

Evaluation of Rational Use of Antiretrovirals before the Dolutegravir Transition in Kinshasa, Democratic Republic of Congo

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Abstract

Background: The ultimate goal of AntiRetroViral Treatments (ART) is to achieve complete immune restoration and lasting viral suppression in the infected patient. In order to ensure the efficacy, safety and accessibility of antiretroviral drugs (ARVs), it is recommended that they should be prescribed according to national guidelines; which are evolving with the various recommendations of the World Health Organization (WHO) and the arrival of newer, more effective and safer molecules. **Objective:** The objective of this study was to assess the rational use of Antiretrovirals in patients treated in Kinshasa before the use of Dolutegravir within the national program in order to assess the correct use of these molecules. **Methods:** This work is a descriptive cross-sectional study to assess the rational use of first-line ARVs among People Living with HIV (PLHIV) in different Centers of Treatment (ATCs) in Kinshasa before the introduction of Dolutegravir. The records of patients on ARVs were randomly and rationally selected in 12 different ATCs for HIV in Kinshasa according to three centers per district in the period from June to September 2018. Information on use and consumption of ARVs, compliance with guidelines, change of therapeutic combination as well as their reasons were consulted for the present study. **Results:** 507 files of PLHIV were collected in the various ATCs. 274 (54.1%) were from female patients. The most represented age group was 26 to 35 years with 192 patients (37.9%). The mean duration of first-line treatment for all patients included was 16.30 ± 5.85 months. The most widely used combination of ARVs overall was TDF +

3TC + EFV at 45.4%. 305 (60.2%) PLHIV kept the same first-line treatment molecule throughout the treatment period with an average treatment duration of 12.9 ± 2.77 months. The most common combination found in this population was TDF + 3TC + EFV (69.2%). 202 (39.8%) PLHIV changed treatment molecule yet respecting the first-line combinations. The average duration of treatment for those who changed molecules was 21.43 ± 7.25 months. Before the change, 112 (55.5%) of these patients were using the ZDV + 3TC + EFV combination. After switching, 105 (52%) of the patients used the TDF + 3TC + NVP combination. The first reason for changing molecules was its unavailability (53.3%) in the ATCs. **Conclusion:** Although some banned molecules are still available in some treatment centers, the guidelines on first-line treatments are respected in different centers in Kinshasa.

Keywords

Rational Use, ARVs, Dolutegravir, Kinshasa

1. Introduction

The Human Immunodeficiency Virus (HIV) is a retrovirus that infects humans, and is responsible for Acquired ImmunoDeficiency Syndrome (AIDS), which is a weakened condition of the immune system making it vulnerable to multiple opportunistic infections.

AntiRetroVirals (ARVs) are molecules used to fight HIV infection. The ultimate goal of AntiRetroViral Treatments (ART) is to achieve complete immune restoration and lasting viral suppression in the infected patient. To ensure efficacy, safety and accessibility, antiretroviral drugs are prescribed according to national guidelines. Nowadays, there are several ARV molecules that have different targets in the life cycle of the virus. They work specifically by inhibiting viral replication and, therefore, slowing the progression of infection. With the arrival of new molecules, the management of ARVs is evolving with the various recommendations of the World Health Organization (WHO) [1].

Rational use of drugs implies that patients receive drugs that are appropriate for their clinical condition, in doses that suit their individual needs, for an adequate period of time, and at the lowest cost for themselves and their communities [2]. Irrational drug use is usually the result of inadequate prescription, and can cause or increase adverse events leading to other illnesses or even death [2]. On the other hand, it is important that the extent and severity of these adverse events be established with a view to either reorienting the management policy or communicating them to patients to improve treatment adherence. The principle of essential drugs stipulates that, at the national level, the choice of a drug line must take into account certain criteria such as the effectiveness of the drug, the inherent risks as well as the needs of the population [3].

In the Democratic Republic of Congo (DRC), since the introduction of ARVs,

Reverse Transcriptase Inhibitors (RTI) as well as those of viral Protease (PI) are widely used despite the various changes in care policies [4]. Previously, in DRC, the preferred scheme was a combination of 2 Nucleoside Reverse Transcriptase Inhibitors (NRTI-Lamivudine/3TC and Zidovudine/ZDV) and 1 Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI-Efavirenz/EFV or Nevirapine/NVP) [5]. In the 2017 revision, the new preferred treatment proposed was a combination of 1 NRTI (3TC), 1 Nucleotide Reverse Transcriptase Inhibitor (nRTI-Tenofovir/TDF) and 1 INNRT (EFV) [4]. Until the transition to Dolutegravir, the alternative regimen consisted of 2 NRTI (CBV = 3TC + ZDV) and 1 INNRT (NVP) [4]. This new proposed treatment had the advantage of diversifying the targets of TARV by introducing a nRTI into the preferential treatment. In all cases, respect and observance of these treatment guidelines have always been essential for the success of ART access programs. All changes in treatment regimen done in the past were motivated by WHO recommendations. However, they have never been evaluated by the national program in order to present the adherence to the treatment nor the achievement.

