Identification, Management, and Outcomes of Combination Antiretroviral Treatment Failure in Adolescents With Perinatal Human Immunodeficiency Virus Infection in Asia

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Background. Combination antiretroviral therapy (cART) failure is a major threat to human immunodeficiency virus (HIV) programs, with implications for individual- and population-level outcomes. Adolescents with perinatally acquired HIV infection (PHIVA) should be a focus for treatment failure given their poorer outcomes compared to children and adults.

Methods. Data (2014–2018) from a regional cohort of Asian PHIVA who received at least 6 months of continuous cART were analyzed. Treatment failure was defined according to World Health Organization criteria. Descriptive analyses were used to report treatment failure and subsequent management and evaluate postfailure CD4 count and viral load trends. Kaplan-Meier survival analyses were used to compare the cumulative incidence of death and loss to follow-up (LTFU) by treatment failure status.

Results. A total 3196 PHIVA were included in the analysis with a median follow-up period of 3.0 years, of whom 230 (7.2%) had experienced 292 treatment failure events (161 virologic, 128 immunologic, 11 clinical) at a rate of 3.78 per 100 person-years. Of the 292 treatment failure events, 31 (10.6%) had a subsequent cART switch within 6 months, which resulted in better immunologic and virologic outcomes compared to those who did not switch cART. The 5-year cumulative incidence of death and LTFU following treatment failure was 18.5% compared to 10.1% without treatment failure.

Conclusions. Improved implementation of virologic monitoring is required to realize the benefits of virologic determination of cART failure. There is a need to address issues related to accessibility to subsequent cART regimens, poor adherence limiting scope to switch regimens, and the role of antiretroviral resistance testing.

Keywords. HIV; adolescent; antiretroviral therapy; treatment failure.

Concerted efforts have been made to improve access to combination antiretroviral therapy (cART) in low- and middle-income countries (LMICs) in response to the World Health Organization's (WHO) "treat all" policy and to meet the Joint United Nations Programme on AIDS (UNAIDS) "90-90-90" target [1, 2]. The expanding access to cART requires a similar approach to treatment monitoring as treatment failure represents a major threat to the success of human immunodeficiency

virus (HIV) programs with implications for individual- and population-level outcomes. Adolescents with perinatally acquired HIV infection (PHIVA) should be a particular focus population for monitoring and optimizing management of treatment failure given their poorer treatment adherence and virologic outcomes compared to younger children, adolescents with horizontally acquired HIV infection, and adults across different resource settings [3–9]. These vulnerabilities result from the unique complexities of managing a chronic, potentially stigmatizing condition, during an adolescent period of biopsychosocial development that poses challenges related to treatment fatigue, engagement in care, disclosure to themselves and others, and evolving health independence for effective lifelong management [10]. Virologic monitoring is the recommended method for monitoring response to antiretroviral therapy (ART) and identifying treatment failure [11].

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However, a reliance on virologic assessment may underestimate the true burden of treatment failure as only 61% of LMICs fully implemented routine HIV viral load (VL) monitoring in 2018 [12]. Despite concerns regarding the accuracy of WHO immunologic criteria in identifying virologic failure [13–17], in the absence of universal routine HIV VL testing, clinical and immunologic criteria for treatment failure remain relevant in guiding antiretroviral management decisions [18].

This study aimed to analyze the identification, management, and outcomes of PHIVA in a regional Asian cohort who encountered clinical, immunologic, and virologic failure on cART by (1) reporting the rates of virologic, immunologic, clinical, and any treatment failure; (2) describing and comparing those with virologic, immunologic, and clinical treatment failure and their subsequent management; (3) evaluating trends in CD4 count and HIV VL with subsequent cART following treatment failure; and (4) comparing the cumulative incidence of death and loss to follow-up (LTFU) between those who experienced treatment failure and those who did not.

