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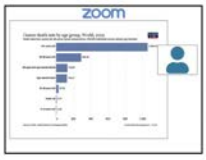

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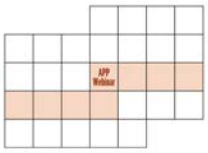

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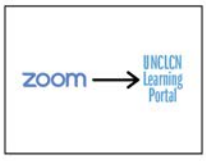

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Thank you for spreading the word!

6

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Our Presenter

Amber B. Cipriani,
PharmD, BCOP

Amber Cipriani, PharmD, BCOP, is a clinical pharmacist specialized in oncology care and pharmacogenomics. She currently serves as the Precision Medicine Pharmacy Coordinator at the University of North Carolina Medical Center where she works to implement initiatives that improve medication use and management through the utilization of technology, genetics, and clinical decision support tools.

She is a member of the Molecular Tumor Board and Precision Oncology Program. She serves as the leader of the Pharmacogenomics Initiative of the Program for Precision Medicine in Health Care (PPMH) at UNC.

Dr. Cipriani's position is a joint funded position with the UNC Eshelman School of Pharmacy, where she serves as a Clinical Assistant Professor coordinates elective courses in pharmacogenomics and hematology/ oncology pharmacotherapy for professional PharmD students.

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Our Presenter

9

Our Presenter

5. Amber Cipriani, PharmD, BCOP, is a clinical pharmacist specialized in oncology care and pharmacogenomics

10

Our Presenter

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4. She currently serves as the Precision Medicine Pharmacy Coordinator at the University of North Carolina Medical Center

11

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3. Enjoyed genetics before going into pharmacy-developed a companion diagnostic genetic test!

12

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2. Joint funded with the Eshelman School of Pharmacy where I coordinate courses and teach

13

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4. She currently serves as the Precision Medicine Pharmacy Coordinator at the University of North Carolina Medical Center
3. Enjoyed genetics before going into pharmacy-developed a companion diagnostic genetic test!
2. Joint funded with the Eshelman School of Pharmacy where I coordinate courses and teach
1. Participates in multiple state and national groups working to implement pharmacogenomic testing

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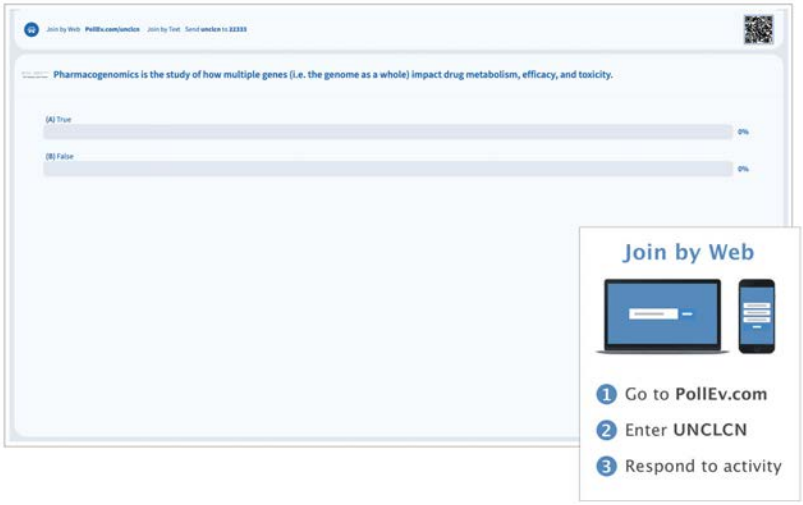
Sample Poll Everywhere Question



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Criteria for Activity Completion:
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Approved Provider Statement:
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Pharmacogenomics is the study of how multiple genes (i.e. the genome as a whole) impact drug metabolism, efficacy, and toxicity.

True 0%

False 0%

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UNC HEALTH

Integrating pharmacogenomic testing into oncology care

Amber Cipriani, PharmD, BCOP

Precision Medicine Pharmacy Coordinator, UNC Health Medical Center

Clinical Assistant Professor, UNC Eshelman School of Pharmacy

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Learning objectives

- Discuss examples of pharmacogenomic relationships for oncology medications.
- Identify resources to aid in interpretation and application of pharmacogenomic tests.
- Describe clinical workflows that integrate pharmacogenomic testing

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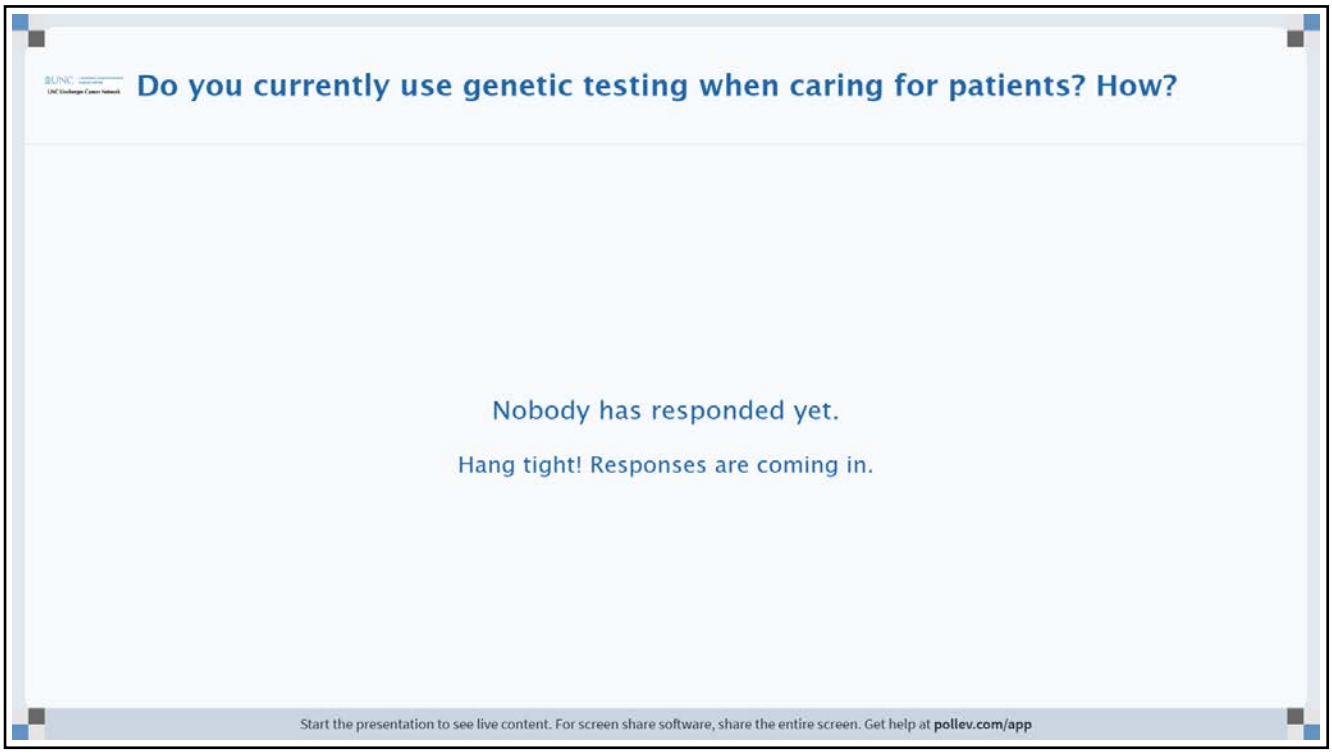

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Background Information

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What is precision medicine?

Precision Medicine Initiative Definition	FDA Definition
"An emerging approach for disease treatment and prevention that takes into account individual variability in genes, microbiomes, environment, and lifestyle for each person"	"An innovative approach to tailoring disease prevention and treatment that takes into account differences in people's genes, environments, and lifestyles"
Goal of Precision Medicine: Target the right treatments to the right patients at the right time	

1. Garrido P, Aldaz A, Vera R, et al. Proposal for the creation of a national strategy for precision medicine in cancer: a position statement of SEOM, SEAP, and SEFH. *Clin Transl Oncol.* 2018;20(4):443-447.
2. US Food and Drug Administration. Precision Medicine. September 27, 2018. Accessed April 12, 2022.

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Pharmacogenetics vs. Pharmacogenomics

Pharmacogenetics

- Study of how a ***single gene*** impacts drug metabolism, efficacy, and toxicity

Pharmacogenomics

- Study of how ***multiple genes*** (i.e. the genome as a whole) impact drug metabolism, efficacy, and toxicity

Whirl-Carrillo M, Huddart R, Gong L, et al. An Evidence-Based Framework for Evaluating Pharmacogenomics Knowledge for Personalized Medicine. *Clin Pharmacol Ther.* 2021;110(3):563-572.

