

Precision Medicine Guided Treatment for Cancer Pain

Effect of CYP2D6 Genotype on Opioid Response:

- Cytochrome P450 2D6 (CYP2D6) is a drug-metabolizing enzyme expressed primarily in the liver.
- CYP2D6-mediated opioids (oxycodone, tramadol, hydrocodone, codeine) are converted to more potent active metabolites by the CYP2D6 enzyme.
 - CYP2D6 metabolizes about 10% of oxycodone into the more potent compound, oxymorphone.
 - CYP2D6 UMs make MORE oxymorphone (may have increased risk of toxicity).
 - CYP2D6 IMs and PMs make LESS oxymorphone (may have decreased efficacy).

How to Interpret CYP2D6 Test Results:

Phenotype	Population Prevalence	Genotype	Enzyme Activity
Poor Metabolizer (PM)	~5-10%	No functional alleles present	Absent
Intermediate Metabolizer (IM)	~2-11%	1 reduced-function AND 1 nonfunctional allele.	Decreased
Extensive/Normal Metabolizer (EM)	~77-92%	2 alleles with full or reduced function OR 1 fully functioning allele AND 1 nonfunctional or reduced-function allele.	Normal
Ultra-Rapid Metabolizer (UM)	~1-2%	> 2 functional alleles	Increased

Source: Crews KR et al. *Clinical pharmacogenetics implementation consortium guidelines for cytochrome P4502D6 genotype and codeine therapy: 2014 update.* Clin Pharmacol Ther. 2014;95(4):376-82.

- A patient's CYP2D6 lab report will reflect the information in this table. For example, it may read as "CYP2D6 *1/*1 (extensive metabolizer phenotype); normal CYP2D6 enzyme activity."

How to Convert from One Opioid to Another

1. Determine the amount of current opioid(s) patient has taken in a 24-hr period that effectively controlled pain. If uncontrolled, use amount taken in past 24-hr period.
2. Calculate "Opioid Equivalent Doses" using table (on right).
3. If pain was effectively **controlled** on current opioid, reduce the new opioid daily dose by 25-50% for cross tolerance.
4. If pain was **uncontrolled** on the current opioid, use 100-125% of the equianalgesic dose.
5. Divide the calculated daily dose of new opioid by the number of doses per day to determine the individual dose

Opioid Equivalent Doses	
Opioid	Oral Dose
Oxycodone	15 mg
Morphine	30 mg
Hydromorphone	7.5 mg
Oxymorphone	10 mg

Source: National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp