## Original Research Article

# Effect of ART2 on the CD4 count and viral load during treatment of second line ART

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### ABSTRACT

**Background:** AIDS first recognized in US summer of 1981 by the U.S. CDC reported. In 1983 HIV was isolated from a patient of lymphadenopathy. This study was for monitoring the change in CD4 count and viral load of PL HIV before and after one year of second line ART in the period of 2016 to 2018.
**Methods:** Study was single centre hospital based and clinical continuous longitudinal, prospective and retrospective, observational at ART plus Centre, Kanpur K.P.S. Institute of Medicine (G.S.V.M. medical college Kanpur) included the all patients on ART1 attending in centre were screened for treatment failure based on clinical, immunological and virological criteria's as decided by SACEP from 2016 to 2018.
**Results:** CD4 count at the time of initiation that of second line ART, there is low CD4 count the mean value is 181.44±85.02 in total subject 118 but 12 month of second line ART 2 treatment mean value of CD4 count 413.01±168.70. After Z test application the value is 13.316, p value 0.0001, MD 231.5, CI is 95%.Viral load value at time of start of second line ART mean value is 80683.85849±293449.2038, after 1 to 12 month of start of second line ART treatment mean value is 350.8559±128.1069, for this Z value is 2.972, p value 0.0033.
**Conclusions:** Second line ART is most effective in treatment after failure with first line ART. CD 4 count increase and viral load decrease and clinical feature improve after treatment of ART 2.

**Keywords:** Acquired immune deficiency syndrome, Antiretroviral therapy, CDC, Human immunodeficiency virus, South Asian Cooperative Environment Programme

## INTRODUCTION

AIDS first recognized in United States in unexplained occurrence of pneumocystis jirovecy in previously healthy homosexual men in Los Angeles and kaposi sarcoma (ks) with and without P. jiroveci and other opportunistic infections in 26 previously healthy homosexual men in New York San Francisco and Los Angeles. HIV is having two strain HIV 1 and HIV 2. HIV 1 was transmitted from chimpanzees and HIV2 is transmitted from sooty mangabey monkey. HIV1 is the cause of the global pandemic while HIV2 progression is very restricted mainly to Western Africa.[1] HIV 1 have three sub group as m; o; n; M (major), O (outlier), N (non major) in which m (major) was worldwide distribution and O (outlier) and N (non major) restricted to West Africa. M (major) consisted in as nine subtypes as A-D, F-H, J and K. Subtypes E and I is recombinant of other type of subtype. Subtype Cis restricted mostly in India and Africa. Subtype B is predominant in Western Europe, the America and Australia. Subtype A is slower progression and subtype d is faster progressionl.[2] Person

with positive HIV serology who have ever had a CD4 lymphocyte count below 200celles/mcl and CD4 lymphocyte percentage below 14% are considered to have aids (current medical diagnosis and treatment 2017).

First time ART should consists of two nucleoside reverse transcriptase inhibitor (NRTI) + Non nucleoside reverse transcriptase.[3]

**Table 1: Representation of regimens and it drugs combination with its indications.**

| Regimen | ARV drug combinations | Indications |
|---|---|---|
| Regimen I | Zidovudine + Lamivudine + Nevirapine | First line Regimen for patients with Hb/9 gm/dl and not on concomitant AU |
| Regimen I (a) | Tenofovir + Lamivudine + Nevirapine | First line Regimen for patients with Hb<9 gm/dl and not on concomitant AU |
| Regimen II | Zidovudine + Lamivudine + Efavirenz | First line Regimen for patients with Hb 9 gm/dl and on concomitant AU |
| Regimen II (a)[4] | Tenofovir + Lamivudine + Efavirenz | First line Regimen for patients with Hb<9 gm/dl and on concomitant AU First line for all patients with Hepatitis B and br Hepatitis C co-infection First line Regimen for pregnant women, with no exposure to sd-NVP in the past |
| Regimen III [5,6] | Zidovudine + Lamivudine + Atazanavir/Ritonavir | Regimen for patients on AZT Containing First line regimen, who develop toxicity to both NVP and EFVAlso Second line regimen for those who are on TDF containing First line regimen if Hb 9 gm/dl |
| Regimen III (a) | Zidovudine + Lamivudine + Lopinavir/Ritonavir | For patients of Regimen Ill who develop severe Atazanavir toxicity First line regimen for patients with HIV-2 infection with Hb / 9 gm/dl |
| Regimen IV | Tenofovir + Lamivudine+ Atazanavir/Ritonavir | Second line regimen for those who are on AZT/d4T containing regimen in the first line Also for patients on TDF containing First line regimen who develop toxicity to both NVP and EFV |
| Regimen IV (a) | Tenofovir + Lamivudine+ Lopinavir/Ritonavir | For patients on Regimen IV who develop severe Atazanavir toxicity First line Regimen for patient with HIV 2 infection with Hb<9 gm/dl First line Regimen for all women exposed to sd-NVP in the past |
| Regimen V[7] | Stavudine+ Lamivudine+ Atazanavir/Ritonavir | Second line for those who are on TDF containing regimen in the First line if Hb< 9 gm/dl |
| Regimen V (a) | Stavudine+ Lamivudine+ Lopinavir/Ritonavir | For patients on Regimen V who develop severe Atazanavir toxicity |

Aim and objective of the study was to see the effectiveness of ART2 and its role on CD4 count and viral load of PL HIV before and after one year of start of second line ART.

