



## RESEARCH PAPER

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## Clinical and immunological profile at the initiation of antiretroviral treatment of HIV-infected patients according to the evolution of WHO recommendations in National Center for Blood Transfusion, Abidjan Cote d'Ivoire

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### Abstract

This retrospective study consisted to show the interest of the various modifications of the WHO guidelines on the clinical, biological parameters of patients HIV. It was conducted with patients followed at the National Center for Blood Donors between 2006 and 2016. Methods: 351 patients were selected and divided into three groups. Group 1 (G 1) had an average level CD4 equal to or less than 200 cells/mm<sup>3</sup>. For the Group 2 (G 2) the number of CD4 was between 200 and 350 cells/mm<sup>3</sup> and the Group 3 (G 3) had a CD4 count of between 350 and 500 cells / mm<sup>3</sup>. These patients were monitored and received regular treatment during 18 months. Blood samples were taken every 6 months and clinical and laboratory assessments were performed. Results: the patients had an average CD4 value of  $290 \pm 8.89$  cells/ mm<sup>3</sup>. The Body Mass Index had increased in G 2 and G 3. CD4 was from  $111.3 \pm 5.48$  cells / mm<sup>3</sup> to  $327.7 \pm 12.16$  cells / mm<sup>3</sup> in G 1, then from  $263.4 \pm 4.16$  cells/mm<sup>3</sup> to  $401.7 \pm 28.37$  cells/mm<sup>3</sup> in G 2 and finally from  $423 \pm 4.18$  cells/mm<sup>3</sup> to  $643.3 \pm 27.60$  cells/mm<sup>3</sup> in G 3. Serum creatinine had increased of 11.71% in G 2 and decreased of 12.73% in G 3. Glutamic Pyruvic Transaminases levels decreased by 6.37% in G 3. Conclusion Antiretroviral therapy initiated at the early stage of infection has benefits on clinically and immunologically changes.

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## Introduction

The introduction of tri-therapy in 1996 has created real hope for people living with HIV/AIDS. This treatment could prolong the life expectancy of these patients. It consists of the combination of three antiretroviral molecules able to inhibit viral replication. Antiretroviral therapy (ART) has resulted in a restoration of CD4 count and reduction of viral load in the body. This treatment was first initiated in industrialized countries and later in developing countries (Desenclos *et al.*, 2013). In 2001, during its special session on HIV, the United Nations set itself the task of facilitating access to ART in resource limited country (ONU, 2001). The purpose of this decision was to reduce disparities between rich countries in the north and very poor in the south because of the expensive cost of such therapy.

Since then, the prognosis of the infection has really changed. The life expectancy of people with HIV / AIDS increased and was similar to that of uninfected people in both industrialized and developing countries (Lepère and Milleri, 2015).

ART initiation at that time was performed at a CD4 threshold of less than 200 cells/mm<sup>3</sup> for all HIV-positive patients in these countries according to WHO recommendations (OMS, 2002). Until 2006, the WHO recommendations announced systematic treatment for any asymptomatic HIV-infected person at the CD4 threshold of less than 200 cells / mm<sup>3</sup> (OMS, 2006). That same year, Professor Yéni and his team gave interesting results in favor of early antiretroviral therapy (Yéni, 2006). This treatment would have the advantage of reducing HIV-related mortality, morbidity and risk of transmission (Bettayeb, 2013).

This theory raised concerns about the potential toxicity of antiretroviral and the risk of developing long-term virus resistance (Piroth, 2008). Nevertheless, it was adopted and the recommended rate was 350 cells / mm<sup>3</sup> in 2010 in southern countries (OMS, 2010). The years that followed were marked by the publication of new WHO

recommendations that introduced tri-therapy at 500 cells / mm<sup>3</sup> in 2013 (OMS, 2013) and systematic treatment for all people with HIV/ AIDS in 2015 (OMS, 2015).

The implementation of these recommendations in Côte d'Ivoire, one of the countries most affected by this pandemic in West Africa (Krou *et al.*, 2012), has led to reformulations of protocols for monitoring patients infected by HIV at the National Center of Blood Donors for the last ten years.

This work is a retrospective study from 2006 to 2016 and its main objective is to show the impact of the different WHO recommendations on the clinical, biochemical and immunological parameters of patients.

