GenoScribe™
BY EMGENEX & GENETRAIT LABORATORIES

300 Portland Street • Columbia, MO 65201
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PHARMACOGENETIC LABORATORY RESULTS

01/27/2015 04:31 PM

Name: [redacted]
Patient ID: 1[redacted]
Specimen ID: 1[redacted]

Gender: F
DOB: 0[redacted]
Race: CAUCASIAN

Specimen Type: BUCCAL SWAB
Collection Date: 01/21/15
Received Date: 01/22/15

ORDERED BY: [redacted]
LOCATION: [redacted]

P: [redacted]
F: [redacted]

CARDIOVASCULAR DISEASE PROFILE

ApoE: Normal Risk

Normal Risk

Cholesterol Management

This patient has a genotype that suggests the patient does not have an elevated risk of coronary heart disease related to these genetic markers.

Statins, a low fat diet, and moderate alcohol usage are expected to be beneficial therapies in lowering LDL in individuals with this genotype.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

STATIN INDUCED MYOPATHY RISK

SLCO1B1: Intermediate Metabolizer

Modification Recommended

Drugs Evaluated: Simvastatin (Zocor), Atorvastatin (Lipitor®), Pitavastatin (Livalo)

This patient has one high risk allele for statin induced myopathy.

Individuals who are heterozygous for (have one copy of) the SLCO1B1*5 allele are estimated to have a 2 to 20 times greater risk of statin induced myopathy than individuals without the variant allele.

Consider alternative medications such as Fluvastatin, Pravastatin and Rosuvastatin, if not otherwise contraindicated.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

THROMBOSIS PROFILE

Prothrombin (Factor II): Normal Risk
Factor V Leiden: Normal Risk
MTHFR A1298C: Normal Risk
MTHFR C677T: Normal Risk

Normal

The absence of a Factor V Leiden 1691A allele and Prothrombin (Factor II) 20210A allele suggests that the patient does not have an elevated risk of venous thrombosis related to these genetic markers.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

WARFARIN METABOLISM

VKORC1: Normal Sensitivity to Warfarin

CYP2C9: Intermediate Metabolizer

Drug Evaluated: Warfarin (Coumadin)

Modification Recommended

This patient has genetic variations within the VKORC1 and/or CYP2C9 genes that predict a reduction in the combined VKORC1 and CYP2C9 enzyme function.

Reduced VKORC1 and CYP2C9 combined enzyme function is expected to reduce the amount of Warfarin necessary to achieve an INR of 2-3.

Consider Warfarin dosages ranging from 3 to 4 mg/day for a patient with these combined VKORC1 and CYP2C9 genotypes. For a patient-specific dosage that includes ethnicity and weight, please use the following website to calculate dosage: http://www.pharmgkb.org/download.action?filename=IWPC_dose_calculator_6-19-09.xls

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

ANTIPLATELET METABOLISM

CYP3A5: Intermediate Metabolizer

CYP3A4: Extensive Metabolizer

CYP2C19: Ultra Metabolizer

Drugs Evaluated: Clopidogrel (Plavix), Ticagrelor (Brilinta®)

Possible Side Effect

This patient has genetic variations within the CYP2C19 gene that predict an increase in the CYP2C19 enzyme function that affects the metabolism of *Clopidogrel*.

Increased CYP2C19 enzyme function is expected to increase the conversion of Clopidogrel to its active form, although in most cases a dosage adjustment is not expected to be necessary. In addition, some studies indicate that the CYP2C19*17 allele is associated with an increased risk of bleeding.

