Gene Tox Lab Solutions

PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION
NAME:	**Patient NA23348**	**SPECIMEN TYPE:**		**Gene Tox Lab Solutions**
ACC #:	NA23348	**COLLECTION DATE:**	1/1/1900	
DOB:	1/1/1900	**RECEIVED DATE:**	1/1/1900	
SEX:		**REPORT DATE:**	11/8/2018	

Comprehensive Pharmacogenetic Report

Risk Management

⚠ Atrial Fibrillation

Increased risk of atrial fibrillation

The patient has a heterozygous mutation in 4q25 variant rs2200733.

Heterozygous mutations in 4q25 variant rs2200733 are associated with 1.7 times increase in risk of atrial fibrillation.

Closely monitor the patient for atrial fibrillations and for other cardiovascular disease risk factors.

✓ Hyperuricemia and Gout

Normal Risk of Gout

The patient carries two copies of ABCG2 rs2231142 C allele.

The ABCG2 rs2231142 C allele is associated with normal ABCG2 activity and subsequent normal renal elimination of uric acid. The patient's genotype is associated with a normal risk of hyperuricemia and gout.

No action is needed for this patient unless other genetic or non-genetic risk factors are present.

⚠ Antipsychotic-Induced Tardive Dyskinesia

Increased Risk of Antipsychotic-Induced Tardive Dyskinesia

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

The genotype results predict that the patient has normal dopamine receptor DRD2 density and functioning. The patient has increased risk for tardive dyskinesia when treated with antipsychotics.

Closely monitor the patient for signs of tardive dyskinesia.

✓ Antipsychotic-Induced Hyperprolactinemia

Normal Risk of Antipsychotic-Induced Hyperprolactinemia

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

The genotype results predict that the patient has normal dopamine receptor DRD2 density and functioning. The patient has normal risk of hyperprolactinemia when treated with antipsychotics.

Monitor the patients closely for any signs of hyperprolactinemia.

✓ Antipsychotic-Induced Weight Gain

Low Risk of Antipsychotic-Induced Weight Gain

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

The genotype results predict that the patient has normal dopamine receptor DRD2 density and functioning. The patient has a normal risk for weight gain when treated with antipsychotics.

Monitor the patient closely for signs weight gain.

✓ Type III Hyperlipoproteinemia

Not Associated with Type III Hyperlipoproteinemia

The patient is negative for both the APOE c.388 T>C (Cys130Arg) and c.526 C>T (Arg176Cys) mutations. The patient's genotype is wild-type, which is the most common genotype in the general population (frequency: >60%).

A patient with wild-type genotype does not have a defect in the apolipoprotein E (APOE), which is an integral structure of lipoprotein particles that have critical roles in blood lipid metabolism and transport. The APOE ε3/ε3 genotype is not associated with increased risk of cardiovascular disease.

No action is needed when a patient is normolipidemic.

⚠ Platelet Hyperactivity

Possible Altered Response to Aspirin

The patient carries one ITGB3 176T>C (Leu59Pro) mutation.
Preliminary studies have found an association between the 176T>C mutation of the integrin β3 gene and the possible resistance to the antithrombotic effects of aspirin. However, because the variability in response to antiplatelet drugs is multifactorial and not caused by single gene mutations, testing for the ITGB3 mutation alone should not be used as a diagnostic tool.

Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

The patient carries one MTHFR C677T mutation (heterozygous). MTHFR enzyme activity is reduced (60% of normal activity).
Patients diagnosed with depression often have low folate levels and homocysteine is a highly sensitive marker of folate status. Functional folate deficiency is indicated by elevated homocysteine. The patient's small reduction in MTHFR activity is not a risk factor for hyperhomocysteinemia.
Patients diagnosed with depression: as lower folate levels are associated with poorer antidepressant response, and baseline levels of folate within the normal range predict antidepressant response, testing for homocysteine levels and serum folate levels may be informative for this patient before prescribing methylfolate as an antidepressant-augmenting agent.

Nitric Oxide Production and Coronary Artery Disease

Normal Risk of Coronary Artery Disease

The patient does not carry the NOS3 G894T risk allele.
The endothelial nitric oxide synthase (NOS3) protein is involved in the synthesis of nitric oxide from L-arginine. The G allele of NOS3 G894T is associated with a normal basal nitric oxide production. The G/G genotype is not associated with an increased risk of developing coronary artery disease, hypertension and ischemic stroke.
No action is needed for this patient unless other cardiovascular risk factors are present.

Alcohol Related Co-morbidities

Normal Alcohol and Acetaldehyde Metabolism After Alcohol Ingestion

ALDH2 rs671 A risk allele or the ADH1B rs1229984 T risk allele are absent.
Test results indicate normal alcohol dehydrogenase (ADH1B) activity and normal aldehyde dehydrogenase activity (ALDH2). ADH1B and ALDH2 play a role in alcohol metabolism. ADH1B is responsible for converting ethanol to acetaldehyde and ALDH2 subsequently converts this acetaldehyde into acetate.

Elevated and sustained aldehyde exposure after frequent alcohol consumption plays a key role in the pathogenesis of tissue and organ damage. In East Asians, abnormal ADH1B and/or ALDH2 activities appears to be associated with various health issues such as cancer, liver and cardiovascular diseases.
Consider optimal drinking habits by reducing the amount and the frequency of alcohol consumption.

Hyperlipidemia/Atherosclerotic Cardiovascular Disease

No increased risk of cardiovascular disease

The patient is a non carrier of the risk alleles in LPA gene for both the variants (rs3798220 and rs10455872).
The patient's genotype is associated with normal lipoprotein levels. The patient has no increased risk of atherosclerosis and cardiovascular disease as compared to the general population unless other risk factors are present.
No action is needed for this patient unless other genetic and non genetic risk factors (e.g. high blood pressure, smoking, diabetes, obesity, high blood cholesterol and excessive alcohol use) are present.

