NETWORK OF T 32 PROGRAMS IN PEDIATRIC CLINICAL PHARMACOLOGY

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PEDIARTIC CLINICAL PHARMACOLOGY JOURNAL CLUB

ONCOLOGY EDITION

December 17, 2013 at Noon EST

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THE TOPIC:

EXPLORING THE CONTROVERSY SURROUNDING GENETIC PREDICTORS OF CISPLATIN-INDUCED OTOTOXICITY

In 2009, Ross and colleagues in Vancouver British Columbia genotyped 220 drug-metabolism genes in pediatric oncology patients and found variants in TPMT and COMT that were linked to cisplatin mediated ototoxicity. Recently Yang et al., attempted to replicate these findings at St Jude's but did not find an association between TPMT/COMT variants and ototoxicity. Around the same time, the British Columbia group attempted to replicate their initial findings, and could not with COMT, but did with TPMT and found an additional transporter ABCC3 with variants that may predict ototoxicity. Clinical Pharmacology and Therapeutics printed both of these opposing articles together in 2013, and just in their most recent issue have also published commentary by Dr. Ratain on this controversy. We will discuss these articles below and the data that has sparked the debate:

1. Pussegoda, K et al. Replication of TPMT and ABCC3 genetic variants highly associated with cisplatin-induced hearing loss in children. CPT. 94, 243-251 (2013).
2. Ratain et al. Challenges in interpreting the evidence for genetic predictors of ototoxicity. CPT. 94, 631-635.
3. Ross, CJ et al; CPNDS consortium. Genetic variants in TPMT and COMT are associated with hearing loss in children receiving cisplatin chemotherapy. Nature Gen. 41, 1345-1349 (2009).
4. Yang JJ et al. The Role of Inherited TPMT and COMT Genetic Variation in Cisplatin-Induced

We invite you to join us for this web-based conference to add to the lively discussion!

Presenters:

Dr. Michael Ferguson of Indiana University

Dr. Behzad Bidadi of Mayo Clinic

Special Guest Reactors

Dr. Mark Ratain of University of Chicago

Dr. Jun Yang of St. Jude's Children's

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