**SUPPLEMENTARY MATERIAL**

**Potential association of *CYPs, COMT, DRD2, 5HTR2A* polymorphisms, and susceptibility to the adverse effect of aripiprazole: preliminary observations.**

***Bartosiewicz et al.***

*DNA extraction and genotyping*

DNA was extracted from whole blood (200 µl) using the nucleic acid isolation kit (GeneMATRIX QUICK BLOOD DNA Purification Kit, Eurx, Poland), according to the manufacturer's protocol. The quality was assessed by agarose gel electrophoresis and quantity was determined spectrophotometrically in a NanoDrop One (Thermo Scientific). Additionally, fluorometric DNA quantification was carried out using a Qubit dsDNA BR assay kit (Invitrogen, Thermo Scientific) and Invitrogen Qubit™ 3.0 Fluorometer (Thermo Scientific) following the manufacturer's protocol.

All patients were genotyped for 71 SNPs/INDELs across 21 genes, plus 5 CNV targets in *CYP2D6* included in the Agena VeriDose Core panel and hybrid *CYP2D6* alleles included in the Agena VeriDose CYP2D6 CNV Panel using MassArray® System (Agena Bioscience). Moreover, three polymorphisms (rs6311, rs6313, and rs6314) in the *5-HTR2A* gene were analyzed using the PCR-RFLP method.

**Table S1** Primers and conditions of PCR-RFLP analysis.

| **Primers** | **Annealing temperature** | **Restriction enzyme (Digestion temperature)** | **Genotype/ Length of products (bp)** |
|---|---|---|---|
| ***5HTR2A* rs6311** | | | |
| F: 5′- CTAGCCACCCTGAGCCTATG -3′<br>R: 5′- ATCATTCACGAGCCCCTCAA -3′ | 55°C | *Msp*I (37°C) | *GG* - 396, 81<br>*GA* – 477, 396, 81<br>*AA* - 477 |
| ***5HTR2A* rs6313** | | | |
| F: 5′- AGCAGAAACTATAACCTGTT -3′<br>R: 5′ - CAAGTGACATCAGGAAATAG -3′ | 55°C | *Msp*I (37°C) | *CC* - 247, 163<br>*CT* – 410, 247, 163<br>*TT* - 410 |
| ***5HTR2A* rs6314** | | | |
| F: 5′- TGAACACAATACCGGCTTTGG -3′<br>R: 5′ - AGCCTATCACACACAGCTCA -3′ | 57°C | *Mva1269*I (37°C) | *CC* - 122, 69<br>*CT* – 191, 122, 69<br>*TT* - 191 |

