






Clinical Pharmacogenetic Dataset

Transforming scientific data into clinical knowledge

The Clinical Pharmacogenetic (PGx) Dataset provides in-depth analysis of the impact of genetic variants of enzymes and transporters on the PK, PD, and safety of drugs in various populations. Available information comes from publications and NDA reviews describing gene-drug interactions (GDI), ethnicity-drug interactions, and case reports.

-  **Detailed study information** regarding design, drug dosing, genetic polymorphisms, population characteristics, PK, PD, and safety results are structured and presented according to the latest PGx scientific consensus. Common metrics for active compounds (percent changes in AUC, plasma concentrations, oral clearance, dose requirements) and metabolites (AUC ratio of metabolite/parent, and formation clearance) are used across all studies to allow metadata analysis of quantitative results.
-  **Study results** are categorized according to the overall impact of genetic variants on drug exposure, PD, and safety/efficacy compared to a reference group (non-carriers of variant).
-  **Comprehensive PK parameters** for parent drugs and their metabolites are available.
-  **Pre-formulated queries** allow users to retrieve an *in vivo* PGx dataset by drug name, gene name, and/or ethnicity.
-  **Results** can be viewed, customized, and downloaded, allowing users to compile and organize the large body of information available.

FROM A CITATION OR NDA/BLA REVIEW

The latest, most relevant, peer-reviewed publications and regulatory documents are identified and fully analyzed. Study protocol and results are manually curated to update the knowledgebase on a daily basis.

NCBI Resources How To

PubMed 30017169[uid]

US National Library of Medicine National Institutes of Health

Format: Abstract - Send to -

Clin Ther. 2018 Jul;40(7):1170-1178. doi: 10.1016/j.clinthera.2018.06.001. Epub 2018 Jul 13.

Effects of CYP2C19 Genetic Polymorphisms on the Pharmacokinetic and Pharmacodynamic Properties of Clopidogrel and Its Active Metabolite in Healthy Chinese Subjects.

Song BL¹, Wan M², Tang D³, Sun C¹, Zhu YB², Linda N¹, Fan HW⁴, Zou JJ⁵.

Author information

Abstract

PURPOSE: Some studies in the white population have shown that carriers of at least 1 loss-of-function allele in the gene that encodes the cytochrome P-450 2C19 isozyme (CYP2C19) have lower levels of the clopidogrel active metabolite (CAM) and a reduced antiplatelet effect of clopidogrel. However, data are limited regarding the association between CYP2C19 genetic variants and exposure to CAM and on the pharmacodynamic properties of CAM in the Chinese population. Data from the white population cannot be extrapolated to the Chinese population because of the marked interethnic differences in CYP2C19 variants. This study was aimed to investigate the influence of CYP2C19 genetic polymorphisms on the pharmacokinetic properties of CAM and the antiplatelet effect of clopidogrel in healthy Chinese volunteers, and to provide evidence for the role of a CYP2C19 genotyping test in predicting the antiplatelet effect of clopidogrel in the Chinese population.

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Search Results for "clopidogrel"

Products listed on this page may not be equivalent to one another.

CLOPIDOGREL BISULFATE	Most often analyzed files: <ul style="list-style-type: none"> Printed labeling Multi-discipline review Chemistry review(s) Other review(s)
PLAVIX	

1

TO A FULLY CURATED DATASET

Prior to integration, all data are carefully and critically evaluated. The richness of each citation, including relevant insights, is exploited, generating a highly detailed dataset.

2

Dosing

Design and Drug Administration
clopidogrel 300 mg oral single dose
Design: Single Dosing, Open-label

Genotyping Method
IPLEX Sequenom MassArray

Alleles Tested
CYP2C19 636A
CYP2C19 636G
CYP2C19 681A
CYP2C19 681G
CYP2C19*2
CYP2C19*3

Genotyping
Phenotyping

CYP2C19	8 Healthy volunteer(s)	10 Healthy volunteer(s)	2 Healthy volunteer(s)
NCBI Gene ↗	volunteer(s)	CYP2C19*1/*2	CYP2C19*2/*2
PharmGKB ↗	(reference)	CYP2C19*1/*3	CYP2C19*2/*3
PharmVar ↗	CYP2C19*1/*1	CYP2C19 Intermediate Metabolizers	CYP2C19*3/*3
	CYP2C19 Normal Metabolizers	Asian	CYP2C19 Poor Metabolizers
	Asian	Chinese	Asian
	Chinese	Male(s)	Chinese
	Male(s)	Non-smokers	Male(s)
	Non-smokers		Non-smokers

Populations with different genotypes

Impact of genetic variations on drug disposition

PK - Pharmacokinetics			
clopidogrel Prodrug PubChem PharmGKB ↗			
Impact of Variant		No	No
AUC (ng/mL*h) Means ± SD	9.62 ± 3.26	9.97 ± 4.31	15.2 ± 0.88
Δ AUC%		3.6	58.0
C _{max} (ng/mL) Means ± SD	3.84 ± 1.94	4.9 ± 2.96	7 ± 1.98
Δ C _{max} %		27.6	82.3
clopidogrel thiol metabolite H4 active metabolite PubChem ↗			
Impact of Variant		Yes	Yes
AUC (ng/mL*h) Means ± SD	61.05 ± 21.63	37.67 ± 11.01	27.08 ± 2.72
Δ AUC%		-38.3*	-55.6*
C _{max} (ng/mL) Means ± SD	45.39 ± 12.57	29.15 ± 7.92	19.55 ± 2.19
Δ C _{max} %		-35.8*	-56.9*

