Sundance DIAGNOSTICS
2525 Arapahoe Avenue, Suite E4-553, Boulder, CO 80302
P: 303 862-2770 F: 303 595-5289 E: support@sundancedx.com

Lifeline- Comprehensive Genetic Test for: Patient 34

Patient:	Patient 34	DOB:	1/1/1900
Accession #:	34	Gender:	
Collection Date:	1/1/1900	Received Date:	1/1/1900
Physician/Ordered By:		Report Generated:	5/10/2016

Risk Management

✓ **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 does not carry the MTHFR C677T or MTHFR A1298C mutation (wild-type). MTHFR enzyme activity is normal.

With a normal MTHFR activity, this patient is unlikely to have elevated plasma levels of homocysteine, which is a known risk factor for cardiovascular diseases and thrombosis. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).

MTHFR enzyme activity is normal.

Guidance Levels

- Action is needed to minimize risk associated with medication. Therapy modification may be required. Increased risk for the indicated condition.
- Increased vigilence and adjustment of medication may be needed. Elevated risk for the indicated condition.
- ✓ Medication can be prescribed according to standard dosage. Typical risk for the indicated condition.

Evidence Levels

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 new knowledge arises.
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.

Potentially Impacted Medications

Category	Drug Class	Use As Directed	Use With Caution	Consider Alternatives
Anticancer Agents	Antifolates	Methotrexate (Trexall)		

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Category	Drug Class	Use As Directed	Use With Caution	Consider Alternatives
Cardiovascular	Angiotensin II Receptor Antagonists	Azilsartan (Edarbi, Edarbyclor) Candesartan (Atacand) Eprosartan (Teveten) Irbesartan (Avapro) Losartan (Cozaar, Hyzaar) Olmesartan (Benicar) Telmisartan (Micardis) Valsartan (Diovan, Entresto)		
	Antianginal Agents	Ranolazine (Ranexa)		
	Antiarrhythmics		Flecainide (Tambocor) Mexiletine (Mexitil) Propafenone (Rythmol)	
	Anticoagulants	Apixaban (Eliquis) Dabigatran Etexilate (Pradaxa) Edoxaban (Savaysa) Fondaparinux (Arixtra) Rivaroxaban (Xarelto)	Warfarin (Coumadin)	
	Antiplatelets	Clopidogrel (Plavix) Prasugrel (Effient) Ticagrelor (Brilinta) Vorapaxar (Zontivity)		
	Beta Blockers	Carvedilol (Coreg) Labetalol (Normodyne, Trandate) Propranolol (Inderal)	Metoprolol (Lopressor) Nebivolol (Bystolic) Timolol (Timoptic)	
	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 (Diabenese) Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide (Micronase) Tolbutamide (Orinase)		
Gastrointestinal	Antiemetics	Dolasetron (Anzemet) Ondansetron (Zofran, Zuplenz) Palonosetron (Aloxi)	Metoclopramide (Reglan)	
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant, Kapidex) Esomeprazole (Nexium) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix) Rabeprazole (Aciphex)		

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Category	Drug Class	Use As Directed	Use With Caution	Consider Alternatives
Infections	Antifungals	Voriconazole (Vfend)		
	Antimalarials	Proguanil (Malarone)		
Pain	Fibromyalgia Agents	Milnacipran (Savella)		
	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) Dihydrocodeine (Synalgos-DC) Fentanyl (Actiq) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Morphine (MS Contin) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta)	Codeine (Codeine; Fioricet with Codeine) Hydrocodone (Vicodin) Oxycodone (Percocet, Oxycontin) Tramadol (Ultram)	
	Antiaddictives		Naltrexone (Vivitrol)	
	Anti-ADHD Agents	Atomoxetine (Strattera) Clonidine (Kapvay) Guanfacine (Intuniv)		

