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.

**Clinical drug interaction profile of idelalisib in healthy subjects.**

Jin F¹, Roeseen T², Zhou Y³, Moyer C¹, Wilbert S², Murray B¹, Ramanathan S¹.

**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 exposed concentrations).
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

Role of the drugs: object (midazolam) vs. precipitant (idelalisib)

Mechanism: Strong inhibition of CYP3A

PK results

Common metrics across all studies

PD and Safety

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 midalozam

Table View of Query Results

Obtain a complete list of in vivo strong inhibitors of CYP3A

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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

ACCESS 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.

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