

Real World Evidence: insights from Italian Cohorts

OC 37 Legacy ART in the modern era: who still receives outdated regimens?

Authors

A. Vergori¹, A. Tavelli^{2,3}, A. Giacomelli⁴, S. Rusconi⁵, S. Nozza⁶, A. Costantini⁷, G. Lapadula⁸, S. Bonora⁹, G. Madeddu¹⁰, R. Gagliardini¹¹, A. Antinori¹¹, A. d'Arminio Monforte², S. Lo Caputo¹

Affiliation

¹Infectious Diseases Unit, Department of Clinical and Surgical Sciences, University of Foggia, Foggia, Italy, ²ICONA Foundation, Milan, Italy, ³National PhD Programme in One Health approaches to infectious diseases and life science research, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy, ⁴III Infectious Diseases Unit, ASST Fatebenefratelli-Sacco, DIBIC Luigi Sacco, Università degli Studi di Milano, Milan, ⁵Infectious Diseases Unit, Ospedale Civile di Legnano, ASST Ovest Milanese, and DIBIC, Università degli Studi di Milano, Milan, ⁶Department of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy, ⁷Clinical Immunology Unit, Azienda Ospedaliero Universitaria delle Marche - Università Politecnica delle Marche, Ancona, Italy, ⁸Department of Infectious Diseases, IRCCS San Gerardo dei Tintori, University of Milano-Bicocca, Monza, Italy, ⁹Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin, Italy, ¹⁰Unit of Infectious Disease, Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, Italy, ¹¹Clinical and Research Infectious Diseases Department, National Institute for Infectious Diseases, Lazzaro Spallanzani IRCCS, Rome, Italy

ABSTRACT

Background: In the INSTI-based antiretroviral therapy (ART) era a number of people with HIV (PWH) is still on guidelines (GLs)-outdated or alternative regimens. We aimed to characterize PWH on such regimens and the related features in clinical centers.

Methods: Cross-sectional analysis in 50 centers of the ICONA cohort including PWH with a last visit in 2024-2025. Regimens were classified as recommended (RecR), outdated (OutR) and alternative (AltR) according to the most recent EACS GLs: OutR were no longer recommended, AltR were considered as alternative to RecR in selected settings (ABC-based regimens, DRV/b+3TC, TDF/F/RPV). Adjusted logistic mixed-effects models including a random intercept for clinical center were used to assess PWH-level and center-level factors associated with use of OutR; center factors were also analyzed for AltR use.

Results: In total, 10,859 (94.9%) of 11,444 PWH were receiving RecR, 2.7% OutR, and 2.4% AltR. Compared with RecR, PWH on OutR were older [median 57.0 (IQR 47.0–63.0) vs 50.0 (40.0–58.0)], more frequently female (33.0% vs 18.8%), and PWID (15.2% vs 7.7%). PWH on OutR showed a longer treatment-experienced profile, with longer ART exposure [13.1y (8.2-21.2) vs 8.0 (3.1-12.0)], higher prevalence of prior AIDS (18.4% vs 14.4%), and of VF on ART (23.6% vs 9.0%), higher number of ART lines [4 (2-6) vs 3 (1-4)], lower median CD4 count at ART start [290.0 (109.0–446.0) vs 329.0 (164.0–490.0) cells/mm³] (Table 1). Higher median total cholesterol and glucose levels were observed in AltR vs RecR. The detailed breakdown of OutR is shown in Figure 1.

In the mixed adjusted models, older age (aOR per 10 y 1.14, 95%CI 1.01-1.29) and longer ART duration (aOR per y 1.09, 95%CI 1.07-1.11) and female sex (aOR 1.40, 95%CI 1.04-1.89) were independently associated with OutR use. MSM showed significantly lower odds (aOR 0.66, 95% CI 0.48–0.91), whereas unemployment was associated with an increased risk (aOR 1.50, 95% CI 1.07-2.10). In contrast, higher total cholesterol levels were associated with only a modest increase in odds (aOR per +10 mg/dL: 1.03, 95% CI 1.00-1.06). In the center-level model, neither

center size nor HIV care model were associated with OutR and AltR use (Table 2). Between-center variation accounted for 19.9% of the variance in use of AltR regimens compared to only 8.0% for OutR, indicating greater standardization across centers in avoiding outdated treatments, but less for AltR.

