PATIENT: Doe , Jane (F) **COLLECTED:** 10/14/2014 **SAMPLE TYPE:** Buccal **ACCESSION:** CL-4194-DM
DOB: 1985-01-01 **RECEIVED:** 12/30/2015 **PHYSICIAN:** Dr. RONALD C MCGLENNEN
PATIENT ID: **REPORTED:** 12/30/2015 **PRACTICE:** Kailos Validation Facility

QUICK SUMMARY

ANTIARRHYTHMICS	RESULTS
Digoxin (LANOXIN®, DIGITEK®)	✓ Consider label recommended dosage if no contraindication.
Flecainide (TAMBACOR™)	⚠ Reduce dose by 50%, record ECG, monitor plasma concentration.
Propafenone (RYTHMOL SR®)	⚠ Reduce dose by 70%, record ECG, monitor plasma concentration.

ANTICOAGULANTS	
Warfarin (COUMADIN®)	⚠ The FDA recommends a daily dosage of 5-7 mg/day. This patient also has VKORC1 variants that could further alter dosing considerations.

ANTIDEPRESSANTS	
Amitriptyline (ELAVIL®) Clomipramine (ANAFRANIL®) Doxepin (SINEQUAN®) Imipramine (TOFRANIL™) Trimipramine (SURMONTIL®)	⊘ Consider alternative drug. If a tricyclic is warranted utilize therapeutic drug monitoring to guide dose adjustment.
Citalopram (CELEXA®) Escitalopram (LEXAPRO®)	✓ Consider label recommended dosage if no contraindication.
Desipramine (NORPRAMIN®) Nortriptyline (PAMELOR™)	⊘ Consider alternative drug. If a tricyclic is warranted consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.
Paroxetine (PAXIL®, PEXEVA®)	⚠ Patient may have a decreased clearance of paroxetine (higher paroxetine plasma concentrations).
Venlafaxine (EFFEXOR®)	⊘ Consider alternate drug (citalopram, sertraline) or adjust dose to clinical response and monitor (O-desmethyl)venlafaxine plasma concentration.

ANTIDIABETICS	
Repaglinide (PRANDIN®) Tolbutamide (ORINASE®)	✓ Consider label recommended dosage if no contraindication.

ANTIEPILEPTICS	
Mephenytoin (MESANTOIN®) Phenytoin (DILANTIN®) Valproic Acid (DEPAKOTE®, STAVZOR®)	✓ Consider label recommended dosage if no contraindication.

ANTIHYPERTENSIVES	
Losartan (COZAAR®, HYZAAR®)	✓ Consider label recommended dosage if no contraindication.
Metoprolol (LOPRESSOR®, TOPROL XL®)	⊘ Select alternative drug (e.g., bisoprolol, carvedilol) or reduce dose by 75%. Risk of heart failure. Be alert to ADEs (e.g., bradycardia, cold extremities).

ANTIPSYCHOTICS	
Aripiprazole (ABILIFY®)	⚠ Poor aripiprazole metabolizer. Reduce maximum dose to 10 mg/day.

Haloperidol (HALDOL®)	Select alternative drug (e.g., pimozide, flupenthixol, fluphenazine, quetiapine, olanzapine, clozapine) or reduce dose by 50%.
Olanzapine (ZYPREXA®)	Consider label recommended dosage if no contraindication.
Risperidone (RISPERDAL®)	Select alternative drug (e.g., quetiapine, olanzapine, clozapine) or be extra alert to ADEs and adjust dose to clinical response.

BENZODIAZEPINES

Diazepam (VALIUM®)	Consider label recommended dosage if no contraindication.

CHEMOTHERAPEUTICS

Capecitabine (XELODO®)	Patient may have an increased risk of drug toxicity.
Cisplatin (PLATINOL) Cyclophosphamide (CYTOXAN®) Fluorouracil (EFUDEX®) Methotrexate (TREXALL™)	Consider label recommended dosage if no contraindication.
Paclitaxel (ABRAXANE®, ONXOL®, TAXOL®)	Patient may have increased risk of neutropenia and neurotoxicity syndromes.
Tamoxifen (NOLVADEX® AND SOLTAMOX®)	Consider aromatase inhibitor for postmenopausal women. Increased risk for relapse of breast cancer.

CORTICOSTEROIDS

Prednisone (DELTASONE®, STERAPRED®)	Consider label recommended dosage if no contraindication.

GENERAL ANESTHETICS

Nitrous Oxide (NITRONOX)	Higher homocysteine levels after anesthesia.

HIV/AIDS

Efavirenz (SUSTIVA®) Nelfinavir (VIRACEPT®)	Patient may have risk of decreased CD4-cell count and decreased virologic response.
Nevirapine (VIRAMUNE®)	Consider label recommended dosage if no contraindication.

IMMUNOSUPPRESSANTS

Cyclosporine (SANDIMMUNE®)	Patient may require a decreased dose to reach target blood concentration. Patient may have increased intracellular and blood concentration of cyclosporine.
Mercaptopurine (PURINETHOL®)	Consider label recommended dosage if no contraindication.
Sirolimus (RAPAMUNE®)	Patient may have decreased metabolism of sirolimus and require a lower dose than normal.
Tacrolimus (PROGRAF®)	Patient may have decreased metabolism of tacrolimus and require a lower dose than normal.

