SESSION 1: CURRENT LANDSCAPE
DPD DEFICIENCY TESTS AND FDA PRODUCT LABELING

U.S. FOOD & DRUG ADMINISTRATION

AACR American Association for Cancer Research

MODERATOR

Michael Pacanowski, PharmD, MPH
U.S. Food and Drug Administration

SPEAKERS

Robert Diasio, MD
Mayo Clinic

Victoria Pratt, PhD
Agena BioScience

Evan Bryson, PharmD, BCOP
U.S. Food and Drug Administration

ADDITIONAL PANELISTS

Sam Abdelghany, PharmD, MHA, BCOP
Smilow Cancer Center at Yale New Haven

D. Max Smith, PharmD, BCPS
Medstar Health & Georgetown University

Jill Bates, PharmD, BCOP, CPT, FASHP
Department of Veterans Affairs

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

The Importance of DPD in 5-FU Treatment: DPD Deficiency Background, Pharmacology, and Testing

Robert B. Diasio MD

Professor/Director Emeritus

Mayo Clinic Cancer Center

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Disclosure Information

I have no financial relationships to disclose.

Toxicity with 5-FU and Capecitabine

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Background:

- 5-FU administered to ~275,000 cancer patients annually in the U.S.†
  - Colon cancer, breast cancer, etc.
  - One of most widely prescribed chemotx worldwide ‡
- 1-in-3* pts - life-threatening toxic side effects (i.e., grade ≥3)
  - Neutropenia, mucositis, severe diarrhea, etc.
- 1,300 people annually die from 5-FU toxicity †
- Toxicity - most common reason for therapy discontinuation
  - Reduces treatment efficacy

† *Public Teleconference Regarding Licensing and Collaborative Research Opportunities for: Methods and Compositions Relating to Detecting Dihydropyrimidine Dehydrogenase (DPD)*, in *Federal Register*, N.I.o.H. Department of Health and Human Services, Editor. 2008, Office of the Federal Register, National Archives and Records Administration. p. 38233.

‡ Commonly stated in literature without primary citation or quantitative evidence

* Lee *et al. J Natl Cancer Inst*. 2014. 106(12).

Importance of DPD with 5-FU Drugs

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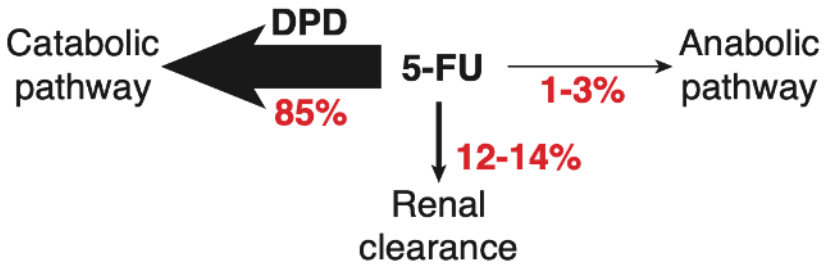
Dihydropyrimidine Dehydrogenase (DPD) inactivates 85% of administered 5-FU



Heggie G et al. 1987. *Cancer Res* 47:2204-6
Diasio RB et al. 1988. *JCI 81:*47-51
Diasio RB et al. 1989. *Clin Pharmacokin* 16:215-237

DPD Deficiency – Initial Case

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Patient 1:

- 40 yr. old WMF previously excellent health

- 3m PTA – Dx. – breast cancer 9/16 lymph nodes "+"

Adjuvant Chemotherapy – CMF Regimen (Cyclophosphamide, Methotrexate, 5-FU)

- During the initial 3 cycles of planned therapy

  - Worsening toxicity (primarily cytopenias) in spite of delay in cycle 2 & 3 therapy and reduction of drug doses.

  - Presented to local hospital comatose with Grade IV cytopenias.

Diasio RB et al. 1988. *JCI* 81:47-51

Laboratory Evidence Suggesting DPD Deficiency

- Plasma uracil levels increased in patient compared to controls by LC-Mass Spectrometry.
- When patient recovered from cytopenias, DPD enzyme activity measured in isolated peripheral blood mononuclear cells.
  - Shown to be absent compared to detectable levels in controls.

