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

Lucia Taramasso (1), Nicola Squillace (2), Elena Ricci (3), Sergio Ferrara (4), Giancarlo Orofino (5), Eleonora Sarchi (6), Emanuele Pontali (7), Giovanni Cenderello (8), Giovanni Francesco Pellicanò (9), Filippo Lagi (10), Elena Salomoni (11), Olivia Bargiacchi (12), Maria Aurora Carleo (13), Luigi Pusterla (14), Salvatore Martini (15), Rita Bellagamba (16), Giordano Madeddu (17), Giuseppe Vittorio De Socio (18), Barbara Menzaghi (19), Goffredo Angioni (20), Katia Falasca (21), Antonio Cascio (22), Antonio Di Biagio (1,23) and Paolo Bonfanti (2) for the CISAI study group.

1 Infectious Disease Clinic, IRCCS Ospedale Policlinico San Martino di Genova, Italy; 2 Infectious Disease Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza - University of Milano-Bicocca, Monza, Italy; 3 Fondazione ASIA, Milan, Italy; 4 Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy; 5 Unit of Infectious Diseases, "Divisione A", Amedeo di Savoia Hospital, Torino, Italy; 6 Infectious Diseases Unit, S.Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy; 7 Department of Infectious Diseases, Galliera Hospital, Genoa, Italy; 8 Infectious Diseases Department, Sanremo Hospital, Sanremo, Italy; 9 Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; 10 AOU Infectious and Tropical Diseases, Careggi Hospital, Florence, Italy; 11 SOC 1 USLCENTRO FIRENZE, Unit of Infectious Diseases, Santa Maria Annunziata Hospital, Florence, Italy; 12 Unit of Infectious Diseases, Ospedale Maggiore della Carità, Novara, Italy; 13 Infectious Diseases and Gender Medicine Unit, Cotugno Hospital, AO dei Colli, Naples, Italy; 14 Infectious Diseases Unit, Ospedale S. Anna, Como, Italy; 15 Department of Infectious Disease, University of Campania Luigi Vanvitelli, Naples, Italy; 16 Clinical and Research Infectious Diseases Department, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy; 17 Unit of Infectious Diseases, Department of Medicine, Surgery and Pharmacy, University of Sassari, Italy; 18 Unit of Infectious Diseases, Santa Maria Hospital, Perugia, Italy; 19 Unit of Infectious Diseases, ASST della Valle Olona – Busto Arsizio (VA), Italy; 20 Infectious Diseases Unit, SS Trinità Hospital, Cagliari, Italy; 21 Clinic of Infectious Diseases, Department of Medicine and Science of Aging, G. D'Annunzio University, Chieti-Pescara, Chieti, Italy; 22 Unit of Infectious Diseases, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy; 23 Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy.

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 February 2024.

Variable	
Female, n (%) **Male, n (%)** **M to F, n (%)**	90 (23.9%) 284 (75.3%) 3 (0.8%)
Age in years, mean (SD)	48.5 (11.2)
Caucasian ethnicity, n (%)	362 (96.0%)
Risk factor for HIV, n (%) **Heterosexual** **MSM** **IVDU** **Other**	 132 (35.0%) 180 (47.8%) 37 (9.8%) 28 (7.4%)
CDC stage, n (%) **A** **B** **C**	 224 (59.4%) 91 (24.1%) 57 (15.1%)
HCV Ab positive, n (%)	44 (11.7%)
CD4 (cells/mm³) , mean (SD) **<200** **≥ 200**	 2 (0.5%) 375 (99.5%)
CD4 (cells/mm³), mean (SD)	842 (351)
BMI (Kg/m²), mean (SD)	25.1 (4.1)
eGFR (mL/min), mean (SD)	86.4 (22.6)
Total cholesterol (mg/dL), mean (SD)	188 (36)
HDL cholesterol (mg/dL), mean (SD)	54 (16)
Blood glucose (mg/dL), mean (SD)	86 (13)
Oral lead-in, n (%)	114 (30.2%)

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; HDL-cholesterol: high-density lipoprotein cholesterol; 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 February 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)

377 PWH were included and observed for median 10 months (IQR, 6-13),(**Table 1**).

Results (II)

Ninety/377 study participants (23.9%) were women, 362 Caucasian (96.0%), most were men who have sex with men (180, 47.8%) and heterosexuals (132, 35.0%), mainly in CDC stage A (224, 60%). Mean age was 48.5 (±11.2) years and median time on ART was 10.0 (IQR 6.3-16.3) years. All were treatment experienced, and Previous ART contained an INSTI in 188 (49.9%) people, a NNRTI in 89 (23.6%), both INSTI+NNRTI in 100 (26.5%). 212 participants (56.2%) had at least one treatment in addition to ART (145 were taking 1-2 other drugs; 67 ≥ 3 other drugs).

Thirty-four PWH (9.0%) discontinued LA treatment after a median of 3 months (range 0-15), of which 24 for AEs (**Table 2**).

