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Laboratory Service Report

1-800-533-1710

MCR

Patient Name TESTINGRNV,2D6CB ATLAS REPORTS	Patient ID SA00060451	Age 8	Gender F	Order # SA00060451
Ordering Phys CLIENT,CLIENT				DOB 06/25/2005
Client Order # SA00060451	Account Information			Report Notes
Collected 07/29/2013 06:00	C7028846-DLMP Rochester 3050 Superior Drive			
Printed 08/14/2013 07:05	Rochester, MN 55901			

Test	Flag Results	Unit	Reference Value	Perform Site*
CYP2D6 Genotype Cascade, B				
RECEIVED: 07/30/2013 13:13 REP	ORTED: 07/30/2013 13:26			
CYP2D6 Phenotype	See Below			MCR
Result:Intermediate to	Extensive metabolizer			
CYP2D6 Star Alleles	2A/4			MCR
-	py of a null allele and one copy d CYP2D6 activity. Additional	of		

This patient has one copy of a null allele and one copy of an allele with increased CYP2D6 activity. Additional descriptions of the effects of the star alleles on CYP2D6 function are found online at Karolinska Database for CYP2D6 gene (http://www.cypalleles.ki.se/cyp2d6.htm) and the Mayo Test Catalog

(http://www.mayomedicallaboratories.com/test-catalog/). CYP2D6 Interpretation

Prodrugs are converted to their active metabolite at a slightly reduced rate which might reduce efficacy of some drugs. Alternatively, drugs that are inactivated by CYP2D6 are metabolized at slightly reduced rate which might increase side effects.

For tamoxifen: Postmenopausal women with this phenotype and early stage breast cancer are not thought to be at a significantly increased risk for breast cancer recurrence when treated with tamoxifen as adjuvant therapy. However, it should be noted that this specific phenotype has not been evaluated adequately in the literature to adequately predict possible outcomes. Patients with this phenotype should not be coadministered CYP2D6 inhibitors (see below), since these medications are known to decrease the metabolic activation of tamoxifen which may increase the risk of breast cancer relapse.

For codeine and tramadol: Codeine is converted to morphine and tramadol is converted to O-desmethyltramadol at a slightly reduced rate so analgesia might be reduced.

For drugs inactivated by CYP2D6 (see below): The drugs are inactivated by CYP2D6 at a slightly reduced rate. Therapeutic drug monitoring should be considered. A three-tiered testing approach was used to identify mutations and copy number variation within the CYP2D6 gene (GenBank numbers AY545216.1 and NM_000106.4). Variations within the CYP2D6 gene are associated with ultra rapid, extensive, intermediate and poor metabolizer predicted phenotypes.

Performing Site Legend on Last Page of Report

Patient Name	Collection Date and Time	Report Status
TESTINGRNV,2D6CB ATLAS REPORTS	07/29/2013 06:00	Final
Page 1 of 4		>> Continued on Next Page >>



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Tier 1 (always performed) consists of the Luminex CYP2D6 Assay. This assay incorporates multiplex polymerase chain reaction (PCR) and multiplex Allele-Specific Primer Extension (ASPE) with Luminex Molecular Diagnostics proprietary Universal Tag sorting system on the Luminex 100 xMAP platform.

Tier 2 consists of copy number variation testing (CNV) performed by TaqMan assay using probes that look for copy number specifically in the CYP2D6 promoter, intron 6 and exon 9 regions. The probes used will not detect CYP2D7 or CYP2D8 pseudogenes. Varying copy number among the probes is used to detect duplications, multiplications and deletions of CYP2D6 as well as CYP2D6-2D7 and CYP2D6-2D7 hybrid genes.

Tier 3 consists of comprehensive sequencing of the CYP2D6 gene and/or CYP2D7-2D6 and CYP2D6-2D7 hybrid genes using a PCR-based method.

The tiered testing is performed sequentially. If a result requires follow up, then the testing is reflexed to the next tier in the cascade. If a result requires no additional follow up in a tier, then testing is stopped and subsequent tier(s) are not performed.

