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Reported case interaction between **Dolutegravir** and **Paclitaxel**

Drugs suspected to be involved in the DDI

Victim

Dolutegravir

Daily Dose

50 (mg)

Dose adjustment performed

No

Administration Route

Oral

Start date

Unknown

End date

Unknown

Perpetrator

Paclitaxel

Daily Dose

100 (mg)

Dose adjustment performed

No

Administration Route

Intravenous

Start date

Unknown

End date

Unknown

Complete list of drugs taken by the patient

Antiretroviral treatment

Dolutegravir

Emtricitabine/Tenofovir-DF

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

Paclitaxel 100mg/m² iv every 3 weeks; valaciclovir 500mg oral once-daily

Clinical case description

Gender

Male

Age

50

eGFR (mL/min)

>60

Liver function impairment

No

Description

A male patient with HIV infection was a candidate for second-line treatment of Kaposi's sarcoma with paclitaxel 100 mg/m² administered intravenously every three weeks. His current combination antiretroviral therapy (cART) consisted of dolutegravir/tenofovir disoproxil fumarate/emtricitabine (DTG/TDF/FTC).

According to the Liverpool HIV drug interaction checker, a potential interaction exists between dolutegravir and paclitaxel. In vitro data suggest that paclitaxel activates the pregnane X receptor (PXR) and could therefore induce UGT1A1, potentially decreasing dolutegravir concentrations. Therapeutic drug monitoring (TDM) of dolutegravir was performed before and one week after paclitaxel administration. The baseline dolutegravir trough concentration was 1.36 mg/L, and one week after paclitaxel dosing it was 1.30 mg/L. These findings did not demonstrate

any clinically relevant change in dolutegravir exposure, and both values were within the therapeutic range.

HIV viral load remained undetectable throughout the course of Kaposi's sarcoma treatment.

Clinical Outcome

No unwanted outcome

Editorial Comment

This case describes a 50-year-old patient on antiretroviral therapy with TDF/FTC+DTG for HIV infection who initiated paclitaxel treatment for KS. Since paclitaxel may theoretically reduce DTG concentrations through PXR activation and subsequent UGT1A1 induction, DTG therapeutic drug monitoring (TDM) was performed before and one week after paclitaxel initiation, showing very similar concentrations at both time points, within the therapeutic range for DTG.

This interaction has not been formally studied and the quality of evidence is low; therefore, real-life TDM data, such as in the present case, are of particular interest. This is even more relevant for a potential interaction still frequently encountered in clinical practice, such as the treatment of Kaposi's sarcoma in people living with HIV, even when virologically suppressed.

Nevertheless, DTG levels were measured before and one week after starting paclitaxel. It remains uncertain whether one week is sufficient for paclitaxel to reach steady state and therefore whether DTG concentrations at this time point are truly representative of the interaction between the two drugs,

or if further decreases in DTG levels could still occur. A relatively recent article (Bettonte, S., Berton, M., Stader, F. et al. Management of Drug Interactions with Inducers: Onset and Disappearance of Induction on Cytochrome P450 3A4 and Uridine Diphosphate Glucuronosyltransferase 1A1 Substrates. Eur J Drug Metab Pharmacokinet 48, 353–362 (2023). <https://doi.org/10.1007/s13318-023-00833-9>) concluded that “our simulations suggest that an inducer should be administered for at least 14 days before conducting interaction studies to reach maximal induction,” although they also suggest that induction may occur more rapidly with UGT1A1 than with CYP3A4.

It would therefore be interesting to know whether the authors of this case have DTG levels obtained at two weeks or later, or additional evidence to justify performing TDM at one week, and whether longer-term virological outcomes are available. Importantly, maintaining virological suppression in a patient with prior undetectable viral load on triple ART does not necessarily exclude the possibility of a clinically relevant reduction in DTG concentrations.

University of Liverpool Recommendation

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

For more information [click here](#)

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