KARKINOS

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Version 1 | XXXXXXXXXX

Whole Genome Sequencing Germline Testing Report

LIMS No.	**XXXXXXXXXX**	**Hosp. Sample ID**	XXXXXXXXXX
Name	**XXXXXXXXXX**	**Specimen type**	Blood
Age | Gender	XXXXXXXXXX	**Collection date**	XXXXXXXXXX
Test Code	XXXXXXXXXX	**Report date**	XXXXXXXXXX
		Referring hospital	XXXXXXXXXX
		Referred by physician	XXXXXXXXXX

Executive Summary

Analysis identified a total of 57 clinically actionable Pharmacogenomic variants.

Analysis identified a heterozygous variant (c.127G>A, p.Ala43Thr) in the SDHB gene associated with Autosomal Dominant Pheochromocytoma. Additional incidental findings include a heterozygous variant (c.68_69delAG, p.Glu23Valfs*17) in BRCA1 gene linked to Autosomal Dominant Familian Breast and Ovarian Cancer.

Analysis additionally identified carrier status in CFTR gene (c.350G>A, Autosomal Recessive Cystic Fibrosis).

Genomic Findings

Incidental Actionable Germline Variants : 2

Incidental Germline Variants (Carrier Status) : 1

Copy Number/Structural Variants : 0

Mitochondrial DNA Variants : 0

Clinically Actionable Pharmacogenomics marker(s) : 57

Significant Genomic Findings

Incidental and Clinically Actionable Germline variants

Gene / Transcript / Variant Type	Variant	Zygosity	Coverage / VAF	Disorder / Inheritance	Variant Classification / Attributes
SDHB NM_003000.3 missense variant	1:17044834 c.127G>A p.Ala43Thr	**Heterozygous**	25 56.00%	Pheochromocytoma Autosomal Dominant	**Likely pathogenic Attributes: PM2, PM1, PP3, PM5**
BRCA1 NM_007294.4 frameshift deletion	c.68_69delAG p.Glu23Valfs*17 17:43124028 rs80357914 Exon 2	**Heterozygous**	31 55.2%	Breast-ovarian cancer familial 1- Autosomal Dominant	**Pathogenic Attributes: PM1,PVS1,PM2,PP5**

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Incidental Germline variants (Carrier Status)

Gene / Transcript / Variant Type	Variant	Zygosity	Coverage / VAF	Disorder / Inheritance	Variant Classification / Attributes
CFTR **NM_000492.4** **missense variant**	7:117530975 c.350G>A p.Arg117His	**Heterozygous**	31 53%	Cystic fibrosis Autosomal Recessive	**Pathogenic** **Attributes:** **PM1,PM2,PP3,PP5**

Copy Number variants
No variant detected.

Structural variants
No variant detected.

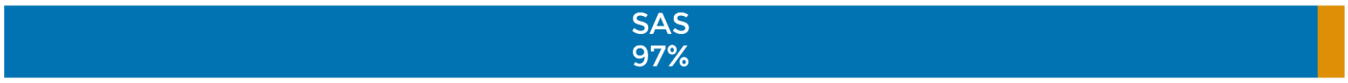
Mitochondrial DNA Variants
No variant detected.

HLA Alleles

HLA-A	HLA-B	HLA-C	HLA-DQA1	HLA-DQB1	HLA-DRB1
A*32:01	B*35:01	C*04:01	-	DQB1*03:01	DRB1*10:01
A*68:01	B*40:06	C*15:02	-	DQB1*05:01	DRB1*11:01

Genomic Population Ancestry Insights

Superpopulation Ancestry



Individual Population Breakdown

Superpopulation Breakdown

South Asian Ancestry (SAS)	97.0%	European Ancestry (EUR)	2.0%
		Others	1.0%

Individual Population Breakdown

Gujarati (GIH)	25.0%	Punjabi (PJL)	17.0%
Bengali (BEB)	21.0%	Tamil (STU)	15.0%
Telugu (ITU)	19.0%	British (GBR)	2.0%
		Others	1.0%

Pharmacogenomic Associations

signify variants which suggest dosage modification and **signify variants which suggest potential for adverse drug reaction.**

