Taylor & Francis
Taylor & Francis Group

Acta Clinica Belgica
International Journal of Clinical and Laboratory Medicine

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/yacb20

A characterization of the HIV population with limited/exhausted treatment options: a multicenter Belgian study

Rakan Nasreddine, Gilles Darcis, Jean Cyr Yombi, Paul De Munter, Eric Florence, Jens Van Praet, Rémy Demeester, Sabine D. Allard, Melanie Schroeder, Ange-Clarisse Dusabineza, Marc Delforge & Stéphane De Wit, on behalf of the Belgian Research on AIDS and HIV Consortium (BREACH)

To cite this article: Rakan Nasreddine, Gilles Darcis, Jean Cyr Yombi, Paul De Munter, Eric Florence, Jens Van Praet, Rémy Demeester, Sabine D. Allard, Melanie Schroeder, Ange-Clarisse Dusabineza, Marc Delforge & Stéphane De Wit, on behalf of the Belgian Research on AIDS and HIV Consortium (BREACH) (2024) A characterization of the HIV population with limited/exhausted treatment options: a multicenter Belgian study, Acta Clinica Belgica, 79:3, 153-159, DOI: 10.1080/17843286.2024.2359184

To link to this article: https://doi.org/10.1080/17843286.2024.2359184

Published online: 30 May 2024.

Submit your article to this journal

Article views: 84

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=yacb20

ACTA CLINICA BELGICA
2024, VOL. 79, NO. 3, 153–159
https://doi.org/10.1080/17843286.2024.2359184

Taylor & Francis
Taylor & Francis Group

Check for updates

A characterization of the HIV population with limited/exhausted treatment options: a multicenter Belgian study

Rakan Nasreddine[a], Gilles Darcis[b], Jean Cyr Yombi[c], Paul De Munter[d], Eric Florence[e], Jens Van Praet[f], Rémy Demeester[g], Sabine D. Allard[h], Melanie Schroeder[i], Ange-Clarisse Dusabineza[j], Marc Delforge[a] and Stéphane De Wit[a], on behalf of the Belgian Research on AIDS and HIV Consortium (BREACH)

[a]Department of Infectious Diseases, Saint-Pierre University Hospital, Brussels, Belgium; [b]Department of Infectious Diseases, Liège University Hospital, Liège, Belgium; [c]Department of Internal Medicine and Infectious Diseases, Cliniques Universitaires Saint-Luc, Brussels, Belgium; [d]Department of General Internal Medicine, Leuven University Hospital, Katholieke Universiteit Leuven, Leuven, Belgium; [e]Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium; [f]Department of Nephrology and Infectious Diseases, AZ Sint-Jan Brugge-Oostende, Brugge, Belgium; [g]Department of Internal Medicine and Infectious Diseases, University Hospital of Charleroi, Lodelinsart, Belgium; [h]Department of Internal Medicine and Infectious Diseases, Universitair Ziekenhuis Brussel, Brussels, Belgium; [i]Medical Affairs, ViiV Healthcare, Middlesex, UK; [j]Medical Affairs, ViiV Healthcare, Wavre, Belgium

ABSTRACT

Objective: Describe the prevalence and characteristics of people living with HIV (PLWH) in Belgium with limited/exhausted treatment options.

Methods: A cross-sectional, multicenter study involving adult treatment-experienced individuals with limited/exhausted treatment options defined as having a multi-drug resistant HIV-1 or a history of multiple treatment changes. The primary outcome was to determine the prevalence of these individuals and classify them based on their two most recent consecutive HIV-1 viral loads (VLs): suppressed (2 VLs < 50 copies/mL), intermediate (≥1 VL between 50–200 copies/mL), or unsuppressed (2 VLs > 200 copies/mL). Secondary outcome was to characterize the participants included in this analysis.

