clinical cases DDIs

Date of report 05 Jul 2024

Reported case interaction between **Ritonavir** and **Vinblastine**

Drugs suspected to be involved in the DDI

Perpetrator
Ritonavir

Daily Dose
100 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Ongoing

Victim
Vinblastine

Daily Dose
Unknown

Dose adjustment performed
No

Administration Route
Intravenous

Start date
Unknown

End date
Unknown

Complete list of drugs taken by the patient

Antiretroviral treatment

Atazanavir (with Ritonavir or Cobicistat)
Emtricitabine/Tenofovir-DF

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

Doxorubicin, bleomycin, vinblastine and dacarbazine

Clinical case description

Gender

Female

Age

60

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 60-year-old woman with HIV-1 on antiretroviral therapy (emtricitabine/tenofovir-DF, and ritonavir-boosted atazanavir) developed Hodgkin's lymphoma. The patient initiated ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) chemotherapy and presented with neutropenia and severe hypokalemia. The next ABVD cycle was scheduled with a 50% dose reduction of doxorubicin and dacarbazine, as well as granulocyte-colony stimulating factor therapy. Despite this, she was re-admitted for febrile neutropenia and refractory hypokalemia. Hypokalemia was considered part of proximal tubular renal dysfunction, and other causes of hypokalemia were excluded. Due to suspicion of drug-drug interactions between antiretrovirals and vinblastine, ritonavir-boosted atazanavir was switched to dolutegravir, and the patient

continued with emtricitabine/tenofovir. In the subsequent ABVD cycles, no neutropenia or hypokalemia were observed. Vinblastine is metabolized by the hepatic P450 cytochrome isoenzyme CYP3A4; therefore, concomitant administration with protease inhibitors may increase plasma levels of vinblastine. Vinblastine is also a substrate and inhibitor of the multidrug resistance-associated protein 2 (MRP2) transporter in the proximal renal tubule. Inhibition of this renal transporter by vinblastine, as well as by ritonavir, could increase tenofovir exposure, contributing to renal toxicity. Therefore, a possible explanation for this case is that the hypokalemia could be a result of tenofovir-mediated tubular damage triggered by the increased vinblastine and tenofovir exposures mediated by ritonavir.
This case was published by Cordova E, et al. Int J STD AIDS 2017.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

6 - Probable

Editorial Comment

Vinblastine is metabolized by CYP3A4, and concentrations may increase due to inhibition of CYP3A4, resulting in the

potential for an increased incidence of adverse events. Coadministration of vinblastine with protease inhibitors is independently associated with WHO grade III-IV neutropenia, as seen in the present clinical case.
In addition to excessive concentrations of vinblastine, increased exposure to tenofovir when co-administered with boosters, mediated through inhibition of MRP2, could have also contributed to renal tubular toxicity in this case. A higher risk of renal impairment has been reported in people receiving tenofovir disoproxil fumarate in combination with a ritonavir or cobicistat-boosted protease inhibitor.
This clinical case underscores the need to avoid boosted antiretroviral regimens whenever possible, especially in complex patients such as those receiving chemotherapy for cancer.

University of Liverpool Recommendation

■ Potential interaction - may require close monitoring, alteration of drug dosage or timing of administration

For more information click here

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