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2D6 codeine	Analgesic	CYP2D6*1 *1/*4	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 codeine	Analgesic	CYP2D6*4 *1/*4	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 hydrocodone	Analgesic	CYP2D6*4 *1/*4	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 hydrocodone	Analgesic	CYP2D6*1 *1/*4	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 tramadol	Analgesic	CYP2D6*1 *1/*4	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 tramadol	Analgesic	CYP2D6*4 *1/*4	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 tramadol	Analgesic	CYP2D6*1 *1/*4	**Drug Efficacy**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 codeine	Analgesic	CYP2D6*1 *1/*4	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 tramadol	Analgesic	CYP2D6*1 *1/*4	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 codeine	Analgesic	CYP2D6*4 *1/*4	**Drug Efficacy**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 codeine	Analgesic	CYP2D6*1 *1/*4	**Drug Efficacy**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2D6 tramadol	Analgesic	CYP2D6*4 *1/*4	**Drug Efficacy**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 tropisetron	Antiemetic	CYP2D6*1 *1/*4	**Drug Efficacy**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 ondansetron	Antiemetic	CYP2D6*4 *1/*4	**Drug Efficacy**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 ondansetron	Antiemetic	CYP2D6*1 *1/*4	**Drug Efficacy**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 tropisetron	Antiemetic	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 tropisetron	Antiemetic	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 metoprolol	Cardiovascular disorders	CYP2D6*1 *1/*4	**Dosage Modification**	**Lower Dose**	**Intermediate Metabolizer**	**1A**
	CYP2D6 metoprolol	Cardiovascular disorders	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 metoprolol	Cardiovascular disorders	CYP2D6*4 *1/*4	**Dosage Modification**	**Lower Dose**	**Intermediate Metabolizer**	**1A**
	CYP2D6 propafenone	Cardiovascular disorders	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 flecainide	Cardiovascular disorders	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 metoprolol	Cardiovascular disorders	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 flecainide	Cardiovascular disorders	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2C9 fluvastatin	Cardiovascular disorders	CYP2C9*1 *1/*3	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 fluvastatin	Cardiovascular disorders	CYP2C9*3 *1/*3	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 fluvastatin	Cardiovascular disorders	CYP2C9*1 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 fluvastatin	Cardiovascular disorders	CYP2C9*3 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 omeprazole	Gastroenterology	CYP2C19*2 *2/*38	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 lansoprazole	Gastroenterology	CYP2C19*2 *2/*38	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 omeprazole	Gastroenterology	CYP2C19*2 *2/*38	**Drug Efficacy**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 pantoprazole	Gastroenterology	CYP2C19*2 *2/*38	**Drug Efficacy**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 lansoprazole	Gastroenterology	CYP2C19*2 *2/*38	**Drug Efficacy**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 dexlansoprazole	Gastroenterology	CYP2C19*2 *2/*38	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 pantoprazole	Gastroenterology	CYP2C19*2 *2/*38	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 warfarin	Hematology	CYP2C9*3 *1/*3	**Dosage Modification**	Lower Dose	Intermediate Metabolizer	1A
	CYP2C9 warfarin	Hematology	CYP2C9*1 *1/*3	**Dosage Modification**	Higher Dose	Intermediate Metabolizer	1A

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2C9 warfarin	Hematology	CYP2C9*3 *1/*3	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 warfarin	Hematology	CYP2C9*1 *1/*3	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 warfarin	Hematology	CYP2C9*3 *1/*3	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 clopidogrel	Hematology	CYP2C19*2 *2/*38	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 acenocoumarol	Hematology	CYP2C9*1 *1/*3	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1B
	CYP2C9 acenocoumarol	Hematology	CYP2C9*3 *1/*3	**Dosage Modification**	Lower Dose	Intermediate Metabolizer	1B
	CYP2C9 acenocoumarol	Hematology	CYP2C9*1 *1/*3	**Dosage Modification**	Higher Dose	Intermediate Metabolizer	1B
	CYP2C19 clopidogrel	Hematology	CYP2C19*2 *2/*38	**Drug Efficacy; Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 clopidogrel	Hematology	CYP2C19*2 *2/*38	**Drug Efficacy**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 warfarin	Hematology	CYP2C9*1 *1/*3	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 acenocoumarol	Hematology	CYP2C9*3 *1/*3	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1B
	warfarin	Hematology	chr10:94645745 G/A AG	**Dosage Modification**	Lower Dose	-	1A
	VKORC1 warfarin	Hematology	chr16:31093557 G/A GG	**Dosage Modification**	Higher Dose	-	1B

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP4F2 warfarin	Hematology	chr19:15879621 C/T CC	**Dosage Modification**	Lower Dose	-	1A
	VKORC1 acenocoumarol	Hematology	chr16:31096368 C/T CC	**Dosage Modification**	Higher Dose	-	1A
	VKORC1 warfarin	Hematology	chr16:31091000 C/T TT	**Dosage Modification**	Higher Dose	-	1B
	VKORC1 warfarin	Hematology	chr16:31092475 A/G GG	**Dosage Modification**	Higher Dose	-	1B
	VKORC1 warfarin	Hematology	chr16:31093188 C/G CC	**Dosage Modification**	Higher Dose	-	1B
	VKORC1 warfarin	Hematology	chr16:31096368 C/T CC	**Dosage Modification**	Higher Dose	-	1A
	VKORC1 phenprocoumon	Hematology	chr16:31096368 C/T CC	**Dosage Modification**	Higher Dose	-	1A
	TPMT azathioprine	Immunology	TPMT*1 *1/*1	**Dosage Modification**	Higher Dose	Normal Metabolizer	1A
	CYP3A5 tacrolimus	Immunology	CYP3A5*3 *3/*3	**Dosage Modification**	Lower Dose	Poor Metabolizer	1A
	IFNL3;IFNL4 peginterferon alfa-2a;peginterferon alfa-2b;ribavirin;telaprevir	Infectious Diseases	chr19:39248147 C/T CT	**Drug Efficacy**	Decreased Response	-	1A
	IFNL3;IFNL4 peginterferon alfa-2a;peginterferon alfa-2b;ribavirin	Infectious Diseases	chr19:39248147 C/T CT	**Drug Efficacy**	Decreased Response	-	1A
	IFNL3;IFNL4 boceprevir;peginterferon alfa-2a;peginterferon alfa-2b;ribavirin	Infectious Diseases	chr19:39248147 C/T CT	**Drug Efficacy**	Decreased Response	-	1A

