RESOLVE MDx

PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION
NAME:	**Sample Report**	**SPECIMEN TYPE:**	DNA	David Smalley
ACC #:	M18002311	**COLLECTION DATE:**	9/12/2018	PGt Controls
DOB:	9/12/2018	**RECEIVED DATE:**	9/12/2018	
SEX:	Female	**REPORT DATE:**	1/17/2019	

Clinical Health Panel

Current Patient Medications

Effexor, Warfarin, Plavix

Effexor | VENLAFAXINE

Non-Response to Venlafaxine (CYP2D6: Ultra-Rapid Metabolizer)

ACTIONABLE

The patient has a decreased CYP2D6 activity which may result in elevated plasma concentrations of venlafaxine at standard doses. Consider an alternative medication or consider prescribing venlafaxine at a reduced dose and be extra alert for adverse events; adjust the dose based on tolerability and therapeutic monitoring.

If therapeutic drug monitoring is utilized, the sum of venlafaxine and O-desmethylvenlafaxine (an active metabolite) plasma concentrations should be used for efficacy. While the sum of the parent and the active metabolite are informative for efficacy, a higher parent (venlafaxine) concentration may be associated with higher side effects, including QT prolongation.

Warfarin | COUMADIN®

Moderate Sensitivity to Warfarin (CYP2C9 *1/*2; VKORC1 -1639G>A G/A)

ACTIONABLE

Initiation Therapy: a dose decrease may be required. Consider using the following warfarin dose range provided in the FDA-approved label: **3-4 mg/day.** OR consider using a personalized dose as calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 8-10 days.

Plavix | CLOPIDOGREL

Normal Response to Clopidogrel (CYP2C19: Normal Metabolizer)

ACTIONABLE

Clopidogrel can be prescribed at standard label-recommended dosage.

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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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Risk Management

⚠ 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 positive for both the APOE c.388 T>C (Cys130Arg) and the APOE c.526 C>T (Arg176Cys) mutations. The patient's genotype is ε2/ε4 (frequency: 0.73-2.9%).

The APOE E2 form is associated with a slower conversion of IDL to LDL, lower plasma cholesterol, and higher triglycerides. The APOE E4 confers a limitation of HDL binding to its receptor, and is associated with increased plasma cholesterol, LDL, and triglycerides. Individuals with the APOE ε2/ε4 genotype may have higher lipid levels.

Consider dietary adjustments (very low fat diet) and lipid-lowering therapy based on lipid profiles and other risk factors.

✓ 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.

✓ 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 (heterozygous). MTHFR enzyme activity is reduced (60% of normal activity).

The patient's small reduction in 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).

The patient's MTHFR activity is slightly reduced.

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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	Azilsartan (Edarbi®, Edarbyclor®) Candesartan (Atacand®) Eprosartan (Teveten®) Irbesartan (Avapro®) Olmesartan (Benicar®) Telmisartan (Micardis®) Valsartan (Diovan®, Entresto®)	Losartan (Cozaar®, Hyzaar®)	
	Antianginal Agents	Ranolazine (Ranexa®)		
	Antiarrhythmics		Mexiletine (Mexitil®) Propafenone (Rythmol®)	Flecainide (Tambocor®)
	Anticoagulants	Apixaban (Eliquis®) Betrixaban (Bevyxxa®) Dabigatran Etexilate (Pradaxa®) Edoxaban (Savaysa®) Fondaparinux (Arixtra®) Rivaroxaban (Xarelto®)	Warfarin (Coumadin®)	
	Antiplatelets	Clopidogrel (Plavix®) Prasugrel (Effient®) Ticagrelor (Brilinta®) Vorapaxar (Zontivity®)		
	Beta Blockers	Atenolol (Tenormin®) Bisoprolol (Zebeta®) Carvedilol (Coreg®) Labetalol (Normodyne®, Trandate®) Nebivolol (Bystolic®) Propranolol (Inderal®) Timolol (Timoptic®)		Metoprolol (Lopressor®)
	Diuretics	Torsemide (Demadex®)		
	Statins	Atorvastatin (Lipitor®) Lovastatin (Mevacor®, Altoprev®, Advicor®) Pitavastatin (Livalo®) Pravastatin (Pravachol®) Rosuvastatin (Crestor®) Simvastatin (Zocor®)	Fluvastatin (Lescol®)	
Diabetes	Meglitinides	Nateglinide (Starlix®) Repaglinide (Prandin®, Prandimet®)		
	Sulfonylureas	Chlorpropamide (Diabinese®) Glimepiride (Amaryl®) Glipizide (Glucotrol®) Glyburide (Micronase®) Tolbutamide (Orinase®)		