**Table S2** List of all analyzed genes and polymorphisms.

| Gene | Variant | Nucleotide change | Type of variant | Amino acid changes/star allele | Functional consequence |
|---|---|---|---|---|---|
| *ABCB1* | rs1045642 | c.3435C>T | Synonymous | No | Decreased activity |
| *APOE* | rs429358 | c.388T>C | Missense | Cys130Arg | E3 isoform – normal lipoprotein metabolism<br>E2 and E4 isoforms – abnormal lipoprotein metabolism |
| | rs7412 | c.526C>T | Missense | Arg176Cys | |
| *COMT* | rs4680 | c.472G>A | Missense | Val158Met | The *A* (Met) variant - lower thermostability and activity of the enzyme. |
| *CYP1A2* | rs2069514 | g.-3860G>A | 5'UTR | Located in the enhancer region. | Decreased enzymatic activity |
| | rs762551 | g.-163C>A | Intron | No | Altered enzymatic activity. |
| | rs12720461 | g.-729C>T | Intron | | Decreased enzymatic activity. |
| | rs56107638 | g.3533G>A | Splice donor | Located in intron 6. Splicing defect. | Decreased enzymatic activity. |
| | rs72547513 | g.558C>A | missense | Phe186Leu | Decreased enzymatic activity. |
| *CYP2B6* | rs3745274 | c.516G>A | Missense | Gln172His | Decreased function. |
| | rs28399499 | c.983T>C | Missense | Ile328Thr | No function. |
| *CYP2C19* | rs4244285 | c.681G>A | Synonymous | Splice defect | No function |
| | rs4986893 | c.636G>A | Stop codon | Trp212Stop | No function |
| | rs28399504 | c.1A>G | Missense | Located in the start codon. Met1Val | No function |
| | rs56337013 | c.1297C>T | Missense | Arg433Trp | No function |
| | rs72552267 | c.395G>A | Missense | Arg132Gln | No function |
| | rs72558186 | g.19294T>A | Splice donor | splice defect | No function |
| | rs41291556 | c.358T>C | Missense | Trp120Arg | No function |
| | rs12248560 | g.-806C>T | 5' Flanking region | Increased expression | Increased function |
| *CYP2C9* | rs1799853 | c.430C>T | Missense | Arg144Cys | Decreased function. |
| | rs1057910 | c.1075A>C | Missense | Ile359Leu | No function |
| | rs56165452 | c. 1076T>C | Missense | Ile359Thr | Decreased function. |
| | rs28371686 | c.1080C>G | Missense | Asp360Glu | Decreased function. |
| | rs9332131 | c.818delA | Frameshift | Lys273fs | No function |
| | rs7900194 | c.449G>A | Missense | Arg150His | Decreased function. |
| | rs28371685 | c.1003C>T | Missense | Arg335Trp | Decreased function. |
| | rs9332239 | c.1465C>T | Missense | Pro489Ser | Decreased function. |
| | rs72558187 | c.269T>C | Missense | Leu90Pro | No function |
| | rs72558190 | c.485C>A | Missense | Ser162Stop | No function |
| **Gene** | **Variant** | **Nucleotide change** | **Type of variant** | **Amino acid changes/star allele** | **Functional consequence** |
| *CYP2D6* | rs16947 | g.2850C>T | Missense | Arg296Cys | Normal function |
| | rs1135840 | g.4180G>C | Missense | Ser486Thr | Normal function |

| | | | | | |
|---|---|---|---|---|---|
| | rs35742686 | g.2549delA | Frameshift | Arg259fs | No function |
| | rs3892097 | g.1846G>A | Splice acceptor | splice defect | No function |
| | rs5030655 | g.1707delT | Frameshift | Trp152fs | No function |
| | rs5030867 | g.2935A>C | Missense | His324Pro | No function |
| | rs5030865 | g.1758G>T | Stop gained | Gly169Stop | No function |
| | rs5030656 | g.2613_2615delAGA (g.2615_2617delAAG) | Inframe deletion | Lys281del | Decreased function |
| | rs1065852 | g.100C>T | Missense | Pro34Ser | Decreased function |
| | rs201377835 rs5030863 | c.883G>C | Splice acceptor | splice defect | No function |
| | rs5030862 | g.124G>A | Missense | Gly42Arg | No function |
| | rs5030865 | g.1758G>A | Stop gained | Gly169Arg | Decreased function |
| | rs72549357 | g.137-138insT | Frameshift | Leu47fs | No function |
| | rs28371706 | g.1023C>T | Missense | Thr107Ile | Decreased function |
| | dup4125_4133 | 4135_4136insTGCCCACTG | Insertion | *18 | No function |
| | rs72549353 | c.2539_2542delAACT | Frameshift | Thr256fs | No function |
| | rs72549354 | c.1973_1974insG | Frameshift | Leu213fs | No function |
| | rs59421388 | g 3183G>A | Missense | Val338Met | Decreased function |
| | rs28371725 | g.2988G>A | Intron | splice defect | Decreased function |
| *CYP3A4* | rs55785340 | c.664T>C | Missense | Ser222Pro | Function not assigned. |
| | rs4987161 | c.566 T>C | Missense | Phe189Ser | Function not assigned. |
| | rs35599367 | g.15389C>T | Intron | splice defect | Function not assigned. |
| *CYP3A5* | rs28365083 | g.27289C>A | Missense | Thr398Asn | No function. |
| | rs776746 | g.6986A>G | Splice acceptor | splice defect | No function. |
| | rs10264272 | c.624G>A | Synonymous | splice defect | No function. |
| | rs41303343 | g.27131_27132insT | Frameshift | Thr346fs | No function. |
| *DRD2* | rs1800497 | c.2137G>A | Missense | Glu>Lys | Decreased activity |
| *F2* | rs1799963 | c.*97G>A | 3`UTR | 3`-UTR | ↑ risk of venous thrombosis |
| *F5* | rs6025 | c.1601G>A | Missense | | ↑ risk of venous thrombosis |
| *GLP1R* | rs1042044 | c.780A>C/T | Missense | Leu260Phe | No function. |
| | rs6923761 | c.502G>A/C | Missense | | No function. |
| | rs2300615 | c.510-1135T>G | | | No function. |

