clinical cases DDIs

Date of report 21 Jan 2021

Reported case interaction between **Doravirine** and **Isavuconazole**

Drugs suspected to be involved in the DDI

Victim
Doravirine

Daily Dose
100 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Dec. 1, 2020

End date
Ongoing

Perpetrator
Isavuconazole

Daily Dose
200 (mg)

Dose adjustment performed
No

Administration Route
Intravenous

Start date
Dec. 1, 2020

End date
Dec. 15, 2020

Complete list of drugs taken by the patient

Antiretroviral treatment

Doravirine
Dolutegravir
Emtricitabine/Tenofovir-AF

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

Isavuconazole, liposomal amphotericin B, trimethoprim-sulfamethoxazole, mirtazapine, dexamethasone.

Clinical case description

Gender

Transgender

Age

35

eGFR (mL/min)

>60

Liver function impairment

No

Description

35-year old transgender woman with history of long lasting HIV-infection and poor adherent to ARV therapy. Multidrug-resistant HIV strain requiring a complex ARV regimen, including FTC-TAF, Darunavir/c and dolutegravir 50mg bid. Admitted due to poor clinical status and subacute pneumonia, initially suspected of being miliary tuberculosis or PjP, but later confirmed as disseminated (lung, liver and bone marrow involvement) progressive histoplasmosis. Severely immunosuppressed (CD4 cell count=18/ul, VL=350000 copies/mL) at admission. Treatment was initiated with liposomal amphotericin B and the ARV regimen (FTC-TAF, DRV/c, DTG double dose) was re-initiated. Clinical course was very bad, requiring ICU admission and mechanical ventilation due

to respiratory worsening. It was then decided to add a second antifungal drug, and isavuconazole (200mg tid first day, later 200mg daily) was then initiated. To reduce the risk of severe DDI, DRV/c was replaced by doravirine. DTG and FTC-TAF were continued Clinical course was slowly favorable (VL=76 copies, CD4=203 at one month) but the patient presented a new deterioration of the clinical condition, which was considered as probably due to IRIS, and which finally improved on steroids. Patient is currently well, on maintenance therapy with itraconazole and the same ARV regimen. Immunological and clinical outcome were favorable with no detected toxicity.

Clinical Outcome

No unwanted outcome

Editorial Comment

Isavuconazole can be considered a moderate inhibitor of CYP3A4/5, and a mild inhibitor of uridine diphosphate-glucuronosyltransferases (UGT), as well as a mild inhibitor of organic cation transporter 2 (OCT2), P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP). Doravirine is primarily metabolised by CYP3A, and medicinal products that induce or inhibit CYP3A are expected to affect the clearance of doravirine. Co-administration of doravirine and inhibitors of CYP3A may result in increased plasma concentrations of doravirine. However, no dose adjustment is needed when doravirine is co-administered with CYP3A inhibitors.

University of Liverpool Recommendation

⚠ Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment is unlikely to be required

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