METHODS

The Therapeutics Research, Education, and AIDS Training (TREAT) Asia Pediatric HIV Observational Database (TApHOD) of the International Epidemiology Databases to Evaluate AIDS (IeDEA) Asia-Pacific network is a regional collaboration evaluating HIV management and outcomes from 16 pediatric HIV services across 6 countries (Cambodia, India, Indonesia, Malaysia, Thailand, and Vietnam). The regional collaboration, established in 2007, collects data during routine care incorporating demographics, HIV diagnosis, laboratory results, WHO clinical events, and ART. Clinical care across the TApHOD network typically involves clinic attendance every 2–4 months, with CD4 count and HIV VL monitoring varying between 2 and 12 months (CD4 count often monitored more frequently than HIV VL). Data are transferred from clinic sites to a centralized database at the Kirby Institute (University of New South Wales, Sydney, Australia) for management and statistical analysis. For this study, PHIVA (aged 10–19 years) who received at least 6 months of continuous cART and had at least 1 data entry for WHO clinical stage, CD4 count, or HIV VL between 1 January 2014 and 31 December 2018 was included. Ethics approvals were obtained through the human research ethics committees at participant sites, the Kirby Institute, and the coordination center at TREAT Asia/amfAR (Bangkok, Thailand).

Definitions

Perinatal HIV infection was determined by mode of transmission as recorded by participant sites. The adolescent age range and period of adolescence was defined as 10–19 years of age. Continuous cART was defined as concomitant use of at least

3 antiretroviral agents with no more than a 2-week break in treatment. A switch in cART was defined as a change in at least 1 antiretroviral drug class or the addition of a new antiretroviral drug class. Viral suppression was defined as site-reported “undetectable” HIV VL. A detectable HIV VL threshold of ≤ 50 copies/mL was used by most sites (range, 10–400 copies/mL). Treatment failure for children (<10 years of age) and adolescents was defined in accordance with the WHO 2016 criteria [18]. For adolescents, clinical treatment failure was defined as a new or recurring WHO clinical stage IV event or death after 6 months of continuous cART. Immunologic treatment failure was defined as a CD4 count ≤ 250 cells/ μ L following clinical treatment failure or a CD4 count <100 cells/ μ L after 6 months of continuous cART. Virologic treatment failure was defined as consecutive HIV VLs ≥ 1000 copies/mL 3–12 months apart after at least 6 months of continuous cART. LTFU was defined as more than a 365-day absence of data prior to the date of last data transfer from clinic sites. Date of LTFU was assigned 365 days following the last recorded visit date.

Statistical Analysis

Descriptive analyses were used to report characteristics of the study population and PHIVA who met virologic, immunologic, clinical, or any treatment failure criteria. Virologic, immunologic, and clinical treatment failure events were not considered mutually exclusive if participants concurrently met multiple treatment failure criteria. Treatment failure rates were calculated by dividing the number of events by person-years of observation. The observation period commenced on the date 6 months of continuous cART was achieved during adolescence (baseline) and ceased on either the date of death, LTFU, clinic transfer, last data transfer from clinic sites, or day prior to the participant's 20th birthday. CD4 count and HIV VL trends following treatment failure were analyzed separately for immunologic and virologic treatment failure and stratified by whether participants switched cART or not within 6 months of treatment failure. The start date for analyzing CD4 count and HIV VL trends was either the date of treatment failure (for those who did not switch cART) or the date of cART switch (for those who switched). CD4 counts were reported at 6-month intervals with a 3-month window period and HIV VLs reported at 12-month intervals with a 6-month window period (as virologic monitoring was less frequent than immunologic monitoring). Kaplan-Meier survival estimates were used to compare the cumulative incidence, with 95% confidence intervals (CIs), of death or LTFU between PHIVA who experienced treatment failure and PHIVA who did not. For the treatment failure cohort, follow-up commenced the date of their first treatment failure event during adolescence. For the cohort that did not experience treatment failure, follow-up commenced the date at which 6 months of continuous cART had been achieved during adolescence. Follow-up finished on the date of death, LTFU,

clinic transfer, last data transfer from clinic sites, or day prior to the participant's 20th birthday. Those who experienced a treatment failure event contributed to the non-treatment failure cohort until they experienced a treatment failure event, at which time they began contributing to the treatment failure cohort. All statistical analyses were performed using Stata version 14.2 version (StataCorp LP, College Station, Texas).