| Gene | Variant | Nucleotide change | Type of variant | Amino acid changes/star allele | Functional consequence |
|---|---|---|---|---|---|
| *5HTR2A* | rs6311 | -1438G>A | Promoter region | | *A* allele - greater promoter activity, *AA* genotype - higher receptor density. |
| | rs6313 | 102C>T | Synonymous | p.Ser34= | Probably affect mRNA secondary structure. The *C* allele is less transcriptionally active due to methylation. |
| | rs6314 | 1354C>T | Missense | His452Tyr | The *T* (Tyr) variant would decrease the receptor's ability to activate C and D phospholipase. |
| *MTHFR* | rs1801133 | c.665C>T | Missense | Ala222Val | rs1801133 |
| | rs1801131 | c.1286A>C | Missense | Glu429Ala | Decreased activity. |
| *OPRM1* | rs1799971 | c.118A>G | Missense | Asn44Asp | Worse response to opioids |
| *PNPLA5* | rs5764010 | c.608-169G>A | | | |
| *SLCO1B1* | rs4149056 | c.521T>C | Missense | Val174Ala | No function |
| *SULT4A1* | rs763120 | c.743-374A>G | | | Related with metabolism of monoamines |
| *VKORC1* | rs9923231 | c.-1639G>A | Promoter region | | Decreased expression |

**Table S3** Demographic and clinical parameters of studied groups and subgroups.

| Group | | N (%) | Age (y) | Weight (kg) | Height (m) | BMI (kg/m$^2$) | ARI dose [mg] | Duration of ARI therapy (N/y) | Adverse drug effects |
|---|---|---|---|---|---|---|---|---|---|
| **WR** (ARI subgroup) | All | 13 (100) | 36.50 (± 10.08) | 81.45 (±24.93) | 1.70 (± 0.11) | 24.68 (± 9.92) | Oral/2.5-30/day LAI/Once-monthly/400 | 9/ >1<br>3/ <1 | not observed<br>ARI monotherapy |
| | Males | 7 (54) | | | | | | | |
| | Females | 6 (46) | | | | | | | |
| **WR** (ARI+SGA subgroup) | All | 51 (100) | 35.86 (± 10.19) | 83.01 (±15.40) | 1.74 (± 0.10) | 27.35 (±4.98) | Oral/7.5-30/day LAI/Once-monthly/400 | 19/ >1<br>32/ <1 | not observed<br>ARI in combination with other SGAs |
| | Males | 34 (67) | | | | | | | |
| | Females | 17 (33) | | | | | | | |
| **BR** | All | 10 (100) | 35.30 (± 12.54) | 74.85 (± 20.01) | 1.69 (± 0.10) | 25.95 (± 4.71) | Oral/3.75-30/day LAI/Once-monthly/400 | 5/ >1<br>5/ <1 | observed ADE<br>ARI was switched to another SGAs |
| | Males | 6 (60) | | | | | | | |
| | Females | 4 (40) | | | | | | | |
| | | | **p = 0.964** | **p = 0.549** | **p = 0.275** | **p = 0.709** | | | |