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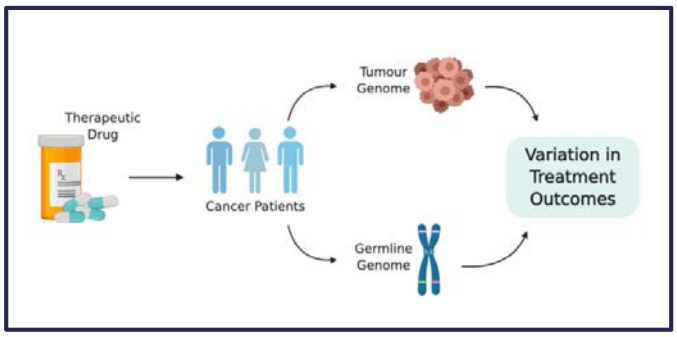
Germline versus somatic mutations



https://commons.wikimedia.org/wiki/File:Cancer_Pharmacogenomics.png

Germline	Somatic
Heritable	Not heritable
In all cells (usually)	Tumor specific
Detected with a cheek swab or blood test	Detected with a tumor sample or blood test

Cancer Genetics Overview (PDQ®)–Health Professional Version. Accessed 19 January 2023. https://www.cancer.gov/about-cancer/causes-prevention/genetics/overview-pdq#_2594 25

25

Pharmacogenetics in Oncology: **Tumor biomarkers applied to drug selection**

26

Case #1

LP is a 51-year-old male who initially presented with SOB for 6 months

LP's chest x-ray was concerning, so computed tomography (CT) was conducted and confirmed presence of a mass in the lung

A biopsy was obtained, and LP was diagnosed with metastatic non-small cell lung cancer (NSCLC)

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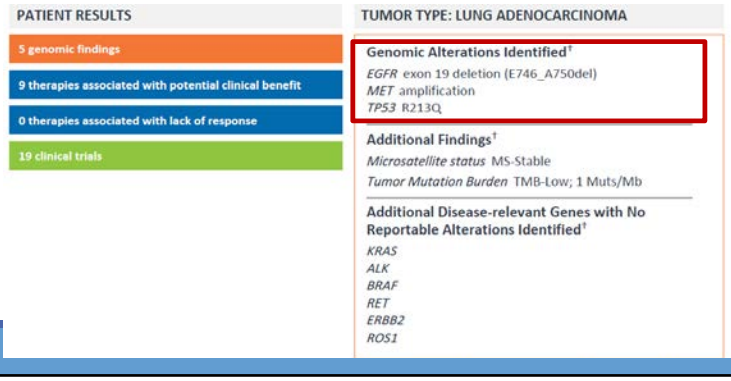
Case #1

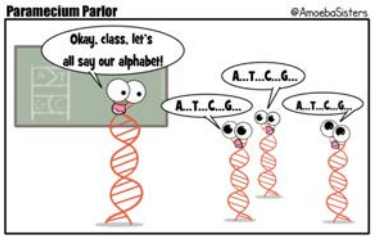
- Tissue obtained from LP's biopsy was sent to anatomic pathology, who prepared a specimen block using a formalin-fixed paraffin embedded (FFPE) protocol
- DNA isolated from the tumor specimen was analyzed for genetic changes associated with cancer using DNA sequencing
- The following results were obtained:



28

Somatic testing: Next-Generation Sequencing (NGS)

- "High-throughput": Utilizes DNA sequencing technologies that can process multiple DNA sequences in parallel (cancer.gov)
- For Patients: Think of it as a very fancy spell-checker for tumor DNA!



Examples of NGS tests used at UNC Health sites

Platform	Sample Type	# of Genes
Foundation CDx	Tumor tissue	324
Foundation CDx Liquid	Blood	311
Guardant	Blood	73
Neogenomics	Tumor tissue	Varies by disease
Tempus xT	Tumor tissue/blood	648

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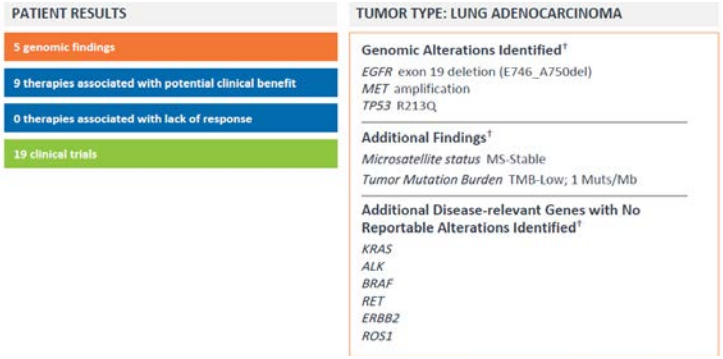
Example of Results

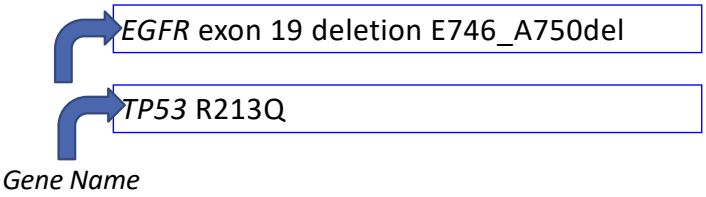


EGFR exon 19 deletion
E746_A750del

TP53 R213Q

30

Example of Results



** Remember our test is looking at the DNA level, but we are concerned with how the gene product (protein) is malfunctioning in cancer

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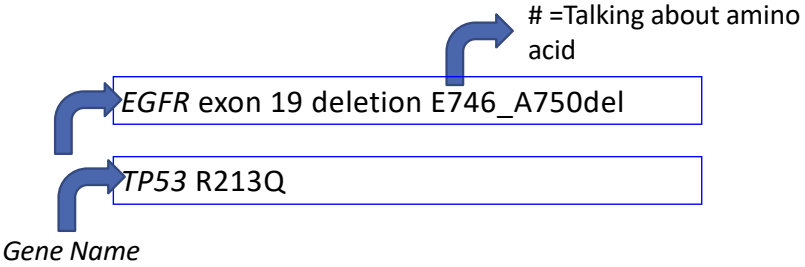
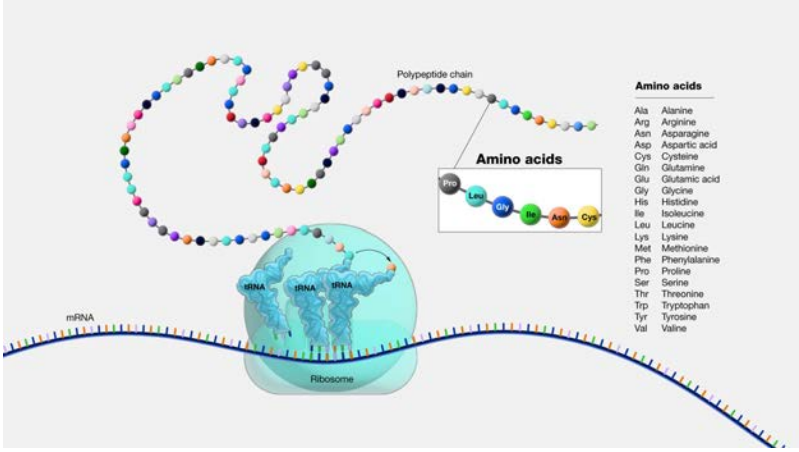
Example of Results



32

Example of Results



EGFR exon 19 deletion E746_A750del

TP53 R213Q

Image from: https://www.genome.gov/genetics-glossary/Amino-Acids

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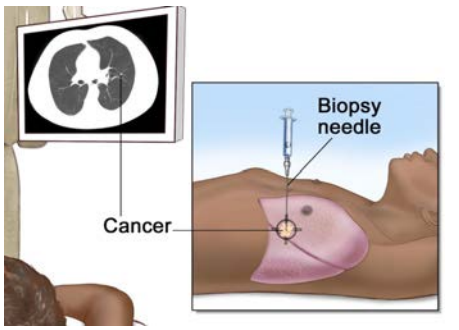
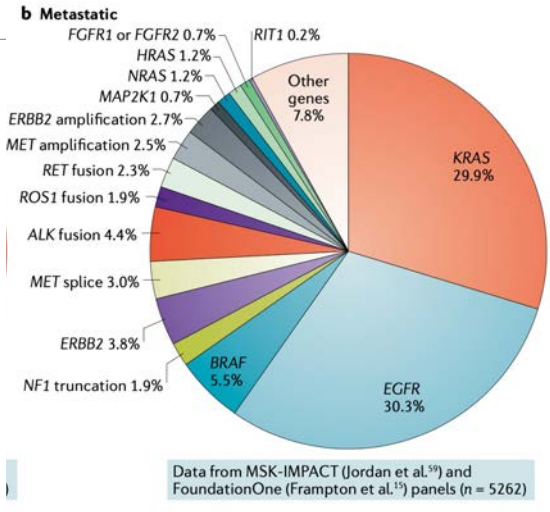
What do we do with somatic tumor testing results?





Skoulidis F, Heymach JV. Co-occurring genomic alterations in non-small-cell lung cancer biology and therapy. *Nat Rev Cancer*. 2019;19(9):495-509.
Image from: https://www.cancer.gov/types/lung/patient/non-small-cell-lung-treatment-pdq

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Biomarker-directed therapy for advanced NSCLC

EGFR Exon 19 deletion/L858R (15%)
- Afatinib
- Erlotinib (+/- VEGF inhibitor)
- Dacomitnib
- Gefitinib
- Osimertinib

ALK rearrangement (2-8%)
- Alectinib
- Brigatinib
- Ceritinib
- Crizotinib
- Lorlatinib

ROS1 rearrangement (1-2%)
- Ceritinib
- Crizotinib
- Entrectinib
- Repotrectinib
- Lorlatinib*

RET rearrangement (1-2%)
- Selpercatinib
- Pralsetinib
- Cabozantinib

MET exon 14 skip (2-4%)
- Capmatinib
- Crizotinib
- Tepotinib

BRAF V600E (1-2.5%)
- Dabrafenib/trametinib
- Encorafenib/binimetinib
- vemurafenib

NTRK 1/2/3 fusion (0.2%)
- Entrectinib
- Larotrectinib

KRAS G12C (13%)
- Sotorasib *
- Adagrasib*

EGFR exon 20 insertion
- Amivantamab*

ERBB2 (HER2) mutation
- Trastuzumab deruxtecan*
- Trastuzumab emtansine*

* Denotes used as second line therapy

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.1.2024.