Results (III)

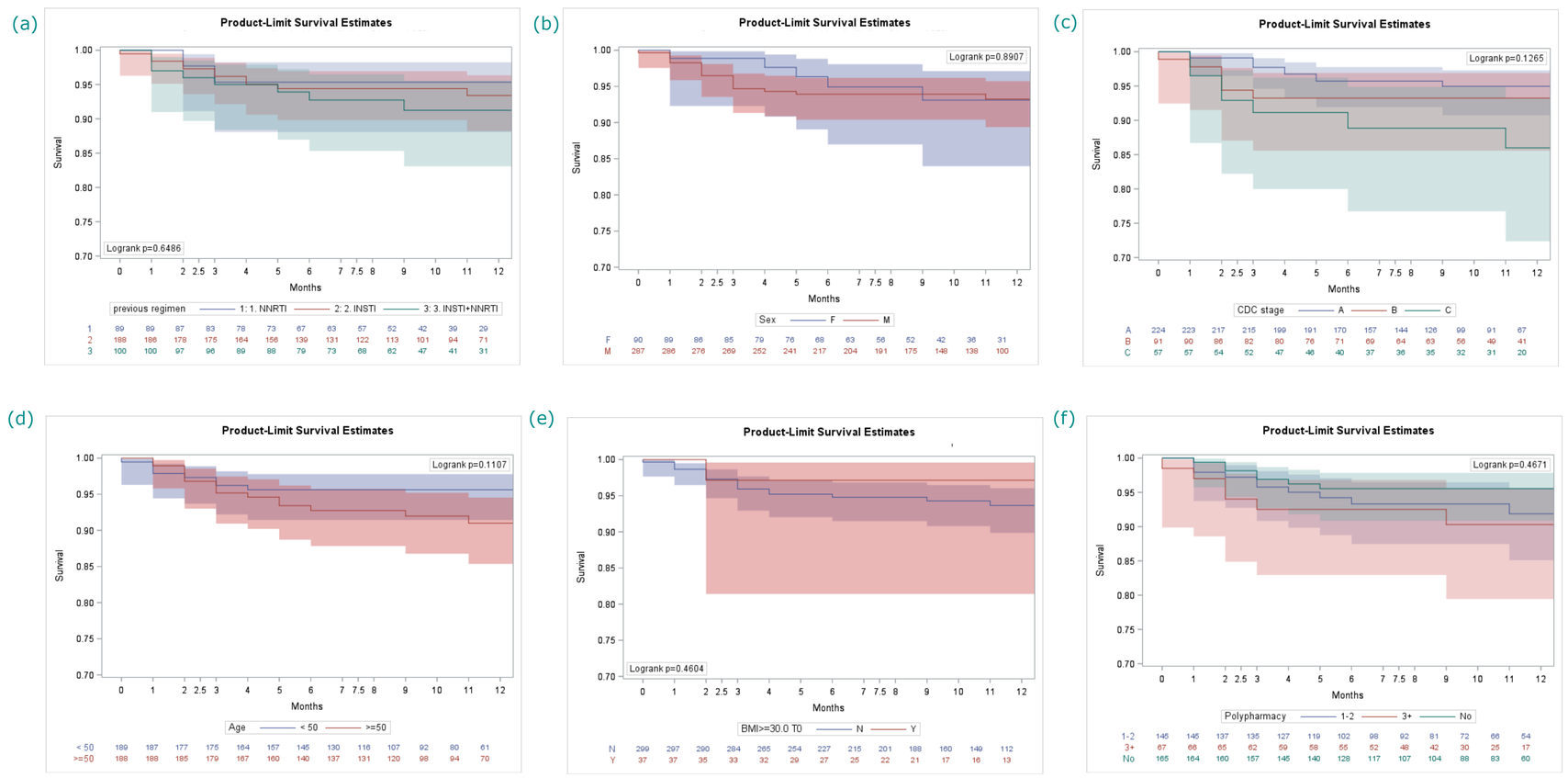
CAB+RPV LA was discontinued for reasons other than adverse events in 10 study participants: 4 people (1.1%) because of virological failure, and 6 (1.6%) for other reasons [lost to follow-up (N=1), pregnancy (N=1), resistance to RPV assessed during the lead-in period (N=1), change of residence (n=1), and inconvenience with injection schedule (N=2)]. The probability of AE leading to discontinuation was not influenced by previous ART, sex, BMI, age, risk factor for HIV, oral lead-in or concomitant treatments (p >0.1 for all, **Figure 1**). PWH in CDC stage C were more likely to discontinue (p=0.0476), and this result was confirmed at the multivariate analysis including all these factors (adjusted hazard ratio 3.00, 95% confidence interval 1.11-8.12, p=0.030).

