

e-PKGene Version 2.0 New features

Three main Search Sections

1 Search for Articles 2 Search for Quantitative Results 3 Summaries

Compound: Submit Search for a synonym

Gene: Submit Search for a synonym

Population: Submit

- 1- Enhanced search for articles
- 2- NEW QUERIES: Search by Quantitative Results
- 3- Summaries: drug summaries updated

Search by synonyms for compounds and genes: click on the link “search by synonym” and type in the new box displayed.

SUBMIT to access the search results

Search for Articles (enhanced current main Search)

Gene: [NCBI Gene](#) [Gene Summary](#) 1
219 articles found

Compound: (R)-amlodipine (1), (R)-lansoprazole (1), (R)-methadone (3), (R)-norverapamil (1)

Populations: African-American (3), Africans (7), Asians (85), Blacks (11)

CYP3A5 (219)

Citations Impact of Variant

Showing 1 to 10 of 219 entries Search:

Year	Article	Studies	Title	NDA / Case Report
2011	22433	2	Ticagrelor NDA	NDA
2010	201532	3	Eribulin	NDA
2013	23574377	1	Severe acute nephrotoxicity in a kidney transplant patient despite low tacrolimus levels: a possible interaction between donor and recipient genetic polymorphisms.	Case Report
2012	21210843	1	Atypical pharmacokinetics of atazanavir in an HIV-1-infected patient.	Case Report

Number of studies for each citation

Retrieve NDAs and case reports

- 1- Access to e-PKGene summaries, link to useful websites.
- 2- Show number of studies performed for each article
- 3- NDA/Case Report are now easily retrieved from the list of articles.

Impact of variant Box redesigned

Gene CYP3A5 [NCBI Gene](#) [Gene Summary](#) { Edit }

219 articles found

Compound

- sildenafil (1)
- siodosin (1)
- simvastatin (3)
- sirolimus (6)

Populations

- Asians (1)
- Caucasians (3)
- Chinese (1)
- Europeans (1)

1 CYP3A5 (219) / sirolimus (6) / Caucasians (3)

Citations **Impact of Variant**

CYP3A5*1/*1
CYP3A5*1/*3

Yes	No
sirolimus 16815317	none reported 2

CYP3A5*1/*3

Yes	No
none reported	sirolimus 17192769 23018254

- 1- Refine the search will narrow the number of citations relevant for a specific compound or population. "Clear Field" option by clicking on another or the previous selection.
- 2- Positive impact is highlighted in red, and non-impact in green. No results appears as "none reported"

Search for Quantitative Results

QUERY

Search for Articles **Search for Quantitative Results** Summaries

Compounds [Search for a synonym](#)

Genes [Search for a synonym](#)

Populations

Submit

One or multiple selections are possible for compounds, genes and populations. SUBMIT to access the quantitative results.

RESULTS

My DIB / Pharmacogenetics

clonidogrel

1

- > summary file
- > PubChem
- > ChemSpider
- > search for articles

Compounds clonidogrel

Genes CYP2C19

14 articles containing 19 relevant measurements

2

You can search/filter individual columns, reorder the columns (drag and drop the column headers), and hide columns you don't need. When you use "Copy to Clipboard" or "Download" you will get the data in the same state as the table.

PK measurements PD measurements

Showing 1 to 10 of 22 entries

3

Additional measurements which are not involved in the determination of Overall Impact are currently hidden.

4

How we determine Overall Impact

Show / Hide Columns Print View Copy to Clipboard Download

Compound	Gene	Genotype (reference)	Genotype	Phenotype (reference)	Phenotype	Race / Ethnicity (reference)	Race / Ethnicity	Overall Impact	Study Design
prasugrel metabolite R-138727	CYP2C19	CYP2C19*1/*1	CYP2C19*1/*2	Homozygous wild-type	Heterozygous variant			No	Retrospective study

- 1- Click to access useful websites, summaries or articles for compounds and genes
- 2- Customize the table according to your points of interest: drag and drop column headers, hide columns you don't need or show columns which are hidden by default.
- 3- Criteria to define the overall impact of variant on drug exposure.
- 4- Download to Excel

RESULTS ANALYSIS

PK measurements PD measurements

Showing 1 to 5 of 5 entries (filtered from 22 total entries)

4

Show / Hide Columns Print View Copy to Clipboard Download

3

Compound	Gene	Genotype (reference)	Genotype	Phenotype	Overall Impact	AUC or AUC(0-infinity) % Δ	Cmax % Δ	Article	Study Design	Number of Subjects	Route of Administration
			*2/			-50					
clopidogrel-H4 (R-130964)	CYP2C19	CYP2C19*1/*1	CYP2C19*2/*2 CYP2C19*2/*3	Poor Metabolizers	Yes	-43.4*	-39.23*	18532997	Single Dosing	9	oral
clopidogrel-H4 (R-130964)	CYP2C19	CYP2C19*1/*1 CYP2C19*1/*17	CYP2C19*1/*2 CYP2C19*1/*3 CYP2C19*2/*2	Slow Metabolizers	Yes	-38.51*	-36.57*	22374717	Single Dosing	8	oral
clopidogrel	CYP2C19	CYP2C19*1/*1	CYP2C19*2/*2 CYP2C19*2/*3	Poor Metabolizers	Yes	193.92*	370.31*	18323861	Single Dosing	8	oral
prasugrel metabolite R-138727	CYP2C19	CYP2C19*1/*1	CYP2C19*2/*2	Poor Metabolizers	No	-16.36	-27.22	17900275	Retrospective study	1	oral
prasugrel metabolite R-138727	CYP2C19	CYP2C19*1/*1	CYP2C19*2/*2 CYP2C19*2/*3	Poor Metabolizers	No	-20.22	-16.11	21689142	Random Crossover	11	oral

1

2

25 records per page

Direct link to the display of the article

- 1- Sort and Search by allelic variant or SNPs
- 2- Refine by % change levels
- 3- Level of significance of the study
- 4- The table displays the results which match the selection criteria

Quantitative results for pharmacodynamic measurements.