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Gastrointestinal	Antiemetics	Aprepitant (Emend-oral®) Dronabinol (Marinol®) Fosaprepitant (Emend-i.v®) Granisetron (Sancuso®, Sustol®) Metoclopramide (Reglan®) Rolapitant (Varubi®)	Dolasetron (Anzemet®) Netupitant-Palonosetron (Akynzeo®) Palonosetron (Aloxi®)	Ondansetron (Zofran®, Zuplenz®)
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant®, Kapidex®) Esomeprazole (Nexium®) Lansoprazole (Prevacid®) Omeprazole (Prilosec®) Pantoprazole (Protonix®) Rabeprazole (Aciphex®)		
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®)		
	Fibromyalgia Agents	Milnacipran (Savella®)		
Pain	Muscle Relaxants	Carisoprodol (Soma®) Cyclobenzaprine (Flexeril®, Amrix®) Metaxalone (Skelaxin®) Methocarbamol (Robaxin®)	Tizanidine (Zanaflex®)	
	NSAIDs	Ibuprofen (Advil®, Motrin®) Ketoprofen (Orudis®) Ketorolac (Toradol®) Nabumetone (Relafen®) Naproxen (Aleve®) Sulindac (Clinoril®)	Celecoxib (Celebrex®) Diclofenac (Voltaren®) Flurbiprofen (Ansaid®) Indomethacin (Indocin®) Meloxicam (Mobic®) Piroxicam (Feldene®)	
	Opioids	Alfentanil (Alfenta®) Buprenorphine (Butrans®, Buprenex®) Fentanyl (Actiq®) Hydromorphone (Dilaudid®, Exalgo®) Levorphanol (Levo Dromoran®) Meperidine (Demerol®) Methadone (Dolophine®) Oxymorphone (Opana®, Numorphan®) Sufentanil (Sufenta®) Tapentadol (Nucynta®)	Benzhydrocodone (Apadaz®) Dihydrocodeine (Synalgos-DC®) Hydrocodone (Vicodin®) Morphine (MS Contin®) Oxycodone (Percocet®, Oxycontin®)	Codeine (Codeine; Fioricet® with Codeine) Tramadol (Ultram®)

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Psychotropic	Antiaddictives	Bupropion (Wellbutrin®, Zyban®, Aplenzin®, Contrave®)	Naltrexone (Vivitrol®, Contrave®)	
	Anti-ADHD Agents	Guanfacine (Intuniv®)	Amphetamine (Adderall®, Evekeo®) Clonidine (Kapvay®) Dexmethylphenidate (Focalin®) Dextroamphetamine (Dexedrine®) Lisdexamfetamine (Vyvanse®) Methylphenidate (Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®)	Atomoxetine (Strattera®)
	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®) Phenobarbital (Luminal®) Pregabalin (Lyrica®) Primidone (Mysoline®) Rufinamide (Banzel®) Tiagabine (Gabitril®) Topiramate (Topamax®) Valproic Acid (Depakote®, Depakene®) Vigabatrin (Sabril®) Zonisamide (Zonegran®)	Fosphenytoin (Cerebyx®) Phenytoin (Dilantin®)	
	Antidementia Agents	Galantamine (Razadyne®) Memantine (Namenda®)	Donepezil (Aricept®)	
	Antidepressants	Desvenlafaxine (Pristiq®) Duloxetine (Cymbalta®) Escitalopram (Lexapro®) Fluoxetine (Prozac®, Sarafem®) Levomilnacipran (Fetzima®) Mirtazapine (Remeron®) Nefazodone (Serzone®) Sertraline (Zoloft®) Trazodone (Oleptro®) Vilazodone (Viibryd®) Vortioxetine (Trintellix®)	Amoxapine (Amoxapine®) Citalopram (Celexa®) Fluvoxamine (Luvox®) Maprotiline (Ludiomil®)	Amitriptyline (Elavil®) Clomipramine (Anafranil®) Desipramine (Norpramin®) Doxepin (Silenor®) Imipramine (Tofranil®) Nortriptyline (Pamelor®) Paroxetine (Paxil®, Brisdelle®) Protriptyline (Vivactil®) Trimipramine (Surmontil®) Venlafaxine (Effexor®)