Analysis of the CYP3A4 and CYP3A5 genes predict normal CYP3A4 and CYP3A5 related enzymatic function. Co-administration of other drugs that inhibit the CYP2C19, CYP3A4 or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these medications.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

OPIATE METABOLISM

CYP3A5: Intermediate Metabolizer

CYP2D6: Extensive Metabolizer

CYP3A4: Extensive Metabolizer

CYP2C19: Ultra Metabolizer

Drugs Evaluated: Codeine, Hydrocodone (Lortab®, Vicodin®), Dihydrocodeine (Synalgos®-DC), Fentanyl (Abstral®, Actiq®, Fentora®, Onsolis), Oxycodone (Percocet®, Oxycontin®), Methadone (Dolophine®), Meperidine (Demerol®), Ketamine (Ketalar®), Tramadol (Ultram®)

Modification Recommended

This patient has genetic variations within CYP2C19 the gene that predicts an increase in the CYP2C19 enzyme function.

Increased CYP2C19 enzyme function is expected to increase the clearance of Meperidine, as well as increase the production of the metabolite Normeperidine. Increased CYP2C19 enzyme function may also increase the clearance of Methadone.

Consider alternative medications such as Codeine, Hydrocodone, Dihydrocodeine, Oxycodone, Tramadol, Ketamine, Fentanyl, Morphine, Oxymorphone, or Hydromorphone, if not otherwise contraindicated.

Analysis of the CYP2D6, CYP3A4 and CYP3A5 genes predict normal CYP2D6, CYP3A4 and CYP3A5 related enzymatic function. Co-administration of other drugs that inhibit the CYP2D6, CYP2C19, CYP3A4 or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these medications.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

NSAID METABOLISM

CYP2C9: Intermediate Metabolizer

Drugs Evaluated: Aspirin (Bayer), Celecoxib (Celebrex®), Diclofenac (Voltaren®-XR), Flurbiprofen (Ansaid®), Ibuprofen (Advil®, Motrin®), Meloxicam (Mobic®), Naproxen (Aleve®, Anaprox®), Mefenamic Acid (Ponstel®), Valdecoxib (Bextra), Piroxicam (Feldene®)

Modification Recommended

This patient has genetic variations within the CYP2C9 gene that predict a reduction in the CYP2C9 enzyme function that affects the metabolism of several NSAIDs.

Reduced CYP2C9 enzyme function is expected to slow clearance of Aspirin, Celecoxib, Diclofenac, Flurbiprofen, Ibuprofen, Mefenamic Acid, Meloxicam, Naproxen, Piroxicam, and Valdecoxib.

Consider alternative medications such as Acetaminophen, Indomethacin, Ketoprofen, or Sulindac, if not otherwise contraindicated.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

METHOTREXATE METABOLISM

SLCO1B1: Intermediate Metabolizer

Drug Evaluated: Methotrexate (Rheumatrex®, Trexall™, Otrexup)

Modification Recommended

This patient has genetic variations within the SLCO1B1 gene that predict a reduction in the OATP1B1 transporter protein function that affects the metabolism Methotrexate.

Reduced OATP1B1 transporter protein function is expected to reduce the clearance of Methotrexate.

Consider reduced Methotrexate dosages or alternative medications, if not otherwise contraindicated.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

ANGIOTENSIN RECEPTOR BLOCKER (ARB) METABOLISM

CYP2C9: Intermediate Metabolizer

CYP3A5: Intermediate Metabolizer

CYP3A4: Extensive Metabolizer

Drugs Evaluated: Losartan (Cozaar®), Irbesartan (Avapro®)

Modification Recommended

This patient has genetic variations within the CYP2C9 gene that predict a reduction in the CYP2C9 enzyme function that affects the metabolism of Irbesartan and *Losartan.*

Reduced CYP2C9 enzyme function is expected to slow clearance of Irbesartan and to reduce the conversion of Losartan to active metabolites.

Consider alternative medications such as Olmesartan, Valsartan, Candesartan, Telmisartan and Eprosartan, if not otherwise contraindicated.

