clinical cases DDIs

Date of report 14 Feb 2020

Reported case interaction between **Ritonavir** and **Rivaroxaban**

Drugs suspected to be involved in the DDI

Perpetrator
Ritonavir

Daily Dose
200 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Ongoing

Victim
Rivaroxaban

Daily Dose
10 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir (with Ritonavir or Cobicistat)
Ritonavir
Lamivudine
Tenofovir-DF
Etravirine
Raltegravir

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

Rivaroxaban, lamotrigine, levetiracetam, gemfibrozil, pantoprazole and terbinafine

Clinical case description

Gender

Male

Age

52

eGFR (mL/min)

>60

Liver function impairment

No

Description

52-year-old Caucasian male with HIV infection diagnosed in 1984. Receiving salvage therapy including darunavir/ritonavir 600 mg/100 mg twice daily, lamivudine 150 mg twice daily, tenofovir 300 mg once daily, etravirine 200 mg twice daily and raltegravir 400 mg twice daily, which resulted in virological HIV suppression (<20 copies/ml). In January 2012, the patient presented a fracture of the right malleolus, which led to surgery. The postoperative period was uneventful and the patient returned home with a prescription for rivaroxaban 10 mg once daily for six weeks. Two weeks after the start of anticoagulant treatment the rivaroxaban plasma level was

253 µg/l (expected peak concentration 125µg/l for 10 mg once daily). The patient was informed of the elevated result and was advised to halve the dosage of rivaroxaban. No additional rivaroxaban measurements were performed. At the end of February 2012, while on a work trip in Mexico, the patient called his HIV physician to complain about acute bloody diarrhoea. At this point, the patient was advised immediately to stop rivaroxaban and to go to the emergency unit. The patient was treated with intravenous hydration and ciprofloxacin 500 mg twice daily with complete resolution of the bloody diarrhoea. Alternative causes for the gastrointestinal bleeding were excluded. Since the treatment for the prevention of venous thromboembolism was almost completed, no other anticoagulant was further prescribed. This case was publshed in Swiss Med Wkly. 2014 Jan 22;144:w13906. doi: 10.4414/smw.2014.13906 by Lakatos B et al.

Clinical Outcome

Loss of efficacy

Drug Interaction Probability Scale (DIPS)

Score

7 - Probable

Editorial Comment

It is not recommended to use ritonavir in patients receiving rivaroxaban, due to the risk of increased bleeding. Inhibition of CYP3A and P-gp lead to increased plasma levels and pharmacodynamic effects of rivaroxaban which may lead to an increased bleeding risk. Coadministration of rivaroxaban (10 mg single dose) and ritonavir (600 mg every 12 hours) increased rivaroxaban AUC and Cmax by 153% and 55%. Norvir Summary of Product Characteristics, AbbVie Ltd, September 2016.

University of Liverpool Recommendation

- These drugs should not be coadministered

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