SESSION 3: FUTURE DIRECTION
WHERE DO WE GO FROM HERE

U.S. FOOD & DRUG ADMINISTRATION

AACR American Association for Cancer Research®

MODERATOR

William Pierce, PharmD, MPH, BCPS
U.S. Food and Drug Administration

SPEAKERS

Christina Wu, MB, BCh, MD
Mayo Clinic at Arizona

ADDITIONAL PANELISTS

Robert Schuck, PharmD
U.S. Food and Drug Administration

Patricia LoRusso, DO, PhD (hc), FAACR
Yale Cancer Center

Karen Merritt
Advocates for Universal DPD/DPYD Testing

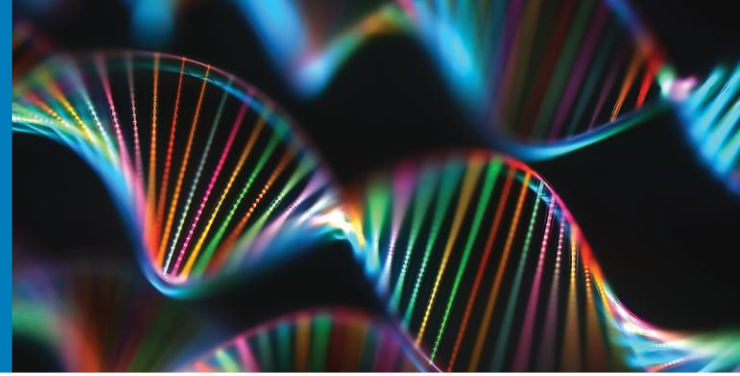
Alan Venook, MD
University of California, San Francisco

Victoria Pratt, PhD
Agena BioScience

FDA-AACR Workshop on

TO TEST OR NOT TO TEST – THAT IS THE QUESTION: DPD DEFICIENCY AND WEIGHING POTENTIAL HARMS

January 16, 2025 I Bethesda, MD



Current State Of *DPYD* Genotype Testing at Mayo Clinic

Christina Wu, MD

Professor of Medicine

Division of Hematology/Oncology

Mayo Clinic, Arizona

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DPYD Testing Available at Mayo Clinic

Test ID	DPDQ DPYD Genotype V	DPYDG DPYD Full Gene Sequencing
Variants tested	*2A.*7, *8, *10, *13, rs67376798, rs75017182, and rs115232898 alleles	Full gene sequencing
Turnaround Time	3-10 days	5-10 days
Lab location	Rochester	Rochester
Fees	$289.52	$522.52

Example DPYD Test Laboratory Report

DPYD Phenotype	Normal metabolizer
DPYD Activity Score	2.00
DPYD Genotype	No variants were detected in the DPYD gene.

INTERPRETATION

No reportable variants were detected in DPYD (activity score of 2). Normal dosing of fluoropyrimidines is supported by this genotype.

In addition, there is no evidence of carrier status or affected status for autosomal recessive DPD deficiency.

This result decreases the likelihood of, but does not rule out, the presence of a pathogenic DPYD variant. Clinical correlation is recommended. A genetic consultation may be of benefit.

Note: in an individual with no reportable variants the expected combined activity score is 2.

METHOD SUMMARY

Genotyping is performed using a PCR-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the segment of DNA that contains the polymorphism. If the detection probe is an exact match to the target DNA, the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected. (TaqMan SNP Genotyping Assays User Guide, Applied Biosystems)

5FU Dosing Recommendations

Phenotype	Alleles	Activity Score	5FU dosing
Normal metabolizer	2 normal function alleles	2	No dose change
Intermediate metabolizer	2 reduced function alleles Or 1 normal and 1 reduced function allele	1-1.5	50% dose reduction
Poor metabolizer	2 non-functioning alleles Or 1 reduced function and 1 non-functioning allele	0-0.5	Do not recommend dosing

Dosing is based on Clinical Pharmocogenetics Implementation Consortium (CPIC) guidelines

DPYD Testing Practice: Breast Cancer Disease Group

- Discussion at 3-site (Minnesota, Arizona, Florida) disease group
- Not routinely testing for *DPYD* genotype
- Consensus that *DPYD* genotype testing should be discussed with patients as an option, prior to starting capecitabine or 5FU.
- Patients are counselled on test turnaround time, how results will affect drug dosing, and patients may have to pay out-of-pocket for testing

DPYD Testing Practice: Gastrointestinal Cancer Disease Group

- Discussion at 3-site (Minnesota, Arizona, Florida) disease group
- Also not routinely testing for *DPYD* genotype

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PATIENT PERSPECTIVE

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SPEAKER

Asal Sayas
White House Office of Science & Technology Policy

CONCLUDING REMARKS

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Workshop Feedback Survey:

SPEAKERS

Paul Kluetz, MD
U.S. Food and Drug Administration

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President, American Association for Cancer Research®