Pharmacogenetic Stratification:
Prevent Adverse Drug Reactions and identify the Most Effective Drug

Pharmacogenetics (PGx), the relationship between genetic variation and inter-individual variability in drug response, has the potential to personalize medications to the genetic make-up of an individual.

PGx-guided dosing is becoming the standard of care in oncology and is gaining acceptance for characterizing therapeutic efficacy and preventing adverse drug reactions (ADR) for many medications.

Regulatory bodies like the US FDA and professional societies, the Clinical Pharmacogenetic Implementation Consortium (CPIC) and the Dutch Pharmacogenetic Working Group (DPWG) publish guidelines on gene variations and drug response, emphasizing clinical relevance and applicability, enabling translation of genetic test results into actionable prescribing decisions for specific drugs.

A recent investigation into ADR-related hospitalization concluded that 30% of ADRs at admission were caused by at least one drug with PGx guidelines, suggesting many ADRs may have been predicted by PGx testing[1].

Decision modeling to evaluate cost-effectiveness of a one-time PGx test to prevent ADRs over a patient's lifetime indicated:
For every 1000 40-year olds tested, PGx can prevent 95 projected ADR-related emergency department/outpatient clinic visits, 6 projected ADR-related hospitalizations and 3 projected ADR-related deaths over a lifetime[2].

Consequently, PGx results should ideally be available preemptively prior to prescribing decisions involving high-risk drugs with PGx guidelines, consistent with the vision that a patient's genetic variation be considered an inherent patient characteristic[3], as are age, weight, renal function, and allergy status.

CODEINE - Ultrarapid ***CYP2D6*** Metabolizer can suffer life threatening respiratory depression
CLOPIDOGREL - Poor ***CYP2C19*** Metabolizers have impaired ability to activate the medication, reducing therapeutic efficacy
WARFARIN - variations in ***CYP2C9*** and ***VKORC1*** affect dosage for therapeutic INR range
SSRI'S, SNRI'S - PGx-guided dosing helped identify medications with tolerable side effects specially in patients who had failed multiple previous treatments
PPI'S - Rapid ***CYP2C19*** Metabolizers have reduced plasma concentration of the drug reflecting reduced therapeutic efficacy
ABACAVIR, CARBAMAZEPINE, ALLOPURINOL - prospective genotyping for ***HLA*** variants can prevent hypersensitivity and adverse reactions
FLUOROURACIL - prospective genotyping for reduced ***DPYD*** function resulted in lower incidences of severe toxicities, 73% in historic controls vs. 28% in genotype-guided cohort

1. Chan SL et al., *Br J Clin Pharmacol* (2016) 82:1636–1646
2. Alagoz O et al., *Pharmacogenomics* (2016) 16:129-36
3. Hamburg MA, Collins FS, *N Engl J Med* (2010) 363:301–4