clinical cases DDIs

Date of report 21 Jun 2019

Reported case interaction between **Cobicistat** and **Quetiapine**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Feb. 10, 2019

End date
Ongoing

Victim
Quetiapine

Daily Dose
25 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir (with Ritonavir or Cobicistat)
Etravirine
Maraviroc

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

Quetiapine, folic acid, rosuvastatin, fenofibrate, trazodone, tibolone, flurazepam, delorazepam

Clinical case description

Gender

Female

Age

49

eGFR (mL/min)

>60

Liver function impairment

No

Description

Patient is followed for psychiatric disorders (olygophrenie, depression/anxiety); HIV+ since 20 years, incomplete adherence in the past and several RAMs in the RT and PR genes. She was admitted to the ward for fever and bilateral otitis after having interrupted her ARVs (incomplete efficacy before and worsening neuropsychiatric symptoms with darunavir/cobicistat + maraviroc + dolutegravir). We re-started her antiretroviral therapy using darunavir/cobicistat (800/150 mg twice daily) plus etravirine (200 twice daily) and maraviroc (300 mg twice daily). She showed a good tolerability to the new regimen with no psychiatric or gastrointestinal complains. Quetiapine trough concentrations

were in range (119 ng/mL, range 100-500) and she was discharged with no other modifications in her therapy.

Clinical Outcome

No unwanted outcome

Editorial Comment

In this case a DRV/Cobi dose 800/150 mg every 12 hours was used, maybe to overcome PI resistance, for compliance reasons and taking into consideration the potential interaction between DRV/cobi and etravirine (see below). However, this is not the recommended dose of DRV/cobi, and this limits the generalization of this report. If DRV/cobi (instead of DRV/r) is to be used with etravirine, there is a potential DDI that could markedly decrease DRV concentrations (Moltó J et al. JAC 2018; 73:732-7) with potential risk of virological failure (However, that study was done with DRV/cobi once-daily, but not with DRV/cobi twice-daily). Quetiapine trough concentrations were within the normal range (although close to the lower margin). However, quetiapine daily doses in this patient were of 25 mg/daily, which are far below the usual dose (200-800 mg/daily). Although the European product label for quetiapine contraindicates the drug with CYP3A4 inhibitors (such as cobicistat), the US product label recommends reducing quetiapine to 1/6 of the original dose in that setting. However, the 25 mg daily dose used in this case is even lower than 1/6 of the lowest usual dose. Of note, a multidirectional DDI with quetiapine and ARV might be possible in this patient, as etravirine can act as a CYP3A4

inducer, potentially lowering quetiapine concentrations (and partially compensating the cobi inhibitory effect; quality of evidence: very low).

University of Liverpool Recommendation

- These drugs should not be coadministered

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