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Resources to identify biomarker directed therapies

- Disease Specific Guidelines (NCCN)
- Laboratory reports
- FDA Table of Pharmacogenomic Biomarkers in Drug Labeling
- OncoKB
- My Cancer Genome
- Precision Medicine Knowledge Base

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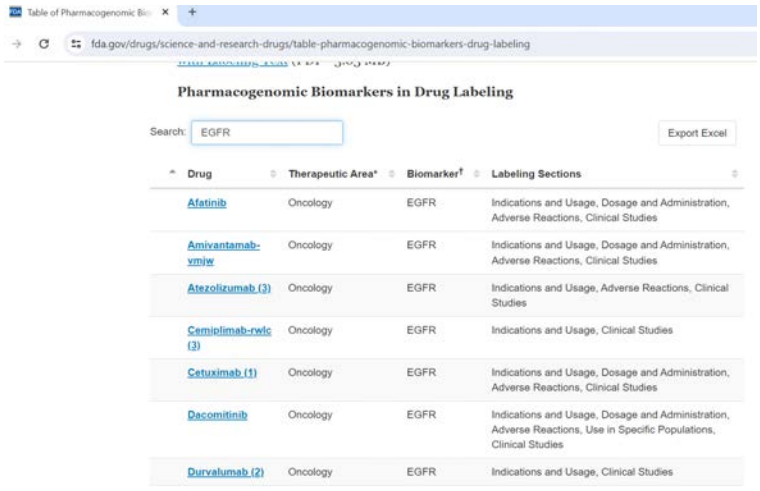

FDA Table of Pharmacogenomic Biomarkers in Drug Labeling

https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling
(So, bookmark it or use your search engine…)

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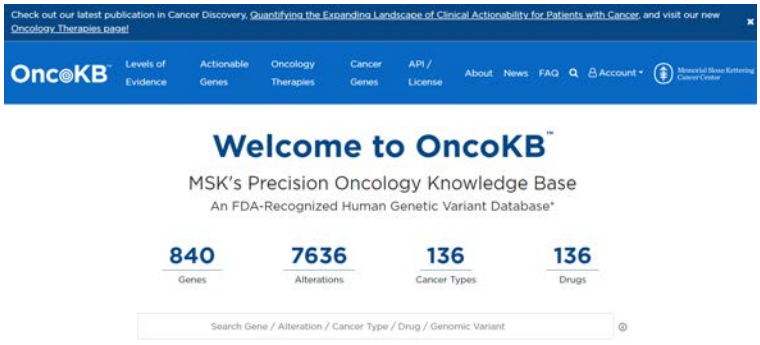

OncoKB

https://www.oncokb.org/

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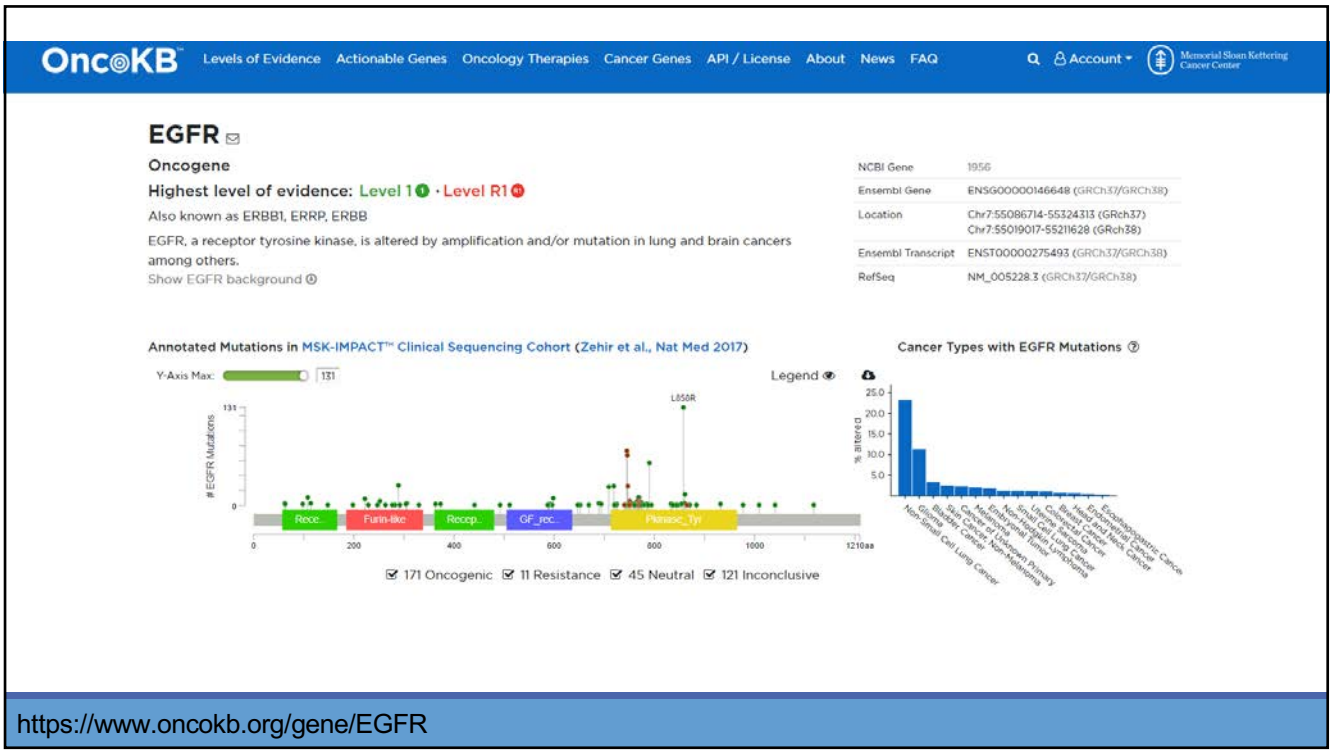
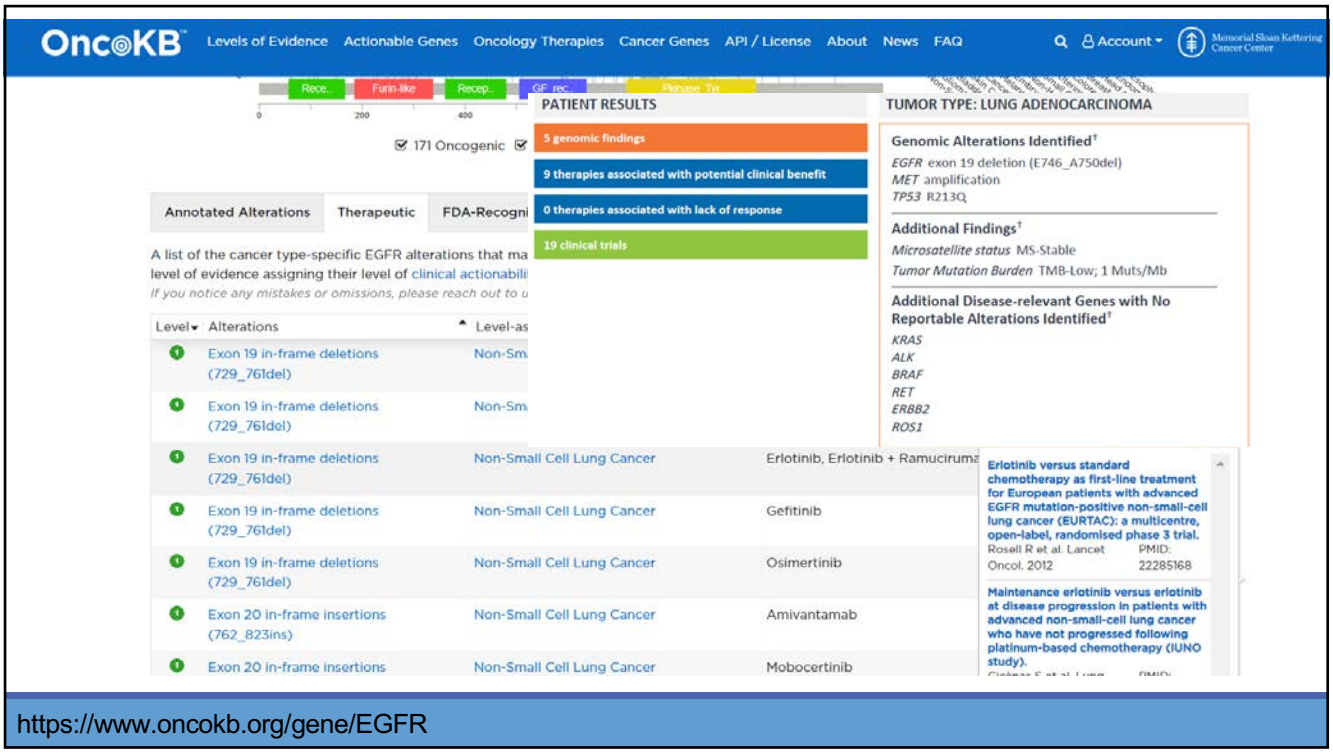


https://www.oncokb.org/gene/EGFR

39



https://www.oncokb.org/gene/EGFR

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First Line Treatments EGFR Mutant NSCLC

EGFR Inhibitor	Dose	Tolerability	Notes
Erlotinib	150 mg PO daily	Acneiform rash, diarrhea	Reversible inhibitor
Gefitinib	250 mg PO daily	LFTs, diarrhea, rash	Reversible inhibitor Re-approved as first line therapy
Afatinib	40 mg PO daily	Higher rates of serious adverse events, diarrhea, stomatitis, treatment related deaths	Irreversible inhibitor Also inhibits HER2
Dacomitinib	45 mg PO daily	Higher rates of serious adverse events, diarrhea, stomatitis, treatment related deaths	Irreversible inhibitor Also inhibits HER2
Osimertinib	80 mg PO daily	Lower rates of diarrhea/rash Pneumonitis, ↓ LVEF	Irreversible inhibitor Active against T790M resistance mutation

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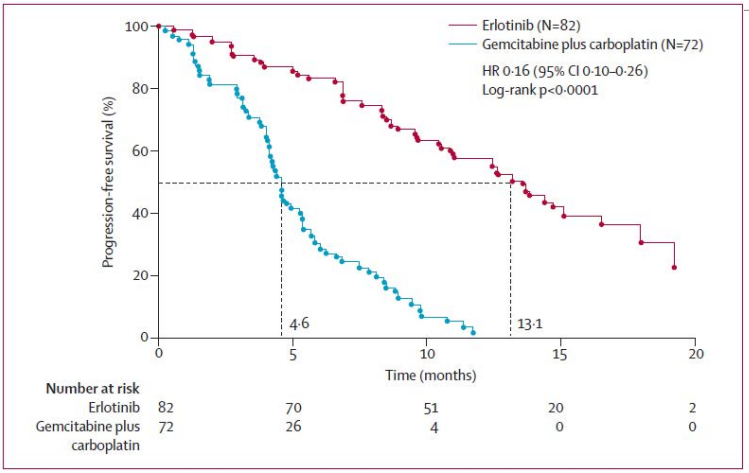
Ugggh…Why are we going through all of this trouble!