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2C19 voriconazole	Infectious Diseases	CYP2C19*2 *2/*38	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2B6 efavirenz	Infectious Diseases	CYP2B6*1 *1/*4	**Dosage Modification**	Higher Dose	Rapid Metabolizer	1A
	IFNL3 interferons;peginterferon alfa-2a;peginterferon alfa-2b;ribavirin	Infectious Diseases	chr19:39252525 T/G TT	**Drug Efficacy**	Increased Response	-	1B
	IFNL4 peginterferon alfa-2a;peginterferon alfa-2b;ribavirin	Infectious Diseases	chr19:39248513 CTT/CG TT/TT	**Drug Efficacy**	Increased Response	-	1B
	CYP2C9 lornoxicam	NSAID	CYP2C9*1 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 flurbiprofen	NSAID	CYP2C9*1 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 flurbiprofen	NSAID	CYP2C9*3 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 lornoxicam	NSAID	CYP2C9*3 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 tenoxicam	NSAID	CYP2C9*3 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 piroxicam	NSAID	CYP2C9*1 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 piroxicam	NSAID	CYP2C9*3 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C9 meloxicam	NSAID	CYP2C9*1 *1/*3	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2C9 meloxicam	**NSAID**	CYP2C9*3 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 ibuprofen	**NSAID**	CYP2C9*1 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 ibuprofen	**NSAID**	CYP2C9*3 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 tenoxicam	**NSAID**	CYP2C9*1 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 celecoxib	**NSAID**	CYP2C9*1 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 celecoxib	**NSAID**	CYP2C9*3 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 phenytoin	**Neurology**	CYP2C9*1 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 phenytoin	**Neurology**	CYP2C9*3 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 phenytoin	**Neurology**	CYP2C9*1 *1/*3	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 siponimod	**Neurology**	CYP2C9*3 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 siponimod	**Neurology**	CYP2C9*1 *1/*3	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C9 phenytoin	**Neurology**	CYP2C9*3 *1/*3	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2D6 tamoxifen	Oncology	CYP2D6*1 *1/*4	**Drug Efficacy**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 tamoxifen	Oncology	CYP2D6*4 *1/*4	**Drug Efficacy**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	TPMT mercaptopurine	Oncology	TPMT*1 *1/*1	**Dosage Modification**	Higher Dose	Normal Metabolizer	1A
	CYP2D6 tamoxifen	Oncology	CYP2D6*4 *1/*4	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	EGFR gefitinib	Oncology	chr7:55191822 T/G TT	**Drug Efficacy**	Decreased Response	-	1A
	NUDT15 mercaptopurine	Oncology	chr13:48045719 C/T CC	**Dosage Modification**	Higher Dose	-	1A
	NUDT15 mercaptopurine	Oncology	NUDT15*1 *1/*1	**Dosage Modification**	Higher Dose	Normal Metabolizer	1A
	CYP2D6 tamoxifen	Oncology	CYP2D6*1 *1/*4	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 escitalopram	Psychiatry	CYP2C19*2 *2/*38	**Drug Metabolism**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2C19 citalopram	Psychiatry	CYP2C19*2 *2/*38	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 atomoxetine	Psychiatry	CYP2D6*1 *1/*4	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 amitriptyline	Psychiatry	CYP2D6*1 *1/*4	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A
	CYP2D6 amitriptyline	Psychiatry	CYP2D6*4 *1/*4	**Adverse Drug Reaction**	Abnormal / Priority / High Risk	Intermediate Metabolizer	1A

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2D6 imipramine	**Psychiatry**	CYP2D6*1 *1/*4	**Dosage Modification**	**Lower Dose**	**Intermediate Metabolizer**	**1A**
	CYP2D6 imipramine	**Psychiatry**	CYP2D6*4 *1/*4	**Dosage Modification**	**Lower Dose**	**Intermediate Metabolizer**	**1A**
	CYP2C19 amitriptyline	**Psychiatry**	CYP2C19*2 *2/*38	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 nortriptyline	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 trimipramine	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 desipramine	**Psychiatry**	CYP2D6*4 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 desipramine	**Psychiatry**	CYP2D6*1 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 atomoxetine	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 doxepin	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 doxepin	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 desipramine	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 desipramine	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 paroxetine	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2D6 paroxetine	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 imipramine	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 aripiprazole	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 aripiprazole	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 venlafaxine	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 venlafaxine	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 risperidone	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 risperidone	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 imipramine	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 trimipramine	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 haloperidol	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 haloperidol	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2D6 nortriptyline	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 clomipramine	**Psychiatry**	CYP2D6*1 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C19 clomipramine	**Psychiatry**	CYP2C19*2 *2/*38	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C19 doxepin	**Psychiatry**	CYP2C19*2 *2/*38	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 nortriptyline	**Psychiatry**	CYP2D6*1 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C19 citalopram	**Psychiatry**	CYP2C19*2 *2/*38	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C19 sertraline	**Psychiatry**	CYP2C19*2 *2/*38	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 atomoxetine	**Psychiatry**	CYP2D6*4 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C19 trimipramine	**Psychiatry**	CYP2C19*2 *2/*38	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2C19 imipramine	**Psychiatry**	CYP2C19*2 *2/*38	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 imipramine	**Psychiatry**	CYP2D6*4 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 imipramine	**Psychiatry**	CYP2D6*1 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2D6 venlafaxine	**Psychiatry**	CYP2D6*4 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 venlafaxine	**Psychiatry**	CYP2D6*1 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 fluvoxamine	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 fluvoxamine	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 zuclopenthixol	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 zuclopenthixol	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 clomipramine	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 clomipramine	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 amitriptyline	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 amitriptyline	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 vortioxetine	**Psychiatry**	CYP2D6*4 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 vortioxetine	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**

	Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
	CYP2D6 atomoxetine	**Psychiatry**	CYP2D6*1 *1/*4	**Drug Metabolism**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 nortriptyline	**Psychiatry**	CYP2D6*4 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CYP2D6 clomipramine	**Psychiatry**	CYP2D6*4 *1/*4	**Adverse Drug Reaction**	**Abnormal / Priority / High Risk**	**Intermediate Metabolizer**	**1A**
	CFTR ivacaftor / tezacaftor	**Pulmonary disorders**	chr7:117559590 ATCT/A CTT/CTT	**Drug Efficacy**	**Decreased Response**	**-**	**1A**

