SONOGEN

CeGaT

SONOGEN XP report for Petra Musterfrau - brief version

First name:	Petra	**Laboratory patient ID:**	12345
Last name:	Musterfrau	**Report date:**	January 19, 2021
Date of birth:	October 25, 1965		
Gender:	female		
Treatment:	abacavir, acenocoumarol, allopurinol, amitriptyline, aripiprazole, atazanavir, atomoxetine, atorvastatin, azathioprine, brexpiprazole, capecitabine, carbamazepine, carisoprodol, carvedilol, celecoxib, cevimeline, chloroquine, citalopram, clobazam, clomipramine, clopidogrel, clozapine, codeine, dapsone, darifenacin, desipramine, diclofenac, doxepin, efavirenz, eltrombopag, escitalopram, ethinyl estradiol, fesoterodine, flecainide, fluorouracil, flurbiprofen, fluvoxamine, glyburide, haloperidol, ibuprofen, iloperidone, imipramine, irinotecan, isoniazid, lansoprazole, lornoxicam, meloxicam, mercaptopurine, metoprolol, mirtazapine, mivacurium, morphine, nelfinavir, nortriptyline, olanzapine, omeprazole, ondansetron, oxcarbazepine, oxycodone, pantoprazole, paroxetine, pazopanib, peginterferon alfa-2a, peginterferon alfa-2b, perphenazine, phenprocoumon, phenytoin, pimozide, piroxicam, propafenone, propofol, rasburicase, ribavirin, risperidone, rosuvastatin, sertraline, sevoflurane, simvastatin, siponimod, streptomycin, succinylcholine, tacrolimus, tak-390mr, tamoxifen, tenoxicam, tetrabenazine, thioridazine, tioguanine, tramadol, trimipramine, tropisetron^{CS}, venlafaxine, voriconazole, vortioxetine, warfarin, zuclopenthixol		

PGx profile

Gene	Genotype	Predicted phenotype	Effect	Tested alleles
CYP2C9	*1/*2	IM*2	slow metabolism	*1, *2, *3, *4, *5, *6, *8, *11, *12, *13, *15, *25, *27
CYP2D6	*2/*4A	IM	slow metabolism	*1, *2, *3, *4, *4A, *4J, *4K, *4M, *5, *6, *6C, *7, *8, *9, *10, *10B, *11, *12, *14A, *14B, *15, *17, *18, *19, *20, *21, *29, *31, *34, *38, *39, *40, *41, *42, *44, *47, *51, *56A, *56B, *57, *62, *65, *69, *91, *92, *96, *100, *101, CNV
POR	*1/*28	increased function	fast metabolism	*1, *28
UGT1A1	*1/*6	IM	slow metabolism	*1, *6, *7, *27, *28, *29, *36, *37, *80
VKORC1	-1639GA	decreased function	increased drug efficacy	-1639A, -1639G
CACNA1S	WT/WT	normal risk	normal risk of adverse events	520T, 3257A, WT
CYP2B6	*1/*1	NM	normal metabolism	*1, *2, *4, *5, *6A, *7, *8, *9, *12, *13, *16, *18, *19, *20, *22, *26, *28, *34, *35, *38
CYP2C19	*1/*1	NM	normal metabolism	*1, *2, *3, *4A, *4B, *5, *6, *7, *8, *9, *10, *16, *17, *19, *22, *24, *25, *26, *36
CYP3A4	*1/*1	*22 non-carrier	normal metabolism	*1, *2, *17, *22
CYP3A5	*3/*3	non-expresser	normal metabolism	*1, *2, *3, *3+2, *6, *7
CYP4F2	*1/*1	NM	normal metabolism	*1, *3
DPYD	*1/*1	NM	normal metabolism	*1, *2A, *3, *7, *8, *10, *12, *13, 2846T, HapB3
HLA-A	*02:01/*24:02	normal risk	normal risk of adverse events	
HLA-B	*40:02/*46:01	normal risk	normal risk of adverse events	

