

# IONIC DNA System

Personalized Pharmacogenomic Analysis Report

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## Variant-Based Drug Risk Summary

rsID	Gene	Drug(s)	Phenot. Category	Significance	Chromosome	Position	Ref	Alt	Genotype	Notes	Summary
rs1801133	MTHFR	atorvastatin	Metabolism	PK	1	11856378	G	A	0/1	NaN	: Metab Clinical signific yes.

rs1801131	MTHFR	5,10-methylenetetrahydrofolate	Efficacy	not stated	1	11856378	G	A	0/1	Please note that alleles have been complemented to the positive strand. Case study of a patient with the AG genotype whose response to pharmacotherapy was improved by the addition of folate supplementation	: Efficacy Clinical significance not stated
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rs1801131	MTHFR	bevacizumab, capecitabine, cisplatin, docetaxel, epirubicin, oxaliplatin, trastuzumab	Efficacy	yes	1	11856378G	A	0/1	Patients with the AA genotype had decreased progression-free survival and overall survival in multivariable analysis. However, note that these were only a "nominally" significant associations: formally significant was defined as $p<0.0026$ , and nominally significant as $p<0.05$ . No association with response was found. Please note that alleles have been complemented to the plus chromosomal strand.	:: Efficacy Clinical significance: yes.: Efficacy Clinical significance: yes.
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rs1801133	MTHFR	disulfiram	Efficacy	yes	1	11856378	G	A	0/1	The drop in percentage of cocaine-positive urines for patients with the CT and TT genotypes over the 10 weeks of disulfiram treatment was significantly greater compared to those with the CC genotype. Please note alleles have been complemented to the positive chromosomal strand.	Synop Variant rs1801133 affects respon to disulfir Pheno Efficac Clinica signific yes.
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rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	Alleles were given as C and T. Response measured as relapse-free survival and overall survival.	: Efficacy Clinical significance no.
rs1801133	MTHFR	capecitabine	Metabolism	yes	PK	1	11856378	A	0/1	as measured by increase in elimination half-life of capecitabine.	:: Metab Clinical significance yes.

rs1801131	MTHFR	benazepril	Efficacy	yes	1	11856378	G	A	0/1	When in a haplotype with rs1801131 allele G, and where only one copy of this GG haplotype was present. Patients with this haplotype had a significantly lower diastolic and systolic blood pressure (DBP and SBP) response to benazepril between baseline and 15 days of treatment, as compared to those with any other haplotype. Please note alleles have been complemented to the plus chromosomal strand.	Synop Variant rs1801131 in gene MTHF affects respon to benaze Pheno Efficac Clinica signific yes.
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rs1801131	MTHFR	methotrexate	Efficacy	yes	1	11856378	G	A	0/1	Alleles given as C and T. Efficacy of treatment was measured as change of DAS28 from start of treatment to 6months after initiation of treatment. Effect seen in patients receiving monotherapy for methotrexate. In combination with MTHFR A1298C, patients with 677CC-1298CC or 677TT-1298AA had better response to methotrexate by DAS28 change. (p=0.013).	Synop Variants rs1801131 in gene MTHFR affects response to methotrexate. Phenotype: Efficacy of Clinical significance: yes.
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rs1801133	MTHFR	antipsychotics: chlorpromazine, clozapine, haloperidol, olanzapine, quetiapine, risperidone	Efficacy	yes	1	11856378	G	A	0/1	<p>response is measured by PANSS (Positive and Negative Syndrome Scale), alleles complemented to plus chromosomal strand. In initial evaluation of whole cohort (men and women) authors stated "A; significantly higher mean score was also found in those having MTHFR CT genotype compared with CC and TT; patients. "</p> <p>"Higher negative Positive and Negative Syndrome Scale scores were significantly associated with women and having the CT genotype for MTHFR c.677C&gt;T (<math>\beta</math> = 4.25; p = 0.008) compared with CC patients. "</p>	: Efficacy Clinically significant yes.
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rs1801133	MTHFR	methotrexate	Metabolism	PK	1	11856378	G	A	0/1	NaN	:: Metabolic Clinical significance no.
rs1801133	MTHFR	methotrexate	Metabolism	PK	1	11856378	G	A	0/1	No significant association between this variant and methotrexate concentrations at 72 or 96 hours. Variant described as C677T in the paper and mapped to rs1801133 by PharmGKB. Please note that alleles have been complemented to the positive strand.	:: Metabolic Clinical significance no.

rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	No significant association between variant and relapse-free survival, overall survival or event-free survival. Please note that alleles have been complemented to the positive strand.	Efficacy of clinical significance
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rs1801131	MTHFR	methotrexate	Metabolism	PK	1	11856378	G	A	0/1	Patients carrying at least one A allele had significantly higher AUC of methotrexate than patients with the GG genotype. Please note that alleles have been complemented to the positive strand.	:: Metabolic Clinical significance yes.
rs1801131	MTHFR	methotrexate	Metabolism	PK	1	11856378	G	A	0/1	Please note that alleles have been complemented to the positive strand.	:: Metabolic Clinical significance yes.

rs1801133	CLCN6, MTHFR	methotrexate	Metabolism	PK	1	11856378G	A	0/1	Please note that alleles have been complemented to the positive strand.	:
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rs1801131	MTHFR	methotrexate	Efficacy	yes	1	11856378	G	A	0/1	Patients with the AA genotype had better overall survival than patients with the AG or GG genotypes. Variant referred to in the paper as C677T. Please note that alleles have been complemented to the positive strand.	Synop Variants rs1801131 in MTHFR gene affects response to metho Pheno Efficacy Clinical signific yes.
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rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	No significant difference in relapse-free survival between genotype groups. Please note that alleles have been complemented to the positive strand.	Efficacy Clinical significance.
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rs1801133	5-LCN6, methotrexate	Metabolism	PK	1	11856378G	A	0/1	Please note that alleles have been complemented to the positive strand. This variant is referred to as 677C>T is the paper and was mapped to rs1801133 by PharmGKB. The AA genotype was not found in the cohort.
	MTHFR							

rs1801133	CLCN6, MTHFR	methotrexate	Metabolism	no	PK	1	11856378	G	A	0/1	Please note that alleles have been complemented to the positive strand.	
rs1801133	MTHFR	methotrexate	Metabolism	yes	PK	1	11856378	G	A	0/1	SNP is referred to in the paper as 677 C>T and was mapped to rs1801133 by PharmGKB. Please note that alleles have been complemented to the positive strand.	:: Metabolic Clinical significance yes.



