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SHORT COMMUNICATION

Durability of Long-Acting Cabotegravir + Rilpivirine in Virologically Suppressed Adults Living With HIV: A Multicenter Observational Cohort in Tuscany (LAHIV)

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ABSTRACT

To evaluate the durability of long-acting cabotegravir (CAB) plus rilpivirine (RPV), available in Italy since June 2022, for maintaining HIV-1 virological suppression. This multicentric observational study included 191 virologically suppressed adults (HIV-RNA < 50 copies/mL) from 11 centers in Tuscany, followed from first CAB + RPV injection until discontinuation, death, or last visit. Discontinuation was defined as regimen switch or two consecutive missed doses, virological failure (VF) as two consecutive HIV-RNA > 50 copies/mL or a single > 1000 copies/mL. Kaplan–Meier survival analysis assessed discontinuation rates. Follow-up was 209.5 person-years with a median of 1 year (IQR 0.5–1.5). Median age was 51 years (IQR 43–58); 81.7% were male; median ART duration was 13.8 years (IQR 8.7–20.2). Eighteen participants (9.2%) discontinued due to adverse events (3.7%), VF (2.6%), personal choice (2.1%), medical decision (0.5%), or loss to follow-up (0.5%). Overall discontinuation was 8.5/100 person-years (95% CI: 5.4–13.6). VF incidence was 2.3/100 person-years (95% CI 0.9–5.7). All VFs, occurred within 28 weeks, except one at Week 72 with resistance mutations. Discontinuation rates were slightly higher than clinical trials but consistent with real-world data. The VF incidence was slightly higher than reported in prior reports, highlighting the need for real-life clinical monitoring.

1 | Introduction

In recent years, the introduction of long-acting (LA) antiretroviral therapies has marked a significant cornerstone in the therapeutic approach to HIV infection. Since 2022, the intramuscular combination of cabotegravir (CAB), an integrase strand transfer inhibitor (INSTI), and rilpivirine (RPV), a non-nucleoside reverse transcriptase inhibitor (NNRTI), has been approved in Europe for use in virologically

suppressed individuals clinically stable and without known resistance to either agent. The aim is to reduce the burden of daily oral antiretroviral therapy (ART), potentially improving adherence and quality of life for selected people living with HIV (PLWH). However, its implementation requires careful consideration, particularly in light of emerging evidence on factors that may be associated with an increased risk of virological failure (VF), such as prior resistance to NNRTIs or INSTIs, genotype A6, and a high body mass index., as well as low plasma concentrations of rilpivirine [1] Pivotal trials such as ATLAS, FLAIR, and ATLAS-2M have demonstrated the noninferiority of this regimen compared with standard daily oral ART in terms of virological efficacy and safety [2–5].

Nonetheless, real-world data remain limited, particularly regarding adherence to scheduled injections and long-term outcomes in routine clinical settings. In Italy, the use of CAB + RPV LA therapy has been gradually introduced in specialized HIV clinics since late 2022. In this study, we report the findings of a prospective multicenter cohort study conducted across 11 infectious diseases and STI centers in Tuscany. The aims are to describe clinical characteristics and virological outcomes of PLWH initiating LA CAB + RPV in real-life clinical practice.

2 | Materials and Methods

We conducted a multicenter, real-world, observational cohort study to evaluate the virological outcomes and durability of LA CAB + RPV regimen in clinical practice. The study included adults living with HIV who were virologically suppressed at baseline (HIV-RNA < 50 copies/mL) and initiated CAB + RPV treatment at 1 of 11 participating centers in Tuscany, Italy (10 Infectious Diseases units and 1 Dermatology unit).

Eligible participants were at least 18 years old, had a confirmed HIV-RNA < 50 copies/mL prior to switching, had signed informed consent, and had at least one documented follow-up HIV-RNA measurement after initiating treatment. Follow-up began prospectively from the first CAB + RPV injection and continued until the earliest of the following events: discontinuation of the regimen for any reason, death, or the last available clinical visit (data freeze: May 12, 2025).

