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Doravirine plus lamivudine (DOR/3TC) two-drug regimen as a maintenance antiretroviral therapy in virally suppressed persons living with HIV

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Background, Objectives

- Drug-reduced ART is now a suitable therapeutic option in PLHIV with sustained viral suppression, which allows to limit the long-term cumulated toxicity of certain drugs (1).
- Two-drug regimens are increasingly used as maintenance strategies. They are all based on INSTIs or boosted PIs. However, all PLHIV are not able to receive INSTIs or boosted PIs, especially in case of intolerance or drug-drug interactions.
- In the era of highly effective ART, only one study has evaluated the virological efficacy of a two-drug regimen based on NNRTI plus NRTI. Kahlert, et al. demonstrated that nevirapine plus lamivudine (NVP/3TC) was able to maintain the control of the viral replication (HIV-RNA <50 copies/mL) in 19 patients over 144 weeks (2).
- Doravirine has a high genetic barrier, a good tolerance and no drug-drug interactions, we assume that DOR/3TC two-drug regimen is a suitable ART in virally suppressed patients, able to maintain the virological success.
- **We report here on a series of PLHIV who received doravirine plus lamivudine (DOR/3TC), to assess the ability of this two-drug regimen to maintain plasma HIV-RNA <50 copies/mL.**

Methods

- This observational, non-interventional study included all adults who initiated DOR/3TC between 09/01/2019 and 01/31/2022, in order to have at least 24 weeks of follow-up, in five French HIV refence centres: Quimper, Pitié-Salpêtrière (Paris), Rennes, Pointe-à-Pitre and Marseille. ART prescriptions were made during routine follow-up by HIV physicians.
- Clinical and biological data were collected from local NADIS database (3). All patients signed a consent for the collection and the use of their anonymized data. Past HIV-RNA and -DNA genotypes were analyzed, when available.
- The primary outcome was the rate maintenance of virological success (no virological failure [VF]: confirmed HIV-RNA ≥50 copies/mL or single HIV-RNA ≥200 copies/mL, or ≥50 copies/mL with ART change) at W48. Secondary outcomes included: strategy success rate (HIV-RNA <50 copies/mL with no ART change) at W48, number of strategy discontinuations over follow-up, evolution of CD4 count, CD4/CD8 ratio over follow-up.
- Changes in CD4 count, CD4/CD8 ratio were assessed using the Wilcoxon test. Statistical tests were processed using STATA v.14.

Results

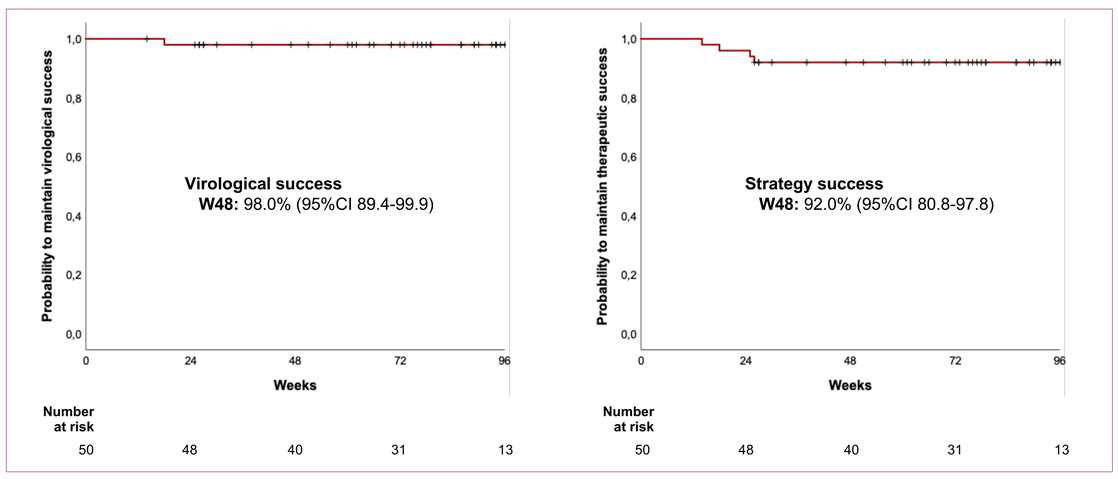
Table. Baseline patients' characteristics (N=50).

