IVIVE of Transporter-Mediated Clinical Drug-Drug Interactions in Industry –

An Update from the IQ Transporter Working Group

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on behalf of the IQ DMLG/CPLG Transporter Working Group

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Overview of IQ Consortium

The International Consortium for Innovation and Quality in Pharmaceutical Development (IQ) is a technically-focused organization of pharmaceutical and biotechnology companies with a mission of advancing science and technology to augment the capability of member companies to develop transformational solutions that benefit patients, regulators and the broader R&D community.

IQ Member Companies:

AbbVie    Bayer HealthCare
Agios     Biogen
Alexion   Blueprint Medicines
Alkermes  Boehringer Ingelheim
Allergan  Bristol-Myers Squibb
Asgen, Inc. Celgene
Astellas  Daiichi Sankyo
AstraZeneca Eisai, Inc.
Baxter Healthcare Eli Lilly and Company
EMD Serono Endo Pharmaceuticals
Genentech Gilead Sciences
GlaxoSmithKline Incyte Corporation
Infinity Ironwood Pharmaceuticals
Johnson & Johnson
Merck & Co. Novartis
Otsuka Pfizer
Pierre Fabre Roche
Sanofi Seattle Genetics
Shire Sunovion
Takeda Teva
Theravance Biopharma UCB Pharma
Vertex, Inc.

www.iqconsortium.org
Project Overview

Problem Statement:
Data from transporter DDI studies can be challenging to interpret as victims are frequently substrates of multiple transporters and inhibitors may inhibit multiple transporters/enzymes. Consequently, the need for and timing of clinical transporter DDI studies could benefit from additional scholarship.

IQ DMLG/CPLG Transporter Project Overview:
Collect in vitro and clinical transporter data on member company drugs and NMEs to:

(1) probe the in vitro to in vivo correlation of transporter drug interactions
(2) identify the overall magnitude of the interactions, their clinical implications, and evaluate the regulatory decision trees.
Data Collection

• **In vitro transporter studies**
  • Basic study design
  • Individual transporter assay results

• **Clinical transporter studies**
  • Reason for study initiation
  • Basic study design
  • Mean pharmacokinetic results
  • Clinical implications

• **Basic compound information** necessary for the interpretation of in vitro and clinical studies
Expected Results

• Evaluation of the regulatory transporter decision trees and, if appropriate, suggest refinement(s).
• An improved understanding of predictability of clinically relevant transporter-mediated DDIs from in vitro data.
• Determination of the magnitude of transporter-mediated DDIs using clinical data for compounds from various companies, therapeutic areas/targets, and probe substrates/inhibitors.
• Understanding the clinical implications of transporter based drug-drug interactions.

Summary of results will be communicated in a white paper (mid 2018)
Q&A