IFNL3	rs12979860-CC	favorable response genotype	high drug-dependent response rate	rs12979860-C, rs12979860-T
MT-RNR1	WT/WT	normal risk	normal risk of adverse events	1095C, 1494T, 1555G, WT
NUDT15	*1/*1	NM	normal risk of adverse events	*1, *3
RYR1	WT/WT	normal risk	normal risk of adverse events	103C, 130T, 487T, 488T, 742A, 742C, 982T, 1021A, 1021C, 1201T, 1209G, 1565C, 1589A, 1597T, 1598A, 1654T, 1840T, 1841T, 6487T, 6488A, 6502A, 6617G, 6617T, 7007A, 7039delGAG, 7048A, 7063T, 7124C, 7282A, 7300A, 7304A, 7354T, 7360T, 7361A, 7372T, 7373A, 7522A, 7522T, 7523A, 9310A, 11969T, 14387G, 14477T, 14497T, 14512G, 14545A, 14582A, 14693C, WT
SLCO1B1	*1a/*1a	normal function	normal drug efficacy	*1a, *5
TPMT	*1/*1	NM	normal metabolism	*1, *2, *3A, *3B, *3C, *4

For HLA-A, the risk allele *31:01 was considered for phenotpe classification.
For HLA-B, the risk alleles *15:02, *57:01 and *58:01 were considered for phenotype classification.

Drug - PGx interactions of current treatment

	Normal risk	Use with caution	High risk
abacavir HLA-B normal risk (*57:01-negative)	• Use abacavir per standard dosing guidelines.		
acenocoumarol Intermediate acenocoumarol sensitivity (incl. CYP4F2)		• **Patient may need reduced acenocoumarol dose.** Consider maintenance dose of 1.4-3 mg/day (10-20.5 mg/week). • **Check INR more frequently.** • Be aware that other factors, such as clinical/demographic factors, drug interactions or other genes may influence the acenocoumarol dose requirement.	
allopurinol HLA-B normal risk (*58:01-negative)	• Follow drug label dosing recommendation.		
amitriptyline CYP2D6 IM, CYP2C19 NM		• High dose (e.g. depression): **Consider 25% reduction of recommended starting dose**. Utilize TDM to guide dose adjustment. • Low dose (e.g. neuropathic pain): Initiate therapy with recommended starting dose, but monitor closely for side effects.	
aripiprazole CYP2D6 IM		• Follow drug label dosing recommendation. • **Be alert to increased plasma concentrations of aripiprazole and increased risk of ADRs.**	
atazanavir UGT1A1 IM	• Follow drug label dosing recommendation.		
atomoxetine CYP2D6 IM		• **Start with 40 mg/day.** If no clinical response and in the absence of adverse events after 2 weeks increase dose to 80 mg/day to approach 400 ng /ml peak plasma concentration.	
atorvastatin SLCO1B1 normal function	• Follow drug label dosing recommendation.		
azathioprine Normal thiopurine metabolism	• Follow drug label dosing recommendation.		
brexpiprazole CYP2D6 IM	• Follow drug label dosing recommendation.		
capecitabine DPYD NM	• Follow drug label dosing recommendation.		
carbamazepine HLA-A normal risk, HLA-B normal risk (*15:02-negative)	• Follow drug label dosing recommendation.		
carisoprodol CYP2C19 NM	• Follow drug label dosing recommendation.		
carvedilol CYP2D6 IM	• Follow drug label dosing recommendation.		
celecoxib CYP2C9 IM*2	• Follow drug label dosing recommendation.		
cevimeline CYP2D6 IM		• Follow drug label dosing recommendation. • **Be alert to increased risk of ADRs.**	
citalopram CYP2C19 NM	• Follow drug label dosing recommendation.		
clobazam CYP2C19 NM	• Follow drug label dosing recommendation.		