**METHODS**

This was clinical (assessment with investigation) continuous longitudinal, prospective and retrospective, observational, single centre hospital-based study at ART Centre, Kanpur.

This study was conducted in ART plus centre K.P.S. Post Graduate Institute of Medicine (G.S.V.M. Medical College, Kanpur) tertiary care teaching hospital (G.S.V.M. Medical College, Kanpur).

The entire patient on 1st line ART treating attending in our centre was screen for treatment failure of based on clinical, immunological and virological criteria as

decided by SACEP and duration of study was 2016 to 2018.

*Inclusion criteria*

- Patient over the age of 18 years at pre-inclusion and monitored under outpatient condition.
- Documented HIV-1 (group M) infection regardless of clinical stage and CD4 lymphocyto-count (taken in 6 months)
- Patient with treatment failure after first-line antiretroviral treatment with a combination including a non-nucleoside reverse transcriptase inhibitor and two nucleoside reverse transcriptase inhibitors, failure.
- Adherence (>80%) to first-line antiretroviral treatment (questionnaire) at pre inclusion.
- Patient agrees not to take any concomitant medication during the trial without informing the investigator.

- Informed consent
- For women in childbearing age: negative pregnancy test at inclusion, with no plan of pregnancy in the coming 12 months and agreeing to use mechanical contraception (with or without hormonal contraception) during the study.

### Exclusion criteria

- Infection with HIV-2 or HIV-1 groups O or N or HIV 1+2.
- Adherence (<80%) to first-line antiretroviral treatment at pre inclusion.
- Participation in any other clinical trial.
- Presence of an uncontrolled, ongoing opportunistic infection or of any severe of progressive disease.
- First-time treatment with a protease inhibitor, Abacavir.
- Not interested to participate in study.
- Severe hepatic insufficiency.
- Creatinine clearance calculated by Cockcroft-Gault formula <50 ml/min.
- Hb≤8 g/dl
- Platelets < 50,000 cells / mm$^3$
- Neutrophiles<500 cells / mm$^3$
- Pregnancy or lactation.

### Blood sample collection

On admission, 10 ml of peripheral venous blood was collected from the antecubital vein by an autoclaved syringe using 20 gauze needles. The blood was allowed to clot at room temperature for at least half an hour. The glass tube with clotted blood was centrifuged at 2000 rpm for 20 minutes and the centrifugation was repeated once more to remove the red cells completely. The supernatant serum, devoid of cellular elements, was separated from the clot and placed in two acid cleaned small test tubes.

### Viral load testing

Patient of HIV suspecting first line ART failure send to BHU Varanasi Department of Microbiology, IMS BHU Banaras.

### Estimation of viral load

In BHU viral load was tested quantitatively real time PCR from HIV RNA by PCR machine.

### Measuring

Viral load was typically reported as copies of HIV in a milliliter (mL) of blood. Changes in viral load are usually reported as a log change (in powers of 10). For example, a three log increase in viral load (3 Log10) is an increase of 103 or 1000 times the previously reported level, while a drop from 500,000 to 500 copies would be a three-log-drop (also 3 Log10).

CD4 count is done by BD facts flow machine by kit and report is analysed and given same day.

### RESULTS

In this study there are 118 HIV patients was included in this study and it was conducted K.P.S. Institute of Medicine (G.S.V.M. medical college Kanpur). Investigation of CD4 count and viral load was done to HIV patients. CD4 count at starting of second line ART was 181.44±85.02and after 1 year of second line ART was 413.01±168.70 and viral load at the start of second line ART 80683.85±293449 and viral load after 6 Month of Second Line ART was 350.85±128.1069. Mean value of CD 4 Count at the time of start of ART2 181.44±85.01 and mean value of CD4 count after one year of start of ART2 413.01±168.69.

Mean difference 231.57, p value 0.0001 CI 95%. And Mean value of viral load at the time of start of ART2 80683.85±293449.20 and mean value of viral load after one to six months of start of ART2 385.45±122.80. Mean difference 80248 p value is 0 .0033 z score is 2.972 CI 95%.

