CERTARA

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-excipient 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

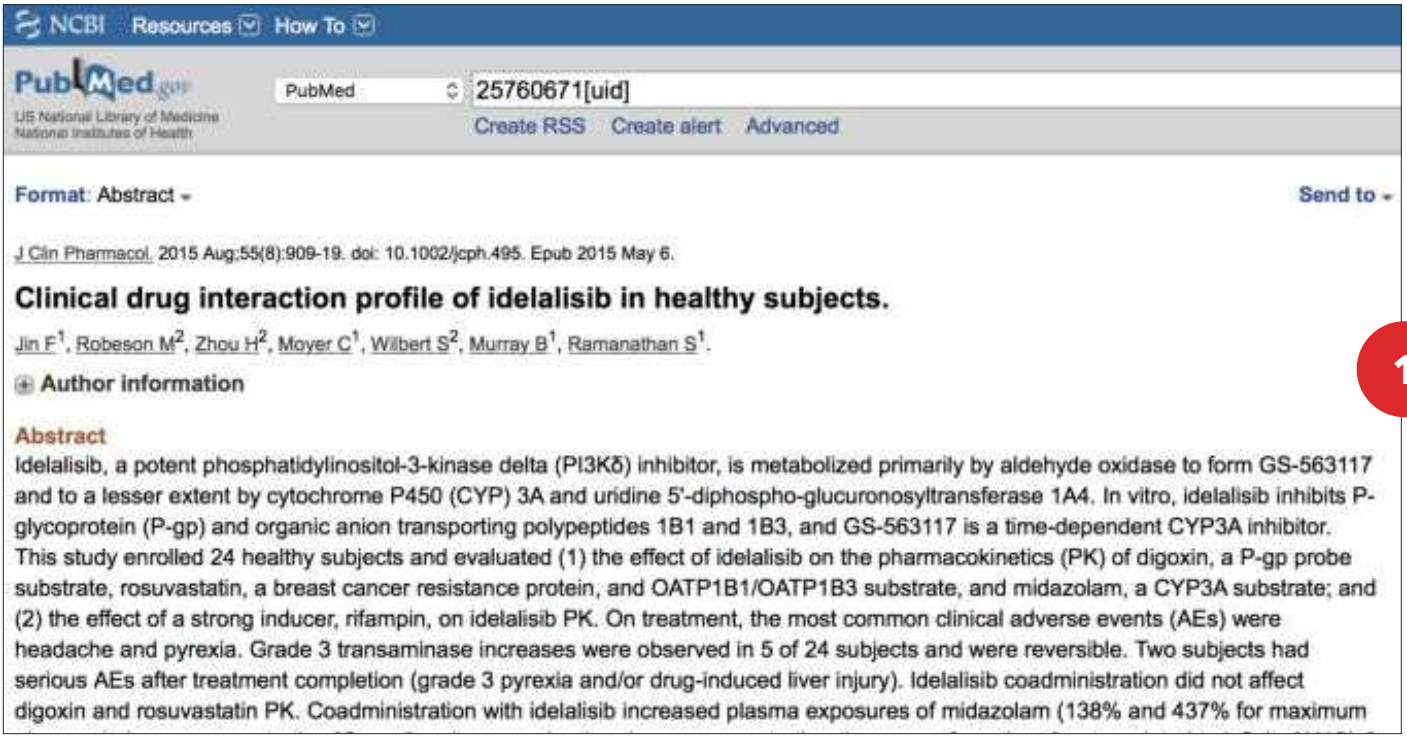
- **Comprehensive PK parameters** for object (victim) drugs and their metabolites, as well as precipitant (perpetrator) concentrations (when measured) are available.

