Original research article

INTERNATIONAL JOURNAL OF STD & AIDS

International Journal of STD & AIDS
2024, Vol. 35(11) 873–883

DOI: 10.1177/09564624241263122
journals.sagepub.com/home/std
Sage

Treatment patterns and preferences of people living with HIV starting or switching antiretroviral therapy: Real-world evidence from Portugal

Liliana Pedro[1], Alexandra Zagalo[2], Raquel Tavares[3], Patrícia Pacheco[4], Joaquim Oliveira[5], Inês Vaz Pinto[6], Rosário Serrão[7], Sandra Tavares[8], Paula Brito[9], Fernando Maltez[10], Isabel Neves[11], Alexandre Carvalho[12], Eugénio Teófilo[13], Joana Almeida[14] and Inês Lains[14]

Abstract

Background: There is a lack of up-to-date real-life evidence on antiretroviral therapy (ART) strategies among people living with HIV (PLWH) in Portugal. This study aimed to describe the treatment strategy used in PLWH either initiating or switching ART.
Methods: Non-interventional, cross-sectional, multicenter study carried out between December 2019 and October 2021 in Portugal.
Results: A total of 237 PLWH were included in this study, 171 of whom were ART-experienced and 66 were ART-naïve. The study showed that triple regimens were the most common ART strategy and integrase strand transfer inhibitors-based therapy was the most frequently used therapeutic class in both ART-naïve and ART-experienced PLWH. Nevertheless, about a third of PLWH who started a triple regimen transitioned to a dual regimen. Patient-reported outcomes revealed high HIV literacy and similar ART preferences in both groups.
Conclusions: This real-world study showed that triple regimens were the most widely used ART strategy, even after the European AIDS Clinical Society guidelines introduced the recommendation of a dual regimen for naïve patients. The cohorts of this study presented a high level of HIV literacy at the time of inclusion. Our findings highlighted that taking pills only once a day is considered a very important feature for most patients.

Keywords

Antiretroviral therapy, antiretroviral therapy-experienced patient, antiretroviral therapy-naïve patient, HIV, quality of life

Date received: 31 January 2024; revised: 3 May 2024; accepted: 13 May 2024

[1] Department of Internal Medicine, Hospital de Portimão, Centro Hospitalar Universitário Do Algarve, Portimão, Portugal
[2] Department of Infectious Diseases, Hospital Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal
[3] Department of Infectiology, Hospital Beatriz Ângelo, Loures, Portugal
[4] Department of Infectiology, Hospital Prof. Dr Fernando da Fonseca, Amadora, Portugal
[5] Department of Infectiology, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal
[6] Department of Internal Medicine, Hospital de Cascais, Cascais, Portugal
[7] Department of Infectious Diseases, Hospital de São João, Centro Hospitalar Universitário de São João, Porto, Portugal
[8] Department of Infectiology, Hospital de Vila Real, Centro Hospitalar Trás-os-Montes e Alto Douro, Vila Real, Portugal
[9] Department of Infectiology, Hospital Garcia de Orta, Almada, Portugal
[10] Department of Infectiology, Hospital Curry Cabral, Centro Hospitalar Universitário Lisboa Central, Lisboa, Portugal
[11] Department of Infectiology, Hospital Pedro Hispano, Unidade Local de Saúde de Matosinhos, Matosinhos, Portugal
[12] Department of Internal Medicine, Hospital de Braga, Braga, Portugal
[13] Department of Internal Medicine, Hospital dos Capuchos, Centro Hospitalar Universitário Lisboa Central, Lisboa, Portugal
[14] Medical Affairs Department, MSD Portugal, Paço de Arcos, Portugal

Corresponding author:
Inês Lains, MSD Portugal, Quinta da Fonte, 19, Paço de Arcos 2770-192, Portugal.
Email: ines.cardoso@merck.com

Introduction

Infection with human immunodeficiency virus (HIV) has become increasingly acknowledged as a manageable chronic disease, due to the advent of antiretroviral therapy (ART) that significantly increased the life expectancy of people living with HIV (PLWH).[1,2] HIV treatment is currently recommended for all PLWH, regardless of $CD4^+$ T cell count or clinical stage[3–5] to prevent HIV-related morbidity and mortality and reduce transmission risk.[6] Hence, unforeseen numbers of PLWH are currently receiving treatment throughout life to maintain prolonged viral suppression.[7] The need for life-long treatment that meets patient convenience, efficacy, and safety may require regimen switches.[4,8]

The development of novel antiretroviral agents is now focused not only on improving long-term efficacy and safety but also on reducing the treatment impact on PLWH's lifestyle, using simpler dose regimens to increase treatment adherence[9,10] and quality of life (QoL). Sociodemographic, clinical characteristics, and local guidelines[11] can also influence the ART choice.[10]

Adequate selection of ART either for starting or switching treatment is a key matter for long-term virological control success. However, to our knowledge, real-life evidence on ART prescribing patterns in ART-naïve and ART-experienced PLWH in Portugal is still missing.

This study aimed to characterize ART strategies for both ART-naïve and ART-experienced PLWH in a real-world setting in Portugal. The sociodemographic and clinical profile, treatment preferences, QoL, and HIV literacy of PLWH were also explored.

Methods

Study design and patients

This is a retrospective, multicenter cross-sectional, non-interventional study conducted between December 2019 and October 2021 in 15 HIV units of Portuguese hospitals. This study included HIV-1-positive people aged ≥18 years who were either starting or switching ART at the time of the study inclusion and who had available data on age, gender at birth, HIV diagnosis date, current prescribed ART regimen, $CD4^+$ T cell count, and viral load. Patients were excluded if they were participating in a clinical trial or were unable or unwilling to comply with the study requirements.

Independent Ethics Committees approved the study (Table S1), which was conducted according to applicable national regulations and to the Helsinki Declaration of the World Medical Association updated in 2013. Written informed consent was obtained from all patients.

Endpoints and assessments

The primary endpoint analyzed the proportion of ART-naïve and ART-experienced PLWH for three parameters related to the most recently prescribed ART: regimen (dual or triple or other regimens), schedule therapy (once daily or twice daily or other), and therapeutic class for triple regimen (protease inhibitors [PI]-based therapy or integrase strand transfer inhibitors [INSTI]-based therapy, or non-nucleoside reverse transcriptase inhibitor [NNRTI]-based therapy). In ART-experienced PLWH, it was further analyzed their first ART regimen and the switch to a different ART regimen since the first ART.