*statistically significant

Impact of genetic variations on drug efficacy

PD - Pharmacodynamics			
Measurements			
• Coagulation and Hemostasis Parameters			
Protocol			
Blood samples for platelet aggregation testing were processed within 2 hours of collection. Maximum platelet aggregation (MPA) was measured by light-transmittance aggregometry in platelet-rich plasma after stimulation with 10 μmol/L adenosine diphosphate using a 4-channel LBY-NJ aggregometer. Platelet aggregation was expressed as the maximal percentage change of light transmission from baseline using platelet-poor plasma as a reference. Inhibition of platelet aggregation (IPA) was calculated as: IPA _t = (MPA ₀ - MPA _t) / MPA ₀ X 100%			
where IPA _t is the IPA at time t, and MPA _t and MPA ₀ are MPA at times t and baseline, respectively. Platelet aggregation in this integrated analysis was assessed at 4 and 24 hours after the administration of a single 300-mg dose of clopidogrel.			
clopidogrel Prodrug PubChem PharmGKB ↗			
Impact of Variant	Yes	Yes	Yes
Inhibition platelet aggregation (%) Means ± SD	56.5 ± 6	37.7 ± 12.01	24.2 ± 18.9
Δ Inhibition platelet aggregation%		-33.3*	-57.2*
maximum platelet aggregation (%) Means ± SD	32 ± 5.7	48.7 ± 7.7	61 ± 9.6

Clopidogrel exposure is significantly impacted in CYP2C19 poor metabolizers.

What other drugs have an AUC change of at least 2-fold in carriers of CYP2C19 loss-of-function alleles?

POWERFUL TOOL FOR DATA INTEGRATION: FROM ONE CITATION TO METADATA ANALYSIS

The data are formatted for immediate use and can be filtered and re-arranged to allow meta-analysis of multiple results.

Query all drugs exhibiting exposure increases of at least 2-fold in CYP2C19 poor metabolizers

Search for Citations
Search for Quantitative Results

Compounds

Genes

Populations

[Search for a synonym](#)

[Search for a synonym](#)

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Table View of Query Results

Multiple formats for viewing and downloading

Filter

Showing 1 to 100 of 1,107 entries (filtered from 2,429 total entries)

Select columns Copy Excel CSV Print

Genotype (reference)	Genotype	Phenotype (reference)	Phenotype	Overall Impact	Compound	Route of administration	Dose	AUC or AUC(0-infinity) % Δ	CL/F or CL % Δ
			x CYP2C19 Poor Metabolizers						
CYP2C19*1/*1, CYP2C19*1/*2	CYP2C19*2/*2	CYP2C19 Intermediate Metabolizers, CYP2C19 Normal Metabolizers	CYP2C19 Poor Metabolizers		(R)-lansoprazole sulfone	oral	60 mg	22655.3	
CYP2C19*1/*1	CYP2C19*2/*2, CYP2C19*2/*3, CYP2C19*3/*3	CYP2C19 Normal Metabolizers	CYP2C19 Poor Metabolizers	Yes	(R)-mephobarbital	oral	200 mg	9100.0*	-98.9*
CYP2C19*1/*1	CYP2C19*2/*2, CYP2C19*2/*3	CYP2C19 Normal Metabolizers	CYP2C19 Poor Metabolizers		lansoprazole sulfone	oral	30 mg	8277.8*	
CYP2C19*1/*1	CYP2C19*2/*2, CYP2C19*2/*3	CYP2C19 Normal Metabolizers	CYP2C19 Poor Metabolizers		lansoprazole sulfone	oral	30 mg	7139.4*	-98.8*
CYP2C19*1/*1	CYP2C19*2/*2, CYP2C19*2/*3	CYP2C19 Normal Metabolizers	CYP2C19 Poor Metabolizers		omeprazole sulfone	IV	20 mg	5895.0*	

Obtain a complete list of drugs that may need dosing adjustment in CYP2C19 poor metabolizers

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CLINICAL PGX DATASET IN NUMBERS

(as of October 16, 2023)

3,248 / **10,084**
in vivo PGx citations / *in vivo* PGx entries

104 / **275**
in vivo PGx NDAs/BLAs / *in vivo* PGx entries

Dedicated *in vitro* PGx queries with **10** possible searches

707 / **1,590**
 citations on PGx efficacy (PD) / entries

714 / **1,140**
 citations on PGx safety (side effects) / entries

307 case reports

725 drugs involved in *in vivo* PGx

APPLICATIONS OF THE CLINICAL PGx DATASET



PROVIDES CONTEXT for RESULTS OBTAINED with candidate compounds



HELPS DEVELOP OVERALL REGULATORY STRATEGY and optimize clinical PGx trials:

- Refines inclusion/exclusion criteria
- Helps select dose, duration, and timing of drug administration in the context of PGx
- Provides PK variability data for power calculations
- Quickly identifies known substrates of enzymes/transporters among marketed drugs to understand GDI risk



SUPPORTS STATIC PREDICTIONS and PBPK MODELING with input parameters



ACCESSES REGULATORY GDI STUDIES for recently marketed drugs



PROVIDES REFERENCE RESOURCE for ASSESSMENT of DRUG INTERACTION SAFETY



HELPS IMPLEMENT PERSONALIZED MEDICINE in the context of GDI and gene-DDI

To learn more, visit www.druginteractionsolutions.org
or email DIDBase@Certara.com



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