All CAB + RPV injections were administered in hospital outpatient settings by trained nursing staff under physician supervision, according to the product characteristics. No home-based administration was performed.

VF was defined as either two consecutive HIV-RNA values > 50 copies/mL or a single value > 1000 copies/mL. The threshold of 50 copies/mL was adopted following the definition of virological rebound according to EACS guidelines (v.12.1). In this study, discontinuation for any cause was defined as the interruption of the CAB + RPV regimen for any reason (clinical, virological, organizational, or individual preference).

Loss to follow-up was defined as the absence of any clinical contact or HIV-RNA measurement for at least 6 months after the last scheduled injection, without evidence of treatment continuation elsewhere.

Loss to follow-up was considered a discontinuation, whereas death was not; however, no deaths occurred during the study period.

Incidence rates of treatment discontinuation and VF were calculated per 100 person-years of follow-up. Kaplan–Meier survival analysis was used to estimate the cumulative probability of remaining on treatment without discontinuation.

When the last HIV-RNA measurement did not coincide with the final clinical visit—since certain visits for long-acting injections did not include blood sampling—the most recent available HIV-RNA value was carried forward for descriptive analyses, provided that the participant was still receiving CAB + RPV treatment. Observation time for the calculation of VF rates was censored at the date of the last clinical visit, irrespective of the timing of the last HIV-RNA measurement. Statistical analyses included χ^2 tests, nonparametric tests, and Kaplan–Meier methods to assess time-to-event outcomes.

2.1 | Ethics

The study received the approval by each independent local Ethics Committee (Study Coordination Site Protocol Number 23666_oss). All the participants provided written informed consent for the use of their data for research purposes. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

3 | Results

A total of 191 PLWH were included in this real-world multicenter cohort, contributing 209.5 person-years of follow-up. The median follow-up duration was 1.0 year (IQR 0.5–1.5). The cohort was made up of 81.7% cisgender men ($n = 156$), 17.8% ($n = 34$) cisgender women, and one transgender woman (0.5%) (Table 1).

The median age at baseline was 51 years (IQR 43–58), and participants had been ART for a median of 13.8 years (IQR 8.7–20.2). At the time of CAB + RPV initiation, the median CD4+ T-cell count was 830 cells/μL (IQR 634–1068), with a median CD4/CD8 ratio of 1.0 (IQR 0.7–1.4). Participants had been virologically suppressed for a median of 4.9 years (IQR 0.9–10.7). Notably, a substantial proportion ($n = 45$; 25.8%) were hepatitis B core antibody (HBcAb) positive, indicating past or occult HBV infection. No biochemical/clinical evidence of HBV reactivation was observed among HBcAb-positive individuals during follow-up. Before the switch, 84 individuals (44.0%) were receiving dual therapy and 107 (56.0%) were on a triple regimen. Only 6.8% were on tenofovir disoproxil fumarate-based regimens immediately prior to the switch. At baseline, a historical genotype was available for 63.8% of participants ($n = 122$). Among these, 22/122 (18.0%) showed at least one major resistance mutation to reverse transcriptase (RT) (Table 1). No cases of integrase inhibitor (INSTI) resistance were detected. Two participants had high-level resistance to RPV according to the Stanford algorithm. In addition, 29/122 (23.8%) harbored other mutations. Overall, 20.4% of participants underwent an oral lead-in phase before receiving the first injection.

TABLE 1 | Clinical/demographic characteristics of adults with HIV-1, ART experienced with HIV-RNA level < 50 copies/mL switching to cabotegravir and rilpivirine in Tuscany, Italy.