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Rheumatology	Antipsychotics	Aripiprazole (Abilify®, Aristada®) Asenapine (Saphris®) Brexpiprazole (Rexulti®) Cariprazine (Vraylar®) Iloperidone (Fanapt®) Loxapine (Loxitane®, Adasuve®) Lurasidone (Latuda®) Paliperidone (Invega®) Pimavanserin (Nuplazid®) Quetiapine (Seroquel®) Thioridazine (Mellaril®) Thiothixene (Navane®) Trifluoperazine (Stelazine®) Ziprasidone (Geodon®)	Chlorpromazine (Thorazine®) Clozapine (Clozaril®) Fluphenazine (Prolixin®) Olanzapine (Zyprexa®) Perphenazine (Trilafon®) Pimozide (Orap®)	Haloperidol (Haldol®) Risperidone (Risperdal®)
	Benzodiazepines	Alprazolam (Xanax®) Clobazam (Onfi®) Clonazepam (Klonopin®) Diazepam (Valium®)		
	Other Neurological Agents	Deutetrabenazine (Austedo®) Dextromethorphan / Quinidine (Nuedexta®) Flibanserin (Addyi®) Valbenazine (Ingrezza®)	Tetrabenazine (Xenazine®)	
	Anti-Hyperuricemics and Anti-Gout Agents	Colchicine (Mitigare®) Febuxostat (Uloric®) Lesinurad (Zurampic®)		
	Immunomodulators	Apremilast (Otezla®) Leflunomide (Arava®) Tofacitinib (Xeljanz®)		
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®) Tamsulosin (Flomax®) Terazosin (Hytrin®)		
	Antispasmodics for Overactive Bladder	Darifenacin (Enablex®) Fesoterodine (Toviaz®) Mirabegron (Myrbetriq®) Oxybutynin (Ditropan®) Solifenacin (Vesicare®) Tolterodine (Detrol®) Trospium (Sanctura®)		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra®) Sildenafil (Viagra®) Tadalafil (Cialis®) Vardenafil (Levitra®)		

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Dosing Guidance

Amitriptyline
Elavil®

Non-Response to Amitriptyline (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Consider an alternative drug, or prescribe amitriptyline at an increased dose and monitor the plasma concentration of amitriptyline and metabolites.

Atomoxetine
Strattera®

Non-Response to Atomoxetine (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

The patient may fail to achieve adequate plasma levels of atomoxetine if the drug is prescribed at standard recommended doses. Consider prescribing atomoxetine with careful titration and monitoring for reduced efficacy. There is insufficient data to calculate dose adjustment. Or consider an alternative medication.

Clomipramine
Anafranil®

Non-Response to Clomipramine (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Consider an alternative drug, or prescribe clomipramine at an increased dose and monitor the plasma concentration of clomipramine and desmethylclomipramine.

Codeine
Codeine; Fioricet® with Codeine

Increased Response to Codeine (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient is a ultra-rapid metabolizer, greatly increased morphine levels are expected, and the patient is at high risk of toxicity when taking codeine. The ultra-rapid conversion of codeine to morphine in breast feeding mothers can result in high and unsafe levels of morphine in the breast milk potentially causing life threatening respiratory depression in the breastfed infant. Avoid prescribing codeine, and consider an alternative opioid or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Desipramine
Norpramin®

Non-Response to Desipramine (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Consider an alternative drug, or prescribe desipramine at increased dosage and observe the patient for decreased efficacy. Adjust dosage in response to desipramine and metabolites plasma concentrations and clinical response.

Doxepin
Silenor®

Non-Response to Doxepin (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Consider an alternative drug or increase doxepin dose by 100%. Adjust maintenance dose according to nordoxepin plasma concentrations.

Flecainide
Tambocor®

Altered Response to Flecainide (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Titrate carefully and consider adjusting the dose in response to plasma concentration and ECG monitoring, OR consider an alternative drug. Examples of alternatives drugs not affected by CYP2D6 include: sotalol, disopyramide, quinidine, and amiodarone.

Haloperidol
Haldol®

Non-Response to Haloperidol (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Consider an alternative drug, or prescribe haloperidol at the standard dose and adjust dosage to achieve a favorable clinical response. Be alert to decreased haloperidol plasma concentrations.

Imipramine
Tofranil®

Non-Response to Imipramine (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Consider an alternative drug or consider prescribing imipramine at an increased dose, then adjust dosage in response to imipramine and desipramine plasma concentrations.

