Table 1: The key loss of function *DPYD* gene variants that should be assessed in patients prior to treatment.

Common name	Nucleotide variant, amino acid change, ID number		Enzyme activity (relative to normal)	[b]Minor allele frequency (global)	Recommended dosage adjustment for heterozygote carriers (partial deficiency[c])
***2A**	c.1905+1G>A **exon 14 skipping** rs3918290	**Non-functional** protein missing aa residues 581-635.	None	0.0043	50%
***13**	c.1679T>G **I560S** rs55886062	Missense mutation affects the cofactor binding and **substantially decreases activity.**	None	0.0006	50%
***9B**	c.2846 A>T **D949V** rs67376798	SNP affects the electron transfer mechanism, which is key for activity. **Low function protein.**	Decreased	0.0052	>25%
Hap-B3[a]	c.1129-5923C>G **Intronic** rs75017182	Intronic variant which affects pre-mRNA splicing. Truncated **non-functional protein.**	Decreased	0.0048	>25%

[a]The haplotype includes c.1236G>A & c.483+18G>A (rs56038477 & rs56276561, with MAF=0.0181 & 0.0153 respectively). [b]Little is known about the minor allele frequency of these variants in people of Māori or Pacific Island ancestry. Individuals of East Asian ancestry have very low prevalence of HapB3 (MAF>0.0000) and *2A (MAF=0.0000) compared with Europeans or South Asians (MAF=0.000 and 0.0034, respectively). There is an additional loss of function variant observed in people of African ancestry (rs115232898, Y186C, with MAF=0.0183). [c]Dosages should not be increased to standard dosage at subsequent cycles based on treatment tolerance. 5-FU and capecitabine use is *contraindicated* in individuals who are homozygous loss of function variant for these alleles (complete deficiency). However, recent studies have demonstrated that extremely low doses (<1% of a standard dose) achieve suitable therapeutic 5-FU plasma concentrations and are safe.[18] Individuals who are compound heterozygote (carrier of more than one of these variant alleles) should be considered as having a complete enzyme deficiency.