clinical cases DDIs

Date of report 26 Mar 2021

Reported case interaction between **Bictegravir** and **Metformin**

Drugs suspected to be involved in the DDI

Perpetrator
Bictegravir

Daily Dose
50 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Ongoing

Victim
Metformin

Daily Dose
1455 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Bictegravir/Emtricitabine/Tenofovir-AF

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

No other drugs

Clinical case description

Gender

Male

Age

62

eGFR (mL/min)

>60

Liver function impairment

No

Description

Case series

The glycemic control under metformin treatment before and after the initiation of a bictegravir containing regimen was evaluated retrospectively in 20 people living with HIV (75% were males; mean age 62 +/- 7 years). The mean metformin dose was 1455 +/- 726 mg daily (ranging from 500 to 3000 mg daily). No clinically significant differences were observed in the glucose fasting values when comparing values pre- versus post- bictegravir initiation (fasting blood glucose 134 +/- 33 versus 128 +/- 24 mg/dL, mean difference -2.2%; P = 0.311). Similarly, no differences were observed for HbA1c (48 +/- 11 versus 50 +/- 10 mmol/mol, mean difference +2%; P = 0.907). The same observation applied when comparing fasted glucose or HbA1c values before and after initiation of bictegravir in individuals receiving metformin daily doses > 1000 mg (fasting blood glucose 130 +/- 33 versus 124 +/- 24

mg/L; P = 0.504 and HbA1c 49 +/- 12 versus 52 +/- 10 mmol/mol; P = 0.863). No individuals experienced episodes of hypoglycaemia or lactic acidosis after initiating bictegravir. All individuals included in the study had a normal renal function or mild renal dysfunction. In conclusion, this study provides evidence from a real-life setting that coadministration of bictegravir and metformin did not result in statistically and/or clinically relevant effects on glycaemic control. This observation was confirmed also for daily doses of metformin >1000 mg. This study has been published (Cattaneo D et al. J Antimicrob Chemother 2021 [epub ahead of print]).

Clinical Outcome

No unwanted outcome

Editorial Comment

Coadministration of bictegravir with metformin increased metformin Cmax and AUC by 28% and 39% due to inhibition of renal OCT2 and MATE1 transporters by bictegravir. However, the pharmacodynamic characteristics of metformin (including glucose reduction, increases in active GLP-1 and plasma lactate) were not affected by coadministration with bictegravir. The European product label for Biktarvy indicates that no dose adjustment is required upon coadministration in patients with normal renal function, but for patients with moderate renal impairment, close monitoring should be considered when starting coadministration of bictegravir with metformin, due to increased risk for lactic acidosis in these

patients (and a dose adjustment of metformin should be considered if required).

University of Liverpool Recommendation

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

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