Other Findings

Variants of Uncertain Significance

Gene / Transcript / Variant Type	Variant	Zygosity	Coverage / VAF	Disorder / Inheritance	Variant Classification / Attributes
COL1A2 NM_000089.4 missense variant	7:94427672 c.3313G>A p.Gly1105Ser	**Heterozygous**	47 68.09%	Osteogenesis imperfecta type III Autosomal Dominant	**Uncertain significance Attributes: PP2**
TTN NM_001267550.2 missense variant	2:178532292 c.104323C>G p.Arg34775Gly	**Heterozygous**	39 41.03%	Cardiomyopathy dilated 1G Autosomal Dominant	**Uncertain significance Attributes: PM2, PP2, PP3**
FLNC NM_001458.5 missense variant	7:128841530 c.2084G>A p.Arg695His	**Heterozygous**	47 48.94%	Arrhythmogenic right ventricular dysplasia, familial Autosomal Dominant	**Uncertain significance Attributes: PM2, PP2**
MYH14 NM_024729.4 missense variant	19:50293586 c.5245C>T p.Arg1749Cys	**Heterozygous**	53 37.74%	Deafness, autosomal dominant 4A Autosomal Dominant	**Uncertain significance Attributes: PM2, PP2**

Pharmacogenomic Associations

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38500899 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38444211 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;iso	**Anaesthesiology**	chr19:38457545 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
flurane;methoxyflurane;sevoflurane;succinylcholine						
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38500655 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S desflurane	**Anaesthesiology**	chr1:201091993 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38455471 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38448673 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38440829 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38580094 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38500654 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyfl	**Anaesthesiology**	chr19:38455359 A/C AA	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
urane;sevofluran e;succinylcholine						
RYR1 desflurane;enflur ane;halothane;iso flurane;methoxyfl urane;sevofluran e;succinylcholine	**Anaesthesiology**	chr19:38448712 G/C GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S methoxyflurane	**Anaesthesiology**	chr1:201091993 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S enflurane	**Anaesthesiology**	chr1:201060815 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S methoxyflurane	**Anaesthesiology**	chr1:201060815 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S sevoflurane	**Anaesthesiology**	chr1:201060815 C/T CC	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
CACNA1S halothane	**Anaesthesiology**	chr1:201060815 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S isoflurane	**Anaesthesiology**	chr1:201060815 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S succinylcholine	**Anaesthesiology**	chr1:201060815 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S enflurane	**Anaesthesiology**	chr1:201091993 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S halothane	**Anaesthesiology**	chr1:201091993 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S isoflurane	**Anaesthesiology**	chr1:201091993 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S succinylcholine	**Anaesthesiology**	chr1:201091993 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S sevoflurane	**Anaesthesiology**	chr1:201091993 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflur	**Anaesthesiology**	chr19:38451842 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
ane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine						
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38512321 G/AGG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38543832 G/T GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38499644 TGGA/T GAG/GAG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38584989 T/C TT	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38499993 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38496283 C/G CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38500898 C/G CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38499655 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38457546 G/T GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38446710 G/C GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38499731 G/C GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38451850 C/G CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38444212 G/T GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38580370 C/G CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyfl	**Anaesthesiology**	chr19:38580004 A/G AA	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
urane;sevofluran e;succinylcholine						
RYR1 desflurane;enflur ane;halothane;iso flurane;methoxyfl urane;sevofluran e;succinylcholine	**Anaesthesiology**	chr19:38580440 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
RYR1 desflurane;enflur ane;halothane;iso flurane;methoxyfl urane;sevofluran e;succinylcholine	**Anaesthesiology**	chr19:38455528 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
RYR1 desflurane;enflur ane;halothane;iso flurane;methoxyfl urane;sevofluran e;succinylcholine	**Anaesthesiology**	chr19:38500642 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
RYR1 desflurane;enflur ane;halothane;iso flurane;methoxyfl urane;sevofluran e;succinylcholine	**Anaesthesiology**	chr19:38500643 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
RYR1 desflurane;enflur ane;halothane;iso flurane;methoxyfl urane;sevofluran e;succinylcholine	**Anaesthesiology**	chr19:38500636 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
RYR1 desflurane;enflur ane;halothane;iso flurane;methoxyfl urane;sevofluran e;succinylcholine	**Anaesthesiology**	chr19:38499670 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
RYR1 desflurane;enflur ane;halothane;iso flurane;methoxyfl urane;sevofluran e;succinylcholine	**Anaesthesiology**	chr19:38499997 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38499223 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38440802 T/C TT	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CACNA1S desflurane	**Anaesthesiology**	chr1:201060815 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38580114 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38494579 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38494564 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38494565 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38580403 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
RYR1 desflurane;enflurane;halothane;isoflurane;methoxyflurane;sevoflurane;succinylcholine	**Anaesthesiology**	chr19:38499975 G/A GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
SLCO1B1 pitavastatin	**Cardiovascular disorders**	chr12:21178615 T/C TT	**Drug Metabolism**	**Increased Metabolism**	**-**	**1A**
SLCO1B1 lovastatin;lovastatin acid	**Cardiovascular disorders**	chr12:21178615 T/C TT	**Drug Metabolism**	**Increased Metabolism**	**-**	**1A**
SLCO1B1 pitavastatin	**Cardiovascular disorders**	SLCO1B1*37 *1/*37	**Drug Metabolism**	**Normal / Routine / Low Risk**	**Normal Function**	**1A**
SLCO1B1 rosuvastatin	**Cardiovascular disorders**	SLCO1B1*37 *1/*37	**Drug Metabolism**	**Normal / Routine / Low Risk**	**Normal Function**	**1A**
SLCO1B1 rosuvastatin	**Cardiovascular disorders**	SLCO1B1*1 *1/*37	**Drug Metabolism**	**Normal / Routine / Low Risk**	**Normal Function**	**1A**
SLCO1B1 atorvastatin	**Cardiovascular disorders**	SLCO1B1*1 *1/*37	**Drug Metabolism**	**Normal / Routine / Low Risk**	**Normal Function**	**1A**
SLCO1B1 pravastatin	**Cardiovascular disorders**	SLCO1B1*1 *1/*37	**Drug Metabolism**	**Normal / Routine / Low Risk**	**Normal Function**	**1A**
SLCO1B1 lovastatin	**Cardiovascular disorders**	chr12:21178615 T/C TT	**Adverse Drug Reaction**	**Decreased Risk**	**-**	**1A**
SLCO1B1 pitavastatin	**Cardiovascular disorders**	SLCO1B1*1 *1/*37	**Drug Metabolism**	**Normal / Routine / Low Risk**	**Normal Function**	**1A**
SLCO1B1 rosuvastatin	**Cardiovascular disorders**	SLCO1B1*1 *1/*37	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**Normal Function**	**1A**
SLCO1B1 atorvastatin	**Cardiovascular disorders**	SLCO1B1*37 *1/*37	**Drug Metabolism**	**Normal / Routine / Low Risk**	**Normal Function**	**1A**
SLCO1B1 simvastatin;simvastatin acid	**Cardiovascular disorders**	SLCO1B1*1 *1/*37	**Drug Metabolism**	**Normal / Routine / Low Risk**	**Normal Function**	**1A**
ABCG2 rosuvastatin	**Cardiovascular disorders**	chr4:88131171 G/T GT	**Drug Metabolism**	**Decreased Metabolism**	**-**	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
SLCO1B1 rosuvastatin	Cardiovascular disorders	chr12:21178615 T/C TT	**Adverse Drug Reaction**	Decreased Risk	-	1A
SLCO1B1 fluvastatin	Cardiovascular disorders	chr12:21178615 T/C TT	**Adverse Drug Reaction**	Decreased Risk	-	1A
SLCO1B1 fluvastatin	Cardiovascular disorders	chr12:21178615 T/C TT	**Drug Metabolism**	Increased Metabolism	-	1A
SLCO1B1 pravastatin	Cardiovascular disorders	chr12:21178615 T/C TT	**Adverse Drug Reaction**	Decreased Risk	-	1A
SLCO1B1 atorvastatin	Cardiovascular disorders	chr12:21178615 T/C TT	**Adverse Drug Reaction**	Decreased Risk	-	1A
SLCO1B1 simvastatin	Cardiovascular disorders	SLCO1B1*1 *1/*37	**Adverse Drug Reaction**	Normal / Routine / Low Risk	Normal Function	1A
SLCO1B1 pravastatin	Cardiovascular disorders	SLCO1B1*1 *1/*37	**Adverse Drug Reaction**	Normal / Routine / Low Risk	Normal Function	1A
SLCO1B1 fluvastatin	Cardiovascular disorders	SLCO1B1*1 *1/*37	**Adverse Drug Reaction**	Normal / Routine / Low Risk	Normal Function	1A
SLCO1B1 atorvastatin	Cardiovascular disorders	SLCO1B1*1 *1/*37	**Adverse Drug Reaction**	Normal / Routine / Low Risk	Normal Function	1A
SLCO1B1 fluvastatin	Cardiovascular disorders	SLCO1B1*1 *1/*37	**Drug Metabolism**	Normal / Routine / Low Risk	Normal Function	1A
SLCO1B1 simvastatin	Cardiovascular disorders	chr12:21178615 T/C TT	**Adverse Drug Reaction**	Decreased Risk	-	1A
SLCO1B1 lovastatin	Cardiovascular disorders	SLCO1B1*1 *1/*37	**Adverse Drug Reaction**	Normal / Routine / Low Risk	Normal Function	1A
SLCO1B1 simvastatin;simvastatin acid	Cardiovascular disorders	chr12:21178615 T/C TT	**Drug Metabolism**	Increased Metabolism	-	1A
SLCO1B1 pravastatin	Cardiovascular disorders	chr12:21178615 T/C TT	**Drug Metabolism**	Increased Metabolism	-	1A
SLCO1B1 lovastatin;lovastatin acid	Cardiovascular disorders	SLCO1B1*1 *1/*37	**Drug Metabolism**	Normal / Routine / Low Risk	Normal Function	1A