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	Fever	Other	Causal correlation with therapy	Days since first injection
1	F, 59	3TC/DTG	Yes, G 3	No	No	Certain	132
2	M, 67	3TC/DTG	Yes, G 2	Yes, G 2	No	Certain	56
3	M, 55	RPV/DTG	Yes, G 2	No	No	Certain	29
4	M, 40	RPV/DTG	Yes, G 2	No	No	Certain	28
5	M, 61	RPV/DTG	Yes, G 2	No	No	Certain	56
6	F, 54	FTC/TAF/BIC	Yes, G 2	No	No	Certain	445
7	M, 55	FTC/TAF/RPV	Yes, G 1	No	No	Certain	64
8	M, 35	FTC/TAF/BIC	No	Yes, G 3	No	Certain	112
9	M, 44	RPV/DTG	No	Yes, G 2	Arthromyalgia, G 2	Possibile	87
10	M, 49	3TC/DTG	No	Yes, G 2	No	Probable	1
11	M, 32	3TC/DTG	No	Yes, G 1	No	Unlikely	94
12	F, 65	RPV/DTG	No	Yes, G 1	No	Possible	181
13	M, 56	3TC/ABC/RPV	No	No	difficulty walking, G 3 ; weight gain, G 1	Unlikely for both	87
14	M, 46	RPV/DTG	No	No	Arthromyalgia, G NA	Certain	30
15	M, 59	FTC/TAF/BIC	No	No	Arthromyalgia, G 1	Probable	19
16	M, 51	RPV/DTG	No	No	Rash, G 2	Possible	140
17	M, 31	FTC/TAF/BIC	No	No	Arthromyalgia, G 4	Certain	63
18	M, 54	FTC/TAF/RPV	No	No	Acute pancreatitis, G 4	Probable	67
19	M, 66	FTC/TAF/RPV	No	No	Glycaemic decompensation, G 3	Possible	98
20	F, 41	FTC/TAF/BIC	No	No	Migraine, G 2	Certain	31
21	M, 62	FTC/TAF/BIC	No	No	Hepatitis, G 3	Probable	92
22	F, 62	3TC/DTG	No	No	Rash, G 3	Possible	143
23	M, 50	FTC/TAF/BIC	No	No	Altered emotionality, G 3	Probable	339
24	F, 58	RPV/DTG	NA	NA	NA	NA	283

3TC: lamivudine; ABC abacavir; BIC: bictegravir; 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) in strata of previous ART regimen (a), sex (b), CDC stage (c), age (d), body mass index (BMI) (e), number of other drugs concomitant to CAB+RPV (f).



ART: antiretroviral thrapy; 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 for AE was higher in this real-life cohort than in registrational trials, while high virological efficacy was seen, with 1% virological failure. To continue the active surveillance of AE in cohort studies will be critical to understanding the key to LA persistence.

CISAI STUDY GROUP

Coordinators: Paolo Bonfanti (Monza), Antonio Di Biagio (Genova). Data Management and Analysis: Elena Delfina Ricci (Milano). Health Informatic Service: L.D. Magnoni, M. Bonetto (Genova, Healthropy); M. Giacomini (Genova, DIBRIS). Participating centers: E. Sarchi, G. Chichino, C. Bolla (Alessandria); A. Saracino, D. Fiordelisi (Bari); L. Calza (Bologna); B. Menzaghi, M. Farinazzo, F. Franzetti (Busto Arsizio); G. Angioni, M. Buffa (Cagliari); P. Maggi, A. Masiello, F. Simeone (Caserta); G. Bruno, B. M. Celesia (Catania); C. Grosso (Cesena); K. Falasca (Chieti); L. Pusterla, G. Chieffo (Como); A. Mastroianni, G. Guadagnino (Cosenza); F. Franzetti, S. Rusconi (Legnano); S. Carradori (Ferrara); E. Salomoni (Firenze); F. Lagi (Firenze); A. Di Biagio, L. Taramasso, M. Bassetti (Genova); E. Pontali, A. Parisini, F. Del Puente (Genova); C. Molteni, A. Pandolfo, S. Piconi (Lecco); S. Rusconi, M. Franzetti (Legnano); G. F. Pellicanò, (Messina); L. Valsecchi, L. Cordier, S. Parisini (Milano); F. Conti (Milano); A. Bandera, A. Gori (Milano); D. Motta, M. Merli, M. Puoti (Milano); P. Bonfanti, N. Squillace, M. Rossi, E. Pollastri, N. Corti (Monza); S. Martini (Napoli); V. Esposito, M.A. Carleo (Napoli); O. Bargiacchi,; A. Cascio, M. Trizzino (Palermo); R. Gulminetti, L. Pagnucco (Pavia); G. V. De Socio, G. Gamboni, D. Altobelli, D. Francisci (Perugia); E. Mazzotta, G. Parruti (Pescara); S. Cicalini, R. Bellagamba, A. Antinori (Roma); P. Morelli (Humanitas); G. Cenderello (Sanremo); G. Madeddu, M. S. Mameli (Sassari); G. Orofino, M. Guastavigna (Torino); M. Lanzafame, A. Delama (Trento); A. Londero, A. Giacinta, C. Tascini (Udine); G. Battagin, V. Manfrin (Vicenza).

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