Molecular analysis identified no clinically significant genetic variations within the CYP3A4 or CYP3A5 genes that affect the metabolism of ARB medications. Co-administration of other drugs that inhibit CYP2C9, CYP3A4 or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these drugs.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

ANTIARRHYTHMIC METABOLISM

CYP3A5: Intermediate Metabolizer

CYP2D6: Extensive Metabolizer

CYP3A4: Extensive Metabolizer

Drugs Evaluated: Flecainide (Tambocor), Propafenone (Rythmol SR®)

Normal

Molecular analysis identified no clinically significant genetic variations within the CYP2D6, CYP3A4, or CYP3A5 genes that affect the metabolism of Flecainide or *Propafenone.*

Manufacturer dosage recommendations, as listed on the product insert, are expected to apply to this patient for Flecainide and Propafenone. Co-administration of other drugs that inhibit the CYP2D6, CYP3A4, or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these drugs.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

METOPROLOL METABOLISM

CYP2D6: Extensive Metabolizer

Drug Evaluated: Metoprolol (Lopressor®, Toprol®)

Normal

Molecular analysis identified no clinically significant genetic variations within the CYP2D6 gene. Thus, normal enzymatic activity associated with this gene is predicted.

Manufacturer dosage recommendations, as listed on the product insert, are expected to apply to this patient for Metoprolol, if not otherwise contraindicated. Co-administration of other drugs that inhibit the CYP2D6 enzyme, and other genetic and non-genetic factors may alter the efficacy or toxicity of this medication.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

TRICYCLIC ANTIDEPRESSANT METABOLISM

CYP3A5: Intermediate Metabolizer

CYP2D6: Extensive Metabolizer

CYP3A4: Extensive Metabolizer

CYP2C19: Ultra Metabolizer

Drugs Evaluated: Desipramine (Norpramin®), Amoxapine, Nortriptyline (Pamelor™), Amitriptyline (Elavil), Clomipramine (Anafranil™), Doxepin (Sinequan®, Silenor™, Prudoxin™), Imipramine (Tofranil®), Trimipramine (Surmontil®)

Modification Recommended

This patient has genetic variations within the CYP2C19 gene that predict an increase in the CYP2C19 enzyme function.

Increased CYP2C19 enzyme function is expected to increase the rate of conversion of Amitriptyline, Clomipramine, Doxepin, Imipramine and Trimipramine to active metabolites.

If not otherwise contraindicated, consider Desipramine, Nortriptyline, or Amoxapine because CYP2C19, CYP3A4 and CYP3A5 enzymes are not major metabolic pathways for these medications.

Molecular analysis identified no clinically significant genetic variations within the CYP2D6, CYP3A4 or CYP3A5 genes that affect the metabolism of tricyclic antidepressant medications. Co-administration of other drugs that inhibit CYP2D6, CYP2C19, CYP3A4 or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these drugs.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

SELECT SSRI/SNRI METABOLISM

CYP2D6: Extensive Metabolizer

CYP2C19: Ultra Metabolizer

Drugs Evaluated: Venlafaxine (Effexor®), Sertraline (Zoloft®), Citalopram (Celexa®), Escitalopram (Lexapro®)

Normal

Molecular analysis identified no clinically significant genetic variations within the genes CYP2D6 or CYP2C19 that affect the metabolism of Venlafaxine, Sertraline, Citalopram or Escitalopram.

Manufacturer dosage recommendations, as listed on the product insert, are expected to apply to this patient for Venlafaxine, Sertraline, Citalopram or Escitalopram, if not otherwise contraindicated. Co-administration of other drugs that inhibit CYP2D6 or CYP2C19 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these drugs.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

HYPERHOMOCYSTEINEMIA RISK

MTHFR A1298C: Normal Risk

MTHFR C677T: Normal Risk

Normal

The absence of the necessary combinations of the MTHFR 677T and MTHFR 1298C alleles which increase the risk of hyperhomocysteinemia suggests that this patient does not have an elevated risk of hyperhomocysteinemia related to these genetic markers.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

SELECT PSYCHOTROPIC DRUGS

CYP2C9: Intermediate Metabolizer

CYP2D6: Extensive Metabolizer

Drugs Evaluated: Risperidone (Risperdal®), Phenytoin (Dilantin®), Haloperidol (Haldol®), Thioridazine (Mellaril®), Aripiprazole (Abilify®)

Modification Recommended

This patient has genetic variations within the CYP2C9 gene that predict a reduction in CYP2C9 enzyme function that affects the metabolism of Phenytoin.

