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Original Research Article

Retrospective analysis of a cohort of HIV-infected patients on antiretroviral therapy in Abidjan (2003 to 2017)

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ABSTRACT

Background: Antiretroviral therapy (ART) has been successful in improving clinical outcomes for HIV-positive patients, but efforts are needed to improve life expectancy and quality of life. This study aimed to analyze a long-term ART cohort and assess patients' life expectancy.
Methods: A retrospective cohort study was conducted at the infectious and tropical diseases department of the University Teaching Hospital of Treichville from 2003 to 2017. Data analysis was done using VBA access and XLSTAT 2018 excel software. Patients on post-exposure chemoprophylaxis and prevention of mother-to-child transmission were excluded.
Results: Out of 19,567 patient records, 49.60% were included, 72.43% were in 1st line, and 50.10% were over 50 years old, mostly female 58.49%, 98.4% HIV1. 74.31% had a CD4/mm^3 (Nadir) count <350. The patients were essentially on the 2IN+INN regimen (72.31%), TDF + XTC + EFV (20.57%). The average duration under treatment 6.15 [0-13.67] ±3.94 years, the average duration under a line of treatment 4.33 [0-14.04] ±2.96 years. Life expectancy was 10.37 years. It is higher in patients on 2IN+IPr (12.21 years) versus 10.12 years in patients on 2IN+INN. The comparison of duration on a line according to the CD4 counts and the line of treatment did not show a significant difference p>0.05.
Conclusions: The study concluded that ART significantly improved the life expectancy of patients, adherence could be improved to further enhance the benefits of ART. The use of new combinations of ART may reduce events related to non-compliance.

Keywords: Life expectancy, HIV, ART, University Teaching Hospital of Treichville

INTRODUCTION

The expansion and scaling up of access to antiretroviral therapy (ART) has improved clinical outcomes for HIV-positive patients in resource-limited countries.[1] Overall, results from program studies have all demonstrated a decrease in mortality and reduction in opportunistic infections, as well as restoration of immunity with a gain in CD4 counts in infected patients on ART.[2-5] International recommendations have gradually increased CD4 levels; from 200 cells/µl to 350 cells/µl and 500 cells/µl in 2003, 2010 and 2013 respectively.[6] The new 2016 recommendations call for universal treatment for all HIV-infected patients regardless of CD4 level.[6]

In Côte d'Ivoire, through the support of donors (Global Fund, PEPFAR, World Bank) in December 2007, accessibility to antiretroviral was largely improved. According to UNAIDS estimates, there is a decline in prevalence among the general population, which fell from 4.7% in 2005 to 3.4% in 2009.[6] The number of functional HIV transmission prevention sites from mother to child has reached the number of 554 (in 2009) out of the 720 health centers offering ANC, i.e. a coverage of 77%. There

are currently 549 VCT sites, representing 95% health district coverage. The number of people on treatment increased from 32.30% in 2006 to 48% in 2009.

The infectious and tropical diseases department is the reference center for the care of patients infected with HIV AIDS in Côte d'Ivoire. Consisting of a multidisciplinary team (physicians, pharmacists, nurses, social workers, counselors), it provides clinical and therapeutic activities as well as clinical trials. It is the ideal service to evaluate the decade of care for HIV-infected patients in Côte d'Ivoire in the context of a country with limited resources. It houses a pharmacy dedicated to the storage and dispensing of treatments.[7]

To our knowledge, very few studies of antiretroviral management in patients examine outcomes of efficacy of triple antiretroviral therapy, long-term survival of patients with more than 10 years of follow-up as well as long-term side effects ,[8-10] and long-term information from other cohort studies and clinical trials is scarce.[11,12]

After more than a decade of caring for infected patients living with HIV AIDS at the University Teaching Hospital of Treichville, it is important to take stock of the activity of dispensing antiretroviral drugs in this department. The purpose of this article is to retrospectively analyze patient data by highlighting the role of the pharmacist in the activities of dispensing antiretroviral drugs through a long-term ART cohort (ALT).

METHODS

Type of study

This was a retrospective cohort study of HIV-infected patients in the department of infectious and tropical diseases of the University Teaching Hospital of Treichville in Abidjan from 2003 to 2017 (14 years). It used information collected in the database (PILOT ARV).

Patients

These were treatment-naive patients taking their antiretroviral medications in the in-house pharmacy. These patients met the criteria for initiation of treatment published in all WHO recommendations. Patients on exclusive cotrimoxazole, chemoprophylaxis of post-exposure antiretroviral therapy and prevention of mother-to-child transmission were excluded from the study.

