dk), where midazolam dose is adjusted to total body weight or age, may lead to both supra- and subtherapeutic doses respectively, in children with obesity. However, confirmatory studies are needed.

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036

PHYSIOLOGICALLY BASED PHARMACOKINETIC MODELS TO PREDICT FETAL EXPOSURE TO ANTIVIRAL DRUGS

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Background Physiologic changes associated with pregnancy may have a large impact on drug disposition. The goal of this study was to build PBPK maternal-fetal models to predict the fetal exposure to antiviral drugs including emtricitabine and acyclovir.

Methods PBPK models were built in the Open Systems Pharmacology Software Suite version 7.3 (www.open-systems-pharmacology.org). The maternal-fetal PBPK model structure was developed in MoBi and exported to PK-Sim for population simulations. Placental transfer was parameterized based on data from ex vivo cotyledon perfusion experiments. The predictive performance of the PBPK models was evaluated via comparison with in vivo data. The pregnancy data for those drugs were from in vivo maternal and fetal blood samples taken at delivery.

Results In the acyclovir ex vivo experimental data simulation, the fitted was 0.056 L/h (95% confidence interval: 0.043 - 0.069 L/h) and the fitted was 0.49 (95% confidence interval: 0.39 - 0.59). The predicted ratio between acyclovir in vivo concentrations in the umbilical vein plasma and the maternal plasma ranged from 0.37 - 0.77, whereas the observed ratios were slightly higher and ranged from 0.61 - 1.1.¹ The previously published, and CLpl (1.49 l/h) parameters² were applied to the emtricitabine maternal-fetal PBPK model, and the emtricitabine concentrations in the umbilical cord were adequately predicted.

Conclusion These results increase the confidence in applying PBPK models to predict maternal and fetal drug exposure. Improved maternal-fetal PBPK models may streamline and accelerate the performance of pharmacokinetic and safety studies for drugs in pregnant women.

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USE OF ALBENDAZOLE IN CHILDREN WITH ASYMPTOMATIC TOXOCARIASIS

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Background Human toxocariasis is highly prevalent and its global importance may be greatly underestimated. Toxocariasis occurs mainly in childhood by ingestion of parasite eggs from contaminated environment. During migration in human tissues the *Toxocara* larvae can cause several symptoms including eye involvement, but the majority of patients are asymptomatic. Eosinophilia is a marker of activity of this disease. There are no studies supporting the treatment of asymptomatic patients. **Methods** To evaluate the effectiveness of albendazole (10–15 mg/kg/day BID for 15 days) a randomized, placebo-controlled trial was carried out in asymptomatic children (ClinicalTrials.gov #NCT00755560). Treatment response was defined as mean absolute reduction in eosinophil counts, 12 months after treatment.

Demographic, complete blood count, liver and renal function and stool parasite exam were assessed at diagnosis, and every 4 months during follow up. Inclusion criteria: age 2 to 15 years, reactive toxocara excretory-secretory substances (TES) by ELISA, eosinophils >1100/mm³, normal fundoscopy and non geohelminthic infection.

Results The 45 enrolled subjects, median age 5.3 years (range 2–13), were randomized in a 1: 1 relationship.

At 12-month follow-up, eosinophil median was: 1008/mm³ (IQ₂₅₋₇₅:680 to 2023) in placebo group and median of 1360/mm³ (IQ₂₅₋₇₅:761 to 2226) in albendazole group (p = 0.37).

Kinetics of specific antibody titers by the ELISA showed an erratic pattern. No differences were observed in the values between the 2 treatment groups.

Both groups had minor adverse events and no patient needed to discontinue medication. In asymptomatic patients with toxocariasis, albendazole was not effective to reduce eosinophil counts.

Conclusion Given that toxocariasis is a neglected disease, in order to evaluate the effectiveness of albendazole or other drugs, further studies need to be conducted.

Disclosure(s) Nothing to disclose

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POPULATION PHARMACOKINETICS OF GANCICLOVIR AFTER ORAL VALGANCICLOVIR IN RENAL TRANSPLANT CHILDREN

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