Metoprolol

Possible Non-Responder to Metoprolol (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Lopressor®

The patient may experience a decrease in the pharmacological effect when taking metoprolol at standard dosage. Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol, or prescribe metoprolol at a higher dose. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol, or prescribe metoprolol at a higher dose. If metoprolol is prescribed, titrate the dose to a maximum of 250% of the normal dose in response to efficacy and adverse events.

Nortriptyline
Pamelor®

Non-Response to Nortriptyline (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or prescribe nortriptyline at an increased dose and monitor the plasma concentration of amitriptyline and hydroxynortriptyline.

Ondansetron
Zofran®, Zuplenz®

Non-Response to Ondansetron (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

A substantially decreased antiemetic effect has been reported in CYP2D6 ultra-rapid metabolizers when taking standard doses of this medication. Consider prescribing an alternative drug not metabolized by CYP2D6 such as granisetron.

Paroxetine
Paxil®, Brisdelle®

Reduced Response to Paroxetine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. Consider an alternative medication.

Protriptyline
Vivactil®

Non-Response to Protriptyline (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Consider alternative drugs or prescribe protriptyline at increased dosage and observe the patient for decreased efficacy. Adjust dosage in response to protriptyline and metabolites plasma concentrations and clinical response.

Risperidone
Risperdal®

Non-Response to Risperidone (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, OR prescribe risperidone , be extra alert to insufficient response, and adjust dosage in response to clinical response and adverse events.

Tramadol
Ultram®

Increased Response to Tramadol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is at high risk of toxicity when taking tramadol at standard dosing. Consider reducing tramadol dose by 30%. Careful monitoring for side effects (nausea, vomiting, constipation, respiratory depression, confusion, urinary retention) and weekly titration are recommended. In case of toxicity, consider alternative opioids other than codeine, or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

The accelerated conversion of tramadol to its active metabolite can result in high and unsafe levels of this metabolite in breast milk potentially causing life threatening respiratory depression in the breastfed infant. Use of tramadol should be avoided in breastfeeding mothers.

Trimipramine
Surmontil®

Non-Response to Trimipramine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or consider prescribing trimipramine at an increased dose, then adjust dosage in response to trimipramine plasma concentrations.

Venlafaxine
Effexor®

Non-Response to Venlafaxine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is unlikely to achieve adequate serum levels of venlafaxine and O-desmethylvenlafaxine when taking standard doses of venlafaxine. Consider an alternative drug, or increase the venlafaxine dose to a maximum of 150% of the normal dose and monitor venlafaxine and O-desmethylvenlafaxine plasma concentrations.

Amoxapine
Amoxapine®

Possible Non-Response to Amoxapine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, amoxapine is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Patients with increased CYP2D6 function may metabolize amoxapine more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. There are no established dosing adjustments for patients with increased CYP2D6 function; therapy must be initiated cautiously and adjusted according to the patient's response.

Amphetamine
Adderall®, Evekeo®

Poor Response to Amphetamine salts (COMT: Low COMT Activity) — **INFORMATIVE**

The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, amphetamines should be administered at the lowest effective dose, and dosage should be individually adjusted.

Benzhydrocodone
Apadaz®

Possible Altered Response to Benzhydrocodone (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Benzhydrocodone is a prodrug of hydrocodone and is converted to active hydrocodone by intestinal enzymes. Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 ultrarapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Celecoxib
Celebrex®

Possible Sensitivity to Celecoxib (CYP2C9: Intermediate Metabolizer) — **INFORMATIVE**

Celecoxib can be prescribed at standard label-recommended dosage and administration. Evaluate response the first week and be alert to gastrointestinal adverse events.

Chlorpromazine
Thorazine®

Possible Non-Response to Chlorpromazine (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. Subjects with increased CYP2D6 function will metabolize chlorpromazine more rapidly which can result in sub-therapeutic drug concentrations. Consider a standard dose and adjust dosage according to the patient's tolerability and response. Higher doses may be necessary to achieve efficacy.

Citalopram
Celexa®

Decreased Response to Citalopram (FKBP5: Homozygous for rs4713916 G allele) — **INFORMATIVE**

FKBP5 is involved in the response to stress and in the pathogenesis of mood disorders. The patient does not carry the A allele of FKBP5 variant rs4713916. Preliminary studies indicate that his genotype is associated with a decreased response to citalopram.

