Supplementary Table 5. SNP covariable analysis on pemetrexed clearance in the full model using stepwise forward inclusion

Factor	Compared genotypes	OFV	ΔOFV*
Ordinal	**Structural base model + eGFR on CL and BSA on Vc**	**-743.8**	
SLC19A1	Mut/Mut vs Mut/WT vs WT/WT	-745.3	-1.6
GGH	Mut/Mut vs Mut/WT vs WT/WT	-745.1	-1.3
FPGS	Mut/Mut vs Mut/WT vs WT/WT	-744.8	-1.0
ABCC2	Mut/Mut vs Mut/WT vs WT/WT	-744.3	-0.6
Dichotomous			
		-743.8	
SLC19A1	WT/WT vs other	-744.3	-0.5
	Mut/Mut vs other	-744.4	-0.6
GGH	WT/WT vs other	-744.7	-0.9
	Mut/Mut vs other	-743.8	-0.0
FPGS	WT/WT vs other	-744.5	-0.8
	Mut/Mut vs other	-744.3	-0.5
ABCC2	WT/WT vs other	-743.8	-0.0
	Mut/Mut vs other	-744.2	-0.5

* To determine model fit, ΔOFV was used according to the likelihood ratio test following a chi-squared distribution. In the stepwise forward inclusion, the threshold for significant improvement of the model was set at $p < 0.01$ (dichotomous: ΔOFV > 6.64, df =1 or ordinal: ΔOFV > 9.21, df =2). In the backward elimination significant worsening of the model was set at $p < 0.005$ (Δ OFV > 7.88, df =1).

†Structural model: Two-compartment model in terms of pemetrexed clearance (CL), central distribution volume (Vc), intercompartimental clearance (Q) and peripheral volume of distribution (Vp), including between-patient variability on CL and proportional error model describing between-patient variability

Abbreviations: OFV, objective function value; CL, pemetrexed clearance; Vc, central volume of distribution; Vp, peripheral volume of distribution; BSA, body surface area; eGFR, estimated glomerular filtration rate; Mut, mutant; WT, wildtype