MUSCLE RELAXANTS

Carisoprodol (SOMA®)	Consider label recommended dosage if no contraindication.

NSAIDS

Celecoxib (CELEBREX®) Diclofenac (VOLTAREN®, CATAFLAM®)	Consider label recommended dosage if no contraindication.

OPIOIDS

Buprenorphine (SUBUTEX®)	✅ Consider label recommended dosage if no contraindication.
Codeine (TYLENOL® #3) Hydrocodone (LORTAB®, VICODIN®) Oxycodone (OXYCONTIN®, PERCOCET®) Tramadol (ULTRAM®)	🚫 Consider alternative analgesics such as morphine or a nonopioid. Patient has greatly reduced metabolism of narcotic analgesics, leading to insufficient pain relief.

PLATELET AGGREGATION INHIBITORS

Clopidogrel (PLAVIX®)	⚠️ Consider label recommended dosage if no contraindication. Be alert to increased platelet inhibition, decreased residual platelet aggregation, and increased risk of bleeding complications.

PROTON PUMP INHIBITORS

Lansoprazole (PREVACID®) Omeprazole (PRILOSEC®) Pantoprazole (PROTONIX®)	✅ Consider label recommended dosage if no contraindication.

STATINS

Atorvastatin (LIPITOR®) Pravastatin (PRAVACHOL®) Rosuvastatin (CRESTOR®) Simvastatin (ZOCOR®, SIMCOR®)	✅ Consider label recommended dosage if no contraindication.

THROMBOPHILIA

Thrombophilia	🚫 Increased risk of deep vein thrombosis. Avoid oral contraceptives.

IMPORTANT

This Quick Summary provides a brief overview of the predicted response of the patient. This information is based solely on the genotype information and is not based on a complete patient profile. Detection or absence of variants does not replace the need for therapeutic monitoring. Physicians should consider the information contained in the Details section, as well as consider current prescriptions, family history, presenting symptoms, and other factors before making any clinical or therapeutic decisions.

✅ No negative assertions based on genotype.

⚠️ Genotype may present increased risk or decreased effectiveness; prescribe with caution.

🚫 Genotype may present increased risk or decreased effectiveness; select alternative drug.

GENE SUMMARY

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*4/*4	🚫 Poor Metabolizer
CYP2C19	*1/*17	⚠️ Rapid Metabolizer
CYP2C9	*1/*1	✅ Extensive (Normal) Metabolizer
CYP3A4	*1/*1	✅ Extensive (Normal) Metabolizer
F2/F5	Positive	🚫 Increased Thrombophilia Risk

DETAILED INFORMATION

Amitriptyline	CYP2C19 *1/*17 *Rapid metabolizer.*	Evidence ★★★
	The patient is a rapid metabolizer of Amitriptyline. Consider an alternative drug. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments. Expect increased metabolism of Amitriptyline when compared to extensive metabolizers.	
	CYP2D6 *4/*4 *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Amitriptyline. Consider alternative drug (e.g., citalopram, sertraline). If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Patient may have greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. Minor clinical effect: QTc prolongation (<450 ms female, <470 ms male); INR increase < 4.5; Kinetic effect.	
Aripiprazole	CYP2D6 *4/*4 *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Aripiprazole. The Dutch Pharmacogentics Working Group Guideline recommends reducing the maximum dose to 10 mg/day (67% of the maximum recommended daily dose). Clinical effect: long-standing discomfort (48-168 hr) without permanent injury e.g. failure of therapy with tricyclic antidepressants, atypical antipsychotic drugs; extrapyramidal side effects; parkinsonism; ADE resulting from increased bioavailability of tricyclic antidepressants, metoprolol, propafenone (central effects e.g. dizziness); INR 4.5-6.0; neutropenia 1.0-1.5x10^9/l; leucopenia 2.0-3.0x10^9/l; thrombocytopenia 50-75x10^9/l.	
Atorvastatin	ABCB1 rs1045642 A/G (HET)	Evidence ★
	Consider label recommended dosage of Atorvastatin if no contraindication.	
	CYP3A5 *3/*3 *Poor metabolizer.*	Evidence ★
	Consider label recommended dosage of Atorvastatin if no contraindication.	
	SLCO1B1 rs4149056 T/T (WT)	Evidence ★
	Consider label recommended dosage of Atorvastatin if no contraindication.	
Buprenorphine	CYP3A4 *1/*1 *Extensive (normal) metabolizer.*	Evidence ★
	The patient is predicted to be an extensive (normal) CYP3A4 metabolizer. Buprenorphine is metabolized by N-dealkylation via CYP3A4 into norbuprenorphine. Although CYP3A4 is the major enzyme responsible for buprenorphine metabolism, chemical inhibition of CYP3A4 does not appear to significantly affect buprenorphine concentrations. Caution is recommended when co-administering buprenorphine with drugs that affect CYP3A4 activity. Examples of CYP3A4 inhibitors include protease inhibitors, macrolide antibiotics, chloramphenicol, azole antifungals and nefazodone.	
Capecitabine	MTHFR rs1801131 G/G (HOM)	Evidence ★★
	Patients with the homozygous genotype may have increased response and increased risk of drug toxicity in people treated with Capecitabine.	
	MTHFR rs1801133 G/G (WT)	Evidence ★★
	Consider label recommended dosage of Capecitabine if no contraindication.	
	ABCB1 rs1045642 A/G (HET)	Evidence ★
	Patients with the heterozygous rs1045642 genotype may have increased risk of hand-foot syndrome when treated with capecitabine for colorectal neoplasms.	