The department also has an inpatient unit and an outpatient unit. The clinical unit has about 120 beds for the hospitalization of patients with infectious and tropical diseases. Patients are put on treatment during outpatient consultations. Antiretroviral medication is provided by a multidisciplinary team of hospital practitioners, pharmacists, nurses and social workers. A weekly meeting is held by the team to ensure the start of the treatment. The pharmacy is located in the outpatient unit. It includes all the facilities to ensure the dispensation of ARVs in complete confidentiality (antiretroviral drugs under key, locked cupboard.

Pilot ARV databases

This database was designed by the pharmacists of the said department and the applications were made ergonomic within the framework of the IDEA project. The software was made from the ACCESS program associated with visual basic application. It has several tabs (Initial assessment; Patient follow-up, stock management and drug dispensing). It is a software to assist in the dispensation and management of antiretroviral drugs. Patient data are recorded daily in the database. This tool makes it possible to monitor the regularity of patient follow-up and to track lost patients. The software allows to measure the patients' compliance, to do the medication reconciliation and to avoid iatrogenic errors and drug interactions. This software allows to give the computerized history.

Dispensation

Pharmacists dispense antiretroviral drugs and counsel patients to optimize treatment. They reinforce the therapeutic education of patients with the help of counselors and social workers.

Supply chain

In the Republic of Cote d'Ivoire, HIV commodities are almost exclusively funded and procured by international donor agencies such as the global fund to fight AIDS, tuberculosis and malaria (GFATM) and the United States President's emergency plan for AIDS relief (PEPFAR). The New Public Health Pharmacy is responsible for stockpile and drug management. It oversees the entire drug supply system, while the Ministry through the National HIV/AIDS care program develops national guidelines on HIV treatment. Each province has a provincial warehouse operated as a semi-independent entity under contract by donors for the storage and distribution of drugs to the various health zones.

Measured information

The PILOT ARV database allowed us to collect information: frequency of prescriptions patients, biological monitoring, and duration on a treatment line and life expectancy on treatment.

Ethical consideration

This study was conducted with due regard to the protection of patients' privacy by anonymizing the data used in the study. The study was carried out in compliance with the rights and safety of patients, ensuring that the dignity of the patients is always respected.

Statistical analysis of data

Data analysis was performed using PILOT VBA Access and XLSTAT 2018 excel. Differences were considered significant at a=5% risk. Chi-square and Kruskal–Wallis tests were used for sample comparison.

RESULTS

Of the 19567 patient records collected, 50.40% were excluded for lack of information and missing data. A total of 330057 prescriptions were dispensed to the 9706 patients included in our study during our study period (Figure 1).

In total, out of the 9706 patients collected, 7030 (72.43%), 2589 (26.67%), 87 (0.90%) were respectively in 1st, 2nd and 3rd line treatment. 58.49% were female, 98.49% were HIV 1, the majority (72.31%) on the 2IN +INN protocol (Table 1). In 2017, the treatment line was mainly the TDF+3, F (TC) combination (20.57%) during the study period (Table 2). Prior to 2017, the average time on treatment for patients was 6.15 years with extremes of 0 and 14.04 years. The average time on a line of treatment was 4.33 years with lows at 0 and highs at 13.67 years (Table 3).

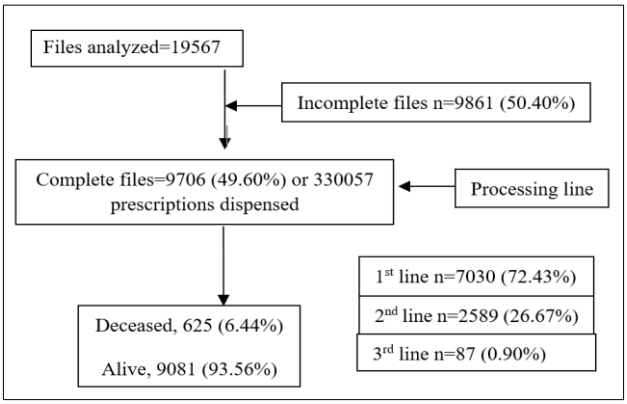

Figure 1: Patient cohort.

The average age at treatment initiation was 39.92 years and 50.29 years during our study period. The average duration of treatment was 10.37 years. With 12.21 years, the line of treatment that had the greatest impact on the life expectancy of patients was the 2nd line (Table 4).