Results: There were 119 individuals included (prevalence of 0.97%; 119 of 12 282 in care). The majority were aged > 50 years (88.2%), women represented 35.3%, and individuals were primarily White (54.7%). Median (IQR) $CD4^+$ T-cell count was 635 (400–875) cells/μL and most (42%) were on a 3-drug ART regimen. Overall, 87.4% were classified as suppressed, 9.2% as intermediate, and 3.4% as unsuppressed. On multivariable analysis, $CD4^+$ T-cell count < 200 cells/μL was associated with being classified as intermediate or unsuppressed ($p = 0.004$).

Conclusion: In this analysis of PLWH in Belgium, individuals with limited/exhausted treatment options represented a small fraction. Most were on a 3-drug ART regimen, were virologically suppressed, and had a $CD4^+$ T-cell count within normal range. A small proportion were not virologically suppressed while others, despite being suppressed, were on ≥ 4-drug ART regimens. As such, new therapeutic options are needed to achieve and maintain virologic suppression in such individuals while decreasing their pill burden.

ARTICLE HISTORY
Received 31 January 2024
Accepted 20 May 2024

KEYWORDS
HIV; multi-drug resistant HIV-1; extensive treatment history; limited/exhausted treatment options; Belgium

Introduction

Many potent antiretrovirals are currently available for the treatment of HIV. Despite this, there is a subset of people living with HIV-1 (PLWH), that either because they have a multi-drug resistant (MDR) HIV-1 or have had to endure multiple treatment switches due to comorbidities, drug-drug interactions (DDIs), or tolerability issues, are unable to receive a standard antiretroviral therapy (ART) regimen from the remaining available treatment options. These individuals therefore, could be considered to have limited/exhausted treatment options and as such, are potentially at risk of virologic non-suppression and subsequent progression of their illness. Even though the population of PLWH with limited/exhausted treatment options has changed over time, as a result of the introduction of new antiretroviral (ARV) classes, recent data concerning this population are limited. In this context, this study sought out to describe the prevalence and characteristics of PLWH with limited/exhausted treatment options in daily clinical practice in Belgium.

Methods

Study design and population

In this cross-sectional, observational, multicenter study, we evaluated all treatment-experienced PLWH, aged ≥18 years, that were in care at one of the participating centers. A person in care was defined as having had at least 1 contact (in-person, by telephone, or by videoconference) with their HIV specialist and performed at least 1 standard laboratory analysis, including an HIV-1 viral load (VL) and $CD4^+$ T-cell count, within 12 months

CONTACT Rakan Nasreddine rakan.nasreddine@stpierre-bru.be Department of Infectious Diseases, Saint-Pierre University Hospital, Rue Haute 322, Brussels 1000, Belgium

© Belgian Society of Internal Medicine and Royal Belgian Society of Laboratory Medicine (2024)

prior to the index date of 1 April 2022. A participant was eligible for inclusion if they fulfilled one of two criteria for what was protocol-defined as having limited/exhausted treatment options. In order to avoid any overlap among the inclusion criteria, a participant was first screened for inclusion based on criterion A. If this was fulfilled, then the participant was included and as such, was not screened for criterion B. However, if the resistance data did not fulfill criterion A or was not available, then participants were screened for inclusion based on criterion B.

