Poster

[P27-3] P27-3: Anti-infective drugs (8): Antiviral

Chair: Birgit C. P. Koch, The Netherlands

Wed. Sep 27, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

(Wed. Sep 27, 2017 12:30 PM - 1:30 PM Annex Hall)

[P27-3-4] Effects of cobicistat and ritonavir on tenofovir plasma concentrations

Dario Cattaneo[1], Sara Baldelli[2], Davide Giacomelli[3], Davide Minisci[4], Cristina Mazzali[5], Paola Meraviglia[6], Cristina Gervasoni[7] (1.Luigi Sacco University Hospital, 2.Luigi Sacco University Hospital, 3.Luigi Sacco University Hospital, 4.Luigi Sacco University Hospital, 5.Politecnico di Milano, 6.Luigi Sacco University Hospital, 7.Luigi Sacco University Hospital)

Keywords: HIV, therapeutic drug monitoring, drug-to-drug interactions

Background

Co-administration of tenofovir alafenamide (TAF) with ritonavir or cobicistat resulted in increased tenofovir plasma concentrations. Here we aimed to assess the effect of ritonavir and cobicistat on tenofovir concentrations in patients treated with tenofovir disoproxil fumarate (TDF).

Methods

HIV-positive patients from our database receiving TDF-containing antiretroviral therapies (ART) for at least one month and with at least one assessment of tenofovir plasma trough concentrations were considered (n=510). Uni- and multivariate regression analyses were carried out considering tenofovir concentration as the dependent variable and clinical characteristics of the enrolled patients as independent covariates. Independent variables with p-values <0.20 at univariate analysis where introduced in the multivariate model.

Results

Enrolled patients were given TDF in combination with protease inhibitors/ritonavir (PIs/r, n=212), non-nucleoside reverse transcriptase inhibitors (NNRTIs, n=176), integrase inhibitors (INIs, dolutegravir or raltegravir, n=46) or with elvitegravir/cobicistat coformulation (n=76). Patients' age, body weight, sex, serum creatinine levels and concomitant ART resulted significantly associated with tenofovir plasma trough concentrations. The highest drug concentrations were measured in patients given elvitegravir/cobicistat (161±113 ng/mL), being significantly higher than values measured in patients given PIs/ritonavir (147±125 ng/mL), INIs (113±74 ng/mL) or NNRTIs (109±62 ng/mL).

As exploratory analysis we looked also at the distribution of tenofovir concentrations clustered according to single components of the ART regimens. Important differences on tenofovir exposure were found between the class of PIs/r, with atazanavir and lopinavir showing the highest tenofovir concentrations compared with amprenavir or darunavir, respectively (163±145 and 164±120 ng/mL versus 112±96 or 107±68 ng/mL, respectively).

Conclusions

The importance of some clinical covariates in predicting tenofovir overexposure was confirmed. We also provided solid evidence that coadministration of TDF with elvitegravir/cobicistat resulted in significantly higher tenofovir concentrations compared with other ART regimens. The boosting effect of ritonavir was less evident. Indeed, tenofovir concentrations measured in patients given TDF with atazanavir or lopinavir were comparable to those measured in those treated with elvitegravir/cobicistat. Conversely, coadministration of amprenavir/ritonavir or darunavir/ritonavir resulted in tenofovir concentrations comparable to those

measured in patients treated with NNRTIs or INIs. Accordingly, the dose of TDF should be reduced according to the companion ARVs.