Calcium Channels Function and Bipolar Disorder

Risk of Bipolar Disorder: Caucasians - Normal; Asians - Increased

The patient carries two copies of the rs1006737 G allele and two copies of the rs1051375 G allele. Caucasians: Risk allele for CACNA1C rs1006737 is absent. Asians: Risk alleles of CACNA1C rs1051375 are present.
The patient does not carry a variant in the gene coding for the voltage-dependent calcium channel L-type, alpha 1C subunit (CACNA1C). This genotype is associated with a normal neuronal depolarization and a normal mood regulation function. This genotype has been associated with lower rates of mood disorder recurrence and a normal risk of bipolar disorder in Caucasians. The patient carries two copies of the risk alleles for bipolar disorder in Asians. Preliminary studies report that this genotype is associated with lower age of onset of bipolar disease in Asians. However, the exact functional significance of this variant remains unknown.

Bipolar disorder is a polygenic disorder and, as such, several genes are implicated in the etiology of the disease. Identification of one or more risk alleles in genes such as CACNA1C cannot replace standard clinical diagnostic tests, and this test should not be used as a diagnostic test for bipolar disorder.

✓ Coronary Artery Disease

No increased risk for coronary artery disease

The patient does not carry the variants rs1333049 and rs1075278 within the 9p21 region.

Unless other risk factors are present, non-carriers of 9p21 rs1333049 and rs10757278 variants do not have an increased risk of coronary artery disease compared to the general population.

No action is needed for this patient unless other genetic and non-genetic risk factors (*e.g.,* high blood pressure, smoking, diabetes, obesity, high blood cholesterol, excessive alcohol use) are present.

✓ Thrombophilia

No Increased Risk of Thrombosis

The patient does not carry the Factor V Leiden G1691A mutation or Factor II G20210A mutation (wild-type).

The patient's risk of thrombosis is not increased (average risk of clotting is about 1 in 1000 for anyone in a year). However, because this test cannot find all of the inherited reasons for abnormal clotting, other factors may affect this risk assessment.

Unless other genetic and/or circumstantial risk factors are present (e.g., smoking or obesity...), estrogen-containing contraceptive and hormone replacement therapy can be used by the patient.

✓ Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient carries one MTHFR C677T mutation and one A1298C mutation (compound heterozygous). MTHFR enzyme activity is reduced.

The patient's reduced MTHFR activity is not a risk factor for hyperhomocysteinemia. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).

Testing total plasma homocysteine level may be beneficial. Hyperhomocysteinemia can be treated with nutritional supplementation.

⊗ A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	**ACTIONABLE** Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA, EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.
⚠ Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.	
✓ The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.	**INFORMATIVE** There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

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Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Anesthesia	Injectable Anesthetics		Propofol (Diprivan®)	
Anticancer Agents	Antifolates		Methotrexate (Trexall®)	
Cardiovascular	Angiotensin II Receptor Antagonists	Candesartan (Atacand®) Eprosartan (Teveten®) Olmesartan (Benicar®) Telmisartan (Micardis®) Valsartan (Diovan®, Entresto®)		
	Antianginal Agents	Nitroglycerin (Gonitro®, Minitran®, Nitro-Dur®, Nitromist®, Nitrostat®)		
	Anticoagulants	Apixaban (Eliquis®) Betrixaban (Bevyxxa®) Dabigatran Etexilate (Pradaxa®) Edoxaban (Savaysa®) Fondaparinux (Arixtra®) Rivaroxaban (Xarelto®)	Warfarin (Coumadin®)	
	Antiplatelets	Prasugrel (Effient®) Ticagrelor (Brilinta®) Vorapaxar (Zontivity®)		Clopidogrel (Plavix®)
	Beta Blockers	Atenolol (Tenormin®) Bisoprolol (Zebeta®) Labetalol (Normodyne®, Trandate®)		
	Calcium Channel Blockers		Verapamil (Covera-HS®, Verelan®, Isoptin®)	
	Diuretics	Hydrochlorothiazide (Esidrix®, Microzide®)		
	Statins	Atorvastatin (Lipitor®) Fluvastatin (Lescol®) Lovastatin (Mevacor®, Altoprev®, Advicor®) Pitavastatin (Livalo®) Pravastatin (Pravachol®) Rosuvastatin (Crestor®) Simvastatin (Zocor®)		
Diabetes	Biguanides	Metformin (Glucophage®)		
	Meglitinides	Nateglinide (Starlix®) Repaglinide (Prandin®, Prandimet®)		
	Antiemetics	Aprepitant (Emend-oral®) Fosaprepitant (Emend-i.v®) Granisetron (Sancuso®, Sustol®) Rolapitant (Varubi®)		

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Gastrointestinal	**Proton Pump Inhibitors**	Dexlansoprazole (Dexilant®, Kapidex®) Esomeprazole (Nexium®) Lansoprazole (Prevacid®) Omeprazole (Prilosec®) Pantoprazole (Protonix®) Rabeprazole (Aciphex®)		
Gaucher Disease	**Endocrine-Metabolic Agents**	Imiglucerase (Cerezyme®) Miglustat (Zavesca®) Taliglucerase alfa (Elelyso®) Velaglucerase alfa (Vpriv®)		
Infections	**Antifungals**	Amphotericin B (AmBisome®, Abelcet®) Anidulafungin (Eraxis®) Caspofungin (Cancidas®) Fluconazole (Diflucan®) Isavuconazonium (Cresemba®) Itraconazole (Sporanox®) Micafungin (Mycamine®) Posaconazole (Noxafil®) Voriconazole (Vfend®)		
	Anti-HIV Agents	Dolutegravir (Tivicay®, Triumeq®) Raltegravir (Isentress®, Dutrebis®)		
	Antimalarials	Proguanil (Malarone®)		
	Interferons	Peginterferon alfa-2a (Pegasys®) Peginterferon alfa-2b (Pegintron®, Sylatron®)		
	Fibromyalgia Agents	Milnacipran (Savella®)		
	Muscle Relaxants	Carisoprodol (Soma®) Cyclobenzaprine (Flexeril®, Amrix®) Metaxalone (Skelaxin®) Methocarbamol (Robaxin®)		
	NSAIDs	Ketoprofen (Orudis®) Ketorolac (Toradol®) Nabumetone (Relafen®) Naproxen (Aleve®) Sulindac (Clinoril®)		

