

The Role of Pharmacogenomic Data in Pediatric Therapeutics

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Genesis of the Topic

- During the pediatric-focused safety review of Sustiva (efavirenz) at the Sept. 2016 Pediatric Advisory Committee (PAC) meeting, the PAC discussed the role of therapeutic drug levels, the risks to rapid metabolizers, how pharmacogenomic testing may be useful, and whether this information should be added to labeling. The PAC welcomed a future discussion of these general issues.
- During the PAC discussion, it was noted that the Panel on Anti-Retroviral Therapy and Medical Management of HIV-Infected Children recommends that efavirenz generally not be used in children less than 3 years of age. If use of efavirenz is unavoidable due to the clinical situation, investigational doses of efavirenz in this age group are suggested (see investigational dosing tables at the below URL); evaluation of CYP2B6 genotype is required prior to use.
 - <https://aidsinfo.nih.gov/guidelines/html/2/pediatric-arv-guidelines/123/efavirenz>

Presentations

1. Pharmacogenomics in Pediatric Product Development and Labeling
 - Dionna Green, MD, Office of Clinical Pharmacology (OCP), CDER
2. Case Studies in Pharmacogenetics
 - Michael Pacanowski, PharmD, MPH, OCP, CDER
3. Analytical and Clinical Validation of Pharmacogenetic Tests
 - Kellie B. Kelm, PhD, Office of In Vitro Diagnostic Devices and Radiological Health, CDRH
4. Clinical Implementation of Precision Therapeutics in Children
 - J. Steven Leeder, PharmD, PhD, Children's Mercy Hospital and Clinics, Kansas City, MO

Examples to Stimulate Discussion



- SUSTIVA[®] (efavirenz)
 - CYP3A and CYP2B6 are the major isozymes responsible for efavirenz metabolism.
- DEPAKENE (valproic acid)
 - Contraindication of known mitochondrial disorders caused by mutations in mitochondrial DNA Polymerase γ (POLG).
- STRATTERA[®] (atomoxetine)
 - Route of atomoxetine elimination is CYP2D6 metabolism.
- PLAVIX (clopidogrel bisulfate)
 - Clopidogrel is a prodrug activated by multiple CYP450 enzymes, including CYP2C19.

Discussion Topic 1 (of 2)

Based on your clinical experience and the information provided to you at this meeting, please discuss the role of pharmacogenomic testing in your care of patients. In this discussion, please consider the following topics: situations that merit ordering a pharmacogenomic test before prescribing a medication; challenges that may arise in obtaining and/or using this information; situations where you would request a pharmacogenomic test to explore an association with a serious adverse drug effect experienced by a patient; and the source(s) of pharmacogenomic information that you (and other pediatric practitioners) may use to inform your clinical practice.



Discussion Topic 2 (of 2)

Please discuss the specific role of product labeling to inform your use of pharmacogenomic data in your clinical pediatric practice. In this discussion, please address the location in the product label (e.g., a boxed warning, contraindication, warning and precautions, dosage and administration). As examples, please discuss the issues you would consider in deciding whether to order a POLG test prior to prescribing valproic acid or a CYP2D6 test prior to prescribing atomoxetine. Finally, please discuss how you would describe pharmacogenomic testing to your patients/parents.

Thank you.

