Immuno-virological and Clinical Follow-up of HIV-2 Patients Receiving BIC/FTC/TAF

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BACKGROUND

- HIV-2 infection remains a significant health problem in West Africa. Integrase inhibitors (INSTI) are an important class of drugs for treating HIV-2 infection given the limited number of drugs active against this virus.
- Bictegravir (BIC) is active in vitro against HIV-2 (1). While the clinical efficacy of raltegravir (RAL) and dolutegravir (DTG) is well established, the clinical efficacy of BIC for treating patients living with HIV-2 (PLHIV-2) has not been reported.
- High level of evidence for the treatment of HIV-2 remains scarce and powerful designs such as randomized clinical trials are difficult to implement
- Given the lack of randomized trials, observational studies currently provide an important tool to establish treatment guidelines

METHODS

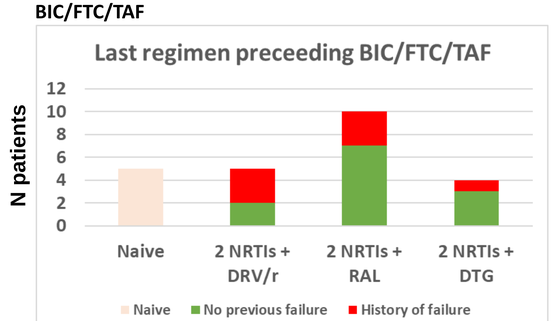
- We studied retrospectively 24 PLHIV-2 followed in the Infectious Diseases Unit at Bichat Hospital, Paris, France, and treated with BIC/FTC/TAF.
- Data were obtained from medical chart recorded in the medical record system Nadis®, designed for the medical follow-up of HIV-infected patients after written informed consent. Data were censored at February 10th 2023.
- Lymphocyte CD4 count and pVL were performed at our institution. By April 2013, a pVL quantification assay with a detection threshold of 40 cps/mL became available. HIV-2 resistance mutations were assessed in RNA or DNA according to pVL value and physician request.
- BIC, FTC and TFV plasma C24h levels were determined 24 h after the last drug intake on the same sample as pVL, using a validated UHPLC-MS/MS method. Limits of quantification were 10 ng/mL for both BIC and FTC and 5 ng/mL for TFV.

BIC/FTC/TAF: effective in the treatment of naive or pretreated **PLHIV-2** in a non comparative retrospective study

RESULTS

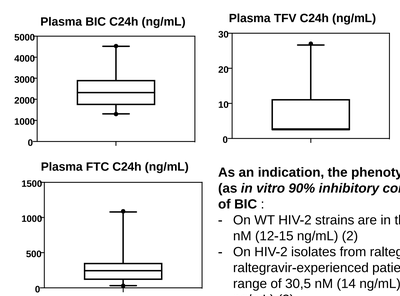
- Twenty four PLVIH-2 received BIC/TAF/FTC, 14 women and 10 men; 22 of them were included in the ANRS CO5 HIV-2 cohort. All except 2 were born in West Africa. CDC stage was A in 14, B in 4 and C in 5 patients. Median age was 58 yrs [IQR 53-61] , median time since HIV-2 infection diagnosis was 19 yrs [IQR 8-23] and median nadir CD4 cell count was 319/mm3 [IQR 174-432]. Zenith pVL was < 100 cps/mL in 13 patients and detectable in 11 patients with a median value of 597 cps/mL [IQR 513-567].
- Five patients were treament naïve and 19 were receiving ARVs with a median of 2 [IQR 1-3] previous regimens. ARVs preceeding switch to BIC/FTC/TAF was a backbone of 2 NRTIs combined with DRV/r in 5 patients, RAL in 10 patients and DTG in 4 patients. Eight of these 19 pretreated patients had an history of treatment failure (Figure 1). Genotypic resistance testing, available in 5 out of these 8 patients, did not show any resistance mutation for INSTI.
- At time of BIC/FTC/TAF initiation, median CD4 cell count was 580/mm3 [IQR 380-697]. Three patients only, all naive, had detectable viral load (57, 94 and 130 cps/mL) with a viral load assay threshold of 40 cps/mL.
- At time of evaluation, the median duration of BIC/FTC/TAF treatment was 27.8 months [IQR 16.4-36.2]. One patient discontinued BIC/FTC/TAF due to weight increase. Viral load was < 40 cps/mL in all patients. Median CD4 cell count was 615 cells/mm3 [IQR 472-787], p = 0.29 by Wilcoxon signed rank test when compared with CD4 at time of BIC/FTC/TAF initiation. Considering the delta CD4 cell count, the mean CD4 count change was 54 ± 248 cells in the whole population and 106 ± 166 cells in the subgroup of naive patients (n=5).
- Drugs C24h levels were available in 20 patients. Pharmacological results are depicted in Figure 2. BIC C24h value was at least 20 fold the value of IC90 of BIC on HIV-2 strains.

FIGURE 1. Antiretroviral therapy before initiation of BIC/FTC/TAF



DRV/r: darunavir/ritonavir, RAL: raltegravir, DTG: dolutegravir, NRTI:nucleoside

FIGURE 2. Median (IQR5-95%) BIC, FTC and TFV C24h (20 patients)



As an indication, the phenotypic susceptibility (as *in vitro 90% inhibitory concentration*, IC_{90}) of BIC :

- On WT HIV-2 strains are in the range of 27-35 nM (12-15 ng/mL) (2)
- On HIV-2 isolates from raltegravir-naives and raltegravir-experienced patients, are in the range of 30,5 nM (14 ng/mL) and 156,1 nM (70 ng/mL) (3)

CONCLUSIONS

- In this retrospective study, BIC/FTC/TAF appeared promising in the treatment of HIV-2 infection.
  - ✓ All subjects had an undetectable pVL at time of evaluation, but pVL at time of BIC/FTC/TAF initiation was > 40 cps/mL in 3 patients only
  - ✓ Assessment of immunological response showed a small but positive gain of CD4 between initiation of BIC/FTC/TAF and follow-up. Unlike in HIV-1 infection, poor CD4 recovery is common in PLVIH-2 receiving ART, even with INSTI. This increase was more important in the 5 naïve patients, as previously shown with DTG (4)
  - ✓ Pharmacological results confirmed the good adherence to treatment and the favorable plasma pharmacokinetics

- INSTI-based ART is the recommended treatment of HIV-2 infection and RAL has been widely used but is given twice daily (5). BIC/FTC/TAF has many advantages: once daily administration, single treatment regimen including TAF that has efficacy against hepatitis B virus and low renal toxicity

- More data in ARV-naïve PLVIH-2 with detectable pVL at time of ART initiation should now be obtained to confirm the value of this combination in the treatment of HIV-2 infection

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