clinical cases DDIs

Date of report 28 Jun 2019

Reported case interaction between **Raltegravir** and **Mineral supplements**

Drugs suspected to be involved in the DDI

Victim
Raltegravir

Daily Dose
1600 (mg)

Dose adjustment performed
Yes

Administration Route
Oral

Start date
July 16, 2018

End date
Oct. 18, 2018

Perpetrator
Mineral supplements

Daily Dose
Unknown

Dose adjustment performed
No

Administration Route
Oral

Start date
July 2, 2018

End date
Oct. 18, 2018

Complete list of drugs taken by the patient

Antiretroviral treatment

Emtricitabine/Tenofovir-DF
Raltegravir

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

Iron supplements, rifampin, isoniazid, azithromycin, prednisone, sulfamethoxazole trimethoprim, omeprazole ferrous sulfate, vitamin B12, folic acid

Clinical case description

Gender

Male

Age

32

eGFR (mL/min)

>60

Liver function impairment

No

Description

32 years old HIV+ men, diagnosed with disseminated TB in July 2018. He initiated treatment for tuberculosis in July 2018 and, because of concomitant anemia, he also received iron supplements (ferrous sulfate), vitamin B12 and folic acid. ART with TDF/FTC plus RAL (800 mg/12h because of concomitant treatment with rifampin) was initiated 2 weeks after TB treatment. In September 2018 the patient had improved. However, despite assuring good adherence to ART, severe immune depression persisted (CD4 count 26/µL, 6%) and virologic failure was confirmed (HIV-1 RNA 282.575 copies/mL). A genotypic resistance test showed resistance associated mutations to NRTI (M184V) and INSTI (E92Q, N155H). Considering good adherence to ART and adequate

RAL dosing, VF was assumed to be possibly a consequence of interactions between RAL and iron supplements (not staggered at least 4 hours). ART was changed to TDF/FTC+DRV/r+DTG (50 mg/12h), rifampin was changed to rifabutin (150 g/24h), and iron supplements were withdrawn. Virologic suppression (<40 copies/mL) was achieved after 2 months.

Clinical Outcome

Loss of efficacy

Drug Interaction Probability Scale (DIPS)

Score

5 - Probable

Editorial Comment

Raltegravir binds to divalent cations (Including iron) at the gastro-intestinal tract which results in chelation and in a reduction in raltegravir absortion. Administration of raltegravir should be separated at least 4 hours form iron supplements. In this context, recommended dose of raltegravir is 400 mg twice daily instead of 1200 mg once daily. In this case, an additional reduction of raltegravir exposure due to rifampicin may be expected (although raltegravir dose was doubled, as recommended in raltegravir prescribing information).

University of Liverpool Recommendation

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

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