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Clinical Organ Impairment Dataset

Transforming scientific data into clinical knowledge

The Clinical Organ Impairment Dataset contains study results from renal and hepatic impairment studies.

- **Detailed study information** regarding design, population, degree of organ impairment, 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 the severity of the disease:

  →Users can focus on a specific object drug or disease severity (mild, moderate, or severe)

  → Explicit changes in exposure can be searched
  (Example: "*Find all drugs with at least 2-fold change in AUC in patients with a specific degree of impairment*")

- **Comprehensive PK parameters** for the object drug and its metabolites are available for each population studied and are compared to a healthy control population.

- **Several pre-formulated queries** allow users to retrieve the organ impairment dataset by drug name, changes in exposure, or disease severity. allowing users to compile and organize the large body of information available.

- **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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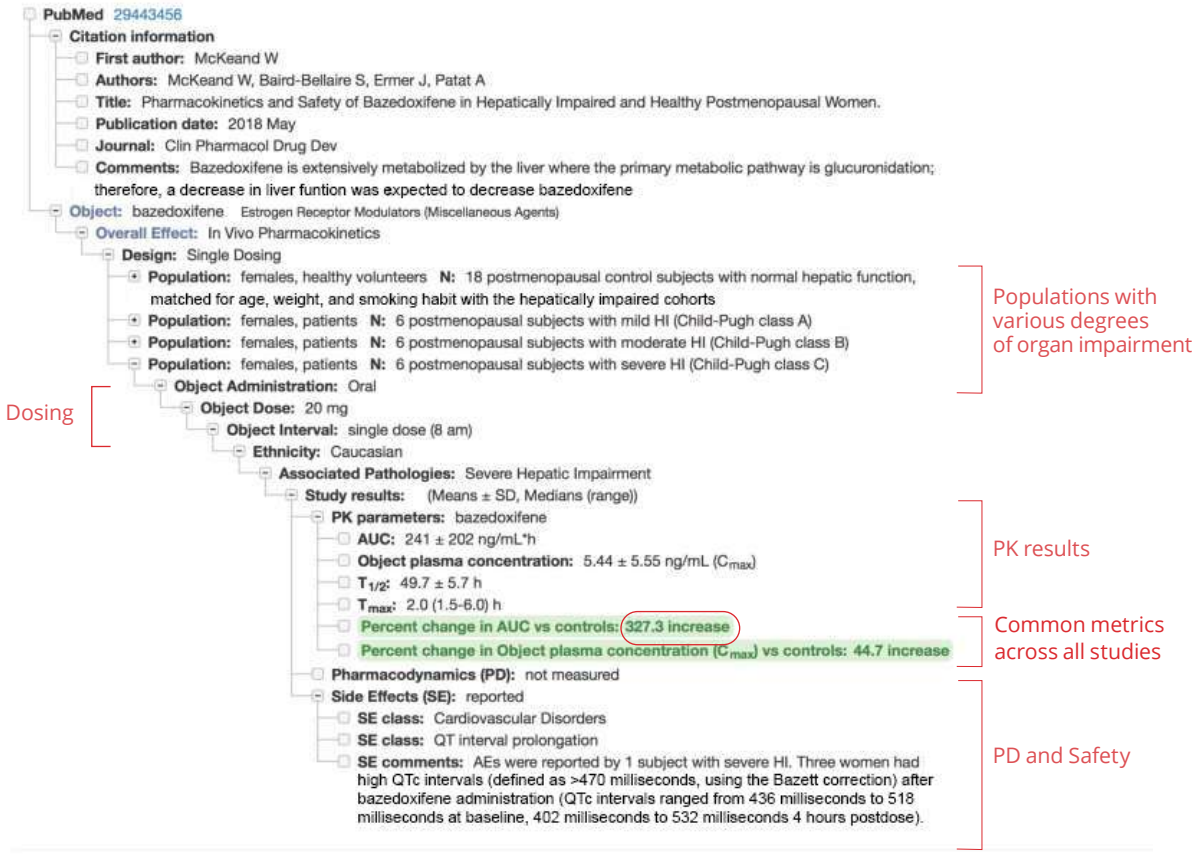

Bazedoxifene shows an AUC increase of 327.3% in patients with severe hepatic impairment.
What other drugs have an AUC change of at least 2-fold in these patients?