rs1801133	MTHFR	methotrexate	Metabolism	PK	1	11856378	G	A	0/1	Please note that alleles have been complemented to the positive strand. Patients with the AG genotype did not have significantly different methotrexate plasma levels compared to those with the GG genotype.	:: Metabolic Clinical significance yes.
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rs1801133	MTHFR	methotrexate	Metabolism	PK	1	11856378	G	A	0/1	No significant difference in allele frequency between patients with delayed methotrexate excretion and those with normal methotrexate excretion.	:: Metabolic Clinical significance no.
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rs1801131	MTHFR	methotrexate	Efficacy	no	1	11856378G	A	0/1	alleles : complement to plus chromosomal strand. Response measured by ESR, erythrocyte sedimentation rate; TJC, tender joints counts; SJC, swollen joints counts; DAS28, Disease Activity Score in 28 joints. "DAS28 was decreased after the post-treatment in 677TT and 1298AC, but was not statistically significant."
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rs1801133	MTHFR	capecitabine, fluorouracil	Dosage	yes	1	11856378	G	A	0/1	"differences were not present in male patients."	Dosage Clinical significance yes.
rs1801133	MTHFR	methotrexate	Toxicity, yes Metabolism/PK		1	11856378	G	A	0/1	Half life and AUC was significantly increased and elimination rate, volume of distribution and total body clearance was significantly decreased.	:: Toxicity Metabolism Clinical significance yes.
rs1801133	MTHFR	capecitabine, fluorouracil, leucovorin, oxaliplatin	Efficacy	yes	1	11856378	G	A	0/1	FOLFOX : (54.4%) and CAPOX (45.6%) regimens. Measured as cumulative survival over 100 months since diagnosis.	Efficacy Clinical significance yes.

rs1801133	MTHFR	risperidone	Efficacy	no	1	11856378	G	A	0/1	Please note that alleles have been complemented to the positive strand.	: Efficacy Clinical significance no.
rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	Please note: alleles have been complemented to the plus chromosomal strand.	: Efficacy Clinical significance no.
rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	Please note: alleles have been complemented to the plus chromosomal strand.	: Efficacy Clinical significance no.
rs1801133	MTHFR	mercaptopurine methotrexate	Dosage	no	1	11856378	G	A	0/1	NaN	:: Dosage Clinical significance no.

rs1801131	MTHFR	methotrexate	Toxicity	no	1	11856378G	A	0/1	Discontinuation due to adverse effects. Please note that alleles have been complemented to the plus chromosomal strand.	rs1801131 in gene MTHF affects respon to metho Clinical signific ent
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rs1801131	MTHFR	antineoplastic agents	Efficacy	no	1	11856378	G	A	0/1	No significant difference in response rate or progression-free survival time was seen between the genotypes. Patients were either receiving FOLFOX/XELOX or FOLFIRI regimens (respectively: fluorouracil, leucovorin, oxaliplatin; capecitabine, oxaliplatin; fluorouracil, leucovorin, irinotecan). Please note alleles have been complemented to the plus chromosomal strand.	Efficacy Clinical significance no. rate progression-free survival time was seen between the genotypes. Patients were either receiving FOLFOX/XELOX or FOLFIRI regimens (respectively: fluorouracil, leucovorin, oxaliplatin; capecitabine, oxaliplatin; fluorouracil, leucovorin, irinotecan). Please note alleles have been complemented to the plus chromosomal strand.
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rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	NaN	: Efficacy Clinical significance no.
rs1801133	MTHFR	methotrexate	Efficacy	yes	1	11856378	G	A	0/1	"MTHFR 677TT ... associated with over 4-fold increased risk for nonresponse." Alleles complemented to plus chromosomal strand.	Synopsis Variant rs1801133 is associated with gene MTHFR affects response to methotrexate. Phenotype Efficacy Clinical significance yes.
rs1801133	MTHFR	methotrexate	Metabolism	yes	1	11856378	G	A	0/1	AA vs GG and AG vs GG were statistically significant.	:: Metabolism Clinical significance yes.



rs1801131	MTHFR	Platinum Efficacy no compounds	1	11856378	G	A	0/1	Patients : were Efficacy treated Clinical with significant cisplatin no. or carboplatin in combination with a third-generation drug (gemcitabine, paclitaxel, pemetrexed or vinorelbine). No significant association with overall response rate (ORR) overall survival (OS) or progression-free survival (PFS) was found for this SNP. Please note that alleles have been complemented to the plus chromosomal strand.
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rs1801133	MTHFR	folic acid, hydroxychloroquine, methotrexate, sulfasalazine	Efficacy	no	1	11856378	G	A	0/1	NaN	: Efficacy Clinical significance no.
rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	NaN	: Efficacy Clinical significance no.
rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	In this study those with a "favourable" MTHFR genotype (ie. 677CC/rs1801133 or 1298AA/rs1801133) were treated with a higher dose.	: Efficacy Clinical significance no.

rs1801133	MTHFR	folic acid	Metabolism	no PK stated	1	11856378	G	A	0/1	Please note that alleles have been complemented to the positive stand. Case study of a patient with the A allele at rs1801133 and the G allele at rs1801131 who subsequently responded to folate supplementation	:: rs1801133 in gene MTHF affects response to folic acid. Phenotype Metabolic Clinical significance not stated
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rs1801133	MTHFR	benazepril	Efficacy	no	1	11856378	G	A	0/1	No significant differences in the change of systolic blood pressure between baseline and after 15 days of benazepril treatment was seen between the genotypes. Please note alleles have been complemented to the plus chromosomal strand.	Synop Variant rs1801133 in gene MTHFR affects response to benazepril. Phenocopy. Efficacy. Clinical significance no.
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rs1801133	MTHFR	benazepril	Efficacy	yes	1	11856378	G	A	0/1	Patients with the AA genotype had a greater change in diastolic blood pressure between baseline and after 15 days of treatment, compared to those with the AG and GG genotypes. Please note alleles have been complemented to the plus chromosomal strand.	Synopsis Variant rs1801133 in the MTHFR gene affects response to benazepril. Phenotype: Efficacy. Clinical significance: yes.
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rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	Also, with increasing copies of rs1801133 G, there was also an increase in the association between rs1801131 and methotrexate response.	: Efficacy Clinical significance no.
rs1801133	CLCN6, MTHFR	methotrexate	Efficacy	yes	1	11856378	G	A	0/1	Non-response was classified by DAS28 >3.2 at two consecutive evaluations (minimum period of at least 6 months of MTX therapy).	Variant rs1801133 in CLCN6 MTHFR affects response to methotrexate. Phenotype Clinical significance yes.

