P094

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

Pascale Perfezou[1], Nolwenn Hall[1], Jean-Charles Duthe[1], Basma Abdi[2], Sophie Seang[3], Anne-Geneviève Marcelin[2], Christine Katlama[3], Romain Palich[3]

1. Public Health Center, Quimper Hospital, Quimper, France
2. Sorbonne University, Virology Department, Pitié-Salpêtrière Hospital, AP-HP, Pierre Louis Epidemiology and Public Health Institute (iPLESP), INSERM 1136, Paris, France
3. Sorbonne University, Infectious Diseases Department, Pitié-Salpêtrière Hospital, AP-HP, Pierre Louis Epidemiology and Public Health Institute (iPLESP), INSERM 1136, Paris, France

Background

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

Methods

- This observational, non-interventional study included all virologically suppressed adults who initiated DOR/3TC between 09/01/2019 and 01/31/2022, with at least 24 weeks of follow-up, in five French HIV treatment 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 the local NADIS database (3). All patients signed a consent for collection and use of their anonymized data. Past HIV-RNA and -DNA genotypes were analyzed, when available.
- The primary outcome was maintenance of virological suppression (HIV-RNA <50 copies/mL) at W48. Virological failure [VF] was defined as a confirmed HIV-RNA ≥50 copies/mL, or a single HIV-RNA ≥200 copies/mL, or ≥50 copies/mL with ART change). Secondary outcomes included: strategy success rate (no VF and no ART change for non-virological reasons) at W48, number of discontinuations over follow-up, evolution of CD4 count and 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

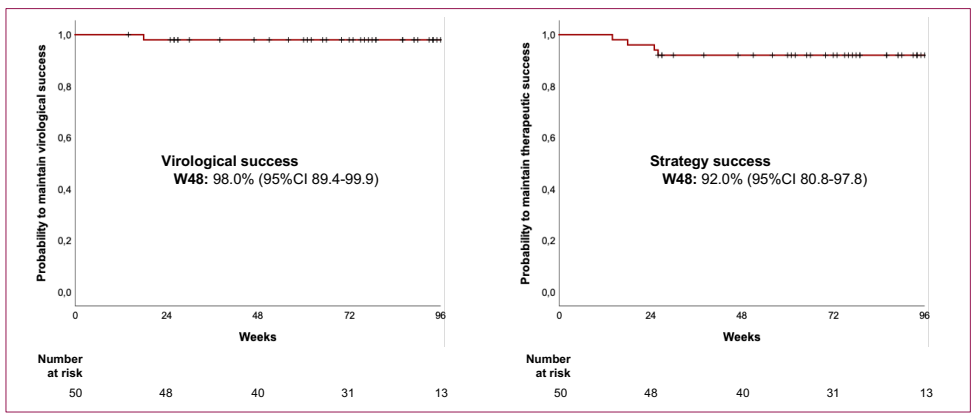
Table. Baseline patients' characteristics (N=50).

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 (insomnia: n=1, digestive disorder: n=2).

Conclusions

- **This preliminary observational study shows that DOR/3TC two-drug regimen maintains high levels of viral suppression in highly ART experienced PLHIV with very long term viral suppression, and good CD4+T cells count. We observed only one VF over the study period, in a patient who stopped treatment, with low-level of HIV-RNA. Importantly, there was also 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 with very long term viral suppression limiting generalizability of the results.

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

ACKNOWLEDGMENTS:
Cédric Arvieux, Isabelle Lamaury, Amélie Ménard

HIV Drug Therapy 30 GLASGOW 2022 | HYBRID YEARS