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Pain	**Opioids**	Alfentanil (Alfenta®) Buprenorphine (Butrans®, Buprenex®) Fentanyl (Actiq®) Hydrocodone (Vicodin®) Hydromorphone (Dilaudid®, Exalgo®) Levorphanol (Levo Dromoran®) Meperidine (Demerol®) Morphine (MS Contin®) Oxymorphone (Opana®, Numorphan®) Sufentanil (Sufenta®) Tapentadol (Nucynta®)	Methadone (Dolophine®)	
Psychotropic	**Antiaddictives**	Acamprosate (Campral®) Disulfiram (Antabuse®)	Bupropion (Wellbutrin®, Zyban®, Aplenzin®, Contrave®) Levodopa / Carbidopa (Sinemet®) Naltrexone (Vivitrol®, Contrave®)	
	Anti-ADHD Agents	Amphetamine (Adderall®, Evekeo®) Dextroamphetamine (Dexedrine®) Guanfacine (Intuniv®) Lisdexamfetamine (Vyvanse®)	Dexmethylphenidate (Focalin®) Methylphenidate (Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®)	
	Anticonvulsants	Brivaracetam (Briviact®) Carbamazepine (Tegretol®, Carbatrol®, Epitol®) Eslicarbazepine (Aptiom®) Ethosuximide (Zarontin®) Ezogabine (Potiga®) Felbamate (Felbatol®) Gabapentin (Neurontin®) Lacosamide (Vimpat®) Lamotrigine (Lamictal®) Levetiracetam (Keppra®) Oxcarbazepine (Trileptal®, Oxtellar XR®) Perampanel (Fycompa®) Pregabalin (Lyrica®) Rufinamide (Banzel®) Tiagabine (Gabitril®) Topiramate (Topamax®) Valproic Acid (Depakote®, Depakene®) Vigabatrin (Sabril®)	Phenobarbital (Luminal®) Primidone (Mysoline®) Zonisamide (Zonegran®)	
	Antidementia Agents	Memantine (Namenda®)		
	Antidepressants	Citalopram (Celexa®) Escitalopram (Lexapro®) Levomilnacipran (Fetzima®) Sertraline (Zoloft®) Trazodone (Oleptro®) Vilazodone (Viibryd®)	Amitriptyline (Elavil®) Clomipramine (Anafranil®) Doxepin (Silenor®) Imipramine (Tofranil®) Trimipramine (Surmontil®)	

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	Antipsychotics	Asenapine (Saphris®) Cariprazine (Vraylar®) Loxapine (Loxitane®, Adasuve®) Lurasidone (Latuda®) Olanzapine (Zyprexa®) Pimavanserin (Nuplazid®) Thiothixene (Navane®) Trifluoperazine (Stelazine®) Ziprasidone (Geodon®)	Clozapine (Clozaril®) Risperidone (Risperdal®)	
	Benzodiazepines	Alprazolam (Xanax®) Clonazepam (Klonopin®) Diazepam (Valium®)	Clobazam (Onfi®)	
	Mood Stabilizers	Lithium (Eskalith®, Lithobid®)		
	Other Neurological Agents	Flibanserin (Addyi®)		
Rheumatology	Anti-Hyperuricemics and Anti-Gout Agents	Allopurinol (Zyloprim®, Liopurin®, Aloprim®) Colchicine (Mitigare®) Febuxostat (Uloric®)		
	Immunomodulators	Apremilast (Otezla®) Tofacitinib (Xeljanz®)	Leflunomide (Arava®)	
	Other Antirheumatic Agents		Sulfasalazine (Azulfidine®, Sulfazine®)	
Transplantation	Immunosuppressants	Tacrolimus (Prograf®)		
Urologicals	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride (Avodart®) Finasteride (Proscar®)		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral®) Doxazosin (Cardura®) Silodosin (Rapaflo®) Terazosin (Hytrin®)		
	Antispasmodics for Overactive Bladder	Oxybutynin (Ditropan®) Solifenacin (Vesicare®) Trospium (Sanctura®)		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra®) Sildenafil (Viagra®) Tadalafil (Cialis®) Vardenafil (Levitra®)		

Dosing Guidance

Clopidogrel
Plavix®

Reduced Response to Clopidogrel (CYP2C19: Intermediate Metabolizer) — ACTIONABLE

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Scott S A SA, Sangkuhl K K, Stein C M CM, Hulot J-S JS, Mega J L JL, Roden D M DM, Klein T E TE, Sabatine M S MS, Johnson J A JA, Shuldiner A R AR, . Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update., Clin. Pharmacol. Ther. 2013 08;94 (3):317-23.

Amitriptyline
Elavil®

Moderate Sensitivity to Amitriptyline (CYP2C19: Intermediate Metabolizer) — ACTIONABLE

Amitriptyline should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Bupropion
Wellbutrin®, Zyban®, Aplenzin®, Contrave®

Possible Altered Response to Bupropion (CYP2B6: Unknown Phenotype) — INFORMATIVE

Bupropion is metabolized to its active metabolite hydroxybupropion by CYP2B6. This metabolite contributes to the therapeutic effects of bupropion when used as a smoking cessation agent or as an antidepressant. Until additional information is available for this genotype, bupropion can be prescribed at standard label-recommended dosage with careful monitoring of the patient's response. Therapeutic monitoring of hydroxybupropion levels may be considered to guide dosing adjustment if needed.

Zhu A Z X AZ, Cox L S LS, Nollen N N, Faseru B B, Okuyemi K S KS, Ahluwalia J S JS, Benowitz N L NL, Tyndale R F RF. CYP2B6 and bupropion's smoking-cessation pharmacology: the role of hydroxybupropion., Clin. Pharmacol. Ther. 2012 11;92(6):771-7.
Høiseth Gudrun G, Haslemo Tore T, Uthus Linda H LH, Molden Espen E. Effect of CYP2B6*6 on Steady-State Serum Concentrations of Bupropion and Hydroxybupropion in Psychiatric Patients: A Study Based on Therapeutic Drug Monitoring Data., Ther Drug Monit 2015 09;37(5):589-93.