Reduced CYP2C9 enzyme function is expected to decrease the rate of clearance of Phenytoin.

When considering Phenytoin, a standard loading dose and a 25% reduction of the manufacturer recommended maintenance dose is recommended in conjunction with therapeutic drug monitoring.

Molecular analysis identified no clinically significant genetic variations within the CYP2D6 gene that affect the metabolism of Haloperidol, Risperidone, Aripiprazole and Thioridazine. Co-administration of other drugs that inhibit the CYP2D6 or CYP2C9 enzymes, and other genetic and non-genetic factors, may alter the efficacy or toxicity of these medications.

Result electronically approved and reported on 01/27/2015 by K. Elias, Ph.D.

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

Genotyping Summary

Gene	Tested Alleles	Patient Genotype	Predicted Patient Phenotype
Prothrombin (Factor II)	G20210A	G/G	Normal Risk
Factor V Leiden	1691G>A	G/G	Normal Risk
MTHFR A1298C	A1298C	A/C	Normal Risk
MTHFR C677T	C677T	C/T	Normal Risk
ApoE	E2, E3, E4	E3/E3	Normal Risk
CYP2C9	*1, *2, *3, *4, *5, *6, *8, *11, *27	*1/*3	IM
CYP2C19	*1, *2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *17	*1/*17	UM
CYP2D6	*1, *2, *3, *4, *4J, *4K, *4M, *5, *6, *6C, *7, *8, *9, *10, *12, *14, *14B, *17, *29, *34, *35, *39, *41, *64, *65, *69, *70	*17/*35	EM
CYP3A4	*1, *1B, *2, *3, *12, *16, *17, *22	*1/*1	EM
CYP3A5	*1, *1D, *2, *3A, *3B, *3C, *6, *7, *8, *9	*3A/*3A	IM
VKORC1	-1639 G>A	G/G	Normal Sensitivity to Warfarin
SLCO1B1	*1, *5	*1/*5	IM

EM = Normal Metabolizer, IM = Intermediate Metabolizer, PM = Poor Metabolizer, UM = Ultra Metabolizer

Laboratory Director: Charlotte L. Phillips, Ph.D. NY Laboratory Director: Karol S. Elias, Ph.D.

All testing is completed by PTC Laboratories, doing business as GeneTrait Laboratories, 300 Portland Street, Columbia MO 65201. This test was developed and its performance characteristics determined by PTC Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration. Tests are completed on a Life Technologies QuantStudio 12K Flex RT-PCT System with OpenArray Block and this laboratory has verified the 99.7% genotyping accuracy of the testing platform. All genotyping is performed in duplicate. The assay is not designed to detect any genetic variants not specifically listed in this report. CLIA: 26D2056029

Phenotype	Definition (as used in this report)
Normal Function	Drug metabolism through the tested enzymatic pathway(s) is normal. No risk factors/variants were identified.
Normal Risk	No risk factors or variants were identified.
Elevated Risk	Variants that are known to increase risk for specific conditions were identified.
Extensive Metabolizer (EM)	Drug metabolism through the tested enzymatic pathway(s) is normal.
Ultra Metabolizer (UM)	Drug metabolism through the tested enzymatic pathway(s) is faster than normal.
Intermediate Metabolizer (IM)	Drug metabolism through the tested enzymatic pathway(s) is slower than normal.
Poor Metabolizer (PM)	Drug metabolism through the tested enzymatic pathway(s) is extremely reduced.
Heterozygous	One of the two chromosomes carries a normal DNA sequence and the other carries the variant at the tested locus.
Homozygous	Both chromosomes carry the same variant DNA sequence at the tested locus.

