clinical cases DDIs

Date of report 03 Feb 2020

Reported case interaction between **Elvitegravir** and **Warfarin**

Drugs suspected to be involved in the DDI

Perpetrator
Elvitegravir

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Victim
Warfarin

Daily Dose
7 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Complete list of drugs taken by the patient

Antiretroviral treatment

Elvitegravir/Cobicistat/Emtricitabine/Tenofovir-DF

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

Warfarin 7 mg once daily

Clinical case description

Gender

Male

Age

42

eGFR (mL/min)

>60

Liver function impairment

No

Description

42-year-old HIV-infected man with a medical history of recurrent bilateral lower extremity deep venous thromboembolism requiring indefinite anticoagulation (target INR 2-3). Warfarin dose was stable at 7 mg once daily (50 mg per week) for approximately 2 years with concomitant antiretroviral treatment consisting of efavirenz plus emtricitabine and tenofovir-DF. Due to central nervous side effects, antiretroviral treatment was switched to elvitegravir/cobicistat plus emtricitabine and tenofovir-DF. After 20 days on elvitegravir/cobicistat, INR became subtherapeutic. Warfarin dose was gradually increased to 11 mg once daily (80 mg per week) in order to maintain a therapeutic INR. This case has been published by Good BL et al. AIDS 2015; 29:985-6.

Clinical Outcome

Loss of efficacy

Drug Interaction Probability Scale (DIPS)

Score

7 - Probable

Editorial Comment

Warfarin is a racemic mixture consisting of 2 enantiomers. The S-enantiomer (more potent) undergoes metabolism by CYP2C9. The R-enantiomer is primarily metabolized by CYP1A2, CYP3A4 and CYP2C19. The observed drug-drug interaction is explained by elvitegravir inducing effect on CYP2C9 resulting in the lower exposure of R-enantiomer (more potent). The patient required a 60% warfarin dosage increase. Of interest, INR values did change 20 days after changing antiretroviral therapy which might be possibly explained by efavirenz long half-life and consequently delayed time to reach elvitegravir induction steady-state.

University of Liverpool Recommendation

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

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