Pharmacogenetic Passport

Pharmacogenetic guidelines and clinical annotations connected to influential DNA changes

sampleName

Contents

0.1 Patient haplotypes

Gene	Phylogenetic method[1]	Set method[2]
VKORC1	H2 / H7	H2 / *2
CYPC191	*1 / *3	*1 / *18

[1]Method using phylogenetic trees to find closest 'relative' to patient alleles. Trees can be seen in Appendix A.

[2]Method looking for overlap of haplotype non-reference variants and patient non-reference variants. Reference variants are filtered out of both sets prior to comparison. Top 5 hits can be seen in Appendix 2.

0.2 Drug-gene connections

Drug	Gene	Guideline	Annotations[3]
Warfarin	VKORC1	Yes	*Level 1-2*: 15 *Level 3-4*: 13
Warfarin	CYPC191	Yes	*Level 1-2*: 15 *Level 3-4*: 13

[3]Level 1A and 1B clinical annotations meet the highest levels of criteria and are manually curated by PharmGKB. Level 1A annotations contain a variant-drug combination in a CPIC or medical society endorsed PGx guideline, or, implemented at a PGRN site, or, in another major health system. Level 1B annotations contain a variant-drug combination where the preponderance of evidence shows an association. The association must be replicated in more than one cohort with significant p-values, and, preferably with a strong effect size. Lower levels (3-4) are less significant and may only be based on a single study or case report, which may be performed in vitro.(PHARMGKB)

0.3 Haplotype Guidelines

0.3.1 Acenocoumarol

VKORC1

Patient haplotype **H1/H2** — **H1/*2**

Genotype	Therapeutic Dose Recommendation	Level of Evidence	Clinical Relevance
VKORC1 [variant:rs9934438] AG	None	Published controlled studies of good quality* relating to phenotyped and/or genotyped patients or healthy volunteers, and having relevant pharmacokinetic or clinical endpoints.	Minor clinical effect (S): QTc prolongation (;450 ms ;470 ms); INR increase; 4.5 Kinetic effect (S).
VKORC1 [variant:rs9934438] AA	Check INR more frequently.	Published controlled studies of good quality* relating to phenotyped and/or genotyped patients or healthy volunteers, and having relevant pharmacokinetic or clinical endpoints.	Minor clinical effect (S): QTc prolongation (;450 ms , ;470 ms); INR increase ; 4.5 Kinetic effect (S).

0.4 Clinical Annotations

0.4.1 Acenocoumarol

VKORC1

Class 2A **rs9934438** *GA* Patients with the AG genotype may have decreased dose of acenocoumarol or phenprocoumon as compared to patients with genotype GG. Other genetic and clinical factors may also influence the dose of acenocoumarol or phenprocoumon.

PRSS53

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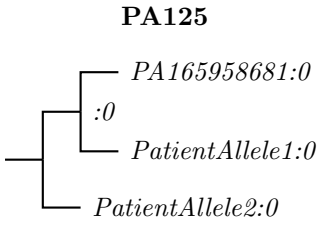
0.5 Appendix 1: Haplotype trees



0.6 Appendix 2: Top 3 haplotypes

	test	Allele 1	Allele 2
		*1	*1
CYP2D6	*2	*2	
	*3	*3	

0.7 Appendix 3: Low level annotations

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