Zhou C, Wu YL, Chen G, et al. Erlotinib versus chemotherapy as first-line treatment for patients with advanced EGFR mutation-positive non-small-cell lung cancer (OPTIMAL, CTONG-0802): a multicentre, open-label, randomised, phase 3 study. *Lancet Oncol*. 2011;12(8):735-742.

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Case #2

43

What therapy would you recommend for RG?

Use OncoKB (https://www.oncokb.org) to assist in answering this question and determine if there are any FDA-approved therapies (OncoKB level 1 evidence) specific to her mutation profile

a. Osimertinib
b. Olaparib
c. Capmatinib
d. Crizotinib

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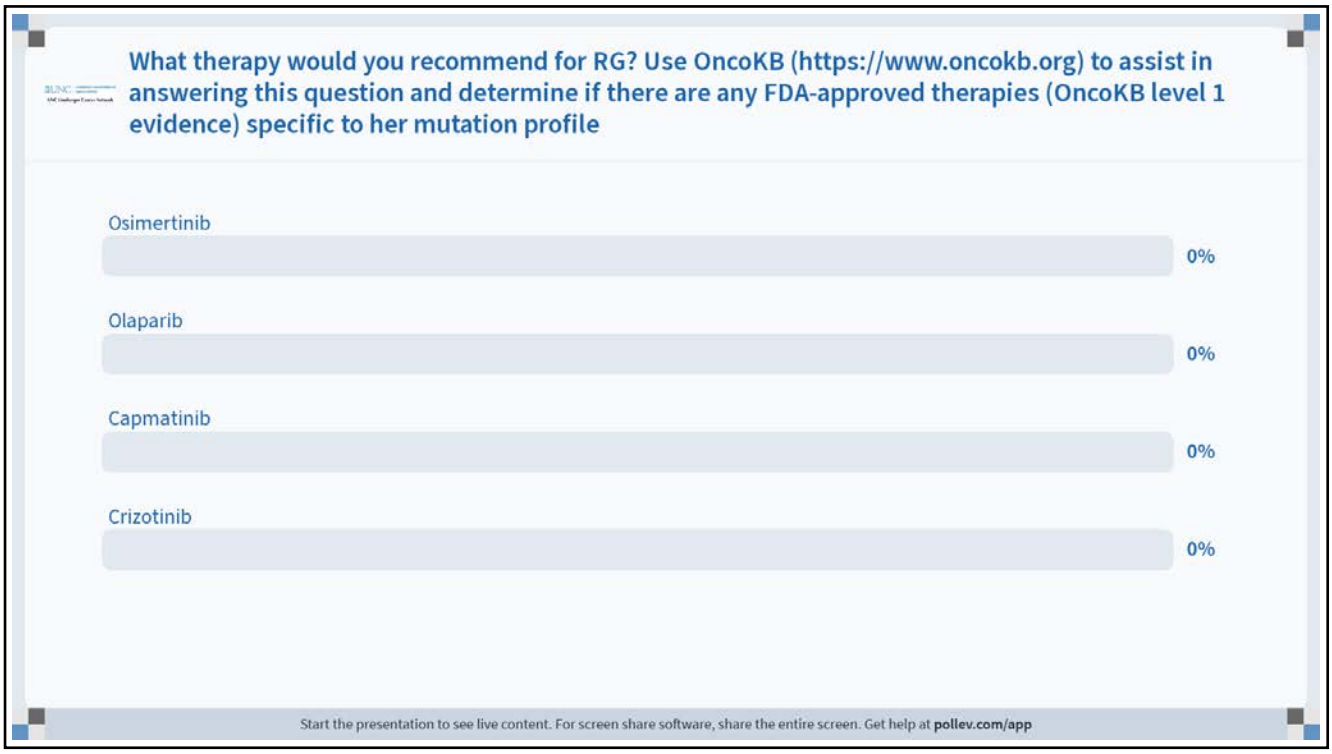
What therapy would you recommend for RG? Use OncoKB (https://www.oncokb.org) to assist in answering this question and determine if there are any FDA-approved therapies (OncoKB level 1 evidence) specific to her mutation profile
Osimertinib
0%
Olaparib
0%
Capmatinib
0%
Crizotinib
0%
Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollev.com/app

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Pharmacogenetics in Oncology:
Germline biomarkers applied to drug dosing

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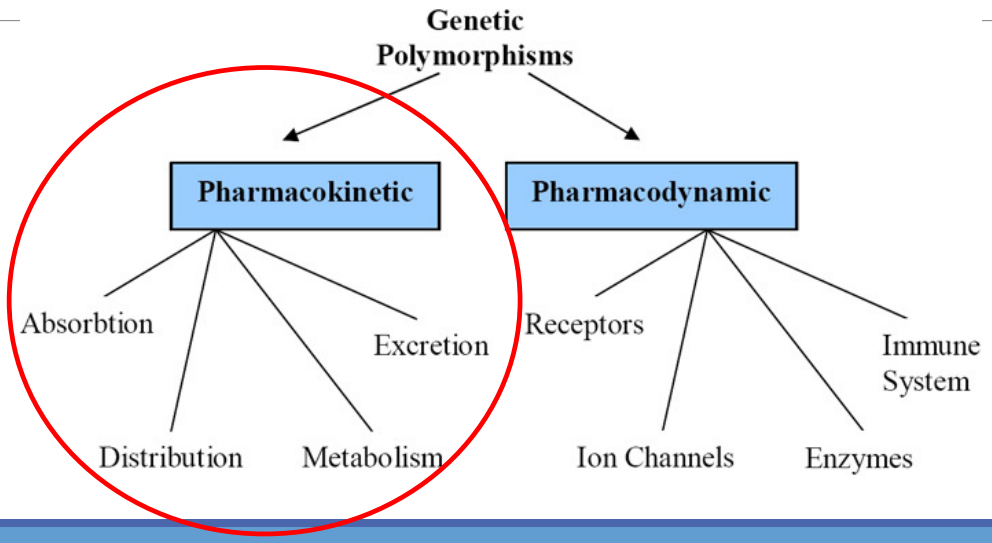
PHARMACOGENETIC BASICS



https://www.nature.com/scitable/topicpage/pharmacogenomics-and-personalized-medicine-643/

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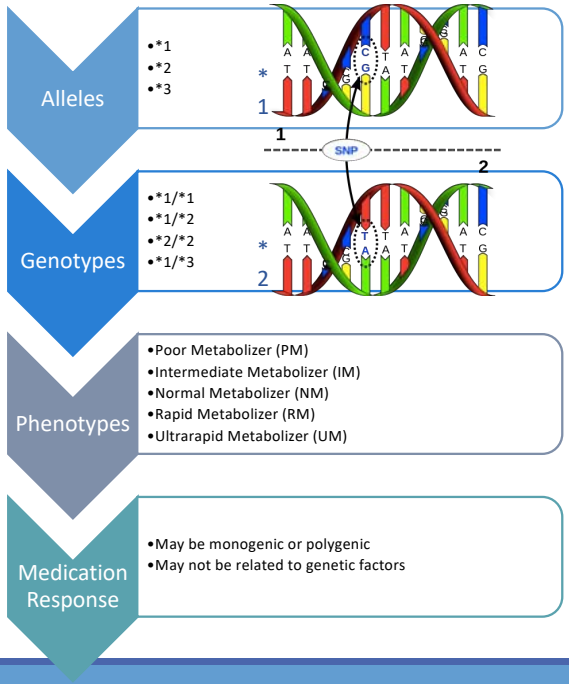
PHARMACOGENETIC BASICS

Allele = a specific genetic sequence at a location in the genome
- Think of as an alternative "spelling" of the gene instructions
- Star nomenclature
- SNP = single nucleotide polymorphism

Genotype = individual's collection of genes
- For each gene, you get one copy from your mom and one copy from your dad

Diplotype = the two "spellings" that a person has for a given gene

Phenotype = individual's observable trait
- The phenotype is predicted by the genetics, but other variables can change it



https://www.genome.gov/genetics-glossary

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Behavioral health	Cardiology	Oncology	Gastroenterology
amitriptyline aripiprazole atomoxetine brexpiprazole citalopram clomipramine desipramine doxepin escitalopram fluvoxamine imipramine mirtazapine nortriptyline paroxetine protriptyline risperidone sertraline trimipramine venlafaxine vortioxetine	clopidogrel hydralazine quinidine simvastatin warfarin	belinostat capecitabine eliglustat fluorouracil irinotecan mercaptopurine tamoxifen thioguanine	dexlansoprazole esomeprazole lansoprazole omeprazole ondansetron pantoprazole rabeprazole
Transplant	**Pain management**	**Infectious disease**	**Neurology**
tacrolimus	celecoxib codeine flurbiprofen ibuprofen meloxicam methadone oxycodone piroxicam tramadol	abacavir atazanavir efavirenz nevirapine voriconazole	phenytoin siponimod pimozide
	Rheumatology	**Ear, eye, nose, throat**	
	azathioprine	dextromethorphan	

And many more…

FDA Table of PGx Associations

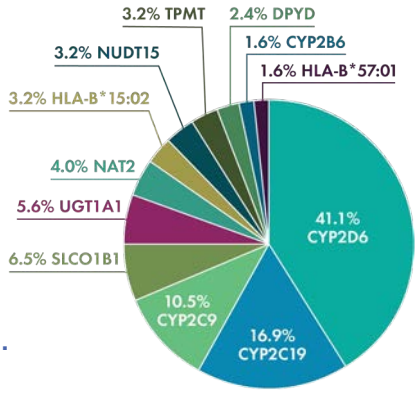

Table of pharmacogenetic associations. U.S. Food and Drug Administration. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

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Case #3

SK is a 55-year-old male with newly diagnosed stage IV colorectal cancer

His oncologist orders a DPYD genotype and finds that SK carries the DPYD *2A allele

You are seeing the patient to initiate cycle 1 of FOLFIRI (5-fluorouracil, leucovorin, irinotecan)

You see the genetic result in the patient's chart, but have no idea why the physician ordered it or what to do with it

50

Case #3 FOLFIRI

Leucovorin

400 mg/m^2 IV on day 1 to match duration of irinotecan infusion

5-Fluorouracil

400 mg/m^2 IV bolus on day 1 followed by 2,400 mg/m^2 IV over 46 hours (as a continuous infusion) started after bolus

Irinotecan

180 mg/m^2 IV over 30-90 minutes on day 1

Leucovorin, 5-Fluorouracil, Irinotecan. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed April 12, 2022.