N – number, y – year
ADE - adverse drug effects (agitation, anxiety, somnolence, hypertension, akathisia, increased sleep latency, weight gain, reduced motor activity, concentration difficulties).
ARI subgroup – aripiprazole monotherapy
ARI+SGA subgroup - aripiprazole with other antipsychotic drugs
BMI – body mass index
BR – badly reacting group (aripiprazole has been replaced by another drug due to adverse effects)
LAI - long-acting injection
SGA - second-generation antipsychotic
WR – well-reacting group (the sum of ARI and ARI+SGA subgroups)

**Table S4** Genotype/haplotype/phenotype frequencies of all analyzed polymorphisms.

| Gene/variants | Genotypes/ Haplotypes/ Phenotypes | Frequency (%) | | | |
|---|---|---|---|---|---|
| | | Total | BR | WR | |
| | | | | ARI | ARI+SGA |
| *ABCB1* | *G/G* | 26.4 | 30.0 | 23.1 | 26.5 |
| | *G/A* | 45.8 | 70.0 | 53.8 | 38.8 |
| | *A/A* | 27.8 | 0.0 | 23.1 | 34.7 |
| *APOE* | *E2/E2* | 1.5 | 0.0 | 0.0 | 2.2 |
| | *E2/E3* | 16.9 | 14.3 | 8.3 | 19.6 |
| | *E2/E4* | 1.5 | 14.3 | 0.0 | 0.0 |
| | *E3/E3* | 61.5 | 42.9 | 75.0 | 60.9 |
| | *E3/4* | 18.5 | 28.6 | 16.7 | 17.4 |
| *COMT* | *G/G* | 29.6 | 44.4 | 23.1 | 28.6 |
| | *G/A* | 38.0 | 55.6 | 53.8 | 30.6 |
| | *A/A* | 32.4 | 0.0 | 23.1 | 40.8 |
| *CYP1A2* | UM | 53.0 | 77.8 | 61.5 | 45.5 |
| | NM | 47.0 | 22.2 | 38.5 | 54.5 |
| | **1F/*1F* | 50.0 | 66.7 | 61.5 | 43.2 |
| | **1A/*1F* | 40.9 | 33.3 | 30.8 | 45.4 |
| | **1A/*1A* | 9.1 | 0.0 | 7.7 | 11.4 |
| *CYP2B6* | **1/*1* | 56.2 | 77.8 | 46.2 | 54.9 |
| | **1/*6* | 35.6 | 22.2 | 46.2 | 35.3 |
| | **6/*6* | 8.2 | 0.0 | 7.7 | 9.8 |
| *CYP2C19* | UM | 4.4 | 0.0 | 16.7 | 2.1 |
| | NM | 67.6 | 66.7 | 66.7 | 68.1 |
| | IM | 25.0 | 33.3 | 16.7 | 25.5 |
| | PM | 2.9 | 0.0 | 0.0 | 4.3 |
| *CYP2C9* | **1/*1* | 70.6 | 55.6 | 69.2 | 73.9 |
| | **1/*2* | 17.6 | 11.1 | 15.4 | 19.6 |
| | **1/*3* | 10.3 | 22.2 | 15.4 | 6.5 |
| | **2/*2* | 1.5 | 11.1 | 0.0 | 0.0 |
| *CYP2D6* | UM | 12.9 | 25.0 | 0.0 | 13.6 |
| | NM | 41.9 | 62.5 | 30.0 | 40.9 |
| | IM | 43.5 | 12.5 | 70.0 | 43.2 |
| | PM | 1.6 | 0.0 | 0.0 | 2.3 |
| *CYP3A4/5* | NM | 8.8 | 11.1 | 0.0 | 10.6 |
| | IM | 83.8 | 77.8 | 100.0 | 80.9 |
| | PM | 7.4 | 11.1 | 0.0 | 8.5 |
| *DRD2* | *WT/WT* | 63.0 | 77.8 | 46.2 | 64.7 |
| | *WT/Taq1A* | 35.6 | 22.2 | 53.8 | 33.3 |
| | *Taq1A/Taq1A* | 1.4 | 0.0 | 0.0 | 2.0 |
| *F2* | *WT/WT* | 98.6 | 100.0 | 92.3 | 100.0 |
| | *WT/G20210A* | 1.4 | 0.0 | 7.7 | 0.0 |
| *F5* | *WT/WT* | 91.8 | 90.0 | 76.9 | 96.0 |
| | *WT/R5060Q* | 8.2 | 10.0 | 23.1 | 4.0 |
| *GLP1R (rs1042044)* | *A/A* | 18.1 | 22.2 | 0.0 | 21.6 |
| | *A/C* | 43.1 | 33.3 | 41.7 | 45.1 |
| | *C/C* | 38.9 | 44.4 | 58.3 | 33.3 |
| *GLP1R (rs2300615)* | *G/G* | 0.0 | 0.0 | 0.0 | 0.0 |
| | *G/T* | 44.4 | 33.3 | 75.0 | 39.2 |
| | *T/T* | 55.6 | 66.7 | 25.0 | 60.8 |
| *GLP1R (rs6923761)* | *A/A* | 10.1 | 11.1 | 8.3 | 10.4 |
| | *A/G* | 39.1 | 55.6 | 33.3 | 37.5 |
| | *G/G* | 50.7 | 33.3 | 58.3 | 52.1 |