The secondary endpoints included the description of sociodemographic and clinical data retrieved from patients' medical charts, and self-reported questionnaires (QoL, treatment preferences, and HIV literacy) completed at the inclusion study visit.

QoL was assessed through the 31-item WHOQOL-HIV-BREF[12,13] questionnaire covering six domains: physical, psychological, independence, social relationships, environment, and spirituality. Test results were transformed into a scale of 0 (lower QoL) to 100 (higher QoL). Treatment preferences were evaluated by a 24-item questionnaire covering four main domains of treatment (benefits, tolerability/toxicity, long-term effects and administration characteristics) and results were ranked as most versus least important options. HIV literacy was assessed through a questionnaire with four multiple-choice questions, classified as an overall score for correct answers (range: 0-4). For single-answer questions, the correct answer was classified with one point; for multiple-answer questions, the mean/median of the individual scores obtained by each patient was determined as the ratio between the number of correct options selected and the number of correct answers possible (range: 0-1).

Statistical methods

Sociodemographic and clinical data were summarized using quantitative (mean, standard deviation [SD], median, and interquartile range) and qualitative variables (counts and percentages). Student's t-test or Mann-Whitney non-parametric test were used for quantitative variables, and Chi-Square test or Fisher Exact test were used for categorical variables. Statistical comparisons were performed for a significance level of 0.05. No imputation of missing data was performed.

Results

Patient and disease characteristics

This study included a total of 237 PLWH: 171 ART-experienced and 66 ART-naïve PLWH. Sociodemographics, comorbidity and concomitant therapy, clinical and HIV infection-related characteristics of PLWH at inclusion in the study are shown in Table 1. The mean age of total PLWH was 45 years and almost 70% were male at birth and had a full-time job. Over 70% had education up to secondary school, never

Table 1. Sociodemographics, comorbidity and concomitant therapy, clinical, and HIV infection-related characteristics in the overall population, ART-experienced, and ART-naïve PLWH at inclusion.

	Overall population (*n* = 237)	ART-experienced (*n* = 171)	ART-naïve (*n* = 66)	*p*-value
Sociodemographics				
Age, mean (SD[a]), years	45.3 (12.5)	48.1 (11.6)	38.1 (11.9)	[b]
≥50 years, *n* (%)	92 (38.8)	78 (45.6)	14 (21.2)	
Gender at birth, male, *n* (%)	164 (69.2)	108 (63.2)	56 (84.8)	**.002**
Origin, *n* (%)[c]				**.007**
Portugal	170 (71.7)	126 (73.7)	44 (66.7)	
Brazil	25 (10.5)	12 (7.0)	13 (19.7)	
Angola	14 (5.9)	11 (6.4)	3 (4.5)	
Guinea-Bissau	7 (2.9)	5 (2.9)	2 (3.0)	
Cape Verde	6 (2.5)	6 (3.5)	0 (0.0)	
Other	15 (6.3)	11 (6.4)	4 (6.1)	
Education, *n* (%) (*n* = 212)				.393
None	6 (2.8)	4 (2.6)	2 (3.4)	
1st, 2nd or 3rd cycle	74 (34.8)	60 (39.0)	14 (24.1)	
Secondary & post-secondary school	90 (42.5)	61 (39.6)	29 (50.0)	
Higher education	42 (19.8)	29 (18.8)	13 (22.4)	
Employment, *n* (%) (*n* = 231)				—
Full-time	159 (68.8)	108 (65.5)	51 (77.3)	
Other[d]	72 (31.2)	57 (34.5)	15 (22.7)	
BMI, Kg/m^2 (*n* = 196)				[b]
Median (IQR[e])	23.8 (21.5-27.1)	23.9 (21.6-27.9)	23.6 (20.9-26.1)	
Smoking, *n* (%) (*n* = 229)				.283
Current smoker	93 (40.6)	70 (41.9)	23 (37.1)	
Former smoker	28 (12.2)	23 (13.8)	5 (8.1)	
Never smoked	108 (47.2)	74 (44.3)	34 (54.8)	
Illicit drug use, *n* (%) (*n* = 230)				.062
Current user	9 (3.9)	5 (3.0)	4 (6.1)	
Former user	47 (20.4)	40 (24.0)	7 (10.6)	
Never used	174 (75.7)	122 (73.1)	52 (78.8)	
Alcohol use disorder, *n* (%) (*n* = 236)	15 (6.4)	13 (7.6)	2 (3.0)	.313
Comorbidity and concomitant therapy				
Non-AIDS related comorbidities, *n* (%)[f]	147 (62.0)	117 (68.4)	30 (45.5)	[b]
Hypercholesterolemia	52 (21.9)	47 (27.4)	5 (7.5)	[b]
Arterial hypertension	41 (17.3)	35 (20.5)	6 (9.1)	[b]
Depression	16 (6.8)	11 (6.4)	5 (7.5)	[b]
Chronic anxiety	16 (6.8)	12 (7.0)	4 (6.1)	[b]
Diabetes mellitus	14 (5.9)	13 (7.6)	1 (1.5)	[b]
Non-ART concomitant treatments, *n* (%)[g]	109 (46.0)	90 (52.6)	19 (28.8)	[b]
Antihypertensives	37 (33.9)	32 (35.6)	5 (26.3)	[b]
Lipid-lowering agents	36 (33.6)	33 (37.1)	3 (16.7)	[b]
Antidepressants/anxiolytics	24 (22.0)	18 (20.0)	6 (31.6)	[b]
Antiplatelet/anticoagulants	14 (13.0)	13 (14.6)	1 (5.3)	[b]
Insulin/oral antidiabetics	13 (11.9)	12 (13.3)	1 (5.3)	[b]
HIV infection-related characteristics				
HIV Duration of infection, (months)				[b]
Median (IQR[e])	74.0 (3.0-192.0)	144.0 (60-216.5)	1.0 (0.0-2.0)	
Mode of transmission, *n* (%)				**<.001**
Heterosexual sex	103 (43.5)	81 (47.4)	22 (33.3)	
Men who have sex with men	69 (29.1)	33 (19.3)	36 (54.5)	
Intravenous drug use	37 (15.6)	35 (20.5)	2 (3.0)	