## Material and methods

### *Framework and study population*

The study was conducted at the National Center for Blood donors located in Abidjan (Ivory Coast). 351 individuals were selected among patients registered between 2006 and 2016.

The inclusion criteria were as below: HIV patients, men or women between the ages of 18 and 60, who started ART for the first time and monitored regularly for at least 18 months Patients co-infected with viral hepatitis (C or B) and tuberculosis, Irregular patient at the medical follow-up and those whose follow-up did not reach 18 months were excluded from this population.

The population was subdivided into three (3) groups. The group 1 (G 1) consisting of 130 patients whose initial CD4 count was less than or equal to 200 cells / mm<sup>3</sup>, they were selected between 2006 and 2009. The group 2 (G 2), selected between 2010 and 2013, was 114.

They had an initial CD4 count of between 200 and 350 cells / mm<sup>3</sup>. And lastly group (G 3) consisting of 107 people whose initial CD4 count was between 350 and 500 cells / mm<sup>3</sup>. This group was recruited

between 2014 and 2016. These subdivisions took into account the different WHO recommendations applied for the care of patients.

#### *Treatments*

During the 18 months of the study, the selected patients received antiretroviral treatment. Blood samples were taken every 6 months: at the initiation of trip-therapy ( $M_0$ ), the sixth month ( $M_6$ ), the twelfth month ( $M_{12}$ ) and the eighteenth month ( $M_{18}$ ). Clinical, biochemical and immunological parameters were measured.

#### *Clinical data*

The clinical parameters measured are as follows:

**Body Mass Index (BMI):** It is measured using a height chart (m) and a weight gain scale (kg). It is obtained by the ratio of the body mass on the size squared:

$$IMC = \frac{m}{t^2}$$

**The karnofsky index (KI):** it is a stratified scale of 0 to 100% which makes it possible to estimate the capacity of mobility of the patients.

**Brachial Perimeter (BP):** refers to the circumference of the arm measured between the shoulder and the elbow in the middle of the brachial biceps. It allows to estimate the lean mass of the patient and is measured in mm with a tape measure.

#### *Immunological parameters*

It was done using Muse made by Guava Auto Technologies (USA). This flow cytometer measures the total lymphocytes (CD4) in the blood. Whole

blood is collected in special tubes contained an anticoagulant (EDTA).

#### *Hematological parameters*

Hematologic parameters such as white blood cells, platelets and hemoglobin levels were measured using the SYSMEX KX-2IN controller.

The blood samples taken for this purpose were collected in the EDTA tubes, homogenized and brought to the automaton for analysis.

#### *Biochemical parameters*

A FULLY automate was used to measure blood glucose, serum creatinine and pyruvic glutamic transaminases (TGP). Blood samples were taken in tubes without anticoagulant and centrifuged at 4000 rpm for 5 minutes. After decantation for 10 to 15 minutes, 20  $\mu$ l of serum were taken and distributed in microtubes for analysis.

#### *Data processing*

The processing of data was performed using Anova one-way of Graph Pad Prism software version 5.01 (Microsoft USA). The results were expressed as mean  $\pm$ SD (standard deviation) and the statistical analysis of the data was performed by Turkey's multiple comparison test. The test was considered significant at a value of  $p < 0.050$

## **Results-discussion**

#### *Clinical parameters*

##### *Body mass index (BMI)*

The results of the study of the body mass index are shown in table 1.

**Table 1.** Body mass index measured during treatment.

Group(G)	$M_0$ (BMI(kg/mm <sup>2</sup> ))	$M_6$ (BMI (kg/mm <sup>2</sup> ))	$M_{12}$ (BMI (kg/mm <sup>2</sup> ))	$M_{18}$ (BMI (kg/mm <sup>2</sup> ))
G 1	21,96 $\pm$ 0,41	22,35 $\pm$ 0,62	22,39 $\pm$ 0,54	22,62 $\pm$ 0,62
G 2	22,08 $\pm$ 0,62	22,78 $\pm$ 0,57	24,36 $\pm$ 0,79	24,77 $\pm$ 0,71*
G 3	24,82 $\pm$ 0,52	25,34 $\pm$ 0,61*	25,33 $\pm$ 0,68	25,94 $\pm$ 1,37

$M_0$ : initiation of treatment,  $M_6$ : sixth month of treatment,  $M_{12}$ : twelfth month of treatment and  $M_{18}$ : eighteenth month of treatment.

