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Drugs Related Changes of Haemoglobin and CD4 Counts in HIV-Infected Patients on Antiretroviral Therapy

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Abstract
The present study examines the effects of antiretroviral therapy (ART) on two basic immuno-haematological parameters over time. We performed a retrospective study of HIV-infected treatment-naïve patients starting a first line ART between June 2014 and January 2015, and followed-up for 12 weeks. On the whole, 254HIV-infected treatment naive patients were enrolled: 100 patients on tenoforvir (TDF) based regimen was compared with 102 and 52 non-TDF based regimen and treatment-naïve patients respectively. Samples were collected at three different points (at baseline, 4 weeks and 12 weeks).CD4 and haemoglobin (Hb) were found to be significantly higher (p=0.001) in the TDF group as compared to non-TDF groups after 12 weeks of follow-up, although there was no significant difference between the Non-TDF group and ART-naive group at 4 and 12 weeks in both parameters. These results demonstrate that the initiation of a TDF based-regimen is followed by an increase in lymphocyte proliferation and lymphocyte-mediated cytotoxicity compared to other non-TDF based-regimen group. However we suggest that TDF should be part of an antiretroviral regimen in immunosuppressed patients at risk of anaemia.
Keywords: *HIV, Tenoforvir (TDF), CD4 and immunosuppressed*

INTRODUCTION

Several longitudinal studies have described infection with human immunedeficiency virus (HIV) causes a progressive dysfunction of the immune system in which there is reduced number of circulating CD4 T cells[1] which is preceded by increased levels of circulating HIV RNA. This predicts disease progression, with development of acquired immune deficiency syndrome (AIDS) and death in the absence of therapy. The CD4 count is the most important laboratory indicator of immune function in HIV-infected patients. It also

the strongest predictor of subsequent used to assess immunity, disease progression and survival according to findings from clinical trials and cohort studies[.2]. Thus CD4 is used to assess a patient's immunologic response to antiretroviral therapy. CD4 count response to ART varies widely but a poor CD4 response in patients with viral suppression is rarely an indication for modifying an ARV regimen.

Low Heamoglobin (Hb) also characterizes the malfunction of the immune system in HIV infection and has been suggested as additional predictive markers of HIV disease progression.[3].New treatment strategies, including the use of effective HIV-specific protease inhibitors such as tenofovir (TDF) or lavimidine, have swept the scientific community withhope caused by dramatic reductions of viral load and similar increases of CD4 cell counts.[4]. Similarly the use of protease inhibitors and triple therapy in clinical practice has been associated with a marked lowering of HIV-related morbidity.[5]. However, clinical reports of severe opportunistic infections in the presence of satisfactory responses to antiretroviral treatment as evaluated by increases in CD4 cell counts [6], have suggested that an increase in CD4 cell count may not always be accompanied by a similar augmentation of the functional capacity of the immune system, or that specific immune defects may persist despite treatment-induced reconstitution of other parts of the immune system.

MATERIALS AND METHOD
Study population

A longitudinal study of 254 HIV-infected naive patients was started between June 2014 and January 2015 at the HIV clinic of the University of Port Harcourt teaching hospital, a reference hospital for tropical infection and disease located in Port Harcourt, Nigeria. HIV-infected Naïve Patients never exposed to ART were invited to participate in the study so far they can be allocated in to any of the three groups; patients to be place on TDF regimen, patients to be place on Non-TDF

regimen and HIV-infected patients that will not be exposed to antiretroviral therapy during the study period. From every patient's social-demographics details of age, sex, occupation, education, income, and HIV status (CD4 T-lymphocyte count) were recorded at the time of recruitment in to the study. Samples were collected at three times point (at baseline, after 4 weeks and after 12 weeks of follow-up). Periods of drug interruption for any reason, if occurring, were discounted. Treatment was provided without any cost to patients.

Statistical analysis

Continuous values are given as mean and standard deviation while categorical data are given as percentages. The three groups of patients analyzed were first compared using chi-squared for categorical data and pair tests for continuous variables. The level of significance was 0.05. All statistical analyses were performed using SPSS version 20.0 software package (SPSS Inc., Chicago, Illinois, USA).