RESULTS

Study Population

A total 3530 PHIVA had ever received care within the TApHOD network between January 2014 and December 2018, of whom 3196 (90.5%) received at least 6 months of continuous cART with available data and were included in the study. Of the 334 PHIVA excluded, 55 (16.5%) had not received cART, 234 (70.0%) had received <6 months of continuous cART, and 45 (13.5%) had received 6 months of continuous cART without available data. [Table 1](#) summarizes the characteristics of the study population. Median cART duration by study entry was 6.9 (interquartile range [IQR], 4.2–8.6) years and the median follow-up period was 3.0 (IQR, 1.6–4.5) years. The median follow-up period for those without HIV VL results (n = 540) was 1.0 (IQR, 0.4–2.4) year and for those with 1 HIV VL result (n = 664) was 1.6 (IQR, 0.9–2.7) years (of whom 530/664 [79.8%] were suppressed). For those with at least 2 HIV VL results (n = 1992), the median follow-period was 3.6 (IQR, 2.5–4.5) years. Two hundred thirty (7.2%) PHIVA experienced 292 treatment failure events at a rate of 3.78 (95% CI, 3.37–4.24) per 100 person-years. This included 153 PHIVA who experienced 161 virologic treatment failure events at a rate of 2.08 (95% CI, 1.79–2.43) per 100 person-years, 118 PHIVA who experienced 128 immunologic treatment failure events at a rate of 1.66 (95% CI, 1.39–1.97) per 100 person-years, and 11 PHIVA who experienced 11 clinical treatment failure events at a rate of 0.14 (95% CI, .08–.26) per 100 person-years. [Table 2](#) shows the characteristics of PHIVA who experienced virologic, immunologic, clinical, or any treatment failure. There were similar proportions of nonnucleoside reverse transcriptase inhibitor (NNRTI)- and protease inhibitor (PI)-based cART regimens, as well as first and subsequent cART regimens, across virologic and immunologic treatment failure cohorts. Those with virologic treatment failure had a higher median CD4 count (341 [IQR, 131–513] cells/μL) compared to those with immunologic treatment failure (53 [IQR, 24–78] cells/μL) or clinical treatment failure (26 [IQR, 24–27] cells/μL). Treatment failure during childhood had occurred for 120 of 230 (52.2%) PHIVA, with the highest proportion occurring for PHIVA with clinical treatment failure (9/11 [81.8%]), followed by immunologic treatment failure (76/118 [64.4%]) and virologic treatment failure (74/153 [48.4%]). Six of 128 (4.7%) immunologic treatment failure events concurrently met virologic treatment failure criteria.

Table 1. Characteristics of Study Population (N = 3196)

Characteristic	No. (%)
Male sex	1604 (50.2)
Country	
Cambodia	607 (19.0)
India	121 (3.8)
Indonesia	163 (5.1)
Malaysia	226 (7.1)
Thailand	1072 (33.5)
Vietnam	1007 (31.5)
Clinic setting	
Urban	1931 (60.4)
Semirural	1066 (33.4)
Rural	199 (6.2)
Age at cART initiation, y	
Median (IQR)	5.9 (3.5–8.5)
<5	856 (26.8)
5–9	1873 (58.6)
≥10	467 (14.6)
Baseline ^a CD4 count, cells/μL	
Median (IQR)	739 (524–988)
≥500	2264 (70.8)
350–499	342 (10.7)
200–349	173 (5.4)
<200	149 (4.7)
Missing	268 (8.4)
Baseline ^a HIV viral load, copies/mL	
Suppressed	1599 (50.0)
Unsuppressed (<1000)	215 (6.7)
1000–9999	86 (2.7)
≥10 000	152 (4.8)
Missing	1144 (35.8)
Median data points available per participant (range)	
Clinical	5 (1–24)
Immunologic	4 (0–20)
Virologic	2 (0–24)
Baseline ^a WHO clinical stage	
I/II	3114 (97.4)
III/IV	82 (2.6)
Baseline ^a cART regimen	
NNRTI based	2358 (73.8)
PI based	780 (24.4)
Other ^b	58 (1.8)
Prior treatment failure (at age <10 y)	
Virologic	414 (13.0)
Immunologic	276 (8.6)
Clinical	283 (8.9)
Any	781 (24.4)
Prior cART switch	
Subjects	871 (27.3)
Median age, y (IQR)	8.3 (5.9–11.1)
Follow-up	
Deaths	31 (1.0)
Median age at death, y (IQR)	15.6 (12.1–17.1)
LTFU	113 (3.6)
Median age at LTFU, y (IQR)	16.8 (14.8–18.4)

Data are presented as no. (%) unless otherwise specified.

Abbreviations: cART, combination antiretroviral therapy; HIV, human immunodeficiency virus; IQR, interquartile range; LTFU, loss to follow-up; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor; WHO, World Health Organization.

^aDate at which 6 months of continuous cART had been achieved as an adolescent.