G 1: CD4 cell count  $\leq$  200 cells / mm<sup>3</sup>, G 2: CD4 cell count between 200 and 350 cells / mm<sup>3</sup> and

G 3: CD4 cell count between 350 and 500 cells / mm<sup>3</sup>. \* :  $p < 0,05$ .

BMI has increased significantly ( $p < 0.05$ ) compared to  $M_0$  in G2 and G3. These increases were respectively to 12,18% after 18 months and to 2,09% after 6 months.

The average values of BMI obtained in these groups at the beginning are relatively similar to those measured by Kouakou and Attia (2009), Kouamé (2010) and

Sako *et al.* (2012). In fact, Kouakou and Attia (2009) obtained an initial BMI equal to 19.8 kg / m<sup>2</sup> for patients with a CD4 count of 148 cells / mm<sup>3</sup>. Regarding Sako *et al.* (2012), they had an average BMI of 21.40 kg / m<sup>2</sup> in patients with an initial CD4 count of 242 cells / mm<sup>3</sup>. Kouamé (2010) measured a BMI of  $23.5 \pm 3.7$  kg / m<sup>2</sup> for patients with an initial mean CD4 count of 457 cells / mm<sup>3</sup>.

**Table 2.** Evolution of hematological parameters during treatment.

hematological parameters	Groups	$M_0$	$M_6$	$M_{12}$	$M_{18}$
White blood cells (cells/mm <sup>3</sup> )	G 1	4466±115,6	4231±171	4560±259,2	4433±179,7
	G 2	4231±192,6	4252±191,1	3931±134,8	4081±174
	G 3	4646±146	4320±115	4328±167,6	4355±179,7
Hemoglobin (g/dl)	G 1	11,40±0,18	11,70±0,23	11,56±0,27	11,81±0,25
	G 2	11,40±0,22	11,65±2,22	11,73±0,24	11,66±0,23
	G 3	12,11±0,18	12,43±0,16	12,52±0,24	12,76±0,25
Platelets (cells /mm <sup>3</sup> )	G 1	247,2±8,078	249,3±13,98	241,9±13,68	268±17,47
	G 2	269,9±11,92	269,4±12	259,3±12,37	256±10,6
	G 3	231,1±7,82	244,1±8	237,5±8,61	230,6±9,28

$M_0$ : initiation of treatment,  $M_6$ : sixth month of treatment,  $M_{12}$ : twelfth month of treatment and  $M_{18}$ : eighteenth month of treatment.

G 1: CD4 cell count  $\leq 200$  cells / mm<sup>3</sup>, G 2: CD4 cell count between 200 and 350 cells / mm<sup>3</sup> and

G 3: CD4 cell count between 350 and 500 cells / mm<sup>3</sup>.

This study did not show any significant variation in G 1 during the period of treatment. This result corroborates those of Tovi (2014). significant increases ( $p < 0.05$ ) of BMI in G 2 and G 3, are similar to the results of Koy *et al.* (2014). These authors obtained a significant ( $p < 0.01$ ) increase in the BMI of patients on ART after 12 months of follow-up. These different results obtained of BMI as a function of the initial CD4 level confirm the results obtained by Kouakou and Attia (2009). Their results showed a correlation between the CD4 count and the change in body mass index. Thus, the weight gain would be higher in patients with high CD4 count at initiation of ART.

#### Karnofsky index (KI)

KI reached to 100% in G1 and G2 After six months of treatment. However, these increase in measured KI in G 1 and G 2 was not significant compared to  $M_0$  (Figure 1) Sako *et al.* (2012) had less than 100% KI in

patients whose mean CD4 count was less than 350 cells / mm<sup>3</sup> at initiation of triple therapy.

These results are different from those obtained by Tovi (2014). She had, indeed, obtained 100% KI for CD4 level equal to 200 cells / mm<sup>3</sup> at the initiation of antiretroviral treatment. KI below 100% in the studied group reflects, indeed, the presence of morbidity cases (Stage 3 and 4 of HIV according to WHO) in the population. According to Moh (2014), morbidity is associated with a low CD4 count. After six months of treatment, KI reaches the optimum level of 100% in G 1 and G 2. These results reflect the effectiveness of antiretroviral therapy.