Citalopram
Celexa®

Reduced Response to Citalopram (HTR2A: Heterozygous for the A allele (rs7997012)) — **INFORMATIVE**

The patient is heterozygous for HTR2A variant rs7997012. Preliminary studies report that heterozygous HTR2A variant rs7997012 may be associated with an unfavorable response to citalopram.

Citalopram
Celexa®

Possible Reduced Response to Citalopram (GRIK4: Reduced Response to Citalopram) — **INFORMATIVE**

The patient's genotype indicates the presence of one copy of the GRIK4 favorable allele and one copy of the GRIK4 unfavorable allele. The patient may or may not benefit from citalopram therapy.

Clonidine
Kapvay®

Possible Altered Response to Clonidine (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Treatment with clonidine can cause dose related decreases in blood pressure and heart rate Measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy. Titrate Clonidine slowly in patients with a history of hypotension, and those with underlying conditions that may be worsened by hypotension and bradycardia.

Clozapine
Clozaril®

Unfavorable Response to Clozapine (HTR2A: Homozygous for the C allele (rs6311)) — **INFORMATIVE**

The patient does not carry the HTR2A variant rs6311. Preliminary studies suggest that this genotype may be associated with an unfavorable response to clozapine in patients with European ancestry.

Clozapine
Clozaril®

Non-Response to Clozapine (CYP1A2: Normal Metabolizer - Higher Inducibility) **INFORMATIVE**

Smokers have a high risk for non-response at standard doses and may require higher doses. There is an association between high clozapine doses and the risk of seizures, and therefore careful monitoring is recommended during dosing adjustment. Smoking cessation will increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Dexmethylphenidate
Focalin®

Poor Response to Dexmethylphenidate (COMT: Low COMT Activity) **INFORMATIVE**

The patient's genotype result predicts a reduced therapeutic 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.

Dextroamphetamine
Dexedrine®

Poor Response to Dextroamphetamine (COMT: Low COMT Activity) **INFORMATIVE**

The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, dextroamphetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

Diclofenac
Voltaren®

Possible Sensitivity to Diclofenac (CYP2C9: Intermediate Metabolizer) **INFORMATIVE**

Diclofenac is extensively metabolized by hydroxylation and direct glucuronidation. About 50% of diclofenac is eliminated as a 4-hydroxymetabolite, a reaction mediated by CYP2C9. Other CYP enzymes including CYP2C8, CYP2C19 and CYP3A4 are also involved in the formation of a 5-hydroxymetabolite. A substantial portion of the drug is also directly glucuronidated by UGT2B7 and UGT2B4. Individuals with decreased CYP2C9 activity (i.e intermediate metabolizers) should be closely monitored for increased gastrointestinal adverse events when prescribed diclofenac and lower doses may be more appropriate for these patients.

Dihydrocodeine
Synalgos-DC®

Possible Altered Response to Dihydrocodeine (CYP2D6: Ultra-Rapid Metabolizer) **INFORMATIVE**

Increased conversion of dihydrocodeine to the more active metabolite dihydromorphine is expected in CYP2D6 ultra-rapid metabolizers. This may result in an exaggerated response. Adequate pain relief can be achieved by decreasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if signs of overdose (excessive sleepiness, confusion, or shallow breathing) are reported.

Dolasetron
Anzemet®

Possible Altered Response to Dolasetron (CYP2D6: Ultra-Rapid Metabolizer) **INFORMATIVE**

The reduction of dolasetron to its active metabolite hydrodolasetron is mediated by a carbonyl reductase. Hydrodolasetron is further eliminated by multiple routes, including renal excretion and by glucuronidation or hydroxylation by CYP2D6. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower hydroxydolasetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Dolasetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Donepezil
Aricept®

Possible Altered Response to Donepezil (CYP2D6: Ultra-Rapid Metabolizer) **INFORMATIVE**

When compared to a normal metabolizer, a ultra-rapid metabolizers has a 24% increase in donepezil clearance. The clinical significance of this increase is not well documented. Consider using a standard dosing regimen and adjust dosage in response to clinical response and tolerability.

Fluphenazine
Prolixin®

Possible Non-response to Fluphenazine (CYP2D6: Ultra-Rapid Metabolizer) **INFORMATIVE**

Fluphenazine is metabolized by CYP2D6, CYP1A2 and other enzymes. **Patients with increased CYP2D6 function will metabolize fluphenazine more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations.** There are no established dosing adjustments for patients with increased CYP2D6 function therefore, therapy must be initiated cautiously with oral or parenteral fluphenazine hydrochloride. When the pharmacological effects and an appropriate dosage are apparent, an equivalent dose of fluphenazine decanoate (IM or SC) may be administered and subsequent dosage adjustments may be necessary.

