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500 Chipeta Way, Salt Lake City, Utah 84108-1221

phone: 801-583-2787, toll free: 800-522-2787

Tracy I. George, MD, Chief Medical Officer

Patient Report

Patient Age/Gender: Male

Specimen Collected: 16-Sep-21 14:54

Cytochrome P450 Genotyping Panel | Received: 16-Sep-21 14:54 Report/Verified: 16-Sep-21 14:56 Procedure Result Units Reference Interval

CYP PANEL Specimen Whole Blood CYP2C19 Genotype Negative CYP2C8 Genotype Negative Negative CYP2C9 Genotype CYP2D6 Genotype Negative CYP3A4 Genotype Negative CYP3A5 Genotype Negative CYP PANEL See Note f1 i1

Interpretation

Result Footnote

f1: CYP PANEL Interpretation

The following CYP2C19 allele(s) were detected: Neg/Neg. This result predicts the normal metabolizer phenotype.

Recommendation: Guidelines for genotype-based dosing are published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and can be found at: https://www.pharmgkb.org/.

The following CYP2C8 allele(s) were detected: Neg/Neg. This result predicts the normal metabolizer phenotype.

The following CYP2C9 allele(s) were detected: Neg/Neg. This result predicts the normal metabolizer phenotype.

Recommendation: Guidelines for genotype-based dosing are published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and can be found at: https://www.pharmgkb.org/.

The following CYP2D6 allele(s) were detected: Neg/Neg. This result predicts the normal metabolizer phenotype with an activity score estimated at 2 of 2.

Recommendation: Guidelines for genotype-based dosing are published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and can be found at: https://www.pharmgkb.org/.

The following CYP3A4 allele(s) were detected: Neg/Neg. This result predicts the normal metabolizer phenotype.

The following CYP3A5 allele(s) were detected: Neg/Neg. This result predicts the normal metabolizer phenotype.

Recommendation: Guidelines for genotype-based dosing are published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and can be found at: https://www.pharmgkb.org/.

This result has been reviewed and approved by

<u>Test Information</u>

i1: CYP PANEL Interpretation

BACKGROUND INFORMATION: Cytochrome P450 Genotyping Panel

*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab

Unless otherwise indicated, testing performed at:

ARUP Laboratories

500 Chipeta Way, Salt Lake City, UT 84108

Laboratory Director: Tracy I. George, MD

ARUP Accession: 21-259-900124

Report Request ID: 15048455

Printed: 16-Sep-21 15:01

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Patient Age/Gender: Male

Test Information

il: CYP PANEL Interpretation

CHARACTERISTICS: The cytochrome P450 (CYP) isozymes 2C19, 2C8, 2C9, 2D6 and the CYP3A subfamily are involved in the metabolism of many drugs. Variants in the genes that code for CYP2C19, CYP2C8, CYP2C9, CYP2D6, CYP3A4 and CYP3A5 will influence pharmacokinetics of respective substrates, and may predict or explain non-standard dose requirements, therapeutic failure or adverse reactions.

INHERITANCE: Autosomal codominant.

CAUSE: Gene variants affect enzyme expression or activity.

VARIANTS TESTED:

Variants are numbered according to the following transcripts: CYP2C19 (NM_000769), CYP2C8 (NM_000770), CYP2C9 (NM_000771), CYP2D6 (M33388 sequence), CYP3A4 (NM_017460) and CYP3A5 (NM 000777).