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PHARMACOGENETIC LABORATORY RESULTS

02/09/2015 03:02 PM

Name: [redacted]
Patient ID: [redacted]
Specimen ID: [redacted]

Gender: M
DOB: [redacted]
Race: CAUCASIAN

Specimen Type: BUCCAL SWAB
Collection Date: 01/29/15
Received Date: 02/05/15

ORDERED BY: [redacted]
LOCATION: [redacted]

P: [redacted]
F:

CARDIOVASCULAR DISEASE PROFILE

ApoE: Normal Risk

Normal Risk

Cholesterol Management

This patient has a genotype that suggests the patient does not have an elevated risk of coronary heart disease related to these genetic markers.

Statins, a low fat diet, and moderate alcohol usage are expected to be beneficial therapies in lowering LDL in individuals with this genotype.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

STATIN INDUCED MYOPATHY RISK

SLCO1B1: Intermediate Metabolizer

Modification Recommended

Drugs Evaluated: Simvastatin (Zocor), Atorvastatin (Lipitor®), Pitavastatin (Livalo)

This patient has one high risk allele for statin induced myopathy.

Individuals who are heterozygous for (have one copy of) the SLCO1B1*5 allele are estimated to have a 2 to 20 times greater risk of statin induced myopathy than individuals without the variant allele.

Consider alternative medications such as Fluvastatin, Pravastatin and Rosuvastatin, if not otherwise contraindicated.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

THROMBOSIS PROFILE

Prothrombin (Factor II): Normal Risk
Factor V Leiden: Increased Risk
MTHFR A1298C: Normal Risk
MTHFR C677T: Normal Risk

Elevated Risk

This patient has two high risk alleles for venous thrombosis. Individuals who are homozygous for (have two copies of) the Factor V Leiden variant allele have approximately 80 times greater risk of venous thrombosis than individuals without the variant alleles. Consultation with a medical geneticist, genetic counselor or hematologist is recommended for further guidance.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

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WARFARIN METABOLISM

VKORC1: Medium Sensitivity to Warfarin

CYP2C9: Intermediate Metabolizer

Drug Evaluated: Warfarin (Coumadin)

Modification Recommended

This patient has genetic variations within the VKORC1 and/or CYP2C9 genes that predict a reduction in the combined VKORC1 and CYP2C9 enzyme function.

Reduced VKORC1 and CYP2C9 combined enzyme function is expected to reduce the amount of Warfarin necessary to achieve an INR of 2-3.

Consider Warfarin dosages ranging from 3 to 4 mg/day for a patient with these combined VKORC1 and CYP2C9 genotypes. For a patient-specific dosage that includes ethnicity and weight, please use the following website to calculate dosage: http://www.pharmgkb.org/download.action?filename=IWPC_dose_calculator_6-19-09.xls

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

ANTIPLATELET METABOLISM

CYP2C19: Intermediate Metabolizer

CYP3A5: Intermediate Metabolizer

CYP3A4: Extensive Metabolizer

Drugs Evaluated: Clopidogrel (Plavix), Ticagrelor (Brilinta®)

Modification Recommended

This patient has genetic variations within the CYP2C19 gene that predict a reduction in the CYP2C19 enzyme function that affects the metabolism of *Clopidogrel*.

Reduced CYP2C19 enzyme function is expected to reduce the conversion of Clopidogrel to its active form.

Consider alternative medications such as Ticagrelor, Dipyridamole, Prasugrel, or Cangrelor, if not otherwise contraindicated.

