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Patient Report

Patient Age/Sex: Unknown

Specimen Collected: 21-Dec-21 14:05

Warfarin Sensitivity Genotyping |Received: 21-Dec-21 14:08 Report/Verified: 21-Dec-21 14:14

Procedure	Result	Units	Reference Interval
WARF PAN Specimen	Whole Blood		
CYP2C9 Genotype	Negative		
CYP2C9 Phenotype	Normal		
CYP2C Cluster Geno	Negative		
CYP2C Cluster Pheno	Normal		
CYP4F2 Genotype	Neg/Neg		
4F2 Phenotype	Normal		
VKORC1 Genotype	Neg/Neg		
VKORC1 Pheno	Low Sensitivity		
WARF PAN Interpretation	See Note [f1 i1]		

Result Footnote

f1: WARF PAN Interpretation

The following CYP2C9 allele(s) were detected: Neg/Neg. This result predicts the normal metabolizer phenotype, with an activity score of 2 of 2.

Recommendation: Guidelines for genotype-based dosing are published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and other organizations. See: https://www.pharmgkb.org/

The 2C cluster variant (rs12777823) was not detected. This result predicts a normal phenotype and is not expected to contribute to warfarin dosing estimates.

CYP4F2 is associated with Vitamin K recycling. No variant alleles were detected suggesting no impact to warfarin dosing, based on this gene.

VKORC1 is the therapeutic target for warfarin. No variant alleles were detected suggesting no impact to warfarin dosing, based on this gene.

Gene-based dosing calculators such as www.WarfarinDosing.org are available. The Clinical Pharmacogenetics Implementation Consortium (CPIC) and other organizations also offer gene-based guidance for warfarin dosing.

This result has been reviewed and approved by Sherin Shaaban, M.D., Ph.D.

Test Information

i1: WARF PAN Interpretation

BACKGROUND INFORMATION: Warfarin Sensitivity (CYP2C9, CYP2C cluster, 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) isozyme 2C9 is involved in the metabolism of many drugs. Variants in the gene that codes CYP2C9 may influence pharmacokinetics of substrates such as warfarin, and may predict or explain non-standard dose requirements, therapeutic

Test Information

i1: WARF PAN Interpretation

failure or adverse reactions. Variants in the VKORC1 and CYP4F2 genes may predict sensitivity to warfarin. The CYP2C cluster variant, rs12777823, common in people of African descent, with a minor allele frequency of approximately 25 percent, is found to be associated with warfarin dose in this population. Genetic information and non-genetic factors can be used in combination with warfarin dose calculators, such as through www.WarfarinDosing.org.
INHERITANCE: Autosomal codominant.
CAUSE: CYP2C9 and CYP2C cluster variants are associated with reduced dose requirements. The VKORC1*2 allele is associated with reduced expression of the warfarin target, vitamin K epoxide reductase (VKOR), and a reduced dose requirement. The CYP4F2 variant is associated with an increased dose requirement.
VARIANTS TESTED:
(Variants are numbered according to the following transcripts: CYP2C9 NM_000771, 2C cluster rs12777823, CYP4F2 NM_001082 and VKORC1 NM_024006).

Negative: No variants detected is predictive of the *1functional alleles.

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.818del
CYP2C9*8: rs7900194, c.449G>A
CYP2C9*11: rs28371685, c.1003C>T
CYP2C9*12: rs9332239, c.1465C>T
CYP2C9*13: rs72558187, c.269T>C
CYP2C9*15: rs72558190, c.485C>A

CYP2C rs12777823, g.96405502 G>A

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 CYP2C9, CYP2C cluster, CYP4F2 and VKORC1 variants will be detected by this panel, and assumptions about phase and content are made to assign alleles. Publicly available sources such as the www.pharmvar.org or www.pharmgkb.org provide guidance on phenotype predictions and allele frequencies.

Test Information

i1: WARF PAN Interpretation

Diagnostic errors can occur due to rare sequence variations. Risk of therapeutic failure or adverse reactions with 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.

Please note the information contained in this report does not contain medication recommendations, and should not be interpreted as recommending any specific medications. Any dosage adjustments or other changes to medications should be evaluated in consultation with a medical provider.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.