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

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CYP2C19*2: rs4244285, c.681G>A; rs12769205, c.332-23A>G
CYP2C19*3: rs4986893, c.636G>A
CYP2C19*4: rs28399504, c.1A>G
CYP2C19*5: rs56337013, c.1297C>T
CYP2C19*6: rs72552267, c.395G>A
CYP2C19*7: rs72558186, c.819+2T>A
CYP2C19*8: rs41291556, c.358T>C
CYP2C19*9: rs17884712, c.431G>A
CYP2C19*10: rs6413438, c.680C>T
CYP2C19*15: rs17882687, c.55A>C
CYP2C19*17: rs12248560, c.-806C>T
CYP2C19*35: rs12769205, c.332-23A>G
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.818del
CYP2C9*8: rs7900194, c.449G>A
CYP2C9*9: rs2256871, c.752A>G
CYP2C9*11: rs28371685, c.1003C>T
CYP2C9*12: rs9332239, c.1465C>T
CYP2D6*2: rs16947, g.2850C>T; rs1135840, g.4180G>C
CYP2D6*2A: rs1080985, g.-1584C>G; rs16947, g.2850C>T; rs1135840, g.4180G>C
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Test Information

```
CYP PANEL Interpretation
CYP2D6*3: rs35743686, g.2549del
CYP2D6*4: rs1065852, g.100C>T; rs3892097, g.1846G>A; rs1135840, g.4180G>C
CYP2D6*5: gene deletion
CYP2D6*6: rs5030655, g.1707del; rs1135840, g.4180G>C
CYP2D6*7: rs5030867, g.2935A>C
CYP2D6*8: rs5030865, g.1758G>T; rs16947, g.2850C>T; rs1135840, g.4180G>C
CYP2D6*9: rs5030656, g.2615 2617del
CYP2D6*10: rs1065852, g.100C>T; rs1135840, g.4180G>C
CYP2D6*11: rs1080985, q.-1584C>G; rs201377835, q.883G>C; rs16947, q.2850C>T;
rs1135840, g.4180G>C
CYP2D6*12: rs5030862, g.124G>A; rs16947, g.2850C>T; rs1135840, g.4180G>C
CYP2D6*13: a CYP2D7-derived exon 1 conversion
CYP2D6*14: rs5030865, q.1758G>A; rs16947, q.2850C>T; rs1135840, q.4180G>C
CYP2D6*15: rs774671100, g.137 138insT
CYP2D6*17: rs28371706, g.1023C>T; rs16947, g.2850C>T; rs1135840, g.4180G>C
CYP2D6*29: rs16947, g.2850C>T; rs59421388, g.3183G>A; rs1135840, g.4180G>C
CYP2D6*35: rs769258, g.31G>A; rs16947, g.2850C>T; rs1135840, g.4180G>C; rs1080985,
g.-1584C>G
CYP2D6*36: a CYP2D6*10 carrying a CYP2D7-derived exon 9 conversion
CYP2D6*36-*10: a CYP2D6*36 and a CYP2D6*10 in tandem
CYP2D6*40: rs28371706, g.1023C>T, rs16947, g.2850C>T; rs1135840, g.4180G>C;
rs72549356, c.1863 1864ins TTTCGCCCCTTTCGCCCC
CYP2D6*41: rs16947, q.2850C>T; rs28371725, q.2988G>A; rs1135840, q.4180G>C
CYP2D6*45: rs28371710, g.1716G>A; rs16947, g.2850C>T; rs1135840, g.4180G>C
CYP2D6*46: rs28371696, g.77G>A; rs28371710, g.1716G>A; rs16947, g.2850C>T;
rs1135840, g.4180G>C
CYP2D6*49: rs1065852, g.100C>T; rs1135822, g.1611T>A; rs1135840, g.4180G>C
CYP2D6*53: rs1135822, g.1611T>A
CYP2D6*69: rs1065852, g.100C>T; rs16947, g.2850C>T; rs28371725, g.2988G>A;
rs1135840, g.4180G>C
CYP2D6*114: rs1065852, g.100C>T; rs5030865, g.1758G>A; rs16947, g.2850C>T;
rs1135840, g.4180G>C
DUP: complete gene duplications
CYP3A4*1B: rs2740574, c.-392G>A
CYP3A4*15: rs4986907, c.485G>A
CYP3A4*22: rs35599367, c.522-191C>T
CYP3A5*3: rs776746, c.219-237A>G
CYP3A5*6: rs10264272, c.624G>A
CYP3A5*7: rs41303343, c.1035dup
CLINICAL SENSITIVITY: Drug-dependent.
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Patient Age/Gender: Male

Test Information

i1: CYP PANEL Interpretation

METHODOLOGY: Polymerase chain reaction (PCR) and fluorescence monitoring. ANALYTICAL SENSITIVITY AND SPECIFICITY: Greater than 99 percent. LIMITATIONS: Only the targeted 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. A combination of the CYP2D6*5 (gene deletion) and a CYP2D6 gene duplication cannot be specifically identified; however, this combination is not expected to adversely affect the phenotype prediction. Diagnostic errors can occur due to rare sequence variations. Risk of therapeutic failure or adverse reactions with gene 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.

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