Abstract SC21 Table 1 Population characteristics at baseline

Variables	N=419
Age (years), Median (IQR)	52 (43-59)
Male sex at birth, n (%)	341 (81.4)
Anti-HCV antibodies positive, n (%)	59 (14.0)
Time from HIV diagnosis (years), Median (IQR)	13.9 (8.8-21.0)
CDC stage C, n (%)	79 (18.8)
Time on antiretroviral therapy (years), Median (IQR)	11.3 (7.0-17.3)
Nadir of CD4+ (cell/μL), Median (IQR)	293 (142-467)
Zenith HIV-RNA (log copies/mL), Median (IQR)	4.98 (4.56-5.51)
CD4+ count (cell/μL) at baseline, Median (IQR)	765 (602-981)
CD4/CD8 ratio at baseline, Median (IQR)	1.05 (0.72-1.44)
HIV subtype B, n (%)	206/255 (80.8)
Body Mass Index, Median (IQR)	24.5 (22.7-26.5)
Previous HAART regimen, n (%):	
- 2NRTI+INI	113 (27.0)
- 2NRTI+NNRTI	53 (12.6)
- 2NRTI+PI	10 (2.4)
- 3TC-based 2DR	160 (38.2)
- RPV+DTG	64 (15.3)
- Other/Unknown	19 (4.5)
Reasons for switch to CAB+RPV, n (%):	
- Simplification	312 (74.5)
- Personal request from PWH	27 (6.4)
- Physician's decision	26 (6.2)
- Other/Unknown reasons	54 (13.9)

Results Of 478 PWH who started CAB/RPV LA across 8 Clinical centers, 419 met inclusion criteria; exclusions were due to BMI >30 kg/m^2 (n=29), prior VF on NNRTIs (n=18), presence of major RPV mutation (n=6), and A1/A6 HIV subtype (n=7). Baseline characteristics are shown in table 1.

During 692 PYFU (median FU 1.9 years), 5 VFs occurred (incidence 0.72 per 100 PYFU). The probability of maintaining VS was 99.1% (±0.5%) at 48 wks and 98.1% (±0.9%) at 144 wks. Cox regression identified no significant predictors of VF. GRT at VF was available for 3 PWH and revealed resistance mutations: 1 participant experienced VF at 19 months after switching from RPV/DTG, developing E138A, M230L, and Q148R; a second, switching from TAF/FTC/RPV, had VF after 12 months with a newly detected Q148K (not present on prior GRT). A third experienced VF after 4 months with K103N, E138K, and Q148R; this latter case received the second injectable dose after 8 wks and had no prior GRT available. Two PWH with a determination of HIV-RNA >1000 cps/mL during FU continued CAB/RPV LA, with subsequent undetectability; one of them, had a HIV-RNA 1021 cps/mL after 24 months, 2 wks after HPV vaccination.

With respect to durability, 56 PWH discontinued CAB/RPV: the main causes of TD were injection-site reactions (ISR) (n=21, 4.9%), regimen intensification (n=10, 2.3%), neurological toxicity (n=7, 1.6%), and patient request (n=5, 1.2%). One participant occurred in HBV acute infection (previous HBsAg and HbcAb negative). 50% of TDs occurred within the first 6 months of FU.

In a sensitivity analysis, which included 138 PWH with known baseline BMI and HIV subtype, we found no VF.

Conclusions These real-world data confirm the high efficacy and tolerability of CAB/RPV LA, supporting their role in individualized antiretroviral care. Although rarely, VF associated with emergence of resistance mutations did occur, including in patients switching from RPV-containing regimens. Larger studies with longer follow-up are needed to identify factors associated with VF and resistance emergence beyond the ones which are already known.

SC22 LIFE AFTER LONG-ACTING THERAPY: WHAT HAPPENS WHEN CAB/RPV IS DISCONTINUED?

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Background The onset of adverse events (AEs) is the main cause of discontinuation of long-acting (LA) cabotegravir+rilpivirine (CAB+RPV) in observational and randomized studies. Nevertheless, data are scarce on the choice of the following oral regimen, on the potential additional AEs that develop during the pharmacokinetic tail of CAB and RPV, and on the virologic outcomes in people who discontinue LA treatment for reasons other than virologic failure (VF).

Materials and Methods This is a multicenter, prospective, observational study conducted within the SCOLTA (Surveillance Cohort Long-Term Toxicity Antiretrovirals) project; it includes people with HIV (PWH) who discontinued LA CAB/RPV therapy after at least one follow-up visit. Descriptive statistics were used to summarize data.

