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

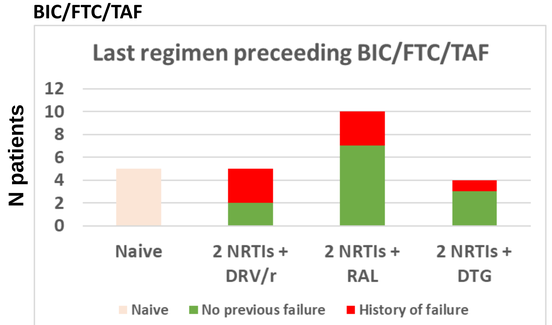
- We studied retrospectively 24 PLHIV-2 followed in the Infectious Diseases Unit at Bichat Hospital, Paris, France, and treated with BIC/FTC/TAF.
- Data were obtained from medical chart recorded in the medical record system Nadis®, designed for the medical follow-up of HIV-infected patients after written 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

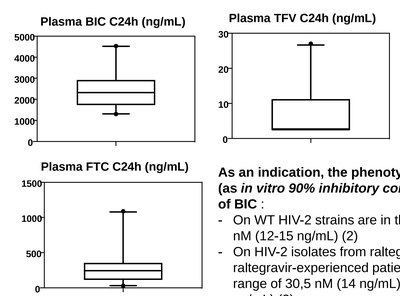
- Twenty four PLVIH-2 received BIC/TAF/FTC, 14 women and 10 men; 22 of them were included in the ANRS CO5 HIV-2 cohort. All except 2 were born in West Africa. CDC stage was A in 15, B in 4 and C in 5 patients. Median age was 58 yrs [IQR 53-61] , median time since HIV-2 infection diagnosis was 19 yrs [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 > 100 cps/mL in 11 patients with a median value of 597 cps/mL [IQR 513-5670].
- 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).
- 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 reverse transcriptase inhibitor

FIGURE 2. Median (IQR5-95%) BIC, FTC and TFV C24h (n = 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-tablet-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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Key information

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