P0146
Paper Poster Session
New treatment options for mycobacterial infections

A pharmacokinetic evaluation of sulfamethoxazole 800 mg once daily in the treatment of tuberculosis

Noor Si Alsaad*[1]

[1]*Umcg, Clinical Phamacy and Pharmacology and, Groningen,, Netherlands*

Background: For treatment of multi drug resistant tuberculosis (MDR-TB) there is a scarcity of antituberculosis drugs. Co-trimoxazole (SXT) is one of the available drug candidates, and already frequently co-prescribed in TB-HIV co-infected patients. However, only limited data are available on pharmacokinetic (PK) and pharmacodynamic (PD) parameters of SXT in TB patients. The objective of this study was to evaluate PKparameters and *in* vitro PD data of the effective part of SXT; sulfamethoxazole (SMX).

Material/methods: In a prospective PK study in patients with drug-sensitive TB (age >18), SXT was administered orally in a dose of 960 mg once daily. One-compartment population pharmacokinetic modelling was performed using Mw\Pharm 3.81 (Mediware, Groningen, The Netherlands). The *ƒ*AUC/MIC ratio and the time period in which the free concentration exceeded the MIC (T>MIC) were calculated.

Results: Twelve patients received 960 mg of SXT on top of first line drugs. The pharmacokinetic parameters of the population model were as follows (mean ± SD): CLm 0.80 ± 0.21 L/h, Vd 0.33 ± 0.04 L*kg-1 corrected lean body mass, fr 0.16 ± 0.06, F 1, Ka 1.04 ± 0.17 h-1, lag time 0.89 ± 1.91 h. Free fraction of SMX was 0.3, but ranged between 0.2-0.4. The geometric mean of the MICs was 8.5 mg/L (range, 4.8-9.5) and of *ƒ* AUC/MIC ratio was 14.7 h.mg/L (range, 10.3-19.2h.mg/L). The percentage of *ƒ* T>MIC ranged between 43 and 100 % of the dosing interval.

Conclusion: The PK and PD data from this study are useful to explore a future dosing regimen of SXT for MDR-TB treatment.