Diasio RB et al. 1988. *JCI* 81:47-51

DPD Deficiency – Initial Case

5-FU Pharmacokinetics

	$t_{1/2}$ (min.)	Clearance ($ml./min./M^2$)	Unchanged 5-FU in 24 hrs. urine % of Dose
"Typical" Patients	13 ± 7	594 ± 198	9.8 ± 1.6

Heggie G et al. 1987. *Cancer Res* 47:2203-2206

Patient 1 (DPD Deficient)	159	70	89.7

Diasio RB et al. 1988. *JCI* 81:47-51

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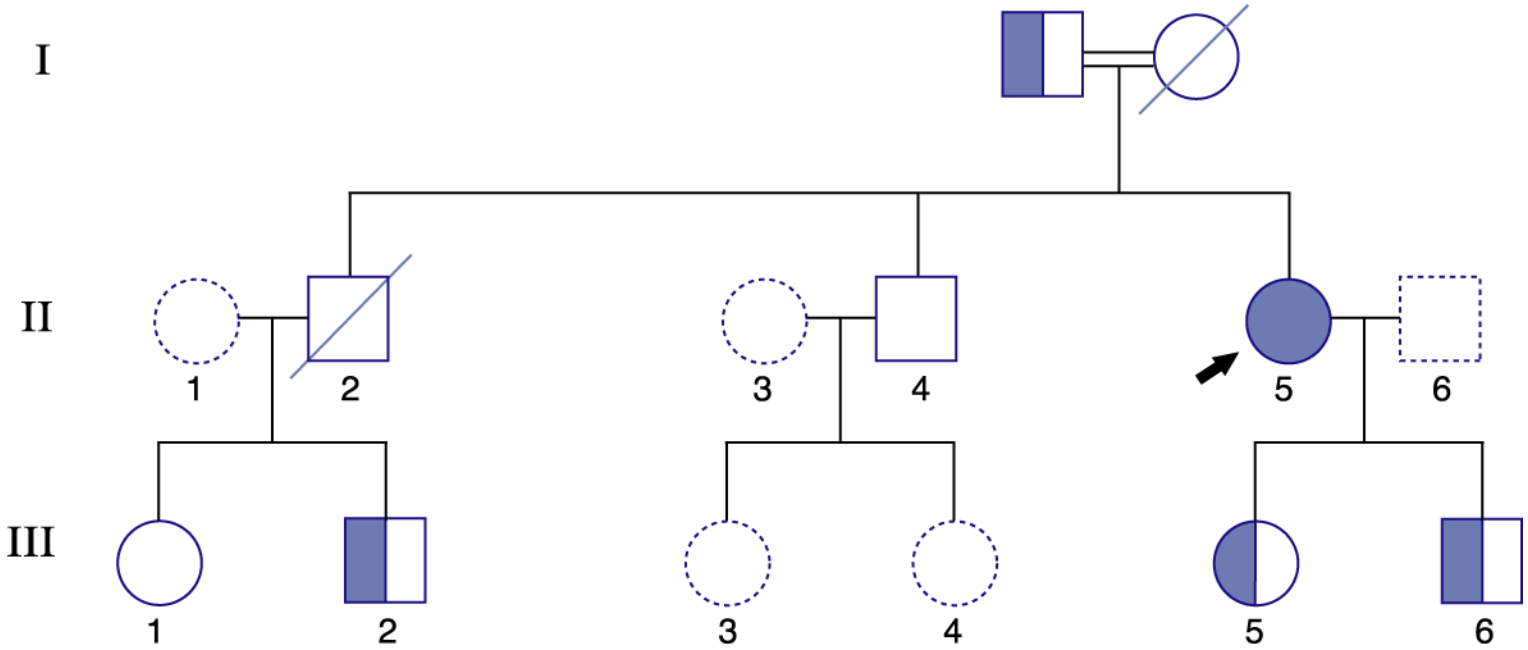
Clinical Manifestations of DPD Deficiency