In 2019, the national program adopted a transition plan to introduce Dolutegravir (DTG) into the preferential first-line ART scheme for the DRC [6]. Dolutegravir (DTG) is an ARV of the Integrase Inhibitor (II) class recommended by WHO to improve the management of People Living with HIV (PLHIV) [1]. This new recommendation introduces a molecule with a different target, thus diversifying TARV.

The objective of this study was to contribute to improving the care of People Living with HIV (PLHIV) by reporting on the rational use of Antiretrovirals in patients treated in different Ambulatory Treatment Centers (ATCs) for HIV infection in Kinshasa before the use of Dolutegravir in the national program. This will allow health programs to predict its proper use and make necessary arrangements.

2. Methods

2.1. Type of Study

The present work is a descriptive cross-sectional study to assess the rational use of first-line Antiretrovirals (ARVs) in People Living with HIV (PLHIV) in various Ambulatory Treatment Centers (ATCs) in Kinshasa before the introduction of Dolutegravir.

2.2. Population and Study Periods

Patient records were randomly and rationally selected from 12 different ATCs for HIV in Kinshasa according to three centers per district in the period from June to September 2018. Only complete records of patients on first-line treatment who had come for consultation during this period were consulted for the present study. Therefore, all files which were properly kept at the ATCs during the period of the study were considered.

All the files of patients who had been on ART for more than 6 months, who

had regular consultations in the different ACTs, who had come for consultation during the period of the study without no discrimination were included. The algorithm presented on the included **Figure 1** was used to decide on inclusion.

2.3. Parameters of Interest

Information on the use and consumption of ARVs, compliance with guidelines, change of therapeutic combination as well as their reasons were collected for this study.

2.4. Data Collection and Analysis Methods

Patient data on 1st line treatment were collected on a collection sheet and then transcribed into an Excel spreadsheet. Quantitative data was presented as absolute value and percentage, and others as mean \pm standard deviation.

3. Results

Five hundred and seven (507) files of PLHIV were collected in the different ATCs. Two hundred and seventy-four (274) files, or 54.1%, belonged to female patients and 233, or 45.9%, to male patients. The most represented age group was that of 26 to 35 years with 192 patients (37.9%), followed by that of 18 to 25 years (25.0%), that of 36 to 45 years (21.3%) and those aged 46 to 55 years (12.2%). The mean duration of first-line treatment, before the transition, for all patients included in labor was 16.30 ± 5.85 months.

The most widely used combination of first-line molecules overall is that of Tenofovir (TDF) + Lamivudine (3TC) + Efavirenz (EFV) at 45.4% followed by combinations of TDF + 3TC + Nevirapine (NVP) at 20.7%, TDF + Emtricitabine (FTC) + EFV at 14.6%, TDF + FTC + NVP at 11.6%, Stavudine (d4T) + 3TC + NVP at 5.1% and Zidovudine (ZDV) + 3TC + EFV at 2.6% EFV. All of them are first line combinations prescribed by the national program before the transition.

Three hundred and five (305) PLHIV, or 60.2%, have not switched to first-line ART. The average duration of treatment for those who did not change molecules

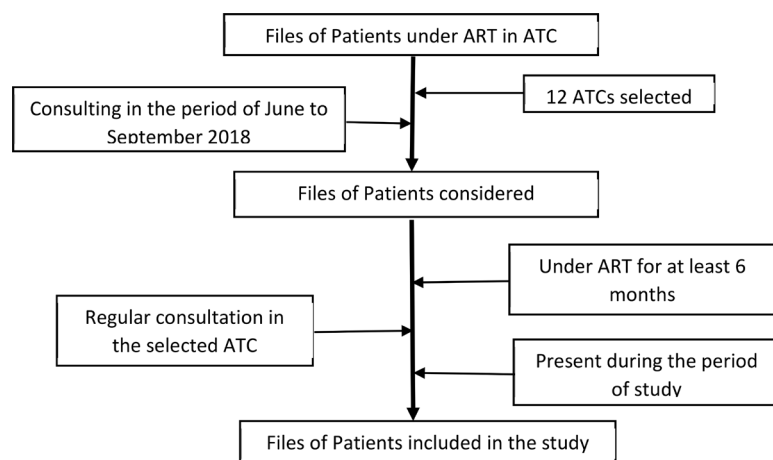


Figure 1. Algorithm used for selection of files.

was 12.9 ± 2.77 months. One hundred and sixty-seven (54.75%) records in this group were female patients while 138 (45.25%) were male patient records. The age group most represented in this group was that of 26 to 35 years old with 123 patients (40.3%), followed by that of 18 to 25 years (30.5%) and that of 36 to 45 years (19.3%).

