clinical cases DDIs

Date of report 22 Sep 2019

Reported case interaction between **Cobicistat** and **Tacrolimus**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
June 15, 2016

End date
Ongoing

Victim
Tacrolimus

Daily Dose
1.5 (mg)

Dose adjustment performed
Yes

Administration Route
Oral

Start date
June 15, 2017

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat
Dolutegravir

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

Tacrolimus, sirolimus, mycophenolate mofetil, trimethoprim/sulfamethoxazole, hidroferol, prednisone, amlodipine, lormetazepam

Clinical case description

Gender

Male

Age

40

eGFR (mL/min)

Hemodialysis

Liver function impairment

No

Description

40-year old man, referred to our centre for evaluation of kidney transplantation. End-stage renal disease secondary to glomerulonephritis in 2006. History of poor compliance to antiretroviral (ARV) therapy, although not documented HIV resistance. Several ARV regimens since 2006 including ATV/r-3TC-AZT, DRV/r-3TC-AZT, DRV/r-3TC-ABC and DRV/r-RAL (ongoing at the time of referral). Persistently detectable VL, around 200-300 copies/mL, while receiving DRV/r-RAL. A genotypic resistance test did not amplify the virus. A pro-viral resistance test was requested. PROT and RT were amplified, with no detectable mutations, INT was not amplified. It was then decided to modify ART to DRV/r 600/100 bid + DTG 50mg bid, becoming rapidly undetectable. Regimen was later

simplified to DRV/c 800/150 qd + DTG 50mg bid. The patient received kidney transplantation in June 2017. Given the extremely limited data available for cobicistat-tacrolimus co-administration, 1.5 mg of tacrolimus was initially given with therapeutic drug monitoring performed 48 and 72hs post-dose. Levels increased up to 23.3 ng/mL. The patient was discharged on tacrolimus 1.5 mg/48hs, which was later modified to 0.5mg/48hs, maintaining tacrolimus plasmatic levels between 7 and 14 ng/mL. One year after kidney transplantation, still on DRV/c 800/150mg QD and dolutegravir 50 mg BID, the patient developed cutaneous SK, adding then sirolimus to the immunosuppressive regimen, at a dose of 0.5mg/ 4 days (sirolimus levels ranging between 3.2 and 6 ng/mL). The patient is currently well, no evidence of SK progression, stable renal function, undetectable HIV VL and CD4 T cells >1000/ul.

Clinical Outcome

No unwanted outcome

Editorial Comment

Coadministration of DRV/cobi with tacrolimus is expected to produce a marked increase in concentrations of tacrolimus through CYP3A4 inhibition. When coadministration occurs, it is recommended a reduction in dose and prolongation of the dosing interval of tacrolimus, as well as therapeutic drug monitoring.

University of Liverpool Recommendation

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

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