- Phenotypically “normal”
- Pharmacogenetic presentation – no medical consequences of DPD deficiency until exposure to drug (e.g., 5-FU). Then, symptoms similar to 5-FU overdose

Family Study of Pt. 1 – DPD Enzyme Levels Demonstrating DPD Deficiency



Johnson MR et al. 2002. *Clin Can Res* 8:768-774

Testing for DPD Deficiency

- Phenotypic Tests
  - Plasma uracil (and dihydrouracil) levels
  - DPP enzyme Test in PBM Cells
- Genotypic Tests
  - Targeted genotyping for 4-5 common alleles; 4 rare
  - *DPYD* Full Gene Sequencing (common & rare alleles)

Diasio RB et al. 2002. *Cancers* 14: 3207

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

Association for Molecular Pathology (AMP)'s Recommendations for Clinical *DPYD* Genotyping Allele Selection

V.M. Pratt, PhD, FACMG

Director, Scientific Affairs, Agena Bioscience, San Diego CA

Adjunct Professor, Clinical Pharmacology, Indiana University School of Medicine, Indianapolis, IN

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Disclosure Information

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Victoria M. Pratt, Ph.D., FACMG

I have the following relevant financial relationships to disclose:

Employee of: Agena Bioscience

About AMP

Mission

The Association for Molecular Pathology is a not-for-profit scientific society that advances the clinical practice, science, and excellence of molecular and genomic laboratory medicine through education, innovation, and advocacy to enable highest quality health care.

Vision

The Association for Molecular Pathology provides global expertise in molecular testing that drives patient care.

Molecular Diagnostics Specialists

3,100+ members worldwide with deep expertise in inherited conditions, oncology, infectious diseases and/or bioinformatics.

- 47% are MDs or MD/PhDs (pathologists)
- 32% are PhDs
- Trainee membership is free (students, residents and fellows)

15.6% are non-U.S. working in 60 countries.

- 8 international affiliates

100% are involved in molecular diagnostics.

Every patient or healthcare provider whose care or work involves molecular testing likely encounters the expertise of an AMP member.

DPYD Genotyping Recommendations:

A Joint Consensus Recommendation of the Association for Molecular Pathology, American College of Medical Genetics and Genomics, Clinical Pharmacogenetics Implementation Consortium, College of American Pathologists, Dutch Pharmacogenetics Working Group of the Royal Dutch Pharmacists Association, European Society for Pharmacogenomics and Personalized Therapy, Pharmacogenomics Knowledgebase, and Pharmacogene Variation Consortium

- **V.M. Pratt, PhD, FACMG**
- On behalf of the AMP Clinical Practice Committee's Pharmacogenomics (PGx) Working Group

AMP PGx Working Group

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Goals

- To develop recommendations defining a minimum set of variants (a “Must-Test” list) that should be included in clinical genotyping assays
- Used by the clinical PGx testing community as a reference for test development

Members

- Subject matter expert representatives from the clinical PGx testing community (US and Europe), including organizational representation from ACMG, CAP, CPIC, DPWG, ESPT, PharmGKB, and PharmVar

Projects – PGx Allele Selection for Clinical Genotyping

- *CYP2C19* - **Pratt VM, et al. *JMD*, 2018;20:269-276**
- *CYP2C9* - **Pratt VM, et al. *JMD*, 2019;21:746-755**
- Warfarin-Related Genes - **Pratt VM, et al. *JMD*, 2020;22:847-859**
- *CYP2D6* - **Pratt VM, et al. *JMD*, 2021;23:1047-1064**
- *TPMT/NUDT15* - **Pratt VM, et al. *JMD*, 2022;24:1079-1088**
- *CYP3A4/CYP3A5* - **Pratt VM, et al. *JMD,* 2023;25:619-629**
- *DPYD* (today’s presentation) - **Pratt VM, et al. *JMD*, 2024;26:851-863**

Variability in *DPYD* Genotyping Tests in the United States

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Table 1. Variant Coverage and Estimated Diagnostic Performance of Commercially Available *DPYD* Genotyping Tests in the United States