For this group, the most common combination found in this population was TDF + 3TC + EFV (69.2%), followed by TDF + FTC + EFV (22.6%), ZDV + 3TC + EFV (4.3%), d4T + 3TC + NVP (2.6%) and TDF + FTC + NVP (1.3%).

Two hundred and two (202) PLHIV, or 39.8%, changed one or two treatment molecules, always keeping the first-line combinations. The average duration of treatment for those who changed molecules was 21.43 ± 7.25 months. One hundred and seven (53.0%) records in this group were female patients while 95 (47.0%) were male patient charts. The age group most represented in this group was that of 26 to 35 years with 69 patients (34.1%), followed by that of 36 to 45 years (24.3%) and that of 46 to 55 years (18.8%).

In this second group, before changing molecules, 55.5% of these patients used the ZDV + 3TC + EFV combination, 24.7% used the TDF + FTC + EFV combination, 16.8% used the TDF + 3TC + EFV combination, 2.5% used the d4T + 3TC + NVP combination, and 0.5% used the TDF + FTC + NVP combination. After changing molecules, 52% of patients used the TDF + 3TC + NVP combination, 27.2% used the TDF + FTC + NVP combination, 9.4% used the TDF + 3TC + EFV combination, 8.9% used the d4T + 3TC + NVP combination, and 2.5% used the TDF + FTC + EFV combination.

Table 1 included in the manuscript present all the above state results. The first reason for changing molecules was its availability (53.3%) in the ATCs, followed by the adverse effects declared by the patient (28.5%) and the decisions taken by the prescriber after consultation (18.2%).

4. Discussion

The objective of this study was to assess the rational use of Antiretrovirals in People Living with HIV under first-line treatment treated in different Ambulatory Treatment Centers (ATCs) in Kinshasa before the use of Dolutegravir in the national program.

Five hundred and seven files of PLHIV were collected in the various ATCs. Two hundred and seventy-four records (274), 54.1%, belonged to female patients and 233, 45.9%, to male patients. The sex ratio in favor of women is very common in the setting in the context of HIV infection; several studies present female patients more present than men [7] [8] [9]. The most represented age group was that of 26 to 35 years with 192 patients (37.9%), followed by that of 18 to 25 years (25.0%), that of 36 to 45 years (21.3%) and those aged 46 to 55 years (12.2%). These results are similar to those presented by various studies in our community where the age group most affected by the HIV epidemic is between 18 and 49 years [7] [8] [9]. The mean duration of first-line treatment for all pa-

tients in labor, before transition, was 16.30 ± 5.85 months on ART. This corroborates data from previous studies showing patients followed for 35 ± 8 months on first-line ART before switching to a higher line [10].

The most widely used combination of molecules is that of Tenofovir (TDF) + Lamivudine (3TC) + Efavirenz (EFV), TLE, at 45.4% followed by combinations of TDF + 3TC + Nevirapine (NVP), TLN, at 20.7%, TDF + Emtricitabine (FTC) + EFV, ART, at 14.6%, TDF + FTC + NVP at 11.6%, Stavudine (d4T) + 3TC + NVP, TRI, at 5.1%, and Zidovudine (ZDV) + 3TC + EFV at 2.6%. The national recommendations are more or less respected in the different structures, however, the use of Stavudine puts many questions on the table. This molecule has

Table 1. Characteristics of the population.

Characteristics	Patients who did not switch treatment (n = 305)	Patients who switched treatment (n = 202)	Total (n = 507)
Sex			
Male	138 (45.25%)	95 (47.0%)	233 (45.9%)
Female	167 (54.75%)	107 (53.0%)	274 (54.1%)
Age Interval (years)			
18 - 25	93 (30.5%)	34 (16.8%)	127 (25.0%)
26 - 35	123 (40.3%)	69 (34.1%)	192 (37.9%)
36 - 45	59 (19.3%)	49 (24.3%)	108 (21.3%)
46 - 55	24 (7.9%)	38 (18.8%)	62 (12.2%)
56 - 65	5 (1.6%)	11 (5.5%)	16 (3.2%)
+65	1 (0.4%)	1 (0.5%)	2 (0.4%)
Average duration of Treatment	12.9 \pm 2.77 months	21.43 \pm 7.25 months	16.30 \pm 5.85 months
Treatment			
TDF + 3TC + EFV	211 (69.2%)	19 (9.4%)	230 (45.4%)
TDF + FTC + EFV	69 (22.6%)	5 (2.5%)	74 (14.6%)
ZDV + 3TC + EFV	13 (4.3%)	0	13 (2.6%)
TDF + FTC + NVP	4 (1.3%)	55 (27.2%)	59 (11.6%)
TDF + 3TC + NVP	0	105 (52.0%)	105 (20.7%)
d4T + 3TC + NVP	8 (2.6%)	18 (8.9%)	26 (5.1%)
Previous Treatment			
TDF + 3TC + EFV	--	34 (16.8%)	34 (16.8%)
TDF + FTC + EFV	--	50 (24.7%)	50 (24.7%)
ZDV + 3TC + EFV	--	112 (55.5%)	112 (55.5%)
TDF + FTC + NVP	--	1 (0.5%)	1 (0.5%)
TDF + 3TC + NVP	--	0	0
d4T + 3TC + NVP	--	5 (2.5%)	5 (2.5%)