Results The study included 700 PWH on LA CAB+RPV, with an observed all-cause therapy interruption rate of 13.3% (93/700) and a median follow-up of 23 months (IQR 14-30). The main reasons for treatment discontinuation were AEs and the subject's decision, accounting for 47.3% (44/93) and 16.1% (11/93) of all interruptions, respectively (table 1). Injection site reactions (ISRs) were the most frequent AE, accounting for 45.5% of cases, followed by arthromyalgias and infectious complications, each accounting for 11.4% of cases (table 2). Excluding people who were lost to follow-up and the deceased, we evaluated the oral regimen selected after LA discontinuation in the remaining study participants. Among the subgroup that discontinued injectables for reasons other than VF, and excluding one subject who returned to the same PI-based therapy that was in place before initiating LA, 100% maintained a NNRTI- and/or INSTI-based regimen without the need to introduce new ARV classes or a PI-based therapy. Considering those who discontinued injectables due to VF, 4 out of 10 people switched to a PI-based regimen (table 3).

Abstract SC22 Table 1–3

Table 1 - **LA CAB+RPV discontinuation rates**

CATEGORY	PWH (N)	RATE (%)
AES	44	47.3
PATIENT'S DECISION	15	16.1
LOST TO FOLLOW-UP	11	11.8
VF	10	10.8
OTHER (*)	6	6.5
DECEASED	4	4.3
PREGNANCY	3	3.2

(*) 3 were hospital relocations, 3 were considered at risk for VF

Abbreviations: PWH, people with HIV; LA, long-acting; CAB, cabotegravir; RPV, rilpivirine; AEs, adverse events; VF, virologic failure.

Table 2 – **AEs classification**

CATEGORY	PWH (N)	RATE (%)
ISRS	20	45.5
ARTHROMYALGIAS	5	11.4
INFECTIOUS COMPLICATIONS (*)	5	11.4
DERMATOLOGIC	3	6.8
CNS	2	4.5
GI	2	4.5
OTHER	4	9.1

(*) 2/5 were specified as HBV infection reactivation; the remaining 3 infectious complications were not further defined.

Abbreviations: PWH, people with HIV; AEs, adverse events; ISRs, injection site reactions; CNS, central nervous system; GI, gastrointestinal; HBV, Hepatitis B Virus.

Table 3 – **oral regimen after LA CAB/RPV discontinuation**

CATEGORY	REGIME POST - LA	PWH (N)	RATE (%)
OTHER	INSTI-based	3	4.0
AES	INSTI+NNRTI-based	8	10.7
AES	INSTI-based	26	34.7
AES	NNRTI-based	9	12.0
AES	PI-based (*)	1	1.3
VF	INSTI-based	5	6.7
VF	PI-based (*)	5	6.7
PREGNANCY	INSTI-based	3	4.0
SUBJECT'S DECISION	INSTI+NNRTI-based	6	8.0
SUBJECT'S DECISION	INSTI-based	6	8.0
SUBJECT'S DECISION	NNRTI-based	3	4.0

(*) One study participant who developed AEs and one who developed VF were already on PI treatment before LA CAB/RPV; the remaining 4 individuals who had to induce a PI-based regimen all underwent VF under LA CAB/RPV.

Abbreviations: LA, long acting; CAB, cabotegravir; RPV, rilpivirine; AEs, adverse events; VF, virologic failure; INSTI, Integrase Strand Transfer Inhibitor; NNRTI, Non-Nucleoside Reverse Transcriptase Inhibitor; PI, Protease Inhibitor.

The resumption of the same drug co-formulation utilized before the LA regimen occurred in 20.0% (2/10), 76.9% (15/65), and 84.1% (37/44) of PWH who interrupted LA due to VF, due to any cause other than VF, and due to AEs, respectively. Overall, 92.1% of regimens after LA interruption were NNRTI (16%), INSTI (57.3%), or NNRTI+INSTI (18.7%)-based. No new AEs were recorded after switching back to oral therapy throughout the whole cohort. Six months after resuming oral therapy, HIV-RNA loads <30 copies/mL and <200 copies/mL were recorded in 96.0% (72/75) and 98.7% (74/75) of individuals, respectively.

Conclusions Among individuals who interrupted injectables for reasons other than VF, the majority returned to the same pre-LA oral co-formulation. The superimposition of CAB+RPV pharmacokinetic tail with an oral NNRTI and/or INSTI-based regimen did not lead to the development of AEs, even in people with a previous AE to CAB or RPV. Six months after the reintroduction of oral therapy, the virologic suppression rate was high throughout the cohort.