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

Physician: Doctor, Example

Patient: Patient, Example

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

Dihydropyrimidine Dehydrogenase (DPYD), 3 Variants

ARUP test code 2012166

DPYD Specimen	Whole Blood
DPYD Genotype	Heterozygous *
DPYD Phenotype	Intermediate *

Interpretation: This patient is heterozygous for the c.2846A>T variant in the DPYD gene. Individuals heterozygous for this DPYD variant are predicted to have intermediate dihydropyrimidine dehydrogenase (DPD) activity (enzyme activity of 30-70 percent of normal). Because 80 percent of administered 5-fluorouracil (5-FU) is normally inactivated by DPD, a decrease in DPD enzymatic activity may lead to increased concentrations of 5-FU and elevated risk for grade III-IV toxicity.

Recommendation: Start fluoropyrimidine therapy with reduced dosing; approximately 50 percent of standard dose is recommended, followed by titration of dose based on patient tolerability and therapeutic drug monitoring. The Clinical Pharmacogenetics Implementation Consortium (CPIC) dosing guidelines for fluoropyrimidines can be found at: https://www.pharmgkb.org/gene/PA145.

This result has been reviewed and approved by [redacted], Ph.D.

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

BACKGROUND INFORMATION: Dihydropyrimidine Dehydrogenase (DPYD), 3 Variants
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:
Non-functional alleles and toxicity risk:
*13 (rs55886062, c.1679T>G) - Increased risk
*2A (rs3918290, c.1905+1G>A) - Greatly increased risk
c.2846A>T (rs67376798) - Increased risk
A result of negative indicates no variants detected and is predictive of *1 functional alleles and normal enzymatic activity.
Allele Frequency by Population:
*13: Caucasian - 0.1 percent; Asian - absent; African American - absent
*2A: Caucasian - 0.47-2.2 percent; Asian - absent; African American - absent
c.2846A>T: Caucasians - 1.1 percent; Asian - absent; African American - absent
CLINICAL SENSITIVITY: Estimated at 31 percent for the DPYD variants analyzed.
METHODOLOGY: Polymerase chain reaction (PCR) and fluorescence monitoring.
ANALYTICAL SENSITIVITY and SPECIFICITY: 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 non-genetic 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 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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VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
DPYD Specimen	21-159-140494	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
DPYD Genotype	21-159-140494	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
DPYD Phenotype	21-159-140494	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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