Conclusions: OutR use appears primarily driven by patient complexity rather than center organization, supporting the need for targeted ART optimization strategies. Notably, OutR and AltR accounted for 5.1% of cases overall. These findings should be interpreted with caution considering the cross-sectional design, potential survivor bias and limited availability of personal and clinical factors influencing the regimen choice. Therefore, the appropriateness of some prescriptions cannot be excluded.

Table 1. Characteristics of study population

Panel A	Recommended regimens (RecR)	Outdated regimens (OutR)	Alternative regimens (AltR)	*p-value	Total
	10,859 (94.9)	309 (2.7)	276 (2.4)		11,444 (100)
Female, n(%)	2,046 (18.8)	102 (33.0)	70 (25.4)	<0.001	2,218 (19.4)
Age, median (IQR)	50.0 (40.0-58.0)	57.0 (47.0-63.0)	51.0 (42.0, 60.0)	<0.001	50.0 (40.0-59.0)
Mode of HIV transmission, n(%)					
Heterosexual	4,410 (40.6)	161 (52.1)	130 (47.1)		4,701 (41.1)
PWIDs	838 (7.7)	47 (15.2)	33 (12.0)		918 (8.0)
MSM	5,156 (47.5)	85 (27.5)	103 (37.3)		5,344 (46.7)
Other/Unknown	455 (4.2)	16 (5.2)	10 (3.6)		481 (4.2)
VS, n(%)	9,528 (88.2)	283 (91.6)	246 (89.1)	0.171	10,055 (88.3)
Current CD4 count, cells/mm ³ , median (IQR)	722.0 (500.0-967.0)	725.0 (508.0-989.0)	732.0 (499.0-1,033.0)	0.394	722.0 (500.0-969.0)
CD4 count at ART start, cells/mm ³ , median (IQR)	329.0 (164.0-490.0)	290.0 (109.0-446.0)	282.5 (103.5-439.5)	<0.001	327.0 (160.0-488.0)
CD4/CD8 at ART start, median (IQR)	0.4 (0.2-0.6)	0.3 (0.2-0.6)	0.3 (0.1-0.5)	0.004	0.4 (0.2-0.6)
History of AIDS, n(%)	1,565 (14.4)	57 (18.4)	53 (19.2)	0.004	9,769 (85.4)
Years on ART, median (IQR)	8.0 (3.1-12.0)	13.1 (8.2-21.2)	8.6 (6.7-12.4)	<0.001	8.1 (3.3-12.2)
VF on ART, n(%)	903 (9.0)	70 (23.6)	43 (16.0)	<0.001	1,016 (9.6)
VF on INSTI, n(%)	413 (4.1)	35 (11.8)	29 (10.8)	<0.001	477 (4.5)
ART lines, median (IQR)	3.0 (1.0-4.0)	4.0 (2.0-6.0)	2.0 (1.0-4.0)	<0.001	3.0 (1.0-4.0)
eGFR_CKD _{epi} , ml/min, median (IQR)	88.1 (74.5-102.0)	88.8 (69.3-100.1)	87.8 (72.6-101.3)	0.144	88.1 (74.3-101.8)
Total cholesterol, median (IQR)	179.0 (154.0-205.0)	187.0 [158.5-213.5]	188.0 (153.5-211.0)	0.005	180.0 (154.0-206.0)
Glucose level, median (IQR)	89.0 (82.0-98.0)	89.0 (82.0-99.0)	93.0 (83.0-101.0)	<0.001	89.0 (82.0-98.0)
HCVAb positivity, n(%)	1,150 (11.1)	66 (21.6)	41 (15.3)	<0.001	9,645 (88.5)
High level of education, n(%)	4,502 (41.5)	112 (36.2)	82 (29.7)	<0.001	4,696 (41.0)
Unemployed, n(%)	1,117 (10.3)	50 (16.2)	44 (15.8)	<0.001	1,211 (10.8)

Abbreviations: PWID, people who inject drugs; MSM, men who have sex with men; VS, virological suppression; VF, virological failure; ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; eGFR, estimated glomerular filtration rate; CKD_{epi}, chronic kidney disease epidemiology collaboration. *p-values refer to comparisons with the contemporary regimen group; chi-square test or Kruskal-Wallis test, as appropriate

