

Date of report 22 Sep 2019

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

# **Drugs suspected to be involved in the DDI**

Perpetrator	Daily Dose
Cobicistat	150 (mg)
Dose adjustment performed No	Administration Route Oral
Start date	End date
June 15, 2016	Ongoing
Victim	Daily Dose
<b>Tacrolimus</b>	1.5 (mg)
Dose adjustment performed	Administration Route
Yes	Oral
Start date	End date
June 15, 2017	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	Age
Male	40
eGFR (mL/min) Hemodialysis	Liver function impairment <b>No</b>

#### 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 coadministration, 1.5 mg of tacrolimus was initially given with therapeutic drug monitoring performed 48 and 72hs postdose. 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

For more information <u>click here</u>