(continued)

Table 1. (continued)

	Overall population (*n* = 237)	ART-experienced (*n* = 171)	ART-naïve (*n* = 66)	*p*-value
Other[h]	28 (11.8)	22 (13.0)	6 (9.1)	
$CD4^+$ T cell count, cells/mL (*n* = 233)				[b]
Median (IQR[e])	519.0 (300.0-751.0)	591.0 (410.5-797.0)	309 (218.3-495.5)	
Plasma RNA VIH (viral load), <100.000 copies/mL, *n* (%) (*n* = 179)	150 (83.8)	125 (96.8)	25 (50.0)	[b]
Time from HIV diagnosis to first ART initiation, (months) (*n* = 234)				**.016**
Median (IQR[e])	1.0 (0.0-16.0)	2.0 (0.0-23.0)	1.0 (0.0-2.0)	

[a]SD: standard deviation; [b]*p*-value not calculated due to the inherent bias of comparing this parameter between ART-naïve and ART-experienced PLWH; [c]The remaining population is from Brazil (overall population = 10.5%, ART-experienced = 7.0%, ART-naïve = 19.7%), Angola (overall population = 5.9%; ART-experienced = 6.4%; ART-naïve = 4.5%), Guinea-Bissau (overall population = 2.9%; ART-experienced = 2.9%; ART-naïve = 3.0%), Cape Verde (overall population = 2.5%; ART-experienced = 3.5%; ART-naïve = 0.0%) and others (overall population = 6.3%; ART-experienced = 6.4%; ART-naïve = 6.1%); [d]Other: part-time (overall population = 1.7%, ART-experienced = 1.8%, ART-naïve = 1.5%), unemployed (overall population = 13.0%, ART-experienced = 13.9%, ART-naïve = 10.6%) student (overall populationl = 3.5%, ART-experienced = 2.4%, ART-naïve = 6.1%), retired (overall population = 8.7%, ART-experienced = 10.3%, ART-naïve = 4.5%), temporarily disabled (overall population = 2.6%, ART-experienced = 3.6%, ART-naïve = 0.0%), disabled (overall population = 0.4%, ART-experienced = 0.6%, Naïve = 0.0%), and housewife (overall population = 1.3%, ART-experienced = 1.8%, ART-naïve = 0.0%); [e]IQR: Interquartile range;[f]Concomitant comorbidities present in more than 5% of patients; [g]Concomitant treatments administered to more than 10% of patients; [h]Other modes of transmission include: mother to child (overall population = 1.3%; ART-experienced = 1.8%; ART-naïve = 0.0%), parenteral (overall population = 0.4%; ART-experienced = 0.6%; ART-naïve = 0.0%), other (overall population = 1.7%; ART-experienced = 1.8%; ART-naïve = 1.5%) and unknown (overall population = 8.4%; ART-experienced = 8.8%; ART-naïve = 7.6%).

used illicit drugs, and were originally from Portugal. Nonetheless, the frequency of PLWH originally from Portugal was significantly higher in the ART-experienced than in the ART-naïve group. In contrast, the ART-naïve group had a significantly higher proportion of PLWH who were male at birth compared with the ART-experienced group.

Regarding the non-AIDS related comorbidities, hypercholesterolemia and arterial hypertension were the most frequent in the ART-experienced group. In the ART-naïve group, arterial hypertension was the most frequent, followed by, at equal ranking, hypercholesterolemia, and depression. The most frequent non-ART concomitant treatments were associated with the most common non-AIDS-related comorbidities.

The main mode of transmission was heterosexual sex in ART-experienced PLWH and men having sex with men in ART-naïve PLWH.

ART-experienced PLWH had a normal median $CD4^+$ T cell count and over 95% had a viral load <100.000 copies/mL, whereas ART-naïve PLWH had a median $CD4^+$ T cell count below the normal range and 50% had a viral load <100.000 copies/mL. The time from HIV diagnosis to first ART initiation was significantly lower in the ART-naïve than ART-experienced PLWH.

ART prescription

A triple drug regimen was the most common recently prescribed regimen during the study period in the overall population and ART-experienced group, and it was also the most common first ART regimen prescribed in the ART-naïve group (Figure 1(A)).

The analysis of the first ART prescribed in both ART-naïve and experienced PLWH revealed that the triple regimen was also the most common regimen prescribed since 1993. The only exception was for the year 1998, with a similar number of patients who received dual and triple regimens as the first ART (Table 2).

Regarding the classes of triple regimens, INSTI was the most common prescribed class, followed by NNRTI and PI in both ART-naïve and ART-experienced PLWH (Figure 1(B)). Concerning the schedule therapy, around 95% of ART-experienced and all ART-naïve PLWH were on a once-daily dosage scheme (Figure 1(C)).

ART switch

In the ART-experienced group, the triple regimen was the dominant ART initiation choice used from 1993 to 2021, except for 1998 (Table 2). However, of the 156 patients who started triple regimens, around one-third switched to dual regimens later in time (Table 3). The number of switches registered varied from one single switch, which was the most frequent number of switches, to six or more switches (Table 3).

Characteristics valued by patients in relation to treatment

The characteristics valued by patients in relation to treatment were, overall, similar between the ART-naïve and ART-experienced PLWH, with treatment efficacy being considered the main benefit. Additionally, the ability to continue treatment even in the presence of other diseases or