rs1801131	MTHFR	methotrexate	Efficacy	yes	1	11856378G	A	0/1	Authors say this variant is associated with non-response in recessive model (minor allele/minor allele vs minor/major + major major and describe variant as C677T). Alleles complemented to plus chromosomal strand.	Synopsis: Variant rs1801131 in gene MTHFR affects response to methotrexate. Phenotype: Efficacy. Clinical significance: yes.
rs1801131	MTHFR	fluorouracil, leucovorin, oxaliplatin	Efficacy	yes	1	11856378G	A	0/1	NaN	: Efficacy. Clinical significance: yes.
rs1801131	MTHFR	methotrexate	Efficacy	no	1	11856378G	A	0/1	NaN	: Efficacy. Clinical significance: no.

rs1801133	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	NaN	: Efficacy Clinical significance no.
rs1801133	MTHFR	methotrexate	Toxicity, no Metabolism/PK		1	11856378	G	A	0/1	NaN	:: Toxicity Metabolism Clinical significance no.
rs1801133	MTHFR	methotrexate	Metabolism/PK	yes	1	11856378	G	A	0/1	NaN	:: Metabolism Clinical significance yes.



rs1801131	MTHFR	methotrexate	Efficacy	no	1	11856378	G	A	0/1	Genotype: AA Efficacy is associated with increased red blood cell folate when treated with methotrexate as compared to genotype GG but this did not correlate with disease activity or red blood cell methotrexate metabolites.
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rs1801133	MTHFR	methotrexate	Toxicity	yes	1	11856378	G	A	0/1	Meta-analysis with 8 studies. Cohorts of pediatrics (6 studies) and adults (2 studies) were also considered separately. In the pediatric and overall cohort, those with the AA genotype had a greater risk of experiencing relapse as compared to those with the AG or GG genotype; no significant result was seen when considering the adult cohort (the authors note that more studies are needed before reliable conclusions can be drawn regarding the influence of rs1801133 on relapse in adults with ALL). Please note alleles have been complemented to the plus chromosomal strand.	..... Variant rs1801133 in gene MTHFR affects response to methotrexate. Clinically significant yes.
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rs1801133	MTHFR	Vitamin B-complex, Incl. Combinations	Efficacy	yes	1	11856378	G	A	0/1	<p>Please note that allele has been complemented to the positive strand. Patients who carried either the A allele of rs1801133 or the G allele of rs1801131 were recruited into the study (genotypes are not given) and given a capsule containing reduced B vitamins and macronutrients or a placebo. Patients taking the B vitamin capsule showed a significant decrease in MADRS score over 8 weeks of treatment compared to those taking placebo.</p>	<p>: Variant rs1801133 in gene MTHF affects response to Vitamin B-com Incl. Combi Phenoc Efficacy Clinical significance.</p>
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rs1801133	MTHFR	fluorouracil	Efficacy	yes	1	11856378	G	A	0/1	Patients receiving Variant 11856378G (A) had a significantly better response to fluorouracil-based chemotherapy. Response gene included MTHFR complete affects response response (CR) to and fluorouracil partial Phenotype response Efficacy (PR). Clinical Non-response significant included yes. progressive disease (PD) and stable disease (SD). Please note that alleles have been complemented to the plus chromosomal strand.
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rs1801133	MTHFR	methotrexate	Metabolism	yes	PK	1	11856378	G	A	0/1	Alleles complement "As depicted in Fig. 1, the MTHFR 677CT/TT genotype exhibited a higher likelihood of delayed clearance compared with the wild-type (OR = 3.056/3.456, P = 0.019/0.009)."	Metab Clinical signific yes.
rs1801133	LCN6, MTHFR	tenofovir	Metabolism	no	PK	1	11856378	G	A	0/1	Significance threshold was set at 4.5E-3.	Metab Clinical signific no.
rs1801133	MTHFR	vitamin b12 and folic acid	Efficacy	yes		1	11856378	G	A	0/1	Full text was unavailable annotation made using abstract.	: Efficacy Clinical signific yes.

rs1801133	MTHFR	methotrexate	Efficacy	yes	1	11856378	G	A	0/1	<p>"In the multivariable analysis, which included smoking, the DHFR rs408626 and MTHFR rs1801133 variants retained a statistically significant association with MTX failure (OR 3.12, P = .017 and OR 2.86, P = .015, respectively in a dominant model). The DHFR rs408626-G and MTHFR rs1801133-C alleles were associated with a higher risk of MTX failure."</p> <p>Alleles complemented.</p>	<p>Synop</p> <p>Varian</p> <p>rs1801133</p> <p>in gene MTHFR affects respor</p> <p>to metho</p> <p>Pheno</p> <p>Efficac</p> <p>Clinica</p> <p>signific</p>
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rs2231142	ABCG2	rosuvastatin	Efficacy	no	3	14131367G	T	0/0	ABCG2 : 421C>A did not significantly affect the lipid-lowering response of rosuvastatin.	Efficacy Clinical significance
rs2231142	ABCG2	allopurinol	Efficacy	yes	3	14131367G	T	0/0	this was significant in both LASSO and New Zealand cohorts and meta-analysis. Good responders were defined as SU <6 mg/dl on allopurinol 300 mg/day and poor responders as SU ≥6 mg/dl despite allopurinol >300 mg/day	Synopsis Variant rs2231142 in gene ABCG2 affects response to allopurinol. Phenotype: Efficacy. Clinical significance: yes.

