clinical cases DDIs

Date of report 19 May 2023

Reported case interaction between **Cobicistat** and **Ticagrelor**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Ongoing

Victim
Ticagrelor

Daily Dose
180 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Dec. 5, 2022

End date
Feb. 16, 2023

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat/Emtricitabine/Tenofovir-AF
Dolutegravir

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

Ticagrelor 180 mg/d; Valsartan/sacubitril 12/13 mg/12h; dapaglifocin10 mg/24h; , atorvastatin 40 mg/24h, AAS 100 mg/24h, espironolactona 25 mg; furosemid2 40 mg 2 pills/ 24h; Vortioxetin 20 mg/24h; citalopram 20 mg/24h; Tamsulosin/solifenacin 0.4 mg+6 mg/24h

Clinical case description

Gender

Male

Age

74

eGFR (mL/min)

60-30

Liver function impairment

No

Description

74 years old man living with HIV since 1986. Heavily treatment experienced because of virological failures and selection of resistance-associated mutations. Salvage therapy in 2007 with TDF/FTC, DRV/r an RAL achieving undetectable viral load. Current ART TAF/FTC, DRV/cobi, DTG (start date unknown).
Comorbidities: Hypertension; ischemic cardiomiopathy (AMI in 2011); Benign prostatic hyperplasia; depression.
In December 2022 he was hospitalized because a new AMI. He required coronary angioplasty and stent insertion and after this procedure, the inhibitor of platelet aggregation ticagrelor was initiated. During the following 2 months, no bleeding

events were observed. However, in February 2023, ticagrelor was switched to prasugrel.
Coadministration of ticagrleor and strong inhibitors of CYP3A4 such as cobicistat is contraindicated, as it may lead to a substantial increase in exposure to ticagrelor and bleeding risk.
Of note, other potential drug-drug interactions were also detected in this patient:

- Atorvastatin and solifenacin are metabolized by CYP3A4 and concentrations are expected to increase due to inhibition of CYP3A4 by cobicistat.
- Sacubitril is converted to the active metabolite LBQ657 by carboxylesterases. LBQ657 is a substrate of OATP1B1/3, OAT1 and darunavir/cobicistat may inhibit OATP1B1 and therefore increase the exposure of sacubitril’s active metabolite. However, signs of toxicity related with these drugs was neither detected.

Clinical Outcome

No unwanted outcome

Editorial Comment

This is an important case as we all struggle with DDI management between boosted PIs and cardiovascular medications. Indeed, cobicistat and ticagrelor may lead to an increased risk for bleeding which did not happen. However, the period of follow-up was only 2 months. I think you can only conclude that there is nu acute (i.e. within 2 months) risk for increaed bleeding.

University of Liverpool Recommendation

- These drugs should not be coadministered

For more information click here

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