






Clinical Drug Interaction Dataset

Transforming scientific data into clinical knowledge

The Clinical Drug Interaction Dataset contains study results from drug-drug, drug-food, drug-natural products, drug-exciptient interaction studies, and case reports.

-  **Detailed study information** regarding design, population, drug dosing, PK, PD, and safety results are extracted from published articles (citations) and NDA reviews. Common metrics (percent changes in AUC, plasma concentrations, oral and renal clearance values) are used across all studies to allow metadata analysis of quantitative results.
-  **Study results** are organized according to the overall effect and mechanism(s) of the interaction:
 - Enzyme and/or transport inhibition, induction, or no effect
 - Other mechanisms, including absorption-based DDI and food-effect
-  **Comprehensive PK parameters** for object (victim) drugs and their metabolites, as well as precipitant (perpetrator) concentrations (when measured) are available.
-  **Multiple pre-formulated queries** allow users to retrieve an in vivo dataset by drug name, therapeutic class, specific enzyme or transporter, changes in exposure, or toxicity (including QT prolongation).
-  **Results** can be viewed, customized, and downloaded in multiple formats, 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 25760671[uid]

Format: Abstract - Send to -

J Clin Pharmacol. 2015 Aug;55(8):909-19. doi: 10.1002/jcph.495. Epub 2015 May 6.

Clinical drug interaction profile of idelalisib in healthy subjects.

Jin F¹, Robeson M², Zhou H², Moyer C¹, Wilbert S², Murray B¹, Ramanathan S¹.

Author information

Abstract

Idelalisib, a potent phosphatidylinositol-3-kinase delta (PI3Kδ) inhibitor, is metabolized primarily by aldehyde oxidase to form GS-563117 and to a lesser extent by cytochrome P450 (CYP) 3A and uridine 5'-diphospho-glucuronosyltransferase 1A4. In vitro, idelalisib inhibits P-glycoprotein (P-gp) and organic anion transporting polypeptides 1B1 and 1B3, and GS-563117 is a time-dependent CYP3A inhibitor. This study enrolled 24 healthy subjects and evaluated (1) the effect of idelalisib on the pharmacokinetics (PK) of digoxin, a P-gp probe substrate, rosuvastatin, a breast cancer resistance protein, and OATP1B1/OATP1B3 substrate, and midazolam, a CYP3A substrate; and (2) the effect of a strong inducer, rifampin, on idelalisib PK. On treatment, the most common clinical adverse events (AEs) were headache and pyrexia. Grade 3 transaminase increases were observed in 5 of 24 subjects and were reversible. Two subjects had serious AEs after treatment completion (grade 3 pyrexia and/or drug-induced liver injury). Idelalisib coadministration did not affect digoxin and rosuvastatin PK. Coadministration with idelalisib increased plasma exposures of midazolam (138% and 437% for maximum

1

U.S. Department of Health & Human Services

FDA U.S. FOOD & DRUG ADMINISTRATION

Home Food Drugs Medical Devices Radiation-Emitting Products Vaccines, Blood & Biologics

Drug Approval Package

FDA Home Drugs Drug Approvals and Databases Drugs@FDA

Zydelig (idelalisib) Tablets
Application No.: 205858
Approval Date: 7/23/2014

Most often analyzed files:

- Printed labeling
- Multi-discipline review
- Chemistry review(s)
- Other review(s)