Criterion A: having an MDR HIV-1 infection based on cumulative resistance data with at least one resistance test occurring between 1 January 2015 and 1 August 2021. MDR HIV-1 was defined as having ≥ 3 ARV classes with ≤ 2 fully active ARVs remaining that can be effectively combined to form a viable new regimen. The nucleoside reverse transcriptase inhibitors (NRTIs) included in resistance testing were abacavir (ABC), didanosine (DDI), emtricitabine (FTC), lamivudine (3TC), stavudine (D4T), tenofovir disoproxil fumarate (TDF)/tenofovir alafenamide (TAF), and zidovudine (AZT). The non-nucleoside reverse transcriptase inhibitors (NNRTIs) included were doravirine (DOR), efavirenz (EFV), etravirine (ETR), nevirapine (NVP), and rilpivirine (RPV). The protease inhibitors (PIs) included were atzanavir (ATV), darunavir (DRV), fosamprenavir (FPV), indinavir (IDV), lopinavir (LPV), nelfinavir (NFV), saquinavir (SQV), and tipranavir (TPV). The integrase strand transfer inhibitors (INSTIs) included were bictegravir (BIC), cabotegravir (CAB), dolutegravir (DTG), elvitegravir (EVG), and raltegravir (RAL). Chemokine coreceptor 5 (CCR5) antagonists were also included in resistance testing. Since several years, fusion inhibitors were no longer incorporated into routine resistance testing being performed in Belgium, because they were no longer commercially available, and as such, were excluded. NRTIs, NNRTIs, PIs, and INSTIs were considered fully active if they were scored by the Stanford algorithm as susceptible (<10 points). A CCR5 antagonist was considered active if it had anticipated activity on tropism assay. Given the approval of new ARVs over time, an individual considered as having an MDR HIV-1 at one point in time could potentially no longer be classified as such when a new active drug becomes available. As such, the reasoning behind selecting the above-mentioned minimum cut-off date for resistance testing was that the date corresponded to when DTG was approved for use in Belgium.

Criterion B: having an extensive treatment history with multiple treatment changes. This was defined as having been treated with at least 3 core agent ARV classes and currently being on their ≥ 4th
regimen containing either DTG twice daily (BID), DRV BID, or ETR + maraviroc (MVC); or having been treated with at least 4 different core agents and currently being on their 4th or subsequent regimen containing either DTG BID, DRV BID, or ETR + MVC.

Study objectives and variables

The primary objective was to determine the prevalence of individuals with limited/exhausted treatment options and subsequently classify them into one of the following categories (based on the 2 most recent consecutive laboratory analyses performed prior to the index date): (i) suppressed, defined as having 2 HIV-1 VLs < 50 copies/mL; (ii) intermediate, defined as having at least one VL between 50–200 copies/mL; and (iii) unsuppressed, defined as having 2 HIV-1 VLs > 200 copies/mL. The secondary objective was to characterize the participants included in this analysis.

Data collected included participant characteristics such as age, gender, race, weight, active co-infection with hepatitis B virus (HBV) and hepatitis C virus (HCV), and co-morbidities, and HIV-related characteristics such as mode of HIV-1 acquisition, prior AIDS-defining illness, time on ART and number of ART regimens prior to the index date, cumulative resistance data, current ART regimen, nadir $CD4^+$ T-cell count along with the current $CD4^+$ and $CD8^+$ T-cell counts, and the two most recent consecutive HIV-1 VLs prior to the index date.

Data source and ethics considerations

Data were gathered from eight HIV reference centers (HRCs) in Belgium between 9 December 2022 and 24 March 2023. These HRCs provide HIV care to more than 80% of PLWH [1], thereby allowing for an adequate sampling of the Belgian HIV population.

This study was conducted in accordance with the General Data Protection Regulation (GDPR) 2016/679. Study-specific informed consent was not required given that this was a cross-sectional study of retrospective variables and the dataset for each participant underwent de-identification prior to extraction. Ethical approval was obtained from a central ethics committee and from site-specific ethics committees prior to data collection.

Statistical analysis

Point prevalence with 95% confidence interval (CI) was calculated as the number of participants fulfilling the inclusion criteria amid the total number of adult PLWH in care at each of the participating HRCs. Categorical values were reported as the number of available and missing data and as percentage. Continuous variables were conveyed as the number of available and missing data, median, and inter-quartile range (IQR). All results

were reported utilizing the pairwise deletion approach for missing data. An ordinal logistic regression analysis using a stepwise variable selection algorithm, utilizing all baseline variables, was performed to explore for associations with being classified as intermediate or unsuppressed. All statistical analyses were conducted using Statistical Analysis System (SAS) software v9.4 (SAS Institute, Inc., Cary, North Carolina, USA).