rs2231142	ABCG2	rosuvastatin	Metabolism	no PK stated	3	14131367G	T	0/0	NaN	: Metab Clinical significance not stated
rs2231142	ABCG2	rosuvastatin	Metabolism	yes PK	3	14131367G	T	0/0	NaN	:: Metab Clinical significance yes.



rs2231142	ABCG2	rosuvastatin	Metabolism	yes	PK	3	14131367G	T	0/0	"The mean C <sub>ss</sub> /D <sub>0</sub> of RST and its metabolites were significantly higher in the subjects carrying the ABCG2 421A than in non-carriers of this allele. The effects of this allele remained significant after being adjusted by the baseline characteristics and false discovery rate; (FDR) (P <sub>adj</sub> < 0.01, FDR < 0.05)."	:: Metabolic Clinical significance yes.
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rs2231142	ABCG2	rosuvastatin	Metabolism	yes	PK	3	14131367	G	T	0/0	This variant is not expected to be affected by clinical rosuvastatin concentrations significantly and potentially affect serum levels of pro-inflammatory and pro-angiogenic markers.	:: Metabolic Clinical significance.
rs2231142	ABCG2	apixaban	Metabolism	yes	PK	3	14131367	G	T	0/0	was significant for 3 measures of PK : AUCss, Cmax,ss, and Cmin,ss.	:: Metabolic Clinical significance.
rs2231142	ABCG2	pitavastatin	Metabolism	no	PK	3	14131367	G	T	0/0	Please note that alleles have been complemented to the positive strand.	:

rs2231142	ABCG2	Opioid anesthetics, Other general anesthetics, volatile anesthetics	Efficacy	yes	3	14131367G	T	0/0	The TT genotype in rs2231142 was significantly associated with a shorter recovery time from general anesthesia compared to the GG and GT genotypes.	:: rs2231142 gene ABOG effects response to Opioid anesthetic Other general anesthetic volatile anesthetic Phenobarbital Efficacy Clinical significance
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rs2231142	ABCG2	gefitinib	Metabolism	PK	3	14131367G	T	0/0	No significant difference in area under the plasma concentration-time curve (AUC) or maximum plasma concentration (Cmax) or trough concentrations (C0) was seen between the genotypes. Please note that alleles have been complemented to the plus chromosomal strand.
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rs2231142	ABCG2	sulfasalazine	Metabolism	yes	PK	3	14131367	G	T	0/0	A single oral dose was given and pharmacokinetic parameters were measured at different times points. Parameters AUC0-48, Cmax and CLtotal/F were all significantly different in individuals with the GT genotype compared to GG, and in individuals with the TT genotype compared to GG and compared to GT. Mean plasma concentrations of Sulfasalazine at all time points were significantly higher in TT subjects compared to GG (0-48 hours, except 0.5 hours).	:: Metabolic Clinical significance yes.
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rs2231142	ABCG2	gefitinib	Metabolism	PK	3	14131367G	T	0/0	No significant difference in median area under the concentration-time curve from 0 to 24 hours (AUC <sub>0-24</sub> ; p=0.323) or trough plasma concentration (C <sub>0</sub> ; p=0.429) was seen between the two genotype groups. Please note that alleles have been complemented to the plus chromosomal strand.
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rs2231141	ABCG2	N-desmethylnaloxone	Metabolism	PK	3	14131367	G	T	0/0	Alleles : complemented to plus chromosomal strand. RS number has typo in paper (effect is reported for ABCG2 c.421C>A and lists in methods as rs2231141.
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rs2231142	ABCG2	sunitinib	Efficacy	no	3	14131367G	T	0/0	The genotype was not associated with progression free survival, or overall survival, or clinical benefit. Clinical benefit was defined as either partial response or stable disease. Please note, alleles have been complemented to the + chromosomal strand.	Synop Variants rs2231142 in ABCG2 gene affects response to sunitinib
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rs2231142	ABCG2	lamotrigine	Metabolism	PK	3	14131367	G	T	0/0	Please note that alleles have been complemented to the positive strand.	
rs2231142	ABCG2	lamotrigine	Dosage	no	3	14131367	G	T	0/0	Please note that alleles have been complemented to the positive strand.	: Dosage Clinical significance no.

rs2231142	ABCG2	methotrexate	Metabolism	PK	3	14131367G	T	0/0	No significant association between this variant and methotrexate concentrations at 72 or 96 hours. Variant described as C421A in the paper and mapped to rs2231142 by PharmGKB. Please note that alleles have been complemented to the positive strand.
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rs2231142	ABCG2	rosuvastatin	Efficacy	yes	3	14131367	G	T	0/0	Volunteers with ABCG2 c.421C>A genotype exhibited significantly higher mean % changes in LDL, apoB and total cholesterol levels as compared to those with the wild-type genotype.	Efficacy Clinical Significance
rs2231142	ABCG2	methotrexate	Metabolism	no	PK	3	14131367	T	0/0	NaN	:

rs2231141	ABCG2	leflunomide	Efficacy	no	3	14131367	G	T	0/0	"79 patients (74 females and five males), ... Seventy patients (88.6% of patients) were receiving leflunomide only; five patients (6.3%) were receiving additionally prednisolone, while nine patients (11.4%) were receiving combined hydroxychloroquine and leflunomide." Authors compared genotypes between "Controlled" RA, DAS 28 score of 3.2 or less and "Poorly controlled" RA with DAS 28 of 3.2 and above.	Synop Varian rs2231 in gene ABCG affects respor to leflunc
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rs2231142	ABCG2	methotrexate	Metabolism	PK	3	14131367	G	T	0/0	No significant difference in allele frequency between patients with delayed methotrexate excretion and those with normal methotrexate excretion.	:
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rs2231141	ABCG2	methotrexate	Metabolism	PK	3	14131367	G	T	0/0	Please note that alleles have been complemented to the positive strand. Patients with the TT genotype did not have significantly different methotrexate plasma levels compared to those with the GG genotype.	: rs2231141 in gene ABCG2 affects response to methotrexate. Phenotype. Metabolic Clinical significance. yes.
rs2231141	ABCG2	pazopanib	Metabolism	PK	3	14131367	G	T	0/0	Alleles complemented to plus chromosomal strand.	:: Metabolic Clinical significance. no.

