clinical cases DDIs

Date of report 31 Oct 2019

Reported case interaction between **Cobicistat** and **Paclitaxel**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Feb. 3, 2019

End date
Ongoing

Victim
Paclitaxel

Daily Dose
205 mg/cycle (mg)

Dose adjustment performed
Yes

Administration Route
Intravenous

Start date
Aug. 19, 2019

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat
Dolutegravir

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

Paliperidone 6 mg BID, mirtazapine 30 mg QD, lorazepam 2 mg QD, levomepromazine 25 mg QD, and alprazolam 0.5 mg PRN (bipolar disorder), transdermal fentanyl 25 mcg/h transdermal patch and pancreatine supplements.

Clinical case description

Gender

Male

Age

50

eGFR (mL/min)

>60

Liver function impairment

No

Description

50 year-old patient, 77 kg, smoker, no enolic habit, ex-drug user (no drug use since 2002), HIV infected since 1987 on ART. HCV was treated in June 2018, with sustained virologic response. Since February 2019 on ART with dolutegravir 50 mg QD and darunavir/cobicistat 800/150 mg QD. A locally advanced pancreas head cancer was diagnosed in July 2019. He started chemotherapy in August 2019 with gemcitabine 1640 mg and (paclitaxel albumin) 205 mg (dose adjusted at 80%), days +1,+8 and +15 every 28 days. On September 18th chemotherapy dose was adjusted to 60% due to patient fragility. According to the treating physician, chemotherapy was acceptably well tolerated: nadir value of neutrophils 2,3 x10^9/L and platelets 63 x 10^9/L in October 2019. He had

had mucositis (grade1 G1), diarrhea (G1), asthenia, cellulitis of the leg and was admitted due to biliary focus sepsis in September. In August 2019 he had an HIV viral load of 63 c/mL and CD4 432 cells/mm3 (18%). On October 24th viral load was <50 c/mL and CD4 861 cells/ mm3.

Clinical Outcome

No unwanted outcome

Editorial Comment

Paclitaxel is predominantly metabolized by CYP2C8 and to a lesser extent by CYP3A4. The literature reports several cases of paclitaxel associated toxicities in patients on PI/ritonavir regimens (Mir O et al. BJCP 2010) due to ritonavir inhibition of both CYP2C8 and CYP3A4 mediated metabolism resulting in higher exposure of paclitaxel. Of interest, cobicistat has no inhibitory effect on CYP2C8 thus boosting by cobicistat might represent an advantage as the main metabolic pathway of paclitaxel is not inhibited thereby mitigating the magnitude of the interaction.

University of Liverpool Recommendation

- These drugs should not be coadministered

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