| Gene/variants | Genotypes/ Haplotypes/ Phenotypes | Frequency (%) | | | |
|---|---|---|---|---|---|
| | | Total | BR | WR | |
| | | | | ARI | ARI |
| *5HTR2A (rs6311)* | *G/G* | 28.2 | 22.2 | 30.8 | 28.6 |
| | *G/A* | 53.5 | 33.3 | 46.2 | 59.2 |
| | *A/A* | 18.3 | 44.5 | 23.1 | 12.2 |
| *5HTR2A (rs6313)* | *C/C* | 33.0 | 33.3 | 30.8 | 32.7 |
| | *C/T* | 49.3 | 22.2 | 46.2 | 55.1 |
| | *T/T* | 18.3 | 44.5 | 23.1 | 12.2 |
| *5HTR2A (rs6314)* | *C/C* | 86.5 | 80.0 | 84.6 | 88.2 |
| | *C/T* | 10.8 | 20.0 | 15.4 | 7.8 |
| | *T/T* | 2.7 | 0.0 | 0.0 | 3.9 |
| *MTHFR (rs1801131)* | *T/T* | 53.4 | 55.6 | 30.8 | 58.8 |
| | *T/G* | 35.6 | 33.3 | 53.8 | 31.4 |
| | *G/G* | 11.0 | 11.1 | 15.4 | 9.8 |
| *MTHFR (rs1801133)* | *G/G* | 43.1 | 44.4 | 41.7 | 43.1 |
| | *G/A* | 40.3 | 33.3 | 41.7 | 41.2 |
| | *A/A* | 16.7 | 22.2 | 16.7 | 15.7 |
| *OPRM1* | *A/A* | 77.8 | 66.7 | 75.0 | 80.4 |
| | *A/G* | 22.2 | 33.3 | 25.0 | 19.6 |
| | *G/G* | 0.0 | 0.0 | 0.0 | 0.0 |
| *PNPLA5* | *C/C* | 89.0 | 70.0 | 84.6 | 94.0 |
| | *C/T* | 11.0 | 30.0 | 15.4 | 6.0 |
| | *T/T* | 0.0 | 0.0 | 0.0 | 0.0 |
| *SLCO1B1* | **1/*1* | 67.6 | 70.0 | 76.9 | 64.6 |
| | **1/*5* | 29.6 | 20.0 | 23.1 | 33.3 |
| | **5/*5* | 2.8 | 10.0 | 0.0 | 2.1 |
| *SULT4A1* | *T/T* | 88.9 | 66.7 | 83.3 | 94.1 |
| | *C/T* | 11.1 | 33.3 | 16.7 | 5.9 |
| | *C/C* | 0.0 | 0.0 | 0.0 | 0.0 |
| *VKORC1* | **1/*1* | 41.1 | 55.6 | 38.5 | 39.2 |
| | **1/*2* | 42.5 | 33.3 | 46.2 | 43.1 |
| | **2/*2* | 16.4 | 11.1 | 15.4 | 17.6 |