	Total ($n = 191$)	
Born in Italy, *n* (%)	163	85.8
Gender, *n* (%)		
• Cisgender woman	34	17.8
• Cisgender man	156	81.7
• Transgender woman	1	0.5
Age at entry, median [IQR]	51	43–58
Risk of HIV transmission, *n* (%)		
• Heterosexual condomless sex	55	28.9
• MSM	105	54.9
• People who inject drugs (PWID)	11	5.7
• Other/not known	20	10.5
Years of undetectable viremia, median [IQR] Missing: 31	4.9	0.9–10.7
AIDS diagnosis, *n* (%)	26	13.6
HBc Ab positive, *n* (%) Missing: 17	45	25.8
HIV-RNA Zenith, Log_{10} copies/mL, median [IQR] Missing: 37	4.9	4.4–5.5
Nadir CD4 (cells/mm^3, median [IQR]) Missing: 30	304	155–430
Years of HIV, median [IQR]	13.8	8.7–20.2
CD4+ T cells at baseline/mm^3, median [IQR]	830	634–1068
CD4/CD8 ratio at baseline, median [IQR]	1.0	0.7–1.4
Type of anchor drug in the preswitch regimen		
• NNRTI	84	43.9
• PI	14	7.3
• INSTI	140	73.2
Number of previous ART regimens, median [IQR]	4	2–5
Preswitch regimen containing rilpivirine	74	38.7
Oral lead-in	39	20.4
Available genotype before the switch	122	63.8
Genotypic profile with major resistance mutations	22 out of 122	18.0
– NNRTI alone	2	
– NRTI alone	13	
– NNRTI + NRTI	5	
– RPV	2	

Abbreviations: ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; NNRTI, non-nucleoside reverse transcriptase inhibitors; NRTI, nucleoside (nucleotide) reverse transcriptase inhibitors; PI, protease inhibitor.

In 15 participants, the date of the last HIV-RNA measurement did not coincide with the final clinical visit. This occurred because certain injection visits did not include blood sampling. Among these individuals, the median time difference between the last HIV-RNA measurement and the final visit was 16 weeks (IQR 16–24; range 8–28).

3.1 | Discontinuations

During follow-up, 18 participants (9.2%) discontinued the CAB + RPV regimen, corresponding to a discontinuation rate of 8.5/100 person-years (95% CI: 5.4–13.6). We did not observe substantial differences between individuals who discontinued therapy and those who did not, except for the duration of virological suppression, which tended to be longer among those who remained on treatment. However, the interquartile range was wide, and the overall sample size limited the strength of this observation (Table 2). Reasons for discontinuation included adverse events ($n = 7$; 3.7%), VF ($n = 5$; 2.6%), voluntary discontinuation ($n = 4$; 2.1%), medical decision ($n = 1$; 0.5%), and loss to follow-up ($n = 1$; 0.5%) (Table 3).

Five participants (2.6%) experienced confirmed VF corresponding to a VF rate of 2.3/100 person-years (95% CI: 0.9–5.7). Most VF episodes (4 out of 5; 80.0%) occurred within the first 28 weeks. All individuals experiencing VF had adhered to the injection schedule. One late VF occurred at Week 72 in a male participant without known baseline resistance who later developed resistance mutations to both NNRTIs (M230L) and INSTIs (N155H, Q146L). Another person with preexisting rilpivirine-associated mutations (98G, 106I, 108I, 181V) also failed treatment.

Other VF cases included one participant with a single HIV-RNA detection of 4660 copies/mL who subsequently regained viral suppression while remaining on CAB + RPV; however, the clinician opted to switch therapy. Another case had two consecutive low-level viral load measurements (> 50 copies/mL and < 200 copies/mL) (genotypic resistance testing not performed); in this instance as well, the treating physician decided to modify the regimen. In a female-at-birth subject with a BMI of 66, previously treated with DTG/3TC and with no resistance mutations at baseline, VF occurred at the eighth administration, due to persistently elevated viremia without the emergence of genotypic resistance. In this case, DTG/3TC had been reintroduced, regaining viral suppression.

Among participants who discontinued due to adverse events (3.7%), a range of symptoms was reported. One case involved a severe injection site reaction resulting in the development of a measurable abscess (Table 3). A smaller proportion of individuals (2.1%) chose to discontinue treatment for nonmedical reasons. Reported motivations included difficulties in managing the logistics of frequent clinic visits—especially in the context of hospitalizations—and challenges in coordinating treatment schedules with work obligations. Additionally, one participant discontinued therapy following a medical decision prompted by the initiation of anticoagulant treatment with rivaroxaban after a diagnosis of atrial fibrillation.