PK measurements PD measurements

Showing 1 to 10 of 13 entries (filtered from 35 total entries)

Show / Hide Columns Print View Copy to Clipboard Download

Compound	Gene	Genotype (reference)	Genotype	Phenotype (reference)	Phenotype	Overall Impact	Inhibition platelet aggregation % Δ	Inhibition platelet aggregation (max change from baseline after a loading dose) % Δ	Inhibition platelet aggregation AUEC (loading dose) % Δ	Platelet reactivity index % Δ
clopidogrel			*2/							
clopidogrel	CYP2C19	CYP2C19*1/*1	CYP2C19*2/*2 CYP2C19*2/*3	Homozygous Extensive Metabolizers	Poor Metabolizers	Yes		-40.25*	-50.58*	
clopidogrel	CYP2C19	CYP2C19*1/*1	CYP2C19*2/*2 CYP2C19*2/*3	Extensive Metabolizers	Poor Metabolizers	Yes				40.4*
clopidogrel	CYP2C19	CYP2C19*1/*1	CYP2C19*2/*2	Homozygous wild-type	Poor Metabolizers	Yes	-90.28*			
clopidogrel	CYP2C19	CYP2C19*1/*1	CYP2C19*2/*2 CYP2C19*2/*3 CYP2C19*3/*3	Extensive Metabolizers	Poor Metabolizers	Yes				

Sort with column headers, reorder (drag and drop columns), filter.

New article display

PubMed 19784640

1 **PK PD Side Effects**

Description >

2 Study 1 >

Study 2 >

Description

PubMed 19784640 [% Δ data](#) [Edit](#) [View in production](#)

CYP3A4*1G genetic polymorphism influences CYP3A activity and response to fentanyl in Chinese gynecologic patients.

European journal of clinical pharmacology, 2010, volume 66, issue 1, pages 61-6

W Zhang, YZ Chang, QC Kan, LR Zhang, ZS Li, H Lu, ZY Wang, QJ Chu, J Zhang

- 1- Click to hide information you are not interested in
- 2- Easy access to 1 study to another

PubMed 19784640

PK PD Side Effects

Description >

Study 1 >

Study 2 >

Study 2

Design and Drug Administration
midazolam 0.1 mg/kg IV single dose
Design: Single Dosing

Genotyping Method
PCR-Restriction fragment length polymorphism (PCR-RFLP)

Alleles Tested
CYP3A4*1G

Comments
CYP3A activity was measured by determining the plasma ratio 1'-hydroxymidazolam/midazolam.

CYP3A4	NCBI Gene Gene Summary	75 Patient(s) (reference) CYP3A4*1/*1 Homozygous wild-type Asians Chinese Female(s) Han Chinese Post-surgery	59 Patient(s) CYP3A4*1/*1G Heterozygous variant Asians Chinese Female(s) Han Chinese Post-surgery	9 Patient(s) CYP3A4*1G/*1G Homozygous variant Asians Chinese Female(s) Han Chinese Post-surgery
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PK - Pharmacokinetics

1'-hydroxymidazolam [PubChem](#) [ChemSpider](#)

Impact of Variant	No	Yes
C ratio (metabolite/parent) Means ± SD	0.46 ± 0.14	0.46 ± 0.12
Δ C ratio (metabolite/parent)%	0.0	-26.09*

* Denotes that the change is statistically significant (P<0.05) or confidence interval outside equivalence boundaries.

All PK, PD and Side effects can be viewed and compared.

Impact of variant for pharmacokinetics and pharmacodynamic measurements is presented along with quantitative data.

PubMed 17534875

PK PD Side Effects

Description >

Study 1 >

Study 2 >

Study 3 >

Study 4 >

Study 5 >

Study 6 >

Study 7 >

Study 8 >

Description

PubMed 17534875 [% Δ data](#)

Associations of ABCB1, ABCC2, and ABCG2 polymorphisms with irinotecan-pharmacokinetics and clinical outcome in patients with advanced non-small cell lung cancer.

Cancer, 2007, volume 110, issue 1, pages 138-47
JY Han, HS Lim, YK Yoo, ES Shin, YH Park, SY Lee, JE Lee, DH Lee, HT Kim, JS Lee

— DJDB's comments

AUC was normalized to 80 mg/m² dose (81 patients were treated with irinotecan 80 mg/m², while 26 patients were treated with irinotecan 65 mg/m²).

With regard to the effect of ABCB1 2677G>T and 3435C>T SNPs on irinotecan and its metabolites disposition, the authors

Quantitative results compared within the article (8 studies) for PK and PD measurements.

PK measurements

PD measurements

Showing 1 to 10 of 57 entries

Show / Hide Columns

Print View

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Download

Article	Year	Compound	Genotype (reference)	Genotype	Overall Impact	Study Design	Number of Subjects	Route of Administration	Dose	Interval
17534875	2007	irinotecan	ABCB1 1236C/ 1236C	ABCB1 1236C/ 1236T	No	Multiple Dosing	57	IV	80 mg/m ²	single dose on days 1 and 8 (with cisplatin 60 mg/m ² on day 1) of 3 weeks cycle
17534875	2007	SN-38	ABCB1 1236C/ 1236C	ABCB1 1236C/ 1236T	No	Multiple Dosing	57	IV	80 mg/m ²	single dose on days 1 and 8 (with cisplatin 60 mg/m ² on day 1) of 3 weeks cycle