DETAILED INFORMATION

Carisoprodol	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Carisoprodol if no contraindication.		
Celecoxib	CYP2C9 *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Celecoxib if no contraindication.		
Cisplatin	MTHFR rs1801133 G/G (WT)		Evidence ★
	Cancer patients with the wild type rs1801133 genotype may have a decreased likelihood of response to chemotherapy and a decreased likelihood of drug toxicity than homozygous patients when treated with cisplatin.		
Citalopram	GRIK4 rs1954787 T/C (HET)		Evidence ★★★
	Patients with the heterozygous genotype may have an increased chance of response to citalopram treatment.		
	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★
	Patient may have decreased drug clearance/metabolism and decreased tolerance when treated with citalopram.		
	HTR2A rs7997012 A/G (HET)		Evidence ★★
	Consider label recommended dosage of Citalopram if no contraindication.		
Clomipramine	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	The patient is a rapid metabolizer of Clomipramine. Consider an alternative drug. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments. Expect increased metabolism of Clomipramine when compared to extensive metabolizers.		
	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Clomipramine. Consider alternative drug (e.g., citalopram, sertraline). If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Patient may have greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. Minor clinical effect: QTc prolongation (<450 ms female, <470 ms male); INR increase < 4.5; Kinetic effect.		
Clopidogrel	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	The patient is an ultrarapid metabolizer of Clopidogrel. The US Food and Drug Administration suggests label-recommended dosage and administration of Clopidogrel. The CPIC Dosing Guidelines report risk of increased platelet inhibition and decreased residual platelet aggregation. Ultrarapid metabolizers may also be associated with an increased risk of bleeding complications.		
	ABCB1 rs1045642 A/G (HET)		Evidence ★
	Consider label recommended dosage of Clopidogrel if no contraindication.		
	CYP3A4 rs2242480 C/C (WT)	*Extensive (normal) metabolizer.*	Evidence ★
	Consider label recommended dosage of Clopidogrel if no contraindication.		

DETAILED INFORMATION

Codeine	CYP2D6 *4/*4 *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Codeine. Patient may have greatly reduced morphine formation following codeine administration, leading to insufficient pain relief. CPIC Dosing Guidelines recommend avoiding codeine use due to lack of efficacy. Consider alternative analgesics such as morphine or a nonopiod. Consider avoiding tramadol. The Dutch Pharmacogenetics Working Group Guideline suggests selecting an alternative drug (e.g., acetaminophen, NSAID, morphine-not tramadol or oxycodone) or be alert to symptoms of insufficient pain relief. Clinical effect: short-lived discomfort (< 48 hr) without permanent injury: e.g. reduced decrease in resting heart rate; reduction in exercise tachycardia; decreased pain relief from oxycodone; ADE resulting from increased bioavailability of atomoxetine (decreased appetite, insomnia, sleep disturbance etc); neutropenia > 1.5x10^9/l; leucopenia > 3.0x10^9/l; thrombocytopenia > 75x10^9/l; moderate diarrhea not affecting daily activities; reduced glucose increase following oral glucose tolerance test.	
Cyclophosphamide	MTHFR rs1801133 G/G (WT)	Evidence ★★
	Consider label recommended dosage of Cyclophosphamide if no contraindication.	
Cyclosporine	ABCB1 rs1045642 A/G (HET)	Evidence ★
	Patients with the heterozygous rs1045642 genotype may have increased intracellular and blood concentration of cyclosporine with transplantation. However contradictory findings have been reported for no association between this variant and dose/efficacy of cyclosporine.	
	CYP3A5 *3/*3 *Poor metabolizer.*	Evidence ★
	Patients with CYP3A5 *3/*3 genotype may require a decreased dose of cyclosporine to reach target blood concentration, although some studies find no association with dosage.	
Desipramine	CYP2D6 *4/*4 *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Desipramine. Consider alternative drug (e.g., citalopram, sertraline). If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Patient may have greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. Minor clinical effect: QTc prolongation (<450 ms female, <470 ms male); INR increase < 4.5; Kinetic effect.	
Diazepam	CYP2C19 *1/*17 *Rapid metabolizer.*	Evidence ★
	The patient is a rarapid metabolizer of diazepam and should have increased metabolism of diazepam (lower AUC and higher clearance of diazepam) compared to poor metabolizers. The patient should emerge from anesthesia more rapidly than poor metabolizers.	
Diclofenac	CYP2C9 *1/*1 *Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Diclofenac if no contraindication.	
Digoxin	ABCB1 rs1045642 A/G (HET)	Evidence ★★
	Consider label recommended dosage of Digoxin if no contraindication.	