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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 drugs exhibiting exposure increases of at least 2-fold in patients with severe hepatic impairment

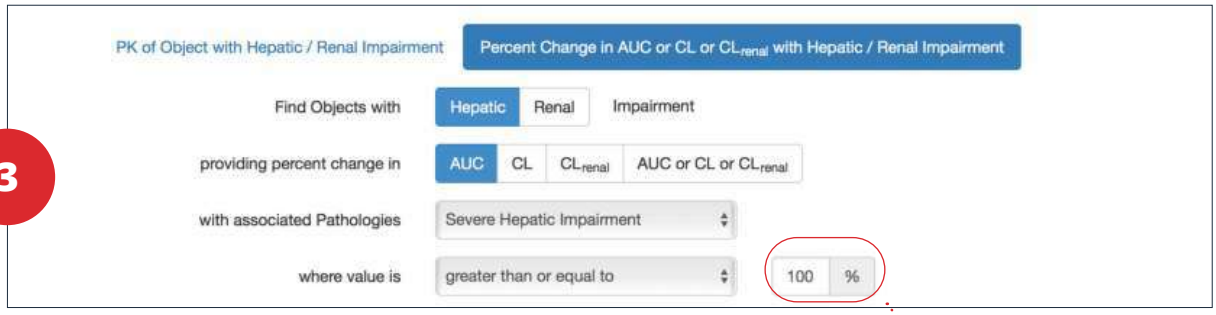

Table View of Query Results

Multiple formats for viewing and downloading

Showing 1 to 100 of 146 entries

Advanced Table Search | Select columns | Copy | Excel | CSV | Print

Object	Object Characteristics	Object Therapeutic Class	Object Administration	Object Dose	Object Interval	Population	AUC	Percent Change AUC	Accession # NDA/BLA #
abemaciclib	CYP1A2 weak inhibitor; CYP3A sensitive substrate	Cancer Treatments → Kinase Inhibitors	Oral	200 mg	single dose	patients (N = 6 subjects with severe HI (Child-Pugh class C))	9310 (49) ng/mL*h	108.7	NDA 208716
acalabrutinib	CYP3A sensitive substrate	Cancer Treatments → Kinase Inhibitors	Oral	100 mg (simulated) (duration not specified)	once daily	males, patients (N = simulated subjects with severe hepatic impairment (number of subjects/trials not provided))	4518.6 ng/mL*h (0-24 h) [PBPK prediction]	442.3	PubMed 356
acalabrutinib	CYP3A sensitive substrate	Cancer Treatments → Kinase Inhibitors	Oral	50 mg	single dose	patients (N = 8 subjects with severe hepatic impairment (Child-Pugh class C))	1169.0 (53.8) ng/mL*h [unbound: 11.5 (32.4) ng/mL*h (0-last) [+259.4%]]	367.3	PubMed 348
acalabrutinib	CYP3A sensitive substrate	Cancer Treatments → Kinase Inhibitors	Oral	50 mg	single dose (capsule)	patients (N = 8 subjects with severe hepatic impairment (Child-Pugh C; scores 10-15))	1169 (53.8) ng/mL*h	416.1	NDA 210259

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Obtain a complete list of drugs that may need dosing adjustment in patients with severe hepatic impairment

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CLINICAL ORGAN IMPAIRMENT DATASET IN NUMBERS

(as of October 16, 2023)

RENAL IMPAIRMENT

1,169 citations / **3,688** entries

302 NDAs/BLAs / **849** entries

HEPATIC IMPAIRMENT

688 citations / **1,715** entries

290 NDAs/BLAs / **715** entries

Dedicated organ impairment queries with **123** possible searches

1,090 possible searches drugs evaluated in organ impairment studies

APPLICATIONS OF CLINICAL ORGAN IMPAIRMENT DATASET

PROVIDES CONTEXT for RESULTS OBTAINED with candidate compouds

HELPS DEVELOP OVERALL REGULATORY STRATEGY and optimize renal and hepatic impairment trials:

- Guides choice of appropriate study design
- Refines inclusion/exclusion criteria for control population and patients with organ impairment
- Helps select dose regimen of object drug
- Provides PK variability data for power calculations

SUPPORTS PBPK MODELING and SIMULATIONS
with drug and disease parameters, changes in exposure validation set

ACCESSES REGULATORY ORGAN IMPAIRMENT STUDIES for recently marketed drugs

PROVIDES REFERENCE RESOURCE for ASSESSMENT of DRUG SAFETY in patients with different severity of renal or hepatic function deficiency

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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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