Table 1: General population characteristics.

Characteristics	1st line	2nd line	3rd line	Total (%)	P*
Age (years)					
<50	3645	1141	57	4843 (49.90)	< 0.0001
≥50	3385	1448	30	4863 (50.10)	
Sex					
F	4167	1462	48	5677 (58.49)	<0.05
M	2863	1127	39	4029 (41.51)	
Weight (kg)					
<30	324	109	1	434 (4.47)	<0.0001
30–70	5399	2052	83	7534 (77.62)	
≥70	1307	428	3	1738’17.91)	
Karnosky (%)					
<70	3501	1276	80	4857 (50.04)	<0.0001
≥70	3529	1313	7	4849 (49.96)	
Viral type					
1	6991	2481	87	9559 (98.49)	<0.0001
2	20	74	0	94 (0.97)	
3	19	34	0	53 (0.55)	
CD4/mm^3 (basic)					
<350	919	295	22	1236 (74.15)	0.91
350-500	153	46	5	204 (12.24)	
≥500	168	56	3	227 (13.62)	
Treatment					
2IN + IG		1	23	24 (0.25)	
2IN + INN	7017	0	1	7018 (72.31)	
2IN + IP	13	463	0	476 (4.90)	
2IN + IPr		1451		1474 (15.19)	
2IN + IPr + IG			63	63 (0.65)	
3IN		674		674 (6.94)	
Grand total	7030 (72.43)	2589 (26.67)	87 (0.90)	9706 (100)	

P* value Kruskal-Wallis test, IN: nucleoside reverse transcriptase inhibitor; NNI: non-nucleoside reverse transcriptase inhibitor PI: protease inhibitor IG: integrase inhibitors

Table 2: Treatment regime according to the lines.

Line	1er line	2e line	3e line	Total (%)
ABC + 3TC + EFV	226			226 (2.33)
AZT + 3TC + EFV	1603			1603 (16.52)
AZT + 3TC + NVP	776			776 (8.00)
D4T + 3TC + EFV	1289			1289 (13.28)
D4T + 3TC + NVP	873			873 (8.99)
TDF + 3, F (TC)+ EFV	1997			1997 (20.57)
ABC + 3TC + AZT		500		500 (5.15)
ABC + 3TC + LPV + RTV		101		101 (1.04)
AZT + 3TC + IDV + RTV		133		133 (1.37)
AZT + 3TC + LPV + RTV		260		260 (2.68)
D4T + 3TC + IDV		112		112 (1.15)
D4T + 3TC + IDV + RTV		111		111 (1.14)
TDF + 3, F (TC) + LPV + RTV		320		320 (3.30)
ABC + 3TC + R; D (LT)			18	18 (0.15)
ABC + 3TC + DRV + RTV			3	3 (0.03)
ABC + 3TC + RLT			6	6 (0.06)
ABC + 3TC +DRV + RLT + RTV			2	2 (0.02)
AZT + 3TC + RLT			2	2 (0.02)
AZT + 3TC + TDF + DRV + RTV			1	1 (0.01)
TDF + 3TC + DLT			13	13 (0.13)
TDF + 3TC + DRV + RTV			8	8 (0.08)
TDF + 3TC + DRV + RTV + DLT			34	34 (0.35)
AUTRES	266	1050		1316 (13.50)
Total	7030	2587	87	9706

Table 3: Average time on treatment in years and on one line.

Parameters	Duration of treatment (years)	Duration under line (years)
Average [min, max]± σ	6.15 [0-14.04] ±3.94	4.33[0-13.67] ±2.96
Median (year)	5.81	3.84

Table 4: Life expectancy and average duration on a protocol.

Line	Protocol	Initial age (years)	Current age (years)	Average duration (years)
1st	2IN + INN	39.78	49.90	10.12
2nd	2IN + IP	40.96	53.17	12.21
	2IN + IPr	40.14	50.93	10.79
	3IN	39.92	50.62	10.70
3rd	2IN + IPr	40.39	49.61	9.22
	2IN + IPr + IG	43.22	48.03	4.81
Grand total		39.92	50.29	10.37

With an age difference of 10.56 years, men had the highest life expectancy during the study period with 53.35 (Table 5).

CD4 gain averaged linearly with an increasing positive correlation coefficient. Growth in CD4 gain was observed over the study period (Figure 2).