DETAILED INFORMATION

Doxepin	CYP2C19 *1/*17 — *Rapid metabolizer.*	Evidence ★★★
	The patient is an ultrarapid metabolizer of Doxepin. Consider an alternative drug. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments. Expect increased metabolism of Doxepin when compared to extensive metabolizers.	
	CYP2D6 *4/*4 — *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Doxepin. Consider alternative drug (e.g., citalopram, sertraline). If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Patient may have greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. Minor clinical effect: QTc prolongation (<450 ms female, <470 ms male); INR increase < 4.5; Kinetic effect.	
Efavirenz	CYP3A5 *3/*3 — *Poor metabolizer.*	Evidence ★★
	Consider label recommended dosage of Efavirenz if no contraindication.	
	ABCB1 rs1045642 A/G (HET)	Evidence ★
	Patients with the heterozygous rs1045642 genotype and HIV who are treated with nelfinavir and efavirenz may have decreased CD4-cell count as compared, decreased virologic response and a decreased, but not absent, risk for toxicity-related failure.	
Escitalopram	CYP2C19 *1/*17 — *Rapid metabolizer.*	Evidence ★★
	Patient may have decreased drug clearance/metabolism and decreased tolerance when treated with escitalopram.	
	HTR2A rs9316233 C/G (HET)	Evidence ★
	Consider label recommended dosage of Escitalopram if no contraindication.	
Flecainide	CYP2D6 *4/*4 — *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Flecainide. The Dutch Pharmacogentics Working Group Guideline recommends reducing dose by 50%, record ECG, monitor plasma concentration. Minor clinical effect: QTc prolongation (<450 ms female, <470 ms male); INR increase < 4.5; Kinetic effect.	
Fluorouracil	MTHFR rs1801133 G/G (WT)	Evidence ★★
	Consider label recommended dosage of Fluorouracil if no contraindication.	
	ABCB1 rs1045642 A/G (HET)	Evidence ★
	Consider label recommended dosage of Fluorouracil if no contraindication.	
Haloperidol	CYP2D6 *4/*4 — *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Haloperidol. The Dutch Pharmacogentics Working Group Guideline recommends reducing dose by 50% or selecting alternative drug (e.g., pimozide, flupenthixol, fluphenazine, quetiapine, olanzapine, clozapine). Clinical effect: long-standing discomfort (48-168 hr) without permanent injury e.g. failure of therapy with tricyclic antidepressants, atypical antipsychotic drugs; extrapyramidal side effects; parkinsonism; ADE resulting from increased bioavailability of tricyclic antidepressants, metoprolol, propafenone (central effects e.g. dizziness); INR 4.5-6.0; neutropenia 1.0-1.5x10^9/l; leucopenia 2.0-3.0x10^9/l; thrombocytopenia 50-75x10^9/l.	

DETAILED INFORMATION

Hydrocodone	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Hydrocodone. This may lead to greatly reduced morphine formation following Hydrocodone administration leading to insufficient pain relief. The CPIC codeine guidelines suggest avoiding use of analgesics metabolized by CYP2D6 (such as Codeine, Hydrocodone, Oxycodeine, Tramadol) and consider alternative analgesics such as morphine or a non-opioid.		
Imipramine	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	The patient is a rapid metabolizer of Imipramine. Consider an alternative drug. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments. Expect increased metabolism of Imipramine when compared to extensive metabolizers.		
	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Imipramine. Consider alternative drug (e.g., citalopram, sertraline). If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Patient may have greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. Minor clinical effect: QTc prolongation (<450 ms female, <470 ms male); INR increase < 4.5; Kinetic effect.		
Lansoprazole	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Lansoprazole if no contraindication.		
Losartan	CYP2C9 *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Losartan if no contraindication.		
Mephenytoin	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★
	Consider label recommended dosage of Mephenytoin if no contraindication.		
Mercaptopurine	MTHFR rs1801133 G/G (WT)		Evidence ★
	Consider label recommended dosage of Mercaptopurine if no contraindication.		
Methotrexate	MTHFR rs1801133 G/G (WT)		Evidence ★★★
	Consider label recommended dosage of Methotrexate if no contraindication.		
	MTHFR rs1801131 G/G (HOM)		Evidence ★
	Patients with the homozygous genotype and non-Hodgkin lymphoma who are treated with methotrexate may have an increased risk of mucositis. Patients with the homozygous rs1801131 genotype and rheumatoid arthritis who are treated with methotrexate may have an increased risk of drug toxicity and adverse events. This association has been contradicted in some studies.		
	MTHFR rs4846051 A/A (HOM)		Evidence ★
	Patients with the heterozygous genotype with rheumatoid arthritis who are treated with methotrexate may have a higher drug toxicity score than wild-type patients.		
	SLCO1B1 rs4149056 T/T (WT)		Evidence ★
	Consider label recommended dosage of Methotrexate if no contraindication.		