rs2231142	ABCG2	rivaroxaban	Metabolism	PK	3	14131367G	T	0/0	Alleles : complement "The majority of patients had taken rivaroxaban 15 mg" Patients had "NVAf undergoing AF catheter ablation".	Metab
rs2231142	ABCG2	pitavastatin	Metabolism	PK	3	14131367G	T	0/0	ABCG2 : 421C4A variant did not appear to be associated with the altered pharmacokinetic of pitavastatin.	Metab

rs2231142	ABCG2	imatinib	Metabolism	yes	PK	3	14131367G	T	0/0	"The C0/D of IM appeared higher in patients with the rs2231142 mutant T-allele (3.98 ± 1.36 ng/ml·mg-1) than that in wild-type GG genotype patients (3.40 ± 1.21 ng/ml·mg-1)."	: rs2231142 in gene ABCG2 affects response to imatinib. Phenotype Metabolism Clinical significance yes.
rs2231142	ABCG2	rosuvastatin	Metabolism	yes	PK	3	14131367G	T	0/0	Alleles complemented to plus chromosome 1 strand. Meta-analysis of 8 studies looking at AUC and Cmax of rosuvastatin.	:: Metabolism Clinical significance yes.



rs2231142	ABCG2	dolutegravir	metabolism	PK	3	14131367G	T	0/0	Alleles complemented to plus chromosomal strand. "ABCG2 c.421C>A (rs2231142) was independently associated with a 28% increase in dolutegravir Cmax; (b = 0.053; P = 0.047) in the homozygous variant. GM Cmax (95% CI); was 3893 (3774–4240) 4346 (3629–5531) and 4994 (single value) ng/mL in the CC, CA and AA genotype groups, respectively." "Pooled samples from three Phase I clinical trials (NCT02219217; NCT02509195 and NCT03094507) and one Phase III clinical trial; (NCT02351908) carried out at the St Stephen's AIDS Trust clinical trial unit; London" From Table one, only one individual was homozygous for minor allele.	: a recom
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rs2231147	ABCG2	felodipine	Metabolism	yes	PK	3	14131367	G	T	0/0	NaN	: rs2231147 in gene ABCG2 affects response to felodipine. Phenocopy Metabolic Clinical significance yes.
rs2231147	ABCG2	apixaban	Metabolism	yes	PK	3	14131367	G	T	0/0	GG	:: genotype Metabolic Clinical significance yes/ has higher concentrations/decreased ratio of apixaban.