Results

Study population

The criteria for having limited/exhausted treatment options were met by 119 individuals resulting in a prevalence of 0.97% (95% CI 0.81–1.1; 119 of 12 282 in care). Of those, 25 (21%) participants were identified based on Criterion A and 94 (79%) on Criterion B (Table 1). The majority were above the age of 50 (88.2%), women represented 35.3% of the cohort, and participants were primarily White (54.7%) and Black (43.7%). The median (IQR) time on ART was 24.8 (21.7–26) years and median (IQR) $CD4^+$ T-cell count was 635 (400–875) cells/μL.

Virologic suppression

Of the 119 participants included, 104 (87.4%) were classified as suppressed, 11 (9.2%) as intermediate, and 4 (3.4%) as unsuppressed (Table 1). The median (IQR) HIV-1 VL for unsuppressed participants was 1 880 (1 140–56 260) copies/mL. On multivariable analysis, having a current $CD4^+$ T-cell count < 200 cells/μL was the only variable found to be significantly associated with being classified as intermediate or unsuppressed (odds ratio [OR] 3.91; 95% CI 1.60–14.18, $p = 0.004$).

Antiretroviral therapy and resistance

The majority of participants were on a 3-drug (42%) ART regimen with 35.3% of individuals on a ≥ 4-drug regimen (Table 1). Overall, the most frequently prescribed treatment was the two-drug regimen of DRV/cobicistat (c) + DTG (9.2%). Resistance data fulfilling criterion A was available for 25/119 (21%) participants. Of those, 22 (88%) had no active NRTI available (tenofovir disoproxil fumarate [TDF] was susceptible in the remaining three participants), 22 (88%) had no active NNRTI available (three participants had 1 NNRTI drug still available), 21 (84%) and 15 (60%) had resistance to atazanavir (ATV) and DRV respectively, and 3 (12%) participants had no active INSTI available. One participant was found to have varying levels of resistance to all ARVs from all classes. Virologic suppression in this individual was achieved by combining twice daily DRV (boosted once daily) with DOR, fostemsavir (FTR), and lenacapavir (LEN).

Discussion

In this study of over 12 000 PLWH in Belgium, the prevalence of individuals with limited/exhausted treatment options was 0.97%. Our cohort shared some similarities with the overall Belgian HIV population [1], such as male predominance (64.7% cohort vs. 65.8% overall) and median $CD4^+$ T-cell count (635 cells/μL cohort vs. 660 cells/μL overall). However, some differences were observed including a higher proportion of individuals aged >50 years (88.2% cohort vs. 47% overall), a finding that is to be expected given the long treatment histories (median time on ART of 24.8 years), and a higher proportion of Black participants (43.7% cohort vs. 34% overall). This finding may tend to indicate that Blacks are at higher risk of exhausting their treatment options. When compared to those born in Western countries, African-born Black individuals tend to be diagnosed at a later stage of infection and have less access to optimal HIV care [2,3]. Given that a significant proportion of the Black HIV population in Belgium are African-born [1], it is possible that the challenges these individuals faced when initially being managed could have played a role in explaining the above-mentioned finding. However, the lack of available data concerning the place of birth of Black participants in this cohort along with the drastic difference in number of participants between our cohort and the overall Belgian HIV population precludes us from forming a definitive conclusion.

Of the 119 participants included, 42% were on a 3-drug ART regimen and 87.4% were virologically suppressed. When dealing with resistance or intolerance for example, the advent of unboosted antiretrovirals such as DTG and DOR has provided clinicians the flexibility to make necessary adjustments to ART regimens, all the while keeping the regimens to two or three drugs and still maintaining virologic suppression. However, as observed in this study, there remains a sizeable proportion of PLWH (34.6%) that despite being virologically suppressed, require a ≥ 4-drug ART regimen to do so. Moreover, a small proportion of the cohort was classified as either intermediate (9.2%) or unsuppressed (3.4%). For those who were classified as intermediate, the absence of longitudinal data on subsequent viral loads, as a result of the cross-sectional nature of the study, precludes us from distinguishing whether this classification could be an indication of impending loss of virologic suppression or rather a benign transitory event. For the participants that were unsuppressed, the median HIV-1 VL observed at the time of unsuppression was 1880 copies/ml with one person having a VL of 56 260 copies/mL. Since resistance data was not available for these individuals, it was not possible to describe to what extent resistance factored in their lack of suppression. However, given the high VL observed for at least one of these

Table 1. Baseline characteristics of the study population.