Clobazam
Onfi®

Possible Sensitivity to Clobazam (CYP2C19: Intermediate Metabolizer) — ACTIONABLE

In CYP2C19 intermediate metabolizers, plasma levels of the active metabolite N-desmethylclobazam were 2-fold higher than those found in CYP2C19 normal metabolizers. The dose adjustment for intermediate metabolizers is not well established, and therefore the recommendation for poor metabolizers is proposed. The starting dose should be 5 mg/day, and dose titration should proceed slowly according to weight. Patients should be titrated initially to 10 mg /day (≤30 kg body weight) or 20 mg/day (>30 kg body weight). If necessary and based upon clinical response, an additional titration to the maximum doses 20 mg/day (≤30 kg body weight) or 40 mg/day (>30 kg body weight) may be started on day 21.

Onfi [package insert]. Deerfield, IL: Lundbeck Inc.; 2013.

Seo Takayuki T, Nagata Rie R, Ishitsu Takateru T, Murata Tsukasa T, Takaishi Chisato C, Hori Masaharu M, Nakagawa Kazuko K. Impact of CYP2C19 polymorphisms on the efficacy of clobazam therapy., Pharmacogenomics 2008 05;9(5):527-37.
Kosaki Kenjiro K, Tamura Kazuyo K, Sato Reiko R, Samejima Hazuki H, Tanigawara Yusuke Y, Takahashi Takao T. A major influence of CYP2C19 genotype on the steady-state concentration of N-desmethylclobazam., Brain Dev. 2004 11;26(8):530-4.

Clomipramine
Anafranil®

Moderate Sensitivity to Clomipramine (CYP2C19: Intermediate Metabolizer) — ACTIONABLE

Clomipramine should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Clozapine
Clozaril®

Risk of Metabolic Syndrome with Clozapine (HTR2C: Heterozygous for the C allele (rs1414334)) — INFORMATIVE

Genetic variation in the Serotonin 2C Receptor (HTR2C) gene is known to be partially involved in the adverse effects to atypical antipsychotic medications. The patient is heterozygous for HTR2C variant rs1414334. The patient may have an increased risk of developing metabolic syndrome when treated with clozapine.

Risselada A J AJ, Vehof J J, Bruggeman R R, Wilffert B B, Cohen D D, Al Hadithy A F AF, Arends J J, Mulder H H. Association between HTR2C gene polymorphisms and the metabolic syndrome in patients using antipsychotics: a replication study., Pharmacogenomics J. 2012 01;12(1):62-7.
Mulder Hans H, Franke Barbara B, van der-Beek van der Annemarie Aart AA, Arends Johan J, Wilmink Frederik W FW, Scheffer Hans H, Egberts Antoine C G AC. The association between HTR2C gene polymorphisms and the metabolic syndrome in patients with schizophrenia., J Clin Psychopharmacol 2007 07;27(4):338-43.

Dexmethylphenidate
Focalin®

Decreased Response to Dexmethylphenidate (COMT: Intermediate COMT Activity) — INFORMATIVE

The patient's genotype result predicts a less optimal response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Cheon Keun-Ah KA, Jun Jin-Yong JY, Cho Dae-Yeon DY. Association of the catechol-O-methyltransferase polymorphism with methylphenidate response in a classroom setting in children with attention-deficit hyperactivity disorder., Int Clin Psychopharmacol 2008 08;23(5):291-8.
Kereszturi Eva E, Tarnok Zsanett Z, Bognar Emese E, Lakatos Krisztina K, Farkas Luca L, Gadoros Julia J, Sasvari-Szekely Maria M, Nemoda Zsofia Z. Catechol-O-methyltransferase Val158Met polymorphism is associated with methylphenidate response in ADHD children. Am J Med Genet B Neuropsychiatr Genet. 2008 11 5;147B(8):1431-5.

Doxepin
Silenor®

Moderate Sensitivity to Doxepin (CYP2C19: Intermediate Metabolizer) — ACTIONABLE

Doxepin should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Imipramine
Tofranil®

Moderate Sensitivity to Imipramine (CYP2C19: Intermediate Metabolizer) — ACTIONABLE

Imipramine should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Leflunomide
Arava®

Increased Sensitivity to Leflunomide (CYP2C19: Intermediate Metabolizer) — INFORMATIVE

Leflunomide is metabolized by CYP2C19 and CYP1A2 to its active metabolite teriflunomide. Preliminary studies indicate that patients with decreased CYP2C19 activity have a higher risk of developing gastrointestinal side effects and hepatotoxicity. There is insufficient data to calculate dose adjustment. If leflunomide is prescribed at standard dosing, monitor closely the patient's response and be alert to increased side effects. Full blood cell count (CBC) and liver function parameters should be checked no more than 6 months before beginning treatment, and every month for the initial 6 months of therapy. Blood pressure should be checked before beginning treatment and periodically thereafter.

Wiese Michael D MD, Schnabl Matthew M, O'Doherty Catherine C, Spargo Llewellyn D LD, Sorich Michael J MJ, Cleland Leslie G LG, Proudman Susanna M SM. Polymorphisms in cytochrome P450 2C19 enzyme and cessation of leflunomide in patients with rheumatoid arthritis., Arthritis Res. Ther. 2014 07;14(4):R163.
Bohanec Grabar Petra P, Grabnar Iztok I, Rozman Blaz B, Logar Dusan D, Tomsic Matija M, Suput Dasa D, Trdan Tina T, Peterlin Masic Lucija L, Mrhar Ales A, Dolzan Vita V. Investigation of the influence of CYP1A2 and CYP2C19 genetic polymorphism on 2-Cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]-2-butenamide (A77 1726) pharmacokinetics in leflunomide-treated patients with rheumatoid arthritis., Drug Metab. Dispos. 2009 09;37(10):2061-8.

