

# Causes of discontinuation of long acting cabotegravir and rilpivirine in clinical practice. Results from the prospective multicenter SCOLTA cohort.

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## Background

Injectable cabotegravir (CAB) and rilpivirine (RPV) long-acting is a new antiretroviral treatment (ART) option for HIV-1 infection in virologically suppressed people with HIV (PWH). The aim of this study is to describe the causes of long-acting (LA) CAB+RPV discontinuation in clinical practice.

**Table 1:** General characteristics of all people with HIV who started long acting cabotegravir+rilpivirine in SCOLTA cohort until January 2024

Variable	
Female, N (%)	53 (22.9%)
Male, N (%)	177 (76.6%)
M to F, N (%)	1 (0.4%)
Age in years, mean (SD)	48.5 (11.9)
Caucasian ethnicity, N (%)	220 (95.2%)
Risk factor for HIV, N (%)	
Heterosexual	75 (32.5%)
MSM	115 (49.8%)
IVDU	19 (8.2%)
Other	22 (9.5%)
CDC stage, N (%)	
A	137 (59.6%)
B	57 (24.8%)
C	36 (15.6%)
HCV Ab positive, N (%)	25 (11.0%)
CD4 (cells/mm <sup>3</sup> ), mean (SD)	2 (0.9%)
< 200	229 (99.1%)
≥ 200	
CD4 (cells/mm <sup>3</sup> ), mean (SD)	849 (351)
BMI (Kg/m <sup>2</sup> ), mean (SD)	25.6 (4.3)
eGFR (mL/min), mean (SD)	86.6 (24.3)
Total cholesterol (mg/dL), mean (SD)	186.3 (37.7)
HDL cholesterol (mg/dL), mean (SD)	53.1 (16.0)
Blood glucose (mg/dL), mean (SD)	89.0 (21.3)
Started with oral lead-in, N (%)	96 (42.7%)

BMI: body mass index; CD4: CD4+ T cells; CDC: center for diseases control and prevention; eGFR: estimated glomerular filtration rate; HCV-Ab: hepatitis C virus antibody; IVDU: intravenous drug use; MSM: men who have sex with men.

## Methods

Observational multicenter prospective SCOLTA (Surveillance Cohort Long-Term Toxicity Antiretrovirals) cohort. PWH who started CAB+RPV LA injectable regimen from July 2022 to January 2024 were included in the present study. Reasons for LA discontinuation were prospectively collected. Probability of discontinuation for adverse events (AE) was assessed through log-rank test, while factors associated with AE were estimated using a Cox proportional-hazards model. P<0.05 was considered statistically significant.

## Results (I)

Among 417 people with HIV (PWH) who started CAB+RPV during the study period, 231 had at least one follow-up visit available and were enrolled in the present study (Table 1).

## Results (II)

Fifty-three/231 (23%) were women, the majority were Caucasian (220, 95%), men who have sex with men (115, 50%) and heterosexuals PWH (75, 32%), mainly in CDC stage A (137, 60%). Mean age at enrolment was 48.5 (±11.9) years and median time on ART was 10 (IQR 5.4-16.1) years. All were treatment experienced, and before LA, the ART regimen contained an integrase inhibitor (INSTI) in 168 (73%) people, a non-nucleoside reverse transcriptase inhibitor (NNRTI) in 120 (52%), both INSTI+NNRTI in 61 (26%) and a protease inhibitor in 3 (1%). 129 study participants (66%) had at least one treatment in addition to ART (86 people were taking 1-2 other drugs; 43 ≥ 3 other drugs). Twenty-one PWH (9%) discontinued LA treatment after a median of 2 months (range 0-6), of which 15 for AEs (Table 2).