	Suppressed *(N = 104)*	Intermediate *(N = 11)*	Unsuppressed *(N = 4)*	Total *(N = 119)*
Age (years), n (%)				
≥50	94 (90.4)	9 (81.8)	2 (50)	105 (88.2)
<50	10 (9.6)	2 (18.2)	2 (50)	14 (11.8)
Gender, n (%)				
Male	70 (67.3)	7 (63.6)	0 (0)	77 (64.7)
Female	34 (32.7)	4 (36.4)	4 (100)	42 (35.3)
Race, n (%)				
White	60 (57.7)	5 (45.5)	0 (0)	65 (54.7)
Black	44 (42.3)	5 (45.5)	3 (75)	52 (43.7)
Other	0 (0)	1 (9)	0 (0)	1 (0.8)
Data not available	0 (0)	0 (0)	1 (25)	1 (0.8)
Weight (kg)				
Median (IQR)	76 (65–84)	70 (65–84)	72 (67–79)	76 (65–84)
Data not available, n (%)	3 (2.9)	0 (0)	0 (0)	3 (2.5)
Co-morbidities, n (%)				
Cardiovascular disease	26 (25)	2 (18.2)	2 (50)	30 (25.2)
Diabetes mellitus	19 (18.3)	3 (27.3)	0 (0)	22 (18.5)
Neurological disease	6 (5.8)	0 (0)	0 (0)	6 (5)
NADM	5 (4.8)	1 (9)	0 (0)	6 (5)
Renal disease	2 (1.9)	0 (0)	0 (0)	2 (1.7)
Active co-infection, n (%)				
HBV	2 (1.9)	0 (0)	1 (25)	3 (2.5)
HCV	0 (0)	0 (0)	0 (0)	0 (0)
Data not available	10 (9.6)	0 (0)	1 (25)	11 (9.2)
HIV Acquisition, n (%)				
Heterosexual	54 (51.9)	7 (63.6)	2 (50)	63 (52.9)
MSM	36 (34.6)	2 (18.2)	0 (0)	38 (31.9)
Other	9 (8.7)	1 (9)	2 (50)	10 (8.4)
Data not available	5 (4.8)	1 (9)	0 (0)	6 (5)
Time since HIV diagnosis (years) Median (IQR)	28.3 (25.9–29.8)	25.7 (24.8–32)	27.6 (25.9–29.8)	28.2 (24.9–32)
Prior AIDS defining illness, n (%)	39 (37.5)	7 (63.6)	1 (25)	47 (43.1)
Nadir $CD4^+$ T-cell count (cells/μL) Median (IQR)	99.5 (29.5–184.5)	16 (4–90)	45 (20–61)	82 (20–180)
Time on ART (years)	25.1 (21.7–26.1)	24.4 (23.8–25.2)	21.5 (18.3–24.6)	24.8 (21.7–26)
Median (IQR)	3 (2.8)	1 (9)	0 (0)	4 (3.4)
Data not available, n (%)				
Number of ARVs received Median (IQR)	15 (13–18)	17 (15–18)	17 (14.5–20)	15 (13–18)
ARVs in current regimen, n (%)				
Two	21 (20.2)	4 (36.4)	2 (50)	27 (22.7)
Three	47 (45.2)	2 (18.2)	1 (25)	50 (42)
Four	25 (24)	4 (36.4)	0 (0)	29 (24.4)
Five	11 (10.6)	0 (0)	1 (25)	12 (10.1)
Six	0 (0)	1 (9)	0 (0)	1 (0.8)

(*Continued*)

Table 1. (Continued).

