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Efficacy and tolerability of long-acting cabotegravir + rilpivirine in real-world setting, 52 weeks results

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Introduction

- Long-acting injectable (LAI) cabotegravir + rilpivirine (CAB+RPV) is the first long-acting antiretroviral regimen approved for virologically suppressed people living with HIV (PLWH) by the FDA in January 2021 (1).
- Despite the available results of the main Phase 3 clinical trials ATLAS (2), FLAIR (3) and ATLAS-2M (4), and predictors associated with confirmed virological failures (CVF) (5), the causes and consequences of CVF remain uncertain.
  Updated data on LAI CAB+RPV from the real-world is necessary to optimize use of this novel LA regimen against potential risks of CVF.

Study Design

- We examined the real-life effectiveness and safety of LAI CAB+RPV in virologically suppressed PLWH treated for up to 52 weeks.

Methods

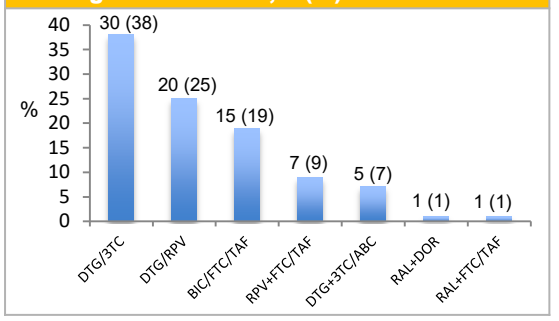
- From February 1st 2023 to May 30th 2024, bimonthly LAI CAB+RPV therapy was offered to 104 PLWH, belonging to the Infectious Diseases Unit of the University of Foggia, after appropriate assessment.
- Participants achieving eligibility criteria switched from combined antiretroviral therapy (cART) to bimonthly LAI CAB (600mg)+RPV (900mg) (without oral lead-in).
- Demographics and laboratory values were recorded in a dedicate database. Data for plasma viral load, CD4+ cell count, ART history, genotypic resistance history, risk factors, number of injections, and safety, including injection site reaction (ISR), were collected.
- Baseline archived HIV-1 resistance-associated mutations (RAMs) were assessed in peripheral blood mononuclear cells (PBMC) of participants with CVF or without GRT history through next-generation sequencing.
- Survival regression model was fitted to evaluate associations between therapeutic efficacy and HIV-RNA suppression status.

Results

PLWH started LAI CAB+RPV

- Of the 104 PLWH, 25 (24%) refused the switch to LAI CAB+RPV for the following reasons:
  - 15 (14%) for preference of the current cART;
  - 2 (2%) for trypanophobia;
  - 2 (2%) for effectiveness-related doubts of LAI CAB+RPV;
  - 6 (6%) for other reasons (not specified).
- 79 (76%) participants accepted the therapeutic switch to LAI CAB+RPV from the previous cART (Figure 1) mainly due to pills fatigue burden (78; 99%), followed by stigma (1; 1%).

Figure 1 **Previous cART of PLWH before starting LAI CAB+RPV, n (%)**

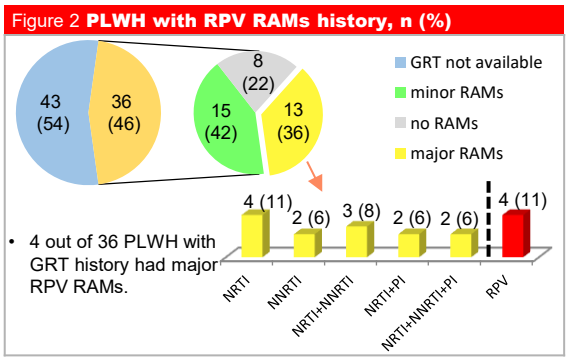


- Characteristics of PLWH started LAI CAB+RPV are shown in Table 1.
- Twelve (15%) had BMI>30 kg/m^2 and 4 (11%) had baseline RPV RAMs (Figure 2).

