


Human *In vitro* Drug Transporter Dataset

Transforming scientific data into clinical knowledge


The Drug Transporter Dataset contains results from *in vitro* transporter studies, where a drug is tested as an inhibitor (precipitant) or a substrate (object) for a given human drug transporter (including variants).


 **Transporter parameters** (IC_{50} , K_i , % inhibition, P_{app} , efflux ratio, uptake ratio, K_m , and V_{max}) and *in vitro*-to-*in vivo* prediction ratios per FDA DDI guidance, along with detailed experimental conditions, are extracted from published articles (citations) and NDA/BLA reviews.

 **Study results** are organized according to the overall effect and mechanism of the interaction:

→ Transporter inhibition entry: drug as inhibitor or non-inhibitor

→ Transporter substrate entry: drug transported or not transported

 **Multiple queries** allow users to retrieve an *in vitro* dataset by drug name, transporter name, or mechanism of the interaction (drug as inhibitor or as substrate).

 **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 28320730[uid]

US National Library of Medicine National Institutes of Health

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Format: Abstract Send to

Drug Metab Dispos. 2017 Jun;45(6):646-656. doi: 10.1124/dmd.116.073932. Epub 2017 Mar 20.

Prediction of the Transporter-Mediated Drug-Drug Interaction Potential of Dabrafenib and Its Major Circulating Metabolites.

Ellens H¹, Johnson M², Lawrence SK², Watson C², Chen L², Richards-Peterson LE².

Author information

Abstract

The BRAF inhibitor dabrafenib was recently approved for the treatment of certain BRAF V600 mutation-positive tumors, either alone or in combination therapy with the mitogen-activated extracellular signal regulated kinase 1 (MEK1) and MEK2 inhibitor, trametinib. This article presents the dabrafenib transporter-mediated drug-drug interaction (DDI) risk assessment, which is currently an important part of drug development, regulatory submission, and drug registration. Dabrafenib and its major circulating metabolites (hydroxy-, carboxy-, and desmethyl-dabrafenib) were investigated as inhibitors of the clinically relevant transporters P-gp, BCRP, OATP1B1, OATP1B3, OCT2, OAT1, and OAT3. The DDI Guidance risk assessment decision criteria for inhibition of BCRP, OATP1B1 and OAT3 were slightly exceeded and therefore a minor DDI effect resulting from inhibition of these transporters remained possible. Biliary secretion is the major excretion pathway of dabrafenib-related material (71.1% of orally administered radiolabeled dose recovered in feces), whereas urinary

1

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

Tafinlar (dabrafenib) Capsules
Application No.: 202806
Approval Date: 05/29/2013

Most often analyzed files:

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

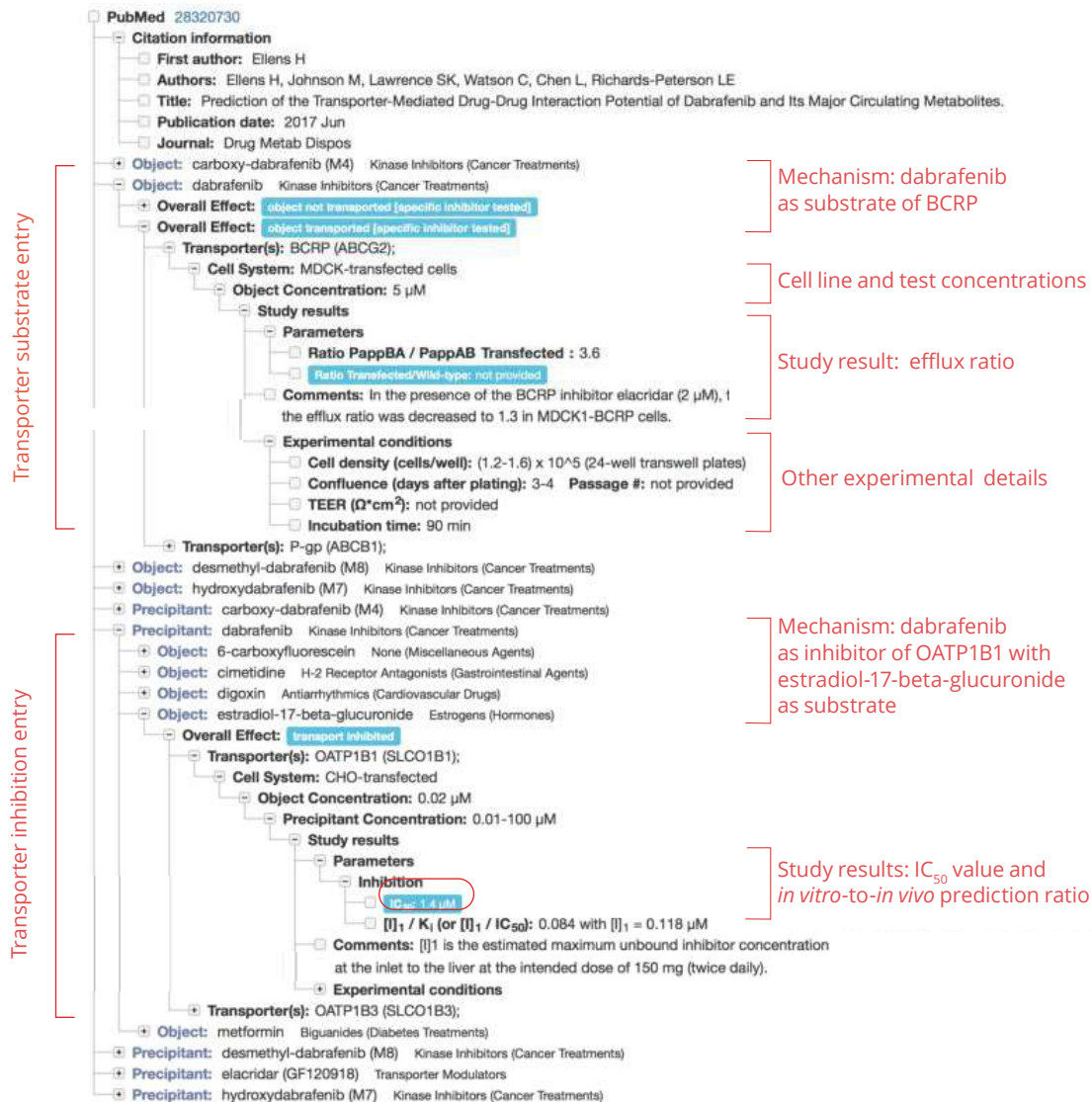
1

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



Dabrafenib inhibits OATP1B1 with an IC₅₀ value of 1.4 µM.
 What other OATP1B1 inhibitors have IC₅₀ values ≤ 10 µM?

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 OATP1B1 inhibitors with $IC_{50} \leq 10 \mu M$

3

Objects and Transporters Transporters with Objects Precipitants and Transporters **Transporters with Precipitants**

Find precipitants which

the following **Transporters**

providing

where value is

Table View of Query Results

4

Showing 1 to 100 of 263 entries (filtered from 771 total entries)

Advanced Table Search Select columns Copy Excel CSV Print

Precipitant	Precipitant Therapeutic Class	Object	System	Object Concentration	Precipitant Concentration	IC ₅₀ (µM)	Accession # or NDA/BLA #	Published
		estrad <input type="text" value="x"/>				-		
bilirubin ditaurate	Miscellaneous Agents → None	estradiol-17-beta-glucuronide	HEK293-transfected cells	2 µM		0.005	PubMed 19560444	2009 Nov 10
glecaprevir	Treatments of AIDS → Protease Inhibitors	estradiol-17-beta-glucuronide	Membrane vesicles	2.0 µM		0.017	PubMed 31167814	2019 Aug
cyclosporine	Immune System Agents → Immunosuppressants	estradiol-17-beta-glucuronide	HEK293-transfected cells		0.003 to 6 µM (30-45 min of pre-incubation)	0.019	PubMed 23179780	2013 Mar
rifamycin	Anti-Infective Agents → Antibiotics	estradiol-17-beta-glucuronide	HEK293-transfected cells	0.02 µM	0.001-30 µM	0.02	PubMed 26700956	2016 Mar
rifamycin	Anti-Infective Agents → Antibiotics	estradiol-17-beta-glucuronide	HEK293-transfected cells	2 µM	0-50 µM (estimated from Fig. 2A)	0.05	PubMed 23886114	2014 Mar
cyclosporine	Immune System Agents → Immunosuppressants	estradiol-17-beta-glucuronide	HEK293-transfected cells	0.02 µM	0.01-3 µM	0.05	PubMed 17901929	2008 May

Obtain a complete list of *in vitro* inhibitors of OATP1B1

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IN VITRO TRANSPORTER DATASET IN NUMBERS

(as of October 16, 2023)

3,248 citations / **350** NDAs/BLAs

16,953 substrate entries / **41,055** inhibition entries

38,259 positive entries / **19,749** negative entries

Dedicated *in vitro* transporter queries with **26** possible searches

108 drug transporters & **38** variants

2,543 compounds as substrates / **4,837** compounds as inhibitors

569 food products & **1,002** herbal medications

APPLICATIONS OF THE IN VITRO METABOLISM DATASET



PROVIDES CONTEXT for RESULTS OBTAINED with candidate compounds



ALLOWS ASSESSMENT of MEASUREMENT VARIABILITY (inter-lab, substrate- and system-dependency, etc.)



SUPPORTS STATIC PREDICTIONS and PBPK MODELING with input parameters



HELPS OPTIMIZE *IN VITRO* STUDY DESIGN (cell system, incubation conditions, test concentrations, choice of substrate/inhibitor, etc.)



ASSISTS with DOSE SELECTION for clinical trials



PROVIDES *IN VITRO* EVIDENCE to EXPLAIN CLINICAL RESULTS and improve understanding of drug interaction mechanisms

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



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