rs2231142	ABCG2	allopurinol	Efficacy	yes	3	14131367G	T	0/0	The authors designated "response" to allopurinol as a reduction of serum uric acid levels to below 6 mg/dL. Mean age was 68 years, 75% were male. The elevated mean baseline SUA before treatment was 8.9 mg/dL. No other SNPs reached genome wide significance.	Synop Variants rs2231142
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rs2231142	ABCG2	dolutegravir	Metabolism	PK	3	14131367	G	T	0/0	mean peak plasma concentration	: a recom
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rs2231142	ABCG2	axitinib	Metabolism	yes	PK	3	14131367G	T	0/0	<p>The authors develop a prediction model and calculated area under the concentration curve (AUC) using 6 SNPs (rs17868323, rs3832043, rs2231142, rs2032582, rs1045642, rs35305980) was compared with actual AUC in 16 patients prospectively which significantly correlated with the objective response rate (P = 0.0002), hand-foot syndrome, P = 0.0055 and hypothyroidism, P = 0.0381, and correlated with actual AUC (P &lt; 0.0001) - the validation study, calculated AUC prior to axitinib treatment precisely predicted actual AUC after axitinib treatment (P = 0.0066).</p>	<p>:: Metabolic Clinical significance yes.</p>
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rs2231142	ABCG2	tacrolimus	Dosage	no	3	14131367G	T	0/0	No significant difference in daily dose of tacrolimus was seen between genotypes of the rs2231142 SNP, at any point between 0 and 60 days after transplant. Please note alleles have been complemented to the plus chromosomal strand.	: Dosage Clinical significance no.
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rs2231142	ABCG2	imatinib	Dosage	no	3	14131367G	T	0/0	No significant association between genotype and chance of requiring an imatinib dose reduction. Please note that alleles have been complemented to the positive strand.	:
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rs2231142	ABCG2	allopurinol	Efficacy	yes	3	14131367G	T	0/0	Good response was defined as serum urate of < 6 mg/dl on a dose of allopurinol on less than 300 mg/day and poor response was defined as serum urate of greater than or equal to 6 mg/dl despite allopurinol of greater than 300 mg/d. The frequency of the GT and TT genotypes was higher in the poor responder group (N=68) than in the good responder group (N=120). This association remained significant even after adjusting for gender, BMI, ethnicity, estimated glomerular filtration rate, diuretic use, and serum urate concentration at baseline.	Synop Variants rs2231142 in gene ABCG2 affects response to allopurinol Phenotype Efficacy Clinical significance yes.
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rs2231142	ABCG2	tacrolimus	Dosage	no	3	14131367G	T	0/0	No significant difference in clearance or blood concentration of tacrolimus was seen between the genotypes of the rs2231142 SNP, at any point between 0 and 60 days after transplant. Please note alleles have been complemented to the plus chromosomal strand.	: Dosage Clinical significance
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rs2231142	ABCG2	fluorouracil, irinotecan, oxaliplatin	Efficacy no	3	14131367	G	T	0/0	Patients were taking either IFL (irinotecan + fluorouracil + leucovorin; n=114), FOLFOX (fluorouracil + oxaliplatin + leucovorin; n=299) or IROX (irinotecan + oxaliplatin; n=107). No significant association was seen between this variant and confirmed response rate, overall survival or time to progression in any of the treatment groups OR all treatment groups considered together. Significance level was set at 0.01.	: Efficacy Clinical significance no.
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rs2231141	ABCG2	methotrexate	Toxicity	no	3	14131367G	T	0/0	Discontinuation due to adverse effects. Please note that alleles have been complemented to the plus chromosomal strand.	rs2231141 in gene ABCG2 affects response to methotrexate. Clinical significance not determined.
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rs2231142	ABCG2	sulfasalazine	Efficacy	yes	3	14131367G	T	0/0	After adjusting for age, baseline DAS28, smoking status and shared epitope positivity, those who carried one or more T allele were more likely to achieve remission after 12 months of treatment. Remission defined as an SDAI of <3.3. Please note that alleles have been complemented to the positive chromosomal strand.	: Efficacy Clinically significant yes.
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rs2231141	ABCG2	antineoplastic agents	Efficacy	yes	3	14131367G	T	0/0	Patients with the GG genotype receiving a FOLFOX/XELOX regimen (respectively: fluorouracil, leucovorin, oxaliplatin, capecitabine, oxaliplatin) had a decreased response rate, as compared to those with the GT or TT genotype. No significant difference in response rate was seen in patients receiving a FOLFIRI regimen (fluorouracil, leucovorin, irinotecan). No significant differences in progression-free survival were seen for either regimen. Please note alleles have been complemented to the plus chromosomal strand.	: a synthesis of the gene ABCG2 and the role of the gene ABCG2 in the response to antineoplastic agents
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rs2231142	ABCG2	granisetron palonosetron	Efficacy no	3	14131367G	T	0/0	There was no significant association between this variant and proportion of patients showing a "complete response" to antiemetic treatment during the first 120 hours after cisplatin-based chemotherapy initiation. Complete response defined as no vomiting episodes or no use of rescue medication. Patients were either receiving granisetron (n=79) or palonosetron (n=77), both in combination with dexamethasone and aprepitant. Please note that alleles have been complemented to the plus chromosomal strand.	: Efficacy Clinical signific no.
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rs2231142	ABCG2	lamotrigine	Efficacy	no	3	14131367G	T	0/0	Alleles given as A and C. Efficacy was determined by monitoring the frequency of patients' epileptic seizures within one year. Each patient was evaluated at 4 weeks after treatment initiation and then at 3-month intervals thereafter. The difference in seizure frequency was based on the difference between the 3-month retrospective baseline frequency and the seizure frequency at 12-month visit, which was reported for the last 3 months prior to the last visit. Good efficacy was defined as seizure-free or a 50% or greater reduction in seizure frequency within a 1-year follow-up period.	Synopsis Variant rs2231142 in gene ABCG2 affects response to lamotrigine. Phenotype Efficacy Clinical significance no.
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rs2231142	ABCG2	lamotrigine	Metabolism	PK	3	14131367	G	T	0/0	Lamotrigine concentrations were measured as steady state in plasma in the early morning before breakfast after at least one month of continuous treatment with lamotrigine monotherapy. Alleles given as A and C.	1008
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rs2231142	ABCG2	sunitinib	Metabolism	yes	PK	3	14131367G	T	0/0	<p>The dose-normalized area under the plasma concentration-time curve from 0 to 24 hours (AUC) for the composite of sunitinib + SU12662 (its active metabolite) was highest for those with the TT genotype, followed by those with the GT genotype then those with the GG genotype (TT&gt;GT&gt;GG). This SNP was identified as a statistically significant variability factor for composite exposure. Please note that alleles have been complemented to the plus chromosomal strand.</p>	<p>: rs2231142 in gene ABCG2 affects response to sunitinib Phenotype Metabolic Clinical significance yes.</p>
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rs2231142	ABCG2	lamotrigine	Metabolism	PK	3	14131367	G	T	0/0	Alleles given as A and C. The concentration was measured as lamotrigine trough concentration / dose normalized by body weight. Included patients had been on lamotrigine monotherapy for at least a month with complete medical records, had normal renal and hepatic functions, and had therapeutic drug monitoring with good compliance.	: a recom
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rs2231147	ABCG2	lamotrigine	Metabolism	PK	3	14131367	G	T	0/0	NaN	:
rs2231147	ABCG2	deferasirox	Metabolism	PK	3	14131367	G	T	0/0	The genotype was not associated with area under the concentration curve (AUC) above the effectiveness cutoff of 360 micrograms/mL as compared in univariate analysis.	Synopsis Variant rs2231147 in gene ABCG2 affects response to deferasirox. Phenomenon: Metabolic Clinical significance: none.
rs2231147	ABCG2	acetaminophen	Metabolism	PK	3	14131367	G	T	0/0	There were no TT homozygotes and only 7 heterozygotes.	: Metabolic Clinical significance: none.

rs2231142	ABCG2	hmg coa reductase inhibitors	Efficacy	yes	3	14131367	G	T	0/0	as part of a three SNP genetic risk score with rs10455872 in LPA and rs2075650 in APOE. Associated allele not explicitly stated but methods reference Tomlinson et al. so used the associated allele from there [PMID:20130569]	: Efficacy Clinical significance yes.
rs2231142	ABCG2	risperidone	Metabolism	yes	3	14131367	G	T	0/0	Alleles complemented to plus chromosome ABCG strand.	: rs2231142 in gene ABCG affects response to risperidone