ARI subgroup – aripiprazole monotherapy.
ARI+SGA subgroup - aripiprazole with other antipsychotic drugs.
BR – badly reacting group (aripiprazole has been replaced by another drug due to adverse effects).
SGA − second-generation antipsychotic.
WR – well-reacting group (the sum of ARI and ARI+SGA subgroups).
Phenotypes: UM − ultrarapid metabolizer, NM − normal metabolizer, IM − intermediate metabolizer, PM − poor metabolizer

**Table S3** List of all analyzed genes and polymorphisms.

| Gene | Variant | Nucleotide change | Type of variant | Amino acid changes/star allele | Functional consequence |
|---|---|---|---|---|---|
| *ABCB1* | rs1045642 | c.3435C>T | Synonymous | No | Decreased activity |
| *APOE* | rs429358 | c.388T>C | Missense | Cys130Arg | E3 isoform – normal lipoprotein metabolism<br>E2 and E4 isoforms – abnormal lipoprotein metabolism |
| | rs7412 | c.526C>T | Missense | Arg176Cys | |
| *COMT* | rs4680 | c.472G>A | Missense | Val158Met | The *A* (Met) variant - lower thermostability and activity of the enzyme. |
| *CYP1A2* | rs2069514 | g.-3860G>A | 5'UTR | Located in the enhancer region. | Decreased enzymatic activity |
| | rs762551 | g.-163C>A | Intron | No | Altered enzymatic activity. |
| | rs12720461 | g.-729C>T | Intron | | Decreased enzymatic activity. |
| | rs56107638 | g.3533G>A | Splice donor | Located in intron 6. Splicing defect. | Decreased enzymatic activity. |
| | rs72547513 | g.558C>A | missense | Phe186Leu | Decreased enzymatic activity. |
| *CYP2B6* | rs3745274 | c.516G>A | Missense | Gln172His | Decreased function. |
| | rs28399499 | c.983T>C | Missense | Ile328Thr | No function. |
| *CYP2C19* | rs4244285 | c.681G>A | Synonymous | Splice defect | No function |
| | rs4986893 | c.636G>A | Stop codon | Trp212Stop | No function |
| | rs28399504 | c.1A>G | Missense | Located in the start codon. Met1Val | No function |
| | rs56337013 | c.1297C>T | Missense | Arg433Trp | No function |
| | rs72552267 | c.395G>A | Missense | Arg132Gln | No function |
| | rs72558186 | g.19294T>A | Splice donor | splice defect | No function |
| | rs41291556 | c.358T>C | Missense | Trp120Arg | No function |
| | rs12248560 | g.-806C>T | 5' Flanking region | Increased expression | Increased function |
| *CYP2C9* | rs1799853 | c.430C>T | Missense | Arg144Cys | Decreased function. |
| | rs1057910 | c.1075A>C | Missense | Ile359Leu | No function |
| | rs56165452 | c. 1076T>C | Missense | Ile359Thr | Decreased function. |
| | rs28371686 | c.1080C>G | Missense | Asp360Glu | Decreased function. |
| | rs9332131 | c.818delA | Frameshift | Lys273fs | No function |
| | rs7900194 | c.449G>A | Missense | Arg150His | Decreased function. |
| | rs28371685 | c.1003C>T | Missense | Arg335Trp | Decreased function. |
| | rs9332239 | c.1465C>T | Missense | Pro489Ser | Decreased function. |
| | rs72558187 | c.269T>C | Missense | Leu90Pro | No function |
| | rs72558190 | c.485C>A | Missense | Ser162Stop | No function |
| **Gene** | **Variant** | **Nucleotide change** | **Type of variant** | **Amino acid changes/star allele** | **Functional consequence** |
| *CYP2D6* | rs16947 | g.2850C>T | Missense | Arg296Cys | Normal function |
| | rs1135840 | g.4180G>C | Missense | Ser486Thr | Normal function |