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Category	Drug Class	Use As Directed	Use With Caution	Consider Alternatives
Psychotropic	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	Donepezil (Aricept) Galantamine (Razadyne) Memantine (Namenda)		
	Antidepressants	Citalopram (Celexa) Desvenlafaxine (Pristiq) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluoxetine (Prozac, Sarafem) Fluvoxamine (Luvox) Levomilnacipran (Fetzima) Mirtazapine (Remeron) Nefazodone (Serzone) Paroxetine (Paxil, Brisdelle) Sertraline (Zoloft) Vilazodone (Viibryd) Vortioxetine (Brintellix)	Amitriptyline (Elavil) Amoxapine (Amoxapine) Clomipramine (Anafranil) Desipramine (Norpramin) Doxepin (Silenor) Imipramine (Tofranil) Maprotiline (Ludiomil) Nortriptyline (Pamelor) Protriptyline (Vivactil) Trimipramine (Surmontil)	Venlafaxine (Effexor)
	Antipsychotics	Aripiprazole (Abilify) Asenapine (Saphris) Brexpiprazole (Rexulti) Chlorpromazine (Thorazine) Haloperidol (Haldol) Loxapine (Loxitane, Adasuve) Lurasidone (Latuda) Paliperidone (Invega) Pimozide (Orap) Quetiapine (Seroquel) Thiothixene (Navane) Trazodone (Oleptro) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Clozapine (Clozaril) Fluphenazine (Prolixin) Iloperidone (Fanapt) Olanzapine (Zyprexa) Perphenazine (Trilafon) Tetrabenazine (Xenazine)	Risperidone (Risperdal) Thioridazine (Mellaril)

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Category	Drug Class	Use As Directed	Use With Caution	Consider Alternatives
	Benzodiazepines	Alprazolam (Xanax) Clobazam (Onfi) Clonazepam (Klonopin) Diazepam (Valium)		
	Other Neurological Agents	Dextromethorphan / Quinidine (Nuedexta)		
Rheumatology	Immunomodulators	Apremilast (Otezla) Leflunomide (Arava) Tofacitinib (Xeljanz)		
Transplantation	Immunosupressants	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

Risperidone (Risperdal)
Actionable

Increased Sensitivity to Risperidone (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider an alternative drug, OR prescribe risperidone, be extra alert of adverse events, and adjust dosage in response to clinical response and tolerability. There is insufficient data to allow calculation of dose adjustment.

Thioridazine (Mellaril)
Actionable

Increased Sensitivity to Thioridazine (CYP2D6 *4/*41 Intermediate Metabolizer)
Reduced cytochrome CYP2D6 activity results in elevated plasma levels of thioridazine, would be expected to augment the prolongation of the QTc interval associated with thioridazine, and may increase the risk of serious, potentially fatal, cardiac arrhythmias, such as Torsades de pointes-type arrhythmias. Such an increased risk may result also from the additive effect of coadministering thioridazine with other agents that prolong the QTc interval. Therefore, thioridazine is contraindicated in patients with reduced levels of CYP2D6 activity.

Venlafaxine (Effexor)
Actionable

Increased Sensitivity to Venlafaxine (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider an alternative drug, OR prescribe venlafaxine, be extra alert of adverse events, adjust dosage in response to clinical response and tolerability. Monitor O-desmethylvenlafaxine plasma concentrations.

Amitriptyline (Elavil)
Actionable

Moderate Sensitivity to Amitriptyline (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider reducing amitriptyline dose by 25% with monitoring of plasma concentrations of amitriptyline and nortriptyline.

Amoxapine (Amoxapine)
Informative

Possible Sensitivity to Amoxapine (CYP2D6 *4/*41 Intermediate Metabolizer)
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. Decreased CYP2D6 activity may result in higher amoxapine concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function therefore, therapy must be initiated cautiously and adjusted according to the patient's response.

Celecoxib (Celebrex)
Informative

Possible Sensitivity to Celecoxib (CYP2C9 *1/*2 Intermediate Metabolizer)
Celecoxib can be prescribed at standard label-recommended dosage and administration. Evaluate response the first week and be alert to gastrointestinal adverse events.

Clomipramine (Anafranil)
Actionable

Moderate Sensitivity to Clomipramine (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider prescribing clomipramine at 25% of recommended standard starting dose. Monitor plasma concentrations of clomipramine and desmethylclomipramine, and titrate accordingly until a favorable response is achieved.