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
SLCO1B1 rosuvastatin	Cardiovascular disorders	chr12:21178615 T/C TT	**Drug Metabolism**	Increased Metabolism	-	1A
SLCO1B1 atorvastatin	Cardiovascular disorders	chr12:21178615 T/C TT	**Drug Metabolism**	Increased Metabolism	-	1A
F5 hormonal contraceptives for systemic use	Contraceptives	chr1:169549811 C/T CC	**Adverse Drug Reaction**	Decreased Risk	-	1A
VKORC1 warfarin	Hematology	chr16:31096368 C/T CC	**Adverse Drug Reaction**	Decreased Risk	-	1B
CYP3A5 tacrolimus	Immunology	CYP3A5*3 *3/*3	**Drug Metabolism**	-	Poor Metabolizer	1B
CYP3A5 tacrolimus	Immunology	CYP3A5*3 *3/*3	**Drug Metabolism**	-	Poor Metabolizer	1A
TPMT azathioprine	Immunology	TPMT*1 *1/*1	**Adverse Drug Reaction**	Normal / Routine / Low Risk	Normal Metabolizer	1A
NUDT15 azathioprine	Immunology	chr13:48045719 C/T CC	**Adverse Drug Reaction**	Normal / Routine / Low Risk	-	1A
CYP3A5 tacrolimus	Immunology	CYP3A5*3 *3/*3	**Drug Metabolism**	-	Poor Metabolizer	1B
MT-RNR1 kanamycin	Infectious Diseases	chrM:1095 T/C T	**Adverse Drug Reaction**	Normal / Routine / Low Risk	-	1A
HLA-A efavirenz	Infectious Diseases	HLA-A*33:03 *24:02/*33:03	**Adverse Drug Reaction**	-	-	1A
CYP2B6 efavirenz	Infectious Diseases	CYP2B6*1 *1/*4	**Drug Metabolism**	Normal / Routine / Low Risk	Rapid Metabolizer	1A
CYP2B6 efavirenz	Infectious Diseases	CYP2B6*4 *1/*4	**Drug Metabolism**	Normal / Routine / Low Risk	Rapid Metabolizer	1A
CYP2B6 efavirenz	Infectious Diseases	CYP2B6*1 *1/*4	**Adverse Drug Reaction**	Normal / Routine / Low Risk	Rapid Metabolizer	1A
HLA-B efavirenz	Infectious Diseases	HLA-B*44:03 *44:03/*51:01	**Adverse Drug Reaction**	-	-	1A