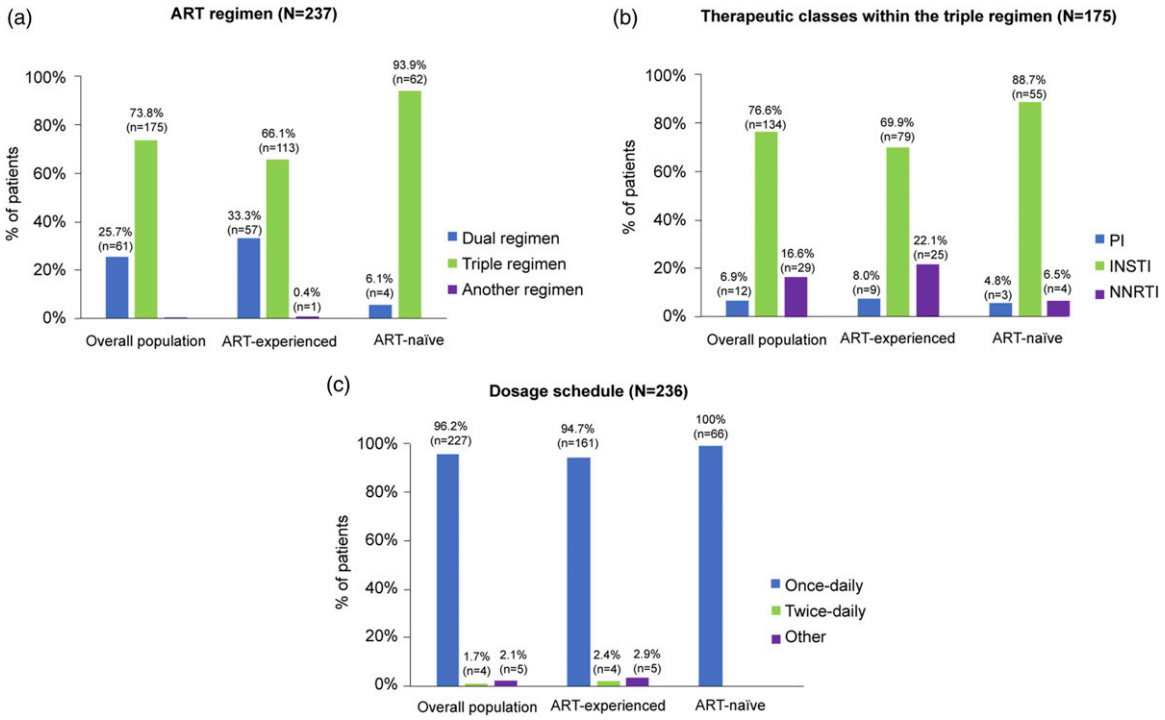

Figure 1. Most recently prescribed ART in the overall population, ART-naïve and ART-experienced PLWH. (a) ART regimen (*N* = 237). (b) Therapeutic classes within the triple regimen (*N* = 175). (c) Dosage schedule (*N* = 236).

conditions was the most important parameter within the category 'tolerability and toxicity'; receiving a treatment that would unlikely cause heart problems and changes in the appearance (shape of the body) was the most important feature within the category 'long-term effects'; and a once-daily regimen was the most important characteristic within the category 'administration characteristics' (Table 4).

Quality of life and HIV literacy

Of all the analyzed domains of the WHOQOL-HIV-BREF questionnaire ('physical', 'psychological', 'independence', 'social relationship', 'environment', 'spirituality', 'general QoL'), only the 'general QoL' domain showed a significant better transformed score for ART-experienced PLWH (68.6 [SD 18.4]) than for ART-naïve PLWH (61.7 [SD 16.5]), $p = .007$ (Table S2).

In respect to HIV literacy, above 90% of PLWH of the overall population knew that HIV infection is caused by a virus, and that HIV can cause AIDS if not treated. Moreover, above 95% of PLWH knew that sexual contact is one of the ways of spreading HIV (Table S3).

Discussion

This real-world study aimed to assess the current characteristics and management of ART-naïve and ART-experienced PLWH in Portugal. We found that triple regimens were the most prescribed ART in both groups, being INSTI-based ART the most commonly used, as recommended by the European guideline.[5] However, around one-third of the ART-experienced PLWH who started ART with triple regimens, switched to dual regimens with time. Although the reasons underlying ART switch were not assessed, improvement in adherence and tolerability, avoidance of toxicity and/or drug-drug interactions may be plausible explanations.[10,14–16]

In 2019, the European AIDS Clinical Society updated the guidelines, recommending as first-line ART not only triple regimens but also, for the first time, a dual regimen (dolutegravir + lamivudine).[17] Despite the increase of 8.5 percentage points in the dual regimen prescription from 2020 to 2021 in the ART-naïve group, that trend was not observed in the ART-experienced patients who switched ART in the same years of observation (2020-2021). Therefore, it will be necessary to collect more data to determine whether the recent recommendation of dual regimen as a first-line treatment has had an impact on the management of PLWH in Portuguese clinical practice.

This study also characterized PLWH in Portugal at a sociodemographic and clinical level, as these features are known to play a role on treatments' choice.[10] Most PLWH were male at birth and sex was the main mode of HIV transmission. These characteristics reflect the latest data from the WHO regarding HIV/AIDS surveillance in Western Europe, that reports a 2.4 male-to-female ratio and sex as the main transmission mode (71.3%), concerning new diagnoses in 2022.[18]

Table 2. Year of ART initiation and ART regimens prescribed in the ART-naïve group and ART-experienced group.

	Dual regimen *n* (%)	Triple regimen *n* (%)	Another regimen *n* (%)
ART-naïve			
2020	1 (2.6)	38 (97.4)	0 (0.0)
2021	3 (11.1)	24 (88.9)	0 (0.0)
ART-experienced			
1993	0 (0.0)	1 (100.0)	0 (0.0)
1994	0 (0.0)	0 (0.0)	1 (100.0)
1997	1 (33.3)	2 (66.7)	0 (0.0)
1998	1 (50.0)	1 (50.0)	0 (0.0)
1999	0 (0.0)	2 (100.0)	0 (0.0)
2000	0 (0.0)	4 (100.0)	0 (0.0)
2001	1 (20.0)	4 (80.0)	0 (0.0)
2002	0 (0.0)	1 (100.0)	0 (0.0)
2003	0 (0.0)	11 (91.7)	1 (8.3)
2004	0 (0.0)	9 (100.0)	0 (0.0)
2005	1 (33.3)	2 (66.7)	0 (0.0)
2006	0 (0.0)	7 (100.0)	0 (0.0)
2007	0 (0.0)	5 (100.0)	0 (0.0)
2008	0 (0.0)	4 (100.0)	0 (0.0)
2009	0 (0.0)	13 (100.0)	0 (0.0)
2010	0 (0.0)	6 (100.0)	0 (0.0)
2011	0 (0.0)	10 (90.9)	1 (9.1)
2012	0 (0.0)	7 (100.0)	0 (0.0)
2013	0 (0.0)	2 (100.0)	0 (0.0)
2014	0 (0.0)	7 (100.0)	0 (0.0)
2015	2 (18.2)	9 (81.8)	0 (0.0)
2016	1 (12.5)	7 (87.5)	0 (0.0)
2017	2 (16.7)	10 (83.3)	0 (0.0)
2018	0 (0.0)	9 (100.0)	0 (0.0)
2019	0 (0.0)	16 (94.1)	1 (5.9)
2020	0 (0.0)	3 (100.0)	0 (0.0)
2021	0 (0.0)	3 (100.0)	0 (0.0)