RESULTS

A total of two hundred and sixty seven patients were recruited in to the study from June 2014 to January 2015. Complete data were obtained from 254 patients while 13 patients were lost to follow-up. Of the 254 patients, 202 patients started a first line antiretroviral therapy (100 Patients on TDF and 102 patients on Non-TDF Antiretroviral therapy) and during the study period all patients met inclusion and exclusion criteria. Among these 202 enrolled patients, 100 (39.37%) initiated tenofovir-containing regimen, 102 (40.16%) initiated tenofovir-sparing regimens and 52 (20.47%) antiretroviral Naïve patients. Baseline demographic characteristics and laboratory features were compared among the groups.

Table 1: Age and Sex Characteristics of the study population

	Mean Age	No. of patient	Std. Deviation	P-Value
SEX				
Male	36.92	85 (33.46%)	7.69	
Female	33.70	169 (66.54%)	7.97	**(Z-test)** **p = 0.002**
Total	**34.77**	**254 (100%)**	**8.01**	
ART Regimen group				
TDF	35.23	100 (39.37%)	7.68	
N-TDF	35.49	102 (40.16%)	8.68	**(ANOVA)** **p = 0.069**
D-NAIVE	32.50	52 (20.47%)	6.93	
Total	**34.77**	**254 (100%)**	**8.02**	

Values in parenthesis showed the percentage of patients in the study population