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About 5-fluorouracil (5FU)

Mechanism of Action

- Inhibits thymidylate synthetase, incorporation into DNA and RNA to block normal biosynthesis

Route of Administration

- Intravenous
- Oral formulation = capecitabine

Most Common Adverse Effects

- Bone marrow suppression (anemia, thrombocytopenia, neutropenia), diarrhea, mucositis, cardiac toxicity

FDA-Labeled Indication

- Colon cancer, gastric cancer, pancreatic cancer, breast cancer

Molecules. 2008 Aug; 13(8): 1551–1569.
Fluorouracil [Package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/012209s040lbl.pdf

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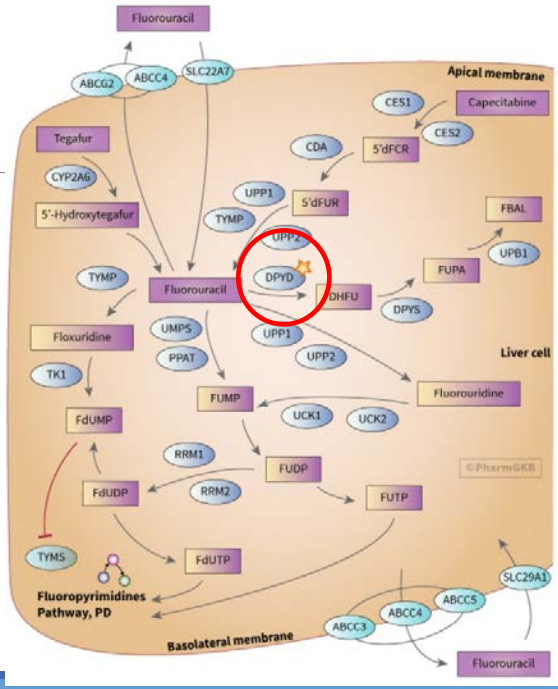
5FU metabolism



https://www.pharmgkb.org/pathway/PA150653776

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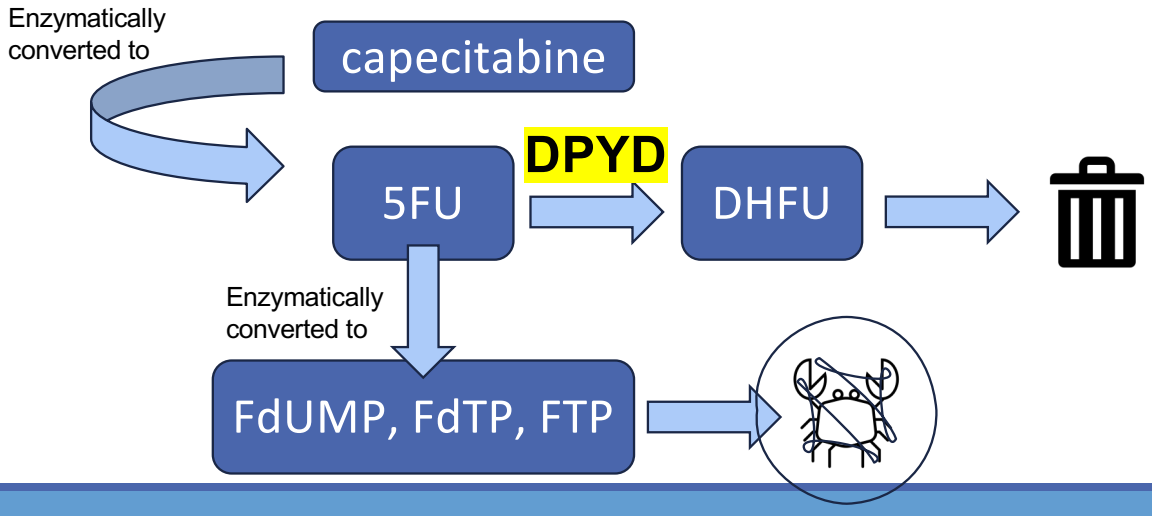
Fluorouracil (5FU) metabolism (Taylor's version)



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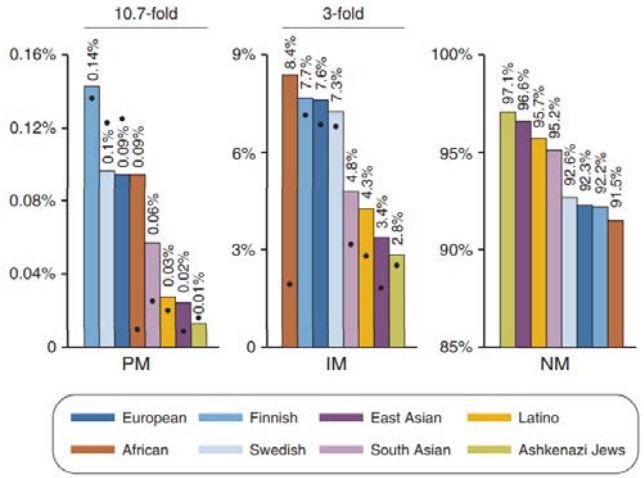
Individual differences in DPYD activity

- Turns out, there is considerable differences in activity of DPYD between individuals
- This activity is linked to the person's genotype for DPYD
- Knowing a genotype, we can predict a phenotype
- The prevalence of DPYD deficiency is rare, but it can cause serious toxicity to 5FU….



Br J Cancer. 2020;123(12):1782-1789.

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Impact of DPYD deficiency on 5FU toxicity

- Depending on the level of DPYD activity, patients treated with standard doses of 5FU had anywhere from a 2-10-fold increase in toxicities, such as myelosuppression and diarrhea
- FATALITIES HAVE BEEN REPORTED IN THOSE WHO LACK ANY DPYD ACTIVITY WHO ARE TREATED WITH NORMAL DOSES OF 5FU

Lancet Oncol. 2015 Dec;16(16):1639-50.;
Pharmacogenomics. 2019 Aug;20(13):931-938.
Cancer Chemother Pharmacol. 2006 Aug;58(2):272-5.

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What should we do?

Clinical Pharmacogenomics Implementation Consortium (CPIC)

- 26 guidelines on drug-gene interactions that require clinical attention
- Tells you "what to do"
- Does NOT tell you who, when, and how to do the genetic testing

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CPIC guidelines: DPYD and 5FU

CPIC UPDATE

Table 2 Recommended dosing of fluoropyrimidines[a] by DPD phenotype

Phenotype	Implications for phenotypic measures	Dosing recommendations	Classification of recommendations[b]
DPYD normal metabolizer	Normal DPD activity and "normal" risk for fluoropyrimidine toxicity.	Based on genotype, there is no indication to change dose or therapy. Use label-recommended dosage and administration.	Strong
DPYD intermediate metabolizer	Decreased DPD activity (leukocyte DPD activity at 30% to 70% that of the normal population) and increased risk for severe or even fatal drug toxicity when treated with fluoropyrimidine drugs.	Reduce starting dose based on activity score followed by titration of dose based on toxicity[c] or therapeutic drug monitoring (if available). **Activity score 1:** Reduce dose by 50% **Activity score 1.5:** Reduce dose by 25% to 50%	**Activity score 1:** Strong **Activity score 1.5:** Moderate
DPYD poor metabolizer	Complete DPD deficiency and increased risk for severe or even fatal drug toxicity when treated with fluoropyrimidine drugs.	**Activity score 0.5:** Avoid use of 5-fluorouracil or 5-fluorouracil prodrug-based regimens. In the event, based on clinical advice, alternative agents are not considered a suitable therapeutic option, 5-fluorouracil should be administered at a strongly reduced dose[d] with early therapeutic drug monitoring.[e] **Activity score 0:** Avoid use of 5-fluorouracil or 5-fluorouracil prodrug-based regimens.	Strong

[a]5-fluorouracil or capecitabine. [b]Rating scheme described in Supplement. [c]Increase the dose in patients experiencing no or clinically tolerable toxicity in the first two cycles to maintain efficacy; decrease the dose in patients who do not tolerate the starting dose to minimize toxicities. [d]If available, a phenotyping test (see main text for further details) should be considered to estimate the starting dose. In the absence of phenotyping data, a dose of <25% of the normal starting dose is estimated assuming additive effects of alleles on 5-FU clearance. [e]Therapeutic drug monitoring should be done at the earliest timepoint possible (e.g., minimum timepoint in steady state) in order to immediately discontinue therapy if the drug level is too high.

