Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	[redacted]/1991
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

UPD Glucuronosyltransferase 1A1 (UGT1A1) and Dihydropyrimidine Dehydrogenase (DPYD) Genotyping

ARUP test code 3019841

DPYD Genotyping Specimen	Whole Blood
DPYD Allele 1	*1
DPYD Allele 2	*1
DPYD Phenotype	Normal
DPYD Interpretation	See Note Activity Score:2 Interpretation: No dihydropyrimidine dehydrogenase (DPYD) gene variants were detected in this individual suggesting the presence of *1 functional alleles. This result predicts the normal metabolizer phenotype for dihydropyrimidine dehydrogenase (DPD) and normal risk for 5-FU toxicity. Recommendation: Guidelines for genotype-based dosing are published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and can be found at: https://cpicpgx.org/ and https://www.pharmgkb.org/. This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Dihydropyrimidine Dehydrogenase (DPYD)
CHARACTERISTICS: 5-fluorouracil (5-FU) is the most frequently used chemotherapeutic drug for the treatment of many types of cancer, particularly colorectal adenocarcinoma. Grade III-IV drug toxicity attributed to 5-FU occurs in approximately 16 percent of patients, and may include hematologic, gastrointestinal, and dermatologic complications. In some cases, this toxicity can cause death. When 5-FU is metabolized in the body, approximately 80 percent is catabolized by the dihydropyrimidine dehydrogenase (DPD) enzyme. Variants in the DPYD gene can lead to reduced 5-FU catabolism, resulting in the aforementioned toxicity complications.
INHERITANCE: Autosomal codominant.
CAUSE: DPYD gene mutations.
DPYD Variants Tested:
(Variants are numbered according to NM_000110 transcript)
Nonfunctional alleles and increased toxicity risk:
    c.1024G>A (rs183385770)
    c.1774C>T (rs59086055)
    *13 (c.1679T>G, rs55886062)
    *2A (c.1905+1G>A, rs3918290)

    Decreased function alleles and increased toxicity risk:
    c.557A>G (rs115232898)
    c.868A>G (rs146356975)
    c.2279C>T (rs112766203)
    c.2846A>T (rs67376798)
    c.1129-5923C>G (rs75017182)

Functional alleles and normal enzymatic activity:
    *1 indicates no variants detected.

METHODOLOGY: Polymerase chain reaction (PCR) and fluorescence monitoring.
ANALYTICAL SENSITIVITY and SPECIFICITY: Greater than 99 percent.
LIMITATIONS: Only the targeted DPYD variants will be detected by this panel. Diagnostic errors can occur due to rare sequence variations. 5-FU drug metabolism, efficacy, and risk for toxicity may be affected by genetic and nongenetic factors that are not evaluated by this test. Genotyping does not replace the need for therapeutic drug monitoring or clinical observation.

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 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.

UGT1A1 Genotyping Specimen	Whole Blood
UGT1A1 Genotyping Allele 1	(TA)6 or *1
UGT1A1 Genotyping Allele 2	(TA)6 or *1

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

UGT1A1 Genotyping Interpretation

See Note

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

Homozygous UGT1A1 (TA)6: Two copies of the UGT1A1 *1 (TA)6 were detected predicting a normal metabolizer status This is associated with normal UGT1A1 enzyme levels. This genotype has not been associated with Gilberts syndrome (benign familial hyperbilirubinemia).

This result has been reviewed and approved by [redacted]

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

ALLELIC FREQUENCY:
  *1(TA)6: Caucasians 0.61, Asians 0.84, African Americans 0.47
  *28(TA)7: Caucasians 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 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.

EER DPYD UGT1A1

See Note

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Authorized individuals can access the ARUP Enhanced Report
with an ARUP Connect account using the following link.

Your local lab can assist you in obtaining the patient
report if you don't have a Connect account.
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[redacted]

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
DPYD Genotyping Specimen	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
DPYD Allele 1	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
DPYD Allele 2	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
DPYD Phenotype	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
DPYD Interpretation	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
UGT1A1 Genotyping Specimen	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
UGT1A1 Genotyping Allele 1	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
UGT1A1 Genotyping Allele 2	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
UGT1A1 Genotyping Interpretation	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
EER DPYD UGT1A1	25-219-126636	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

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