clomipramine CYP2D6 IM, CYP2C19 NM		• High dose (e.g. depression): **Consider 25-30% reduction of recommended starting dose**. Utilize TDM to guide dose adjustment. • Low dose (e.g. neuropathic pain): Initiate therapy with recommended starting dose, but monitor closely for side effects.	
clopidogrel CYP2C19 NM	• Follow drug label dosing recommendation.		
clozapine CYP2D6 IM	• Follow drug label dosing recommendation.		
codeine CYP2D6 IM		• Use label recommended age- or weight-specific dosing. • Be careful with concomitant use of CYP2D6 inhibitors, CYP3A4 inhibitors and CYP3A4 inducers. Accordingly, a dose increase or reduction may be necessary. • **If no response, consider alternative analgesics** such as morphine or a non-opioid.	
darifenacin CYP2D6 IM	• Follow drug label dosing recommendation.		
desipramine CYP2D6 IM		• High dose (e.g. depression): **Consider 25% reduction of recommended starting dose**. Utilize TDM to guide dose adjustments. • Low dose (e.g. neuropathic pain): Initiate therapy with recommended starting dose, but monitor closely for side effects.	
diclofenac CYP2C9 IM*2	• Follow drug label dosing recommendations.		
doxepin CYP2D6 IM, CYP2C19 NM		• High dose (e.g. depression): **Consider 20-25% reduction of recommended starting dose**. Utilize TDM to guide dose adjustments and monitor the effect and side effects. • Low dose (e.g. neuropathic pain): Initiate therapy with recommended starting dose, but monitor closely for side effects.	
efavirenz CYP2B6 NM	• Follow drug label dosing recommendation.		
escitalopram CYP2C19 NM	• Follow drug label dosing recommendation.		
fesoterodine CYP2D6 IM	• Follow drug label dosing recommendation.		
flecainide CYP2D6 IM			• **Reduce dose by 25%**, record ECG, monitor plasma concentration.
fluorouracil DPYD NM	• Follow drug label dosing recommendation.		
flurbiprofen CYP2C9 IM*2	• Follow drug label dosing recommendation.		
fluvoxamine CYP2D6 IM	• Follow drug label dosing recommendation.		
glyburide CYP2C9 IM*2	• Follow drug label dosing recommendation.		
haloperidol CYP2D6 IM	• Follow drug label dosing recommendation.		
ibuprofen CYP2C9 IM*2	• Follow drug label dosing recommendations.		
iloperidone CYP2D6 IM		• **Be alert to ADEs.** • **Patient may need a dose reduction.**	
imipramine CYP2D6 IM, CYP2C19 NM		• High dose (e.g. depression): **Consider 25-30% reduction of recommended starting dose**. Utilize TDM to guide dose adjustment and monitor the effect and side effects. • Low dose (e.g. neuropathic pain): Initiate therapy with recommended starting dose, but monitor closely for side effects.	

irinotecan UGT1A1 IM		• Follow drug label dosing recommendation. • Be alert to increased risk of ADRs at higher doses.	
lansoprazole CYP2C19 NM		• Initiate standard starting daily dose. • **Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis.** Daily dose may be given in divided doses. • **Monitor for efficacy.**	
lornoxicam CYP2C9 IM*2	• Follow drug label dosing recommendation.		
meloxicam CYP2C9 IM*2	• Follow drug label dosing recommendations.		
mercaptopurine normal thiopurine metabolism	• Follow drug label dosing recommendation.		
metoprolol CYP2D6 IM		• **Heart failure: select alternative drug** (e.g., bisoprolol, carvedilol) **or reduce dose by 50%.** • **Other indications: be alert to ADEs** (e.g., bradycardia, cold extremities) **or select alternative drug** (e.g., atenolol, bisoprolol).	
mirtazapine CYP2D6 IM	• Follow drug label dosing recommendation.		
nelfinavir CYP2C19 NM	• Follow drug label dosing recommendation.		
nortriptyline CYP2D6 IM		• High dose (e.g. depression): **Consider 25-40% reduction of recommended starting dose**. Utilize TDM to guide dose adjustments. • Low dose (e.g. neuropathic pain): Initiate therapy with recommended starting dose, but monitor closely for side effects.	
omeprazole CYP2C19 NM		• Initiate standard starting daily dose. • **Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis**. Daily dose may be given in divided doses. • **Monitor for efficacy.**	
ondansetron CYP2D6 IM	• Follow drug label dosing recommendation.		
oxcarbazepine HLA-B normal risk (*15:02-negative)	• Follow drug label dosing recommendation.		
oxycodone CYP2D6 IM		• **Be alert to symptoms of insufficient pain relief.**	
pantoprazole CYP2C19 NM		• Initiate standard starting daily dose. • **Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis**. Daily dose may be given in divided doses. • **Monitor for efficacy.**	
paroxetine CYP2D6 IM	• Follow drug label dosing recommendation.		
pazopanib UGT1A1 IM	• Follow drug label dosing recommendation.		
peginterferon alfa-2a IFNL3-favorable-response genotype	• **High response rates** in treatment naïve patients. • Approximately 90% chance for SVR after 24–48 weeks of treatment. Weighs in favor of using PEG-interferon-alfa and ribavirin-containing regimens.		
peginterferon alfa-2b IFNL3-favorable-response genotype	• **High response rates** in treatment naïve patients. • Approximately 90% chance for SVR after 24–48 weeks of treatment. Weighs in favor of using PEG-interferon-alfa and ribavirin-containing regimens.		