#### Brachial Perimeter (BP)

The evolution of BP in G1 and G3 was not significant during the traitement. On the other side, BP increased significantly in G 2 between  $M_0$  and  $M_{18}$ , ranging from  $290 \pm 8.944$  mm to  $391.5 \pm 15.62$  mm.

This increase was of 32.96%. (Figure 2). Brachial perimeter values measured in G 2 showed a very significant increase ( $p < 0.01$ ) similar to the results obtained by Koy *et al.* (2014). Changes in brachial perimeter indicate an increase or decrease in energy reserves. There is, in fact, a link between HIV

infection and the nutritional status of patients. During an HIV infection, the immune system activates to fight against the invasion of the virus. This activation causes profound changes that can disrupt the patient's metabolism (Hommes *and al.*, 1991).

**Table 3.** Evolution of biochemical parameters as a function of the initial CD4 level at initiation of treatment.

Biochemical parameters	Groups	M <sub>0</sub>	M <sub>6</sub>	M <sub>12</sub>	M <sub>18</sub>
serum creatinine (UI/l)	G 1	8,95±0,21	7,91±0,39	8,86±0,37	8,83±0,34
	G 2	10,67±0,44	11,68±0,31	11,62±0,33	11,93±0,22
	G 3	11,23±0,25	10,67±0,25	9,75±0,23**	9,80±0,39*
TGP (UI/l)	G 1	21,38±1,109	22,31±1,71	20,55±1,50	23,78±1,91
	G 2	24,69±1,86	24,62±1,55	25,72±1,58	26,44±1,53
	G 3	25,58±1,58	25,02±1,72*	23,95±2,17**	23,71±2,98
blood glucose (g/l)	G 1	0,83±0,02	0,80±0,03	0,80±0,02	0,83±0,03
	G 2	0,83±0,01	0,82±0,01	0,80±0,01	0,86±0,01
	G 3	0,86±0,01	0,85±0,01	0,86±0,04	0,92±0,06

M<sub>0</sub>: initiation of treatment, M<sub>6</sub>: sixth month of treatment, M<sub>12</sub>: twelfth month of treatment and M<sub>18</sub>: eighteenth month of treatment.

G 1: CD4 cell count  $\leq 200$  cells / mm<sup>3</sup>, G 2: CD4 cell count between 200 and 350 cells / mm<sup>3</sup> and

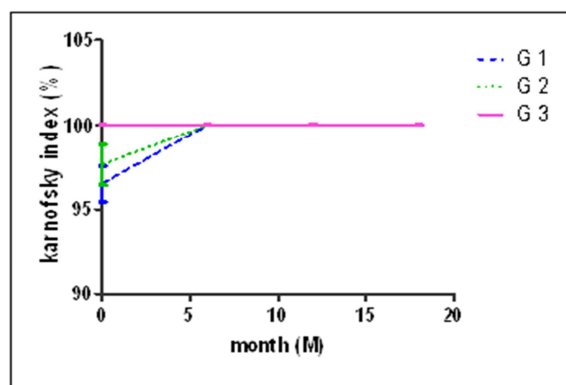
G 3: CD4 cell count between 350 and 500 cells / mm<sup>3</sup>.

\* :  $p < 0,05$  ;

\*\* :  $p < 0,01$  ;

\*\*\* :  $p < 0,001$ .

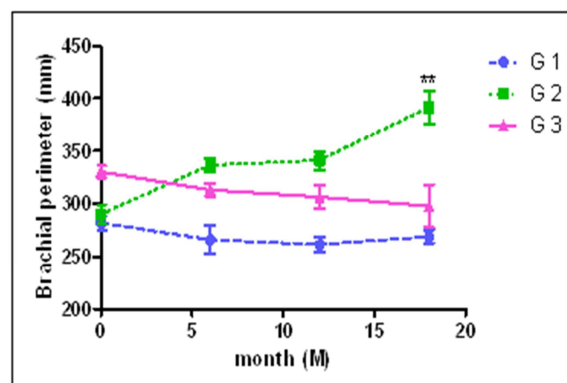
These modifications, characterized by the synthesis of new cells involved in the immune response, induce a protein expenditure of 15 g / day.



