clinical cases DDIs

Date of report 17 Mar 2026

Reported case interaction between **Cobicistat** and **Tacrolimus**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
June 5, 2024

End date
Ongoing

Victim
Tacrolimus

Daily Dose
0,5 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
June 5, 2024

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat/Emtricitabine/Tenofovir-AF

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

Tacrolimus, mycophenolate, methylprednisolone, atorvastatin, cotrimoxazole, famotidine, furosemide, calcium carbonate, amlodipine, calcium acetate, insulin, repaglinide, asprin, bisoprolol, prasugrel, darbepoetin, valgancyclovir,

Clinical case description

Gender

Male

Age

55

eGFR (mL/min)

60-30

Liver function impairment

No

Description

A 55-year-old man with a history of end-stage chronic kidney disease (ESKD) secondary to HIV-associated nephropathy underwent deceased-donor kidney transplantation. Immunosuppressive therapy consisted of basiliximab, tacrolimus, mycophenolate, and methylprednisolone. Prior to transplantation, antiretroviral therapy (ART) was switched from etravirine plus darunavir/ritonavir to dolutegravir plus rilpivirine to minimize the risk of drug–drug interactions. At the time of transplantation, HIV viral load was undetectable and the CD4 count was 230 cells/mm³.

Three months after transplantation, during an intensive care unit (ICU) admission due to septic shock, plasma HIV viral load increased to 1,920 copies/mL (confirmed at 17,000

copies/mL). At that time, the tacrolimus dose was 3.5 mg every 12 hours. Due to concerns about ART failure, and in the absence of prior resistance data, ART was switched to darunavir/cobicistat/emtricitabine/tenofovir alafenamide. Based on prior clinical experience, tacrolimus dosing was adjusted to 0.5 mg every 72 hours. Tacrolimus trough concentrations ranged from 5.2 to 19.3 ng/mL (target range: 5–15 ng/mL), without reported adverse events. HIV viral load subsequently returned to undetectable levels.

Genotypic resistance testing performed prior to switching ART revealed no resistance-associated mutations. Despite the favorable clinical outcome, switching to an alternative ART regimen with a high genetic barrier to resistance and a lower potential for interaction with tacrolimus may be considered.

Clinical Outcome

No unwanted outcome

Editorial Comment

Transplantation requiring immunosuppression remains challenging in people living with HIV (PWH), particularly in those who are heavily treatment-experienced. Tacrolimus is a commonly prescribed immunosuppressive agent, while boosted darunavir is frequently used in PWH with known or suspected prior virological failure and resistance.

Cobicistat is a potent inhibitor of CYP3A4 and P-glycoprotein (P-gp), and therefore cobicistat-boosted darunavir is expected to significantly increase tacrolimus plasma

concentrations, potentially leading to toxicity. Although tacrolimus dosing routinely requires close monitoring and adjustment to ensure adequate immunosuppression while minimizing adverse effects, coadministration with cobicistat-boosted darunavir necessitates substantial dose reduction and/or prolongation of the dosing interval, along with intensified therapeutic drug monitoring (TDM).
Concomitant use typically requires markedly reduced tacrolimus doses in all patients, often with extended dosing intervals. More frequent monitoring of tacrolimus concentrations is essential until stable therapeutic levels are achieved. Díaz and colleagues (Infect Dis Ther. 2021;10:1055–1064) proposed an approach consisting of administering a single low dose (e.g., 1 mg), followed by daily TDM, with redosing only when tacrolimus concentrations reach the lower limit of the target range. This process is repeated until an appropriate dosing interval is established.
In PWH undergoing transplantation and receiving tacrolimus, an unboosted antiretroviral regimen is generally preferred to minimize drug–drug interactions. However, this case illustrates that when cobicistat-boosted darunavir is required, coadministration can be safe and effective if managed appropriately with careful dose adjustment and close monitoring.

University of Liverpool Recommendation

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

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