Flurbiprofen
Ansaid®

Possible Sensitivity to Flurbiprofen (CYP2C9: Intermediate Metabolizer) — **INFORMATIVE**

The patient may have high plasma levels of the drug. Flurbiprofen can be prescribed at standard label-recommended dosage and administration with closer monitoring for gastrointestinal side effects.

Fluvastatin
Lescol®

Possible Sensitivity to Fluvastatin (CYP2C9: Intermediate Metabolizer) — **ACTIONABLE**

Increased fluvastatin plasma concentrations due to reduced CYP2C9 activity may occur, resulting in myopathy/hepatotoxicity. Consider monitoring the patient for treatment-related adverse effects, and adjust dose as needed. Other adverse events and predisposing factors include advanced age (≥65), diabetes, hypothyroidism, renal or hepatic impairments, high statin dose, CYP2C9 inhibitors, ABCG2 inhibitors, and female gender.

Fluvoxamine
Luvox®

Possible Reduced Response to Fluvoxamine (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. There is insufficient data to calculate dose adjustments and careful titration is recommended until a favorable response is achieved. An alternative medication not metabolized by CYP2D6 can also be considered.

Fosphenytoin
Cerebyx®

Moderate Sensitivity to Fosphenytoin (CYP2C9: Intermediate Metabolizer) — **ACTIONABLE**

Fosphenytoin is a prodrug of phenytoin. The genotype results indicate that the patient is a CYP2C9 intermediate metabolizer. Plasma concentrations of phenytoin are likely to increase, resulting in an increased risk of mild to moderate neurological toxicity. Consider a standard loading dose, and reduce the maintenance dose by 25%. Evaluate response and serum concentrations after 7-10 days. Be alert to neurological concentration-related adverse events.

Hydrocodone
Vicodin®

Possible Altered Response to Hydrocodone (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower hydrocodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Indomethacin
Indocin®

Possible Sensitivity to Indomethacin (CYP2C9: Intermediate Metabolizer) — **INFORMATIVE**

Indomethacin is metabolized mainly by O-demethylation to its inactive metabolite O-desmethylindomethacin, a reaction catalyzed by CYP2C9. At standard doses, indomethacin plasma concentrations may be higher in individuals with decreased CYP2C9 function. Although indomethacin can be prescribed at standard label recommended-dosage and administration, a closer monitoring for signs of gastrointestinal toxicity during long-term administration is recommended.

Lisdexamfetamine
Vyvanse®

Poor Response to Lisdexamfetamine (COMT: Low COMT Activity) — **INFORMATIVE**

The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, lisdexamfetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

Losartan
Cozaar®, Hyzaar®

Possible Decreased Response to Losartan (CYP2C9: Intermediate Metabolizer) — **INFORMATIVE**

Losartan is metabolized to its active metabolite by CYP2C9 and CYP3A4. The patient's genotype predicts a reduced exposure to losartan's active metabolite and a possible reduced hypotensive effect. Losartan can be prescribed at label-recommended dosage and administration with additional monitoring of the patient's response.

Maprotiline
Ludiomil®

Possible Non-response to Maprotiline (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Patients with increased CYP2D6 function may metabolize maprotiline more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. **There are no established dosing adjustments for patients with increased CYP2D6 function. Seizures have been associated with the use of maprotiline especially at high doses. Therefore, therapy must be initiated at a standard dose and gradually increased in small increments according to the patient's response.**

Meloxicam
Mobic®

Possible Sensitivity to Meloxicam (CYP2C9: Intermediate Metabolizer) — **INFORMATIVE**

Meloxicam plasma concentrations may be higher in individual with decreased CYP2C9 function. A reduction in meloxicam dosage may be needed with a closer monitoring for signs of gastrointestinal toxicity during long-term administration.

Methotrexate
Trexall®

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

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.

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

Poor Response to Methylphenidate (COMT: Low COMT Activity) — **INFORMATIVE**

The patient's genotype result predicts a reduced therapeutic 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.

Mexiletine
Mexitil®

Altered Response to Mexiletine (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Because mexiletine plasma concentrations may be decreased, consider adjusting dose in response to mexiletine plasma concentration and ECG monitoring, until a favorable response in achieved.