**Fig. 1.** Karnofsky index measured during treatment. M<sub>0</sub>: initiation of treatment, M<sub>6</sub>: sixth month of treatment. M<sub>12</sub>: twelfth month of treatment and M<sub>18</sub>: eighteenth month of treatment. G 1: CD4 cell count  $\leq 200$  cells / mm<sup>3</sup>, G 2: CD4 cell count between 200 and 350 cells / mm<sup>3</sup> and G 3: CD4 cell count between 350 and 500 cells / mm<sup>3</sup>.

According to Macalan (2001), this energy expenditure can cause a nutritional imbalance that can lead to a

severe decrease in anthropometric values (brachial perimeter) (Moore *et al.*, 1993). Promoting the restoration of the immune system induces a better nutritional status characterized by an increase in the brachial perimeter.



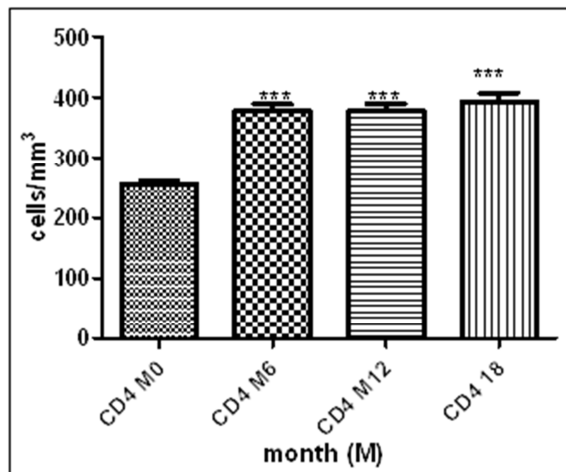
**Fig. 2.** Brachial parameter measured during treatment. M<sub>0</sub>: initiation of treatment, M<sub>6</sub>: sixth month of treatment, M<sub>12</sub>: twelfth month of treatment and M<sub>18</sub>: eighteenth month of treatment. G 1: CD4 cell count  $\leq 200$  cells / mm<sup>3</sup>, G 2: CD4 cell count between 200 and 350 cells / mm<sup>3</sup> and G 3: CD4 cell count between 350 and 500 cells / mm<sup>3</sup>.

\*\* :  $p < 0,01$ .

### Immunological parameters

#### CD4 Evolution of all patients

The average value of CD4 of all patients treated with ART was  $290 \pm 8.94$  cells /  $\text{mm}^3$  at  $M_0$  this value increased gradually of 16.06% after six months of treatment, of 17.55% at  $M_{12}$  and finally of 35% at  $M_{18}$ . These increases were highly significant ( $p < 0.001$ ) compared with  $M_0$  (Figure 3).



**Fig. 3.** Evolution of CD4 count in the general population during treatment  $M_0$ : initiation of treatment.  $M_6$ : sixth month of treatment,  $M_{12}$ : twelfth month of treatment and  $M_{18}$ : eighteenth month of treatment.

\*\*\* :  $p < 0.001$ .

#### CD4 evolution in G 1

The initial mean of the number of CD4 in this group was  $111.3 \pm 5.48$  cells /  $\text{mm}^3$  at  $M_0$ . It increased and reached  $251 \pm 9.91$  cells /  $\text{mm}^3$  at  $M_6$ , a highly significant ( $p < 0.001$ ) increase of 125.51% over  $M_0$ . This rate continued to increase to reach a maximum of  $327.7 \pm 13.16$  cells /  $\text{mm}^3$  at  $M_{18}$ , a highly significant increase ( $p < 0.001$ ) of 194.42% compared to  $M_0$  (Figure 4).

#### CD4 evolution in G 2

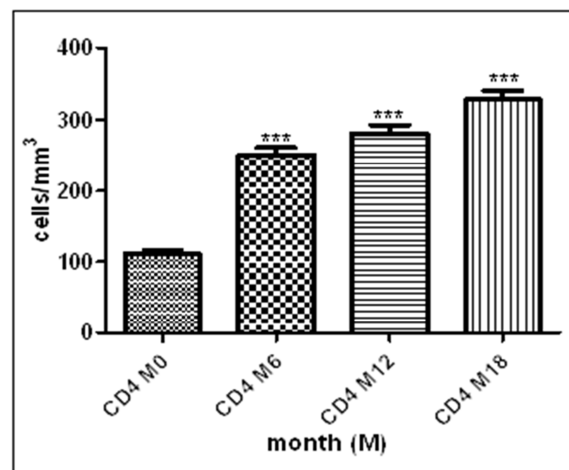
CD4 measured at  $M_0$  of G 2 gave an average of  $269.7 \pm 4.16$  cells /  $\text{mm}^3$ . This rate peaked at  $M_6$  ( $401.7 \pm 28.37$  cells /  $\text{mm}^3$ ), a highly significant ( $p < 0.001$ ) increase of 48.94% over  $M_0$ .

