Clinical Pharmacogenetic Dataset

Transforming scientific data into clinical knowledge
The Clinical Pharmacogenetic (PGx) Dataset provides in-depth analysis of the impact of genetic variants of enzymes and transporters on the PK, PD, and safety of drugs in various populations. Available information comes from publications and NDA reviews describing gene-drug interactions (GDI), ethnicity-drug interactions, and case reports.

**Detailed study information** regarding design, drug dosing, genetic polymorphisms, population characteristics, PK, PD, and safety results are structured and presented according to the latest PGx scientific consensus. Common metrics for active compounds (percent changes in AUC, plasma concentrations, oral clearance, dose requirements) and metabolites (AUC ratio of metabolite/parent, and formation clearance) are used across all studies to allow metadata analysis of quantitative results.

**Study results** are categorized according to the overall impact of genetic variants on drug exposure, PD, and safety/efficacy compared to a reference group (non-carriers of variant).

**Comprehensive PK parameters** for parent drugs and their metabolites are available.

**Pre-formulated queries** allow users to retrieve an *in vivo* PGx dataset by drug name, gene name, and/or ethnicity.

**Results** can be viewed, customized, and downloaded, allowing users to compile and organize the large body of information available.

druginteractionsolutions.org
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.

Most often analyzed files:
- Printed labeling
- Multi-discipline review
- Chemistry review(s)
- Other review(s)
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.

**Dosing**

<table>
<thead>
<tr>
<th>Design and Drug Administration</th>
<th>Genotyping Method</th>
<th>Alleles Tested</th>
</tr>
</thead>
</table>
| clopidogrel 300 mg oral single dose | iPLEX Sequenom MassArray | CYP2C19 636A  
CYP2C19 636G  
CYP2C19 681A  
CYP2C19 681G  
CYP2C19*2  
CYP2C19*3 |
| Design: Single Dosing, Open-label | 8 Healthy volunteer(s) (reference)  
CYP2C19*1/*1  
CYP2C19*1/*3  
CYP2C19 Intermediate Metabolizers  
Asian  
Chinese  
Male(s)  
non-smokers | 2 Healthy volunteer(s)  
CYP2C19*2/2  
CYP2C19*2/3  
CYP2C19*3/3  
CYP2C19 Poor Metabolizers  
Asian  
Chinese  
Male(s)  
non-smokers |

**Impact of genetic variations on drug disposition**

- Clopidogrel exposure is significantly impacted in CYP2C19 poor metabolizers.

**Impact of genetic variations on drug efficacy**

- What other drugs have an AUC change of at least 2-fold in carriers of CYP2C19 loss-of-function alleles?

*statistically significant
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 CYP2C19 poor metabolizers**

**Table View of Query Results**

- Filter
- Multiple formats for viewing and downloading

Obtain a complete list of drugs that may need dosing adjustment in CYP2C19 poor metabolizers.
CLINICAL PGx DATASET IN NUMBERS  
(as of April 16, 2020)

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
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<td>Safety (side effects)</td>
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<tr>
<td>Drugs involved in PGx</td>
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</tbody>
</table>

APPLICATIONS OF THE CLINICAL PGx DATASET

- **Provides context for results obtained with candidate compounds**
- **Helps develop overall regulatory strategy and optimize clinical PGx trials:**
  - Refines inclusion/exclusion criteria
  - Helps select dose, duration, and timing of drug administration in the context of PGx
  - Provides PK variability data for power calculations
  - Quickly identifies known substrates of enzymes/transporters among marketed drugs to understand GDI risk
- **Supports static predictions and PBPK modeling**
  with input parameters
- **Accesses regulatory GDI studies for recently marketed drugs**
- **Provides reference resource for assessment of drug interaction safety**
- **Helps implement personalized medicine in the context of GDI and gene-DDI**

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