Levodopa / Carbidopa
Sinemet®

Unfavorable Response to Levodopa/Carbidopa Treatment of Cocaine Addiction (DBH: Normal Dopamine Beta-Hydroxylase Activity) — INFORMATIVE

Dopamine β-hydroxylase (DBH) is the final enzyme in norepinephrine biosynthesis, catalyzing the oxidative hydroxylation of dopamine to norepinephrine. The patient does not carry the T allele of DBH rs1611115, which is significantly associated with low DBH activity. Preliminary studies indicate that levodopa/carbidopa treatment offers no additional benefit when compared to placebo for treating cocaine addiction in patients with this genotype. Replication of these results in a larger cohort is still needed to validate these findings.

Liu Shijing S, Green Charles E CE, Lane Scott D SD, Kosten Thomas R TR, Moeller Frederick G FG, Nielsen David A DA, Schmitz Joy M JM. The influence of dopamine β-hydroxylase gene polymorphism rs1611115 on levodopa/carbidopa treatment for cocaine dependence: a preliminary study., Pharmacogenet. Genomics 2014 06;24(7):370-3.

Methadone
Dolophine®

Unknown Sensitivity to Methadone (CYP2B6: Unknown Phenotype) — INFORMATIVE

Until additional information is available, prescribe methadone with careful monitoring. If a genotype effect is suspected based on patient response, adjust dosage accordingly, or prescribe an alternative medication.

Dobrinas Maria M, Crettol Séverine S, Oneda Beatrice B, Lahyani Rachel R, Rotger Margalida M, Choong Eva E, Lubomirov Rubin R, Csajka Chantal C, Eap Chin B CB. Contribution of CYP2B6 alleles in explaining extreme (S)-methadone plasma levels: a CYP2B6 gene resequencing study., Pharmacogenet Genomics 2013 01;23(2):84-93.
Kharasch Evan D ED, Regina Karen J KJ, Blood Jane J, Friedel Christina C. Methadone Pharmacogenetics: CYP2B6 Polymorphisms Determine Plasma Concentrations, Clearance, and Metabolism., Anesthesiology 2015 10;123(5):1142-53.
Kringen Marianne K MK, Chalabianloo Fatemeh F, Bernard Jean-Paul JP, Bramness Jørgen G JG, Molden Espen E, Høiseth Gudrun G. The combined effect of CYP2B6 genotype and other candidate genes on a steady-state serum concentration of methadone in opioid maintenance treatment., Ther Drug Monit 2017 07; ():.

Methotrexate

Increased risk for methotrexate toxicity (MTHFR: Reduced MTHFR Activity) — INFORMATIVE

Trexall®

The patient carries the MTHFR 677 T allele resulting in a reduced MTHFR activity. **Malignancy:** Leukemia or lymphoma patients who are treated with methotrexate standard regimens might have an increased likelihood of treatment interruptions due to methotrexate toxicity. Consider at least a 25% reduction in methotrexate starting dose, followed by titration based on toxicity. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment. **Nonmalignant conditions:** a limited number of studies found an association between the MTHFR 677 T allele and methotrexate-induced toxicity in rheumatoid arthritis patients. However, there is insufficient data to calculate dose adjustment. Monitor patient closely for increased side effects and adjust the dose accordingly. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment.

De Mattia Elena E, Toffoli Giuseppe G. C677T and A1298C MTHFR polymorphisms, a challenge for antifolate and fluoropyrimidine-based therapy personalisation., Eur J Cancer 2009 04;45(8):1333-51.
Choi Yun Jung YJ, Park Hyangmin H, Lee Ji Sung JS, Lee Ju-Yeon JY, Kim Shin S, Kim Tae Won TW, Park Jung Sun JS, Kim Jeong Eun JE, Yoon Dok Hyun DH, Suh Cheolwon C. Methotrexate elimination and toxicity: MTHFR 677C>T polymorphism in patients with primary CNS lymphoma treated with high-dose methotrexate., Hematol Oncol 2016 10;():.
Zhao Ming M, Liang Liang L, Ji Liwei L, Chen Di D, Zhang Yatong Y, Zhu Yuanchao Y, Ongaro Alessia A. MTHFR gene polymorphisms and methotrexate toxicity in adult patients with hematological malignancies: a meta-analysis., Pharmacogenomics 2016 7;17(9):1005-17.

Methylphenidate

Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®

Decreased Response to Methylphenidate (COMT: Intermediate COMT Activity) **INFORMATIVE**

The patient's genotype result predicts a less optimal response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Cheon Keun-Ah KA, Jun Jin-Yong JY, Cho Dae-Yeon DY. Association of the catechol-O-methyltransferase polymorphism with methylphenidate response in a classroom setting in children with attention-deficit hyperactivity disorder., Int Clin Psychopharmacol 2008 08;23(5):291-8.

Naltrexone

Vivitrol®, Contrave®

Altered Response to Naltrexone (OPRM1: Normal OPRM1 Function) **INFORMATIVE**

Treatment of alcohol dependence: the patient has the OPRM1 118AA wild-type genotype that is associated with a poorer outcome with naltrexone therapy. Naltrexone-treated patients not carrying the OPRM1 118A>G G allele are less likely to respond to this drug, and may have higher relapse rates than those who are carriers of this allele. This association has not been reported consistently across studies.

Kranzler Henry R HR, Armeli Stephen S, Covault Jonathan J, Tennen Howard H. Variation in OPRM1 moderates the effect of desire to drink on subsequent drinking and its attenuation by naltrexone treatment., Addict Biol 2013 01;18(1):193-201.
Chamorro Antonio-Javier AJ, Marcos Miguel M, Mirón-Canelo José-Antonio JA, Pastor Isabel I, González-Sarmiento Rogelio R, Laso Francisco-Javier FJ. Association of μ-opioid receptor (OPRM1) gene polymorphism with response to naltrexone in alcohol dependence: a systematic review and meta-analysis., Addict Biol 2012 04;17(3):505-12.
Coller Janet K JK, Cahill Sharon S, Edmonds Carolyn C, Farquharson Aaron L AL, Longo Marie M, Minniti Rinaldo R, Sullivan Thomas T, Somogyi Andrew A AA, White Jason M JM. OPRM1 A118G genotype fails to predict the effectiveness of naltrexone treatment for alcohol dependence., Pharmacogenet. Genomics 2011 11;21(12):902-5.