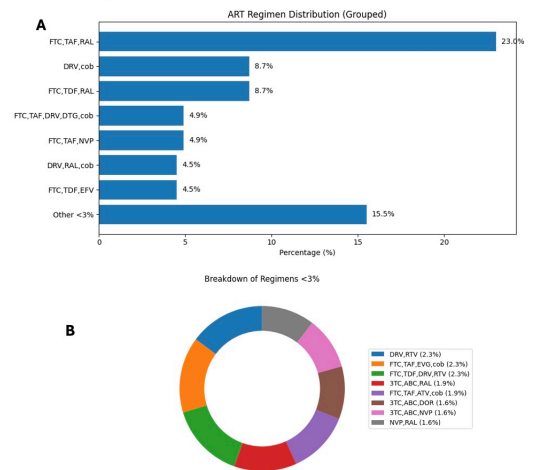
Definitions: Virological suppression (VS) was defined as HIV RNA <50 copies/mL. Virological failure (VF) was defined as two consecutive HIV RNA measurements >200 copies/mL or a single value >1000 copies/mL after initial VS (HIV RNA <50 copies/mL)

Table 2. Multilevel logistic regression analyses showing patient-level factors associated with OutR (a), centre-level factors associated with OutR (b), and centre-level factors associated with AltR (c)

a	OR	95%CI	p	aOR*	95%CI	p		
Age, per 10 years older	1.47	1.34	1.61	<.001	1.14	1.01	1.29	0.039
Sex, Female	2.14	1.67	2.74	<.001	1.40	1.04	1.89	0.027
Born-Italy	1.42	1.03	1.96	0.031	1.09	0.76	1.58	0.628
Mode HIV transmission								
Heterosexual	1			1.00				
IDU	1.50	1.07	2.11	0.019	0.94	0.65	1.37	0.762
MSM	0.43	0.33	0.57	<.001	0.70	0.50	0.97	0.032
Other/Unknown	0.92	0.54	1.57	0.762	1.08	0.60	1.93	0.796
Education								
Higher	1			1.00				
Lower	1.89	1.42	2.50	<.001	1.13	0.83	1.53	0.432
Unknown	1.01	0.76	1.35	0.94	1.21	0.89	1.65	0.226
Occupation								
Unemployed	1.63	1.19	2.23	<.001	1.52	1.09	2.13	0.014
CD4 ART start <350 cells/mm ³	1.38	1.09	1.74	0.008	1.10	0.86	1.41	0.451
HIV-RNA ART start > 5 log	0.91	0.71	1.15	0.412				
Years on ART, per 1 more	1.11	1.09	1.13	<.001	1.09	1.07	1.11	<.001
Total Cholesterol, per 10 mg/dl increase	1.05	1.02	1.08	0.001	1.03	1.00	1.06	0.023
Fasting-Glucose, per 10 mg/dl increase	1.03	0.99	1.08	0.131				
Metabolic Syndrome	1.37	1.06	1.76	0.015	1.15	0.88	1.52	0.301

*Adjusted for the factors showed in table

Figure 1: Distribution of current OutR (A) and donut chart showing the composition of less frequent OutR (<3%) (B)



b	aOR*	95%CI	p	
N. PWH in care for center				
>2000	1			
1001-2000	0.72	0.36	1.43	0.354
<1000	1.30	0.68	2.48	0.436
HIV care model				
Full ID rotation	1			
Dedicated HIV staff (fixed PWH)	1.00	0.27	3.70	0.995
Dedicated HIV staff (rotating pool)	0.82	0.47	1.41	0.467

*Adjusted for the factors showed and age, sex, mode HIV transmission, year on ART, job

c	aOR*	95%CI	p	
N. PWH in care for center				
>2000	1			
1001-2000	0.66	0.25	1.75	0.404
<1000	0.73	0.28	1.90	0.521
Organization HIV outpatient				
Full ID rotation	1			
Dedicated Staff, fixed for PWH	2.50	0.41	15.34	0.323
Dedicated Staff, pool of physicians	0.93	0.43	2.00	0.856

*Adjusted for the factors showed and age, sex, mode HIV transmission, year on ART, job