clinical cases DDIs

Date of report 03 Feb 2020

Reported case interaction between **Cobicistat** and **Simvastatin**

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
Unknown

Victim
Simvastatin

Daily Dose
Unknown

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Complete list of drugs taken by the patient

Antiretroviral treatment

Elvitegravir/Cobicistat/Emtricitabine/Tenofovir-AF

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

simvastatin

Clinical case description

Gender

Male

Age

50

eGFR (mL/min)

<30

Liver function impairment

No

Description

Middle aged HIV infected patient who developed a severe rhabdomyolysis 2 weeks after being switched to elvitegravir/ cobicistat, emtricitabine, tenofovir alafenamide while on treatment with simvastatin (dose unknown). Within 2 weeks, the patient developed severe muscle pain and reduced micturition as well as a dark discoloration of the urine. Laboratory analyses showed severe renal impairment (eGFR 12 mL/min), postassium 6.1 mmol/L, very high transaminase levels (ALT > 2279 U/L; AST > 5193 U/L) and creatinine kinase > 200000 U/L. The patient was diagnosed with rhabdomyolysis and secondary acute renal failure and underwent dialysis. After discontinuation of the antiretroviral treatment and simvastatin, creatinine kinase and transaminase levels decreased rapidly so that dialysis could be stopped after 2 months. This case has been published by Perrone C et al. AIDS 2018; 32:676-677.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

7 - Probable

Editorial Comment

This drug-drug interaction occurred because of cobicistat strong inhibitory effect on CYP3A4, the main enzyme contributing to simvastatin metabolism. Coadministration of simvastatin with strong CYP3A4 inhibitors is estimated to increase simvastatin exposure by 100 fold (Stader F et al. Antimicrob Agent Chemother 2018). Given the large magnitude of the drug-drug interaction and related high risk of rhabdomyolysis, coadministration of simvastatin with boosted antiretroviral agents is contra-indicated.

University of Liverpool Recommendation

- These drugs should not be coadministered

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