clinical cases DDIs

Date of report 13 Oct 2020

Reported case interaction between **Cobicistat** and **Voriconazole**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
June 1, 2015

End date
June 1, 2017

Victim
Voriconazole

Daily Dose
400 (mg)

Dose adjustment performed
Yes

Administration Route
Oral

Start date
June 10, 2015

End date
Aug. 10, 2015

Complete list of drugs taken by the patient

Antiretroviral treatment

Elvitegravir/Cobicistat/Emtricitabine/Tenofovir-DF
Darunavir (with Ritonavir or Cobicistat)

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

Voriconazole, dexamethasone, ipratropium, salbutamol, salmeterol

Clinical case description

Gender

Male

Age

50

eGFR (mL/min)

>60

Liver function impairment

No

Description

Middle-aged male patient with HIV since 1987, treated since the early 1990s with several ARV regimens and experienced multiple virological failures causing an MDR strain (62V/65R/101E/181C/184I mutations, conferring resistance to lamivudine/ emtricitabine/didanosine/abacavir/nevirapine/efavirenz/rilpivirine/etravirine and partial resistance to tenofovir). Relevant medical history: COPD. He had an undetectable viral load high CD4 lymphocyte count on 800/100 mg of darunavir/ritonavir once daily and 400 mg of raltegravir twice daily at the time of consultation. He was admitted for a respiratory infection and treated with broad-spectrum antibiotics and high doses of systemic steroids with incomplete response. Then, invasive pulmonary aspergillosis was diagnosed. ARV regimen was changed to enfuvirtide,

zidovudine, tenofovir and raltegravir at the usual doses, to avoid DDI between ritonavir and voriconazole 200mg twice daily (ritonavir induces the CYP2C19 isoenzyme, leading frequently to insufficient drug levels of voriconazole). Later, ART regimen was changed again (due to intolerance to enfuvirtide injections and to get a simplification) to elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate 150/150/200/300 mg once daily and 800 mg of darunavir once daily (cobicistat has a theoretically better drug–drug interaction profile, due to the more selective 3A4 isoenzyme inhibition than ritonavir) Vorizonazole levels were monitored (and a complete PK curve over 24 hs was performed), requiring increase in doses up to 400mg twice daily to maintain target levels (1 mg/mL). Patient completely resolved the pulmonary aspergillosis, with no relapse. This case has been already published: Ambrosioni J et al. J Antimicrob Chemother. 2016 Apr;71(4):1125-7. doi: 10.1093/jac/dkv449. https://pubmed.ncbi.nlm.nih.gov/26755498/

Clinical Outcome

No unwanted outcome

Editorial Comment

Coadministration of voriconazole with darunavir/ritonavir has not been studied. Coadministration with ritonavir alone (100 mg twice daily) decreased voriconazole AUC by ~39%. Voriconazole should not be combined with boosted darunavir unless an assessment of the benefit/risk ratio justifies the use of voriconazole. Consider TDM, such as in this clinical

case. Coadministration of voriconazole with elvitegravir/cobicistat has not been studied. Voriconazole is a strong inhibitor of CYP3A4 and may increase plasma concentrations of elvitegravir/cobicistat. Concentrations of voriconazole may also increase. When coadministration is required, an assessment of benefit/risk ratio is recommended to justify the use of voriconazole. Consider TDM, such as in this clinical case.

University of Liverpool Recommendation

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

For more information click here