P108 PHARMACOKINETICS OF MYCOPHENOLIC ACID FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN CHILDREN

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Background Mycophenolate mofetil (MMF) is increasingly used in children with systemic lupus erythematosus (SLE). Monitoring of its active metabolite, mycophenolic acid (MPA), is performed for individual dosage adjustment of MMF and is based on determination of area under the plasma concentration-time curve (AUC_{12h}) of MPA. The objective of this monocentric study is to describe the pharmacokinetics (PK) of MPA in paediatric patients with SLE or lupus nephritis.

Methods Patients with lupus treated by MMF between January 2009 and July 2018 were included. MPA plasma concentrations (T0, T0.5h, T1h, T2h, T3h, T8h and T12h) were determined by EMIT (enzyme-multiplied immunotechnique) and MPA AUC_{12h} calculated according to trapezoid rule.

Results Twenty-two patients were diagnosed with lupus at 11.5 ± 2.9 years. Clinical presentation was SLE (n=18) or isolated lupus nephritis (n=4). Treatments prior to MMF were steroids and/or immunosuppressants (endoxan, rituximab). Age at initiation of MMF (Cellcept® n=20, Myfortic® n=2) was 12.9 ± 2.6 years.

PK of MPA was performed after 8.2 ± 14.8 months of treatment, under MMF dose of 840 ± 218 mg (577 ± 98 mg/m²). A large interindividual variability in MPA concentration-time profiles was observed with the following mean parameters: C_{max}=4.60 ± 11.70 µg/mL, t_{max}=80 ± 77 min, trough plasma concentration (C₀) = 2.30 ± 1.60 µg/mL and AUC_{0-12h}=46.29 ± 17.39 µg*h/mL.

Conclusion Data on the PK of MPA in lupus children are limited. Our results show the high interindividual variability in MPA exposure after oral administration of MMF. Monitoring of exposure based on AUC in combination with immunological disease parameters will allow to individualise treatment to optimise

Disclosure(s) Nothing to disclose

P109 OPTIMAL DOSING REGIMEN OF CASPOFUNGIN IN CHILDREN: MILLIGRAM PER KILOGRAM OR MILLIGRAM PER SQUARE METER?

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Background Caspofungin is the first echinocandin to be used as a first-line antifungal agent for *Candida* spp. infections in febrile, neutropenic adult and paediatric patients. To date, the optimal dosing of caspofungin in children has not been determined. We evaluated the population pharmacokinetics of caspofungin in children (2–12 years old) and defined an appropriate dose in order to optimize caspofungin treatment in this vulnerable population.

Methods Blood samples were collected from 48 children treated with caspofungin and drug concentrations were quantified by HPLC-MS. Population pharmacokinetic analysis and

Monte-Carlo simulation were performed using NONMEM software

Results Data from 48 children was available for population pharmacokinetic analysis. A two-compartment model with first-order elimination had the best fit with the data. Subsequent covariate analysis demonstrated that body surface area had a significant correlation with caspofungin pharmacokinetics compared to body weight. Monte Carlo simulation demonstrated that >90% of a simulated paediatric population (age range, 2–12 years) treated with a loading dose of 70 mg/m² followed by a 50 mg/m² maintenance dose once daily would reach a minimum inhibitory concentration of 1 µg/mL, the proposed susceptibility breakpoint for caspofungin against *Candida* spp.

Conclusion The population pharmacokinetics of caspofungin was evaluated and revealed that adjustment of caspofungin based on body surface area is most appropriate for paediatric use.

Disclosure(s) Nothing to disclose

P110 POPULATION PHARMACOKINETICS AND DOSING OPTIMISATION OF IMPENEM IN CHILDREN WITH HAEMATOLOGICAL MALIGNANCIE

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Background Imipenem/cilastatin is widely used for the treatment of children with serious infections. Currently, there is lack of pharmacokinetic studies of imipenem in children with hematological malignancies. Given the significant impact of disease on pharmacokinetics and increased resistance, we aimed to conduct a population based pharmacokinetic study of imipenem and optimize the dosage regimens for this vulnerable population.

Methods After treated with IMP/CS, blood samples of children were collected and the concentration of imipenem were quantified using HPLC-UV. Then, population level pharmacokinetic analysis was conducted using NONMEM software.

Results Data from 56 children (age range: 2.03–11.82 years) with hematological malignancies were collected to conduct a population based pharmacokinetic analysis. In this study, a two-compartment model that followed first-order elimination was found to be best suitable. The parameters of current weight, age and creatinine elimination rate were significant covariates that influenced imipenem pharmacokinetics. As a result, 52.0%, 65.2% and 76.6% of children reached the pharmacodynamic target (70% fT>MIC) against sensitive pathogens with an MIC of 0.5 mg/L at 15, 20 and 25 mg/kg q6h of imipenem, respectively. However, only 17.2% of children achieved the pharmacodynamic target against *Pseudomonas aeruginosa* with an MIC of 2 mg/L at a dose of 25 mg/kg q6h.

Conclusion Population pharmacokinetics of imipenem was assessed in children. The current dosage regimens of imipenem are underdose for resistant pathogens including *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. However, for sensitive pathogens, imipenem has an acceptable pharmacodynamic target rate at a dosage of 25 mg/kg q6h.

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