Clin Pharmacol Ther. 2018 Feb;103(2):210-216.
https://cpicpgx.org/guidelines/guideline-for-fluoropyrimidines-and-dpyd/

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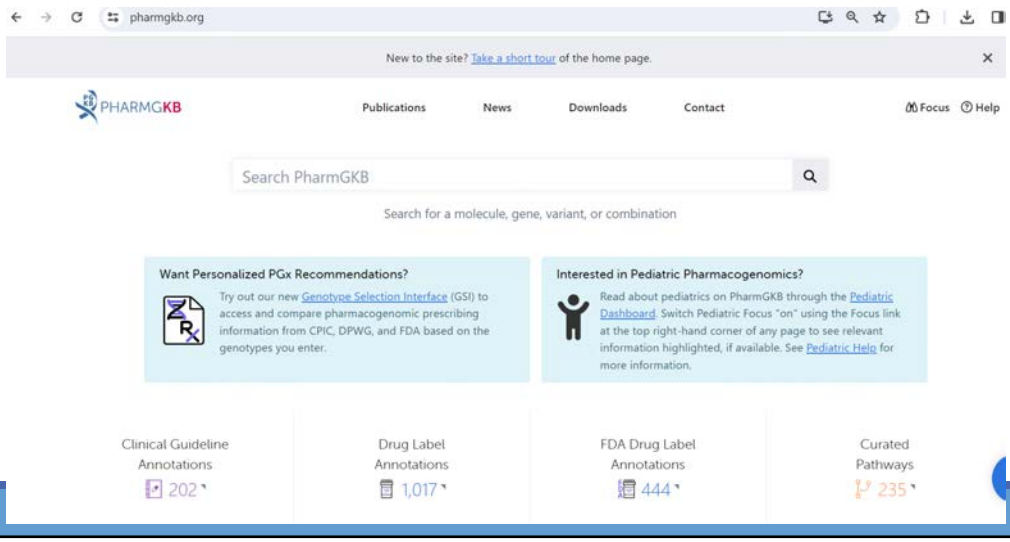
Another resource: PharmGKB



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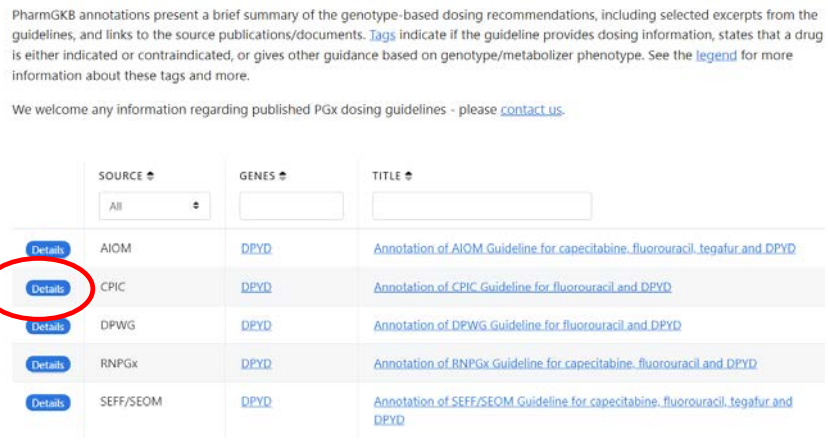
So what should we do?

1. Go to PharmGKB
2. Search for “fluorouracil”
3. Click “Prescribing Info”



https://www.pharmgkb.org/chemical/PA128406956/guidelineAnnotation/PA166122686

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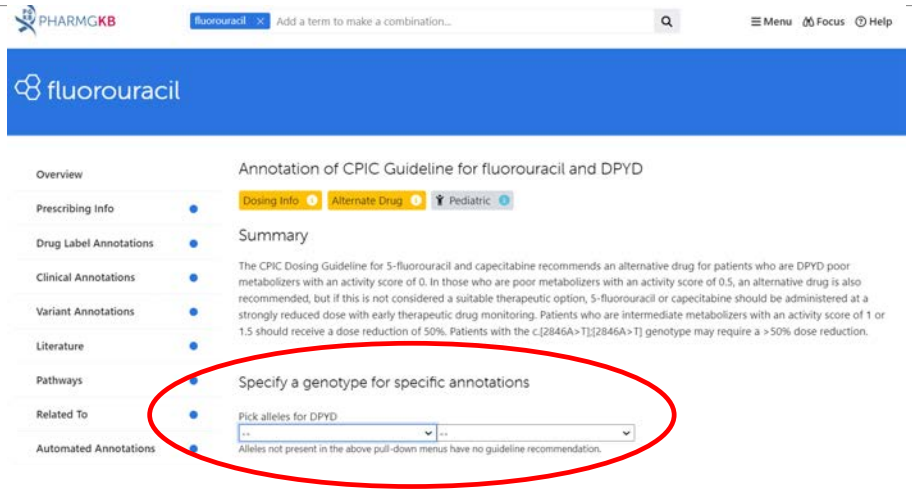
What should we do?



https://www.pharmgkb.org/chemical/PA128406956/guidelineAnnotation/PA166122686

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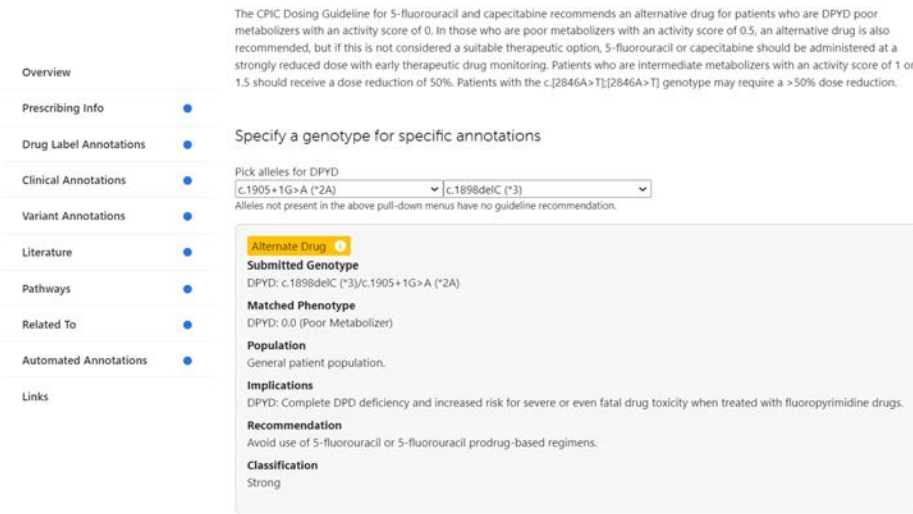
What should we do?



https://www.pharmgkb.org/chemical/PA128406956/guidelineAnnotation/PA166122686

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Dosing of 5FU considering DPYD activity score

Table 1 Nomenclature systems for describing *DPYD* genotype and DPD activity

CPIC activity score	CPIC DPD metabolizer phenotype	Example *DPYD* genotype	Approximate DPD activity	Diplotype	DPD deficiency classification	CPIC recommended starting dose
2.0	Normal metabolizer	*1/*1	100%	Homozygous wildtype	DPD sufficient	Label-recommended dose
1.5	Intermediate metabolizer	*1/p.D949V	75%	Heterozygous variant	Partial DPD deficiency	Reduce dose by 50%
1.0	Intermediate metabolizer	*1/*2A or p.D949V/p.D949V or p.D949V/HapB3	50%	Heterozygous or homozygous variant or compound heterozygous	Partial DPD deficiency	Reduce dose by 50%
0.5	Poor metabolizer	*2A/p.D949V	25%	Compound heterozygous	Partial DPD deficiency[a]	Avoid use or strongly reduce dose (by >75%)
0.0	Poor metabolizer	*2A/*2A or *2A/*13	0%	Homozygous variant or compound heterozygous	Complete DPD deficiency	Avoid use

Activity score is calculated by adding the activity score of the two alleles.
[a]The FDA's definition of "certain compound heterozygous mutations in the DPD gene that results in complete or near complete absence of DPD activity" suggest their recommendations to avoid FP in patients with complete absence of DPD activity also applies to this subgroup.
CPIC, Clinical Pharmacogenetics Implementation Consortium; DPD, dihydropyrimidine dehydrogenase.

Clin Pharmacol Ther. 2023 Oct;114(4):768-779.

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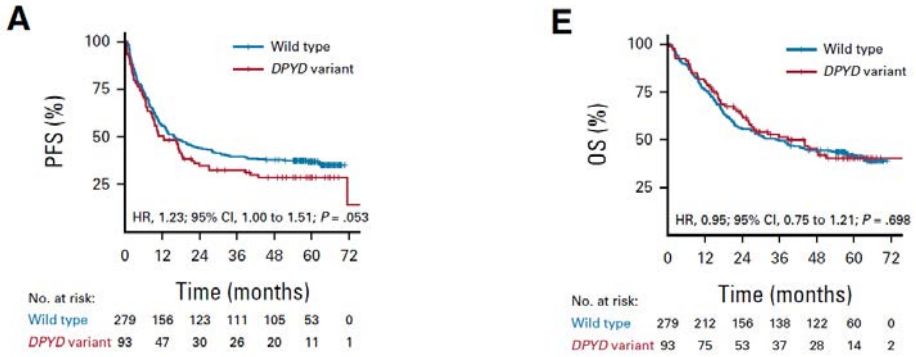
Do dose reductions compromise survival?

Comparison of patients who received dose-reduced 5FU based on the presence of DPYD variants (n=93) to matched controls who received full dose 5FU (n=279)



J Clin Oncol. 2023;41(35):5411-5421.

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But what do the "big guys" say?