The increases at  $M_{12}$  and  $M_{18}$  were highly significant ( $p < 0.001$ ) compared to  $M_0$  with growth rates of 46.71% and 41.26%, respectively (Figure 5).

#### CD4 evolution in G 3

In G 3 the initial CD4 at  $M_0$  rate was  $423 \pm 4.18$  cells /  $\text{mm}^3$ . It increased to  $555.4 \pm 16.94$  cells /  $\text{mm}^3$  at  $M_6$ , a highly significant ( $p < 0.001$ ) increase of 30.89%. This rate progressively increased at  $M_{12}$  and  $M_{18}$ , reaching  $643.3 \pm 27.60$  cells /  $\text{mm}^3$ , a highly significant ( $p < 0.001$ ) increase of 51.61% compared to  $M_0$  (Figure 6).

HIV infection induces lymphopenia; it comes from the dendritic cells that detract HIV-infected CD4 cells. This reduction in the rate of CD4 can be profound or not depending on the stage of evolution of HIV infection. In addition to the lymphopenia induced by the virus, the deterioration of immune system is accompanied by a gradual disparity of cells and mediators involved in the innate and adaptive immune responses (T8 lymphocytes, NK, dendritic cells, interferons, cytokines, chemokines etc.). The CD4 count required for a person in good clinical and immunological condition is estimated to be between 500 and 1500 cells /  $\text{mm}^3$  (Ndazing, 2015). Antiretroviral with their inhibitory effect on the replication of the virus, gradually promote the restoration of the immune system.



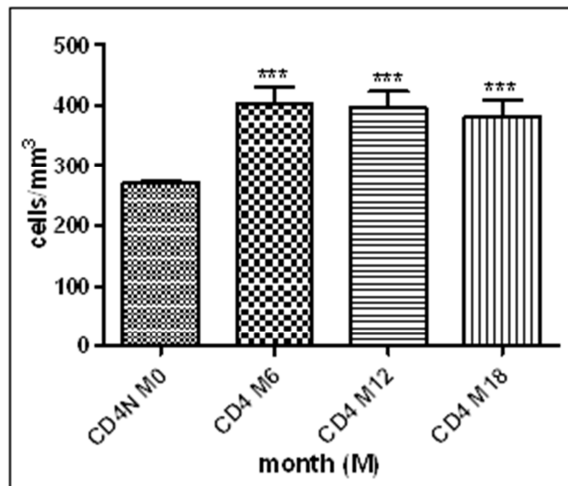
**Fig. 4.** Evolution of CD4 count in G 1 during treatment.  $M_0$ : initiation of treatment,  $M_6$ : sixth month of treatment,  $M_{12}$ : twelfth month of treatment and  $M_{18}$ : eighteenth month of treatment. G 1: CD4 cell count  $\leq 200$  cells /  $\text{mm}^3$ ,

\*\*\* :  $p < 0.001$ .

It is felt by the gradual increase in CD4 count in patients on ART, and this, whatever the initial rate of



CD4 at the initiation of antiretroviral treatment. Thus, for an average CD4 count equal to  $290 \pm 8.94$  cells / mm<sup>3</sup>, at the initiation of antiretroviral therapy in the general population, the CD4 level progressively increased by 16.06%, then 17.55% and finally 35% at M<sub>6</sub>, M<sub>12</sub> and M<sub>18</sub>.



**Fig. 5.** Evolution of CD4 levels in G 2 during treatment. M<sub>0</sub>: initiation of treatment, M<sub>6</sub>: sixth month of treatment, M<sub>12</sub>: twelfth month of treatment and M<sub>18</sub>: eighteenth month of treatment. G 2: CD4 cell count between 200 and 350 cells / mm<sup>3</sup>.

\*\*\* :  $p < 0.001$ .