Characteristic of patients

The mean age of the male and female patients were; 36.92 (33.46%) and, 33.70 (66.54%) years respectively with a statistically significant difference of P = 0.001. The minimum and maximum age of the study population of the male and female patients were; 50:20, and 48:18 years respectively. Figure 1 shows that at baseline there was a statistically significant different between the CD4 of the treatment-Naïve group and the CD4 of the TDF and Non-TDF groups (p=0.000 and 0.000 respectively). After 4 weeks of follow-up, there was an increase in the CD4 of the drug treatment groups but when compared with the treatment Naïve group, the different was highly statistically significant (p=0.000 and 0.000 respectively) (Figure 2). After 12 weeks of exposure and follow there was a significant increase in the TDF group as compared with the treatment Naïve and Non-TDF groups. Although there was no statistically significant different between the TDF group and the Non-TDF group, a significant different was observed between the TDF and the treatment Naïve group (p=0.04) (Figure 3).
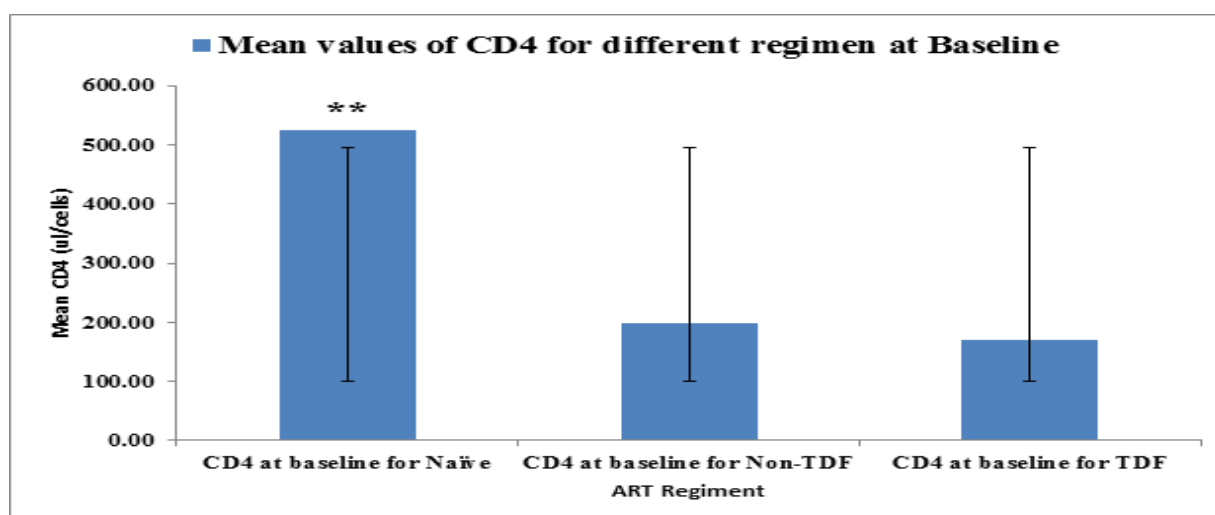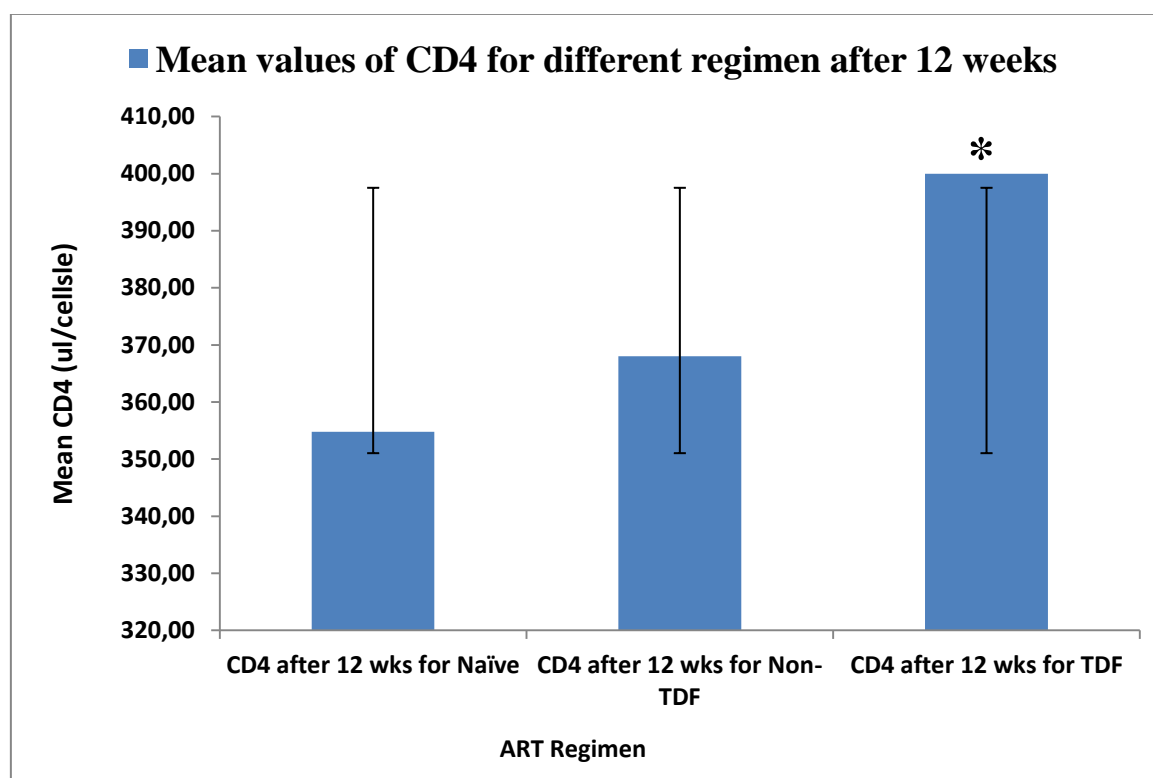