Phenobarbital

Luminal®

Possible Sensitivity to Phenobarbital (CYP2C19: Intermediate Metabolizer) **INFORMATIVE**

CYP2C19 is partly involved in the metabolism of phenobarbital, and although CYP2C19 intermediate metabolizers have a lower clearance of phenobarbital than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, phenobarbital can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Lee Soon Min SM, Chung Jae Yong JY, Lee Young Mock YM, Park Min Soo MS, Namgung Ran R, Park Kook In KI, Lee Chul C. Effects of cytochrome P450 (CYP) 2C19 polymorphisms on pharmacokinetics of phenobarbital in neonates and infants with seizures., Arch. Dis. Child. 2012 05;97(6):569-72.
Mamiya K K, Hadama A A, Yukawa E E, Ieiri I I, Otsubo K K, Ninomiya H H, Tashiro N N, Higuchi S S. CYP2C19 polymorphism effect on phenobarbitone. Pharmacokinetics in Japanese patients with epilepsy: analysis by population pharmacokinetics., Eur. J. Clin. Pharmacol. 2000 07;55(11-12):821-5.
Yukawa E E, Mamiya K K. Effect of CYP2C19 genetic polymorphism on pharmacokinetics of phenytoin and phenobarbital in Japanese epileptic patients using Non-linear Mixed Effects Model approach., J Clin Pharm Ther 2006 06;31(3):275-82.
Anderson, Gail D. "Chemisry, Biotransformation, and Pharmacokinetics." Antiepileptic Drugs. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2002. 496-03. Print.

Primidone

Mysoline®

Possible Sensitivity to Primidone (CYP2C19: Intermediate Metabolizer) **INFORMATIVE**

CYP2C19 is partly involved in the metabolism of primidone, and although CYP2C19 intermediate metabolizers have a lower clearance of phenobarbital (active metabolite) than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, primidone can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Fincham, Richard W., and Dorothy D. Schottelius. "Primidone." Antiepileptic Drugs. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2002. 621-36. Print.

Propofol

Diprivan®

Unknown Response to Propofol (CYP2B6: Unknown Phenotype) **INFORMATIVE**

Altrhough the CYP2B6 metabolizer status is not well characterized, this genotype along with other factors such as old age (>65 years) and associated comorbidities may contribute to delayed emergence from anesthesia. There is insufficient data to allow calculation of dose adjustment; careful monitoring during post-surgery is recommended. The dosing regimen needs to be individualized for each patient, considering the patient's prior propofol dose requirements, age and comorbidities.

Mastrogianni Orthodoxia O, Gbandi Emma E, Orphanidis Amvrosios A, Raikos Nikolaos N, Goutziomitrou Evangelia E, Kolibianakis Efstratios M EM, Tarlatzis Basil C BC, Goulas Antonis A. Association of the CYP2B6 c.516G>T polymorphism with high blood propofol concentrations in women from northern Greece., Drug Metab. Pharmacokinet. 2014 04;29(2):215-8.
Murayama N N, Minoshima M M, Shimizu M M, Guengerich F P FP, Yamazaki H H. Involvement of human cytochrome P450 2B6 in the omega- and 4-hydroxylation of the anesthetic agent propofol., Xenobiotica 2007 07;37(7):717-24.
Court M H MH, Duan S X SX, Hesse L M LM, Venkatakrishnan K K, Greenblatt D J DJ. Cytochrome P-450 2B6 is responsible for interindividual variability of propofol hydroxylation by human liver microsomes., Anesthesiology 2001 01;94(1):110-9.

Risperidone

Risperdal®

Risk of Metabolic Syndrome with Risperidone (HTR2C: Heterozygous for the C allele (rs1414334)) — **INFORMATIVE**

Genetic variations in the Serotonin 2C Receptor (HTR2C) gene in known to be partially involved in the adverse effects associated with atypical antipsychotic medications. The patient is heterozygous for HTR2C variant rs1414334. The patient may have an increased risk of developing metabolic syndrome when treated with risperidone.

Risselada A J AJ, Vehof J J, Bruggeman R R, Wilffert B B, Cohen D D, Al Hadithy A F AF, Arends J J, Mulder H H. Association between HTR2C gene polymorphisms and the metabolic syndrome in patients using antipsychotics: a replication study., Pharmacogenomics J. 2012 01;12(1):62-7.

Sulfasalazine

Azulfidine®, Sulfazine®

Decreased Response to Sulfasalazine For the Treatment of Rheumatoid Arthritis (ABCG2: Normal Function) — **INFORMATIVE**

Rheumatoid Arthritis: The patient carries two copies of ABCG2 rs2231142 C allele. Preliminary data suggests that this genotype may be associated with decreased plasma levels of sulfasalazine which may decrease the likelihood of response to this drug.

Wiese M D MD, Alotaibi N N, O'Doherty C C, Sorich M J MJ, Suppiah V V, Cleland L G LG, Proudman S M SM. Pharmacogenomics of NAT2 and ABCG2 influence the toxicity and efficacy of sulphasalazine containing DMARD regimens in early rheumatoid arthritis., Pharmacogenomics J. 2014 07;14(4):350-5.
Gotanda Keisuke K, Tokumoto Tomoko T, Hirota Takeshi T, Fukae Masato M, Ieiri Ichiro I. Sulfasalazine disposition in a subject with 376C>T (nonsense mutation) and 421C>A variants in the ABCG2 gene., Br J Clin Pharmacol 2015 10;80(5):1236-7.

