clinical cases DDIs

Date of report 28 Sep 2021

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

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, 2005

End date
Feb. 15, 2021

Victim
Paclitaxel

Daily Dose
80 mg/m2 (mg)

Dose adjustment performed
Yes

Administration Route
Intravenous

Start date
Dec. 24, 2020

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Lopinavir/ritonavir
Lamivudine

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

Losartan (50mg), Dexamethasone, Paclitaxel, Pertuzumab (420mg), Trastuzumab (6 mg/kg), Esomeprazole (40mg), Calcium/Vitamin D (2.5mg/800IU)

Clinical case description

Gender

Female

Age

56

eGFR (mL/min)

>60

Liver function impairment

No

Description

Woman, tested HIV-positive in 2000. The treatment initially started with nevirapine, lamivudine and stavudine. In 2001, a M184I/P mutation caused virologic failure (Y181C/P and M36I/P were also found). As a result, the therapy was changed to lopinavir/ritonavir (kaletra) and lamivudine achieving sufficient virologic and immunologic suppression; The most recent CD4 count was measured to be 0.76x10*9/L (0.06x10*9/l at the start of treatment) and viral load 02-2021: < 30 copies/ml (1.25x10*6/l at the start of treatment). She was diagnosed with breast cancer in 2020 and an initial treatment with trastuzumab and fulvestrant was started. Tumor progression was observed, so fulvestrant was switched out for pertuzumab and paclitaxel was added (starting at

24-12). Pertuzumab and trastuzumab were given on day 1 and paclitaxel was given on day 1, 8 and 15. One cycle had the duration of 21 days. Paclitaxel was administered on day 1 and 8 of the first cycle. However on 06-01, just before day 15, the patient had to be hospitalized due to a neutropenic fever. There were also signs of a developing pancytopenia. The day 15 dosage of paclitaxel was cancelled. Cycle 2 was started on 14-01 with 75% of the original paclitaxel dose. All 3 days of the cycle were completed. Again, during this cycle, signs of pancytopenia started to show. Rehospitalization followed because of neutropenic fever, and it was discovered that a severe pancytopenia had developed; leucocyte count: 1.7x109/L (normal value 4.0-10.0x109/L) and neutrophil count: 0.5x109/L (normal value 2.0-7.5x109/L). Kaletra was discontinued and dolutegravir 50mg was started on 15-02. On 18-02, leukocyte and neutrophil count were returned to normal values and the third cycle was initiated with 50% of the original dose of paclitaxel, without signs of recurrent pancytopenia. The remaining cycles were administered at reduced dosages; the fourth cycle at 50% and the fifth and sixth cycle at 60% of the original paclitaxel dose. Cancer treatment response was successful, as tumor remission was observed. Blood count remained within acceptable range during the last three cycles, without recurrent pancytopenia. The new antiretroviral regimen resulted in adequate virologic suppression, and patient acceptation of dolutegravir was good.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

8 - Probable

Editorial Comment

Lopinavir/ritonavir could potentially increase paclitaxel exposure. A pharmacokinetic interaction between ritonavir and paclitaxel probably contributed to the patient developing a severe pancytopenia. Paclitaxel is mainly metabolized by CYP2C8, though a small fraction is metabolized by CYP3A4. Ritonavir is a strong inhibitor of CYP3A4, and to a lesser extent CYP2C8. Inhibition of both metabolic pathway could increase paclitaxel levels, leading to bone marrow toxicity, thus resulting in severe pancytopenia. Furthermore, inhibition of P-glycoprotein transporters could possibly contribute to the observed toxicity.

University of Liverpool Recommendation

- These drugs should not be coadministered

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