Effect of rifabutin in dolutegravir dosing: a case series

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BACKGROUND

Tuberculosis (TB) is the leading cause of death in human immunodeficiency virus (HIV) infected people worldwide.

Rifamycins are potent inducers of the CYP3A4 isoform, which can cause sub-therapeutic concentrations of anti-retroviral drugs.

Rifabutin (RBN) is a less potent inducer of CYP3A4. Pharmacokinetic (PK) studies done on healthy adults showed that rifampin decreased dolutegravir (DTG) concentrations by more than 50 % whereas RBN decreased it by 30%.

Currently there are no studies examining the concomitant use of RBN and DTG.

METHODS

Retrospective analysis of patients in the respiratory care unit (RCU) at Jackson Memorial Hospital in Miami.

Case series of 4 co-infected patients receiving both agents who underwent PK analysis.

We included adult patients, admitted to the RCU, with a concomitant diagnosis of HIV and active TB disease who received DTG and RBN, and for which DTG and RBN plasma concentrations were measured for therapeutic drug monitoring (TDM).

A non-compartmental analysis was performed and the area under the concentration-time curve (AUC) was calculated for DTG and RBN.

RESULTS

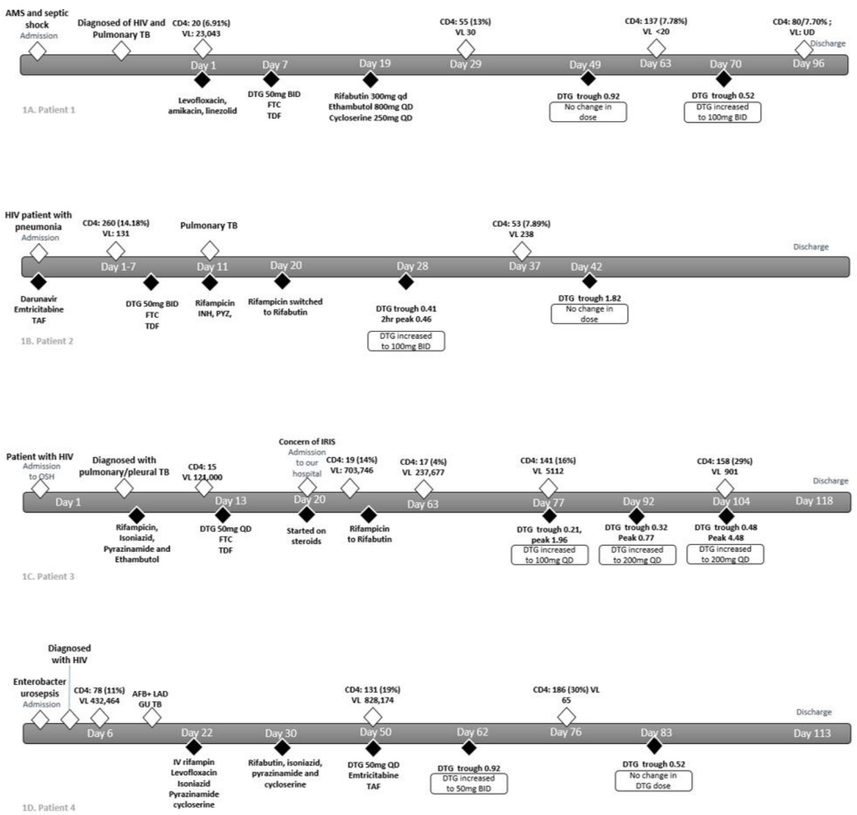

Table 1: Patients' pharmacokinetics of DTG

Patient	Weight (kg)	TDM event#	DTG				
			Dose, mg	Frequency, hr	Expected concentrations mcg/mL Cmax 3.30 Cmin 0.80	$AUC_{0\text{-}tau}$, mcg.hr/mL	$AUC_{0\text{-}24}$, mcg.hr/mL
1	56.5	1	50	12	0.92	7.68	15.36
1	57.6	2	50	12	0.52	10.52[a]	–
2	59	1	50	12	0.41	5.22	10.44
2	58.6	2	100	12	1.82	35.98	71.95
3	70.5	1	50	24	0.21	26.04	26.04
3	71	2	100	24	0.32	13.08	13.08
3	75	3	200	24	0.48	59.52	59.52
4	73.4	1	50	24	0.35	30.38	30.38
4	79.8	2	50	12	1.45	29.34	58.68

RESULTS

Table 2: Patients' pharmacokinetics of RBN

Patient	Weight (kg)	TDM event#	RBN			
			Dose[a], mg	Cmax Expected 0.49-0.90	$AUC_{0\text{-}7}$, mcg.hr/mL	$AUC_{0\text{-}24}$, mcg.hr/mL
1	56.5	1	450	0.65	2.45	–
1	57.6	2	450	0.37	2.44	–
2	59	1	300	0.12	–[b]	–
2	58.6	2	600	0.53	2.26	–
3	70.5	1	300	0.88	4.52	6.58
3	71	2	300	0.26	1.07	–
3	75	3	450	1.01	5.04	7.00
4	73.4	1	300	0.44	2.24	3.22
4	79.8	2	300	0.37	1.93	2.88

CONCLUSIONS

All patients with HIV and TB who were treated with RBN had low concentrations of DTG

Concomitant use of RBN and DTG would benefit from TDM

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