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Clozapine (Clozaril)
Informative

Non-Response to Clozapine (CYP1A2 *1A/*1F Normal Metabolizer - Higher Inducibility)
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.

Codeine (Codeine; Fioricet with Codeine)
Actionable

Possible Non-Response to Codeine (CYP2D6 *4/*41 Intermediate Metabolizer)
Reduced morphine levels are anticipated, and the patient may or may not experience adequate pain relief with codeine. Codeine can be prescribed at standard label-recommended dosage and administration, with monitoring for symptoms of insufficient pain relief. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Desipramine (Norpramin)
Actionable

Moderate Sensitivity to Desipramine (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider prescribing desipramine at 25% of recommended standard starting dose. Monitor plasma concentrations of desipramine and metabolites and titrate accordingly until a favorable response is achieved.

Diclofenac (Voltaren)
Informative

Possible Sensitivity to Diclofenac (CYP2C9 *1/*2 Intermediate Metabolizer)
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.

Doxepin (Silenor)
Actionable

Moderate Sensitivity to Doxepin (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider reducing the doxepin starting dose by 25%, and adjust maintenance dose according to nordoxepin plasma concentrations.

Flecainide (Tambocor)
Actionable

Increased Sensitivity to Flecainide (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider prescribing a lower flecainide dose. When compared to a CYP2D6 normal metabolizer, an intermediate metabolizer may require a 25% dose reduction. Careful titration with ECG recording and monitoring of flecainide plasma concentrations are recommended until a favorable clinical response is achieved.

Fluphenazine (Prolixin)
Informative

Possible Sensitivity to Fluphenazine (CYP2D6 *4/*41 Intermediate Metabolizer)
Fluphenazine is metabolized by CYP2D6, CYP1A2 and other enzymes. **Decreased CYP2D6 activity may result in higher fluphenazine concentrations potentially leading to higher adverse events such as extrapyramidal symptoms**. There are no established dosing adjustments for patients with decreased 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.

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Flurbiprofen (Ansaid)
Informative

Possible Sensitivity to Flurbiprofen (CYP2C9 *1/*2 Intermediate Metabolizer)
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)
Actionable

Possible Sensitivity to Fluvastatin (CYP2C9 *1/*2 Intermediate Metabolizer)
Increased fluvastatin plasma concentrations due to reduced CYP2C9 activity may occur, resulting in myotoxicity/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.

Fosphenytoin (Cerebyx)
Actionable

Moderate Sensitivity to Fosphenytoin (CYP2C9 *1/*2 Intermediate Metabolizer)
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.

Hydrocodone (Vicodin)
Informative

Possible Altered Response to Hydrocodone (CYP2D6 *4/*41 Intermediate Metabolizer)
Decreased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 intermediate metabolizers. However, there is insufficient evidence whether these patients have decreased analgesia when taking hydrocodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Iloperidone (Fanapt)
Actionable

Moderate Sensitivity to Iloperidone (CYP2D6 *4/*41 Intermediate Metabolizer)
Because iloperidone is associated with QTc prolongation, caution is warranted when prescribing the drug in patients with reduced CYP2D6 activity. Iloperidone must be titrated slowly from a low starting dose to avoid orthostatic hypotension. If patients taking iloperidone experience symptoms that could indicate the occurrence of cardiac arrhythmias (e.g., dizziness, palpitations, or syncope), the prescriber should initiate further evaluation, including cardiac monitoring.

Imipramine (Tofranil)
Actionable

Moderate Sensitivity to Imipramine (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider 25% reduction of recommended starting dose , then titrate in response to imipramine and desipramine plasma concentrations.

Indomethacin (Indocin)
Informative

Possible Sensitivity to Indomethacin (CYP2C9 *1/*2 Intermediate Metabolizer)
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.

Maprotiline (Ludiomil)
Informative

Possible Sensitivity to Maprotiline (CYP2D6 *4/*41 Intermediate Metabolizer)
Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Decreased CYP2D6 activity results in higher maprotiline concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function therefore, therapy must be initiated at a low dosage and gradually adjusted according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.