^bOther regimens included NNRTI/PI based (n = 30), integrase inhibitor based (n = 21), entry inhibitor based (n = 6), and nucleoside reverse transcriptase inhibitor based (n = 1).

Treatment Failure Management and Outcomes

Of the 292 treatment failure events, there were 31 (10.6%) that switched cART at a median of 77 (IQR, 63–126) days following treatment failure (Table 2). For the 31 cART switches, 25

(80.6%) had switched from a first cART regimen and 6 (19.4%) had switched from at least a second cART regimen (data not shown). Furthermore, among the 31 cART switches, 23 (74.2%) involved a switch from NNRTI- to PI-based cART, 5 (16.1%)

Table 2. Characteristics of Adolescents With Perinatally Acquired Human Immunodeficiency Virus Infection With Virologic, Immunologic, Clinical, and Any Treatment Failure

Characteristic	Virologic Failure	Immunologic Failure	Clinical Failure	Any Treatment Failure
Adolescents ^{a,b} , No.	153	118	11	230
Events ^{b,c} , No.	161	128	11	292
Median age, y (IQR) ^c	15.7 (13.3–17.9)	16.3 (12.9–18.6)	12.8 (10.7–17.6)	15.9 (13.1–18.1)
Sex ^a				
Male	74 (48.4)	59 (50)	3 (27.3)	114 (49.6)
Female	79 (51.6)	59 (50)	8 (72.7)	116 (50.4)
Site ^a				
Urban	85 (55.6)	61 (51.7)	9 (81.8)	123 (53.5)
Semirural	61 (40.0)	48 (40.7)	0	91 (39.6)
Rural	7 (4.6)	9 (7.6)	2 (18.2)	16 (6.9)
Current cART ^c				
NNRTI based	75 (46.6)	57 (44.5)	4 (36.4)	134 (45.9)
PI based	78 (48.5)	61 (47.7)	7 (63.6)	140 (48.0)
Other	8 (5.0)	10 (7.8)	0	18 (6.1)
cART regimen ^c				
First	86 (53.4)	67 (52.3)	4 (36.4)	154 (52.7)
Subsequent	75 (46.6)	61 (47.7)	7 (63.6)	138 (47.3)
CD4 count, cells/ μ L ^c				
Median (IQR)	341 (131–513)	53 (24–78)	26 (24–27)	86 (40–348)
≥ 500	35 (21.7)	0	0	35 (12.0)
350–499	27 (16.8)	0	0	27 (9.2)
200–349	27 (16.8)	1 (0.8)	0	28 (9.6)
<200	41 (25.5)	127 (99.2)	2 (18.2)	162 (55.5)
Missing	31 (19.3)	0	9 (81.8)	40 (13.7)
HIV viral load, copies/mL ^c				
Suppressed	0	5 (3.9)	0	5 (1.7)
Unsuppressed and <1000	0	5 (3.9)	0	5 (1.7)
1000–9999	60 (37.3)	4 (3.1)	0	63 (21.6)
$\geq 10\ 000$	101 (62.7)	46 (36.0)	0	142 (48.6)
Missing	0	68 (53.1)	11 (100)	77 (26.4)
Age at cART initiation, y ^a				
Median (IQR)	6.8 (4.5–9.1)	7.0 (5.0–9.1)	6.1 (3.6–9.1)	6.8 (4.6–9.1)
<5	24 (15.7)	14 (11.9)	2 (18.2)	36 (15.6)
5–9	105 (68.6)	84 (71.2)	8 (72.7)	157 (68.3)
≥ 10	24 (15.7)	20 (17.0)	1 (9.1)	37 (16.1)
Prior treatment failure (at age <10 y) ^a				
No	79 (51.6)	42 (35.6)	2 (18.2)	110 (47.8)
Yes	74 (48.4)	76 (64.4)	9 (81.8)	120 (52.2)
Attrition ^a				
Death	8 (5.2)	10 (8.5)	5 (45.5)	22 (9.6)
Loss to follow-up	6 (3.9)	2 (1.7)	0	8 (3.5)
Subsequent cART ^{c,d}				
No cART switch	142 (88.2)	116 (90.6)	11 (100)	261 (89.4)
cART switch	19 (11.8)	12 (9.4)	0	31 (10.6)

Data are presented as no. (%) unless otherwise specified.

Abbreviations: cART, combination antiretroviral therapy; HIV, human immunodeficiency virus; IQR, interquartile range; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

^aAnalysis conducted per participant.