Table 1 **Characteristics of PLWH started LAI CAB+RPV**

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS	
Variables	**Total (n=79)**
Gender, n (%)	
Cisgender males	55 (70)
Cisgender females	24 (30)
Ethnicity, n (%)	
Caucasian	76 (96)
Black	3 (4)
Age, years, median (IQR)	50 (41-58)
BMI, kg/m^2, median (IQR)	**25.4 (22.4-28.5)**
HIV infection duration, years, median (IQR)	17 (8-22)
Risk factor, n (%)	
Men who have Sex with Men (MSM)	33 (42)
Heterosexual	36 (45)
People who inject drugs	10 (13)
Past co-infections, n (%)	24 (30)
HBV	9 (11)
HCV	11 (14)
HBV/HCV	4 (5)
VIRO-IMMUNOLOGICAL CHARACTERISTICS	
Variables	**Total (n=79)**
HIV-1 subtype, n (%)	
B	**21 (27)**
CRF02_AG	**1 (1)**
F1	**1 (1)**
Unknown	**56 (71)**
PLWH with historical GRT, n (%)	
Plasma, n (%)	36 (46)
RPV-associated Y181C, n (%)	**2 (5)**
RPV-associated E138A, n (%)	**1 (3)**
RPV-associated L100I, n (%)	**1 (3)**
Not associated-RPV RAMs	**32 (89)**
GRT on PBMC at Baseline, n (%)	12 (15)
RPV-associated Y181C, n (%)	**1 (8)**
RPV-associated M230I, n (%)	**2 (17)**
RPV-associated E138A, n (%)	**3 (25)**
Not associated-RPV RAMs	**6 (50)**
Duration of viral suppression, years, median (IQR)	8.9 (5.7-13.1)
Target not detected at switch, n (%)	75 (95)
Baseline CD4+/CD8+ ratio, median (IQR)	1.2 (0.8-1.6)
Baseline CD4+ T-cells, cells/mm^3, median (IQR)	857 (656-1,253)
Baseline CD8+ T-cells, cells/mm^3, median (IQR)	755 (589-1,048)
At least one failure before switch, n (%)	20 (25)
NNRTI-failure before switch, n (%)	8 (11)
RPV-associated failure	3 (4)
EFV-associated failure	3 (4)
NVP-associated failure	2 (3)
INSTI-failure before switch, n (%)	0 (0)

Figure 2 **PLWH with RPV RAMs history, n (%)**



- 4 out of 36 PLWH with GRT history had major RPV RAMs.

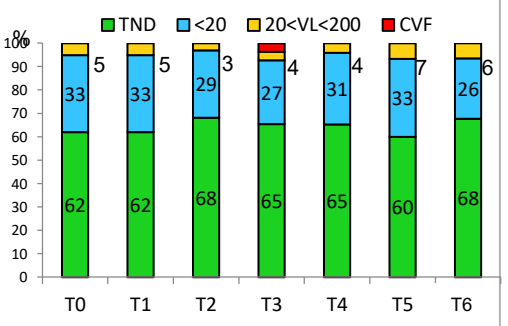
Results 2. Efficacy

- With a median observational follow-up of 55 weeks (IQR 24-63), considering participants with at least two doses of LAI CAB+RPV, 67 (92%) maintained HIV-RNA <50 copies/mL (Figure 3a).
- Six (8%) interrupted treatment with LAI CAB+RPV: 2 had CVF, 1 ISR, 2 moved to other centres and 1 had doubt on LAI CAB+RPV efficacy.
- Treatment adherence was high in most of the PLWH (97%); one missed the second injection, and another one received the third dose 9 days later the scheduled date. Both maintained viral suppression.
- Both CVF presented BMI<30 kg/m^2 and B subtype:
  - The first CVF is a 47-year-old woman with a viral rebound of 3614 copies/mL. Patient switched to BIC/TAF/FTC. Since the last visit carried out on 30/04/2024, the woman has been virologically suppressed.
  - The second CVF is a 58-year-old man with a viral rebound of 19130 copies/mL. Patient switched to BIC/TAF/FTC on 02/05/2024.
- For both CVF, post-failure GRT was performed; no CAB and/or RPV related RAMs were detected.
- PLWH with detectable HIV-RNA in the last 36 months before LAI CAB+RPV, were more likely to have detectable viral load during treatment (p-value<0.0001) (Figure 3b).

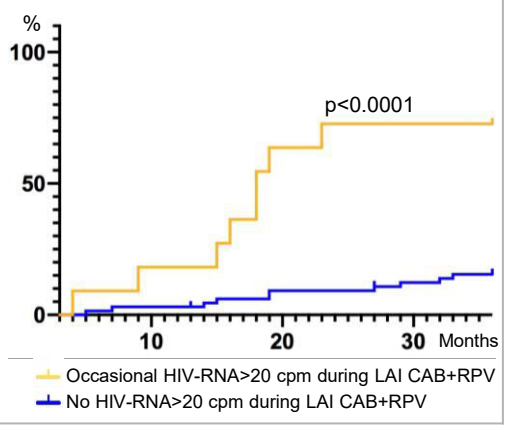
Figure 3 **Efficacy results of LAI CAB+RPV at 52 weeks**

a) Percentages of the viral load (VL) ranges detected at each injection time-point (T).

TND: Target not detected



b) Higher probability of HIV-RNA remaining suppressed during LAI CAB+RPV in those without detectable HIV-RNA in 36 months prior to switch (blue).



Conclusions

- In this real-life study, LAI CAB+RPV therapy was safe and effective in most PLWH (92%) that maintained viral suppression up to 52 weeks.
- Two CVF occurred and no RAMs were detected in both of them.

References

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5. Cutrell AG, et al.. Exploring predictors of HIV-1 virologic failure to long-acting cabotegravir and rilpivirine: a multivariable analysis. AIDS. 2021 Jul 15;35(9):1333-1342. doi: 10.1097/QAD.0000000000002883.