	Suppressed *(N = 104)*	Intermediate *(N = 11)*	Unsuppressed *(N = 4)*	Total *(N = 119)*
Most common ART regimens at index date, n (%)	DRV/c + DTG − 11 (10.7) DRV/r + ETR + RAL − 9 (8.7) DRV/c + DTG + MVC − 5 (4.8) DRV/c/FTC/TAF + DTG − 4 (3.8)	DRV/r + DTG − 2 (18.2) DRV/c/FTC/TAF + DTG − 2 (18.2) BIC/FTC/TAF + MVC − 1 (9.1) DTG/3TC + DOR − 1 (9.1)	DRV/r + DTG − 2 (50) ATV/r + DTG + MVC − 1 (25) DRV/c + ABC/3TC/DTG + RPV − 1 (25)	DRV/c + DTG 11 (9.2) DRV/r + ETR + RAL 9 (7.6)
Individuals on twice daily DTG or	5 (4.8)	2 (18.2)	0 (0)	7 (5.9)
DRV, n (%)	79 (76)	5 (45.5)	4 (100)	88 (73.9)
Included via criterion A				
Included via criterion B				
$CD4^+$ T-cell count at index date (cells/μL), n (%)				
<200	3 (2.9)	1 (9.1)	2 (50)	6 (5)
200–349	11 (10.6)	1 (9.1)	1 (25)	13 (10.9)
350–499	18 (17.3)	3 (27.3)	1 (25)	22 (18.5)
≥500	72 (69.2)	6 (54.5)	0 (0)	78 (65.6)
$CD4^+/CD8^+$ ratio at index date	0.7 (0.4–1)	0.3 (0.1–0.6)	0.3 (0.1–0.4)	0.6 (0.4–1)
Median (IQR)				
Value of HIV-1 VL ≥ 50 copies/mL	N/A	102 (40–198)	1880 (1140–56260)	171 (65–1240)
Median (IQR)				
Criteria of inclusion, n (%)				
Criterion A	20 (19.2)	5 (45.5)	0 (0)	25 (21)
Criterion B	84 (80.8)	6 (54.5)	4 (100)	94 (79)

IQR, inter-quartile range; NADM, non-AIDS-defining malignancy; HBV, hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men; ART, antiretroviral therapy; ARV, antiretrovirals; DRV/c; darunavir/cobicistat; DTG, dolutegravir; DRV/r; darunavir/ritonavir; ETR, etravirine; RAL, raltegravir; MVC, maraviroc; FTC/TAF, emtricitabine/tenofovir alafenamide; BIC, bictegravir; 3TC, lamivudine; DOR, doravirine; ATV/r; atazanavir/ritonavir; ABC, abacavir; RPV, rilpivirine.

participants, sub-optimal adherence or intolerance to the treatment regimen could have played a role in their virologic non-suppression. Despite this, these individuals still represent a possible source of dissemination of potentially MDR HIV-1 among newly infected individuals. Furthermore, we found that having a $CD4^+$ T-cell count of < 200 cells/μL at the time of analysis was significantly associated with being classified as intermediate or unsuppressed (OR 3.91; $p = 0.004$). Of course, given that being classified as intermediate or unsuppressed implied varying forms of detectable viremia, this finding could simply be a consequence of the progression of illness in these individuals. However, some reports have indicated that lower $CD4^+$ T-cell counts were associated with an increased risk of viral rebound [4] while others have suggested that the extent of $CD4^+$ T-cell depletion strongly predicts HIV reservoir size which in turn, could act as an essential determinant of virologic failure [5,6].

