clinical cases DDIs

Date of report 08 May 2019

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

Drugs suspected to be involved in the DDI

Perpetrator
Lopinavir/Ritonavir

Daily Dose
800/200 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Jan. 1, 2004

End date
Ongoing

Victim
Clopidogrel

Daily Dose
75 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Nov. 1, 2014

End date
May 1, 2015

Complete list of drugs taken by the patient

Antiretroviral treatment

Lopinavir/ritonavir

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

Aspirin, clopidogrel, enalapril, bisoprolol, atorvastatin and omeprazole

Clinical case description

Gender

Male

Age

45

eGFR (mL/min)

>60

Liver function impairment

No

Description

45-year-old male with HIV infection diagnosed since 2004. Following diagnosis, he started cART with lopinavir/ritonavir plus tenofovir/emtricitabine, which was later simplified to darunavir/ritonavir monotherapy. The patient maintained complete virologic suppression throughout the follow-up. In November 2014, he complained of progressive dyspnea, being diagnosed with acute pulmonary edema secondary to severe systolic dysfunction. A significant stenosis at the anterior descending coronary artery was shown by coronary angiography, and a conventional stent was implanted. The patient started treatment with aspirin, clopidogrel, enalapril, bisoprolol, atorvastatin and omeprazole, with no change in his antiretroviral regimen. Six months later, the patient had an episode of chest pain, accompanied by electrocardiographic signs of acute anterior myocardial

infarction, and evidence of thrombosis of the implanted stent. He then underwent thromboaspiration and implantation of a drug-eluting stent, and clopidogrel was replaced by prasugrel. No changes were made in his antiretroviral regimen. After two years of follow-up, the patient had no evidence of further ischemic events.

Clinical Outcome

Loss of efficacy

Drug Interaction Probability Scale (DIPS)

Score

6 - Probable

Editorial Comment

Clopidogrel and prasugrel are both metabolized to their active forms through the CYP3A4 pathway. Inhibition of CYP3A4 by ritonavir may have led to subtherapeutic plasma concentrations of active clopidogrel, putting the patient at risk of a recurrence of his coronary disease. Co-administration of ketoconazole with clopidogrel decreased the concentrations of the active metabolite of clopidogrel by 22%-29%, with a subsequent decrease in the antiaggregant effect of 28%-33%. Although co-administration of ketoconazole with prasugrel also decreased the plasma concentration of the active metabolite of prasugrel, such a decrease did not result in a decrease in its antiaggregant

effect. (Farid NA, Payne CD, Small DS, et al. Cytochrome P4503A inhibition by ketoconazole affects prasugrel and clopidogrel pharmacokinetics and pharmacodynamics differently. Clin Pharmacol Ther 2007; 81 (5): 735-41).

University of Liverpool Recommendation

- These drugs should not be coadministered

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