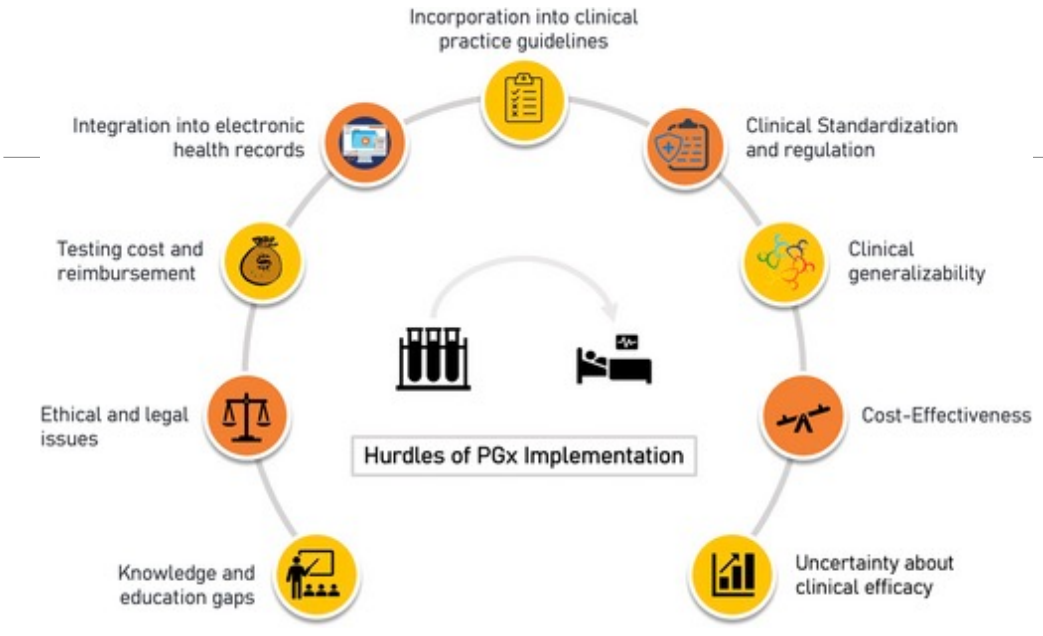
- DPYD testing is recommended in European guidelines, but not yet by American groups

---------- **WARNINGS AND PRECAUTIONS** ----------

- **Increased Risk of Serious or Fatal Adverse Reactions in Patients with Low or Absent Dipyrimidine Dehydrogenase Activity:** Withhold or permanently discontinue fluorouracil in patients with evidence of acute early-onset or unusually severe toxicity, which may indicate near complete or total absence of dipyrimidine dehydrogenase (DPD) activity. No fluorouracil dose has been proven safe in patients with absent DPD activity. (5.1)

Clin Pharmacol Ther. 2023 Oct;114(4):768-779

65



Psychiatry Clin. Neurosci. Rep. 2022;1:e26.

66

Is that all the genetic testing you need?

Genes & Drugs (CPIC Level A)

CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A5	CYP4F2	DPYD
• Efavirenz	• Celecoxib • Fluvastatin • Fosphenytoin • Ibuprofen • Meloxicam • Phenytoin • Piroxicam • Siponimod • Warfarin	• Amitriptyline • **Citalopram** • Clopidogrel • **Escitalopram** • Lansoprazole • Omeprazole • Pantoprazole • Sertraline • Voriconazole	• Atomoxetine • Codeine • Nortriptyline • **Ondansetron** • Paroxetine • Pitolisant • Tamoxifen • **Tramadol** • Vortioxetine	• Tacrolimus	• Warfarin	• **Fluorouracil** • **Capecitabine**

HLA-A	HLA-B	NUDT15	SLCO1B1	TPMT	UGT1A1	VKORC1
• Carbamazepine	• Abacavir • Allopurinol • Carbamazepine • Fosphenytoin • Oxcarbazepine • Phenytoin	• Azathioprine • Mercaptopurine • Thioguanine	• Atorvastatin • Fluvastatin • Lovastatin • Pitavastatin • Pravastatin • Rosuvastatin • Simvastatin	• Azathioprine • Mercaptopurine • Thioguanine	• Atazanavir • **Irinotecan**	• Warfarin

https://cpicpgx.org/genes-drugs/

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Case #4

TR is a 10-year-old African American female diagnosed with acute lymphoblastic leukemia (ALL)

She presents for a follow-up visit for monitoring of mercaptopurine (6-MP), which she is prescribed at a dose of **7.5 mg/m² three times per week**

You notice that the usual dose for 6-MP is **75 mg/m² daily**

Her organ function is completely normal, and her CBC is within normal limits to continue the drug

Could this dosing be a mistake? Could there be a pharmacogenetic "force" at work here?

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Case #4 Question

Which of the following is the reason for a **10-fold dose reduction** of mercaptopurine for ST?

Use PharmGKB (https://www.pharmgkb.org/) to assist in answering this question

a. She is a UGT1A1 poor metabolizer (UGT1A1 *28/*28)
b. She is a NUDT15 intermediate metabolizer (NUDT15 *1/*2)
c. She is a TPMT poor metabolizer (TPMT *3A/*3A)
d. She is a child, and thus metabolizes mercaptopurine different than adults

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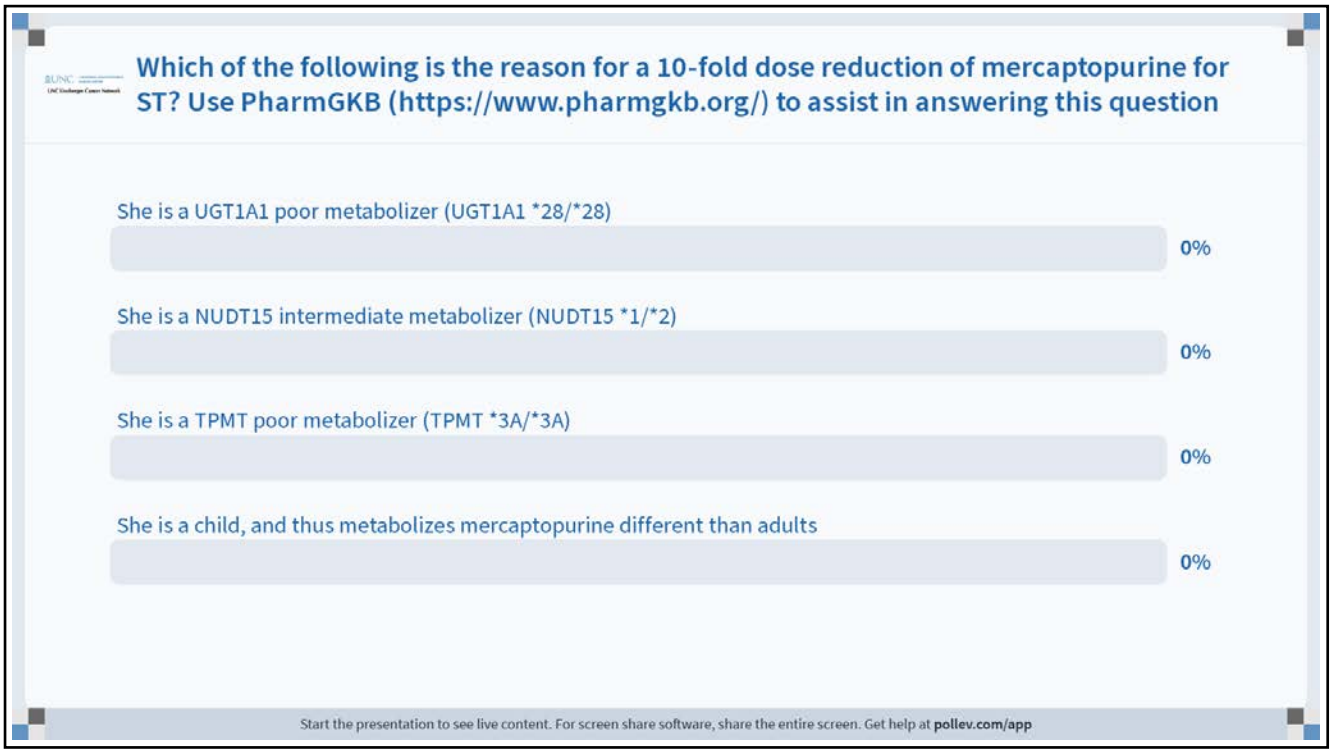

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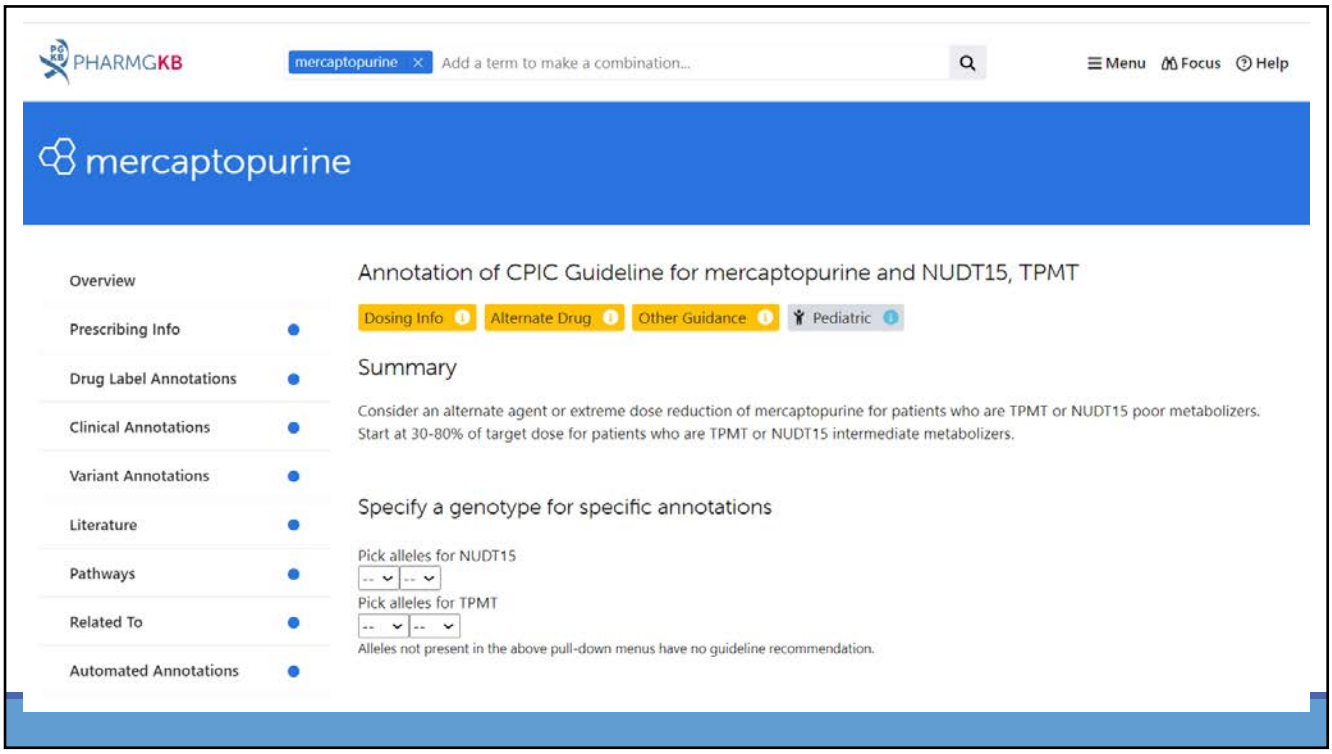

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Workflow solutions: Clinical Decision Support

Would you rather….