In each of these group, the measured of the number of CD4 T-cells showed an significant increase ( $p < 0.001$ ) after 6 months of treatment, during the follow-up period. These results are similar to those of Okome *et al.* (2007) and show the interest of antiretroviral therapy in restoring the immune system (Abokon *et al.*, 2014). The rate of evolution of CD4 after six months of treatment in G 1 was 125.51% while that of G 3 was 30.89%. These results are relatively similar to those of Lozès *et al.* (2012) and Bernard Hirshel according to Fontenay (1994). They obtained respective evolution rates of 275% for an initial CD4 level equal to 137 cells / mm<sup>3</sup> and 36.26% for an initial rate of 477 cells / mm<sup>3</sup>.

The immune restoration induced by tri- therapy is generally performed like a slope according to Sovaila *et al.* (2015). The first slope, induced after the initiation of the treatment, is more important and intense. It is characterized by a massive production of

CD4 after six months of treatment. This intense activation of the immune system is related to the deep depletion of the organism in CD4 and also to the presence of possible opportunist infections. In group 1, CD4 production was 125.5% after six months of treatment, however, this production was unable to increase CD4 levels above 500 cells / mm<sup>3</sup>. However, this intense CD4 production in this group failed to raise the CD4 level above the threshold of 500 cells / mm<sup>3</sup>. While in G 3, CD4 production in the range of 30% increase the level of CD4 to more than 600 cells / mm<sup>3</sup>. As a result, it appears that on antiretroviral therapy, the CD4 count reaches the required level when the threshold at initiation is high. Also, when the threshold at initiation is low, the rate of CD4 has difficulty going up to the threshold of 500 cells / mm<sup>3</sup>. Otherwise, it will take a longer time under ARV to reach a normal CD4 level for a low CD4 level at initiation. Indeed, the administration of an ARV treatment at the threshold of CD4 of less than 500 cells / mm<sup>3</sup> would correspond to a treatment during the stage of primary infection. At this stage, HIV reservoirs are formed (Cheret, 2014). Tri-therapy although not allowing their true destruction, prevent their constitution (Geeraert *et al.*, 2008). Early treatment also restores the number and anti-HIV activity of NK cells (Vasan *et al.*, 2007) and dendritic cells (Killian *et al.*, 2006).

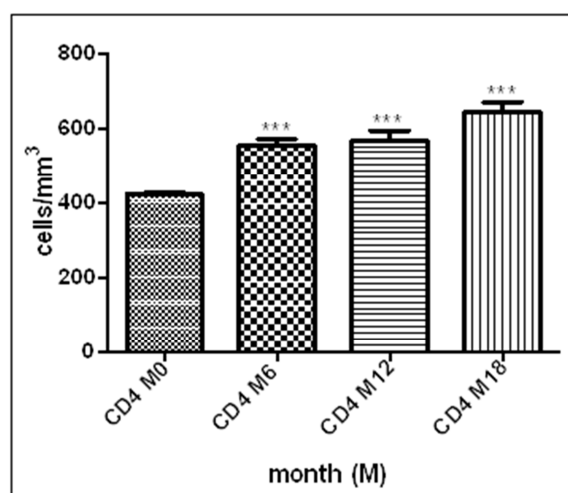
Late treatment, that is, an initial CD4 threshold of less than 200 cells / mm<sup>3</sup>, has no effect on NK cell decline induced by infection and on HIV reservoirs.

The second CD4 production slope under antiretroviral therapy is lower than the first, indicating the regulation of the immune response on antiretroviral drugs.

The evolution rate of CD4 after 18 months of treatment in POP 3 was 51.61% compared to M<sub>0</sub>, ie 20.72% between M<sub>6</sub> and M<sub>18</sub>. This could be explained by the regulation of the intensity of the immune response and because of the absence of viral load; this one having been eliminated during the first slope of production. According to Fontenay (1994), CD4

production during primary infection helps normalize CD4 levels.

When treatment is late, the intensity of second-slope production may be important to raise CD4 levels to the required level. This would justify the rate of evolution of CD4 at 194.42% after 18 months of treatment in G 1 ie increase of CD4 production of 68.91% between M6 and M18 in this group. In this case, the evolution of the CD4 count requires an intense activation of the immune system that could lead to a generalized inflammation of it: the inflammatory immune reconstitution syndrome (Sovaila *et al.*, 2015).