## Results (III)

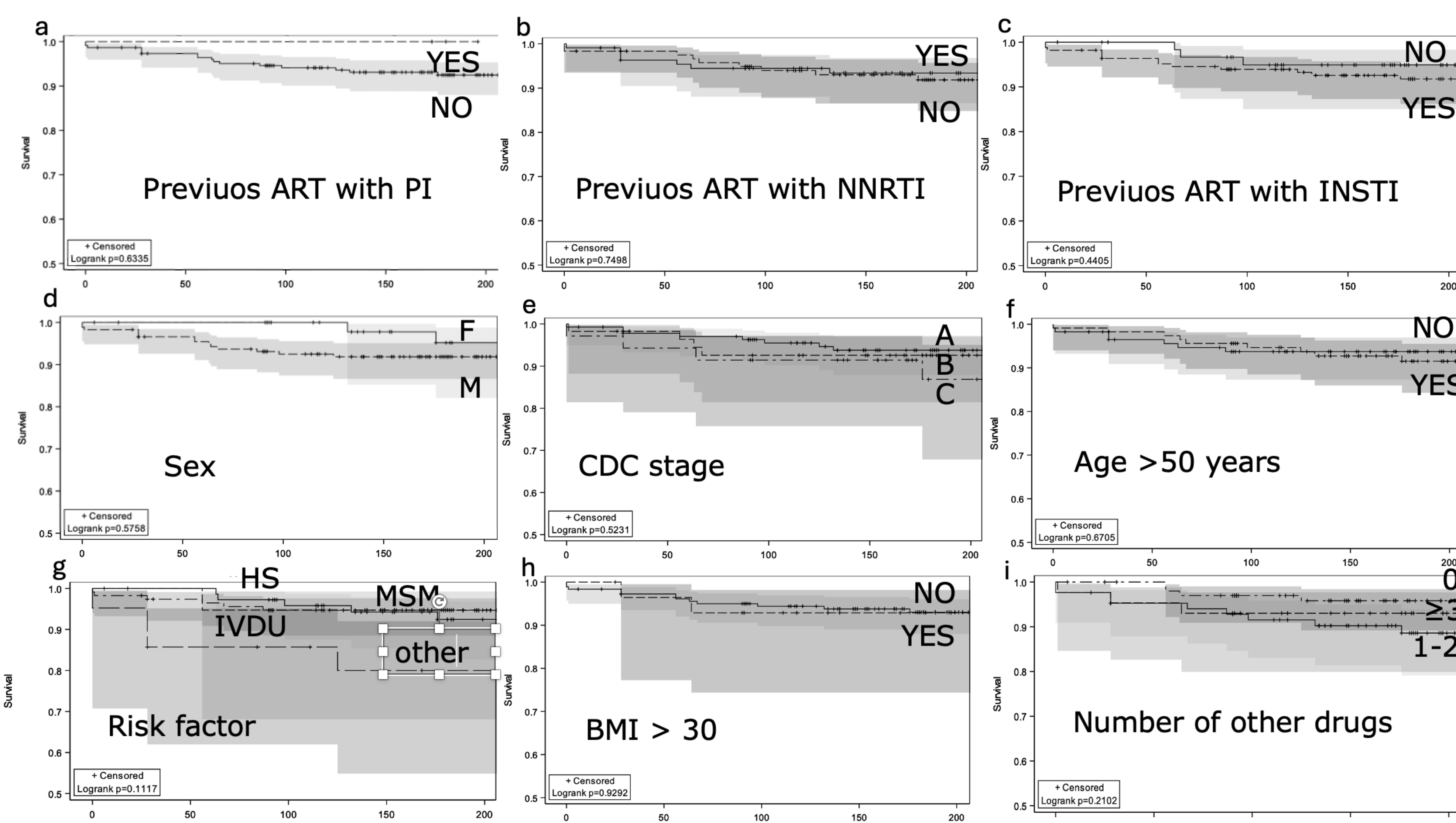
The probability of AE leading to discontinuation was not influenced by previous ART treatments, sex, body mass index, CDC stage, age, risk factor for HIV, concomitant treatments or by oral lead-in (p >0.1 for all, Figure 1). Other six persons discontinued treatment, due to lost to follow up (N=1), pregnancy (N=1), virologic failure (N=2), resistance to RPV (N=1) and inconvenience with injection schedule (N=1). In the case of discontinuation due to RPV resistance, information about the presence of resistance was acquired after the LA regimen had already been started, but despite this, HIV-RNA remained suppressed during follow up under LA treatment until discontinuation.

**Table 2.** Adverse events leading to discontinuation of long-acting therapy with cabotegravir/rilpivirine in SCOLTA cohort.

	Sex at birth, age	Previous regimen	Pain/local reaction	Pyrexia	Other	Days since first injection	Oral lead-in	Causal correlation with therapy
1	M, 61	RPV/DTG	Grade 2	No	No	56	Yes	Certain
2	M, 55	RPV/DTG	Grade 2	No	No	1	No	Certain
3	F, 59	3TC/DTG	Grade 3	No	No	132	No	Certain
4	M, 40	RPV/DTG	Grade 2	No	No	1	No	Certain
5	M, 67	3TC/DTG	Grade 2	Grade 2	No	1	Yes	Both certain
6	M, 55	FTC/TAF/RPV	Grade 1	Grade NA	No	1	Yes	Certain
7	M, 35	FTC/TAF/BIC	No	Grade 3	No	29	Yes	Certain
8	M, 49	3TC/DTG	No	Grade 2	No	1	No	Likely
9	M, 44	RPV/DTG	No	Grade 2	Arthromyalgia, grade 2	87	No	Possible
10	F, 65	RPV/DTG	No	Grade 1	Gastrointestinal, grade NA	148	Yes	Possible
11	M, 66	FTC/TAF/RPV	No	No	Glycemic decompensation, grade 3	63	No	Possible
12	M, 54	FTC/TAF/RPV	No	No	Acute pancreatitis, grade 4	40	Yes	Likely
13	M, 51	RPV/DTG	No	No	Rash, grade 2	125	No	Possible
14	M, 31	FTC/TAF/BIC	No	No	Arthromyalgia, grade 4 Erectile dysfunction, grade NA	35	Yes	Certain
15	F, 41	FTC/TAF/BIC	No	No	Headache, grade 2	During lead-in	Yes	Certain

3TC: lamivudine; ABC abacavir; BIC: bicitegravir; DTG: dolutegravir; FTC: emtricitabine; G: grade of adverse event; NA: not available; RPV: rilpivirine; TAF: tenofovir alafenamide.

**Figure 1.** Cumulative probability of discontinuation of rilpivirine (RPV) and cabotegravir (CAB) due to previous ART regimen (a-c), sex (d), CDC stage (e), age (f), risk factor for HIV (g), body mass index (BMI) (h), number of other drugs concomitant to CAB+RPV (i).



ART: antiretroviral therapy; F: female; HS: heterosexuals; INSTI: integrase inhibitors; IVDU: intravenous drug use; M: male; MSM: men who have sex with men; NNRTI: non-nucleoside reverse transcriptase inhibitors; PI: protease inhibitors.

## Conclusions

The frequency of LA CAB/RPV interruptions in SCOLTA was higher than expected based on data derived from clinical trials. The possible interpretation could be that in clinical practice PWHs and clinicians tolerate a lower degree of severity of an adverse event than in the context of randomized trials. Studies exploring the PWH perspective will be critical to understanding the key to LA persistence.

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