clinical cases DDIs

Date of report 03 Mar 2020

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
Dec. 15, 2015

End date
Sept. 23, 2019

Victim
Atorvastatin

Daily Dose
40 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
April 8, 2013

End date
Sept. 23, 2019

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat
Lamivudine

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

Nebivolol 5mg/day; Ramipril 2,5mg/day; Insuline, Linagliptine 5mg/day; Pregabalin 150mg/day; Omeprazole 20 mg/day; Omega-3 fatty acids 1000mg/day; Acetylsalicylic acid 300mg/day; Atorvastatin/Ezetimibe 40/10 mg/day; Calcifediol 0,266 mcg every 2 weeks

Clinical case description

Gender

Male

Age

59

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 59-year-old man, smoker and with chronic alcohol use. He was diagnosed with HIV when he was hospitalized because a stroke in 2013. ART was initiated in 2013 and since 2015 he was receiving DRV/c (800/150 mg) + 3TC (300 mg), maintain undetectable plasma viral load. He was also on treatment with Atorvastatin/Ezetimibe (40/10mg) since 2013 because of dyslipidemia and Nebivolol+Ramipril because of hypertension. In addition, he presented chronic renal disease (estimated FGR 69 mL/min). In September 2019 the patient presented with rhabdomyolysis and impairment of renal function. Statin was suspended, ART was switched to DTG/3TC and corticosteroid treatment along immunoglobulins was

initiated. Progressive improvement of clinical symptoms and laboratory abnormalities were observed. A muscle biopsy showed rhabdomyolysis and absence of histopathological signs suggestive of autoimmune myopathy, being the final diagnosis immune-mediated necrotizing myopathy associated with statins. Despite no adverse events during 4 years of treatment with atorvastatin 40 mg and darunavir/cobicistat, the patient finally presented statins associated myopathy probably related with the high atorvastatin plasma concentrations resulting of the CYP3A4 inhibition by cobicistat.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

3 - Possible

Editorial Comment

Coadministration of darunavir/cobicistat (800/150 mg once daily) and atorvastatin (10 mg) increased atorvastatin AUC and Cmax by 290% and 319% due to inhibition of CYP3A4, OATP1B1 and BCRP by darunavir/cobicistat. However, atorvastatin did not affect darunavir/cobicistat exposure. When administration of atorvastatin and darunavir/cobicistat is required, it is recommended to initiate atorvastatin with the

lowest dose, and titrate to desired response while monitoring for safety. A daily dose of 40 mg atorvastatin should not be exceeded with careful safety monitoring. (Note, the US product label for Prezcobix states not to exceed atorvastatin 20 mg/day.)

University of Liverpool Recommendation

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

For more information click here