Analysis of the CYP3A4 and CYP3A5 genes predict normal CYP3A4 and CYP3A5 related enzymatic function. Co-administration of other drugs that inhibit the CYP2C19, CYP3A4 or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these medications.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

OPIATE METABOLISM

CYP2C19: Intermediate Metabolizer

CYP3A5: Intermediate Metabolizer

CYP2D6: Extensive Metabolizer

CYP3A4: Extensive Metabolizer

Drugs Evaluated: Codeine, Hydrocodone (Lortab®, Vicodin®), Dihydrocodeine (Synalgos®-DC), Fentanyl (Abstral®, Actiq®, Fentora®, Onsolis), Oxycodone (Percocet®, Oxycontin®), Methadone (Dolophine®), Meperidine (Demerol®), Ketamine (Ketalar®), Tramadol (Ultram®)

Normal

Molecular analysis identified no clinically significant genetic variations within genes CYP2D6, CYP2C19, CYP3A4 and CYP3A5 that affect the metabolism of Codeine, Hydrocodone, Dihydrocodeine, Fentanyl, Oxycodone, Methadone, Meperidine, Ketamine and Tramadol. Thus, normal enzymatic activity associated with these genes is predicted.

Manufacturer dosage recommendations, as listed on the product insert, are *expected to apply to this patient for these medications, if not otherwise* contraindicated. Co-administration of other drugs that inhibit the CYP2D6, CYP2C19, CYP3A4 or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these medications.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

NSAID METABOLISM

CYP2C9: Intermediate Metabolizer

Drugs Evaluated: Aspirin (Bayer), Celecoxib (Celebrex®), Diclofenac (Voltaren®-XR), Flurbiprofen (Ansaid®), Ibuprofen (Advil®, Motrin®), Meloxicam (Mobic®), Naproxen (Aleve®, Anaprox®), Mefenamic Acid (Ponstel®), Valdecoxib (Bextra), Piroxicam (Feldene®)

Modification Recommended

This patient has genetic variations within the CYP2C9 gene that predict a reduction in the CYP2C9 enzyme function that affects the metabolism of several NSAIDs.

Reduced CYP2C9 enzyme function is expected to slow clearance of Aspirin, Celecoxib, Diclofenac, Flurbiprofen, Ibuprofen, Mefenamic Acid, Meloxicam, Naproxen, Piroxicam, and Valdecoxib.

Consider alternative medications such as Acetaminophen, Indomethacin, Ketoprofen, or Sulindac, if not otherwise contraindicated.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

METHOTREXATE METABOLISM

SLCO1B1: Intermediate Metabolizer

Drug Evaluated: Methotrexate (Rheumatrex®, Trexall™, Otrexup)

Modification Recommended

This patient has genetic variations within the SLCO1B1 gene that predict a reduction in the OATP1B1 transporter protein function that affects the metabolism Methotrexate.

Reduced OATP1B1 transporter protein function is expected to reduce the clearance of Methotrexate.

Consider reduced Methotrexate dosages or alternative medications, if not otherwise contraindicated.

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INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

ANGIOTENSIN RECEPTOR BLOCKER (ARB) METABOLISM

CYP2C9: Intermediate Metabolizer

CYP3A5: Intermediate Metabolizer

CYP3A4: Extensive Metabolizer

Modification Recommended

Drugs Evaluated: Losartan (Cozaar®), Irbesartan (Avapro®)

This patient has genetic variations within the CYP2C9 gene that predict a reduction in the CYP2C9 enzyme function that affects the metabolism of Irbesartan and Losartan.

Reduced CYP2C9 enzyme function is expected to slow clearance of Irbesartan and to reduce the conversion of Losartan to active metabolites.

Consider alternative medications such as Olmesartan, Valsartan, Candesartan, Telmisartan and Eprosartan, if not otherwise contraindicated.

Molecular analysis identified no clinically significant genetic variations within the CYP3A4 or CYP3A5 genes that affect the metabolism of ARB medications. Co-administration of other drugs that inhibit CYP2C9, CYP3A4 or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these drugs.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

ANTIARRHYTHMIC METABOLISM

CYP3A5: Intermediate Metabolizer

CYP2D6: Extensive Metabolizer

CYP3A4: Extensive Metabolizer

Normal

Drugs Evaluated: Flecainide (Tambocor), Propafenone (Rythmol SR®)

Molecular analysis identified no clinically significant genetic variations within the CYP2D6, CYP3A4, or CYP3A5 genes that affect the metabolism of Flecainide or Propafenone.