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
MT-RNR1 streptomycin	**Infectious Diseases**	chrM:1494 C/T C	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-RNR1 gentamicin	**Infectious Diseases**	chrM:1494 C/T C	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-RNR1 tobramycin	**Infectious Diseases**	chrM:1494 C/T C	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-RNR1 gentamicin	**Infectious Diseases**	chrM:1095 T/C T	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-ND1;MT-RNR1 gentamicin	**Infectious Diseases**	chrM:1555 A/G A	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-RNR1 kanamycin	**Infectious Diseases**	chrM:1555 A/G A	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-RNR1 streptomycin	**Infectious Diseases**	chrM:1555 A/G A	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CYP2B6 efavirenz	**Infectious Diseases**	chr19:41006936 G/T GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
NAT2 Drugs For Treatment Of Tuberculosis;isoniazid	**Infectious Diseases**	NAT2*4 *4/*6	**Adverse Drug Reaction**	-	-	**1B**
MT-RNR1 aminoglycoside antibacterials	**Infectious Diseases**	chrM:1095 T/C T	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-RNR1 aminoglycoside antibacterials	**Infectious Diseases**	chrM:1494 C/T C	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
CYP2B6 efavirenz	**Infectious Diseases**	chr19:41006936 G/T GG	**Drug Metabolism**	**Increased Metabolism**	-	**1A**
MT-RNR1 streptomycin	**Infectious Diseases**	chrM:1095 T/C T	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-RNR1 kanamycin	**Infectious Diseases**	chrM:1494 C/T C	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-RNR1 tobramycin	**Infectious Diseases**	chrM:1555 A/G A	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
MT-RNR1 amikacin	**Infectious Diseases**	chrM:1555 A/G A	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
MT-RNR1 aminoglycoside antibacterials	**Infectious Diseases**	chrM:1555 A/G A	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97450065 TG/T GG	**Gene Activity**	**Increased Activity**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97573863 C/T CC	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97573943 C/A CC	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97593343 C/A CC	**Gene Activity**	**Increased Activity**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97579893 G/C GG	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97699474 T/C TT	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
DPYD capecitabine	**Oncology**	chr1:97579893 G/C GG	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97740410 GATGA/G ATGA/ATGA	**Gene Activity**	**Increased Activity**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97515787 A/C AA	**Gene Activity**	**Increased Activity**	-	**1A**
DPYD capecitabine	**Oncology**	chr1:97515787 A/C AA	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97234991 G/T GG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97691776 G/A GG	**Gene Activity**	**Increased Activity**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97450058 C/T CC	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
DPYD fluorouracil	**Oncology**	chr1:97515865 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
DPYD fluorouracil	**Oncology**	chr1:97515839 T/C TT	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
DPYD fluorouracil	**Oncology**	chr1:97305364 C/T CC	**Gene Activity**	**Increased Activity**	**-**	**1A**
DPYD fluorouracil	**Oncology**	chr1:97450058 C/T CC	**Gene Activity**	**Increased Activity**	**-**	**1A**
DPYD fluorouracil	**Oncology**	chr1:97515787 A/C AA	**Adverse Drug Reaction**	**Decreased Risk**	**-**	**1A**
DPYD tegafur	**Oncology**	chr1:97082391 T/A TT	**Adverse Drug Reaction**	**Decreased Risk**	**-**	**1A**
DPYD tegafur	**Oncology**	chr1:97450058 C/T CC	**Adverse Drug Reaction**	**Decreased Risk**	**-**	**1A**
DPYD tegafur	**Oncology**	chr1:97515787 A/C AA	**Adverse Drug Reaction**	**Decreased Risk**	**-**	**1A**
DPYD fluorouracil	**Oncology**	chr1:97450190 G/A GG	**Adverse Drug Reaction**	**Decreased Risk**	**-**	**1A**
NUDT15 mercaptopurine	**Oncology**	NUDT15*1 *1/*1	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**Normal Metabolizer**	**1A**
TPMT mercaptopurine	**Oncology**	TPMT*1 *1/*1	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**Normal Metabolizer**	**1A**
DPYD fluorouracil	**Oncology**	chr1:97079071 C/A CC	**Gene Activity**	**Increased Activity**	**-**	**1A**
DPYD capecitabine	**Oncology**	chr1:97450058 C/T CC	**Adverse Drug Reaction**	**Decreased Risk**	**-**	**1A**
DPYD fluorouracil	**Oncology**	chr1:97883329 A/G AG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**
DPYD fluorouracil	**Oncology**	chr1:97082391 T/A TT	**Gene Activity**	**Increased Activity**	**-**	**1A**
DPYD capecitabine	**Oncology**	chr1:97883329 A/G AG	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	**-**	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
DPYD fluorouracil	**Oncology**	chr1:97450068 A/G AA	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97450190 G/A GG	**Gene Activity**	**Increased Activity**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97515923 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97699535 T/C TT	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97699474 T/C TT	**Gene Activity**	**Increased Activity**	-	**1A**
DPYD capecitabine	**Oncology**	chr1:97305364 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD capecitabine	**Oncology**	chr1:97082391 T/A TT	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
DPYD capecitabine	**Oncology**	chr1:97515839 T/C TT	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD capecitabine	**Oncology**	chr1:97699535 T/C TT	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD capecitabine	**Oncology**	chr1:97450068 A/G AA	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD capecitabine	**Oncology**	chr1:97573863 C/T CC	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97579893 G/C GG	**Gene Activity**	**Increased Activity**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97305364 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97082391 T/A TT	**Adverse Drug Reaction**	**Decreased Risk**	-	**1A**
DPYD fluorouracil	**Oncology**	chr1:97573943 C/A CC	**Gene Activity**	**Increased Activity**	-	**1A**
DPYD capecitabine	**Oncology**	chr1:97515865 C/T CC	**Adverse Drug Reaction**	**Normal / Routine / Low Risk**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
CYP2B6 sertraline	Psychiatry	CYP2B6*1 *1/*4	**Drug Metabolism**	Normal / Routine / Low Risk	Rapid Metabolizer	1A
CYP2B6 sertraline	Psychiatry	CYP2B6*4 *1/*4	**Drug Metabolism**	Normal / Routine / Low Risk	Rapid Metabolizer	1A
CYP3A4 quetiapine	Psychiatry	CYP3A4*1 *1/*1	**Drug Metabolism**	-	-	1A
CYP2A6 nicotine	Psychoactive	CYP2A6*1 *1/*18	**Drug Metabolism**	-	-	1B
CFTR ivacaftor	Pulmonary disorders	chr7:117642472 G/A GG	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117642451 G/A GG	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117535285 T/G TT	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117534363 G/A GG	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117530974 C/T CC	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117530953 G/C GG	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117530955 C/A CC	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117509089 C/T CC	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117509069 C/T CC	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117611649 C/T CC	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117611650 G/A GG	**Drug Efficacy**	Unknown Response	-	1A
CFTR ivacaftor	Pulmonary disorders	chr7:117606695 C/T CC	**Drug Efficacy**	Unknown Response	-	1A