DETAILED INFORMATION

Metoprolol	CYP2D6 *4/*4 *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Metoprolol. The Dutch Pharmacogentics Working Group Guideline warns of risk of heart failure and to select alternative drug (e.g., bisoprolol, carvedilol) or reduce dose by 75%. Other indications: be alert to ADEs (e.g., bradycardia, cold extremities) or select alternative drug (e.g., atenolol, bisoprolol). Clinical effect: long-standing discomfort (48-168 hr) without permanent injury e.g. failure of therapy with tricyclic antidepressants, atypical antipsychotic drugs; extrapyramidal side effects; parkinsonism; ADE resulting from increased bioavailability of tricyclic antidepressants, metoprolol, propafenone (central effects e.g. dizziness); INR 4.5-6.0; neutropenia 1.0-1.5x10^9/l; leucopenia 2.0-3.0x10^9/l; thrombocytopenia 50-75x10^9/l.	
Nelfinavir	ABCB1 rs1045642 A/G (HET)	Evidence ★
	Patients with the heterozygous rs1045642 genotype and HIV who are treated with nelfinavir and efavirenz may have decreased CD4-cell count, a decreased virologic response and a decreased, but not absent, risk for toxicity-related failure.	
Nevirapine	CYP3A5 *3/*3 *Poor metabolizer.*	Evidence ★★
	Patients with the CYP3A5 *3/*3 genotype and HIV infection who are treated with nevirapine may have increased clearance of the drug as compared to patients with the *1/*3 or *1/*1 genotype. Association with clearance was not found in a larger cohort in a separate study. Patients may also have differences in alanine aminotransferase levels, but association with toxicity has not been reported.	
	ABCB1 rs1045642 A/G (HET)	Evidence ★★
	Consider label recommended dosage of Nevirapine if no contraindication.	
Nitrous Oxide	MTHFR rs1801131 G/G (HOM)	Evidence ★
	Patients with the homozygous rs1801131 genotype may have higher homocysteine levels after nitrous oxide anesthesia.	
	MTHFR rs1801133 G/G (WT)	Evidence ★
	Consider label recommended dosage of Nitrous Oxide if no contraindication.	
Nortriptyline	CYP2D6 *4/*4 *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Nortriptyline. Consider alternative drug (e.g., citalopram, sertraline). If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Patient may have greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. Minor clinical effect: QTc prolongation (<450 ms female, <470 ms male); INR increase < 4.5; Kinetic effect.	
	ABCB1 rs1045642 A/G (HET)	Evidence ★
	Patients with the heterozygous rs1045642 genotype and depression who are treated with nortriptyline may have a decreased, but not absent, likelihood to develop postural hypotension.	
Olanzapine	HTR2A rs6313 G/G (WT)	Evidence ★
	Consider label recommended dosage of Olanzapine if no contraindication.	
	HTR2A rs7997012 A/G (HET)	Evidence ★
	Consider label recommended dosage of Olanzapine if no contraindication.	

DETAILED INFORMATION

Omeprazole	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Omeprazole if no contraindication.		
Oxycodone	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★
	The genotype predicts that the patient is a Poor Metabolizer for Oxycodone. Consider using an alternate drug rather than oxycodone (not codeine or tramadol) or be alert to insufficient pain relief. The Dutch Pharmacogenetics Working Group Guideline indicates that there is insufficient data to allow calculation of dose adjustment. Clinical effect: short-lived discomfort (< 48 hr) without permanent injury: e.g. reduced decrease in resting heart rate; reduction in exercise tachycardia; decreased pain relief from oxycodone; ADE resulting from increased bioavailability of atomoxetine (decreased appetite, insomnia, sleep disturbance etc); neutropenia > 1.5x10^9/l; leucopenia > 3.0x10^9/l; thrombocytopenia > 75x10^9/l; moderate diarrhea not affecting daily activities; reduced glucose increase following oral glucose tolerance test.		
Paclitaxel	CYP3A4 rs12721627 G/G (WT)	*Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Paclitaxel if no contraindication.		
	ABCB1 rs1045642 A/G (HET)		Evidence ★
	Patients with the heterozygous rs1045642 genotype may have increased risk of Neutropenia and Neurotoxicity Syndromes when treated with paclitaxel in cancer patients as compared to patients with homozygous genotype		
Pantoprazole	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Pantoprazole if no contraindication.		
Paroxetine	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer of Paroxetine. The Dutch Pharmacogenetics Working Group Guideline makes no dosing recommendation. Minor clinical effect: QTc prolongation (<450 ms men, <470 ms women); INR increase < 4.5. Kinetic effect.		
	HTR2A rs6313 G/G (WT)		Evidence ★
	Consider label recommended dosage of Paroxetine if no contraindication.		
Phenytoin	CYP2C9 *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Phenytoin if no contraindication.		
	ABCB1 rs1045642 A/G (HET)		Evidence ★
	African American patients with epilepsy and the heterozygous genotype may have increased likelihood of drug resistance when treated with phenytoin. However no associations have been found between this variant and increased response to phenytoin in Asians.		
	CYP2C9 rs9332131 A/A (WT)	*Extensive (normal) metabolizer.*	Evidence ★
	Consider label recommended dosage of Phenytoin if no contraindication.		
Pravastatin	SLCO1B1 rs4149056 T/T (WT)		Evidence ★★
	Consider label recommended dosage of Pravastatin if no contraindication.		
Prednisone	ABCB1 rs1045642 A/G (HET)		Evidence ★
	Consider label recommended dosage of prednisone if no contraindication.		