| | | | | | |
|---|---|---|---|---|---|
| | rs35742686 | g.2549delA | Frameshift | Arg259fs | No function |
| | rs3892097 | g.1846G>A | Splice acceptor | splice defect | No function |
| | rs5030655 | g.1707delT | Frameshift | Trp152fs | No function |
| | rs5030867 | g.2935A>C | Missense | His324Pro | No function |
| | rs5030865 | g.1758G>T | Stop gained | Gly169Stop | No function |
| | rs5030656 | g.2613_2615delAGA (g.2615_2617delAAG) | Inframe deletion | Lys281del | Decreased function |
| | rs1065852 | g.100C>T | Missense | Pro34Ser | Decreased function |
| | rs201377835 rs5030863 | c.883G>C | Splice acceptor | splice defect | No function |
| | rs5030862 | g.124G>A | Missense | Gly42Arg | No function |
| | rs5030865 | g.1758G>A | Stop gained | Gly169Arg | Decreased function |
| | rs72549357 | g.137-138insT | Frameshift | Leu47fs | No function |
| | rs28371706 | g.1023C>T | Missense | Thr107Ile | Decreased function |
| | dup4125_4133 | 4135_4136insTGCCCACTG | Insertion | *18 | No function |
| | rs72549353 | c.2539_2542delAACT | Frameshift | Thr256fs | No function |
| | rs72549354 | c.1973_1974insG | Frameshift | Leu213fs | No function |
| | rs59421388 | g 3183G>A | Missense | Val338Met | Decreased function |
| | rs28371725 | g.2988G>A | Intron | splice defect | Decreased function |
| *CYP3A4* | rs55785340 | c.664T>C | Missense | Ser222Pro | Function not assigned. |
| | rs4987161 | c.566 T>C | Missense | Phe189Ser | Function not assigned. |
| | rs35599367 | g.15389C>T | Intron | splice defect | Function not assigned. |
| *CYP3A5* | rs28365083 | g.27289C>A | Missense | Thr398Asn | No function. |
| | rs776746 | g.6986A>G | Splice acceptor | splice defect | No function. |
| | rs10264272 | c.624G>A | Synonymous | splice defect | No function. |
| | rs41303343 | g.27131_27132insT | Frameshift | Thr346fs | No function. |
| *DRD2* | rs1800497 | c.2137G>A | Missense | Glu>Lys | Decreased activity |
| *F2* | rs1799963 | c.*97G>A | 3`UTR | 3`-UTR | ↑ risk of venous thrombosis |
| *F5* | rs6025 | c.1601G>A | Missense | | ↑ risk of venous thrombosis |
| *GLP1R* | rs1042044 | c.780A>C/T | Missense | Leu260Phe | No function. |
| | rs6923761 | c.502G>A/C | Missense | | No function. |
| | rs2300615 | c.510-1135T>G | | | No function. |

| Gene | Variant | Nucleotide change | Type of variant | Amino acid changes/star allele | Functional consequence |
|---|---|---|---|---|---|
| *5HTR2A* | rs6311 | -1438G>A | Promoter region | | *A* allele - greater promoter activity, *AA* genotype - higher receptor density. |
| | rs6313 | 102C>T | Synonymous | p.Ser34= | Probably affect mRNA secondary structure. The *C* allele is less transcriptionally active due to methylation. |
| | rs6314 | 1354C>T | Missense | His452Tyr | The *T* (Tyr) variant would decrease the receptor's ability to activate C and D phospholipase. |
| *MTHFR* | rs1801133 | c.665C>T | Missense | Ala222Val | rs1801133 |
| | rs1801131 | c.1286A>C | Missense | Glu429Ala | Decreased activity. |
| *OPRM1* | rs1799971 | c.118A>G | Missense | Asn44Asp | Worse response to opioids |
| *PNPLA5* | rs5764010 | c.608-169G>A | | | |
| *SLCO1B1* | rs4149056 | c.521T>C | Missense | Val174Ala | No function |
| *SULT4A1* | rs763120 | c.743-374A>G | | | Related with metabolism of monoamines |
| *VKORC1* | rs9923231 | c.-1639G>A | Promoter region | | Decreased expression |