Meloxicam (Mobic)
Informative

Possible Sensitivity to Meloxicam (CYP2C9 *1/*2 Intermediate Metabolizer)
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.

Metoclopramide (Reglan)
Informative

Possible Sensitivity to Metoclopramide (CYP2D6 *4/*41 Intermediate Metabolizer)
There is not data documenting the changes in plasma concentrations of metoclopramide in CYP2D6 intermediate metabolizers. Metoclopramide can be prescribed at standard label-recommended dosage and administration with careful monitoring for possible increased of side effects.

Metoprolol (Lopressor)
Actionable

Increased Sensitivity to Metoprolol (CYP2D6 *4/*41 Intermediate Metabolizer)
Based on the genotype result, this patient may be at risk of excessive beta-blockade when taking metoprolol at standard dosage. Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol, or prescribe metoprolol at a lower dose. When compared to a normal metabolizer, an intermediate metabolizer may require a 50% dose reduction. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol, or prescribe metoprolol at a lower dose. When compared to a normal metabolizer, an intermediate metabolizer may require a 50% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).

Mexiletine (Mexitil)
Actionable

Increased Sensitivity to Mexiletine (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider prescribing a lower mexiletine dose. A slow titration with ECG recording and monitoring of mexiletine plasma concentrations are recommended until a favorable clinical response is achieved.

Naltrexone (Vivitrol)
Informative

Altered Response to Naltrexone (OPRM1 A118G AA Normal OPRM1 Function)
Treatment of alcohol dependence: the patient has the wild-type genotype for OPRM1 that is associated with a poorer outcome with naltrexone therapy. Naltrexone-treated patients not carrying the 118A> G mutation are less likely to respond to this drug, and may have higher relapse rates than those who are carriers of this mutation.

Nebivolol (Bystolic)
Actionable

Normal Sensitivity to Nebivolol (CYP2D6 *4/*41 Intermediate Metabolizer)
Nebivolol can be prescribed at standard label-recommended dosage and administration. Caution is recommended during up-titration until a favorable response is achieved.

Nortriptyline (Pamelor)
Actionable

Moderate Sensitivity to Nortriptyline (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider reducing nortriptyline dose by 25%, then adjust the dose in response of nortriptyline and 10-hydroxynortriptyline plasma concentrations.

Olanzapine (Zyprexa)
Informative

Non-Response to Olanzapine (CYP1A2 *1A/*1F Normal Metabolizer - Higher Inducibility)
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)
Actionable

Possible Altered Response to Oxycodone (CYP2D6 *4/*41 Intermediate Metabolizer)
Decreased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 intermediate metabolizers. However, there is insufficient evidence whether these patients have decreased analgesia when taking oxycodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Perphenazine (Trilafon)
Actionable

Possible Sensitivity to Perphenazine (CYP2D6 *4/*41 Intermediate Metabolizer)
Patients with a decreased CYP2D6 function will eliminate perphenazine more slowly, which can result in higher drug concentrations and possibly more adverse events (extrapyramidal symptoms). Consider close monitoring and dose reduction to avoid toxicity.

Phenytoin (Dilantin)
Actionable

Moderate Sensitivity to Phenytoin (CYP2C9 *1/*2 Intermediate Metabolizer)
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.

Piroxicam (Feldene)
Informative

Possible Sensitivity to Piroxicam (CYP2C9 *1/*2 Intermediate Metabolizer)
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)
Actionable

Moderate Sensitivity to Propafenone (CYP2D6 *4/*41 Intermediate Metabolizer)
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.

Protriptyline (Vivactil)
Actionable

Possible Sensitivity to Protriptyline (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider prescribing protriptyline at 25% of recommended standard starting dose. Monitor plasma concentrations of protriptyline and metabolites and titrate accordingly until a favorable response is achieved.

Tetrabenazine (Xenazine)
Actionable

Normal Sensitivity to Tetrabenazine (CYP2D6 *4/*41 Intermediate Metabolizer)
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 intermediate metabolizers of CYP2D6 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.