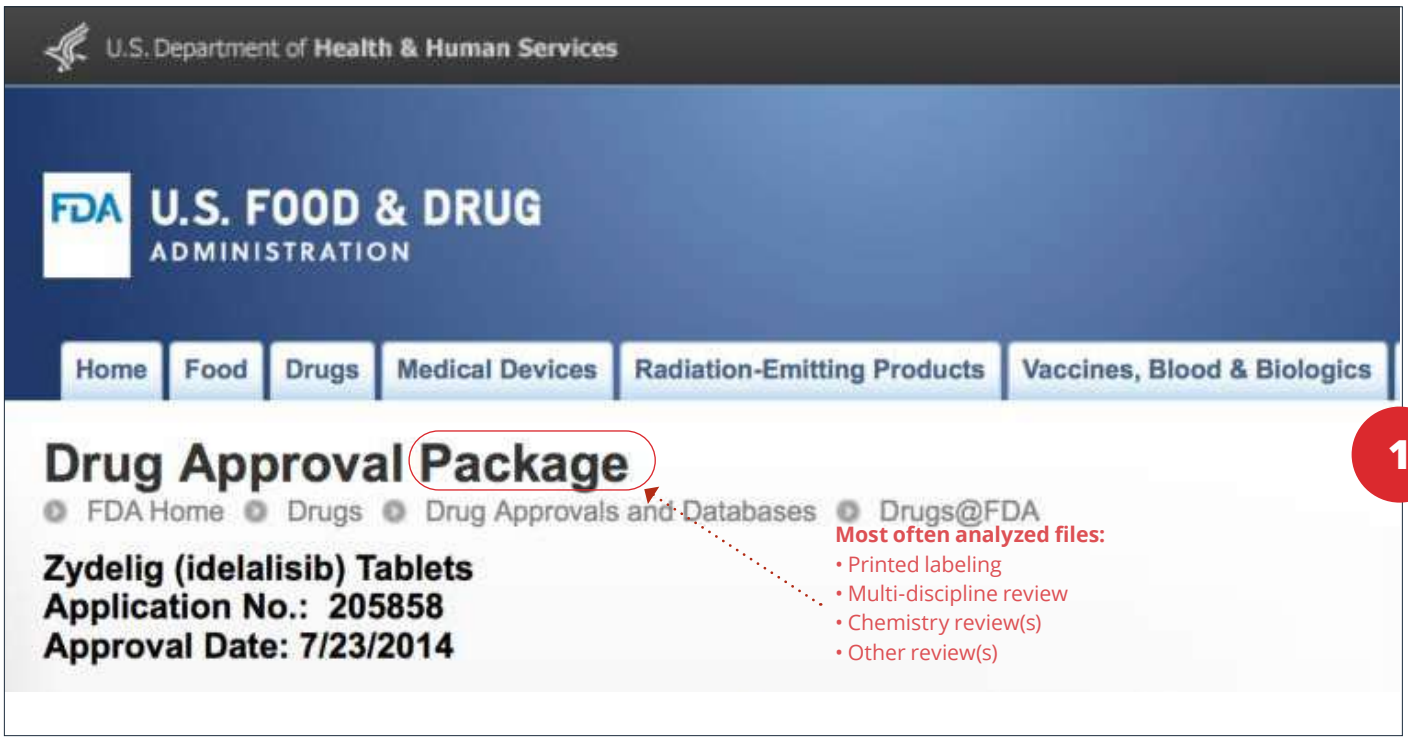
- **Multiple pre-formulated queries** allow users to retrieve an in vivo dataset by drug name, therapeutic class, specific enzyme or transporter, changes in exposure, or toxicity (including QT prolongation).

- **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.