		DPYD Variants Tested								
Laboratory Name	**Test Name (Order Code)**	***2A**	***13**	**c.2846A>T**	**HapB3**	**c.557A>G**	**Other**	**FN Rate**	**Sensitivity**	**NPV**
Color Health	Color Extended and Color Standard panels	X	X					81.6%	18.4%	95.1%
23andMe	*DPYD* Drug Metabolism	X		X				69.4%	30.6%	95.8%
Fulgent Genetics	Picture PGx	X	X	X				65.3%	34.7%	96.0%
ARUP	Dihydropyrimidine dehydrogenase (*DPYD*), 3 Variants (2012166)	X	X	X				65.3%	34.7%	96.0%
Indiana University	Pharmacogenetic *DPYD* Genotyping (53102299)	X	X	X	X	X		0%	100%	100%
Quest	Pharmacogenomics panel (36943)	X			X	X	*2B, *4, *5, *7, *8, *9A, *9B	20.4%	79.6%	98.7%
LabCorp	*DPYD* Genotyping (512275)	X	X	X	X	X		0%	100%	100%
Mayo Clinic Laboratories	*DPYD* Genotype, Varies (DPYDQ)	X	X	X	X	X	*7, *8, *10	0%	100%	100%
OneOme	The RightMed Test	X	X	X	X	X		0%	100%	100%
RPRD	Precision HealthPGx Panel	X	X	X	X	X	*3, *4, *5, *6, *7, *8, *9A, *9B, *10, *11, *12, p.R21Q, p.R21×, p.M166V, p.R592Q, pQu.N635K, p.R886C	0%	100%	100%
Sanford Laboratories	*DPYD* Genotyping (LBOR0149)	X	X	X	X	X	*3, *7, *8, *10, *12	0%	100%	100%
Sinochips Diagnostics	*DPYD* genotyping	X	X	X	X	X	*7, *8, *10, *12	0%	100%	100%
Tempus	*DPYD* test	X	X	X	X	X		0%	100%	100%

Nguyen et al. 2024. *J Natl Compr Canc Netw.* PMID: 38754463

Why Recommend Genotyping For Specific Alleles?

- Option 1: Test all known variants/alleles
  - Not practical – for example - *CYP2D6*, there are currently >145 alleles/sub-alleles!
  - Ongoing updates to known allele list
- Option 2: Sequencing instead of targeted genotyping
  - Current state: a few key pharmacogenes are technically challenging by short-read NGS chemistry
  - Challenges in reporting genotypes and interpreting rare variants/alleles
  - Phenotype-driven vs. preemptively
  - Cost effectiveness
- **Option 3: Adopt a similar approach to ACMG recommendations for *CFTR* testing**
  - Define a minimum set of variants based on multiethnic allele frequency to optimize diagnostic test rate

A Two-Tier Framework

- **Tier 1 -** Minimum "must-test" variants
  - Known effect on protein function and/or gene expression
  - Appreciable minor allele frequency (Tier 1 - ≥0.1% and Tier 2 ≥0.01% cut-offs for *DPYD*) based on gnomAD v4.0.0
  - Available reference materials
  - Technical feasibility to detect variant in a clinical laboratory
- **Tier 2 -** Extended panel
  - Meet at least one but not all the criteria for inclusion in Tier 1
- **Other**
  - Variants with unknown or uncertain function are not recommended for inclusion in clinical test panels

AMP PGx Working Group: *DPYD*

- Part of ongoing effort of the AMP PGx Working Group: 7th deliverable
- Challenges:
  - *DPYD* variants are rarer than CYPs, similar to *TPMT* and *NUDT15*
  - Information on phasing of variants not as well documented
  - *DPYD* testing can be different depending on the clinical indication
    - PGx indication vs. diagnostic testing for autosomal recessive DPD deficiency
  - Limited reference materials for *DPYD*
    - Co-project with CDC GeT-RM to characterize additional DNAs from Coriell Life Sciences (Camden, NJ)
    - https://www.jmdjournal.org/article/S1525-1578(24)00155-7/fulltext