Table 3. ART switches in ART-experienced PLWH.

	n (%)
ART switch (*n* = 167)	
1 switch	64 (38.3)
2 switches	39 (23.4)
3 switches	28 (16.8)
4 switches	11 (6.6)
5 switches	8 (4.8)
≥6 switches	17 (10.2)
Switch from triple to dual regimen (*n* = 156)	52 (33.3)

At the time of inclusion in the study, HIV literacy was high. The fact that almost all ART-naïve PLWH knew that sexual contact is one of the modes of transmission, and yet, it was the main mode of transmission, raises the question of whether these individuals did not know that is possible to have protected sex or if they did but chose to engage in unsafe sexual behavior.[19,20] The proportion of males was significantly higher in the ART-naïve than in the ART-experienced group. This difference may be partly explained by the fact that the main mode of transmission in the ART-naïve group was sex between men, whereas in the ART-experienced group was heterosexual sex. These data could be mirroring recent reports in which 35.2% of the transmission mode, in Western Europe in 2022, was sex between men.[18]

Table 4. Characteristics valued by patients in relation to treatment.

Domains[a]		Overall population (*n* = 237)	ART-experienced (*n* = 171)	ART-naïve (*n* = 66)
Benefits, *n* (%)				
The HIV treatment works very well (reduces the amount of the infection in my body)	Most important	163 (68.8)	117 (70.1)	46 (69.7)
	Least important	4 (1.7)	3 (1.8)	1 (1.5)
The HIV treatment improves my thoughts and feelings about the disease	Most important	10 (4.2)	4 (2.4)	6 (9.1)
	Least important	54 (22.8)	47 (28.8)	7 (10.8)
The HIV treatment improves my social life (spending time with friends or family)	Most important	11 (4.6)	7 (4.2)	4 (6.1)
	Least important	69 (29.1)	42 (25.8)	20 (30.8)
The HIV treatment continues to work well for a long time after I take it	Most important	9 (3.8)	7 (4.2)	2 (6.0)
	Least important	9 (3.8)	8 (4.9)	1 (1.5)
The HIV treatment will allow me to choose more therapy options in the future	Most important	7 (3.0)	7 (4.2)	0 (0.0)
	Least important	30 (12.7)	20 (12.3)	10 (15.4)
Over time, HIV treatment will not stop working well to treat the disease	Most important	3 (1.3)	3 (1.8)	0 (0.0)
	Least important	35 (14.8)	22 (13.5)	13 (20.0)
I can take the HIV treatment safely with other treatments I may need for other diseases conditions	Most important	30 (12.7)	22 (13.2)	8 (12.1)
	Least important	34 (14.3)	21 (12.9)	13 (20.0)
Tolerability/Toxicity, *n* (%)				
The HIV treatment rarely causes feelings of nausea	Most important	43 (18.9)	34 (21.0)	9 (13.6)
	Least important	36 (15.7)	28 (17.1)	8 (12.3)
The HIV treatment rarely causes diarrhea	Most important	5 (2.2)	3 (1.9)	2 (3.0)
	Least important	34 (14.8)	21 (12.8)	13 (20.0)
The HIV treatment rarely causes anxiety, depression, and/or problems with sleeping	Most important	48 (21.1)	27 (16.7)	21 (31.8)
	Least important	23 (10.0)	17 (10.4)	6 (9.2)
I can take the HIV treatment even if I have other diseases or conditions	Most important	109 (47.8)	84 (51.9)	25 (37.9)
	Least important	29 (12.7)	19 (11.6)	10 (15.4)
During HIV treatment, I can get pregnant and/or breastfeed	Most important	23 (10.1)	14 (8.6)	9 (13.6)
	Least important	107 (46.7)	79 (48.2)	28 (43.1)

(continued)

Table 4. (continued)

Domains[a]		Overall population (*n* = 237)	ART-experienced (*n* = 171)	ART-naïve (*n* = 66)
Long-term effects, *n* (%)				
The HIV treatment does not affect my appearance or the way I look (changes in the shape of my body)	Most important	69 (30.1)	43 (25.9)	26 (41.3)
	Least important	68 (30.1)	48 (29.3)	20 (32.3)
It is unlikely that HIV treatment will cause problems with my heart	Most important	98 (42.8)	69 (41.6)	29 (46.0)
	Least important	18 (8.0)	17 (10.4)	1 (1.6)
It is unlikely that HIV treatment will cause problems with my kidneys	Most important	32 (14.0)	25 (15.1)	7 (11.1)
	Least important	10 (4.4)	7 (4.3)	3 (4.8)
It is unlikely that HIV treatment will cause problems with my bone loss	Most important	18 (7.9)	18 (10.8)	0 (0.0)
	Least important	33 (14.6)	28 (17.1)	5 (8.1)
It is unlikely that HIV treatment will cause problems with my cholesterol	Most important	12 (5.2)	11 (6.6)	1 (1.6)
	Least important	97 (42.9)	64 (39.0)	33 (53.2)
Administration characteristics (I), *n* (%)				
I only have to take a few pills	Most important	41 (17.7)	28 (16.9)	13 (19.7)
	Least important	21 (9.2)	16 (9.8)	5 (7.8)
I only have to take my pills once a day	Most important	168 (72.4)	122 (73.5)	46 (69.7)
	Least important	11 (4.8)	6 (3.7)	5 (7.8)
I can take my pills without food	Most important	12 (5.2)	9 (5.4)	3 (4.5)
	Least important	63 (27.6)	47 (28.7)	16 (25.0)
The pills I take are small in size	Most important	11 (4.7)	7 (4.2)	4 (6.1)
	Least important	133 (58.3)	95 (57.9)	38 (59.4)
Administration characteristics (II), *n* (%)				
I have to swallow pills once a day	Most convenient	102 (46.2)	70 (44.6)	32 (50.0)
I have to swallow pills once a week	Most convenient	9 (4.1)	7 (4.5)	2 (3.1)
I have to swallow pills once a month	Most convenient	40 (18.1)	31 (19.7)	9 (14.1)
I have to get an injection once a month (using a needle or syringe)	Most convenient	13 (5.9)	6 (3.8)	7 (10.9)
I have to get an implant twice a year (under the skin)	Most convenient	4 (1.8)	2 (1.3)	2 (3.1)
I have to get an implant once a year (under the skin)	Most convenient	53 (24.0)	41 (26.1)	12 (18.8)