Among participants who remained in follow-up, no missed doses were recorded. The overall probability of remaining on

TABLE 2 | Clinical and demographic characteristics of adults with HIV-1, ART-experienced with HIV-RNA < 50 copies/mL switching to RPV + CAB in Tuscany, Italy, stratified by treatment discontinuation status.

	Not discontinued ($N = 173$)	Discontinued ($n = 18$)	p
Born in Italy, *n* (%)	146 (84.8)	17 (94.4)	0.269
Gender, *n* (%)			0.489
• Cisgender woman	29 (16.7)	5 (27.8)	
• Cisgender man	143 (82.7)	13 (72.2)	
• Transgender woman	1 (0.6)	0 (0)	
Age at entry, median [IQR]	53 [49–57]	51 [43–58]	0.497
Risk of HIV transmission, *n* (%)			0.397
• Heterosexual condomless sex	48 (27.7)	7 (38.9)	
• MSM	94 (54.3)	11 (61.1)	
• IPeople who inject drugs (PWID)	11 (6.4)	0	
• Other/Not known	20 (11.5)	0	
Years of undetectable viremia, median [IQR] Missing: 31	5.3 [1.2–11.0]	0.6 [0.4–5.8]	0.003
AIDS diagnosis, *n* (%)	24 (13.8)	2 (11.1)	0.745
HBc Ab positive, *n* (%) Missing: 17	40 (25.6)	5 (27.8)	0.845
HIV-RNA Zenith, Log_{10} copies/mL, median [IQR] Missing: 37	4.87 [4.42–5.52]	5.08 [4.84–5.53]	0.314
Nadir CD4 (cells/mm^3, median [IQR]) Missing: 30	325 [156–453]	237 [99–314]	0.126
Years of HIV, median [IQR]	13.8 [8.8–20.2]	14.0 [8.4–22.0]	0.919
CD4+ T cells at baseline/mm^3, median [IQR]	833 [634–1079]	803 [637–990]	0.635
CD4/CD8 ratio at baseline, median [IQR]	1.1 [0.7–1.4]	0.9 [0.7–1.2]	0.227
Number of previous ART regimens, median [IQR]	4 [2–5]	4 [4–6]	0.118
Preswitch regimen containing rilpivirine	68 (39.3)	6 (33.3)	0.621
Oral lead-in	37 (21.4)	2 (11.1)	0.303

Abbreviations: INSTI, integrase strand transfer inhibitor; MSM, males who have sex with males; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; ART, antiretroviral therapy.

treatment over time is illustrated in the Kaplan–Meier survival curve (Figure 1).

4 | Discussion

In this multicenter cohort study conducted in Tuscany, we observed rates of discontinuation and VF with CAB + RPV that were broadly consistent with other real-world European reports, although slightly higher VF rates emerged compared with Phase 3 clinical trials. We focused primarily on European cohorts, as they share a healthcare system, follow-up structures, and—critically—VF definitions more comparable to ours than those used in the United States, making cross-study comparisons more directly interpretable.

A distinctive strength of our study is that it captures the real-life, regional, and decentralized implementation of LA CAB + RPV within routine clinical practice. By including both academic and nonacademic infectious diseases centers—often underrepresented in large national cohorts—our cohort reflects the full spectrum of care delivery across Tuscany, encompassing variations in patient profiles and follow-up strategies. This heterogeneity provides an authentic representation of everyday clinical practice and enhances the external validity of our findings, offering nuanced insights into the performance of long-acting therapy in diverse, real-world settings beyond controlled trial conditions. Methodologically, we adopted a conservative VF definition (two consecutive HIV-RNA values > 50 copies/mL or one > 1000 copies/mL followed by treatment switch), which aligns with virological rebound definition in the EACS guidelines but is stricter than the ≥ 200 copies/mL threshold used in the FLAIR, ATLAS, and ATLAS-2M trials. This approach likely captured clinically relevant events that might have been missed with more lenient thresholds.

