Fluorouracil and Capecitabine Dosing Based on *DPYD* Activity Score (DPYD-AS)

Predicted Activity Score	Genotype	Likely *DPYD* Phenotype	Dosing for Fluorouracil and Capecitabine
0	Homozygous (or compound heterozygous) for a non-functional variant	Poor metabolizer	Do not use
0.5	One non-functional PLUS one reduced function variant		Use not recommended If no alternative option, reduce dose by at least 75% PLUS early therapeutic drug monitoring
1.0	Heterozygous for a non-functional variant	Intermediate metabolizer	Reduce dose by 50% Titrate future dose based on clinical judgement†
	Homozygous for a reduced function variant*		
	Compound heterozygous for two reduced function variants		
1.5	Heterozygous for a reduced function variant		
2.0	Variant negative	Normal metabolizer	No dose reduction

*Case reports from patients who are homozygous for c.2846A>T indicate that a dose reduction of more than 50% in the starting dose may be required in some carriers of this genotype.

†Only consider escalating dose if no toxicity in cycle 1 and 2. Increase by a maximum of 10% per cycle.

References

1. Amstutz U, Henricks LM, Offer SM, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing: 2017 Update. Clin Pharmacol Ther 2018;103(2):210-6.
2. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for diphydropyrimidine dehydrogenase genotype and fluropyrimidine dosing: November 2018 update. Available at: https://cpicpgx.org/guidelines/guideline-for-fluoropyrimidines-and-dpyd/