Manufacturer dosage recommendations, as listed on the product insert, are expected to apply to this patient for Flecainide and Propafenone. Co-administration of other drugs that inhibit the CYP2D6, CYP3A4, or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these drugs.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

METOPROLOL METABOLISM

CYP2D6: Extensive Metabolizer

Normal

Drug Evaluated: Metoprolol (Lopressor®, Toprol®)

Molecular analysis identified no clinically significant genetic variations within the CYP2D6 gene. Thus, normal enzymatic activity associated with this gene is predicted.

Manufacturer dosage recommendations, as listed on the product insert, are expected to apply to this patient for Metoprolol, if not otherwise contraindicated. Co-administration of other drugs that inhibit the CYP2D6 enzyme, and other genetic and non-genetic factors may alter the efficacy or toxicity of this medication.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

TRICYCLIC ANTIDEPRESSANT METABOLISM

CYP2C19: Intermediate Metabolizer
CYP3A5: Intermediate Metabolizer
CYP2D6: Extensive Metabolizer
CYP3A4: Extensive Metabolizer

Drugs Evaluated: Desipramine (Norpramin®), Amoxapine, Nortriptyline (Pamelor™), Amitriptyline (Elavil), Clomipramine (Anafranil™), Doxepin (Sinequan®, Silenor™, Prudoxin™), Imipramine (Tofranil®), Trimipramine (Surmontil®)

Normal

Molecular analysis identified no clinically significant genetic variations within genes CYP2D6, CYP2C19, CYP3A4 and CYP3A5 that affect the metabolism of tricyclic antidepressant medications.

Manufacturer dosage recommendations, as listed on the product insert, are expected to apply to this patient if not otherwise contraindicated. Co-administration of other drugs that inhibit CYP2D6, CYP2C19, CYP3A4 or CYP3A5 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these drugs.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

SELECT SSRI/SNRI METABOLISM

CYP2C19: Intermediate Metabolizer
CYP2D6: Extensive Metabolizer

Drugs Evaluated: Venlafaxine (Effexor®), Sertraline (Zoloft®), Citalopram (Celexa®), Escitalopram (Lexapro®)

Modification Recommended

This patient has genetic variations within the CYP2C19 gene that predict a reduction in the CYP2C19 enzyme function that affects the metabolism of Sertraline, Citalopram or Escitalopram.

Reduced CYP2C19 enzyme function is expected to decrease the rate of clearance of Sertraline, Citalopram and Escitalopram. A dosage adjustment is not expected to be necessary for Citalopram or Escitalopram as a result of this reduction in CYP2C19 enzyme function.

When considering Sertraline, a dosage adjustment has not been scientifically established, although the patient should be monitored closely for indications of side effects and adverse drug reactions.

Molecular analysis identified no clinically significant genetic variations within the CYP2D6 gene that affect the metabolism of Venlafaxine. Co-administration of other drugs that inhibit CYP2D6 or CYP2C19 enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of these drugs.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

HYPERHOMOCYSTEINEMIA RISK

MTHFR A1298C: Normal Risk
MTHFR C677T: Normal Risk

Normal

The absence of the necessary combinations of the MTHFR 677T and MTHFR 1298C alleles which increase the risk of hyperhomocysteinemia suggests that this patient does not have an elevated risk of hyperhomocysteinemia related to these genetic markers.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

SELECT PSYCHOTROPIC DRUGS

CYP2C9: Intermediate Metabolizer

CYP2D6: Extensive Metabolizer

Drugs Evaluated: Risperidone (Risperdal®), Phenytoin (Dilantin®), Haloperidol (Haldol®), Thioridazine (Mellaril®), Aripiprazole (Abilify®)

Modification Recommended

This patient has genetic variations within the CYP2C9 gene that predict a reduction in CYP2C9 enzyme function that affects the metabolism of Phenytoin.

Reduced CYP2C9 enzyme function is expected to decrease the rate of clearance of Phenytoin.