**: Significant at p=0.00 and 0.00when CD4at baseline for naïve was compared with CD4 at baseline for Non-TDF and TDF respectively'

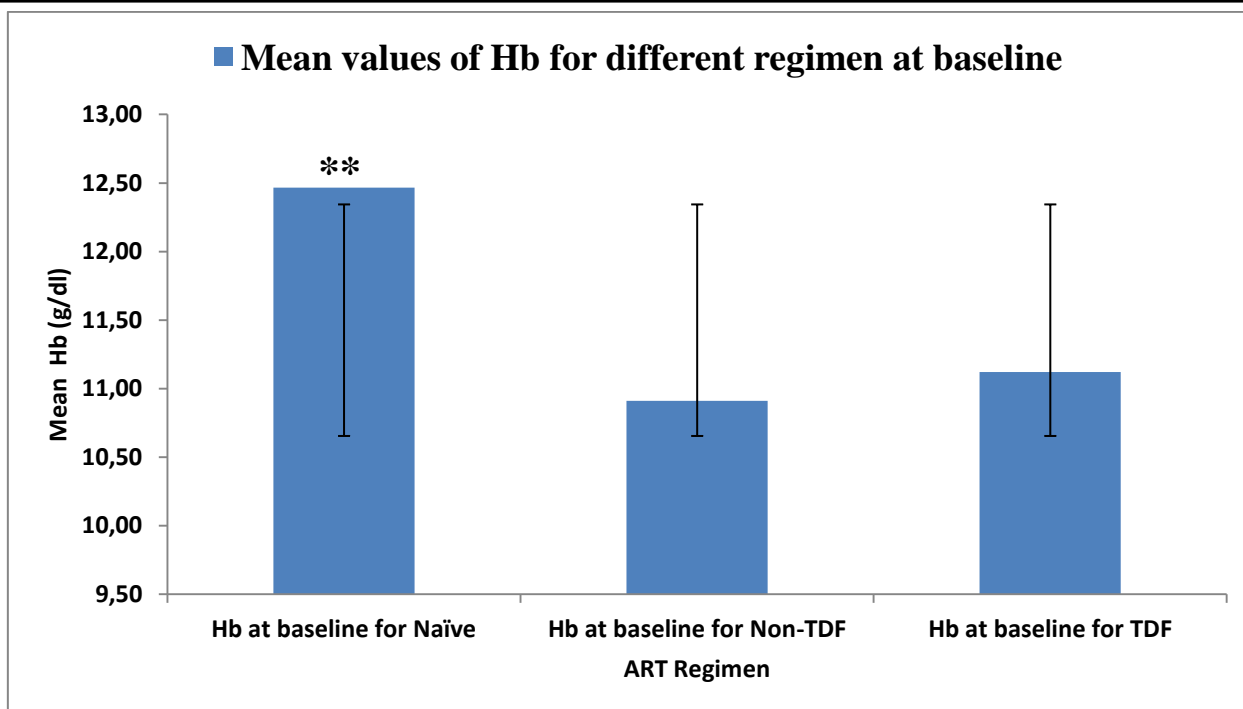**Figure 1:** CD4 of the study population at baseline
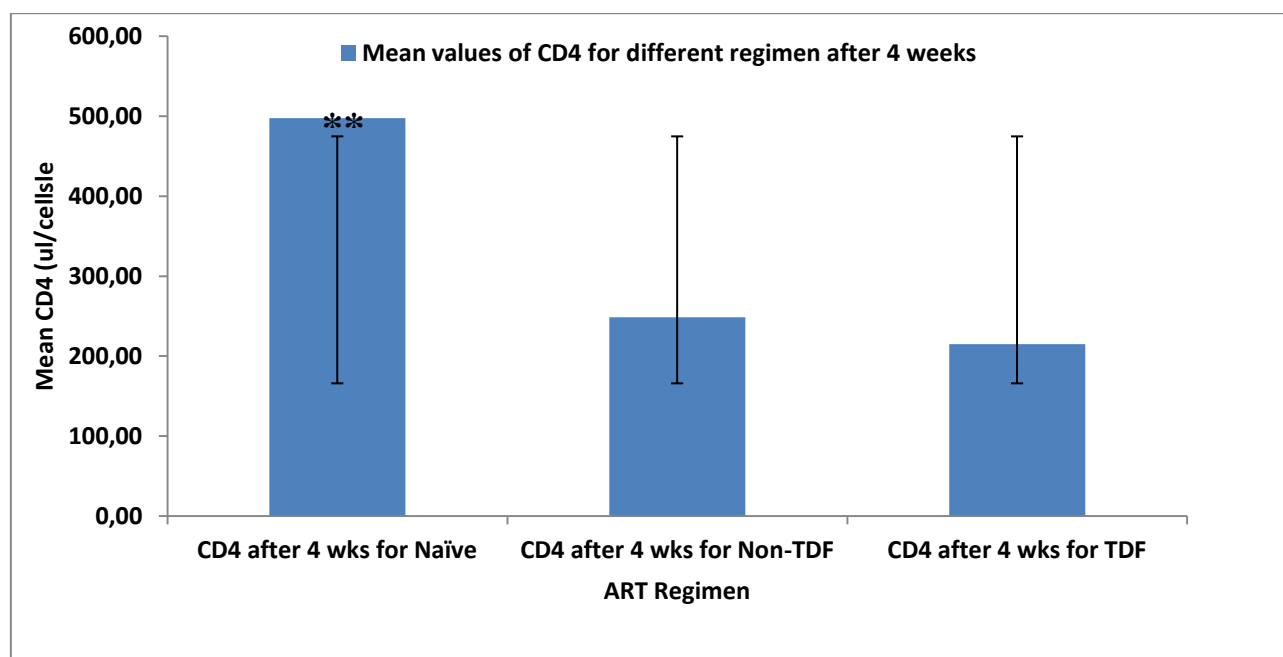
**: Significant at p=0.00 and 0.00when CD4after 4 wks for naïve was compared with CD4 after 4 wks for Non- TDF and TDF respectively