In recent studies, the prevalence of PLWH with limited/exhausted treatment options has been reported to range between < 1% to 16.1% [7–10]. The variations in prevalence are likely explained by the heterogeneity of the populations studied, the period that each study covered (early ART vs. contemporary ART era), and most importantly, the criteria used to identify persons with limited/exhausted treatment options. Indeed, there is no consensus on the definition of these individuals. In the absence of resistance data, some studies have used approaches relying on virologic failure and antiretroviral treatment history [8,9]. Reports that did use genotypic resistance data were mostly conducted in the early ART era [11–17] prior to the availability of 2nd generation INSTIs. Moreover, utilization of the most recent genotypic test rather than cumulative resistance data has resulted in discrepant estimates of prevalence [13,18]. In addition, some studies have focused on the number of antiretroviral drugs or classes to which an individual is resistant [19], rather than how many active drugs are available, which is essential to achieving virologic suppression [20]. Even the cut-offs used to define MDR HIV-1 in terms of the number of active drugs available in each class (2 or 3) or in terms of the Stanford algorithm score (10 or 15) could contribute to the variations in results among the aforementioned studies, including our study. Indeed, the MDR HIV-1 definition utilized in this study, which was believed to most accurately encompass what an MDR HIV was, resulted in only 21% of participants being included based on this criterion.

Strengths of this study include the utilization of a two-component composite definition for PLWH with limited/exhausted treatment options optimizing their identification. However, as this was an observational, cross-sectional study of electronically captured data from daily clinical practice, it was not possible to perform a chart review for each participant in order to collect longitudinal data on the reasons for treatment changes and adherence.

Conclusion

In this analysis of PLWH in Belgium, those with limited/exhausted treatment options represented a small fraction. Most were on a 3-drug ART regimen, were virologically suppressed, and had a $CD4^+$ T-cell count within normal range. A small proportion were not fully suppressed while others, despite being virologically suppressed, were on ≥ 4-drug ART regimens or on regimens, that despite having less antiretrovirals, could have future implications, such as increased cardiovascular risk or DDIs with potential non-HIV medications. Therefore, these regimens may not be the most optimal treatments for the ever-aging HIV population and as such, new therapeutic options such as FTR, LEN, or even broadly neutralizing antibodies (bNAbs) will be needed to ensure virologic suppression in these individuals and correspondingly, decrease their pill burden. In addition, a standardized definition of PLWH with limited/exhausted treatment options will be required in order to accurately identify these individuals in the future.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This study was supported by ViiV Healthcare.

ORCID

Rakan Nasreddine http://orcid.org/0000-0002-1265-1500

Data availability statement

The data that support the findings of this study are available from the corresponding author, RN, upon reasonable request.

References

[1] Sciensano. Epidémiologie du sida et de l'infection à VIH en Belgique. 2021. [cited 2023 Jul 5]. Available from: https://www.sciensano.be/en/biblio/epidemiologie-du-sida-et-de linfection-a-vih-en-belgique-situation-au-31-decembre-2021

[2] Blanas DA, Nichols K, Bekele M, et al. HIV/AIDS among African-born residents in the United States. J Immigr Minor Health. 2013;15(4):718–724. doi: 10.1007/s10903-012-9691-6

[3] Ross J, Akiyama MJ, Slawek D, et al. Undocumented African immigrants' experiences of HIV testing and

linkage to care. AIDS Patient Care STDS. 2019;33 (7):336–341. doi: 10.1089/apc.2019.0036

[4] Miller V, Staszewski S, Sabin C, et al. CD4 lymphocyte count as a predictor of the duration of highly active antiretroviral therapy–induced suppression of human immunodeficiency virus load. J Infect Dis. 1999;180 (2):530–533. doi: 10.1086/314890

[5] Pinkevych M, Cromer D, Tolstrup M, et al. HIV reactivation from latency after treatment interruption occurs on average every 5-8 days—implications for HIV remission. PLOS Pathog. 2015;11(7):e1005000. doi: 10.1371/journal.ppat.1005000

[6] Boulassel MR, Chomont N, Pai NP, et al. CD4 T cell nadir independently predicts the magnitude of the HIV reservoir after prolonged suppressive antiretroviral therapy. J Clin Virol. 2012;53(1):29–32. doi: 10.1016/j.jcv.2011.09.018