perphenazine CYP2D6 IM		• Follow drug label dosing recommendation. • **Be alert to increased risk of side effects**.	
phenprocoumon Intermediate phenprocoumon sensitivity (incl. CYP4F2)		• **Patient may need reduced phenprocoumon dose** (consider dose reduction by 3 to 7 mg/week for maintenance dose)**.** • **Check INR more frequently.** • Be aware that other factors, such as clinical/demographic factors, drug interactions or other genes may influence the phenprocoumon dose requirement.	
phenytoin HLA-B normal risk (*15: 02-negative), CYP2C9 IM*2	• Follow drug label dosing recommendation.		
pimozide CYP2D6 IM		• **Use 80% of the standard maximal dose of pimozide and do not exceed 16 mg/day.**	
piroxicam CYP2C9 IM*2	• Follow drug label dosing recommendations.		
propafenone CYP2D6 IM			• **Adjust dose in response to plasma concentration and record ECG** or • **Select alternative drug** (e.g., sotalol, disopyramide, quinidine, amiodarone).
propofol CYP2B6 NM	• Follow drug label dosing recommendation.		
ribavirin IFNL3-favorable-response genotype	• **High response rates** in treatment naïve patients. • Approximately 70-90% chance for SVR after 24–48 weeks of treatment. Weighs in favor of using PEG-interferon-alfa and ribavirin-containing regimens.		
risperidone CYP2D6 IM		• **Adjust dose to clinical response** - lower doses may be needed.	
rosuvastatin SLCO1B1 normal function	• Follow drug label dosing recommendation.		
sertraline CYP2C19 NM	• Follow drug label dosing recommendation.		
sevoflurane Normal risk of MH	• RYR1 and CACNA1S phenotypes show no contraindication for the use of volatile anesthetics.		
simvastatin SLCO1B1 normal function	• Follow drug label dosing recommendation.		
siponimod CYP2C9 IM*2	• Follow drug label dosing recommendation.		
streptomycin MT-RNR1 normal risk	• Follow drug label dosing recommendation.		
succinylcholine Normal risk of MH	• RYR1 and CACNA1S phenotypes show no contraindication for the use of succinylcholine.		
tacrolimus CYP3A5 non-expresser, POR increased function	• Initiate therapy with standard recommended dose. • **Use TDM to guide dose adjustments.**		
tak-390mr CYP2C19 NM		• Initiate standard starting daily dose. • **Consider increasing dose by 50-100%** for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. • **Monitor for efficacy.**	
tamoxifen CYP2D6 IM			• **Consider alternative hormonal therapy** such as aromatase inhibitor for postmenopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women. • **If aromatase inhibitor use is contraindicated, consider use of a higher tamoxifen dose (40 mg/day).** • **Avoid concomitant use of CYP2D6 inhibitors** (strong to weak)**.**