Morphine
MS Contin®

Altered Response to Morphine (COMT: Low COMT Activity) — **INFORMATIVE**

The patient carries two COMT Val158Met variants, which translates to a reduced COMT function. The patient may require lower doses of morphine for adequate pain control. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

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.

Netupitant-Palonosetron
Akynzeo®

Possible Altered Response to Netupitant-Palonosetron (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Netupitant: Netupitant is extensively metabolized to three major metabolites (desmethyl, N-oxide and a hydroxy-methyl derivatives). Metabolism is mediated primarily by CYP3A4 and to a lesser extent by CYP2C9 and CYP2D6. No genetically guided drug selection or dosing recommendations are available for this drug. Netupitant can be prescribed at standard label-recommended dosage and administration.
Palonosetron: Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Olanzapine
Zyprexa®

Non-Response to Olanzapine (CYP1A2: Normal Metabolizer - Higher Inducibility) — **INFORMATIVE**

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Oxycodone
Percocet®, Oxycontin®

Possible Altered Response to Oxycodone (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Increased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower oxycodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Palonosetron
Aloxi®

Possible Altered Response to Palonosetron (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Perphenazine
Trilafon®

Possible Non-Response to Perphenazine (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Subjects with increased CYP2D6 function will metabolize perphenazine more rapidly, which can result in sub-therapeutic drug concentrations. Consider a dose increase with close monitoring until a favorable response is achieved.

Phenytoin
Dilantin®

Moderate Sensitivity to Phenytoin (CYP2C9: Intermediate Metabolizer) — **ACTIONABLE**

The genotype results indicate that the patient is a CYP2C9 substrate intermediate metabolizer. Plasma concentrations of phenytoin are likely to increase, resulting in an increased risk of mild to moderate neurological toxicity. Consider a standard loading dose, and reduce the maintenance dose by 25%. Evaluate response and serum concentrations after 7-10 days. Be alert to neurological concentration-related adverse events.

Pimozide
Orap®

Possible Non-Response to Pimozide (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

There is insufficient data to calculate dose adjustment, and if pimozide is prescribed at standard dosing, monitor response and be alert to reduced efficacy. Standard starting dose: 1 to 2 mg/day (adult) or 0.05 mg/kg/day (children). Doses may be increased to a maximum of 10 mg/day or 0.2 mg/kg/day.

Piroxicam
Feldene®

Possible Sensitivity to Piroxicam (CYP2C9: Intermediate Metabolizer) — **INFORMATIVE**

Piroxicam plasma concentrations may be higher in individual with decreased CYP2C9 function. Although piroxicam can be prescribed at standard label-recommended dosage and administration, a closer monitoring for signs of gastrointestinal toxicity during long-term administration is recommended.

Propafenone
Rythmol®

Altered Response to Propafenone (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

There is insufficient data to allow calculation of dose adjustment. Titrate carefully and adjust the dose in response to plasma concentration and ECG monitoring. OR consider an alternative drug such as sotalol, disopyramide, quinidine, or amiodarone.

Dose adjustments with co-medications: concurrent use of propafenone along with CYP3A4 inhibitors and CYP2D6 inhibitors may significantly increase the plasma concentration of propafenone and thereby increase the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with both a CYP2D6 inhibitor and a CYP3A4 inhibitor.

⚠ Tetrabenazine

Xenazine®

Unknown Sensitivity to Tetrabenazine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

For treating chorea associated with Huntington's disease: There is insufficient data to calculate dose adjustment, and if tetrabenazine is prescribed, individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 ultra-rapid metabolizers is not defined. The maximum daily dose in normal metabolizers is 100 mg with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

⚠ Tizanidine

Zanaflex®

Possible Non-Response to Tizanidine (CYP1A2: Normal Metabolizer - Higher Inducibility) — INFORMATIVE

There is little evidence regarding the impact of CYP1A2 genetic variants on tizanidine response. Smokers may be at risk for non-response and may require higher doses. There is an association between high tizanidine plasma concentrations and the risk of hypotension and excessive sedation. Therefore, careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to excessive hypotension and sedation. Careful monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

⚠ Warfarin

Coumadin®

Moderate Sensitivity to Warfarin (CYP2C9 *1/*2; VKORC1 -1639G>A G/A) — ACTIONABLE

Initiation Therapy: a dose decrease may be required. Consider using the following warfarin dose range provided in the FDA-approved label: **3-4 mg/day.** OR consider using a personalized dose as calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 8-10 days.

