio; CI, confidence interval.

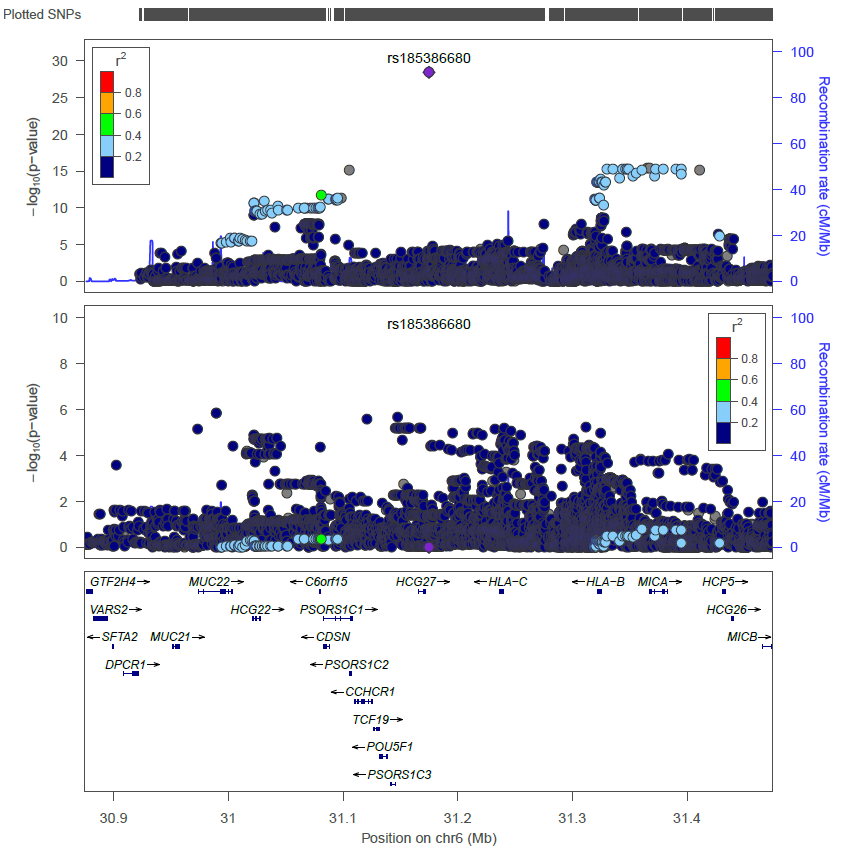
Figure 1. Manhattan plot of the GWAS of ATD-induced agranulocytosis.



-log10 P values on the y axis plotted against ascending physical position on the x axis. The dotted red line represents the genomewide

significance threshold P values 1x10-8.

Figure 2. Regional association plot of the region +/- 300kb of rs185386680.



The upper panel shows the original regional association plot; the middle panel shows the regional association plot after conditioning on the genotype of rs185386680; the lower panel indicates the physical location and location of genes in the region.

Figure 3. Flow diagram for calculating numbers needed to screen to prevent one CMZ/MMI-induced agranulocytosis.

