clinical cases DDIs

Date of report 16 Apr 2024

Reported case interaction between **Cobicistat** and **Amiodarone**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Oct. 22, 2018

End date
May 24, 2023

Victim
Amiodarone

Daily Dose
200 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Feb. 5, 2023

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat/Emtricitabine/Tenofovir-AF

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

Amiodarone 200 mg/day, hidralacine 50 mg/12 h, espironolactone 12.5 mg/day, furosemide 40 mg/day, empagliflozine 10 mg/day, tramadol/paracetamol/12 hours, omeprazole 20 mg/day.

Clinical case description

Gender

Female

Age

58

eGFR (mL/min)

>60

Liver function impairment

No

Description

Patient with HIV infection diagnosed in 2018 with CD4 150 and CV 32,000. She was started on ART with boosted PI due to irregular adherence to medication and controls, achieving good virological control since 2019. In January 2023, she presented to the emergency department for dyspnea and orthopnea, indicative of heart failure in the context of atrial tachycardia. Upon admission to cardiology, valvular heart disease was diagnosed, sinus rhythm was restored with amiodarone. She was discharged in February 2023 with amiodarone, while continuing her usual antiretroviral treatment containing darunavir/cobicistat.
The patient attended follow-up consultations in May 2023, reporting no symptoms and overall good health. Despite the

absence of adverse effects from the co-administration of cobicistat and amiodarone, it was decided to change ART to BIC/FTC/TAF.
Amiodarone is metabolized by CYP2C8 and 3A4, and its exposure may increase due to CYP3A4 inhibition by darunavir/cobicistat, potentially leading to cardiac arrhythmias. The European SmPC for Symtuza contraindicates their coadministration, but the US prescribing information advises caution and clinical monitoring.
Tenofovir alafenamide is a substrate of P-gp, and inhibitors of P-gp such as amiodarone are expected to increase its absorption, thereby increasing systemic concentration. Emtricitabine does not interact with this metabolic pathway. Although darunavir/cobicistat is expected to increase amiodarone plasma concentrations based on theoretical considerations (CYP3A inhibition), the patient received both drugs for 3 months without incident in this particular case. However, the ART was changed as a precautionary measure.

Clinical Outcome

No unwanted outcome

Editorial Comment

The current case highlights the necessity of avoiding pharmacokinetic enhancers whenever possible. Co-medications that may represent a potentially risky drug-drug interaction can be prescribed for primary physicians or other specialists who may be unaware of relevant drug-drug interactions with antiretrovirals, or even unaware of HIV

status of the patient; HIV status is frequently not disclosed to primary care physicians in some settings.
Certain medications, such as drugs for cardiovascular conditions, psychiatric medications or chemotherapy, are particularly dangerous when prescribed in persons with (known or unknown) antiretroviral regimens including pharmacokinetic enhancers. Although this case did not present clinically negative outcomes, the antiretroviral regimen or amiodarone should have been ideally modified beforehand to avoid co-administration.

University of Liverpool Recommendation

- These drugs should not be coadministered

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