The number of prescriptions dispensed has evolved steadily since 2003, even if we observe a sawtooth growth (Figure 3).

No significant difference was observed between CD4 gain, treatment line and life expectancy of patients (Table 6).

Table 5: Life expectancy and gender.

Sex	Initial age	Current age	Age difference (years)
F	37.98	48.21	10.23
M	42.79	53.35	10 .56
Grand total	39.92	50.29	10.37

Table 6: CD4 and treatment lines.

Line duration (years) CD4 rate	Processing line				P value*
≤5	**1st line**	**2nd line**	**3rd line**	**Grand total**	
CD4 ≤350/mm³	655	225	22	902	
350 mm³<CD4≤500 mm³	109	28	5	142	0.052
CD4 >500 mm³	126	42	3	171	
6-10 years					
CD4 ≤350/mm³	190	51	0	241	
350 mm³<CD4 ≤500 mm³	32	14	0	46	0.095
CD4 >500 mm³	24	13	0	37	
>10 years					
CD4 ≤350/mm³	74	19	0	93	
350 mm³<CD4≤500 mm³	12	4	0	16	0.095
CD4>500 mm³	18	1	0	19	
Grand total	1240	397	30	1667	

* Kruskal-Wallis test

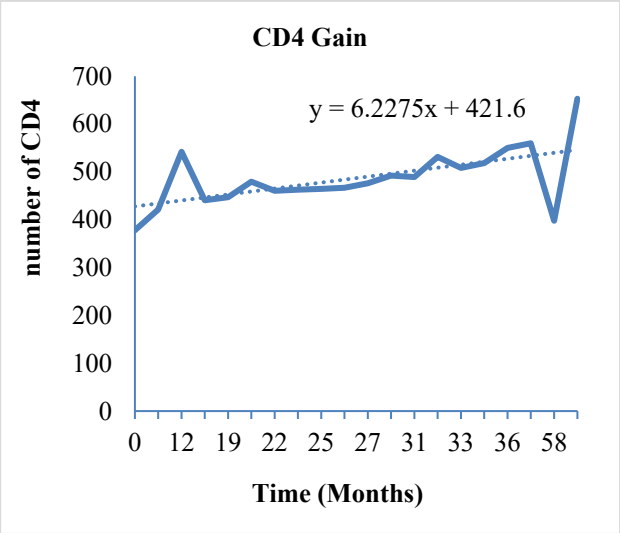

Figure 2: Evolution of the average CD4 rate in the cohort.

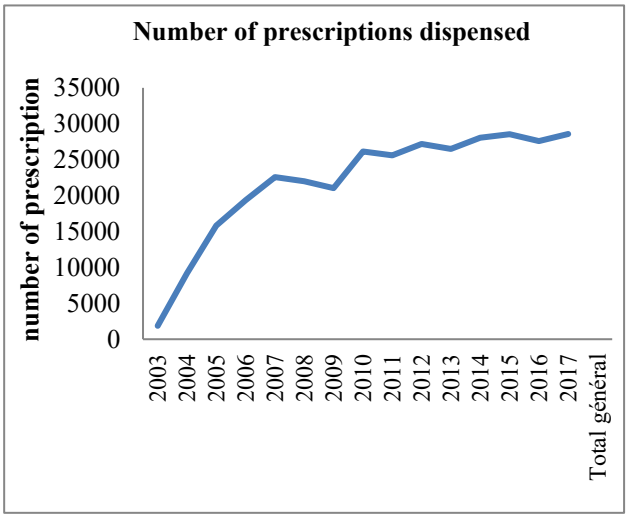

Figure 3: Number of prescriptions dispensed per month.

DISCUSSION

This study showed that the majority of patients 7030 (72.43%) were on 1st line HIV treatment. The results of this study indicating that the majority of HIV patients were treated in the first line are consistent with the treatment protocols recommended by the World Health Organization (WHO) for the management of HIV. First-line drugs for HIV treatment include nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs).[13] Previous studies have also shown that the use of first-line drugs for HIV treatment is associated with significant improvement in patient survival.[14,15] Long-term use of these drugs can lead to drug resistance and treatment failure. Therefore, WHO recommends regular monitoring of viral load and assessment of drug resistance in HIV patients on treatment to ensure treatment efficacy.[13] Studies have shown that regular monitoring of viral load and drug resistance can improve long-term health outcomes for HIV patients.[16,17] Overall, the results of this study in Côte d'Ivoire are consistent with WHO recommendations for HIV management and underscore the importance of regular monitoring of viral load and drug resistance in patients on treatment.