RESOLVE MDx

PATIENT INFORMATION

NAME: **Sample Report**
ACC #: M18002311
DOB: 9/12/2018
SEX: Female

Test Details

Gene	Genotype	Phenotype	Clinical Consequences
ANKK1/DRD2	DRD2:Taq1A G/G	**Unaltered DRD2 function**	Consistent with a normal dopamine receptor D2 function.
Apolipoprotein E	ε2/ε4	**Altered APOE function**	Not associated with type III hyperlipoproteinemia
COMT	Val158Met A/A	**Low COMT Activity**	Consistent with a significantly reduced catechol O-methyltransferase (COMT) function.
CYP1A2	*1F/*1F	**Normal Metabolizer - Higher Inducibility**	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid Metabolism occurs in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
CYP2B6	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP2B6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2C19	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP2C19 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2C9	*1/*2	**Intermediate Metabolizer**	Consistent with a moderate deficiency in CYP2C9 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2D6	*1/*1 XN	**Ultra-Rapid Metabolizer**	Consistent with a significant increase in CYP2D6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
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.
F2 **F5**	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	rs4713916 G/G	**Homozygous for rs4713916 G allele**	Consistent with a possible non-response to citalopram.
GRIK4	83-10039T>C T/C	**Reduced Response to Citalopram**	Consistent with a possible non-response to citalopram.
HTR2A	-1438G>A C/C	**Homozygous for the C allele (rs6311)**	The patient does not carry the variant allele at rs6311 which may be associated with greater serotonin 2A receptor gene expression.
HTR2A	rs7997012 A/G	**Heterozygous for the A allele (rs7997012)**	Reduced response to citalopram and escitalopram
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 AA 677C>T CT	**No Increased Risk of Hyperhomocysteinemia**	The patient MTHFR function is reduced slightly. This is not associated with an increased risk for venous thromboembolism.
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.
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.

RESOLVE MDx

PATIENT INFORMATION

NAME: **Sample Report**
ACC #: M18002311
DOB: 9/12/2018
SEX: Female

Alleles Tested: **ANKK1/DRD2** DRD2:Taq1A; **Apolipoprotein E** ε2, ε4, (ε3 is reference); **COMT** Val158Met; **CYP1A2** *1C, *1D, *1F, *1K, *1L, *1V, *1W; **CYP2B6** *6, *9; **CYP2C19** *2, *3, *4, *4B, *5, *6, *7, *8, *9, *17; **CYP2C9** *2, *3, *4, *5, *6, *11; **CYP2D6** *2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *17, *29, *35, *41, *5 (gene deletion), XN (gene duplication); **CYP3A4** *22; **CYP3A5** *1D, *2, *3, *3C, *6, *7, *8, *9; **Factor II** 20210G>A; **Factor V Leiden** 1691G>A; **FKBP5** rs4713916; **GRIK4** 83-10039T>C; **HTR2A** -1438G>A, rs7997012; **MTHFR** 1298A>C, 677C>T; **OPRM1** A118G; **SLCO1B1** 521T>C; **VKORC1** -1639G>A

Disclaimer: Resolve Molecular Diagnostics developed the genotyping-based test. The performance characteristics of this test were determined by Resolve Molecular Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA).

Only a qualified healthcare professional should advise a patient on how to interpret the results and information found in this report. Resolve Molecular Diagnostics will not make any recommendations based on the results of the test performed, therefore, please seek advice from your healthcare provider.

Methodology: All single nucleic polymorphism (SNP) genotyping was performed using Applied BiosystemsTM TaqMan® chemistry on the QuantStudioTM 12K Flex Real-Time PCR System from ThermoFisher Scientific. Array based assays detects listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

Limitations: 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.

Translational Software Disclaimer: The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed.

The pharmacogenetic assay involves use of reporting software and genotype-phenotype associations performed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

RESOLVE MDx

PATIENT INFORMATION

NAME: **Sample Report**
ACC #: M18002311
DOB: 9/12/2018
SEX: Female

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.

RESOLVE MDx

REPORT DETAILS

Patient: Sample Report
DOB: 9/12/2018
ACC #: M18002311

Pharmacogenetic Test Summary

CYP2C19	*1/*1	Normal Metabolizer
CYP2C9	*1/*2	Intermediate Metabolizer
CYP2D6	*1/*1 XN	Ultra-Rapid Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer

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

For a complete report contact Resolve Molecular Diagnostics

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