Figure 2: CD4 of the study population after 12 weeks of exposure
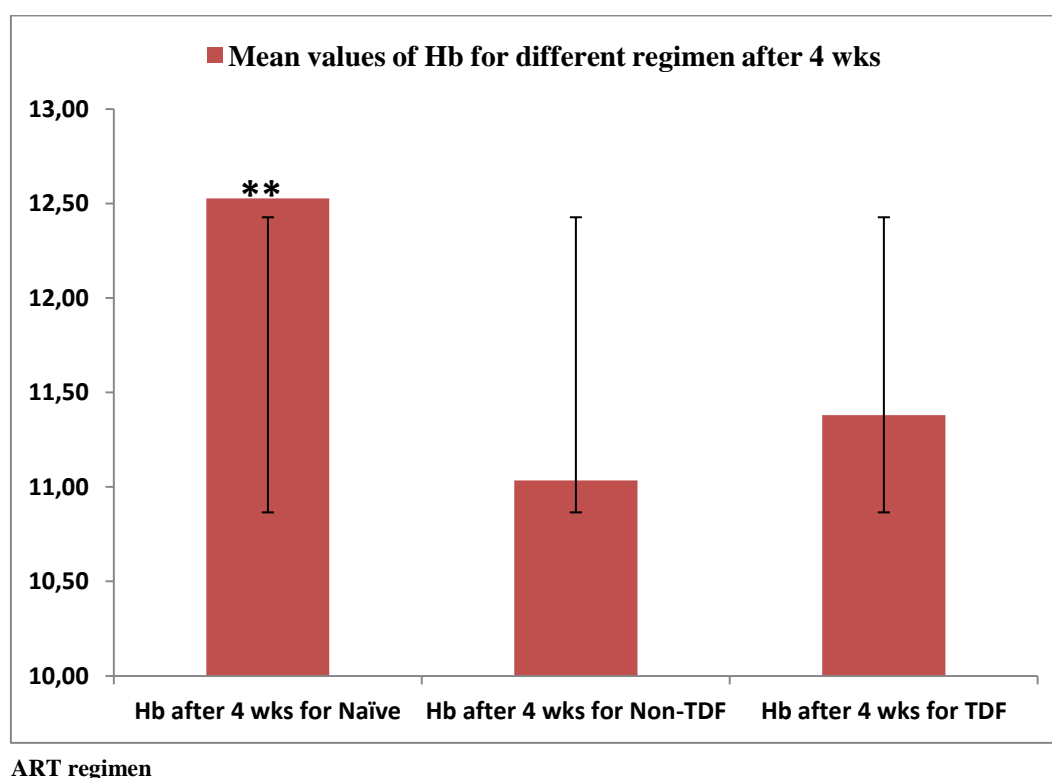

*: Significant at p=0.04 when CD4after 12 wks for TDF was compared with CD4 after 12 wks for naïve.

