Date of report 04 Jul 2024

Reported case interaction between **Dolutegravir** and **Metformin**

Drugs suspected to be involved in the DDI

Perpetrator
Dolutegravir

Daily Dose
50 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Victim
Metformin

Daily Dose
1700 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Complete list of drugs taken by the patient

Antiretroviral treatment

Dolutegravir
Lamivudine

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

Metformin 850 mg BID; enalapril 20 mg BID; rosuvastatin 40 mg QD

Clinical case description

Gender

Female

Age

58

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 58-year-old female with HIV infection diagnosed in 2016. No liver and kidney function impairment. Current BMI 32.7 kg/m^2 (obese). On ART with DTG/3TC (50/300 mg) QD. She was diagnosed with metabolic syndrome (hyperglycemia, hypertension and dyslipidemia), and she was prescribed metformin 850 mg BID. Soon after, she experienced nausea, flatulence and diarrhea. No other symptoms that could be early signs of lactic acidosis (i.e., vomiting, weakness, muscle pain, chills, drowsiness, abdominal pain or discomfort, slow or irregular heartbeat, breathing difficulty) were reported by the patient.
A consultation with the HIV specialist was made. Since dolutegravir is an inhibitor of the renal organic cation transporters (OCT)2 and multidrug and toxin extrusion

transporter (MATE)1, it may increase plasma concentrations of other drugs eliminated via OCT2 or MATE1 such as metformin. Although these side effects reported by the patient are common with metformin, their severity may have been enhanced by co-administration with dolutegravir. After consultation, metformin was changed to semaglutide 1.0 mg subcutaneously once a week, with resolution of the side effects.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

4 - Possible

Editorial Comment

This is a case of a potential drug-drug interaction between dolutegravir and metformin due to inhibition of OCT2 and MATE1 by dolutegravir. Co-administration of metformin with dolutegravir (50 mg QD) increased metformin AUC and Cmin by 79% and 66%. While hypoglycemia has been rarely reported, an observational study in 19 participants receiving both drugs reported gastrointestinal distress (n=3) and hypoglycemic symptoms (n=3) that resulted in metformin dose reduction (n=2) and/or discontinuation (n=2) (Masich A,

et al. Int J STD AIDS 2017;28(12):1229-1233. doi: 10.1177/0956462417695995.). A maximum dose of metformin of 1000 mg daily is advised when co-administered with dolutegravir, as well as monitoring for possible side effects.

University of Liverpool Recommendation

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

For more information click here