DETAILED INFORMATION

Propafenone	CYP2D6 *4/*4 *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Propafenone. The Dutch Pharmacogentics Working Group Guideline recommends reducing dose by 70%, recording ECG, and monitoring plasma concentration. Clinical effect: long-standing discomfort (48-168 hr) without permanent injury e.g. failure of therapy with tricyclic antidepressants, atypical antipsychotic drugs; extrapyramidal side effects; parkinsonism; ADE resulting from increased bioavailability of tricyclic antidepressants, metoprolol, propafenone (central effects e.g. dizziness); INR 4.5-6.0; neutropenia 1.0-1.5x10^9/l; leucopenia 2.0-3.0x10^9/l; thrombocytopenia 50-75x10^9/l.	
Repaglinide	SLCO1B1 rs4149056 T/T (WT)	Evidence ★
	Consider label recommended dosage of Repaglinide if no contraindication.	
Risperidone	CYP2D6 *4/*4 *Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer of Risperidone. The Dutch Pharmacogenetics Working Group Guideline recommends selecting an alternative drug (e.g., quetiapine,olanzapine, clozapine) or be extra alert to ADEs and adjust dose to clinical response. Clinical effect: long-standing discomfort (> 168 hr), permanent symptom or invalidating injury e.g. failure of prophylaxis of atrial fibrillation; venous thromboembolism; decreased effect of clopidogrel on inhibition of platelet aggregation; ADE resulting from increased bioavailability of phenytoin; INR > 6.0; neutropenia 0.5-1.0x10^9/l; leucopenia 1.0-2.0x10^9/l; thrombocytopenia 25-50x10^9/l; severe diarrhea.	
	HTR2A rs6311 C/C (WT)	Evidence ★
	Consider label recommended dosage of Risperidone if no contraindication.	
	HTR2A rs6313 G/G (WT)	Evidence ★
	Consider label recommended dosage of Risperidone if no contraindication.	
Rosuvastatin	SLCO1B1 rs4149056 T/T (WT)	Evidence ★
	Consider label recommended dosage of Rosuvastatin if no contraindication.	
Simvastatin	SLCO1B1 rs4149056 T/T (WT)	Evidence ★★★
	Consider label recommended dosage of Simvastatin if no contraindication.	
	ABCB1 rs1045642 A/G (HET)	Evidence ★
	Consider label recommended dosage of Simvastatin if no contraindication.	
	CYP3A5 *3/*3 *Poor metabolizer.*	Evidence ★
	Consider label recommended dosage of Simvastatin if no contraindication.	
Sirolimus	CYP3A5 *3/*3 *Poor metabolizer.*	Evidence ★★
	Patients with the CYP3A5 *3/*3 genotype and who are recipients of transplants may have decreased metabolism of Sirolimus and require a lower dose.	
Tacrolimus	CYP3A5 *3/*3 *Poor metabolizer.*	Evidence ★★★
	Patients with the homozygous CYP3A5*3/*3 genotype and are recipients of a transplantation who are treated with tacrolimus may have decreased metabolism of tacrolimus resulting in increased exposure, and may require a lower dose as compared to normal.	

DETAILED INFORMATION

Tamoxifen	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Tamoxifen. The Dutch Pharmacogentics Working Group Guideline indicates an increased risk for relapse of breast cancer. Consider aromatase inhibitor for postmenopausal women. Clinical effect: Failure of lifesaving therapy e.g. anticipated myelosuppression; prevention of breast cancer relapse; arrhythmia; neutropenia < 0.5x10^9/l; leucopenia < 1.0x10^9/l; thrombocytopenia < 25x10^9/l; life-threatening complications from diarrhea.		
Thrombophilia	F5 rs6025 T/C (HET)		Evidence ★★★
	Patients with a heterozygous rs6025 call in the F5 gene, commonly known as the Leiden mutation, have a higher risk of recurrent thrombosis, and depending on other factors, this risk can climb to at least 5x. One study concludes that heterozygotes for rs6025 have an increased risk of recurrent deep venous thrombosis after a first episode and are therefore candidates for lifelong anticoagulation treatment. Patients with negative family history of thrombotic events should avoid additional risk factors (e.g., obesity, smoking). Patients with positive family history of thrombotic events should avoid estrogen-containing oral contraceptive and select alternative (e.g., copper intrauterine device, progestin-only contraceptive).		
	F2 rs1799963 G/G (WT)		Evidence ★★★
	The patient does not carry the Prothrombin (Factor II: G20210A) Mutation, a common genetic marker associated with inherited thrombophilia.		
Tolbutamide	CYP2C9 *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Tolbutamide if no contraindication.		
Tramadol	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Tramadol. The Dutch Pharmacogentics Working Group Guideline recommends selecting an alternative drug, not oxycodone or codeine, or be alert to symptoms of insufficient pain relief. Clinical effect: short-lived discomfort (< 48 hr) without permanent injury: e.g. reduced decrease in resting heart rate; reduction in exercise tachycardia; decreased pain relief from oxycodone; ADE resulting from increased bioavailability of atomoxetine (decreased appetite, insomnia, sleep disturbance etc); neutropenia > 1.5x10^9/l; leucopenia > 3.0x10^9/l; thrombocytopenia > 75x10^9/l; moderate diarrhea not affecting daily activities; reduced glucose increase following oral glucose tolerance test.		
Trimipramine	CYP2C19 *1/*17	*Rapid metabolizer.*	Evidence ★★★
	The patient is a rapid metabolizer of Trimipramine. Consider an alternative drug. If a tricyclic is warranted, utilize therapeutic drug monitoring to guide dose adjustments. Expect increased metabolism of Trimipramine when compared to extensive metabolizers.		
	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer for Trimipramine. Consider alternative drug (e.g., citalopram, sertraline). If a tricyclic is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Patient may have greatly reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers. Higher plasma concentrations will increase the probability of side effects. Minor clinical effect: QTc prolongation (<450 ms female, <470 ms male); INR increase < 4.5; Kinetic effect.		