been officially withdrawn since 2013 [5]. This molecule was banned by the WHO following the various reported adverse effects [6].

Three hundred and five (60.2%) PLHIV kept the same first-line treatment molecule. The average duration of treatment for those who did not change molecules was 12.9 ± 2.77 months. One hundred and sixty-seven (54.75%) records in this group were female patients while 138 (45.25%) were male patient records. The age group most represented in this group was that of 26 to 35 years with 123 patients (40.3%), followed by that of 18 to 25 years (30.5%) and that of 36 to 45 years (19.3%). The most common combination found in this population was TDF + 3TC + EFV, TLE (69.2%), followed by TDF + FTC + EFV, ART (22.6%), ZDV + 3TC + EFV (4.3%), d4T + 3TC + NVP, TRI (2.6%) and TDF + FTC + NVP (1.3%). These combinations comply with the latest national recommendations on the prescription of first-line ARVs [4] [6].

Two hundred and two (39.8%) PLHIV changed treatment molecules, always keeping the first-line combinations. The average duration of treatment for those who changed molecules was 21.43 ± 7.25 months. Longer exposure to ART is always likely to cause resistance to treatments which often lead to changes in molecules [6] [7]. One hundred and seven (53.0%) records in this group were female patients while 95 (47.0%) were male patient charts. In accordance with the literature, the age group most represented in this group was that of 26 to 35 years with 69 patients (34.1%), followed by that of 36 to 45 years (24.3%) and that of 46 to 55 years (18.8%). In this group, before changing molecules, 55.5% of patients used the ZDV + 3TC + EFV combination, 24.7% used the TDF + FTC + EFV combination, 16.8% used the TDF + 3TC + EFV combination, 2.5% used the d4T + 3TC + NVP combination, and 0.5% used the TDF + FTC + NVP combination. These combinations are no longer up to date on the latest recommendations, they are combinations of previous recommendations [5]. After changing molecules, 52% of patients used the TDF + 3TC + NVP combination, 27.2% used the TDF + FTC + NVP combination, 9.4% used the TDF + 3TC + EFV combination, 8.9% used the d4T + 3TC + NVP combination, and 2.5% used the TDF + FTC + EFV combination. The combinations after switching are closer to current treatment recommendations [4] [6]. Hence the regular change of ART guidelines may be the cause of non-compliance with these recommendations.

Nevertheless for this group, according to the data, the first reason for changing molecules was its availability (53.3%) in the ATCs, followed by adverse effects in the patient (28.5%) and decisions taken by the prescriber (18.2%). This is justified because the supply is made by the national programs which adapt their stocks according to the decisions to change molecules.

5. Limitations of the Study

This is a descriptive cross-sectional study based on patients' files and records. Therefore, only available patients' data have been collected to be presented. The type and the restriction of the study did not allow to record additional informa-

tion such as clinical and biological data of patients. Only available data on patients files could be presented.

6. Conclusion

Although some banned molecules are still available in some treatment centers, the guidelines on first-line treatments are respected in the Kinshasa treatment centers.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations and Acronyms

3TC: Lamivudine
ART: AntiRetroViral Treatment
ART^o: TDF + FTC + EFV
ARV: Antiretroviral
ATC: Ambulatory Treatment Center
CBV: ZDV + 3TC
d4T: Stavudine
DRC: Democratic Republic of Congo
DTG: Dolutegravir
EFV: Efavirenz
FTC: Emtricitabine
HIV: Human Immunodeficiency Virus
II: Inhibitor of Integrase
NVP: Nevirapine
NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor
nRTI: Nucleotide Reverse Transcriptase Inhibitor
NRTI: Nucleoside Reverse Transcriptase Inhibitor
PI: Protease Inhibitor
PLHIV: Person Living With HIV
RTI: Reverse Transcriptase Inhibitor
TDF: Tenofovir
TLE: TDF + 3TC + EFV
TRI: d4T + 3TC + NVP
TRV: TDF + FTC
WHO: World Health Organization
ZDV: Zidovudine.