rs2231142	ABCG2	allopurinol	Dosage	yes	3	14131367G	T	0/0	ABCG2 : genotype Dosage and Clinical diuretic signific use yes. explained 53% of the variability in prediction error.
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rs2231142	ABCG2	tenofovir	Metabolism	yes	PK	3	14131367G	T	0/0	Patients with the GT or TT genotype had a 1.51-fold increase in tenofovir area under the concentration-time curve (AUC) as compared to those with the GG genotype. Multivariable model controlling for age (per decade), body mass index (per 10 percent increase), African American race, ritonavir use, and whether eGFR is less than 70 ml/min per 1.73m2	: Metabolic Clinical significance yes.
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rs2231142	ABCG2	antiepileptic	Efficacy	no	3	14131367G	T	0/0	Please note, alleles have been complemented for the plus strand. Epilepsy patients on antiepileptic drug (AED) treatment were divided into those with drug-responsive or drug-resistant epilepsy and genotypes and allele frequencies were compared. No significant association found with this variant.	: Efficacy Clinical significance no. complemented for the plus strand. Epilepsy patients on antiepileptic drug (AED) treatment were divided into those with drug-responsive or drug-resistant epilepsy and genotypes and allele frequencies were compared. No significant association found with this variant.
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rs2231142	ABCG2	sulfasalazine	Metabolism of PK stated	3	14131367G	T	0/0	<p>The mean AUC(0,48 h) was 3-fold higher and Cmax was 2.5-fold higher in individuals with the TT genotype as compared to individuals with the GG genotype. The apparent oral clearance (dose/AUC(0,48 h)) was 3-fold lower in individuals with the TT genotype as compared to individuals with the GG genotype. The authors reported no differences in sulfasalazine PK between the GG genotype and GT genotype, however a single individual was compound heterozygous at rs72552713 (CT) and rs2231142 (GT) in and altered PK as compared to other individuals who were heterozygous only at rs2231142 (GT). Please note: alleles have been complemented to the + chromosomal strand.</p>	: Metabolic Clinical significance not stated
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rs2231142	ABCG2	atorvastatin	Efficacy	no	3	14131367	G	T	0/0	The authors tested whether significant differences in the following biomarkers that corresponded to genotype (dominant model): triglycerides, HDL-cholesterol, LDL-cholesterol and total cholesterol.	: Efficacy Clinical significance.
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rs2231142	ABCG2	imatinib	Other, Metabolism/PK	yes	3	14131367G	T	0/0	The association was with decreased clearance. Genotype alone was not associated, but genotype enhanced a more major association with body weight, albuminemia and plasma alpha1-acid glycoprotein. There were no TT in this small group(41 GG, 5 GT).
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rs2231142	ABCG2	atorvastatin	Metabolism	PK	3	14131367	G	T	0/0	The AUC of atorvastatin in patients carrying ABCG2 c.421AA tended to be smaller compared with those in patients with c.421CC or c.421CA after its microdosing and therapeutic dosing. However, it did not reach statistical significance.	: Metab Clinical Signific no.
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rs2231142	ABCG2	imatinib	Efficacy	yes	3	14131367G	T	0/0	Direction of relationship not explicitly stated. Assumed minor allele as T and having lower odds ratio of response. Alleles complemented to plus strand as gene is on minus chromosomal strand.	Synopsis of Variant rs2231142 in gene ABCG2 affects response to imatinib. Phenotype: Efficacy. Clinical significance: yes.
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rs2231142	ABCG2	lamotrigine	Metabolism	PK	3	14131367	G	T	0/0	In patients with the AA and AG genotype, steady-state measured and dose-adjusted lamotrigine trough concentration was higher in those administered lamotrigine as compared to the GG genotype and lower in those administered lamotrigine only as compared to the GG genotype.	: a recom
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rs2231141	ABCG2	selumetinib	Metabolism	PK	3	14131367G	T	0/0	Not associated with normalized dose when allele was assessed within ethnic groups (Asian, White, Black) and when all ethnic groups were pooled together.	:
rs2231141	ABCG2	iguratimod	Efficacy	yes	3	14131367G	T	0/0	Alleles complementary to plus strand.	: a synthon of the rs2231141 gene ABCG2 in the gene ABCG2.
rs2231141	ABCG2	apixaban	Metabolism	PK stated	3	14131367G	T	0/0	NaN	: Metab Clinical significance not stated

rs2231141	ABCG2	methotrexate	Metabolism	PK	3	14131367G	T	0/0	The T allele is associated with longer half-life of methotrexate.	: rs2231141 in gene ABCG2 affects response to methotrexate. Pharmacokinetic Clinical significance.
rs2231141	ABCG2	sulfasalazine	Dosage	no	3	14131367G	T	0/0	Exposure: was measured as Cmax and AUC 0-24.	Dosage Clinical significance.
rs2231141	ABCG2	rosuvastatin	Metabolism	PK	3	14131367G	T	0/0	Exposure: was measured as Cmax and AUC 0-24.	Metabolic Clinical significance.
rs2231141	ABCG2	sunitinib	Metabolism	PK	3	14131367G	T	0/0	as measured by C/D Ratio or total Sunitinib Dose-Adjusted Concentration.	:

rs2231142	ABCG2	talinolol	Metabolism	no	PK	3	14131367	G	T	0/0	This was a twin study of monozygotic and dizygotic twins.	: Metabolic Clinical significance no.
rs2231142	ABCG2	gefitinib	Efficacy	no		3	14131367	G	T	0/0	NaN	Synopsis Variant rs2231142 in gene ABCG2 affects response to gefitinib
rs2231142	ABCG2	rosuvastatin	Efficacy	yes		3	14131367	G	T	0/0	as measured by achievement of their LDL cholesterol target (significance given for variants of either CYP3A5*1, 6986A>G, rs776746 and ABCG2; 421C>A, rs2231142).	: Efficacy Clinical significance yes.



rs2231142	ABCG2	granisetron palonosetron	Efficacy no	3	14131367	G	T	0/0	Patients with cancer, treated with cisplatin who had been treated with granisetron and palonosetron. Nausea and vomiting episodes were recorded for the first 120 h post cisplatin. With regard to vomiting events, presence/absence of symptoms and the time of onset were described. Nausea severity was categorized using a 4-point Likert scale (0 = no nausea, 1 = mild nausea, 2 = moderate nausea and 3 = severe nausea) according to the subjective assessment of each patient.	: Efficacy Clinical significance no.
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rs2231142	ABCG2	sunitinib	Metabolism	no PK	3	14131367	G	T	0/0	NaN	:
rs2231142	ABCG2	sorafenib	Metabolism	yes PK	3	14131367	G	T	0/0	measured by concentration (body weight) ratio.; (alleles complemented to plus strand). No TT homozygotes were observed.	Phenotype Metabolic (clinical significance) yes.

rs2231142	ABCG2	n-desethyl-sunitinib, Metabolism/PK sunitinib	Toxicity, no	3	14131367G	T	0/0	in a single case study. Authors state "Therefore we speculated that the extremely high plasma concentration of sunitinib and SU12662 caused by the ABCG2 421 AA genotype might have resulted in severe toxicities to the patient."	Synop Varian rs2231 in gene ABCG affects respon to desec sunitin sunitin Pheno Toxicit Metab Clinica signific
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rs2231142	ABCG2	ceftriaxone	Metabolism	PK	3	14131367G	T	0/0	Please note that alleles have been complemented to the positive strand. No significant association was found between this variant and concentrations of ceftriaxone in the plasma or cerebrospinal fluid (CSF) of patients. There was also no significant association between this variant and ceftriaxone CSF to plasma ratios.
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rs2231142	ABCG2	letermovir	Metabolism	PK	3	14131367G	T	0/0	No significant association between this variant and letermovir AUC.
rs2231142	ABCG2	selumetinib	Metabolism	PK	3	14131367G	T	0/0	Not associated with AUC, AUC0-12 when allele was assessed within ethnic groups (Asian, White, Black) and when all ethnic groups were pooled together. Only P-values for AUC presented here.