AMP Guidelines for *DPYD* Clinical Testing: Tier 1

Variant (NM_000110.4)	Legacy Name	CPIC Defined Function	Activity Value	rsID	DPYD RefSeqGene (LRG_722)	GRCh38.p13 chr 1	HGVS protein Nomenclature	Reference Material Available‡	Multiethnic Allele Frequency (%)
c.1905+1G>A	*2A	No function	0	rs3918290	NG_008807.2: g.476002G>A	NC_000001.11: g.97450058C>T	N/A	Yes	0-0.5%
c.1679T>G	*13	No function	0	rs55886062	NG_008807.2: g.410273T>G	NC_000001.11: g.97515787A>C	NP_000101.2: p.Ile560Ser	Yes	0-0.08%
c.1129-5923C>G, c.1236G>A	HapB3	Decreased function	0.5	rs75017182, rs56038477	NG_008807.2: g.346167C>G, NG_008807.2: g.352197G>A	NC_000001.10: g.97579893G>C, NC_000001.10: g.97573863C>T	N/A, NP_000101.2: p.Glu412=	Yes	0.06-2.4%
c.557A>G	N/A	Decreased function	0.5	rs115232898	NG_008807.2: g.226586A>G	NC_000001.11: g.97699474T>C	NP_000101.2: p.Tyr186Cys	Yes	0-2.1%
c.868A>G	N/A	Decreased function	0.5	rs146356975	NG_008807.2: g.330911A>G	NC_000001.11: g.97595149T>C	NP_000101.2: p.Lys290Glu	Yes	0-0.2%
c.2279C>T	N/A	Decreased function	0.5	rs112766203	NG_008807.2: g.620781C>T	NC_000001.11: g.97305279G>A	NP_000101.2: p.Thr760Ile	Yes	0-0.5%
c.2846A>T	N/A	Decreased function	0.5	rs67376798	NG_008807.2: g.843669A>T	NC_000001.11: g.97082391T>A	NP_000101.2: p.Asp949Val	Yes	0-0.6%

AMP Guidelines for *DPYD* Clinical Testing: Tier 2

Variant (NM_000110.4)	Legacy Name	CPIC Defined Function	Activity Value	rsID	DPYD RefSeqGene (LRG_722)	GRCh38.p13 chr 1	HGVS protein Nomenclature	Reference Material Available‡	Multiethnic Allele Frequency (%)
c.299_302del	*7	No function	0	rs72549309	NG_008807.2: g.185642TCAT[1]	NC_000001.11: g.97740411ATGA[1]	NP_000101.2: p.Phe100fs	Yes	0-0.01%
c.703C>T	*8	No function	0	rs1801266	NG_008807.2: g.234284C>T	NC_000001.11: g.97691776G>A	NP_000101.2: p.Arg235Trp	No	0-0.03%
c.1314T>G	N/A	Decreased function	0.5	rs186169810	NG_008807.2: g.352275T>G	NC_000001.11: g.97573785A>C	NP_000101.2: p.Phe438Leu	Yes	0-0.05%
c.1475C>T	N/A	No function	0	rs72549304	NG_008807.2: g.376451C>T	NC_000001.11: g.97549609G>A	NP_000101.2: p.Ser492Leu	No	0-0.02%
c.1774C>T	N/A	No function	0	rs59086055	NG_008807.2: g.475870C>T	NC_000001.11: g.97450190G>A	NP_000101.2: p.Arg592Trp	Yes	0-0.08%
c.2639G>T	N/A	No function	0	rs55674432	NG_008807.2: g.827444G>T	NC_000001.11: g.97098616C>A	NP_000101.2: p.Gly880Val	No	0-0.08%