Compared with the Italian ICONA cohort—which used the same cut-off of our study—our VF rate was slightly higher (2.3 vs. 1.35 per 100 person-years [95% CI, 0.61–3.01]) [6]. In our series, we included two individuals who spontaneously re-suppressed while continuing CAB + RPV—one with two HIV-RNA measurements < 200 copies/mL and one with a transient HIV-RNA > 4000 copies/mL. In one VF case, RPV-associated resistance mutations were documented before the switch, highlighting the value of reviewing available genotypic resistance testing prior to initiating CAB + RPV LA. This is consistent with prior evidence showing that archived RPV resistance—

TABLE 3 | Reasons for discontinuation of cabotegravir + rilpivirine in a population of adults with HIV-1, ART experienced with HIV-RNA level < 50 copies/mL in Tuscany, Italy.

Previous regimen	viremia (> 50 cp/mL) < 6 months ago	Subtype	BMI at discontinuations	OLI	NNRTI or INSTI-associated mutations on the baseline genotype	Cause	Week	Postregimen
Virological failure								
3TC/DTG	Yes	B	29.5		98G 106I 108I 181V	Virological failure: (4930 cp/mL)—preexisting RPV mutations on RNA. No resistance to INSTIs at failure (RNA test).	4	T/F/DRVc
T/F/DOR	No	N/A	26.6	No	Not detected	Virological failure (2 determinations > 50 cp/mL but < 200 in a previously suppressed individual)—genotypic test not performed at VF.	28	3TC/DTG
3TC/DTG	No	N/A	66	No	Not detected	Virological failure:(6560 cp/mL)—no resistance was recorded at failure (RNA test).	28	3TC/DTG
3TC/DTG	No	B	26	Yes	Not detected	Virological failure (3640)—M230L for NNRTI and N155H and Q146L for INSTIs (RNA test).	72	T/F/DRVc
RPV/DTG	No	B	25.9	No	Not detected	Virological failure (4660 cp/mL) at Week 4, but subsequently dropped to < 50 cp/mL while still on CAB + RPV. No viral resistance was detected, and viral load remained persistently < 50 cp/mL. However, the physician preferred to switch the regimen.	4	RPV/DTG
Toxicity/adverse reaction								
3TC/DTG	No	N/A	N/A	No	N/A	High fever with widespread joint pain and gluteal pain. Walking impairment.	4	3TC/DTG
RPV/DTG	Yes	B	N/A	No	Not detected	Rash	28	RPV/DTG
RPV/DTG	Yes	N/A	20.2	No	N/A	General malaise	4	RPV/DTG
3TC/DTG	No	N/A	25.3	No	N/A	Depression	4	3TC/DTG
T/F/RPV	Yes	N/A	23	No	Not detected	Panic attacks	12	T/F/RPV
3TC/DTG	No		21	No	N/A	Weight gain of 10 kg, worsening of depressive symptoms, insomnia, asthenia.	44	3TC/DTG
T/F/BIC	No	N/A	22.2	Yes	Not detected	Severe site injection reaction (abscess 4.5 × 2.85 cm)	12	3TC/DTG
T/F/BIC	No	B	24.5	No	184V	Voluntary discontinuation: variable and unpredictable work schedule	12	T/F/BIC
3TC/DTG	No	N/A	24.6	No	N/A	Voluntary discontinuation	72	3TC/DTG

(Continues)

TABLE 3 | (Continued)

Previous regimen	viremia (> 50 cp/mL) < 6 months ago	Subtype	BMI at discontinuations	OLI	NNRTI or INSTI-associated mutations on the baseline genotype	Cause	Week	Postregimen
3TC/DTG	No	N/a	22.4	No	K103T	Voluntary discontinuation: reports an increase in "fat mass" (cit.) despite unchanged body weight	96	3TC/DTG
RPV/DTG	Yes	N/A	22	No	N/A	Lost to follow-up	12	//
T/F/RPV	No	N/A	23.4	No	N/A	Excessive clinic visits and local reaction	28	T/F/RPV
3TC/DTG	No	B	45.3	No	Not detected	Medical decision: initiation of rivaroxaban therapy following the onset of atrial fibrillation	44	3TC/DTG