[a]Each patient selected just one answer as most important and one answer as the least important, for each domain (Benefits, Tolerability/Toxicity, Long-term effects, Administration characteristics (I), Administration characteristics (II)) of this questionnaire.

Most PLWH (69%) had a full-time job, contrary to a 2014 study in which most patients (60%) were either unemployed or retired.[21] These findings may reflect the impact played by the improvement of ART during the last decade on factors associated with employment as discrimination/stigma and on PLWH's perception on how their health issues affect their daily work.

Portugal was the most common country of origin in both groups, but the percentage of patients originally from Portugal was significantly lower in the ART-naïve group (who had, on average, less than a year of HIV infection) than in the ART-experienced group (who had, on average, 12 years of HIV infection), reflecting the known immigrant population growth in the last decade.[22] Additionally, due to the high percentage of ART-experienced patients originated from Portugal, we do not anticipate a major impact on the results regarding treatment regimens recommended in other countries.

ART initiation commonly triggers metabolic disorders, especially among those under long-term ART, leading to a BMI increase in ART-experienced patients.[23,24] Nevertheless, the median BMI in ART-experienced patients was within the normal range, suggesting that overweight can be avoided. Despite that, over 20% of ART-experienced PLWH presented cardiometabolic diseases (hypercholesteremia and arterial hypertension). The fact that half of the people were above 50 years old can also play a role, as aging is associated with the emergence of these type of comorbidities.[25]

The significantly shorter time from HIV diagnosis to first ART initiation in ART-naïve than in the ART-experienced PLWH may be the consequence of the 2015 WHO guidelines that started to recommend ART for all adults with HIV regardless of $CD4^+$ T cell count.[26]

At the time of study inclusion, ART-experienced PLWH had a median $CD4^+$ T cell count within the normal range, indicating a controlled disease and good patient monitoring. In contrast, ART-naïve patients had a median $CD4^+$ T count below the normal range and half of them had ≥100.000 copies/mL of viral load. The compromised immune system and a high level of viral load make patients more susceptible to infections.[27] These circumstances may have prompted the lower score attributed by ART-naïve PLWH to the general QoL domain, as assessed by the WHOQOL-HIV BREF tool.

Regarding patients' ART preferences, the most valued parameters in the two groups (with an average age difference of 10 years) were the efficacy of ART, the possibility of being treated with ART even in the presence of other diseases/conditions, and the existence of ART in pills that can be taken once a day. This indicates a consensus in the preferences across age and experience with ART, which is an important insight for improving disease management and patient adherence to the treatment. Our study also showed that most ART-experienced and all ART-naïve PLWH were on a once-daily dosage scheme, an administration characteristic considered as most important for the majority of PLWH. However, in a recent study involving several European countries, 65% of patients expressed worry about forgetting to take their daily dose and 43.3% perceived room for improvement with their HIV medication.[28]

Despite the insights of this study, it is also important to consider its limitations. First, it was an observational and cross-sectional design, with data collected from medical charts. Information for some variables was incomplete or missing as it was collected for purposes other than research. Second, the study was only carried out in HIV centers in Portugal, which restricts the generalization of the findings to a broader population. Third, although this study assessed sociodemographic and clinical characteristics of ART-naïve and ART-experienced patients, it does not allow to derive causal relationships between patient profile and ART choice. Fourth, the number of included ART-naïve PLWH was approximately 2.6 times lower than the ART-experienced PLWH. As the study was conducted during the COVID-19 period, we cannot rule out the possible impact of the pandemic on the number of newly diagnosed patients. It has been described in the literature that the pandemic led to a decrease in HIV testing and, therefore, a decrease in newly diagnosed patients.[29–32] Indeed, the 2022 report on HIV infection in Portugal showed a lower number of HIV diagnoses in 2020 than in 2021 and raised the possibility that those differences were associated with the COVID-19 pandemic.[33] However, the report did not investigate if the reduction in the number of newly diagnosed HIV-positive people was due to a restriction in access to diagnosis, behavioral changes, or other unidentified factors.[33] Regarding ART management, although some studies have shown that the pandemic did not affect treatment management,[34,35] our data do not allow us to draw any conclusion on this matter.

Conclusions

This real-world study provided an updated overview of the characteristics and management of ART-naïve and ART-experienced PLWH in Portugal. Triple regimen was the most prescribed regimen, mainly INSTI-based therapy. However, approximately one-third of the patients from the ART-experienced group that started with triple regimen switched to dual regimen. The vast majority of patients had once-daily dosage schedule, being in accordance with one of their preferences regarding administration characteristics. Overall, the ART preferences were similar between the two groups, suggesting a consensus on the characteristics that PLWH most appreciate. Lastly, the levels of HIV literacy were high, indicating an educational success.

In summary, by assessing real-world ART prescribing patterns, this study has generated evidence on current treatment strategies in the clinical practice in Portugal.

Acknowledgements

The authors would like to acknowledge the START study team (Table S4). Medical writing support for the preparation of this manuscript was provided by Catarina Leitão at Evidenze Health España S.L., funded by MSD Portugal. Statistical analysis was performed by Nilza Gonçalves at KeyPoint (Evidenze Group) and Sara Pinheiro at Evidenze Health España S.L. and funded by MSD Portugal. Responsibility for opinions, conclusions and interpretation of data lies with the authors.

