clinical cases DDIs

Date of report 29 Oct 2021

Reported case interaction between **Etravirine** and **Tacrolimus**

Drugs suspected to be involved in the DDI

Perpetrator
Etravirine

Daily Dose
400 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Nov. 12, 2014

End date
March 10, 2021

Victim
Tacrolimus

Daily Dose
2 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Jan. 1, 2016

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Lamivudine
Raltegravir
Maraviroc
Etravirine

Complete list of all comedications taken by the patient, included that involved in the DDI

Warfarin, mycophenolate, tacrolimus, itraconazole, atorvastatin, omeprazole, solifenacin, citalopram, salbutamol, tramadol, zopiclone, lactulose

Clinical case description

Gender

Male

Age

57

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 57-year-old White British male attended our clinic for rationalisation of his antiretroviral regimen following MDT discussion. The patient was on Lamivudine 100mg OD, Etravirine 200mg BD, Raltegravir 400mg BD and Maraviroc 300mg BD. He was consistently virologically suppressed with a CD4 count of 269 cells mm3 (30%). He was highly treatment experienced with extensive drug resistance (see table 1).

Table 1: Summary of drug resistance mutations

Drug class	Major mutations
NRTIs	M41L, D67N, T69N, K70R, L74V, M184V, T215Y, K219E
NNRTIs	L100I, K103N
PI	Nil
INSTI	Nil

His past medical history included liver transplantation secondary to alcoholic liver disease. Amongst his list of co-medications, he took tacrolimus 2mg OD for transplant rejection and itraconazole 100mg BD for oesophageal candidiasis prophylaxis.

His ARV regimen was simplified to Doravirine 100mg BD, Dolutegravir 50mg OD and Maraviroc 150mg BD. The removal of etravirine, a moderate CYP3A4 inducer, warranted close monitoring of tacrolimus levels to prevent drug-related toxicity (see table 2). Concomitant administration of potent CYP3A4 inhibitor itraconazole made prediction of drug level changes more difficult.

Table 2: Tacrolimus level monitoring post-antiretroviral switch

Day post-switch	Level (mcg/L) (Target range 5-7mcg/L)	Action

7	10.9	Dose reduced to 1mg OD
10	7.1	
13	6.7	
15	7.1	
20	6.3	
22	5.6	
29	5.6	
35	13.2	Dose reduced to 0.5mg OD
42	5.4	

Following completion of post-switch monitoring, a 75% tacrolimus dose reduction was required to maintain therapeutic drug levels. This demonstrates the significance of the enzyme inducing effects of etravirine, even in the presence of a potent CYP3A4 inhibitor. The change in levels from day 7 to 35 suggests that enzyme deinduction follows a prolonged time course following etravirine discontinuation.

Clinical Outcome

No unwanted outcome

Editorial Comment

University of Liverpool Recommendation

■ Potential interaction - may require close monitoring, alteration of drug dosage or timing of administration

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