Warde Medical Laboratory

LABORATORY REPORT

QC ACCOUNT (WARDE)
300 W. TEXTILE
ANN ARBOR MI 48108

EXAMPLE, REPORT W
WX0000003827 M 07/08/1978 46 Y

Referral Testing

Collected: 07/16/2024 14:56 Received: 07/16/2024 14:56

Test Name	Result	Flag	Ref-Ranges	Units	Site
UGT1A1 Genotyping					
UGT1A1 Genotyping Specimen	Whole Blood				ARRL
UGT1A1 Genotyping Allele 1	(TA)6 or *1				ARRL
UGT1A1 Genotyping Allele 2	**(TA)5 or *36**	**AB**			ARRL
UGT1A1 Genotyping Interpretation	See Note				ARRL

Indications for ordering:
- Determine sensitivity to irinotecan or related compounds.
- Confirm a diagnosis of Gilbert syndrome.

Heterozygous UTG1A1 (TA)6/(TA)5: One copy of *1 (TA)6 and one copy of *36 (TA)5 were detected. Clinical data is limited for the impact of the (TA)5 allele; however, enzyme levels are predicted to be normal and predicts a normal metabolizer status. Although not characterized clinically, this genotype is not expected to contribute to Gilbert's syndrome (benign familial hyperbilirubinemia).

This result has been reviewed and approved by Makenzie Fulmer, Ph.D.
BACKGROUND INFORMATION: UDP Glucuronosyltransferase 1A1 (UGT1A1) Genotyping
CHARACTERISTICS: UGT1A1 is responsible for the clearance of drugs (e.g., irinotecan) and endobiotic compounds (e.g., bilirubin). Irinotecan's major active and toxic metabolite (SN-38) is inactivated by the UGT1A1 enzyme and then eliminated via the bile. UGT1A1 gene mutations cause accumulation of SN-38, which may lead to irinotecan-related toxicities (neutropenia, diarrhea).
CAUSE: Variations in TA repeat number in the TATAAA element of the 5'UGT1A1-promoter affects transcription efficiency. The common number of repeats is six [(TA)6, *1 allele], while seven repeats [(TA)7, *28 allele] is associated with reduced transcription activity. Homozygosity for the (TA)7 allele is also associated with Gilbert syndrome (benign familial hyperbilirubinemia).
ALLELES TESTED: *36 allele, (TA)5; *1 allele, (TA)6; *28 allele, (TA)7 and *37 allele, (TA)8.
CLINICAL SENSITIVITY/SPECIFICITY: Risk of irinotecan toxicity by genotype (Br J Cancer. 2004; 91:678-82).
6/6 (*1/*1): diarrhea 17 percent; neutropenia 15 percent
6/7 (*1/*28): diarrhea 33 percent; neutropenia 27 percent
7/7 (*28/*28): diarrhea 70 percent; neutropenia 40 percent

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ALLELIC FREQUENCY:
*1(TA)6: Whites 0.61, Asians 0.84, African Americans 0.47
*28(TA)7: Whites 0.39, Asians 0.16, African Americans 0.43

METHODOLOGY: Polymerase chain reaction followed by size analysis using capillary electrophoresis.
ANALYTICAL SENSITIVITY AND SPECIFICITY: Greater than 99 percent.
LIMITATIONS: Variations in the UGT1A1 gene, other than those targeted, will not be detected. Clinical significance of the rare *36, (TA)5 and *37, (TA)8 alleles in predicting irinotecan toxicities is not well established. Genetic and non-genetic factors other than UGT1A1, may contribute to irinotecan toxicity and efficacy. Diagnostic errors can occur due to rare sequence variations.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the U.S. 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.

EER UGT1A1	See Note				ARRL

Performed By: ARUP Laboratories
500 Chipeta Way
Salt Lake City, UT 84108
Laboratory Director: Jonathan R. Genzen, MD, PhD
CLIA Number: 46D0523979

Reported Date: 07/16/2024 14:56 UGT1A

Performing Site:
ARRL: ARUP REFERENCE LAB 500 Chipeta Way Salt Lake City UT 841081221

LAB: L - LOW, H - HIGH, AB - ABNORMAL, C - CRITICAL, . - NOT TESTED

G316000292
WX0000003827
Printed D&T: 07/16/24 14:56

Ordered By: KAJAL SITWALA, MD, PHD
WX00000000002516

Kajal V. Sitwala, MD, PhD - Medical Director
Form: MM RL1