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

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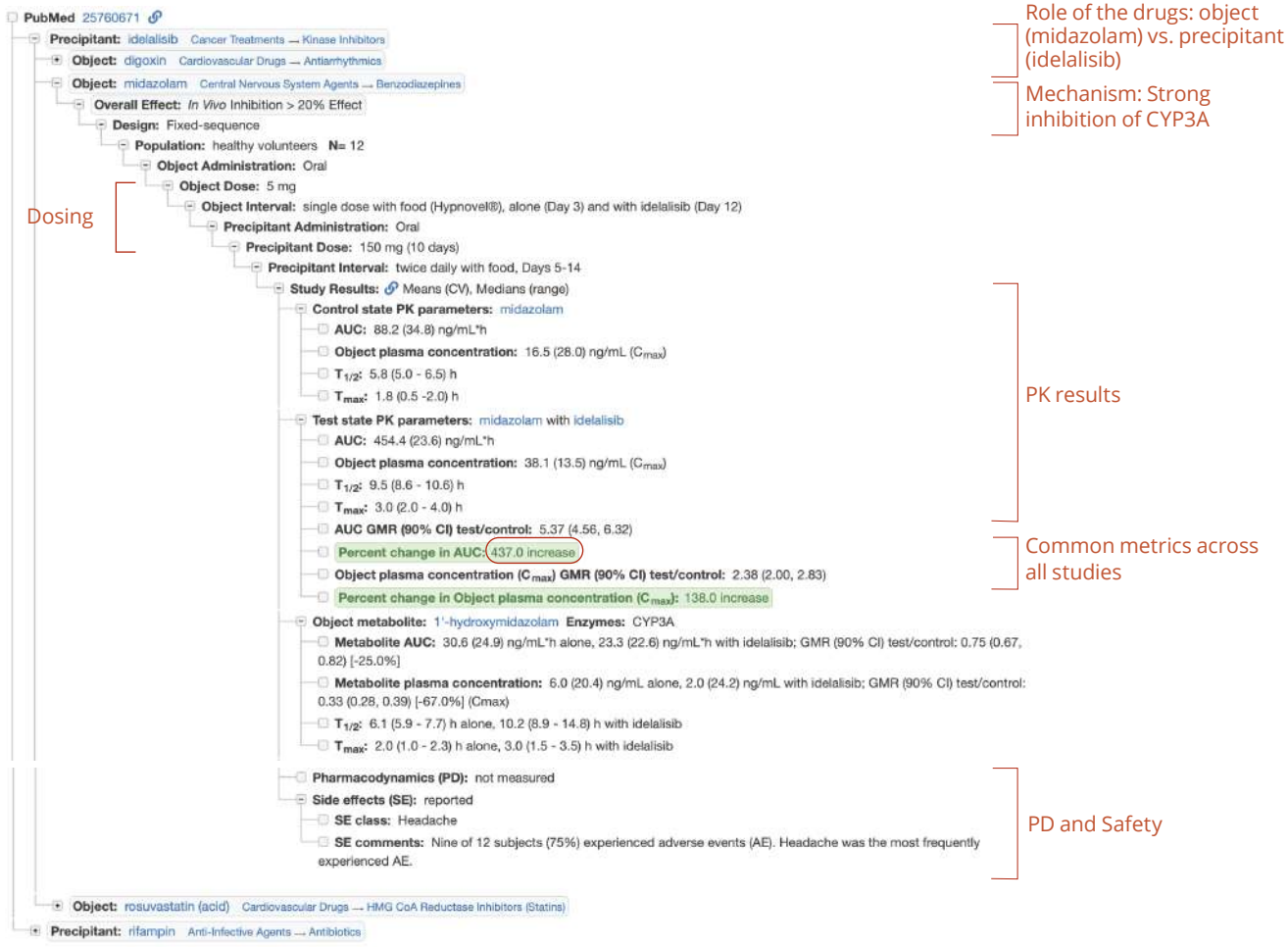

Idelalisib inhibits CYP3A with an AUC increase of 5.2-fold.

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

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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 midalozam

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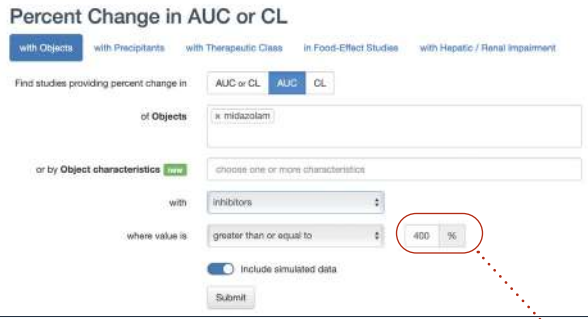

Table View of Query Results

Multiple formats for viewing and downloading

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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

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

CLINICAL DRUG INTERACTION DATASET IN NUMBERS

(as of October 16, 2023)

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

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

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

3,221 entries involving transporter(s)

2,853 case reports

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

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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.

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