clinical cases DDIs

Date of report 22 Jun 2020

Reported case interaction between **Dolutegravir** and **Valproate**

Drugs suspected to be involved in the DDI

Victim
Dolutegravir

Daily Dose
50mg (mg)

Dose adjustment performed
Yes

Administration Route
Oral

Start date
Nov. 15, 2019

End date
Ongoing

Perpetrator
Valproate

Daily Dose
3000 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Nov. 6, 2019

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment
Dolutegravir
Emtricitabine/Tenofovir-DF

Complete list of all comedications taken by the patient, included that involved in the DDI
Valproate Alfusozin Ciprofloxacin Colecalciferol Desloratidin Haldol Lora
Quetiapine Multivitamin

Clinical case description

Gender
Male

Age
50

eGFR (mL/min)
>60

Liver function impairm
No

Description
A 50-year old patient with a new HIV infection (CD4 count 10; VL 300.0
to the hospital for respiratory insufficiency due to PJP and Pasteurella in
with FTC/TDF was started on 14 November 2019. The patient also recei
history mental disorders and drug abuse. The valproate-DTG interactio
clinically relevant. Valproate reduces total DTG concentrations due to p
displacement, free DTG fraction increases, leading to therapeutic free
(Bollen P; 20th International Workshop on Clinical Pharmacology of HIV
DTG plasma trough concentrations were measured in this patient – disp
We decided to measure free DTG concentrations, because of the extrem
2019. Free DTG fraction did not increase and was thus considered to be
DTG was given BID instead of QD to increase plasma concentrations fr
DTG trough concentration increased and the free DTG concentration w

vitro EC90 value of unbound dolutegravir (0.9 µg/L). This case suggests valproate and DTG might be clinically relevant in some patients.

DTG concentrations

Date	Dose	Total DTG	Free DTG
		mg/L	ug/L (% o
18-11-2019	1 dd 50mg	0.71	5.8 (0.8)
22-11-2019	1 dd 50mg	0.09	0.58 (0.6)
02-12-2019	2 dd 50mg	0.39	1.47 (0.4)

Viral load data

Date	VL
07-11-2019	300.000 copies/ml
02-12-2019	600 copies/ml
31-01-2020	900 copies/ml

Clinical Outcome

Loss of efficacy

Drug Interaction Probability Scale (DIPS)

Score

2 - Possible

Editorial Comment

University of Liverpool Recommendation

- No clinically significant interaction expected

For more information click here