

Optimizing Chemotherapy with

**PGx
Oncology**

Using NGS



Employing the genetic information to guide chemotherapy

- Reduces events of drug-toxicity
- Maximises the efficacy of chemotherapeutic regimen
- Provides specific drug dosing recommendations, based on guidelines
 - CPIC (Clinical Pharmacogenetics Implementation Consortium)
 - NCCN (National Comprehensive Cancer Network)
 - DPWG (Dutch Pharmacogenetics Working Group)

Why OncoPGx is required?



>21% of hospitalization to an oncology service are Adverse Drug Reaction (ADR)-related⁽¹⁾



60% ADRs may be preventable⁽¹⁾



Improved prescription of supportive care medication⁽²⁾

Who should get tested?

CANCER PATIENTS

- Likely to be enrolled for / on chemotherapy
- With history of adverse reactions to cancer medications
- With a family history of medication sensitivity
- With other comorbidities like diabetes or cardiovascular disease






Report highlights

Drugs to be 'avoided',
Drugs to be 'used with caution' & Drugs to be 'used as directed'

The genetic variants that impact the drugs

The dosing recommendations based on guidelines: CPIC, NCCN, DPWG

Medications covered by OncoPGx panel

Drug Class	Genes
 Oncology Fluoropyrimidines, Thiopurines, Irinotecan, Tamoxifen	DPYD, NUDT15, RYR1, TPMT, UGT1A1, G6PD, CACNA1S, CYP2C9, CYP2D6, CYP3A5
 Pain Management Nonsteroidal Anti-inflammatory Drugs (NSAIDs), Opioids, Analgesics	
 Gastroenterology Proton-Pump Inhibitors (PPIs)	
 Immunology Immunosuppressants	
 Others Antinauseants, Anesthetics	

Relevance of pharmacogenomics

Drug	Gene	Impact
Thiopurines	TPMT, NUDT15	Loss-of-function variations can cause higher risk of toxicity and life-threatening myelosuppression with conventional dose of thiopurines like azathiopurine/ mercaptopurine/ thioguanine. ⁽³⁾
Fluoropyrimidines	DPYD	Patients with variants can experience significant toxicity when treated with fluoropyrimidines (e.g., 5-FU, capecitabine). ⁽⁴⁾
Tamoxifen	CYP2D6	Loss-of-function variations can produce lower levels of endoxifen thus less inhibition of cancer cell growth. ⁽⁵⁾
Irinotecan	UGT1A1	Dosing of drugs like irinotecan can be tailored based on UGT1A1 genotype to reduce the risk of neutropenia. ⁽⁶⁾
Opioids	CYP2C9, CYP2D6	Can influence palliative care depending on how a patient metabolizes opioids like codeine, tramadol, and morphine. ⁽⁷⁾

Benefits of OncoPGx



Optimizes
chemotherapeutic
regimes



Aids in informed
clinical decision on
chemotherapeutic
regimens



Reduces trial
and error of
medications



Assess risk for drug
selection and dose
adjustments



Reduces drug
toxicity and
adverse effects



Optimizes pain
management along
with chemotherapy



Improves
supportive care



Improves quality
of life

References

1. Lavan HA et al. Adverse Drug Reactions in an Oncological Population: Prevalence, Predictability, and Preventability. *Oncologist*. 2019; doi:10.1634/theoncologist.2018-0476
2. Jai N et al., Pharmacogenomics-guided supportive oncology: A tale of two trials . *Contemporary Clinical Trials*, 2021; doi:10.1016/j.cct.2021.106391
3. Pratt V et al. *TPMT* and *NUDT15* Genotyping Recommendations: A Joint Consensus Recommendation of the Association for Molecular Pathology, 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, and Pharmacogenomics Knowledgebase. *Journal of Molecular Diagnostics*. 2022; 24(10): 1051-1063. <https://doi.org/10.1016/j.jmoldx.2022.06.007>.
4. Sharma BB et al. Pathogenic *DPYD* Variants and Treatment-Related Mortality in Patients Receiving Fluoropyrimidine Chemotherapy: A Systematic Review and Meta-Analysis. *Oncologist*. 2021; 26(12):1008-1016. doi: 10.1002/onco.1396
5. Mulder TAM et al. Clinical *CYP2D6* Genotyping to Personalize Adjuvant Tamoxifen Treatment in ER-Positive Breast Cancer Patients: Current Status of a Controversy. *Cancers(Basel)*. 2021; 13(4):771. doi: 10.3390/cancers13040771
6. Hulshof EC et al. *UGT1A1* genotype-guided dosing of irinotecan: A prospective safety and cost analysis in poor metaboliser patients. *European Journal of Cancer*. 2022; 162: 148 – 157. <https://doi.org/10.1016/j.ejca.2021.12.009>
7. Patel JN et al. Pharmacogenetic (PGx) guided cancer pain management in an oncology palliative medicine (PM) clinic. *Journal of Clinical Oncology*. 2019; 37(31) suppl. https://doi.org/10.1200/JCO.2019.37.31_suppl.117
8. <https://cpicpgx.org/guidelines/>
9. <https://www.knmp.nl/dossiers/farmacogenetica>
10. <https://www.nccn.org/guidelines>