**Fig. 6.** Evolution of CD4 levels in G 3 during treatment. M<sub>0</sub>: initiation of treatment, M<sub>6</sub>: sixth month of treatment, M<sub>12</sub>: twelfth month of treatment and M<sub>18</sub>: eighteenth month of treatment. G 3: CD4 cell count between 350 and 500 cells / mm<sup>3</sup>.

\*\*\* : P<0,001.

#### Hematological parameters

The white blood cell and platelets count in each group did not change significantly ( $p > 0.05$ ) during the study period. (Table II) These results are contrary to those obtained by Tovi (2014), who observed a significant increase in white blood cells after 36 months of treatment. The lack of variation in white blood cell and platelets counts could be explained by the fact that the HIV infection would not have caused any damage to these blood cells. Loua *et al.* (2011) found no significant difference between the white blood cell count of people living with HIV and those

who were not infected with HIV. On the other hand, these results could be explained by the fact that the automaton that was used for their measurement is not efficient enough to detect their increase during the follow-up.

The hemoglobin rates measured in groups G 1, G 2 and G 3 were respectively  $11.40 \pm 0.18$  g / dl,  $11.44 \pm 0.22$  g / dl and  $12.11 \pm 0.18$  g/dl at M<sub>0</sub>. These rates showed a non-significant increase ( $p > 0.05$ ) during treatment. These results are similar to the results obtained by Tovi (2014). On the other hand, they are contrary to those of Nacoulma *et al.* (2007). Knowing that the normal value of hemoglobin is estimated to be at least 12 g / dl, these results indicate the presence of cases of anemia in G 1 and G 2. According to Njonkou (2014), the presence of anemia in these populations could be explained by profound immunosuppression or viral progression of infection due to a low CD4 count (Diallo *et al.*, 2003).

#### Biochemical parameters

The results of the study of the body mass index are shown in table1.

#### Serum creatinine

The mean value of serum creatinine measured in G 2 increased significantly ( $p < 0.05$ ) with a growth rate of 11.71% between M<sub>0</sub> and M<sub>18</sub>. It confirms the results of Tovi (2014). Indeed, the increase in creatinine belong to the toxicity associated to ART or the presence of impaired renal function related to age, black race, or high blood pressure (Izzedine, 2009).

In contrast, serum creatinine measured in G 3 decreased significantly ( $p < 0.001$ ) of 12.73% at M<sub>18</sub> compared to M<sub>0</sub>. In G 3, the rate of creatinine significantly decreased ( $p < 0.001$ ). This corroborates the results of Traoré (2008). The progressive decrease in serum creatinine came from the regulation of this level by antiretroviral (Nyimi *et al.*, 2001).

#### Pyruvic glutamic transaminases (TGP)

The measured of TGP in G 3 level decreased significantly, with respective variations of 2.18% at



M<sub>6</sub> (p <0.05), and 6.37% at M<sub>12</sub> (p <0.01) compared to M<sub>0</sub>. . This result is contrary to those of Mouhari-Touré *et al.* (2011). These authors observed an increase in TGP of 29.8% after one year of follow-up. The decrease in transaminases observed in G 3 is thought to be due to hepatic function regulation of ART.

#### *Blood glucose*

No significant difference was observed in patients' blood glucose levels after initiation of antiretroviral therapy. All patients had a blood glucose level of 0.8 g / dl.

#### **Conclusion**

The present study highlights the interest of the successive modifications of the recommendations of the WHO in recent years. The study of the evolution of clinical parameters showed that patients treated with a high CD4 threshold presented favorable status for a better clinical restoration under antiretrovirals. The study of the evolution of the immunological parameters showed a better restoring of the CD4 number in the group 3 with a CD4 level above 500 cells / mm<sup>3</sup> after treatment. However, this restoration with antiretrovirals must be supported by good observance.

The study of the evolution of hematological parameters revealed an anemia for people treated late. The study of the evolution of the biochemical parameters showed that the treatment carried out in the group 3 did not induce perturbation on the hepatic and renal functions of these patients.

This study should be continued to evaluate the effect of treatment regimens on the CD4 threshold, the side effects associated with long-term early treatment, and to study the incidence of mortality and morbidity in each of the populations studied.

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