

Client: ARUP Physician Services
 321 TESTING ANSR EXTRACT
 Salt Lake City, NY 84108
 UNITED STATES

Physician: TEST,

Patient: 24629 ARUPTEST, WARF 2

DOB

Gender: █████

Patient Identifiers: 546488

Visit Number (FIN): 569415

Collection Date: 5/22/2019 13:38

Warfarin Sensitivity (CYP2C8, CYP2C9, CYP4F2, VKORC1) Genotyping

ARUP test code 3001541

WARF PAN Specimen Saliva

CYP2C8 Genotype Neg/Neg

CYP2C9 Genotype Neg/Neg

CYP4F2 Genotype **Neg/*3** *

VKORC1 Genotype **Neg/*2** *

WARF PAN Interpretation See Note

A Neg result indicates that no variants were detected. All variant alleles are defined based on consensus nomenclature and suggest reduced function of the associated protein(s).

CYP2C8 and CYP2C9 are associated with inactivation of warfarin through metabolism. Variant alleles suggest reduced rates of warfarin metabolism, a prolonged time required to achieve steady-state concentrations, and a reduced dose requirement.

CYP4F2 is associated with vitamin K recycling. Variant alleles suggest an increased dose requirement.

VKORC1 is the therapeutic target for warfarin. Variant alleles suggest increased warfarin sensitivity and a reduced dose requirement.

Dosing calculators such as that available through www.warfarinDosing.org are available to predict loading and therapeutic/maintenance doses.

This result has been reviewed and approved by Gwen McMillin, Ph.D.

H=High, L=Low, *=Abnormal, C=Critical

BACKGROUND INFORMATION: warfarin Sensitivity (CYP2C8, CYP2C9, CYP4F2, VKORC1) Genotyping

CHARACTERISTICS: warfarin sensitivity can lead to a life-threatening overdose event such as excessive bleeding. Genetic variation is recognized to explain a large proportion of variability in warfarin dose requirements. This test may predict individual warfarin sensitivity and non-standard dose requirements. The cytochrome P450 (CYP) isozymes 2C8 and 2C9 are involved in the metabolism of many drugs. Variants in the genes that code for CYP2C8 and CYP2C9 may influence pharmacokinetics of substrates such as warfarin, and may predict or explain non-standard dose requirements, therapeutic failure or adverse reactions. Variants in the VKORC1 and CYP4F2 genes may predict sensitivity to warfarin. Genetic information and non-genetic factors can be used in combination with warfarin dose calculators, such as through www.WarfarinDosing.org.

INHERITANCE: Autosomal co-dominant.

CAUSE: CYP2C8, CYP2C9 and CYP4F2 gene variants affect enzyme expression or activity. The VKORC1*2 allele is associated with reduced expression of the warfarin target, vitamin K epoxide reductase (VKOR), and a reduced dose requirement.

VARIANTS TESTED:
Variants are numbered according to the following transcripts: CYP2C8 (NM_000770), CYP2C9 (NM_000771), CYP4F2 (NM_001082) and VKORC1 (NM_024006).
Negative: No variants detected is predictive of the *1 functional alleles.

CYP2C8*1C: rs17110453, c.-370T>G
CYP2C8*2: rs11572103, c.805A>T
CYP2C8*3: rs10509681, c.1196A>G
CYP2C8*4: rs1058930, c.792C>G

CYP2C9*2: rs1799853, c.430C>T
CYP2C9*3: rs1057910, c.1075A>C
CYP2C9*4: rs56165452, c.1076T>C
CYP2C9*5: rs28371686, c.1080C>G
CYP2C9*6: rs9332131, c.817de1A
CYP2C9*8: rs7900194, c.449G>A
CYP2C9*11: rs28371685, c.1003C>T

CYP4F2*3: rs2108622, c.1297G>A

VKORC1*2: rs9923231, c.-1639G>A

CLINICAL SENSITIVITY: Genetic factors and known non-genetic factors account for approximately 50 percent of the variability in warfarin dose.

METHODOLOGY: Polymerase chain reaction (PCR) and fluorescence monitoring.

ANALYTICAL SENSITIVITY AND SPECIFICITY: Greater than 99 percent.
LIMITATIONS: Only the targeted CYP2C8, CYP2C9, CYP4F2 and VKORC1 variants will be detected by this panel, and assumptions about phase and content are made to assign alleles. Publically available sources such as the www.pharmvar.org or www.pharmgkb.org provide guidance on phenotype predictions and allele frequencies. Diagnostic errors can occur due to rare sequence variations. Risk of therapeutic failure or adverse reactions with CYP2C8 or CYP2C9 substrates may be affected by genetic and non-genetic factors that are not detected by this test. This result does not replace the need for therapeutic drug or clinical monitoring.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

H=High, L=Low, *=Abnormal, C=Critical

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
WARF PAN Specimen	19-142-113007	5/22/2019 1:38:00 PM	5/22/2019 1:50:28 PM	5/22/2019 3:14:00 PM
CYP2C8 Genotype	19-142-113007	5/22/2019 1:38:00 PM	5/22/2019 1:50:28 PM	5/22/2019 3:14:00 PM
CYP2C9 Genotype	19-142-113007	5/22/2019 1:38:00 PM	5/22/2019 1:50:28 PM	5/22/2019 3:14:00 PM
CYP4F2 Genotype	19-142-113007	5/22/2019 1:38:00 PM	5/22/2019 1:50:28 PM	5/22/2019 3:14:00 PM
VKORC1 Genotype	19-142-113007	5/22/2019 1:38:00 PM	5/22/2019 1:50:28 PM	5/22/2019 3:14:00 PM
WARF PAN Interpretation	19-142-113007	5/22/2019 1:38:00 PM	5/22/2019 1:50:28 PM	5/22/2019 3:14:00 PM

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical