

TEST DEFINITION

6/23/2010

Code Name
---- -----------60439 CYP2C19 Sequence Genotype

ORDER CODE	EFF DATE	TC	TITLE	Checking Normals	Print normals (# coded)	Perform Site *
60439(prof 83639	•	2010 Transp 24065	sport temp : Ambient\Refrig OK\Frozen NO			MCR
		31969	2C19 Ger	otype Star Alleles		
		31987	2C19 -80	 D6C>T (*17)		
		24058	2C19 1A	 >G (*4)		
		24059	2C19 358	 BT>C (*8)		
		24060	 2C19 395	 5G>A (*6)		
		24061	 2C19 636	 5G>A (*3)		
		24062	 2C19 681	 LG>A (*2)		
		24063	2C19 IVS	 55+2T>A (*7)		
		24066	TEST COI	riewed by DE ALWAYS MESSAGE - [Z83639S,AS] A combination of bidirectional sequence analysis was used to variants in the promoter as when CYP2C19 gene. These sequences of -806C>T (*17), 1A 636G>A (*3), 681G>A (*2), and sequencing assay will not det	al and dual monodirectional DN test for the presence of yell as exons 1, 3, 4, and 5 contains reactions detect the A>G (*4), 358T>C (*8), 395G>A IVS5+2T>A (*7). This	of (*6),

result in decreased or inactive CYP2C19. Absence of a detectable gene mutation or polymorphism does not rule out 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 aggregation. Individuals who have two defective copies of 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, R-warfarin (less active isomer), proquanil 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

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.

ASR

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.

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CODE	DATE	TC	TITLE	Checking Normals	Print normals (# coded)	Site *					
ORDER	$_{ m EFF}$					Perform					

60439 (continued)

60416 6/9/2010 CYP2C19 Sequencing

Transport temp : Ambient\Refrig OK\Frozen NO

60416 Sequencing

*Performing Site Legend

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CODE TEXT

Total of 0 normals codes

*** End of Report ***