

Date of report 28 Sep 2021

# Reported case interaction between Lopinavir/Ritonavir and Paclitaxel

# **Drugs suspected to be involved in the DDI**

Perpetrator	Daily Dose
<b>Lopinavir/Ritonavir</b>	800/200 (mg)
Dose adjustment performed No	Administration Route Oral
Start date	End date
Jan. 1, 2005	Feb. 15, 2021
Victim	Daily Dose
<b>Paclitaxel</b>	80 mg/m2 (mg)
Dose adjustment performed	Administration Route
<b>Yes</b>	Intravenous
Start date	End date

Ongoing

Start date **Dec. 24, 2020** 

# **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	Age
Female	56
eGFR (mL/min)	Liver function impairment
>60	<b>No</b>

#### 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  $0.76 \times 10^{*9}$ /L ( $0.06 \times 10^{*9}$ /l at the start of treatment) and viral load 02-2021: < 30 copies/ml ( $1.25 \times 10^{*6}$ /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

For more information <u>click here</u>