

COVID-19 in HIV-infected patients: does tenofovir-based ART have an impact?

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Background:

- The nucleotide analogue tenofovir has been hypothesized to be effective in COVID-19, still being a controversial issue. Tenofovir is available as two prodrugs, tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF), both currently essential part of antiretroviral therapy (ART) regimens.
- People living with human immunodeficiency virus (PLWHIV) might be at particularly high risk for severe COVID-19 progression.
- We aim to describe clinical outcomes of COVID-19 in PLWHIV with and without tenofovir-based ART in a national cohort.

Material and Methods:

- Prospective observational multicentric study in Argentina (COVIDARE).
- PLWHIV with confirmed COVID-19 were enrolled from September 2020 to mid-June 2022 by using a standardized data collection form.
- Patients were stratified according baseline ART regimen into two groups: those with tenofovir (either TDF or TAF) and those without.
- Univariate and multivariate analysis were performed to evaluate impact of tenofovir vs. non-tenofovir containing regimens on major clinical outcomes adjusting by potential confounders.

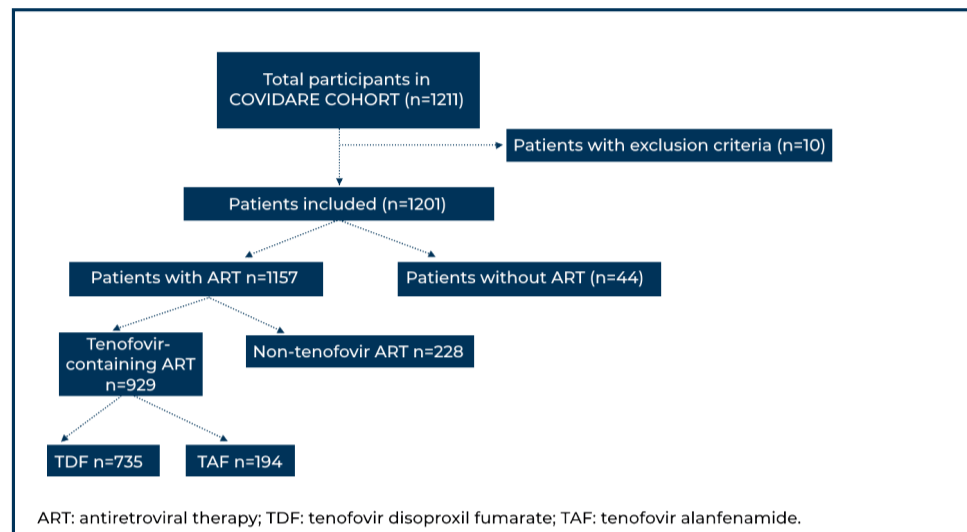
Results:

- 1157 were included, 929 (80%) received tenofovir-based ART (79% TDF, 21% TAF), as shown in figure 1.
- Accompanying drugs included almost universally XTC and for TAF mostly BIC (77%) and for TDF: EFV (32%), DRV/r (39.6%) or DTG (14.4%), among others.
- Non-tenofovir ART was predominantly based on ABC/XTC (63.5%) or single 3TC (19%) as nucleoside analogs + DTG (32%), DRV/R (34.6%) or EFV (20%), among others.
- A comparison between both cohorts is shown in table 1:

Table 1. Demographic profile, clinical characteristics and outcomes of COVID-19 in HIV-infected patients with tenofovir and non-tenofovir based baseline antiretroviral therapy in the COVIDARE cohort, Argentina (2020-2022).

	Tenofovir (TDF/TAF) cohort (n=929)	Non-tenofovir cohort (n=228)	P value
Male sex	612 (65.8%)	145 (63%)	0.091
Age yr (median, IQR)	43 (36-51)	50 (40-57)	0.011
Comorbidities	352(37.8%)	115 (50.4%)	0.001
Obesity	155(16.6%)	37(16.2%)	0.123
Hypertension	41 (4.41%)	39(13.5%)	0.001
Smoking	74(7.96%)	29(12.7%)	0.023
Diabetes	23 (2.47%)	25(10.9%)	0.000
Asthma	5(0.53%)	6 (2.63%)	0.003
Chronic kidney disease	5(0.53%)	16(7.01%)	0.002
Coronary heart disease	11(1.18%)	5(2.19%)	0.706
Virologic suppression	758 (81.5%)	179 (63.4%)	1.00
CD4 T-cell count cel/uL (median, IQR)	598 (434-800)	656.5 (472.5-824)	0.824
Symptomatic COVID-19 (n, %)	891 (95.7%)	221 (96.9%)	0.509
Radiographic abnormalities (n/N, %)	85/197 (45.5%)	24/59 (46.6%)	1.000
Hospitalization	146 (16.4%)	41 (18.72%)	0.119
Oxygen therapy	83 (8.94%)	31 (13.84%)	0.040
COVID-19 therapy	105 (11.3%)	30 (13.3%)	0.618
Mortality	8 (0.86%)	5 (2.22%)	1.00

Figure 1. Flowchart of HIV/COVID coinfected patients in the COVIDARE cohort, Argentina, according to ART status.



- Considering demographics, both groups were similar except for older age in non-tenofovir group.
- Regarding prevalence of symptomatic disease, radiologic findings, hospitalization and mortality no differences were observed between cohorts.
- Oxygen therapy requirement was higher in non-tenofovir group.
- Age and non-tenofovir ART remain associated to requirement of oxygen therapy on multivariate analysis (p= 0.025 and 0.031, respectively) as shown in table 2.

TABLE 2. Variables associated to oxygen requirement COVID-19 in HIV-infected patients in the COVIDARE cohort, Argentina (2020-2022).

Variable	OR	(IC 95%)	p-value
Non-tenofovir ART	1,69	(1,19-2,52)	0,031
Age	1,24	(1,12- 3,23)	0.025
Viral load (c/ml)	0,92	(0,75 -2,86)	0.263
CD4 T-cell count (cel/uL)	0,42	(0,40-1,27)	0,072
Comorbidities	0,22	(0,17-1.07)	0,059

ART: antiretroviral therapy

Conclusions

- No differences were observed in hospitalization and mortality rates in tenofovir vs. non-tenofovir groups. Conversely, requirement of oxygen therapy was associated to older age and non-tenofovir ART which may suggest a protective effect of tenofovir.
- Considering the intrinsic limitations of the observational design of this study, clinical trials are needed to better define impact of tenofovir containing ART in clinical outcomes of COVID-19.
- Our group is currently evaluating the impact of TDF vs. TAF + other therapies in hospitalization and oxygen requirement rates in COVIDARE cohort

References

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