clinical cases DDIs

Date of report 23 Dec 2020

Reported case interaction between **Darunavir** and **Enzalutamide**

Drugs suspected to be involved in the DDI

Victim
Darunavir

Daily Dose
600 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Perpetrator
Enzalutamide

Daily Dose
160 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Complete list of drugs taken by the patient

Antiretroviral treatment

Ritonavir
Dolutegravir
Etravirine
Tenofovir-DF
Emtricitabine

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

enzalutamide

Clinical case description

Gender

Male

Age

58

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 58-year-old male, HIV positive since in 1988 with a history of multiple ART regimens and high level resistance to all NRTIs, all first-generation NNRTIs and PIs (except DRV), was diagnosed with protaste cancer with bone metastases. The patient required a treatment with enzalutamide, a potent CYP3A4 inducer and moderate inducer. At the time of the oncological diagnosis, the patient was treated with TDF (300 mg QD), emtricitabine (200 mg QD), darunavir/r (600/100 mg BID), raltegravir (400 mg QD), etravirine (200 mg QD). The drug interaction with enzalutamide was successfully managed by increasing ritonavir and etravirine doses and by replacing raltegravir with dolutegravir. The antiretoviral regimen in presence of enzalutamide was darunavir/r (600/200 mg BID),

dolutegravir (50 mg BID), etravirine (200 mg BID), TDF (300 mg QD), emtricitabine (200 mg QD). TDM showed that ARV drug levels after adjustment were comparable to those in absence of enzalutamide. After 7 months of concomitant therapy with enzalutamide, prostate-specific antigen improved from 1.1 to 0.1 ng/mL. At more than 2.5 years follow-up, the patient remains virologically suppressed on the same medications. This case was published by Nhean S et al. AIDS 2018.

Clinical Outcome

No unwanted outcome

Editorial Comment

Enzalutamide is a potent enzyme inducer and may lead to loss of efficacy of many commonly used medicinal products. Enzymes that may be induced include CYP3A in the liver and gut, CYP2B6, CYP2C9, CYP2C19, and uridine 5'-diphospho-glucuronosyltransferase (UGTs - glucuronide conjugating enzymes). The transport protein P-gp may also be induced, and probably other transporters as well, e.g. multidrug resistance-associated protein 2 (MRP2), breast cancer resistance protein (BCRP) and the organic anion transporting polypeptide 1B1 (OATP1B1). Co-administration of enzalutamide (160 mg once daily) with single oral doses of sensitive CYP substrates in prostate cancer patients resulted in an 86% decrease in the AUC of midazolam (CYP3A4 substrate), a 56% decrease in the AUC of S-warfarin (CYP2C9 substrate), and a 70% decrease in the AUC of omeprazole

(CYP2C19 substrate). UGT1A1 may have been induced as well.

University of Liverpool Recommendation

- These drugs should not be coadministered

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