The combination therapy of 2IN and IN (72.31%) was the most prescribed therapy over time in the infectious and tropical diseases department. This profile and patient characteristics are consistent with national recommendations in Côte d'Ivoire during the study period. In fact, compliance with national recommendations for prescribing ARV drugs has reduced the risk of errors and drug-related iatrogenic. The progressive substitution of stavudine or indinavir according to WHO recommendations was observed in the treatment of HIV/AIDS in the centers, which reduced adverse effects such as peripheral neuropathy.[18]

This study also showed the introduction of new therapeutic classes, dolutegravir in fixed combinations with 2IN

(tenofovir/lamivudine). These combinations are more effective and better tolerated and allow for increased adherence.[18]

Between 2003 and 2017, the mean duration on treatment overall regardless of treatment line was 6.15 [0-13.67] ±3.94 years in the cohort. ARV treatment kept some patients alive until the time of the study. The study results showing an average treatment duration of 6.15 years are interesting, as they provide information on the duration of treatment for patients with infectious and tropical diseases. However, it is important to note that the duration of treatment can vary depending on many factors, including disease severity, patient response to treatment, drug tolerance, and other individual factors. Comparing these findings with other data in the literature, examining the characteristics of HIV patients on antiretroviral (ARV) therapy in sub-Saharan Africa, the authors showed that the average duration of treatment was 47.5 months, or approximately 3.95 years.[19] This is shorter than the average duration of treatment reported in the study.

The mean duration under one line of treatment was 4.33 [0-14.04] ±2.96 years. The study results showing a mean duration of treatment per line of 4.33 years are interesting, as they provide information on the duration of treatment for patients with infectious and tropical diseases. The duration of treatment per line among HIV patients in Thailand was 3.6 years.[20]

Life expectancy was 10.37 years. It was higher in patients on 2IN+IPr (12.21 years) compared to 10.12 years in patients on 2IN+INN. The results of the study showing a life gain expectancy of 10.37. Life gain expectancy can vary depending on many factors, including disease severity, age, gender and other individual factors. A study examining the life expectancy of HIV patients in North America and Europe showed that the life expectancy of HIV patients has increased significantly in recent years, from 32 years in 1996 to 50 years in 2007. This suggests that advances in treatment have significantly improved clinical outcomes for HIV patients.[21]

The results in Switzerland showed that the life expectancy of HIV patients were 54.4 years, which is considerably higher than the average life expectancy of the Swiss population (82 years). This suggests that advances in treatment have significantly improved the clinical outcomes of HIV patients.[22]

Increasing CD4 counts is a major goal of antiretroviral therapy. Previous studies have also shown an increase in CD4 with regular use of ARV drugs. For example, a study by Vitoria et al (2009) reported a mean CD4 increase of 50 cells/mm³ after six months of ARV therapy in sub-Saharan Africa.[23] In addition, a more recent study showed a mean CD4 increase of 220 cells/mm³ after 12 months of ARV therapy in HIV patients in Ethiopia.[24]

These results suggest that CD4 increase is an expected and common effect of antiretroviral therapy and that the observation of this growth in this study is consistent with findings in the literature. However, it is important to note that CD4 increase may vary depending on many factors, including severity of infection, duration of infection, initial viral load, and adherence to antiretroviral therapy.

The linear increase in CD4 gain observed in this cohort is consistent with the results of other studies in the field of HIV/AIDS treatment. Indeed, a study conducted in India also exposed an increase in CD4 count with prolonged treatment duration in patients on antiretroviral therapy.[25] Another work in Europe also showed that duration of antiretroviral therapy was positively associated with increased CD4 counts.[26]

The results of this study suggest that there is no significant difference between CD4 gain, treatment line, and patient life expectancy. However, it should be noted that these results may differ between studies depending on the study population and the methods used to measure these variables.

The authors found that switching from the first line of treatment to the second line was associated with a decrease in life expectancy among patients, although this difference was not statistically significant.[27]

Regarding CD4 gain, a study, in China showed that patients on antiretroviral therapy with an initial high viral load tended to have a greater increase in CD4 count after 12 months of treatment compared with patients with a lower initial viral load.[28]

Ultimately, the results of this study should be interpreted with caution, as they are based only on data from this specific cohort and cannot be generalized to other populations or settings.

CONCLUSION

ART has significantly increased the life expectancy of HIV-infected patients.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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