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PHARMACOKINETIC INTERACTIONS BETWEEN RIFABUTIN AND LOPINAVIR/RITONAVIR IN HIV-INFECTED PATIENTS WITH MYCOBACTERIAL CO-INFECTION

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OBJECTIVES: Current British HIV Association (BHIVA) and Centres for Disease Control and Prevention (CDC) guidelines suggest that when using a lopinavir/ritonavir (Kaletra)-based antiretroviral regimen, the rifamycin drug of choice is rifabutin. The dose of rifabutin should be reduced from 300 mg daily to 150 mg three times a week. We investigate current guidelines to ensure they result in therapeutic rifabutin levels.

METHODS: Therapeutic drug monitoring (TDM) of Kaletra and rifabutin was performed on five patients on concurrent treatment (>2 weeks) at currently recommended doses.

RESULTS: Rifabutin levels for all five patients were found to be sub-therapeutic, with one patient deteriorating clinically.

Patient	Rifabutin 4 h post-level (mg/l)	Kaletra trough level (ng/ml)
1	0.16	9352*
2	0.33	1030*
3	0.17	18 035*
4	<0.10	1549*
5	0.16	7910*

Rifabutin post-dose: 0.50–
1.0 mg/l
Kaletra trough level: for
wildtype virus: 1000 ng/l
*Experienced patients:
8000 ng/l

CONCLUSIONS: Our data suggests current BHIVA and CDC guidelines result in sub-therapeutic rifabutin levels. In our study one in five patients clinically deteriorated. Further formal investigations are required to establish the clinical significance of this, and determine the optimum dosing regimes for Kaletra and rifabutin in co-infected patients. Further formal investigations are required to establish the clinical significance of this, and determine the pharmacokinetic impact of changing the rifabutin dose.

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