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
CFTR ivacaftor	**Pulmonary disorders**	chr7:117587806 G/A GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117642528 G/T GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117587799 A/C AA	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117587801 T/G TT	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117611640 G/A GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117534318 G/A GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117611620 A/C AA	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117611595 T/G TT	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117603708 C/T CC	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117590409 A/G AA	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117548795 C/A CC	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117540270 G/C GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117611663 T/A TT	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117614699 G/C GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor / lumacaftor	**Pulmonary disorders**	chr7:117559590 ATCT/A CTT/CTT	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117530975 G/A GG	**Drug Efficacy**	**Unknown Response**	-	**1A**

Gene/Drug	Therapeutic Area	Variant / Genotype	Phenotype Category	Implication	Phenotype	Clinical Annotation Level
CFTR ivacaftor	**Pulmonary disorders**	chr7:117509035 G/A GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117664770 G/A GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117587805 G/A GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117587800 G/A GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117540285 G/A GG	**Drug Efficacy**	**Unknown Response**	-	**1A**
CFTR ivacaftor	**Pulmonary disorders**	chr7:117642483 T/C TT	**Drug Efficacy**	**Unknown Response**	-	**1A**

Sequencing and Analysis Details

Variant Classification and Tiers

The variant classification system used in this report is based on joint consensus recommendations of the **American College of Medical Genetics and Association for Molecular Pathology** for evaluation of pathogenicity of sequence variants. PGx summaries stated in the report have been provided by the Clinical Pharmacogenomics Implementation Consortium and PharmGKB which are standard databases for pharmacogenomic variations. The variant classification system used in this report is based on PharmGKB's clinical annotations for pharmacogenomics variants. These annotations incorporate variant-specific prescribing guidance from clinical guidelines and FDA-approved drug labels are created by expert curators who review variant information and provide summaries of how each variant affects a person's response to medication. The clinical annotation scores are assigned based on supporting evidence for a variant to determine the Level of Evidence for the annotation, which can range from 1 to 4, with level 1 indicating the highest level of reliability and supporting evidence.

Level 1 - High Level of Evidence

Level A: Variant-drug pairs with specific prescribing guidance from clinical guidelines or FDA-approved drug labels, supported by at least one publication.
Level B: Variant-drug pairs with strong evidence of association but lacking specific prescribing guidance in clinical guidelines or FDA drug labels, backed by at least two independent publications.

Level 2 - Moderate Level of Evidence

Level A: Variants in known pharmacogenes that have a stronger likelihood of causing drug-related effects, with moderate evidence backing the variant-drug associations
Level B: Variant-drug pairs with a moderate level of evidence supporting the association.

Level 3 - Low Level of Evidence

Level 4 - Unsupported

Other related test findings

N/A

Quality Metrics

WGS Analysis QC metrics: Total Reads: 990987150; Percentage genome covered (>10x): 94.54%; Average Unique Coverage (Count): 45.50x

Methodology

Quality Assessment:
The quality of nucleic acids is assessed using fluorometry (Qubit, Thermo Scientific) and automated gel electrophoresis (Agilent Tape station) assays. Samples after extraction, post-fragmentation and post-Index PCR are assessed by QC. Samples that pass the minimum QC are only taken for the next step of the process.