[7] Priest J, Hulbert E, Gilliam BL, et al. Characterization of heavily treatment-experienced people with HIV and impact on healthcare resource utilization in US commercial and medicare advantage health plans. Open Forum Infect Dis. 2021;8(12):ofab562. doi: 10.1093/ofid/ofab562

[8] Hsu RK, Fusco JS, Henegar CE, et al. Heavily treatment-experienced people living with HIV in the OPERA® cohort: population characteristics and clinical outcomes. BMC Infect Dis. 2023;23(1):91. doi: 10.1186/s12879-023-08038-w

[9] Henegar C, Vannappagari V, Viswanathan S, et al. Identifying heavily treatment-experienced patients in a large administrative claims database. In: [Abstract MOPEB236] 10th IAS Conference on HIV Science; 2019 Jul 21–24; Mexico City, Mexico.

[10] Bajema KL, Nance RM, Delaney JAC, et al. Substantial decline in heavily treated therapy-experienced persons with HIV with limited antiretroviral treatment options. AIDS. 2020;34(14):2051–2059. doi: 10.1097/QAD.0000000000002679

[11] Lima VD, Harrigan PR, Senecal M, et al. Epidemiology of antiretroviral multiclass resistance. Am J Epidemiol. 2010;172(4):460–468. doi: 10.1093/aje/kwq101

[12] Abraham AG, Lau B, Deeks S, et al. Missing data on the estimation of the prevalence of accumulated human immunodeficiency virus drug resistance in patients treated with antiretroviral drugs in North America. Am J Epidemiol. 2011;174(6):727–735. doi: 10.1093/aje/kwr141

[13] Pillay D, Green H, Matthias R, et al. Estimating HIV-1 drug resistance in antiretroviral-treated individuals in the United Kingdom. J Infect Dis. 2005; 192:967–973.

[14] De Luca A, Dunn D, Zazzi M, et al. Declining prevalence of HIV-1 drug resistance in antiretroviral treatment-exposed individuals in Western Europe. J Infect Dis. 2013;207(8):1216–1220. doi: 10.1093/infdis/jit017

[15] Tamalet C, Fantini J, Tourres C, et al. Resistance of HIV-1 to multiple antiretroviral drugs in France: a 6-year survey (1997– 2002) based on an analysis of over 7000 genotypes. AIDS. 2003;17(16):2383–2388. doi: 10.1097/00002030-200311070-00014

[16] Audelin AM, Lohse N, Obel N, et al. The incidence rate of HIV type-1 drug resistance in patients on antiretroviral therapy: a nationwide population-based Danish cohort study 1999–2005. Antivir Ther. 2009;14 (7):995–1000. doi: 10.3851/IMP1412

[17] von Wyl V, Yerly S, Burgisser P, et al. Long-term trends of HIV type 1 drug resistance prevalence among antiretroviral treatment-experienced patients in Switzerland. Clin Infect Dis. 2009;48:979–987. doi: 10.1086/597352

[18] Gill VC, Lynch T, Ramazani S, et al. Reporting on the prevalence of antiretroviral drug resistance in a regional HIV population over 20 years: a word of caution. Antivir Ther. 2017;22(4):277–286. doi: 10.3851/IMP3105

[19] Scherrer AU, von Wyl V, Yang WL, et al. Emergence of acquired HIV-1 drug resistance almost stopped in Switzerland: a 15-year prospective cohort analysis. Clin Infect Dis. 2016;62(10):1310–1317. doi: 10.1093/cid/ciw128

[20] Gandhi RT, Tashima KT, Smeaton LM, et al. Long-term outcomes in a large randomized trial of HIV-1 salvage therapy: 96-week results of AIDS clinical trials group A5241 (OPTIONS). J Infect Dis. 2020;221(9):1407–1415. doi: 10.1093/infdis/jiz281