Author contributions

ET was involved in the study's conceptualization, methodology, and investigation, in the formal analysis of the results, and writing - original draft and review & editing of the manuscript; JA was involved in the study's conceptualization and methodology, and writing - review & editing of the manuscript; IL was involved in the formal analysis of the results and writing - review & editing of the manuscript; LP, AZ, RT, PP, JO, IVP, RS, ST, PB, FM, IN and AC were involved in the investigation and writing – review & editing of the manuscript.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The authors of this manuscript declare: JO participated on advisory boards and speaker for Gilead Sciences, ViiV Healthcare and Sanofi; IL and JA are employees of MSD Portugal; ET participated as a consultant, on advisory boards for MSD Portugal; RT participated as a speaker for MSD, ViiV, Gilead, Janssen; IN has received support from MSD Portugal for training and research activities; LP has participated in advisory boards for MSD and ViiV. The other authors declare no conflicts of interest.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by MSD Portugal [Protocol NIS008356].

ORCID iDs

Alexandre Carvalho https://orcid.org/0000-0001-5683-3181
Inês Lains https://orcid.org/0009-0001-0003-4636

Data availability

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Supplemental Material

Supplemental material for this article is available online.

References

1. Katz IT and Maughan-Brown B. Improved life expectancy of people living with HIV: who is left behind? *Lancet HIV* 2017; 4: e324–e326. DOI: 10.1016/s2352-3018(17)30086-3.
2. Wandeler G, Johnson LF and Egger M. Trends in life expectancy of HIV-positive adults on antiretroviral therapy across the globe: comparisons with general population. *Curr Opin HIV AIDS* 2016; 11: 492–500. DOI: 10.1097/coh.0000000000000298.
3. WHO. *Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach*. Geneva, Switzerland: World Health Organization, 2021.
4. GeSIDA. Executive summary of the GeSIDA/National AIDS Plan consensus document on antiretroviral therapy in adults infected by the human immunodeficiency virus (updated January 2018). *Enferm Infecc Microbiol Clín* 2019; 37: 195–202. DOI: 10.1016/j.eimc.2018.02.010.
5. EACS. *EACS guidelines*. European AIDS Clinical Society, 2021.
6. Albert J, Berglund T, Gisslen M, Gröön P, Sönnerborg A, Tegnell A, Alexandersson A, Berggren I, Blaxhult A, Brytting M, Carlander C, Carlson J, Flamholc L, Follin P, Haggar A, Hansdotter F, Josephson F, Karlström O, Liljeros F, Navér L, Pettersson K, Johansson VS, Svennerholm B, Tunbäck P and Widgren K. Risk of HIV transmission from patients on antiretroviral therapy: a position statement from the Risk of HIV transmission from patients on antiretroviral therapy: a position statement from the Public Health Agency of Sweden and the Swedish Reference Group for Antiviral Therapyublic health agency of Sweden and the Swedish reference group for antiviral therapy. *Scand J Infect Dis* 2014; 46: 673–677. DOI: 10.3109/00365548.2014.926565.
7. Cihlar T and Fordyce M. Current status and prospects of HIV treatment. *Curr Opin Virol* 2016; 18: 50–56. DOI: 10.1016/j.coviro.2016.03.004.
8. Cicconi P, Cozzi-Lepri A, Castagna A, Trecarichi EM, Antinori A, Gatti F, Cassola G, Sighinolfi L, Castelli P and d'Arminio Monforte AICoNA Foundation Study Group. Insights into reasons for discontinuation according to year of starting first regimen of highly active antiretroviral therapy in a cohort of antiretroviral-naive patients. *HIV Med* 2010; 11: 104–113. DOI: 10.1111/j.1468-1293.2009.00750.x.
9. Nachega JB, Mugavero MJ, Zeier M, Vitória M and Gallant JE. Treatment simplification in HIV-infected adults as a strategy to prevent toxicity, improve adherence, quality of life and decrease healthcare costs. *Patient Prefer Adherence* 2011; 5: 357–367. DOI: 10.2147/PPA.S22771.
10. Pedrol E, Viciana P, Arranz A, Pasquau J, Deig E and Tasias MSWITH AUDIT study group. [Reasons for antiretroviral treatment change in HIV+ patients in Spain in 2010-2011. SWITCH AUDIT Study]. *Rev Esp Quimioter* 2014; 27: 93–97.
11. VIH/SID PNpaI. Recomendações Portuguesas para o tratamento da infeção por VIH-1 e VIH- 2 – 2016. VIH/SIDA PNpaI, 2016.
12. Canavarro MC and Pereira M. Factor structure and psychometric properties of the European Portuguese version of a questionnaire to assess quality of life in HIV-infected adults: the WHOQOL-HIV-Bref. *AIDS Care* 2012; 24: 799–807. DOI: 10.1080/09540121.2011.630362.
13. O'Connell KA and Skevington SM. An international quality of life instrument to assess wellbeing in adults who are HIV-positive: a short form of the WHOQOL-HIV (31 items). *AIDS Behav* 2012; 16: 452–460. DOI: 10.1007/s10461-010-9863-0.
14. Chastain D, Badowski M, Huesgen E, Pandit NS, Pallotta A and Michienzi S. Optimizing Optimizing Antiretroviral Therapy in Treatment-Experienced Patients Living with HIV: A Critical

Review of Switch and Simplification Strategies. An Opinion of the HIV Practice and Research Network of the American College of Clinical Pharmacyntiretroviral therapy in treatment-experienced patients living with HIV: a critical review of switch and simplification strategies. An opinion of the HIV practice and research network of the American college of clinical pharmacy. *J Int Assoc Phys AIDS Care* 2019; 18: 2325958219867325. DOI: 10.1177/2325958219867325.