Trimipramine

Surmontil®

Moderate Sensitivity to Trimipramine (CYP2C19: Intermediate Metabolizer) — **ACTIONABLE**

Trimipramine should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Verapamil

Covera-HS®, Verelan®, Isoptin®

Unfavorable Response to Verapamil (CACNA1C: Homozygous for rs1051375 G allele) — **INFORMATIVE**

CACNA1C encodes for an alpha-1 subunit of a voltage-dependent calcium channel. The patient carries two copies of CACNA1C rs1051375 G allele. In hypertensive patients with stable coronary artery disease, the G/G genotype may be associated with an increased risk of adverse outcomes (occurrence of death, nonfatal myocardial infarction, or nonfatal stroke) when prescribed with verapamil compared with atenolol.

Bremer Troy T, Man Albert A, Kask Kalev K, Diamond Cornelius C. CACNA1C polymorphisms are associated with the efficacy of calcium channel blockers in the treatment of hypertension., Pharmacogenomics 2006 04;7(3):271-9.

Warfarin

Coumadin®

Possible Sensitivity to Warfarin (CYP2C9 Indeterminate; VKORC1 -1639G>A G/A) — **INFORMATIVE**

Because the patient's CYP2C9 phenotype or genotype results are unknown, a warfarin initiation dose range cannot be recommended.

Johnson J A JA, Gong L L, Whirl-Carrillo M M, Gage B F BF, Scott S A SA, Stein C M CM, Anderson J L JL, Kimmel S E SE, Lee M T M MT, Pirmohamed M M, Wadelius M M, Klein T E TE, Altman R B RB, . Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 genotypes and warfarin dosing., Clin. Pharmacol. Ther. 2011 09;90(4):625-9.
Coumadin [package insert]. Princeton, NJ: Bristol-Myers Squibb Pharma Company; 2011.

Zonisamide

Zonegran®

Possible Sensitivity to Zonisamide (CYP2C19: Intermediate Metabolizer) — **INFORMATIVE**

CYP2C19 is partly involved in the metabolism of zonisamide, and although preliminary studies show that CYP2C19 intermediate metabolizers have a slightly lower (15%) zonisamide clearance than normal metabolizers, no significant change in the clinical outcome has been reported with this antiepileptic drug. Therefore, zonisamide can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Okada Yusuke Y, Seo Takayuki T, Ishitsu Takateru T, Wanibuchi Atsuko A, Hashimoto Nami N, Higa Yoko Y, Nakagawa Kazuko K. Population estimation regarding the effects of cytochrome P450 2C19 and 3A5 polymorphisms on zonisamide clearance., Ther Drug Monit 2008 08;30(4):540-3.

PATIENT INFORMATION

NAME: **Patient NA23348**
ACC #: NA23348
DOB: 1/1/1900
SEX:

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Test Details

Gene	Genotype	Phenotype	Clinical Consequences
12q15	rs7297610 C/C	**Homozygous for the C allele (rs7297610)**	Favorable response to hydrochlorothiazide in African Americans
4q25	rs2200733 C/T	**Heterozygous for rs2200733 variant**	The patient has a heterozygous mutation in 4q25 variant rs2200733. Heterozygous mutations in rs2200733 are associated with a 1.7 times increase in atrial fibrillation risk.
9p21	rs10757278 A/A rs1333049 G/G	**No increased risk for coronary artery disease**	The patient does not carry the variants rs1333049 and rs10757278 within the 9p21 region. Unless other risk factors are present, non-carriers of 9p21 rs1333049 and rs10757278 variants do not have an increased risk of coronary artery disease compared to the general population.
ABCB1	2677G>T G/G	**Variant Allele Not Present**	Consistent with high transporter expression.
ABCB1	1236T>C C/C	**Homozygous Mutant - Variant Allele Present**	Consistent with decreased transporter expression.
ABCB1	2677G>A G/G	**Variant Allele Not Present**	Consistent with high transporter expression.
ABCB1	1000-44G>A A/A	**Homozygous Mutant - Variant Allele Present**	Consistent with decreased transporter expression.
ABCG2	421C>A C/C	**Normal Function**	Consistent with a normal ABCG2 transporter function. The patient's risk for statin-induced adverse events is normal.
ADRA2A	5749G>A G/G	**Wild Type for rs1800545**	
ALDH2 ADH1B	1369G>A G/G 706A>G C/C	**Normal Alcohol and Acetaldehyde Metabolism After Alcohol Ingestion**	East Asians: ALDH2 rs671 A allele or the ADH1B rs1229984 T allele associated with increased risk of alcohol related co-morbidities are absent.
ANKK1/DRD2	DRD2:Taq1A G/G	**Unaltered DRD2 function**	Consistent with a normal dopamine receptor D2 function.
Apolipoprotein E	ε3/ε3	**Normal APOE function**	Not associated with type III hyperlipoproteinemia - No increased risk of cardiovascular disease
BDNF	434C>T C/T	**Heterozygous for rs6265 T Allele**	Consistent with reduced activity-dependent secretion of BDNF from neurons and impaired BDNF signaling.
C11orf65	rs11212617 C/A	**Heterozygous for the A allele (rs11212617)**	Increased glycemic response to metformin
CACNA1C	5361G>A G/G	**Homozygous for rs1051375 G allele**	Normal function of the L-type calcium channel.
CACNA1C	270344G>A G/G 5361G>A G/G	**Risk of Bipolar Disorder: Caucasians - Normal; Asians - Increased**	The patient does not carry a variant in the gene coding for the voltage-dependent calcium channel L-type, alpha 1C subunit (CACNA1C). This genotype is associated with a normal neuronal depolarization and a normal mood regulation function. This genotype has been associated with lower rates of mood disorder recurrence and a normal risk of bipolar disorder in Caucasians. The patient carries two copies of the risk alleles for bipolar disorder in Asians. Preliminary studies report that this genotype is associated with lower age of onset of bipolar disease in Asians. However, the exact functional significance of this variant remains unknown.
COMT	Val158Met A/G	**Intermediate COMT Activity**	Consistent with a reduced catechol O-methyltransferase (COMT) function.
CYP2B6	Indeterminate	**Unknown Phenotype**	The patient's CYP2B6 metabolism status cannot be determined based on the genotype results. Caution if CYP2B6 drug substrates are prescribed.
CYP2C	g.96405502G>A G/A	**High Sensitivity**	

