## PI-83

PREGNANCY OUTCOME FOLLOWING GESTATIONAL EXPOSURE TO MONTELUKAST: A PROSPECTIVE COTROLLED STUDY. M. Sarkar, BSc Hon, G. Koren, MD, Department of Pharmaceutical Sciences, University of Toronto, Motherisk Program, Division of Clinical Pharmacology & Toxicology, Hospital for Sick Children and University of Toronto, Toronto, ON, Canada.

**BACKGROUND:** Asthma is the most common respiratory crisis complicating pregnancy. Montelukast is prescribed orally for chronic treatment of asthma. Although animal reproductive studies show no evidence of teratogenic effects, there are no human studies assessing possible effects on the developing fetus with *in utero* exposure. Despite known risks associated with poorly controlled asthma, lack of safety data prevents women from using montelukast in pregnancy. Our aim is to evaluate pregnancy outcomes following gestational exposure to montelukast.

**METHODS:** This prospective controlled study enrolls pregnant women who contact Motherisk about exposure to montelukast. These women are followed up using standardized data collection forms. Montelukast-exposed women are compared to a disease-matched group using inhalers for similar indications and a group of women exposed to known non-teratogens. Rates of major anomalies and other adverse outcomes are compared between groups.

**RESULTS:** To date, 64 women exposed to montelukast during 1$^{st}$ trimester have been enrolled, of which 24 have used it throughout pregnancy. Outcomes of this group include: 62 (96.9%) live births, 2 (3.1%) SA and 2 (3.1%) major malformations. Upon comparison to controls, no statistical differences are apparent in these or any other endpoints of interest.

**CONCLUSIONS:** Data collected thus far in this ongoing study appear to suggest no increased risk for major malformations above baseline of 1–3%, following use of montelukast in pregnancy.

## PI-84

PHARMACOKINETICS (PK) AND ABSOLUTE BIOAVAILABILITY (F) OF LINEZOLID (L) IN CYSTIC FIBROSIS (CF) PATIENTS (PTS). M. Reed, PharmD, M. Konstan, MD, M. O'Riordan, MS, J. Blumer, PhD, MD, Case Western Reserve University, National Institute of Child Health and Human Development, PPRU, Cleveland, OH.

**INTRODUCTION:** Methicillin- & vancomycin-resistant bacteria are increasingly responsible for CF exacerbations. L is highly active against these pathogens. We studied L first dose (FD) & steady-state (SS) PK in CF Pts.

**METHODS:** CF pts received L-IV and then orally when indicated as part of their hospitalized clinical care. 12 blood samples & 4 timed urine aliquots were obtained over 24hrs after FD (2$^{nd}$ IV dose held) & 9 blood samples again at SS (dosed q8–12h). Quantitation of L and 2 inactive metabolites were determined by HPLC; standard non-compartment PK methodology was used.

**RESULTS:** 10 pts (5 males) studied thus far; data analyzed for 7. Plasma L concentration-time curves reflect 2-compartment character. Mean(±)SD L PK after FD:t½-4.6 (1.9) hrs;Vd-0.67 (0.09) L/Kg; Cl-2.6 (1) ml/min/Kg. No differences were observed between FD & SS PK. ~18% of IV dose excreted in urine over 24hrs. Median L oral F was 110% of IV dose administered. L metabolites M25 & M23 accounted for ~24% & 5% of parent L plasma concentrations, respectively. These L PK data in CF are consistent with L PK data obtained in 39 non-CF Pts of similar age.

**CONCLUSIONS:** Our preliminary L CF PK data support conventional age-appropriate L dosing & employing a 1 to 1 conversion for IV to oral switch in the treatment of CF patients.

## PI-85

PATTERNS OF DRUG UTILIZATION IN A NEONATAL INTENSIVE CARE UNIT. I. Warrier, MD, W. Du, PhD, G. Natarajan, MD, V. Salari, PhD, J. V. Aranda, MD, PhD, Children's Hospital of Michigan, Detroit, MI.

**BACKGROUND/AIMS:** Pharmacological agents are extensively used in neonatal intensive care settings but their utilization rates in neonates including premature infants is an area that has not been studied in great detail. This study determined the types, patterns and frequency of drug use in sick newborns to identify educational and research priorities in neonatal drug therapy.

**METHODS:** Data that had been prospectively collected in 6860 neonates admitted to the neonatal intensive care unit (ICU) / progressive care nursery (PCN) at a maternity hospital between 1997 and 2003 were analyzed retrospectively.

**RESULTS:** A total of 107 different drugs used in a predominantly African-American (~80%) population were studied . Mean length of ICU/PCN stay was 15±24 days, birthweight (BW) 2494±1002 grams and gestational age (GA) 35±5 weeks. Drug exposure rates (fig 1) were highest for antibiotics. The highest average drug usage was in the 24–27 week GA group at 12.4/infant followed by the <23 week GA category at 10.5/infant. Factors associated with increased risk of drug exposure by multivariate analysis were: Caucasian ethnicity, male gender, GA <28 week and BW <1000 grams.

**CONCLUSIONS:** Antibiotics are the most commonly used drugs, far outweighing any other category, with >90% of infants being exposed to them. Future research and educational efforts should be directed to areas of appropriate antibiotic therapy in neonates with priority assigned to very low birth weight infants.

## PI-86

PHARMACOKINETICS OF RIFAPENTINE IN CHILDREN. M. J. Blake, PhD, MD, S. M. Abdel-Rahman, PharmD, R. F. Jacobs, MD, N. K. Lowery, RN, G. L. Kearns, PharmD, PhD, Children's Mercy Hospitals and Clinics, Univ of Arkansas Med Cntr & Arkansas Children's Hospital Research Institute and Medical Center, Kansas City, MO.

Rifapentine (RIF) is a rifamycin antibiotic approved for the treatment of pulmonary infections caused by *M. tuberculosis* that has potential therapeutic advantages over existing rifamycins. This study was designed to characterize the pharmacokinetics of RIF in children.

**METHODS:** 24 children (7.1 ± 3.3 yr; 27.9 ± 11.9 kg) were enrolled in this open label study. Children received a single oral dose of RIF (150 or 300 mg) followed by repeated blood sampling (n=11) over 32 hr and quantitation of RIF and 25-desacetyl rifapentine (DRF) by HPLC. Pharmacokinetic parameters were determined using a model independent approach.

**RESULTS:** Due to a large degree of intersubject variability, no relationship was observed between weight-normalized dose and exposure. A weak, albeit significant, relationship was observed between age and dose-normalized $AUC_{0\text{-}n}$ and $AUC_{0\text{-}\infty}$ ($r^2$=0.22, p=0.02). Similarly, age appeared to account, in part, for the extent of DRF formation ($r^2$=0.27, p=0.01). In contrast, no correlation was observed between age and dose-normalized $C_{max}$ or Vd/F. Adverse events related to the administration of RIF were mild and included stomach ache (n=1) and vomiting (n=2).

**CONCLUSIONS:** RIF appears to be well tolerated in children 2–12 yr. Given a comparable weight normalized dose, RIF exposure estimates are slightly lower in children than reported for adults. However, putative pharmacodynamic targets for highly susceptible isolates appear to be achieved in the majority of children receiving a RIF dose of 5–10 mg/kg.