

S2 Table. Overview of the variant alleles (mutations) of the various pharmacogenes included in the genotyping panels and the respective genotype-predicted aberrant phenotypes required for gene-drug interaction (GDI) assessments.

Gene	Variant allele panel	Genotype-predicted aberrant phenotypes
CYP2D6 [1]	<p>Non-coding variant alleles:</p> <ul style="list-style-type: none"> • 2D6*3 (rs35742686) • 2D6*4 (rs3892097) • 2D6*6 (rs5030655) <p>Reduced-function variant alleles:</p> <ul style="list-style-type: none"> • 2D6*9 (rs5030656) • 2D6*10 (rs1065852) • 2D6*41 (rs29001518) <p>Copy number analysis:</p> <ul style="list-style-type: none"> • 2D6*5 (whole gene deletion) • multiplication of fully-functional alleles (2D6*1 or *2) 	<p>‘Poor metabolizers’ (PMs): Homozygous carriers of non-coding alleles</p> <p>‘Intermediate metabolizers’ (IMs): Heterozygous carriers of non-coding alleles and homozygous carriers of reduced-function alleles</p> <p>‘Ultrarapid metabolizers’ (UMs): Carriers of three or more functional gene copies</p>
CYP2C19 [1]	<p>Non-coding variant alleles:</p> <ul style="list-style-type: none"> • 2C19*2 (rs4244285) • 2C19*3 (rs4986893/rs57081121) • 2C19*4 (rs28399504) <p>Gain-of-function allele:</p> <ul style="list-style-type: none"> • CYP2C19*17 (rs12248560) 	<p>PMs: Homozygous carriers of non-coding alleles</p> <p>IMs: Heterozygous carriers of non-coding alleles</p> <p>UMs: Hetero- or homozygous carriers of the gain-of-function allele</p>
CYP2C9 [1]	<p>Reduced-function alleles:</p> <ul style="list-style-type: none"> • 2C9*2 (rs1799853) • 2C9*3 (rs1057910) 	<p>PMs: Homozygous carriers of CYP2C9*3</p> <p>IMs: Heterozygous carriers of CYP2C9*3 and homozygous carriers of CYP2C9*2</p>
CYP3A5 [1]	<p>Non-coding variant allele:</p> <ul style="list-style-type: none"> • CYP3A5*3 (rs776746) 	<p>Increased CYP3A5 metabolism: Hetero- or homozygous carriers of CYP3A5*1</p>
SLCO1B1 [2]	<p>Reduced-function allele:</p> <ul style="list-style-type: none"> • 521T>C/*5 (rs4149056) 	<p>Decreased OATP1B1-mediated transport, e.g. of statins: Hetero- or homozygous carriers of the reduced-function allele</p>
VCORK1 [3]	<p>Increased VCORK1-sensitivity:</p> <ul style="list-style-type: none"> • VKORC1*2 (rs9923231) 	<p>Low-dose warfarin responders: Hetero- or homozygous carriers of VKORC1*2</p>

All genotyping assays were validated and had been certified by Norwegian accreditation for routine clinical use. All variant allele analyses were performed using Taqman-based realtime PCR assays.

REFERENCES:

[1] Gaedigk A, Ingelman-Sundberg M, Miller NA, Leeder JS, Whirl-Carrillo M, Klein TE. The Pharmacogene Variation (PharmVar) Consortium: Incorporation of the Human Cytochrome P450 (CYP) Allele Nomenclature Database. Clin Pharmacol Ther. 2018; 103: 399-401.

[2] Kallikoski A, Niemi M. Impact of OATP transporters on pharmacokinetics. British journal of pharmacology. 2009; 158: 693-705.

[3] Owen RP, Gong L, Sagreiya H, Klein TE, Altman RB. VKORC1 pharmacogenomics summary. Pharmacogenetics and genomics. 2010; 20: 642-4.