Direct DNA testing will not detect all variants that result in decreased or increased CYP2D6 enzyme activity. Absence of a detectable gene mutation or polymorphism does not rule out the possibility that a patient has an ultrarapid, intermediate or poor metabolizer phenotype. Please contact the laboratory for a comprehensive list of variations tested in tier one and also for common polymorphism identified during tier three testing (if performed).

Based on the test sensitivity and currently available CYP2D6 polymorphism carrier frequencies, persons of Caucasian descent have approximately a 1 percent risk of having an undetected variation which would impact the predicted phenotype. This risk may be higher or lower in other ethnic groups.

Performing Site Legend on Last Page of Report

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Patient Name	Collection Date and Time	Report Status		
TESTINGRNV,2D6CB ATLAS REPORTS	07/29/2013 06:00	Final		
Page 2 of 4		>> Continued on Next Page >>		



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Patients with an ultrarapid, extensive (normal) or intermediate metabolizer phenotype may have CYP2D6 enzyme activity inhibited by a variety of medications, or their metabolites. The following is a partial listing of drugs known to affect CYP2D6 activity as of the date of this report (see the Cytochrome P450 2D6 Drug Interaction Chart in the Mayo Laboratory Test Catalog).

Drugs known to induce CYP2D6 activity: Dexamethasone and rifampin. Co-administration of these inducers, with other drugs metabolized by CYP2D6, may increase the rate of drug metabolism by CYP2D6, thus impacting the drug's effectiveness or side effect profile.

Drugs known to inhibit CYP2D6 activity: Amiodarone, bupropion, celecoxib, chlorpheniramine, chlorpromazine, cimetidine, cinacalcet, citalopram, clemastine, clomipramine, cocaine, dexmedetomidine, diltiazem, diphenhydramine, doxepin, doxorubicin, duloxetine, escitalopram, fluoxetine, haloperidol, halofantrine, hydroxyzine, indinavir, levomepromazine, methadone, metoclopramide, mibefradil, midodrine, moclobemide, paroxetine, perphenazine, pimozide, quinidine, ranitidine, ritonavir, sertraline, terbinafine, thioridazine, ticlopidine, and tripelennamine. Co-administration, with other drugs metabolized by CYP2D6, may decrease the rate of CYP2D6 metabolism, potentially resulting in an increased risk of toxicity.

Drugs that undergo metabolism by CYP2D6: Alprenolol, amitriptyline, amphetamine, aripiprazole, atomoxetine, carvedilol, chlorpheniramine, chlorpromazine, clonidine, clomipramine, codeine, debrisoquine, desipramine, dextromethorphan, dexfenfluramine, diltiazem, donepezil, duloxetine, flecainide, fluoxetine, fluvoxamine, haloperidol, hydrocodone, iloperidone, imipramine, lidocaine, metoclopramide, methoxyamphetamine, s-metoprolol, mexiletine, minaprine, mirtazapine, nebivolol, nortriptyline, oxycodone, ondansetron, paroxetine, pergolide, perhexiline, perphenazine, phenacetin, promethazine, pimozide, propafenone, propranolol, risperidone, sparteine, sertraline, tamoxifen, thioridazine, timolol, tramadol, venlafaxine and zuclopenthixol.

Performing Site Legend on Last Page of Report

Patient Name TESTINGRNV.2D6CB ATLAS REPORTS	Collection Date and Time 07/29/2013 06:00	Report Status Final
Page 3 of 4		>> Continued on Next Page >>



Laboratory Service Report

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CAUTIONS:

Rare polymorphisms exist that could lead to false negative or positive results. If results obtained do not match the clinical findings (phenotype), additional testing should be considered. Call Mayo Medical Laboratories for instructions for testing patients who have received a bone marrow or liver transplant.

Laboratory developed test.

Reviewed by LAURA TRAIN MCR

* Performing Site:

MCR	Mayo Clinic Laboratories - Rochester Main Campus 200 First St SW Rochester, MN 55905	Lab Director: Franklin R. Cockerill, III, M.D.

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TESTINGRNV,2D6CB ATLAS REPORTS	07/29/2013 06:00	Final
Page 4 of 4		** End of Report **