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Title: Pharmacokinetics of drugs for non tuberculous mycobacterial lung infections

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Body: Successful treatment for Non-Tuberculous Mycobacterial (NTM) infections is easily frustrated. Little is known about the pharmacokinetics (PK) and dynamics of treatment regimens in relation to treatment outcome. Drug concentrations may be an intermedian link. In NTM disease very few PK studies have been performed. We performed a prospective, descriptive pharmacokinetic (PK) study of the plasma pharmacokinetics (full PK-curve) of rifampicin (RIF), ethambutol, clarithromycin, azithromycin, isoniazid and moxifloxacin and their active metabolites in a Dutch series of patients with clinically relevant NTM lungdisease and we compared the results with two other series from the literature. The baseline characteristics are shown in table 1.

baseline characteristics

Patients	14
Male, n (%)	10 (71%)
Mean age (range)	64.3 (43-85)
Ethnicity	Caucasian (100%)
Mean Weight (kg)	71,01
BMI (range)	23.4 (19.0-30.3)
Species	n=

table 1

Table 2 shows the main PK results.

main pharmacokinetic parameters

Drugs used	n=	Mean dose/Kg	Mean Cmax	Mean AUC0-24
Rifampicin	14	8,51 ± 0.74	12.813 ± 4.28	47.833 ± 14.84
Claritromycin	5	7.10 ±0.81	0.426 ± 0.25	2.744 ± 0.76
Azitromycin	2	4.73 ± 1.92	0.183 ± 0.24	2.034 ± 0.85
Ethambutol	13	15.96 ± 1.92	3.275 ± 1.21	26.339 ± 11.36

table 2

Results were generally consistent with the data published in the past by Wallace and Peloquin. Our data showed that rifampicin causes a reduction in clarithromycin and azithromycin serum concentrations. The current study has confirmed the significant PK interactions between rifampicin and clarithromycin and we feel this calls for a reevaluation of the dosing strategies in NTM lung disease as an inadequate response to treatment might be attributed to suboptimal drug exposure.