tenoxicam CYP2C9 IM*2	• Follow drug label dosing recommendations.		
tetrabenazine CYP2D6 IM		• Follow drug label dosing recommendation. • **Be alert to increased risk of ADEs.**	
thioridazine CYP2D6 IM		• **Select alternative drug,** as thioridazine is contraindicated.	
tioguanine Normal thiopurine metabolism	• Follow drug label dosing recommendation.		
tramadol CYP2D6 IM		• **Be alert to decreased efficacy** (symptoms of insufficient pain relief). • **Consider dose increase.** • **If response is still inadequate, select alternative drug**- not oxycodone or codeine-	
trimipramine CYP2D6 IM, CYP2C19 NM		• High dose (e.g. depression): **Consider 25% reduction of recommended starting dose**. Utilize TDM to guide dose adjustment. • Low dose (e.g. neuropathic pain): Initiate therapy with recommended starting dose, but monitor closely for side effects.	
tropisetron[cs] CYP2D6 IM	• Follow drug label dosing recommendation.		
venlafaxine CYP2D6 IM		• **Avoid venlafaxine** or • **If side effects occur reduce the dose** and monitor the effect and side effects or check the plasma concentrations of venlafaxine and O-desmethylvenlafaxine.	
voriconazole CYP2C19 NM	• Follow drug label dosing recommendation.		
vortioxetine CYP2D6 IM	• Follow drug label dosing recommendation.		
warfarin Intermediate warfarin sensitivity (incl. CYP4F2)		• **Calculate dose with warfarin dose algorithm** (e.g. http://www.warfarindosing.org) or • Use recommended warfarin maintenance dose: 2.7-4.3 mg/day (19-30 mg/week). • **Consider higher starting dose** (3-9 mg at day 1 and 2).	
zuclopenthixol CYP2D6 IM		• **Reduce dose by 25%** or • **Select alternative drug.**	

Predictable drug - PGx interactions

Table shows potential interactions of specific drugs with patient's PGx profile. These drugs are related to biomarkers, for which drug label recommendations or dosing guidelines exist, or for which LoE is at least C. For suggested action and detailed information, please indicate drug of interest in patient's treatment and refer to SONOGEN detailed report or consult drug labels or dosing guidelines.

Normal risk		Use with caution	High risk
abacavir (4)	meloxicam (2)	acenocoumarol (1)	flecainide (1)
allopurinol (3)	mercaptopurine (3)	amitriptyline (2)	propafenone (2)
atazanavir (1)	mirtazapine (1)	aripiprazole (2)	tamoxifen (1)
atorvastatin (1)	nelfinavir (1)	atomoxetine (2)	
azathioprine (3)	ondansetron (1)	cevimeline (2)	
brexpiprazole (2)	oxcarbazepine (3)	clomipramine (2)	
capecitabine (2)	paroxetine (1)	codeine (2)	
carbamazepine (4)	pazopanib (2)	desipramine (2)	
carisoprodol (2)	peginterferon alfa-2a (1)	doxepin (2)	
carvedilol (2)	peginterferon alfa-2b (2)	iloperidone (2)	
celecoxib (2)	phenytoin (2)	imipramine (2)	
citalopram (2)	piroxicam (2)	irinotecan (2)	
clobazam (2)	propofol (1)	lansoprazole (1)	
clopidogrel (2)	ribavirin (1)	metoprolol (1)	
clozapine (2)	rosuvastatin (2)	nortriptyline (2)	
darifenacin (2)	sertraline (1)	omeprazole (2)	
diclofenac (1)	sevoflurane (2)	oxycodone (1)	
efavirenz (2)	simvastatin (1)	pantoprazole (2)	
escitalopram (2)	siponimod (4)	perphenazine (2)	
fesoterodine (2)	streptomycin (1)	phenprocoumon (1)	
fluorouracil (2)	succinylcholine (2)	pimozide (4)	
flurbiprofen (2)	tacrolimus (1)	risperidone (1)	
fluvoxamine (1)	tenoxicam (1)	tak-390mr (2)	
glyburide (2)	tioguanine (3)	tetrabenazine (4)	
haloperidol (1)	tropisetron^{CS} (1)	thioridazine (2)	
ibuprofen (1)	voriconazole (2)	tramadol (2)	
lornoxicam (1)	vortioxetine (2)	trimipramine (2)	
		venlafaxine (2)	
		warfarin (2)	
		zuclopenthixol (1)	