^bVirologic, immunologic, and clinical treatment failure events not considered mutually exclusive.

^cAnalysis conducted per treatment failure event.

^dcART switch within 6 months of treatment failure.

involved a switch to integrase inhibitor (INSTI)-based cART, and 3 (9.7%) involved a switch from INSTI- or entry inhibitor-based cART to NNRTI- or PI-based cART. For the 261 treatment failure events without a subsequent cART switch, 129 (49.4%) involved a first cART regimen and 132 (50.6%) involved at least a second cART regimen (data not shown). **Figure 1** compares trends in CD4 count following treatment failure for those who switched cART and those who did not switch. The median CD4 count at the time of any treatment failure was 105 (IQR, 32–424) cells/ μ L for those who switched cART, which improved to 423 (IQR, 126–503) within 6 months of cART switch. For those who did not switch cART, the median CD4 count was 86 (IQR, 40–346) cells/ μ L at the time of treatment failure and 184 (IQR, 32–471) cells/ μ L at 2 years following treatment failure. The divergence in immunologic outcomes was more pronounced following immunologic compared to virologic treatment failure (**Figure 2**). **Figure 3** demonstrates HIV VL trends following any treatment failure event for PHIVA who switched cART and PHIVA who did not. HIV VL suppression was achieved in 4 of 8 (50.0%) PHIVA at 12 months following cART switch; for PHIVA who did not switch cART, HIV VL suppression was achieved by 15 of 92 (16.3%) at 12 months and 13 of 47 (27.7%) PHIVA at 24 months.

Throughout the 5-year study period there were 31 of 3196 (1.0%) deaths at a median age of 15.6 (IQR, 12.1–17.1) years and 113 of 3196 (3.6%) LTFU at a median age of 16.8 (IQR 14.8–18.4) years. Kaplan-Meier survival analyses demonstrated a 5-year cumulative incidence of death or LTFU for the entire cohort of 11.1% (95% CI, 9.2%–13.3%). The 5-year cumulative incidence of death or LTFU for PHIVA following treatment failure was 18.5% (95% CI, 11.6%–28.8%), while the 5-year cumulative incidence of death or LTFU for PHIVA without treatment failure was 10.1% (95% CI, 8.2%–12.4%) (**Figure 4**).

Figure 1. Trends in median CD4 cell count (with 95% confidence intervals) following any treatment failure for those who switched combination antiretroviral therapy (cART) and those who did not.

DISCUSSION

This study demonstrates the burden of treatment failure experienced by a contemporary cohort of PHIVA in Asia on cART, including issues relating to the implementation of virologic monitoring, the small proportion of PHIVA switching cART following treatment failure, and the divergence in outcomes for those who switched cART compared to those who continued on a failed regimen. The overall treatment failure rate in our PHIVA cohort of 3.8 per 100 person-years is lower than that reported by a previous Thai study, which found a virologic treatment failure rate of 7.4 per 100 person-years for adolescents aged 10–13 years and 10.8 per 100 person-years for adolescents aged 14–16 years [19]. The treatment failure rate in our cohort is also lower than that in a South African adolescent cohort demonstrating a virologic failure rate of 8.2 per 100 person-years [6]. Such differences in treatment failure rates are likely to be influenced by access to HIV VL testing, virologic monitoring strategies (eg, routine vs targeted), and definitions of virologic failure across different clinic settings over different calendar periods. The relatively delayed initiation of cART in our cohort reflects the limited infrastructure and treatment policies (eg, criteria-led initiation) in the Asian region during earlier time periods, which has been similarly reported in other LMICs [20].

Virologic assessment determined 55.1% of treatment failure events in this study, and a corresponding HIV VL was present in 46.9% of immunologic treatment failure events and in none of the clinical treatment failure events. Furthermore, 37.7% of our cohort had <2 HIV VL results despite reasonable follow-up periods. This signifies the challenges in implementing universal routine HIV VL testing in LMICs and the ongoing reliance on immunologic and clinical monitoring. Most sites in this analysis conducted HIV VL testing less frequently than CD4 count testing, and some sites could only offer targeted instead of routine virologic monitoring. Multiple studies have demonstrated low sensitivity and poor positive predictive value of immunologic criteria in determining virologic failure [13–17], leading to unnecessary switches in ART. Even though only 4.7% of our immunologic treatment failure events had concurrently met virologic treatment failure, 92.3% (55/60) of those with a corresponding HIV VL at the time of immunologic treatment failure were unsuppressed. Further benefits of virologic monitoring were realized in improved outcomes for those with treatment failure, with the median CD4 count at diagnosis of virologic treatment failure (341 cells/ μ L) being higher than that for immunologic treatment failure (53 cells/ μ L) and clinical treatment failure (26 cells/ μ L).