Age, years, median (IQR)	58 (51-62)
Gender, n (%)	
- Male	34 (68)
- Female	16 (32)
Birth Country, n (%)	
- France	44 (88)
- Other	6 (12)
Transmission group, n (%)	
- Heterosexual	23 (46)
- MSM	21 (42)
- Other	6 (12)
CDC stage C, n (%)	11 (22)
CD4 nadir, cells/mm^3, median (IQR)	258 (145-385)
HIV-RNA zenith, log$_{10}$ copies/mL, median (IQR)	4.79 (3.67-5.32)
Time from HIV diagnosis, years, median (IQR)	24 (16-29)
Time from ART initiation, years, median (IQR)	20 (13-23)
Genotypic sensitivity score, n (%)[a]	
- 2	18/20 (90)
- 1	2[b]/20 (10)
Duration of viral suppression, years, median (IQR)	14 (8-19)
CD4 count, cells/mm^3, median (IQR)	784 (636-889)
CD4/CD8 ratio, median (IQR)	1.16 (0.96-1.50)
Antiretroviral strategy prior to DOR/3TC, n (%)	
- NNRTI-based 3-DR	25 (50)
- INSTI-based 3-DR	11 (22)
- Dolutegravir/lamivudine	6 (12)
- Darunavir/ritonavir/lamivudine	3 (6)
- Other 2-DR	3 (6)
- Boosted PI monotherapy	2 (4)

NOTES. 3-DR: three-drug regimen. 2-DR: two-drug regimen. a. Calculated from cumulative historical HIV-RNA and HIV-DNA genotypes with reverse transcriptase available sequences (N=20). b. These two patients had a documented M184V mutation in past genotypes.

- Forty-three patients were included, with 29 (67%) men, median age: 59 years (IQR 52-63), ART duration: 21 years (14-25), duration of virological suppression: 14 years (8-19), CD4 count: 616/mm3 (774-878). All had pVL <50 copies/mL at study entry.

Figure. Virological and therapeutic success rate under DOR/3TC.



- There was no significant change in the CD4/CD8 ratio (+0.01, p=72), and a significant increase in the CD4 count (+51/mm^3, p=0.031) over the study period.
- All except three were naive to doravine before switching.
- Median follow-up was 79 weeks (IQR 60-96). **The virological success rate was 98.0% (95%CI 89.4-99.9) and the strategy success rate was 92.0% (95%CI 80.8-97.8) at W48.**
- One VF occurred at W18 (HIV-RNA=101 copies/mL), in a patient having briefly stopped his treatment due to intense nightmares; no resistance at baseline; no resistance emergence; HIV-RNA <50 copies/mL after resumption of boosted PI monotherapy.
- There were three strategy discontinuations over the entire study period for adverse event (neuropsychic disorder: n=2, digestive disorder: n=1).

Conclusions

- **This preliminary observational study shows that DOR/3TC two-drug regimen is able to maintain high level of viral suppression in highly experienced PLHIV with long viral suppression, and good CD4+T cells count. We observed only one VF over the study period, in a patient who stopped his treatment, with low-level of HIV-RNA, and, more importantly, with no emergence of resistance. A prospective, randomized trial is now needed to confirm these results.**
- Limitations: retrospective observational study, with non comparative arm, and small population size.

REFERENCES: **Katlama**, *AIDS*, 2017, **Kahlert**, *Plos One*, 2020, **Pugliese**, *HIV Medicine*, 2009

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