ARUP LABORATORIES
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Tracy I. George, MD, Chief Medical Officer

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

Physician: Doctor, Example

Patient: Patient, Example

DOB	10/6/1966
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]

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

BACKGROUND INFORMATION: Dihydropyrimidine Dehydrogenase (DPYD), 3 Variants

Background information for 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.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
DPYD Specimen	18-190-400079	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
DPYD Genotype	18-190-400079	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
DPYD Phenotype	18-190-400079	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