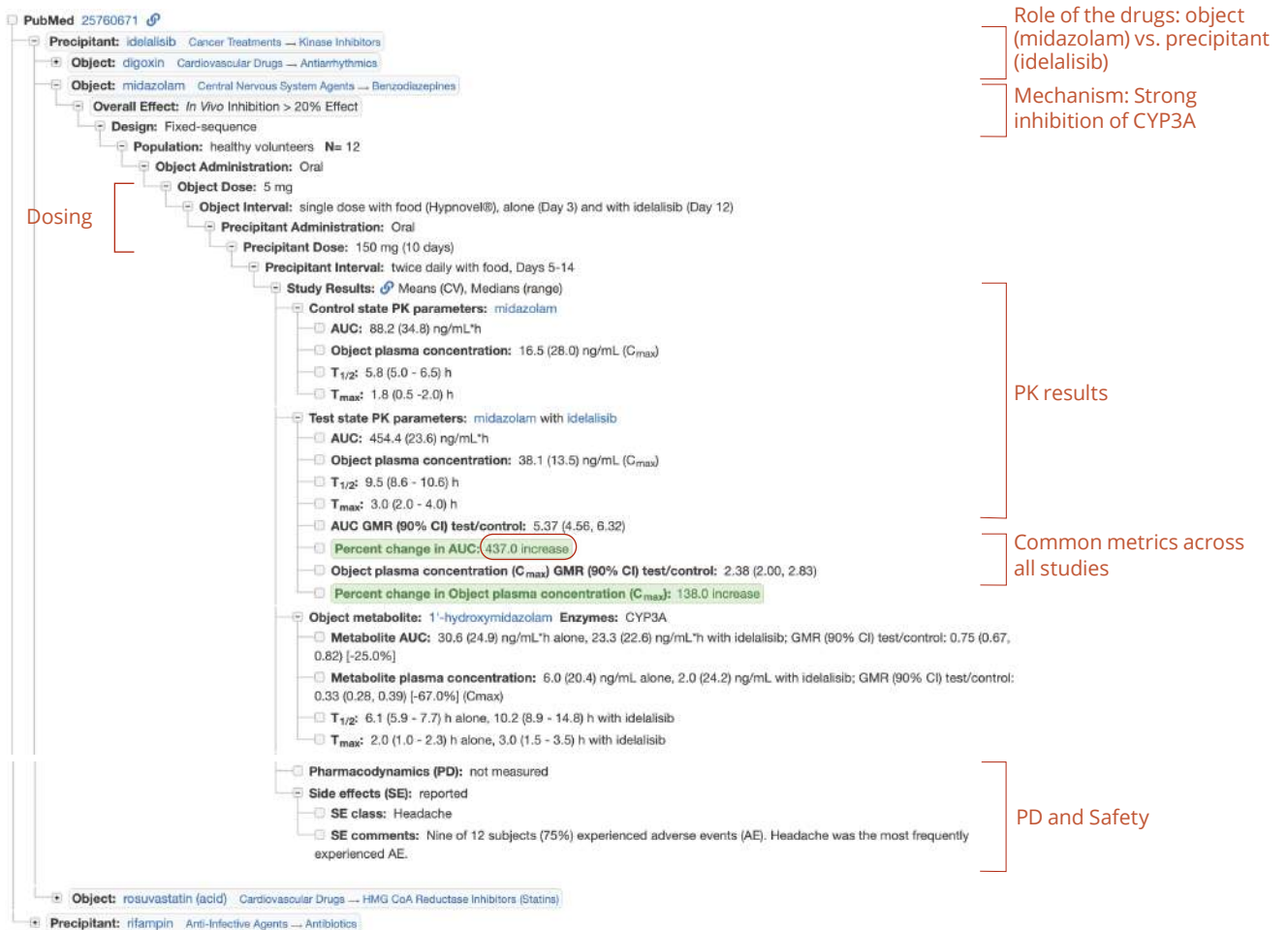
1

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.

Tree View of Citation Data

2



Idelalisib inhibits CYP3A with an AUC increase of 5.2-fold.

What other strong CYP3A inhibitors change the AUC of the index substrate midazolam by at least 5-fold?