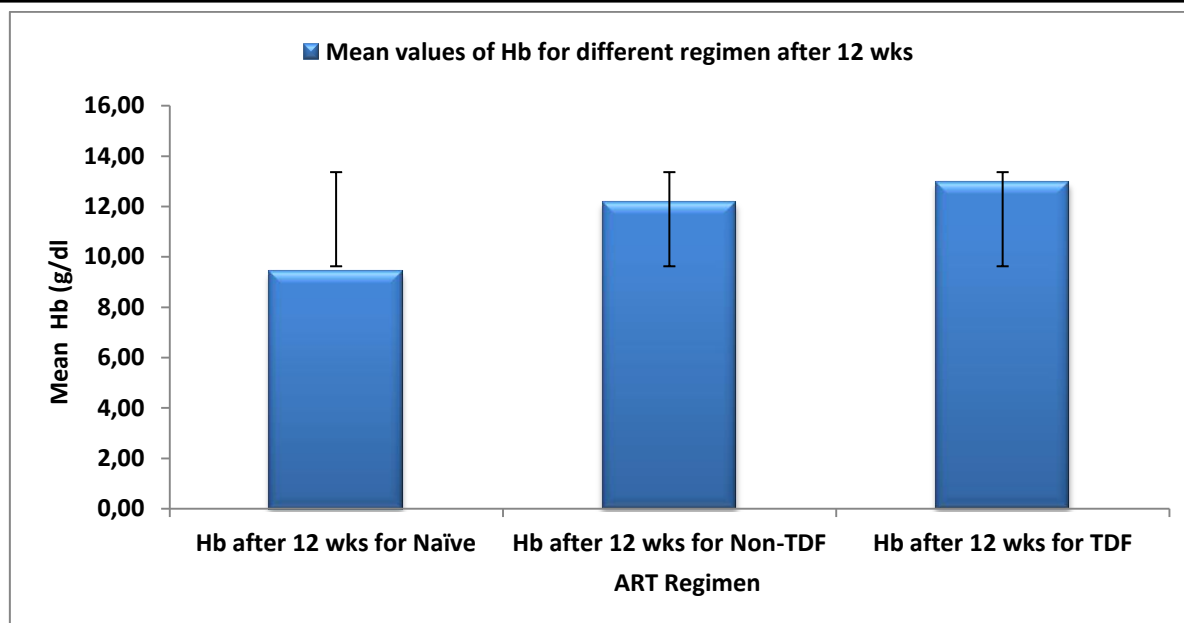**Figure 3: CD4** of the study population after 12 weeks of exposure

Figure 4: Hb of the study population at baseline

**: Significant at p=0.038 and 0.016when Hbat baseline for naïve was compared with Hb at baseline for Non-TDF and TDF respectively

**: Significant at p=0.005 and 0.008when Hb after 4 wks for naïve was compared with Hb after 4 wks for Non-TDF and TDF respectively

Figure 5: Hb of the study population after 4 weeks of exposure

Figure 6: Hb of the study population after 12 weeks of exposure

At baseline, there was a statistical different between the haemoglobin level of the treatment Naïve group as compared to the TDF and Non-TDF groups, this different was statistically significant (p=0.031 and 0.016 respectively) (Figure 4). After 4 weeks there was a noticeable increase in all the groups and the different between the treatment-Naïve group and the TDF and Non-TDF groups was statistically significant (p=0.005 and 0.008 respectively) (Figure 5).

After 12 weeks, there was a decrease in the mean Hb values of the treatment-Naïve group while there was much higher increase in the TDF group as compared with the Non-TDF group (Figure 6).

DISCUSSION

In this longitudinal analysis of HIV-infected patients, we found that HIV-infected patients on TDF regimen had higher CD4 and Hb values than those on Non-TDF regimen. Studies has shown that in HIV-infected patients, it is important to control the viral load at a very lower level in order to maintain a positive CD4 count slope when ART continues at later stages of the infection, particularly from 3 months to more than 24 months after ART initiation.[7].

This study agree with other findings [8,] that HIV-infected patients have an initially delayed CD4 count recovery at 4 weeks after HAART initiation, but at 12 weeks, CD4 count increases tramendiously. This study examines the trend of CD4 count rather than the absolute CD4 count since ART initiation decreases CD4 count. We notice in particular that there is a progressive increased in CD4 of the TDF group after 12 weeks as compared to tenofovir sparing regimen groups (Non-TDF and treatment-naive). This finding is in consistent with other reports.[9-11.]

TDF have been shown to boast the immune system in a non-specific way although a growing number of case reports and cohort studies have described an association between treatment with tenofovir and renal tubulopathy or impaired glomerular filtration rate (GFR) in patients with human immunodeficiency virus (HIV) infection.[12-14.]

Haemoglobin level increased markedly in our series of patients especially after 4 weeks of exposure to antiretroviral therapy and in treatment Naïve patients while haemoglobin is increased markedly in the two drug treatment groups and decrease in the treatment Naïve group after 12 weeks of exposure. From our result it could be believe that tenofovir could be used in the treatment of HIV-infected Patients at risk of severe anemia as compared to the other antiretroviral therapy.

CONCLUSION

Detecting the changes in CD4 and Hb for different treatment regimen is important in the HIV-infected population given its association with increased mortality risk and potential impact on treatment choices. In this longitudinal study of HIV-infected Naïve patients, TDF appeared more sensitive in detecting and boasting the immune system and causing lymphocyte proliferation than other antiretroviral therapy. Additionally, TDF might be used in patients at risk of anemia.

COMPETING INTEREST

The authors have declared that no competing interests exist

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