DETAILED INFORMATION

Valproic Acid	CYP2C9 *1/*1	*Extensive (normal) metabolizer.*	Evidence ★
	Consider label recommended dosage of Valproic Acid if no contraindication.		
Venlafaxine	CYP2D6 *4/*4	*Poor metabolizer.*	Evidence ★★★
	The genotype predicts that the patient is a Poor Metabolizer of Venlafaxine. Insufficient data to allow calculation of dose adjustment. Select alternative drug (e.g., citalopram, sertraline) or adjust dose to clinical response and monitor (O-desmethyl)venlafaxine plasma concentration. Clinical effect: long-standing discomfort (48-168 hr) without permanent injury e.g. failure of therapy with tricyclic antidepressants, atypical antipsychotic drugs; extrapyramidal side effects; parkinsonism; ADE resulting from increased bioavailability of tricyclic antidepressants, metoprolol, propafenone (central effects e.g. dizziness); INR 4.5-6.0; neutropenia 1.0-1.5x10^9/l; leucopenia 2.0-3.0x10^9/l; thrombocytopenia 50-75x10^9/l.		
Warfarin	VKORC1 rs7294 C/T (HET)		Evidence ★★★
	Patients with the heterozygous rs7294 genotype who are treated with warfarin may require a higher dose as compared to patients with the wild-type genotype.		
	CYP2C9 *1/*1. VKORC1 rs9923231 C/C (WT)	*Extensive (normal) metabolizer.*	Evidence ★★★
	The CYP2C9 *1/*1 genotype is a fully functional, extensive (normal) metabolizer of Warfarin, and the VKORC1 wild-type variant is associated with low sensitivity to Warfarin. Recommended daily warfarin doses (mg/day) to achieve a therapeutic INR based on CYP2C9 and VKORC1 genotype using the warfarin product insert approved by the United States Food and Drug Administration: 5-7 mg / day.		
	VKORC1 rs9934438 G/G (WT)		Evidence ★★★
	Consider label recommended dosage of Warfarin if no contraindication.		
	VKORC1 rs17708472 G/A (HET)		Evidence ★★
	Patients with the heterozygous rs17708472 genotype: 1) may require a higher dose of warfarin as compared to patients with the wild-type genotype 2) may have an increased risk of warfarin resistance as compared to patients with the wild-type genotype.		
	VKORC1 rs2359612 G/G (HOM)		Evidence ★★
	Patients with the homozygous rs2359612 genotype who are treated with warfarin may require a higher dose as compared to patients with the heterozygous or wild-type genotype.		
	CYP2C9 rs7900194 G/G (WT)	*Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Warfarin if no contraindication.		
	CYP2C9 rs28371686 C/C (WT)	*Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Warfarin if no contraindication.		
	VKORC1 rs8050894 C/C (WT)		Evidence ★★
	Consider label recommended dosage of Warfarin if no contraindication.		
	CYP2C9 rs28371685 C/C (WT)	*Extensive (normal) metabolizer.*	Evidence ★
	Consider label recommended dosage of Warfarin if no contraindication.		
	CYP2C9 rs9332131 A/A (WT)	*Extensive (normal) metabolizer.*	Evidence ★
	Consider label recommended dosage of Warfarin if no contraindication.		

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KEY FOR VARIANT-DRUG COMBINATION EVIDENCE

Replicated in multiple studies with statistical significance and strong effect size.
Replicated in multiple studies with and without statistical significance and effect size may be minimal.
Not yet replicated or replicated but lacking clear evidence of an association.
Notable information is available and special considerations may be of interest when prescribing for this genotype.
Literature does not indicate additional risks, benefits, or prescription changes to consider for this genotype.