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 strong CYP3A inhibitors exhibiting exposure increases of at least 5-fold of the index substrate midazolam

3

Percent Change in AUC or CL

with Objects with Precipitants with Therapeutic Class in Food-Effect Studies with Hepatic / Renal Impairment

Find studies providing percent change in AUC or CL AUC CL

of Objects

or by Object characteristics

with

where value is %

Include simulated data

Submit

Table View of Query Results

4

Showing 1 to 100 of 122 entries

Advanced Table Search Select columns Copy Excel CSV Print

Object	Object Administration	Precipitant	Precipitant Characteristics	Precipitant Therapeutic Class	Precipitant Administration	Precipitant Dose	Precipitant Interval	Percent Change AUC	Accession # or NDA/BLA #
midazolam	IV	ketoconazole	CYP2C8 weak inhibitor CYP2C9 weak inhibitor CYP3A moderate sensitive substrate CYP3A strong inhibitor P-gp clinical inhibitor P-gp FDA clinical inhibitor QT interval prolongating drug	Anti-infective Agents → Antifungals	Oral	200 mg (1.5 days)	bid (first dose 12 h before midazolam administration)	404.3	PubMed 10579473
midazolam	Oral	boceprevir	CYP3A moderate sensitive substrate CYP3A strong inhibitor CYP3A weak inducer P-gp clinical inhibitor	Anti-infective Agents → Antivirals	Oral	800 mg (6 days)	three times daily (capsules) on Days 1-6 after a meal or snack	405.3	NDA 202258
midazolam	Oral	clarithromycin	CYP2C9 weak inhibitor CYP3A FDA clinical strong index inhibitor CYP3A moderate sensitive substrate CYP3A strong inhibitor OATP1B1 FDA clinical inhibitor OATP1B3 FDA clinical inhibitor P-gp clinical inhibitor P-gp FDA clinical inhibitor QT interval prolongating drug	Anti-infective Agents → Antibiotics	Oral	500 mg (7 days)	bid	405.5	PubMed 9728893
midazolam	Oral	ritonavir	CYP1A2 moderate inducer CYP2B6 moderate inducer CYP2C19 strong inducer CYP2C9 moderate inducer CYP2D6 weak inhibitor	Treatments of AIDS → Protease Inhibitors	Oral	300 mg (9 days)	twice daily starting on study day 1	405.9	PubMed 21937987

Multiple formats for viewing and downloading

Obtain a complete list of *in vivo* strong inhibitors of CYP3A

Copyright © 2023 Certara, USA All Rights Reserved.

CLINICAL DRUG INTERACTION DATASET IN NUMBERS

(as of October 16, 2023)

13,817 / **37,570**
in vivo DDI citations / *in vivo* DDI entries

15,804 / **29,767**
 positive entries / negative entries

43 *in vivo* queries with **388**
 possible searches

3,221 entries involving transporter(s)

2,853 case reports

2,453 / **2,216**
 objects (victims) / precipitants (perpetrators)

APPLICATIONS OF THE CLINICAL DRUG INTERACTION DATASET



PROVIDES CONTEXT for RESULTS OBTAINED with candidate compounds



HELPS DEVELOP OVERALL REGULATORY STRATEGY and optimize clinical drug interaction trials:

- Guides choice of appropriate index drugs and study design
- Refines inclusion/exclusion criteria
- Helps select dose, duration, and timing of administration of object and precipitant drugs
- Provides PK variability data for power calculations
- Quickly identifies known substrates/perpetrators of enzymes/transporters among marketed drugs to understand DDI risk with common co-medications



SUPPORTS STATIC PREDICTIONS and PBPK MODELING with input parameters



ACCESSES REGULATORY DDI STUDIES for recently marketed drugs



PROVIDES REFERENCE RESOURCE for ASSESSMENT of DRUG INTERACTION SAFETY

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



About Certara

Certara accelerates medicines using proprietary biosimulation software, technology and services to transform traditional drug discovery and development. Its clients include more than 2,000 biopharmaceutical companies, academic institutions, and regulatory agencies across 62 countries.

For more information visit www.certara.com or email DIDBase@Certara.com.