Most Recommended Clinically Relevant *DPYD* Variants are Rare in the Population

- Due to extreme toxicity associated with DPD deficiency
  - Variants with at least > 0.1% allele frequency in any subpopulation are recommended as Tier 1
  - c.1679T>G, p.Ile560Ser (legacy *DPYD*13)* or did not meet the Tier 1 allele frequency cutoff
    - ❑ Included in Tier 1 due to its association with extreme toxicity and the European Medicines Agency (EMA) drug label recommendations
- Overall detection rate of recommended panel to identify individuals with impaired DPD function cannot be reliability determined at this time
  - Overall incidence of partial or complete DPD deficiency is not well defined
  - Large percentage of deleterious variants are rare or novel

DPYD Full Gene Sequencing

- Due to large number of rare variants and potential severe toxicities, clinical labs may choose full gene sequencing rather than genotyping but keep in mind…
  - Current ACMG/AMP guidelines for interpreting sequence variants are not designed for interpreting PGx variants
    - Many rare variants encountered in clinical sequencing may ultimately be classified as variants of unknown significance (VUS).
  - Sequencing may detect both common and rare variants, but Sanger or short-read sequencing will not resolve phasing when more than 1 variant is detected

Copy Number Variation: *DPYD* Partial/Whole Gene Deletions

- Exon 4 deletion: Observed at high prevalence in the Finnish population at 2.4% of individuals prescreened for DPD deficiency
  - Another study observed a lower frequency of 0.2% for the deletion in a Canadian population, which included an individual with severe 5-FU toxicity
  - Frequency of deletion likely population specific and vary considerably among different patient populations
- Interstitial deletions of exons 6, 12, and 14-16, and partial and whole gene *DPYD* deletions have been observed with DPD deficiency with variable phenotypes
- Exonic deletions meet the frequency for inclusion in either Tier 1 or 2, but they are not well-defined at this time
  - **<u>Currently no recommendations for routine clinical testing</u>**
  - Could be considered in cases of 5-FU toxicity or DPD deficiency when a single pathogenic variant cannot explain the phenotype

Proficiency Testing/External Quality Assessment*

- Several proficiency testing (PT) or external quality assessment programs are available for *DPYD* genotyping
  - Will need to expand their offerings to meet recommended Tier 1 and 2 variants

Variant (legacy name)	cDNA	Tier	Number (%) CAP	Number (%) RfB	Number (%) SKML	Number (%) EMQN€
rs3918290 (*2A)	c.1905+1G>A	1	63 (98%)	142 (100%)	22 (100%)	73 (100%)
rs72549303 (*3)	c.1898del	none	13 (20%)			
rs1801158 (*4)	c.1601G>A	none				1 (1%)
rs1801159 (*5)	c.1627A>G	none				1 (1%)
rs1801160 (*6)	c.2194G>A	none				47 (64%)
rs72549309 (*7)	c.299_302del	2	15 (23%)		2 (9%)¥	5 (7%)
rs1801266 (*8)	c.703C>T	2	18 (28%)			3 (4%)
rs1801265 (*9A)	c.85T>C	none				2 (3%)
rs1801267 (*9B)	c.2657G>A	none	13 (20%)			2 (3%)
rs1801268 (*10)	c.2983G>T	none				3 (4%)
rs72549306 (*11)	c.1003G>T	none				1 (2%)
rs115232898	c.557A>G	1	27 (42%)			3 (4%)
rs78060119 (*12)	c.1156G>T	none	14 (22%)			2 (3%)
rs55886062 (*13)	c.1679T>G	1	59 (92%)	138 (97%)	22 (100%)	71 (97%)
rs72549310	c.61C>T	none				1 (1%)
rs67376798	c.2846A>T	1	54 (84%)	138 (97%)	22 (100%)	70 (96%)
rs75017182 (HapB3)	c.1129-5923C>G	1	36 (56%)	50 (35%)	22 (100%)	44 (60%)
rs56038477 (HapB3)	c.1236G>A	none				28 (38%)

*Information available at time of publication; inclusion does not represent AMP endorsement

Conclusions

- This AMP joint consensus recommendation is intended to:
  - Promote test standardization of *DPYD* and genotype concordance between laboratories
  - Inform clinical laboratory professionals of which variants to include when designing and validating clinical PGx assays for *DPYD* testing
  - Complementary to other clinical guidelines, e.g., by CPIC and DPWG
- While designed to be inclusive of admixed population, laboratories should consider genetic variation in their population.
  - Modifications may be considered, and labs should justify variant selection
  - Laboratories should follow best practices for assay validation and adhere to regulatory requirements

