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