clinical cases DDIs

Date of report 27 Feb 2020

Reported case interaction between **Ritonavir** and **Clopidogrel**

Drugs suspected to be involved in the DDI

Perpetrator
Ritonavir

Daily Dose
100 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
April 8, 2016

End date
Ongoing

Victim
Clopidogrel

Daily Dose
75 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Nov. 19, 2015

End date
Nov. 30, 2016

Complete list of drugs taken by the patient

Antiretroviral treatment

Ritonavir
Darunavir (with Ritonavir or Cobicistat)

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

clopidogrel, aspirin, olanzapine, diazepam, pantoprazole, escitalopram, buprenorphin

Clinical case description

Gender

Male

Age

56

eGFR (mL/min)

>60

Liver function impairment

No

Description

This patient was a previous intravenous drug user, living with HIV since 2001. Chronic HCV-associated hepatitis with F1 fibrosis. Incomplete adherence in the past, and the selection of RAMs. On DRV/r monotherapy since 2013, in 2015 he suffered from an acute myocardial infarction and he was treated with coronary stent and antiplatelet therapy. Because of the known interaction between clopidogrel and ritonavir, cART was switched to dolutegravir plus lamivudine and rilpivirine. After 3 months on the new cART the patient had severe neuropsychiatric intolerance, and he was switched back to darunavir/ritonavir. Given the impossibility to obtain other antiplatelet agents the patient was followed closely until clopidogrel withdrawal (9 months later). No new coronary syndrome, symptoms or stent stenosis was observed during

the 9 months nor in the available follow up afterwards (3.5 years).

Clinical Outcome

No unwanted outcome

Editorial Comment

Clopidogrel is administered as a prodrug that is metabolized to its active form through the CYP3A4 pathway. Inhibition of CYP3A4 by ritonavir may lead to subtherapeutic plasma concentrations of active clopidogrel, putting the patient at risk of a recurrence of his coronary disease. In this scenario it is recommended either to switch antiretroviral treatment to unboosted regimens, without ritonavir or cobicistat, or to look for alternative antiplatelet agents whose antiaggregant effects are not affected by ritonavir, such as prasugrel.

University of Liverpool Recommendation

- These drugs should not be coadministered

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