AMP PGx Working Group

- **Victoria M. Pratt** (Co-Chair), Indiana University School of Medicine, Agena Bioscience
- **Karen E. Weck** (Chair), University of North Carolina
- **Larisa H. Cavallari**, University of Florida
- **Edward D. Esplin**, Invitae, ACMG representative
- **Makenzie L. Fulmer**, ARUP Laboratories and University of Utah School of Medicine
- **Andrea Gaedigk**, Children's Mercy Kansas City, PharmVar representative
- **Houda Hachad**, AccessDx Laboratory
- **Yuan Ji**, ARUP Laboratories and University of Utah School of Medicine
- **Lisa V. Kalman**, Division of Laboratory Systems, Centers for Disease Control and Prevention
- **Reynold C. Ly**, Nationwide Children's Hospital
- **Ann M. Moyer**, Mayo Clinic, CAP representative
- **Stuart A. Scott**, Stanford University Medical Center
- **Amy J. Turner**, Medical College of Wisconsin and RPRD Diagnostics, Junior Member
- **Ron H.N. van Schaik**, Erasmus MC University Medical Center, ESPT and DPWG representative
- **Michelle Whirl-Carrillo**, Stanford University, CPIC and PharmGKB representative

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- **AMP Clinical Practice Committee**
- **Jacob Ruden, PhD**
- **Robyn Temple-Smolkin, MBA, PhD, HCLD(ABB)**
- **Dr. Karen Weck, AMP PGx Working Group Chair**
- **Ed Esplin, MD, PhD, ACMG representative**
- **Other contributing professional societies**

Contact:

Dr. Victoria Pratt (vicky.pratt@agenabio.com), Co-Chair of the AMP PGx Working Group, for feedback and suggestions

FLUOROPYRIMIDINES AND DPD DEFICIENCY
A REGULATORY HISTORY OF FDA LABELING

EVAN BRYSON, PHARMD, BCOP

ONCOLOGY CENTER OF EXCELLENCE

CONFLICTS OF INTEREST

- None

FDA DRUG LABELING

- Must provide adequate directions for use[1]
- Includes all written, printed, or graphic matter associated with a drug[2]
- Must be updated when new information becomes available that causes the labeling to become inaccurate, false, or misleading[3]
- FDA may require safety labeling changes to drug USPI if the FDA becomes aware of new safety information[4]

FDA: Food and Drug Administration
USPI: United States Prescribing Information

1: 21 CFR 201.5
2. 21 CFR 1.3(a)
3. 21 CFR 201.56(a)(2)
4. FD&C Act, section 505(o)(4)

FLUOROURACIL LABELING

Year	Labeling Changes	DPD Deficiency Updates
1962	FDA approved for the treatment of colorectal cancer	DPD deficiency not discussed in original labeling
2016	Labeling update	New subsection of Warnings and Precautions section added on increased risk of serious or fatal adverse reactions in patients with low or absent DPD activity
2024	Safety labeling changes approved by the FDA	DPD deficiency language updated to align with 2022 capecitabine labeling

CAPECITABINE (XELODA) LABELING

Year	Labeling Changes	DPD Deficiency Updates
1998	FDA approved for the treatment of metastatic breast cancer	DPD deficiency not discussed in original labeling
2003	Labeling update	Contraindication added for all patients with known DPD deficiency
2015	Labeling update	Contraindication for DPD deficiency removed New subsection of Warnings and Precautions section added on increased risk of serious or fatal adverse reactions in patients with low or absent DPD activity
2022	Labeling updated under Project Renewal	Numerous changes made, including a statement to consider pre-treatment testing for DPD deficiency

CURRENT W&P LANGUAGE

5.2 Serious Adverse Reactions from Dihydropyrimidine Dehydrogenase (DPD) Deficiency

Patients with certain homozygous or compound heterozygous variants in the *DPYD* gene known to result in complete or near complete absence of DPD activity (complete DPD deficiency) are at increased risk for acute early-onset toxicity and serious, including fatal, adverse reactions due to XELODA (e.g., mucositis, diarrhea, neutropenia, and neurotoxicity). Patients with partial DPD activity (partial DPD deficiency) may also have increased risk of serious, including fatal, adverse reactions.

