clinical cases DDIs

Date of report 03 Feb 2025

Reported case interaction between **Darunavir** and **Carbamazepine**

Drugs suspected to be involved in the DDI

Victim
Darunavir

Daily Dose
800 (mg)

Dose adjustment performed
Yes

Administration Route
Oral

Start date
Unknown

End date
Unknown

Perpetrator
Carbamazepine

Daily Dose
800 (mg)

Dose adjustment performed
Yes

Administration Route
Oral

Start date
May 1, 2020

End date
Unknown

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat
Raltegravir

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

Carbamazepine 800 mg QD

Clinical case description

Gender

Male

Age

59

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 59-year-old man with HIV, treated with darunavir/cobicistat (800/150 mg once daily) plus raltegravir (400 mg twice daily), was prescribed carbamazepine (200 mg once daily), a metabolic inducer, for recurrent trigeminal neuralgia. Before initiating carbamazepine, the patient's darunavir and raltegravir trough concentrations were 1710 ng/mL and 884 ng/mL, respectively, with a suppressed viral load. With the addition of carbamazepine (200 mg daily), darunavir and raltegravir trough concentrations increased to 2079 ng/mL and 3112 ng/mL, respectively. However, due to a suboptimal response, the carbamazepine dose was increased to 200 mg twice daily, leading to a reduction in darunavir and raltegravir trough concentrations (821 ng/mL and <40 ng/mL, respectively). Over the following months, the carbamazepine

dose was further increased to 800 mg daily, resulting in darunavir trough concentrations as low as 142 ng/mL. The patient was subsequently switched to darunavir/ritonavir (600/100 mg twice daily) with dolutegravir (50 mg twice daily). Serial measurements of darunavir trough concentrations alongside carbamazepine levels demonstrated that carbamazepine induction was dose- and concentration-dependent. While sufficient darunavir levels were maintained at lower carbamazepine doses, daily carbamazepine doses >550 mg or trough concentrations >12.5 mg/mL were associated with a more pronounced induction effect and a higher risk of suboptimal darunavir trough concentrations. No virological failure occurred, likely due to intensive therapeutic drug monitoring (TDM), continuous dose adjustments, and optimal dolutegravir exposure. This case was published by Cattaneo D et al. in Ther Drug Monit 2024; 46:277-280.

Clinical Outcome

No unwanted outcome

Editorial Comment

Co-administration of darunavir/cobicistat or raltegravir with carbamazepine is contraindicated due to the potential for loss of therapeutic efficacy. Theoretically, carbamazepine is expected to decrease darunavir and/or cobicistat plasma concentrations through CYP3A induction. Additionally, carbamazepine induces UGT1A1, which can reduce raltegravir concentrations.

This case illustrates that low doses of carbamazepine have a limited impact on darunavir concentrations, whereas higher doses significantly affect both darunavir and raltegravir levels. This highlights the importance of therapeutic drug monitoring, particularly in cases where there are no alternative therapeutic options or when complex drug interactions are present, even though routine use of this approach is not recommended.
It is also important to note that ritonavir is more resistant to enzyme induction than cobicistat, which allows the co-administration of darunavir/ritonavir with carbamazepine. However, carbamazepine plasma concentrations should be closely monitored to avoid toxicity due to the inhibition of its metabolism by ritonavir or cobicistat.

University of Liverpool Recommendation

- These drugs should not be coadministered

For more information click here

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