When considering Phenytoin, a standard loading dose and a 25% reduction of the manufacturer recommended maintenance dose is recommended in conjunction with therapeutic drug monitoring.

Molecular analysis identified no clinically significant genetic variations within the CYP2D6 gene that affect the metabolism of Haloperidol, Risperidone, Aripiprazole and Thioridazine. Co-administration of other drugs that inhibit the CYP2D6 or CYP2C9 enzymes, and other genetic and non-genetic factors, may alter the efficacy or toxicity of these medications.

Result electronically approved and reported on 02/09/2015 by K. Elias, Ph.D.

Genotyping Summary

Gene	Tested Alleles	Patient Genotype	Predicted Patient Phenotype
Prothrombin (Factor II)	G20210A	G/G	Normal Risk
Factor V Leiden	1691G>A	A/A	Increased Risk
MTHFR A1298C	A1298C	A/A	Normal Risk
MTHFR C677T	C677T	C/C	Normal Risk
ApoE	E2, E3, E4	E3/E3	Normal Risk
CYP2C9	*1, *2, *3, *4, *5, *6, *8, *11, *27	*1/*2	IM
CYP2C19	*1, *2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *17	*1/*2	IM
CYP2D6	*1, *2, *3, *4, *4J, *4K, *4M, *5, *6, *6C, *7, *8, *9, *10, *12, *14, *14B, *17, *29, *34, *35, *39, *41, *64, *65, *69, *70	*2/*41	EM
CYP3A4	*1, *1B, *2, *3, *12, *16, *17, *22	*1/*1	EM
CYP3A5	*1, *1D, *2, *3A, *3B, *3C, *6, *7, *8, *9	*3A/*3A	IM
VKORC1	-1639 G>A	G/A	Medium Sensitivity to Warfarin
SLCO1B1	*1, *5	*1/*5	IM

EM = Normal Metabolizer, IM = Intermediate Metabolizer, PM = Poor Metabolizer, UM = Ultra Metabolizer

INTENDED USE: These genetic tests are intended to be used as an adjunctive test to complement, not replace, other clinical findings in determining the best treatment plan for the patient. In addition to the results contained on this laboratory report, the co-administration of other drugs that inhibit the CYP enzymes, and other genetic and non-genetic factors may alter the efficacy or toxicity of medications mentioned in this report. All reference information is avaliable upon request.

Laboratory Director: Charlotte L. Phillips, Ph.D. NY Laboratory Director: Karol S. Elias, Ph.D.

All testing is completed by PTC Laboratories, doing business as GeneTrait Laboratories, 300 Portland Street, Columbia MO 65201. This test was developed and its performance characteristics determined by PTC Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration. Tests are completed on a Life Technologies QuantStudio 12K Flex RT-PCT System with OpenArray Block and this laboratory has verified the 99.7% genotyping accuracy of the testing platform. All genotyping is performed in duplicate. The assay is not designed to detect any genetic variants not specifically listed in this report. CLIA: 26D2056029

Phenotype	***Definition (as used in this report)***
Normal Function	Drug metabolism through the tested enzymatic pathway(s) is normal. No risk factors/variants were identified.
Normal Risk	No risk factors or variants were identified.
Elevated Risk	Variants that are known to increase risk for specific conditions were identified.
Extensive Metabolizer (EM)	Drug metabolism through the tested enzymatic pathway(s) is normal.
Ultra Metabolizer (UM)	Drug metabolism through the tested enzymatic pathway(s) is faster than normal.
Intermediate Metabolizer (IM)	Drug metabolism through the tested enzymatic pathway(s) is slower than normal.
Poor Metabolizer (PM)	Drug metabolism through the tested enzymatic pathway(s) is extremely reduced.
Heterozygous	One of the two chromosomes carries a normal DNA sequence and the other carries the variant at the tested locus.
Homozygous	Both chromosomes carry the same variant DNA sequence at the tested locus.

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