XELODA is not recommended for use in patients known to have certain homozygous or compound heterozygous *DPYD* variants that result in complete DPD deficiency.

Withhold or permanently discontinue XELODA based on clinical assessment of the onset, duration, and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe reactions, which may indicate complete DPD deficiency. No XELODA dose has been proven safe for patients with complete DPD deficiency. There are insufficient data to recommend a specific dose in patients with partial DPD deficiency.

CURRENT W&P LANGUAGE, CONT

Consider testing for genetic variants of *DPYD* prior to initiating XELODA to reduce the risk of serious adverse reactions if the patient's clinical status permits and based on clinical judgement *[see Clinical Pharmacology (12.5)]*. Serious adverse reactions may still occur even if no *DPYD* variants are identified.

An FDA-authorized test for the detection of genetic variants of *DPYD* to identify patients at risk of serious adverse reactions due to increased systemic exposure to XELODA is not currently available. Currently available tests used to identify *DPYD* variants may vary in accuracy and design (e.g., which *DPYD* variant(s) they identify).

CURRENT LABELING LANGUAGE

Section 12.5: Pharmacogenomics

Four *DPYD* variants have been associated with impaired DPD activity in White populations, especially when present as homozygous or compound heterozygous variants: c.1905+1G>A (*DPYD* *2A), c.1679T>G (*DPYD* *13), c.2846A>T, and c.1129-5923C>G (Haplotype B3). *DPYD**2A and *DPYD**13 are no function variants, and c.2846A>T and c.1129-5923C>G are decreased function variants. The decreased function *DPYD* variant c.557A>G is observed in individuals of African ancestry. This is not a complete listing of all *DPYD* variants that may result in DPD deficiency *[see Warnings and Precautions (5.2)]*.

CURRENT LABELING LANGUAGE

Section 17: Patient Counseling Information

Serious Adverse Reactions from Dihydropyrimidine Dehydrogenase (DPD) Deficiency

Inform patients of the potential for serious and life-threatening adverse reactions due to DPD deficiency and discuss with your patient whether they should be tested for genetic variants of *DPYD* that are associated with an increased risk of serious adverse reactions from the use of XELODA. Advise patients to immediately contact their healthcare provider if symptoms of severe mucositis, diarrhea, neutropenia, and neurotoxicity occur *[see Warnings and Precautions (5.2) and Clinical Pharmacology (12.5)]*.

CONCLUSIONS

- Fluoropyrimidine labeling has evolved over the years
- Current fluoropyrimidine labeling
  - Contains a Warning and Precaution for serious adverse reactions from DPD deficiency
  - States to consider pre-treatment testing
  - Provides information about *DPYD* variants of interest
  - Specifies that patients should be informed about the risk of adverse reactions in patients with DPD deficiency and the role of genetic testing

SESSION 1: CURRENT LANDSCAPE
DPD DEFICIENCY TESTS AND FDA PRODUCT LABELING

U.S. FOOD & DRUG ADMINISTRATION

AACR American Association for Cancer Research

MODERATOR

Michael Pacanowski, PharmD, MPH
U.S. Food and Drug Administration

SPEAKERS

Robert Diasio, MD
Mayo Clinic

Victoria Pratt, PhD
Agena BioScience

Evan Bryson, PharmD, BCOP
U.S. Food and Drug Administration

ADDITIONAL PANELISTS

Sam Abdelghany, PharmD, MHA, BCOP
Smilow Cancer Center at Yale New Haven

D. Max Smith, PharmD, BCPS
Medstar Health & Georgetown University

Jill Bates, PharmD, BCOP, CPT, FASHP
Department of Veterans Affairs