Assay method
The test is performed using a comprehensive whole-genome next-generation sequencing (WGS) approach. Briefly, the extracted nucleic acid from patient blood samples that qualify for quality check is subjected to library preparation using a commercially available kit (Illumina DNA PCR Free Kit) as instructed by the manufacturer (Illumina, Inc.). Libraries that passed the quality check at this stage are normalized, pooled, and sequenced on Illumina Next Generation Sequencing Platform (Illumina NovaSeq X-Plus).

Variant Calling and Annotation:
Alignment, post-processing, and default quality-filtered variant calling were executed on the Illumina DRAGEN Bio-IT platform developed by Illumina Inc., USA. The analysis was facilitated by the 'Dynamic Read Analysis for GENomics' (DRAGEN) v4.2.4 pipeline using the GRCh38 (hg38) human reference genome. Generated VCF files were annotated using VarSeq 2.5.0. Following are the sources and versions of databases used: 1 kg Phase 3, ClinVar 2023-04-06 v2, Golden Helix CancerKb, Genome Asia 100 K variant frequencies, gnomAD Exome variant frequencies 2.1.1 v2, gnomAD Genomes (coding subset) variant frequencies 3.1.2 v2, NHBLBI ESP6500SI-V2-SSA137 exome variant frequencies 0.0.30, RefSeq Genes 110, Sift and polyphen2 missense predictions 2021-04-21.

Variant Assessment:
Variants after annotation were assessed and filtered based on the following criteria- Present in < 1% of the known germline population databases, Read Depth (DP) > 10, Genotype Qualities (GQ) > 20, Variant not reported to be Benign, Likely Benign, Conflicting. The final filtered variants were classified based on the ACMG/AMP guidelines. For pharmacogenomics variants, the generated output files were mapped against Level 1A and 1B variations reported in the PharmGKB database. For SNVs, variants with Read Depth (DP) > 10 were considered. Star alleles were identified using a custom script integrating allele-specific information. Genotype determination and diplotype annotation were performed with reference to the CPIC database, ensuring accurate classification of star alleles.

Limitations

This Report was generated using the materials and methods described above, which required the use of various reagents, protocols, instruments, software, databases, and other items, some of which were provided or made accessible by third parties. A defect or malfunction in any such reagents, protocols, instruments, software, databases, and/or other items may compromise the quality or accuracy of the Report.

Pharmacogenomics association data for this report only includes Level 1A and 1B variants from PharmGKB. Variants with other levels of evidence are not reported. Rare nucleotide changes, which may lead to altered or partial blood group antigen expression or result in null phenotypes, may not be detected by this assay. Consequently, only the variants targeted and cataloged by ISBT are interrogated in this report, and rare nucleotide alterations outside this scope may remain unidentified.

The Report has been created based on or incorporates references to, various scientific manuscripts, references, and other sources of information, including without limitation manuscripts, references, and other sources of information that were prepared by third parties that describe correlations between certain genetic mutations and particular diseases (and/or certain therapeutics that may be useful in ameliorating the effects of such diseases). Such information and correlations are subject to change over time in response to future scientific and medical findings. Karkinos Healthcare makes no representation or warranty of any kind, expressed or implied, regarding the accuracy of the information provided by or contained in such manuscripts, references, and other sources of information. If any of the information provided by or contained in such manuscripts, references, and other sources is later determined to be inaccurate, the accuracy and quality of the Report may be adversely impacted. Karkinos Healthcare is not obligated to notify you of any impact that future scientific or medical research findings may have on the Report.

The Report must always be interpreted and considered within the clinical context, and a physician should always consider the Report along with all other pertinent information and data that a physician would prudently consider prior to providing a diagnosis to a patient or developing and implementing a plan of care for a patient. The Report should never be considered or relied upon alone in making any diagnosis or prognosis. The manifestation of many diseases is caused by more than one gene variant, a single gene variant may be relevant to more than one disease, and certain relevant gene variants may not have been considered in the Report. In addition, many diseases are caused or influenced by modifier genes, epigenetic factors, environmental factors, and other variables that are not addressed by the Report (or that are otherwise unknown). If a germline variant is in question, further testing may be recommended. As such, the relevance of the Report should be interpreted in the context of a patient's clinical manifestations. The Report provided by Karkinos Healthcare is provided on an "AS IS" basis. Karkinos Healthcare makes no representation or warranty of any kind, expressed or implied, regarding the Report. In no event shall Karkinos Healthcare be liable for any actual damages, indirect damages, and/or special or consequential damages arising out of or in any way connected with the Report, your use of the Report, your reliance on the Report, or any defect or inaccurate information included within the Report. Medical knowledge annotation is constantly updated and reflects the current knowledge at the time.

The test performance characteristics were determined by the Molecular Laboratory of Karkinos Healthcare Advanced Center for Cancer Diagnostics and Research. The Report was generated by the Karkinos Healthcare Molecular Laboratory in collaboration as required by the CLIA 1988 regulations. The Report, and the tests used to generate the Report, have not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. The test results have been scientifically shown to be clinically useful. The laboratory is under the process of CAP/CLIA as well as ISO-15189 certifications.

Disclaimer

The tests are carried out in the lab with the presumption that the specimen belongs to the patient named or identified in the bill/test request form.
The test results relate specifically to the sample received in the lab and are presumed to have been generated and transported per specific instructions given by the physicians/laboratory.
The reported results are for information and are subject to confirmation and interpretation by the referring doctor.
Some tests are referred to other laboratories to provide a wider test menu to the customer.
Karkinos shall in no event be liable for accidental damage, loss, or destruction of the specimen, which is not attributable to any direct and mala fide act or omission of Karkinos or its employees. Liability of Karkinos for deficiency of services, or other errors and omissions shall be limited.

Signature | Signature | Signature

**** End of Report ****