

1-800-533-1710

PATIENT NA	ME			PATIENT NUM	BER		AGE	SEX	ACCESSION #
PAM, TESTING2C19R			L3MRNW378	7520		57	F	W3787520	
ORDERING	PHYSICIAN			CLIENT ORDE	₹#				ACCOUNT # LIAISONS
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Attn: May	o Liaisons								
200 First	Street SW								
Rocheste	r, MN 55905								
507-284-8	3202								

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CYP2C19 Sequence Genotype

Sequencing Performed MCR 2C19 Interpretation MCR

This individual has two copies of the gene that produce inactive enzyme. This genotype is associated with the poor metabolizer phenotype. Significant caution should be exercised when treating with drugs metabolized by CYP2C19 and consideration given to using drugs not metabolized by CYP2C19.

2C19 Genotype Star	2/3	MCR
Alleles		
2C19 -806C>T (*17)	C/C	MCR
2C19 1A>G (*4)	A/A	MCR
2C19 358T>C (*8)	T/T	MCR
2C19 395G>A (*6)	G/G	MCR
2C19 636G>A (*3)	G/A	MCR
2C19 681G>A (*2)	G/A	MCR
2C19 IVS5+2T>A (*7)	T/T	MCR
2C19 Reviewed by	John L. Black, M.D.	MCR

This test was developed and its performance characteristics determined by Laboratory Medicine and Pathology, Mayo Clinic, Rochester MN. It has not been cleared or approved by the U.S. Food and Drug Administration.

A combination of bidirectional and dual monodirectional DNA sequence analysis was used to test for the presence of variants in the promoter as well as exons 1, 3, 4, and 5 of the CYP2C19 gene. These sequencing reactions detect the presence of -806C>T (*17), 1A>G (*4), 358T>C (*8), 395G>A (*6), 636G>A (*3), 681G>A (*2), and IVS5+2T>A (*7). This sequencing assay will not detect all the known mutations that result in decreased or inactive CYP2C19. Absence of a detectable gene mutation or polymorphism does not rule out

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the possibility that a patient has an intermediate or poor metabolizer phenotype.

Individuals receiving clopidogrel who have one copy (heterozygous) of the null or deficient CYP2C19 polymorphisms detected by this test will likely require a dose increase to achieve effective inhibition of platelet Individuals who have two defective copies of aggregation. these CYP2C19 deficient alleles (poor metabolizers) may not achieve effective inhibition of platelet aggregation using the standard doses of clopidogrel. An increased dose of clopidogrel, or switching to other antiplatelet drugs such as prasugrel, should be considered for CYP2C19 poor metabolizers. The presence of the *17 promoter polymorphism will increase the expression of the CYP2C19 enzyme encoded by the allele on which it is found. When found in combination with other polymorphisms, we are unable to ascertain the mode of inheritance to predict which allele includes the *17 promoter polymorphism but will make our best prediction of the impact of the findings. Patients with an extensive (normal) or intermediate metabolizer genotype may have CYP2C19 enzyme activity inhibited by a variety of medications or their metabolites. The following is a partial listing of drugs known to affect CYP2C19 activity as of the date of this report. Drugs that undergo metabolism by CYP2C19:

Anticoagulants: clopidogrel

Anticonvulsants: mephenytoin, phenytoin, primidone

Antidepressants: amitriptyline, citalopram, S-citalopram,

clomipramine

Antineoplastic drugs: cyclophosphamide

Antiretroviral: nelfinavir

Proton pump inhibitors: lansoprazole, omeprazole, pantoprazole

Miscellaneous drugs: diazepam, progesterone, propranolol,

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PATIENT I	NAME STING2C19R			PATIENT NUM L3MRNW378			AGE 57	SEX F	ACCESSION # W3787520
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R-warfarin (less active isomer), proguanil

Coadministration may decrease the rate of elimination of other drugs metabolized by CYP2C19.

Drugs known to increase CYP2C19 activity:

carbamazepine

prednisone

rifampin

Coadministration of these drugs increases synthesis of CYP2C19 and increases the rate of elimination of drugs metabolized by CYP2C19.

Drugs known to decrease CYP2C19 activity:

chloramphenicol

cimetidine

felbamate

fluoxetine

fluvoxamine

 $\verb|indomethacin||$

ketoconazole

lansoprazole

modafinil

omeprazole

probenicid

ticlopidine

topiramate

Coadministration will decrease the rate of metabolism of CYP2C19 metabolized drugs, increasing the possibility of toxicity, particularly in heterozygous individuals.

Rapid DNA Extraction

Comment Genomic DNA was extracted.

MCR

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PATIENT NAME			PATIENT NU			AGE	SEX	ACCESSION #
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200 First Street SW								
Rochester, MN 55905								
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MCR	Mayo Clinic Dpt of Lab Med & Pathology	Lab Director: Franklin R. Cockerill, III, M.D.
	200 First Street SW Rochester, MN 55905	

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