rs2231141	ABCG2	sulfasalazine	Other	no	3	14131367	G	T	0/0	No significant difference in likelihood of cessation of sulphasalazine treatment due to adverse effects was seen between those who carried the T allele and those who did not. Most common adverse events were nausea/vomiting and fatigue/lethargy; please refer to paper for full list. Note that alleles have been complemented to the plus chromosomal strand.	:: rs2231141 in gene ABCG2 affects response to the sulfasalazine Phenotype: Other. Clinical significance no.
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rs2231141	ABCG2	methotrexate	Metabolism	no	PK	3	14131367G	T	0/0	TT vs GG and TG vs GG were not statistically significant.	:
rs2231141	ABCG2	voriconazole	Metabolism	yes	PK	3	14131367G	T	0/0	"ABCG2 : a phenotype recom was a also recom associated with recom voriconazole concentrations (p a = recom 0.015) a recom poor a function; recom (PF) or decreased function (DF) patients having higher voriconazole concentrations compared to normal function (NF) patients."	

rs2231142	ABCG2	diazepam	Metabolism	PK	3	14131367	G	T	0/0	effect was seen for both Cmax and t1/2 with t-test but was not significant after Bonferroni correction.	:
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rs2231142	ABCG2	eltrombopag	Metabolism	PK	3	14131367	G	T	0/0	"The clearance of the variant of ABCG2 (rs2231142, G>T) was significantly higher than that of the wild-type (P = .02) (Figure 2A). However, when clearances were normalized by weight, the clearance between the wild-type and variant shows no statistical difference (Figure 2D). No other remarkable difference was noted in the wild-type and variant of CYP1A2 (rs762551, C > A) (Figure 2B,E) and UGT1A1*6 (rs4148323, G>A) (Figure 2C,F)."	:: Metab Clinical signific no.
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rs2231141	ABCG2	imatinib	Efficacy	yes	3	14131367	G	T	0/0	"Patients with a T allele for ABCB1 (rs1045642, rs2032582, and rs1128503) A allele for ABCG2-rs2231141 and G allele for CYP3A5-rs7767 polymorphisms showed better cytogenetic response and molecular response." Alleles complemented.	Synopsis: Variant rs2231141 in gene ABCG2 affects response to imatinib. Phenotype: Efficacy. Clinical significance: significant for ABCG2-rs2231141 and CYP3A5-rs7767 polymorphisms.
rs2231141	ABCG2	clozapine	Metabolism/ PK	yes	3	14131367	G	T	0/0	Alleles complemented to plus chromosome strand. rs2231141 in gene ABCG2 affects response to clozapine.	Synopsis: Variant rs2231141 in gene ABCG2 affects response to clozapine. Phenotype: Metabolism/ PK. Clinical significance: significant for ABCG2-rs2231141.

rs2231142	ABCG2	allopurinol	Efficacy	yes	3	14131367	G	T	0/0	Response to allopurinol was determined by whether serum uric acid concentration decreased following allopurinol treatment. This SNP is in perfect LD with rs45499402.	Synopsis: Variant rs2231142 in the ABCG2 gene affects response to allopurinol. Response to allopurinol was determined by whether serum uric acid concentration decreased following allopurinol treatment. This SNP is in perfect LD with rs45499402.
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rs2231142	ABCG2	rivaroxaban	Metabolism	PK	3	14131367	G	T	0/0	Alleles complemented. "In our dataset, individuals with the ABCG2 421 A/A genotype had considerably higher average values of Vd/F (508.27±72.73 L; P=0.001) and t1/2 (41.04±23.73 h; P=0.000) compared to those with the other genotypes, 421 C/A and 421 C/C, with no statistically significant difference between means." "Individuals carrying two mutant alleles in the ABCG2 SNP tended to have lower AUC, Cmax, and Cl/F (as shown in Table 4) compared to carriers of the wild-type genotype. However, it is essential to note that these differences did not achieve statistical significance (P>0.05)." This was reported for the fasting group which had 2 TT individuals, the fed group had no TT individuals.	:: Metabolic Clinical significance.
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rs2231142	ABCG2	gefitinib	Efficacy	no	3	14131367G	T	0/0	"our meta-analysis provides strong evidence that rs2231142 does not influence the response and toxicity to gefitinib treatment in patients with EGFR-mutated NSCLC." "Three studies analyzed the curative effect indicator, involving 239 patients. No association was observed between the ABCG2 C421A polymorphism and the response to Gefitinib chemotherapy (HR=1.0670; 95%CI= 0.8042-1.4156; p=0.653; I2=0%), as depicted in Figure 2." Alleles complemented	Synop Variation rs2231142 in gene ABCG2 affects respon to gefitini
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[illegible]

rs2231142	ABCG2	rosuvastatin	Metabolism	yes	PK	3	14131367	G	T	0/0	The exposure to rosuvastatin increased by 44% in young subjects (p = 0.0021) with BCRP intermediate function (IF) and by 35% and 59% (p > 0.05 for both) in elderly subjects with BCRP IF and low function. The ABCG2 421C > A polymorphism was identified as a more important determinant than the SLCO1B1 521T > C polymorphism in both elderly and young subjects.	:: Metab Clinical significance yes.
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rs2231142	ABCG2	imatinib	Efficacy	yes	3	14131367G	T	0/0	Alleles complemented. There were no TT homozygotes. "However, a statistically significant difference was noted between the two patient groups regarding the distribution of different genotypes of the ABCG2 C421A polymorphism with predominance of the CA genotype in responder patients (p = 0.0395) (Fig. 2b).; Assessment of molecular response to imatinib based on the BCR-ABL1 transcript level at 12 months. Responders (n = 26); Non-responders (n = 24). "	Synopsis Variant rs2231142 in gene ABCG2 affects response to imatinib Phenotype Efficacy Clinical significance
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