Background Cytomegalovirus (CMV) infection is a major cause of morbidity in solid organ transplant recipients. Valganciclovir (ValG), prodrug of the antiviral ganciclovir, is used to prevent or treat CMV infection in this population. It is controversial in children. As the percentage of patients reaching the pharmacological target is too low with currently used ValG dosing regimen, our aim was to determine ganciclovir population pharmacokinetics in renal transplant children receiving ValG and propose an appropriate dosage regimen.

Methods After transplantation, children receiving ValG were monitored for plasma ganciclovir concentrations using high performance liquid chromatography. Population pharmacokinetics analysis was performed with NONMEM.

Results 1212 samples from 104 renal transplant patients, aged 2 to 20 years, received ValG to prevent (n=80), treat (n=12), or both prevent then treat (n=12) CMV infection. ValG was administered orally at a daily dose of 19.8 ± 10.1 mg/kg (mean ± SD). A two-compartment model with first-order elimination best fitted the data. At steadystate, $AUC_{\text{ss}}$ was $64.5 \pm 23.4$ μg/mLh, apparent clearance (CL/F) was $0.39 \pm 0.14$ L/h/kg, apparent volume of distribution at steadystate (VDss/F) was $2.4 \pm 0.48$ L/kg. Ganciclovir CL/F increased with body surface area, decreased with increasing creatinine clearance and was 15% higher in boys. Central volume of distribution increased with body surface area (BSA) and showed a 14% increase in boys. Internal validation was performed.

Conclusion We have successfully built a pharmacokinetic model allowing to propose dosages adapted individually to the characteristics of renal transplanted children.

Disclosure(s) Nothing to disclose

REFERENCE

Poster Presentations

P01 APPLICATION OF FETO-PLACENTAL-MATERNAL PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODEL TO PREDICT TENOFOVIR CONCENTRATION DURING PREGNANCY

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Background Tenofovir is a drug used in combination with other anti-HIV drugs to treat patients with HIV-1 infection. It is used during pregnancy to reduce the risk of HIV transmission to the child. The aim of this work is to use a Physiologically-Based Pharmacokinetic (PBPK) model for prediction of maternal and fetal tenofovir concentration at birth.

Methods A full Feto-Placental-Maternal PBPK model that includes placenta as a 3-compartment permeability limited organ and 14 compartments for different fetal organs was developed using physiological and drug specific parameters.