Abbreviations: BL, baseline; BMI, body mass index; DTG, dolutegravir; FTC, emtricitabine; F, emtricitabine; INSTI, integrase strand transfer inhibitor; N/A, not available; NNRTI, non-nucleoside reverse transcriptase inhibitors; OLI, oral lead-in; RPV, rilpivirine; T, TAF; 3TC, lamivudine.

together with other recognized risk factors such as HIV-1 subtype A6 and high BMI—should be considered when assessing suitability for long-acting therapy. [7] However, historical genotypic and subtype data are not always available in routine practice, as seen in our cohort, where 63.8% of participants lacked a prior genotype. This reflects a common real-world scenario in which genotypic testing has not always been routinely performed or accessible—for example, in individuals referred from other centers without complete documentation or in earlier years when such testing was not systematically available in all centers. Although this limits the ability to precisely quantify the contribution of archived resistance, it should not be regarded as a barrier to prescribing CAB + RPV LA in appropriately selected and motivated individuals. In these situations, clinical judgment based on ART history and any documented VFs remains central and often provides a sufficiently robust assessment. Notably, all participants who experienced VF in our cohort had a baseline genotype available, suggesting that the absence of older genotypic data did not materially affect the interpretation of resistance-related outcomes.

In the Dutch ATHENA cohort—also an observational study but with a cut-off similar to that of the trials—the rate of loss of virological control was 2%, more closely aligned with our findings, despite differences in VF definitions (≥ 200 copies/mL). [8] While the trials report lower VF rates (~1% at 48 weeks), this may reflect stricter eligibility criteria and more intensive follow-up than in routine care. All VF cases in our cohort occurred despite adherence to the injection schedule, in line with trial data.

The overall discontinuation rate was 8.5/100 person-years, lower than the 11.42/100 PY reported in ICONA. Discontinuations due to adverse events (3.7%) were in line with other European real-world experiences, such as 3.6% (5 out of 138) in a monocentric study from Milan [9] and 7% in ICONA [6]. In our cohort, these were mainly due to significant injection-site reactions, neuropsychiatric symptoms such as difficulty of sleeping, or mood changes (although rare, as reported in a recent review by Bottanelli et al. [10]), and logistical challenges related to frequent clinic visits—barriers also reported in other studies.

Following the analysis of discontinuations, several additional characteristics of our cohort—some of which may be relevant for interpreting real-life data on CAB + RPV LA—deserve consideration.

First, participants who discontinued CAB + RPV had a significantly shorter duration of previous virological suppression compared with those who remained on treatment. Although this may indicate a subgroup with less consolidated adherence or more complex treatment histories, the limited number of events and the substantial variability observed suggest caution in interpretation. Larger cohorts with longer follow-up are required to determine whether shorter prior viral suppression may emerge as an independent predictor of early discontinuation in real-world practice.

Second, in our relatively high proportion of anti-HBc–positive participants, HBV-DNA testing was not systematically performed—as this is not generally indicated in the absence of HBsAg positivity or elevated liver enzymes.

