

TheraGuide 5-FU™

TheraGuide 5-FU™ is the first and only comprehensive test for predisposition for 5-FU toxicity caused by variations in the *DPYD* and *TYMS* genes. It employs full sequencing of the *DPYD* gene and analysis of the *TYMS* gene.

1 in 4 individuals

carry variations in either the *DPYD* or *TYMS* genes that will increase their risk of dose-limiting toxicity.



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Testing for 5-FU Toxicity: *DPYD*

As many as 1 in 3 patients receiving 5-FU related therapy experience dose limiting, and sometimes life-threatening, toxicity that is largely avoidable. Variations in the *DPYD* and *TYMS* genes are associated with up to a 60% risk of severe to life-threatening toxicity to 5-FU or capecitabine. Identification of toxicity risk prior to administering treatment can help physicians provide enhanced therapeutic choices for improved patient outcomes. The following paper investigates the value of pretreatment *DPYD* analysis and its role in clinical practice.

Morel, A. Clinical relevance of different dihydropyrimidine dehydrogenase gene single nucleotide polymorphisms on 5-fluorouracil tolerance. *Mol Cancer Ther* 2006. 5(11): 289-291.

Purpose: To investigate the value of pretherapeutic detection of *DPYD* variants in patients receiving 5-FU-based treatment.

Design and Methods: 487 cancer patients treated with 5-FU were tested for 22 distinct *DPYD* variants. Careful biologic and clinical follow-up was performed. The variants were evaluated for their respective incidence, association with severe or life-threatening toxicity, and effect on clinical management.

Results: Five separate variants were identified in 187 patients. Three of these variants (IVS14+1 G>A, D949V, and I560S) were associated with grade 3 or 4 toxicity at a higher frequency than a cohort of unselected patients (see table below).

<i>DPYD</i> variant	Grade 3 or 4 Toxicity
IVS14+1 G>A, D949V, and I560S	13/21 (62%)
Unselected	44/487 (9%)

Bottom Line: "Pretreatment detection [of *DPYD* variants] could help to avoid severe toxic side effects. This approach is suitable for clinical practice and should be compared or combined with pharmacologic approaches." Full sequence analysis of *DPYD* would likely increase the sensitivity of testing over rates reported here.



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