Among our PHIVA cohort, 24.4% had experienced treatment failure during childhood. Furthermore, for PHIVA who experienced treatment failure during adolescence, 52.2% experienced treatment failure during childhood and 47.3% were on at least their second cART regimen. This highlights

Figure 2. Trends in median CD4 count (with 95% confidence intervals) following immunologic treatment failure (A) and virologic treatment failure (B) for those who switched combination antiretroviral therapy (cART) and those who did not.

issues with cART durability for those with perinatal HIV infection and the impact this has on choosing subsequent ART regimens. Only 10.6% of treatment failure events resulted in a cART switch, of which the majority were switching from a first cART regimen. The low proportion of cART switches identifies issues with access to subsequent cART regimens, poor adherence influencing decisions to switch cART regimens, and/or the role of antiretroviral resistance testing guiding treatment decisions that is not uniformly reported across our network. The limited use of INSTI-based cART, both evident at baseline and following treatment failure, in part reflects the inconsistent access to such regimens in the

region. The low proportion of cART switches following treatment failure is in keeping with experiences in other LMICs, with a West African analysis in children and young adolescents finding that 21 of 322 (6.5%) first-line treatment failure events were followed by a cART switch [21]. Furthermore, in a cohort of adolescents and adults in Myanmar, the gap between first-line cART failure and switch to second-line cART was higher for adolescents and those with perinatal HIV infection [7].

Our results suggest better virologic and immunologic outcomes for those who switched cART compared to those who did not. This advocates for a more proactive approach to switching

Figure 3. Trends in human immunodeficiency virus (HIV) viral load after any treatment failure for adolescents with perinatally acquired HIV infection who switched combination antiretroviral therapy (cART) (A) and those who did not switch cART (B).

Figure 4. Cumulative incidence of death and loss to follow-up following treatment failure and for those who did not experience treatment failure.

cART regimens following treatment failure, which necessitates access to a broader range of cART regimens coupled with the capacity for enhanced treatment adherence support. Furthermore, our survival analysis revealed that almost 1 in 5 PHIVA who experienced treatment failure either died or was LTFU, compared to 1 in 10 PHIVA without treatment failure, thereby identifying a high-risk population that could benefit from enhanced strategies to improve treatment adherence and engagement in care.

The limitations to this study include its observational nature and the potential for incomplete or inconsistent reporting of data. This analysis may underestimate treatment failure due to survival bias associated with analyzing those who remained in care through to adolescence, and having inclusion criteria that permit only 1 data point (that would not meet virologic treatment failure criteria). There are a lack of treatment adherence data to account for nonadherence in determining treatment failure and evaluating outcomes following treatment failure. Antiretroviral resistance is not uniformly reported across our network and therefore the role of resistance testing in guiding treatment decisions could not be assessed. Missing HIV VL data limited the ability to capture the burden of treatment failure and outcomes following treatment failure. Despite the study period beginning in 2014, treatment failure was defined according to the 2016 WHO guidelines, which differs from the 2013 WHO guidelines by including a CD4 count ≤ 250 cells/ μ L following clinical treatment failure and omitting a CD4 count fall to baseline or below as part of the immunologic treatment failure criteria. The 2016 WHO guidelines were chosen to provide a contemporary evaluation of treatment failure that would be more generalizable in the current context of early cART initiation irrespective of immune status.

In conclusion, while the rates of treatment failure in our cohort are lower than has been reported in other LMICs, there are

consistent concerns relating to timely switching to subsequent cART regimens, which has implications for poorer immunologic and virologic outcomes. This identifies a need to address issues related to accessibility to subsequent cART regimens, the influence of poor adherence in deciding to switch regimens, and the role of antiretroviral resistance testing in confirming treatment failure. Improved implementation of routine HIV VL testing is required to realize the benefits of virologic determination of cART failure with better immune status. Those who experience treatment failure are a high-risk population for attrition and should be the focus of enhanced strategies to maintain treatment adherence and engagement in care.

Notes

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