() PGx information included in the drug label; based on Pharmacogenomics Knowledgebase (PharmGKB) and classified into the following categories: (4) required, (3) recommended, (2) actionable, (1) informative

Disclaimer

The present individual treatment optimization proposal and the related information was generated by SONOGEN XP - a clinical decision support and pharmacogenetic expert system. This software is an in vitro medical device and has been developed according to the directive on in vitro diagnostic medical devices (Directive 98/79/EC of the European Parliament and of the Council). The containing information has been collected and reviewed to our best knowledge, however there is no guarantee that it contains the latest scientific findings and that all adverse or important outcomes will be reported in the literature and integrated in the SONOGEN XP software. The responsibility for a correct drug-treatment prescription lies with the treating physician and the user should always apply his independent professional judgement.

Limitation

This pharmacogenetic test will not detect all the known mutations of a gene. Absence of a detectable gene mutation does not rule out the possibility of an altered phenotype due to the presence of an undetected mutation or due to other factors influencing the drug efficacy, such as drug-drug-interactions, comorbidities or lifestyle habits.

Legend

Biomarker Relevance (BR)

	Genetic testing required. The drug label states that a genetic testing should be conducted before using this drug. This requirement may only be for a subset of patients. If the drug label states a test "should be" performed, this is to be interpreted as a requirement.
	Genetic testing recommended. The drug label states that a genetic testing is recommended before using this drug. This recommendation may only be for a subset of patients. If the drug label states a test "should be considered", this is to be interpreted as a recommendation.
	Actionable PGx. The drug label does not discuss testing for gene variants, but does contain information about changes in efficacy, dosage or toxicity (due to such variants). The drug label may mention contraindication of the drug in a subset of patients but does not require or recommend genetic testing.
	Informative PGx. The drug label mentions a gene/protein is involved in the metabolism or pharmacodynamics of the drug but gives no information to suggest that variation in this gene/protein leads to a different response.

Level of Evidence (LoE)

E	The variant-drug combination is based on published incomplete case reports, non-significant studies or in vitro, molecular or functional assay evidence only.
D	The variant-drug combination is based on published case reports, well documented, and having relevant pharmacokinetic or clinical endpoints.
C	The variant-drug combination shows moderate evidence of an association (it is replicated but there may be some studies that do not show statistical significance, and/or the effect size may be small). Or drug label information on PGx relevant genes with potential influence on pharmacokinetics, without information on specific variants.
B	The variant-drug combination shows good evidence of an association (it is replicated in more than one cohort with significant p-values, and preferably will have a strong effect size). Or drug label information on specific variants of PGx relevant genes with potential influence on pharmacokinetics. Or the variant-drug combination and recommendation are reflected in peer reviewed articles.
A	The variant-drug combination is reflected in a pharmacogenetic guideline (e.g. CPIC, DPWG), or implemented at a pharmacogenomic research network site (e.g. www.warfarindosing.org) or in another major health system. Or FDA box warning. Or FDA drug label recommendation on pharmacogenetic testing.

PGx - Phenotype

APS	average pain sensitivity
HPS	high pain sensitivity
IM	intermediate metabolizer
IM*2	IM with one *2 allele or equivalent (*8, *11, *12)
IM*3	IM with one *3 allele or equivalent (*4, *5, *6, *13, *14, *15, *25)
LPS	low pain sensitivity
NM	normal metabolizer
PM	poor metabolizer
PM*2	PM with two *2 alleles or equivalent (*8, *11, *12)
PM*3	PM with two *3 alleles or equivalent (*4, *5, *6, *13, *14, *15, *25)
PM*2/*3	PM with one *2 allele or equivalent (*8, *11, *12) and one *3 allele or equivalent (*4, *5, *6, *13, *14, *15, *25)
RM	rapid metabolizer
UM	ultrarapid metabolizer

For further information, please refer to the detailed report.

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