15. Baril JG, Angel JB, Gill MJ, Gathe J, Cahn P, van Wyk J and Walmsley S. Dual Dual Therapy Treatment Strategies for the Management of Patients Infected with HIV: A Systematic Review of Current Evidence in ARV-Naive or ARV-Experienced, Virologically Suppressed Patientsherapy treatment strategies for the management of patients infected with HIV: a systematic review of current evidence in ARV-naive or ARV-experienced, virologically suppressed patients. *PLoS One* 2016; 11: e0148231. DOI: 10.1371/journal.pone.0148231.
16. Greene M, Steinman MA, McNicholl IR and Valcour V. Polypharmacy, drug-drug interactions, and potentially inappropriate medications in older adults with human immunodeficiency virus infection. *J Am Geriatr Soc* 2014; 62: 447–453. DOI: 10.1111/jgs.12695.
17. Ryom L, Cotter A, De Miguel R, Béguelin C, Podlekareva D, Arribas JR, Marzolini C, Mallon P, Rauch A, Kirk O, Molina JM, Guaraldi G, Winston A, Bhagani S, Cinque P, Kowalska JD, Collins S and Battegay MEACS Governing Board. 2019 update of the European AIDS Clinical Society Guidelines for treatment of people living with HIV version 10.0. *HIV Med* 2020; 21: 617–624. DOI: 10.1111/hiv.12878.
18. Europe ECDPCWRO. *HIV/AIDS surveillance in Europe 2023 – 2022 data*. Stockholm, Sweden: ECDC, 2023.
19. Beyrer C, Baral SD, van Griensven F, Goodreau SM, Chariyalertsak S, Wirtz AL and Brookmeyer R. Global epidemiology of HIV infection in men who have sex with men. *Lancet* 2012; 380: 367–377. DOI: 10.1016/s0140-6736(12)60821-6.
20. Shilo G and Mor Z. Sexual practices and risk behaviors of Israeli adult heterosexual men. *AIDS Care* 2020; 32: 567–571. DOI: 10.1080/09540121.2019.1634786.
21. SER+ and GNP+. *Avaliação do Índice de Estigma das PVV em Portugal Lisboa2014*.
22. Esteves A. Portugal: 2021 census confirms growth in immigrant population, https://ec.europa.eu/migrant-integration/news/portugal-2021-census-confirms-growth-immigrant-population_en (2021).
23. Chen HH, Fu BT, Zhu QY, Lu HX, Luo LH, Chen L, Liu XH, Zhou XJ, Huang JH, Feng XX, Shan GS and Shen ZY. [Dynamic variations of BMI and influencing factors among HIV/AIDS patients receiving highly active antiretroviral therapy in Liuzhou, Guangxi Zhuang Autonomous Region, 2013-2014]. *Zhonghua Liuxingbingxue Zazhi* 2018; 39: 487–490. DOI: 10.3760/cma.j.issn.0254-6450.2018.04.020.
24. Desai KT, Patel PB, Verma A and Bansal RK. Environment and psychosocial factors are more important than clinical factors in determining quality of life of HIV-positive patients on antiretroviral therapy. *Trop Doct* 2020; 50: 180–186. DOI: 10.1177/0049475520908180.
25. Robles NR and Macias JF. Hypertension in the elderly. *Cardiovasc Hematol Agents Med Chem* 2015; 12: 136–145. DOI: 10.2174/1871525713666150310112350.
26. WHO. *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV*. Geneva, Switzerland: WHO, 2015, https://www.who.int/publications/i/item/9789241509565.
27. Damtie D, Yismaw G, Woldeyohannes D and Anagaw B. Common opportunistic infections and their CD4 cell correlates among HIV-infected patients attending at antiretroviral therapy clinic of Gondar University Hospital, Northwest Ethiopia. *BMC Res Notes* 2013; 6: 534. DOI: 10.1186/1756-0500-6-534.
28. van Dyk R, Lammertink B, Appiah A, Plieger H, de los Rios P and Okoli C. Preference for non-daily ART is associated with perceived extent of ART-related emotional, psychosocial, physical, and adherence challenges among people living with HIV in Preference for non-daily ART is associated with perceivedextent of ART-related emotional, psychosocial, physical, andadherence challenges among people living with HIV in theNetherlands and other European countrieshe Netherlands and other European countries. *Popul Med* 2022; 4: 1–13. DOI: 10.18332/popmed/156768.
29. Oka S. HIV testing in COVID-19 pandemic and beyond in Japan. *Glob Health Med* 2021; 3: 356–357. DOI: 10.35772/ghm.2021.01103.
30. DiNenno EA, Delaney KP, Pitasi MA, MacGowan R, Miles G, Dailey A, Courtenay-Quirk C, Byrd K, Thomas D, Brooks JT, Daskalakis D and Collins N. HIV HIV Testing Before and During the COVID-19 Pandemic - United States, 2019-2020esting before and during the COVID-19 pandemic - United States, 2019-2020. *MMWR Morb Mortal Wkly Rep* 2022; 71: 820–824. DOI: 10.15585/mmwr.mm7125a2.
31. Shi L, Tang W, Hu H, Qiu T, Marley G, Liu X, Chen Y, Chen Y and Fu G. The impact of COVID-19 pandemic on HIV care continuum in Jiangsu, China. *BMC Infect Dis* 2021; 21: 768. DOI: 10.1186/s12879-021-06490-0.
32. Desta AA, Woldearegay TW, Gebremeskel E, Alemayehu M, Getachew T, Gebregzabiher G, Ghebremedhin KD, Zgita DN, Aregawi AB and Redae G. Impacts of COVID-19 on essential health services in Tigray, Northern Ethiopia: Impacts of COVID-19 on essential health services in Tigray, Northern Ethiopia: A pre-post study pre-post study. *PLoS One* 2021; 16: e0256330. DOI: 10.1371/journal.pone.0256330.
33. Jorge INdSDR. Infeção por VIH em Portugal - 2022, https://www.backoffice.dgs.pt/upload/DGSv9/ficheiros/i029981.pdf.
34. Dusina A, Lombardi F, Tamburrini E, Onorati F, Petrucci M and Di Giambenedetto S. Home care assistance: has covid-19 had an impact on the complex management of HIV patients? *AIDS Behav* 2023; 27: 1173–1181. DOI: 10.1007/s10461-022-03854-8.
35. Lee D, Chow EPF, Aguirre I, Fairley CK and Ong JJ. Access to HIV Access to HIV Antiretroviral Therapy among People Living with HIV in Melbourne during the COVID-19 Pandemicntiretroviral therapy among people living with HIV in Melbourne during the COVID-19 pandemic. *Int J Environ Res Publ Health* 2021; 18: 12765. DOI: 10.3390/ijerph182312765.