clinical cases DDIs

Date of report 18 Dec 2023

Reported case interaction between **Cobicistat** and **Atorvastatin**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
July 28, 2016

End date
Sept. 8, 2022

Victim
Atorvastatin

Daily Dose
40 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Sept. 4, 2022

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

Clopidogrel 75 mg/24h acetylsalicylic acid 100mg/24h Atorvastatin 40 mg/24h

Clinical case description

Gender

Male

Age

59

eGFR (mL/min)

60-30

Liver function impairment

No

Description

A 59-year-old man diagnosed with HIV in 1985 has been virologically suppressed since 2006. In June 2022, his CD4 count was 345 (17%), and HIV-1 RNA was undetectable. He has been on current ART with DRV_cobi/FTC/TAF since 2016. In August 2022, he was hospitalized due to an acute myocardial infarction. Following a primary angioplasty, the prescribed treatment included clopidogrel (600 mg as a loading dose and then 75 mg/24h), acetylsalicylic acid 100 mg/24h, and atorvastatin 40 mg/24h.
Although there were no observed recurrences of myocardial ischemia or side effects after one month, possibly due to the brief period of co-administration, DRV_cobi/FTC/TAF was changed to BIC/FTC/TAF to avoid potential complications related to drug-drug interactions.

Clopidogrel is a prodrug converted to its active metabolite via CYPs 3A4, 2B6, 2C19, and 1A2. Co-administration of clopidogrel with a potent CYPs 3A4 inhibitor like cobicistat can reduce the concentration of clopidogrel's active metabolite and subsequently its antiplatelet effect. If switching from a boosted regimen isn't feasible, prasugrel should be preferred over clopidogrel.
Additionally, the inhibition of CYP3A4, OATP1B1, and BCRP by cobicistat may lead to two undesired consequences: i) an increase in systemic exposure to atorvastatin, posing a risk of unwanted side effects like myopathy for the patient, and ii) a decrease in atorvastatin concentration within hepatocytes, reducing its therapeutic effect.

Clinical Outcome

No unwanted outcome

Editorial Comment

Data have demonstrated that the decrease in clopidogrel's active metabolite does lead to insufficient inhibition of platelet aggregation Although a comparable decrease of the drug prasugrel's active metabolite AUC has been observed, this decrease did not impair prasugrel's antiplatelet effect. The differential impact on clopidogrel and prasugrel pharmacodynamics effect is in line with clinical observations. Therefore, if switching from a boosted regimen isn't feasible, prasugrel should be preferred over clopidogrel.
For the secondary prevention of acute coronary syndromes an atorvastatin dose of 80mg once daily should be initiated

unless there is a potential drug interactions or high risk of adverse effects. In the case of this drug-drug interaction, the dose of 40mg is the maximum dose that can be administered, so was an appropriate starting dose, accompanied by monitoring for adverse effects, in this clinical scenario. The dose of 40mg should be increased to 80mg after stopping the boosted regimen, in order to ensure optimal management of lipids in the context of secondary prevention.

University of Liverpool Recommendation

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

For more information click here

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