1. Look all this mess up yourself and try to figure out how to understand it

OR

2. Have a warning pop up when your patient is at risk of a drug-gene interaction?

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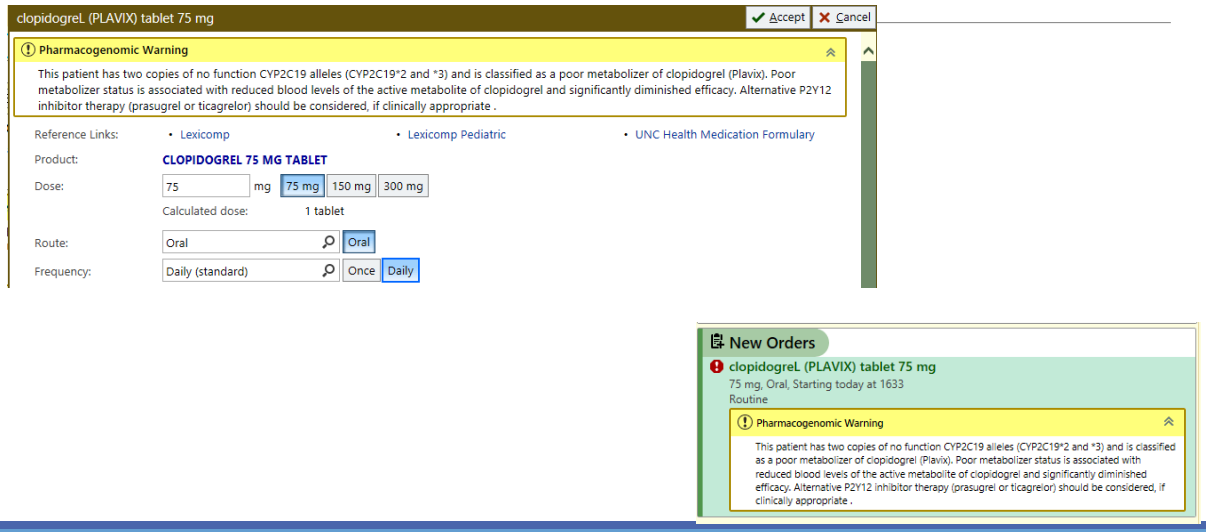
Clinical decision support



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Workflow solutions: Multigene testing

Would you rather…

1. Test for each individual pharmacogene when needed (and wait for the results to return before placing an order)

OR

2. Test for multiple important pharmacogenes at once, so that you have the results on hand when needing to prescribe drugs with pharmacogenetic interactions

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Who is doing multigene testing?

St. Jude

University of Florida

Vanderbilt

NorthShore

Duke

Levine

VA

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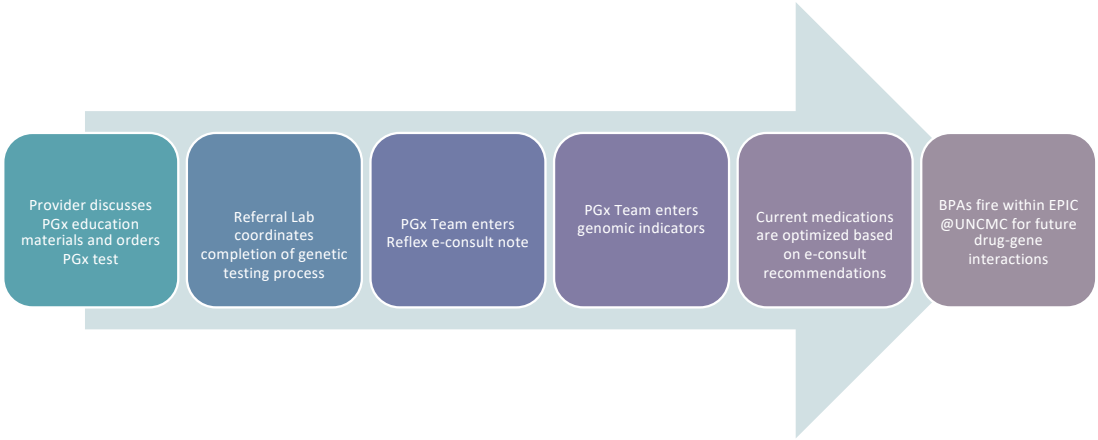
Multigene testing pilot in GI oncology at UNC Health



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Summary

- Targeted therapies used in oncology often require a biomarker test to determine treatment eligibility
- Large somatic tumor sequencing panels are becoming the gold standard in oncology, so your ability to understand the information is crucial to choosing the best treatment
  - RESOURCE: https://www.oncokb.org/
- Germline genetics can impact how a patient responds to treatment due to differences in drug metabolizing enzymes or pharmacodynamic markers
  - RESOURCE: https://www.pharmgkb.org/

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Questions/Comments?

Nobody has responded yet.

Hang tight! Responses are coming in.

Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

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Extra slides (for questions)

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Oncology Specific Resources	Germline Pharmacogenetics Resources
OncoKB	CPIC
My Cancer Genome	PharmGKB
Precision Medicine Knowledge Base	FDA Table of Pharmacogenetic Associations

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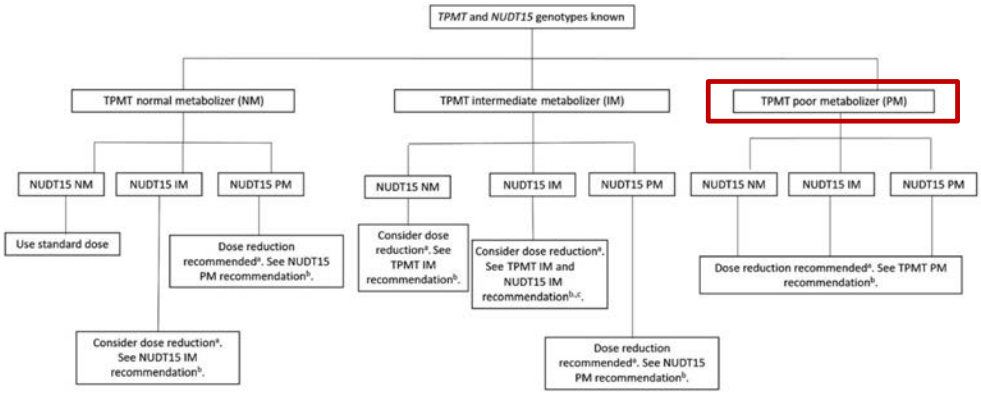
6-Mercaptopurine Dosing



Relling MV, Schwab M, Whirl-Carrillo M, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update. *Clin Pharmacol Ther*. 2019;105(5):1095-1105.

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	Mercaptopurine	
Phenotype	**Implications for mercaptopurine and azathioprine phenotypic measures**	**Dosing recommendations for mercaptopurine**
TPMT poor metabolizer	Extremely high concentrations of TGN metabolites; fatal toxicity possible without dose decrease; no MeTIMP metabolites. Greatly increased risk of thiopurine-related leukopenia, neutropenia, myelosuppression.	For malignancy, start with drastically reduced doses (reduce daily dose[a] by 10-fold and reduce frequency to thrice weekly instead of daily (e.g., 10 mg/m^2/day given just 3 days/week) and adjust doses of mercaptopurine based on degree of myelosuppression and disease-specific guidelines. Allow 4–6 weeks to reach steady-state after each dose adjustment. If myelosuppression occurs, emphasis should be on reducing mercaptopurine over other agents. For nonmalignant conditions, consider alternative nonthiopurine immunosuppressant therapy.[4,26,30,38]

Relling MV, Schwab M, Whirl-Carrillo M, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update. *Clin Pharmacol Ther*. 2019;105(5):1095-1105.

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Thank You . . .

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The Telehealth Team

Tim Poe – Director

Veneranda Obure – Technology Support Specialist

Andrew Dodgson, DPT – Continuing Education Specialist

Jon Powell, PhD – Continuing Education Specialist

Patrick Muscarella – Technology Support Technician

Oliver Marth – Technology Support Technician

Lindsey Reich, MA – Public Communication Specialist

Barbara Walsh, DNP, MPH, MSN, RN – Nurse Planner

The song ***Back Rhodes*** written and performed by **Don Poe**

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Upcoming Live Webinars

learn.unclcn.org

RESEARCH TO PRACTICE Live Webinar

February 28
12:00 PM

Immune (check point) Related Adverse Events
Frances Collichio, MD

PATIENT CENTERED CARE Live Webinar

March 13
12:00 PM

Oncologic Emergencies
Jake Stein, MD, MPH

ADVANCED PRACTICE PROVIDER Live Webinar

March 20
4:00 PM

Physical Therapy Approaches to Oncology Care: Beyond Lymphedema
Sarah Richardson, PT, DPT, CLT, WCS

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Self-Paced, Online Courses

learn.unclcn.org/spoc

RESEARCH TO PRACTICE Self-Paced, Online Course

Update on Prostate Cancer Screening
Marc Bjurlin, DO, MSc, FACOS

RESEARCH TO PRACTICE Self-Paced, Online Course

Genitourinary Cancer Management in North Carolina: Updates for 2023
Hung-Jui (Ray) Tan, MD, MSHPM

PATIENT CENTERED CARE Self-Paced, Online Course

Next Generation Cancer Care Navigation
William A. Wood, MD, MPH

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