CYP2C19	*8/*17	**Intermediate Metabolizer**	Consistent with a moderate deficiency in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2C9	Indeterminate	**Unknown Phenotype**	Test results were obtained for CYP2C9 but one or more analytes failed. The patient's CYP2C9 metabolism status cannot be determined based on the genotype results. Caution if CYP2C9 drug substrates are prescribed.
CYP2D6	Indeterminate	**Unknown Phenotype**	Test results were obtained for CYP2D6 but one or more analytes failed. The patient's CYP2D6 metabolism status cannot be determined based on the genotype results. Caution if CYP2D6 drug substrates are prescribed.
CYP3A4	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP3A5	*3/*3	**Poor Metabolizer**	Consistent with a poor CYP3A5 activity. This phenotype is the most common in the general population. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP4F2	1347G>A A/G	**Heterozygous for the A allele (rs2108622)**	
DBH	-1021C>T C/C	**Normal Dopamine Beta-Hydroxylase Activity**	Consistent with a normal dopamine beta-hydroxylase activity and a normal conversion of dopamine to norepinephrine.
DRD2	rs2283265 C/C	**Homozygous for rs2283265 C allele**	The patient carries two copies of the rs2283265 C allele.
DRD2	-241A>G T/T	**Homozygous for rs1799978 T Allele**	Associated with a favorable response to Risperidone.
F5 **F2**	1691G>A GG 20210G>A GG	**No Increased Risk of Thrombosis**	Unless other genetic or circumstantial risk factors are present, the patient is not expected to have an increased risk for thrombosis.
FKBP5	rs1360780 T/C	**Heterozygous for rs1360780 T allele**	Genotype may be associated with less frequent depressive episodes.
GRIK1	rs2832407 C/C	**Homozygous for rs2832407 C allele**	Glutamate receptor, ionotropic, kainate 1 (GRIK1) belongs to the kainate family of glutamate receptors, which are the predominant excitatory neurotransmitter receptors in the brain. The patient carries two copies of the GRIK1 rs2832407 C allele.
GRIN2B	rs2058878 A/T	**Heterozygous for rs2058878 A allele**	Decreased risk of early relapse and longer abstinence in alcoholics when treated with Acamprosate.
HTR2A	-1438G>A C/T	**Heterozygous for the T Allele (rs6311)**	The patient carries one copy of the variant allele at rs6311 which may be associated with greater serotonin 2A receptor gene expression.
HTR2A	rs7997012 A/A	**Homozygous for the A allele (rs7997012)**	Possible increased response to citalopram and escitalopram
HTR2C	114138144C>G G/C	**Heterozygous for the C allele (rs1414334)**	This genotype is associated with risperidone- and clozapine-induced metabolic syndrome.
HTR2C	-759C>T C/T	**Heterozygous for the C allele (rs3813929)**	Consistent with altered satiety signaling mediated by the serotonin receptor 2C (HTR2C). Increased incidence of metabolic side effects (weight gain, hyperglycemia, hyperlipidemia) with atypical antipsychotic medications.
IFNL3	rs12979860 C/C	**Homozygous for rs12979860 C allele**	Favorable Response to Peginterferon alfa-2a and alfa-2b and Ribavirin Based Regimen for Hepatitic C Genotype 1
ITGB3	176T>C T/C	**Increased Platelet Reactivity**	The patient carries the 176T>C mutation of the integrin β3 gene which is associated with an increased platelet reactivity.

PATIENT INFORMATION

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LPA	rs10455872 A/A rs3798220 T/T	**No increased risk of cardiovascular disease**	The patient is a non carrier of the risk alleles of LPA (rs3798220 and rs 10455872). The patient's genotype is associated with normal lipoprotein levels. The patient has no increased risk of atherosclerosis and cardiovascular disease as compared to the general population unless other risk factors are present.
MTHFR	677C>T CT	**Reduced MTHFR Activity**	The patient carries one MTHFR C677T mutation (heterozygous) and the patient's MTHFR activity is reduced slightly. This is not associated with an increased risk of hyperhomocysteinemia.
MTHFR	1298A>C AC 677C>T CT	**No Increased Risk of Hyperhomocysteinemia**	The patient's MTHFR activity is reduced. However, this change is not associated with increased total plasma homocysteine levels.
NOS3	G894T G/G	**Normal Basal Nitric Oxide Production**	The G/G genotype is not associated with an increased risk of developing coronary artery disease, hypertension and ischemic stroke.
OPRM1	A118G A/A	**Normal OPRM1 Function**	Consistent with a normal OPRM1 receptor signaling efficiency induced by exogenous opioids. This is associated with a good analgesia following standard opioid doses and a poor response to naltrexone.
SLC47A2	-130G>A G/G	**Normal Function**	Normal renal and secretion clearance of metformin
SLCO1B1	521T>C T/T	**Normal Function**	Consistent with a typical SLCO1B1 transporter function. The patient's risk for statin-induced myopathy is not increased.
VKORC1	-1639G>A G/A	**Intermediate Warfarin Sensitivity**	VKORC1 is the site of action of warfarin. The patient may require a decrease in warfarin dosage.

Limitation: This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Absence of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, comorbidities, and lifestyle habits.

Methodology: Array-based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%

Gene Tox Lab Solutions

PATIENT INFORMATION

NAME: **Patient NA23348**
ACC #: NA23348
DOB: 1/1/1900
SEX:

Patient Information Card

This is a summary genetic report for your patient to share with other healthcare providers. The card can be cut out along the dashed line and carried with the patient.

Gene Tox Lab Solutions

REPORT DETAILS

Patient: Patient NA23348
DOB: 1/1/1900
ACC #: NA23348

Pharmacogenetic Test Summary

CYP2C19	*8/*17	Intermediate Metabolizer
CYP2C9	Indeterminate	Unknown Phenotype
CYP2D6	Indeterminate	Unknown Phenotype
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer

MTHFR	677C>T CT	Reduced MTHFR Activity
MTHFR	1298A>C AC 677C>T CT	No Increased Risk of Hyperhomocysteinemia
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity

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