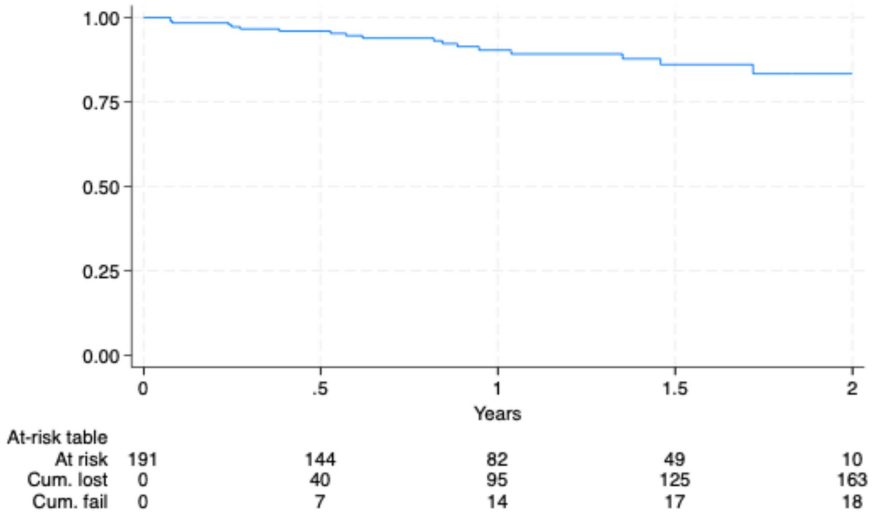

FIGURE 1 | Probability of remaining free from treatment discontinuation for all causes in adults with HIV-1 ART experienced with HIV-RNA level < 50 copies/mL switching to cabotegravir and rilpivirine in Tuscany, Italy. The at-risk table below the graph indicates the number of participants still under observation ("at risk"), cumulatively lost to follow-up ("cum. lost"), and those who discontinued treatment ("cum. fail") at each time point.

Although no biochemical or clinical evidence of HBV reactivation was observed during follow-up, the possibility of reactivation over longer observation underscores the need for continued clinical monitoring [11].

Finally, although women accounted for 17.8% of our cohort, this proportion is comparable to—or higher than—other major European real-world cohorts evaluating CAB + RPV LA (e.g., ICONA [6]: 12%; ATHENA [8]: 9%) and it is also closer to the representation observed in pivotal clinical trials, where female participation ranged between 23% and 28% [2, 3].

This study has several limitations. First, the short observation period reflects the early implementation of LA CAB + RPV in Tuscany, which began in late 2022, and therefore mainly captures early discontinuations and VFs that occurred within the first year of treatment. Furthermore, in a subset of participants, the last HIV-RNA measurement did not coincide with the final clinical visit, as certain injection visits did not include blood sampling; this may have slightly underestimated the number of VFs. Finally, socioeconomic information (e.g., employment or educational status) was not systematically available, although overall adherence to scheduled injections appeared good, with no missed doses among participants who remained in follow-up. Longer observation will be essential to confirm the long-term durability and safety of this therapeutic strategy.

In conclusion, while our VF rate is slightly higher than in clinical trials, LA CAB + RPV demonstrated reassuring effectiveness and tolerability in a heterogeneous real-world environment. The stricter VF definition and inclusion of a wide range of clinical settings provide a nuanced perspective on regimen performance. Longer real-life follow-up data will be essential to fully understand the long-term durability of this strategy.

Author Contributions

Filippo Lagi conceived and coordinated the study, analyzed the data, and drafted the manuscript. Giuseppe Formica drafted the manuscript. Giuseppe Formica, Massimiliano Fabbiani, and Barbara Rossetti contributed to study design, data interpretation, and critical revision of the manuscript. Matteo Piccica, Giuseppe Formica, Alessio Pampaloni, Beatrice Menichini, Silvia Costarelli, Claudia Bianco, Giovanni Sarteschi, Michele De Gennaro, Emanuela Francalanci, Martina Turco, Giuseppe Gasparro, Marco Fognani, Paola Corsi, Marco Pozzi, Gaetana Sterrantino, Mario Tumbarello, Daniela Messeri, Cecilia Costa, Beatrice Anna Adriani, Cesira Nencioni, Danilo Tacconi, Spartaco Sani, Antonella Vincenti, and Luigi Pisano contributed to patient recruitment, data collection, and clinical follow-up. Alessandro Bartoloni supervised the overall project and critically revised the manuscript for important intellectual content. All authors reviewed and approved the final version of the manuscript.

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Ethics Statement

The study received the approval by each independent local Ethics Committee (Study Coordination Site Protocol Number 23666_oss). This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent

All the participants provided written informed consent for the use of their data for research purposes.

Conflicts of Interest

F.L. and B.R. consultant/participated on advisory boards sponsored by ViiV Healthcare, Janssen. M.Fa. received speakers' honoraria, support for travel to meetings, and/or fees for attending advisory boards from Bristol Myers Squibb (BMS), Gilead, Janssen-Cilag, Merck Sharp and Dohme (MSD), and ViiV Healthcare. No personal relationships, academic competition, or intellectual biases that could have inappropriately influenced the work reported in this paper.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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