Timolol (Timoptic)
Actionable

Possible Sensitivity to Timolol (CYP2D6 *4/*41 Intermediate Metabolizer)
Potentiated systemic beta-blockade (e.g., bradycardia) has been reported during timolol treatment by patients with decreased CYP2D6 activity. Monitor patient for treatment-related adverse effects.

Tizanidine (Zanaflex)
Informative

Possible Non-Response to Tizanidine (CYP1A2 *1A/*1F Normal Metabolizer - Higher Inducibility)
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.

Tramadol (Ultram)
Actionable

Possible Non-Responder to Tramadol (CYP2D6 *4/*41 Intermediate Metabolizer)
The patient may need higher doses or may not experience adequate pain relief when taking tramadol. Tramadol dose needs to be individualized and careful weekly titration is recommended. If no response, 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.

Trimipramine (Surmontil)
Actionable

Moderate Sensitivity to Trimipramine (CYP2D6 *4/*41 Intermediate Metabolizer)
Consider 25% reduction of recommended starting dose , then titrate in response to trimipramine plasma concentrations.

Warfarin (Coumadin)
Actionable

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

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Pharmacogenetic Test Results			
Gene	**Genotype**	**Phenotype**	**Clinical Consequences**
CYP1A2	*1A/*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.
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	*4/*41	Intermediate Metabolizer	Consistent with moderate to substantial deficiency in CYP2D6 activity. Increased 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.
Factor II Factor V Leiden	20210G>A GG 1691G>A GG	No Increased Risk of Thrombosis	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.
MTHFR	1298A>C AA 677C>T CC	No Increased Risk of Hyperhomocysteinemia	With a normal MTHFR activity, this patient is unlikely to have elevated plasma levels of homocysteine, which is a known risk factor for cardiovascular diseases and thrombosis. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).
OPRM1	A118G AA	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 TT	Normal Transporter 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.

AllelesTested: CYP1A2 *1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W; **CYP2C19** *2, *3, *4, *4B, *6, *7, *8, *9, *10, *17; **CYP2C9** *2, *3, *4, *5, *6, *8, *11, *27; **CYP2D6** *2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *17, *29, *41, *5 (gene deletion), XN (gene duplication); **CYP3A4** *2, *3, *12, *17; **CYP3A5** *1D, *2, *3, *3B, *3C, *6, *7, *8, *9; **Factor II** 20210G>A; **Factor V Leiden** 1691G>A; **MTHFR** 1298A>C, 677C>T; **OPRM1** A118G; **SLCO1B1** 521T>C, 388A>G; **VKORC1** -1639G>A, 1173C>T

2525 Arapahoe Avenue, Suite E4-553, Boulder, CO 80302
P: 303 862-2770 F: 303 595-5289 E: support@sundancedx.com

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%.

Disclaimer: These tests were developed and characterized by Quantigen Laboratory. The tests in Quantigen's pharmacogenetics panel have not been approved by the Federal Drug Administration. The FDA has determined that such approval is not necessary, provided that the laboratory both (1) maintains its good standing as a clinical testing laboratory with all mandatory accrediting bodies, and (2) continually demonstrates that its testing protocols and procedures achieve a high degree of analytical accuracy.

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 non-FDA approved interpretational software and genotype-phenotype associations performed by Translational Software. A qualified designee within Quantigen Laboratory 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.

Laboratory Certification: CLIA # 15D2076283

Laboratory Director: Michael Berger M.D.

Sundance DIAGNOSTICS
2525 Arapahoe Avenue, Suite E4-553, Boulder, CO 80302
P: 303 862-2770 F: 303 595-5289 E: support@sundancedx.com

Summary Patient Report

Patient: Patient 34 DOB: 1/1/1900 Report Date: 5/10/2016
Ordered By: Gender: Accession #: 34

Pharmacogenetic Test Results

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P: 303 862-2770 F: 303 595-5289 E: support@sundancedx.com

Patient Information Card

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

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Patient Name	DOB	Requisition ID
Patient 34	**1/1/1900**	**34**

Pharmacogenetic Test Summary

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For a complete report contact Sundance Diagnostics

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