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REPORTED GENOTYPES

This panel performs genotyping analysis on key genes and variant hot-spot regions, focused on analyzing loci documented as altering the effectiveness of drug metabolism. Key genotyping results include the following:

ABCB1
rs1045642:A/G Het

CYP2C19
CYP2C19 *1/*17
rs4244285:G/G Wild
rs4986893:G/G Wild
rs28399504:A/A Wild
rs56337013:C/C Wild
rs72552267:G/G Wild
rs72558186:T/T Wild
rs41291556:T/T Wild
rs17884712:G/G Wild
rs6413438:C/C Wild
rs55640102:A/A Wild
rs12248560:C/T Het

CYP2C9
CYP2C9 *1/*1
rs1799853:C/C Wild
rs1057910:A/A Wild
rs28371686:C/C Wild
rs9332131:A/A Wild
rs7900194:G/G Wild
rs28371685:C/C Wild

CYP2D6
CYP2D6 *4/*4
rs16947:G/G Hom
rs1135840:G/G Wild
rs35742686:T/T Wild
rs1135824:T/T Wild
rs1065852:A/A Hom
rs3892097:T/T Hom
rs5030655:A/A Wild
rs5030867:T/T Wild
rs5030865:C/C Wild
rs5030656:CTT/CTT Wild
rs5030863 Unreportable
rs5030862:C/C Wild
rs72549357:A/A Wild
rs28371706 Unreportable
rs59421388:C/C Wild
rs769258:C/C Wild
rs28371725:C/C Wild
rs28371696:C/C Wild

CYP3A4
CYP3A4 *1/*1
rs12721627:G/G Wild
rs2242480:C/C Wild
rs12721629:G/G Wild
rs4987161:A/A Wild
rs72552799:C/C Wild
rs67784355:G/G Wild
rs4986909:G/G Wild
rs35599367:G/G Wild

CYP3A5
CYP3A5 *3/*3
rs776746:C/C Wild

F2
rs1799963:G/G Wild

F5
rs6025:T/C Het

GRIK4
rs1954787:T/C Het

HTR2A
rs7997012:A/G Het
rs9316233:C/G Het
rs6313:G/G Wild
rs6311:C/C Wild

MTHFR
rs1801133:G/G Wild
rs1801131:G/G Hom
rs4846051:A/A Hom

SLCO1B1
rs4149056:T/T Wild

VKORC1
rs9923231:C/C Wild
rs9934438:G/G Wild
rs17708472:G/A Het
rs2359612:G/G Hom
rs7294:C/T Het
rs8050894:C/C Wild

Reported genotype calls are all displayed with respect to the positive DNA strand. Variants indicated as homozygous (Hom) or heterozygous (Het) differ from the GRCh37/hg19 reference sequence (Wild). This report is limited to the following star-alleles: CYP2D6: *1, *2, *3B, *3, *4, *5, *6, *6C, *7, *8, *9, *10, *11, *12, *14B, *14A, *15, *17, *29, *35A, *41 & *46. CYP2C19: *1, *2, *3, *4, *5, *6, *7, *8, *9, *10, *12 & *17. CYP2C9: *1, *2 & *3. CYP3A5: *1 & *3. CYP3A4: *1, *8, *11, *12, *13, *16, *17 & *22. Any genotype identified as a default star-allele (CYP2D6 *2, CYP2C19 *1, CYP2C9 *1, CYP3A5 *3, CYP3A4 *1) indicates the absence only of the other alleles listed and does not imply that other variants in the gene are absent. Full allele deletions and duplications are only analyzed for the CYP2D6 gene. This test does not report polymorphisms other than those specifically listed, and mutations in other genes associated with drug metabolism will not be detected. Rare diagnostic errors may occur if variations occur in primer site locations.

DISCLAIMER

The information presented on this report is provided as supplementary health information. The results presented are intended for use by a physician, pharmacist or other healthcare professional to advise a patient on the use of prescribed medications. This test is not a 510k cleared test, but managed by CMS and FDA under the Clinical Laboratory Improvement Amendment (CLIA) as a LDT. The ordering physician is responsible for the diagnosis and management of disease and decisions based on the data provided. Results are dependent on adequate specimen collection and processing.

METHODOLOGY

Genomic DNA is extracted from dry buccal swabs using magnetic particle processing. DNA from patient samples are amplified with primers specific for ABCB1, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, F2, F5, GRIK4, HTR2A, MTHFR, SLCO1B1 & VKORC1 using Nested Patch PCR (Varley, et. al.). Positive and negative controls are used with each run. Patient samples, positive, and negative controls are sequenced using a MiSeq (Illumina). Sequences are analyzed using alignment and base call algorithms with Kailos Blue Software for the presence or absence of single nucleotide base changes, insertions and deletions. LR-PCR utilized for confirmation of CYP2D6 duplications and deletions. Results and recommendations are compiled as part of a medical report.

Genetic testing was performed in the Kailos Genetics CLIA facility at 601 Genome Way; Huntsville, Al. 35806. CLIA#: 01D2016114. Medical Director: Ronald McGlennen MD, FCAP, FACMG, ABMG.

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This report was reviewed and approved for release by CLIA Lab Manager & Supervisor: Michele R. Erickson-Johnson, PhD, MB (ASCP)[CM]

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