**Table 2: CD4 count in study before 1year of start of study, at initiation of study and after 1year after start of study.**

| Range | 1 year before start of 2nd line ART | Initiation of 2nd line ART | 1 year after of 2nd line |
|---|---|---|---|
| <200 | 4 | 74 | 2 |
| >200 | 114 | 44 | 116 |

In this study CD4 count of study subject at one year before at the initiation of 2nd line ART and one year start of 2nd line ART. Our study show that CD4 count decrease at the initiation of 2nd line ART and CD4 count more than 200 the subject is increase after one year of start of ART 2,44 to 116 less than 200 subject is increase 74 from 4 one year before of start of ART2.

**Table 3: Viral load at start of second line ART.**

| Viral load | No. of subjects | Percentage |
|---|---|---|
| >10000 | 107 | 90% |
| <10000 | 11 | 10% |

In this study the distribution of viral load more than study subject on basis of viral load at the time of initiation of ART2. In our study the no of subject of viral load more than 10000 is 107 and less than 10000.

In this study there is showing relationship between CD4 Count at Start and at One Year of Second Line ART were as CD4 count at starting of second line ART mean 181.44±85.02 and CD4 count after 1 year of start of

second line ART with a mean and SD 413.01±168.70. Mean difference 231.57 p value 0.0001 CI 95%.

**Table 4: Relationship between CD4 count at start and at one year after of second line ART.**

|  | CD4 count at start of second line ART | CD4 count after 1 year of start of second line ART |
|---|---|---|
| Mean±SD | 181.44±85.02 | 413.01±168.70 |

**Table 5: Relationship between mean value and SD of viral load of start of second ART and after 6 month of second line ART.**

|  | Viral load at the start of second line art | Viral load after 6 month of second line art |
|---|---|---|
| Mean±SD | 80683.85±293449 | 350.85±128.1069 |

In this study there is showing relationship between mean value and SD of viral load of start of second ART2 and after 6 month of second line ART were as viral load at the start of second line ART2 mean 80683.85±293449 and viral load after 6 month of second line ART2mean and SD 350.85±128.1069

Mean difference 80248 p value is 0.0033 z score is 2.972 CI 95%.

**Table 6: Representation of regime of second line ART in study subjects.**

| Regimens | No. of subjects | Percentage |
|---|---|---|
| TLATV/R | 35 | 63% |
| ZLATV/R | 74 | 30% |
| TLLP/R | 5 | 4% |
| ZLLP/R | 4 | 3% |

In this study antiretroviral drugs included was TLATV/R Tenofovir+Lamivudine+Atanzanavir+Ritonivir there are 35 patients are given treatment i.e. 63%, ZLATV/R Zaduvidine+Lamivudibne+Atanzanavir+Ritonivir there are 74 patients are given treatment i.e. 30%, TLLP/R Tenofovir+Lamivudine+Lopinavir+Ritonavir there are 5 patients are given treatment i.e. 4%, ZLLP/R-Zaduvuvidine+Lamivudine+Lopinavir +Ritonavir there are 4 patients are given treatment i.e. of 3%. More number of patients are then TLATV/R.

## DISCUSSION

CD4 count and Viral load at the time of initiation that of second line ART, there is low CD4 count the mean value is 181.44 in total 118 subject standard deviation that is 85.02 in total subject 118 but at 6 month/12 month of second line ART 2 treatment mean value is CD4 count 413.01 and SD 168.70. For this Z TEST applied the Z value is 13.316, p value is 0.0001, mean difference 231.5,

confidence interval 95%, this shows significance of second line ART treatment and effectiveness of second line of ART IS 127%.Viral load value at time of start of second line ART mean value is 80683.85849 and SD is 293449.2038, after 1 to 6 month of start of second line ART treatment mean value is 350.8559 and SD is 128.1069, for this z value is 2.972, p value is 0.0033, mean difference 80298, it is suggestive of significance of value and effectiveness of ART2 is 99%.

Dishank Patel et al overall outcome of out of 126 patients, 82 received regimen V [zidovudine (ZDV) + lamivudine (3TC) + tenofovir (TDF) + boosted lopinavir (LPV/r)] and 44 received regimen Va (3TC + TDF + LPV/r).[8] A significant (p <0.0001) increase in mean body weight and marked reduction in number of patients categorized as WHO stage III/IV was observed at 12 months of second line ART. Moreover, a significant immune reconstitution with increase in mean CD4 count and viral suppression (PVL<400 copies/ml) in 103 (82%) patients (p <0.0001) was also observed. A total of 83 ADRs were observed in 69 (55%) patients, the most common being dyslipidemia followed by anemia ero status disclosure Sciences, Early outcome of second line antiretroviral therapy in treatment-experienced human immunodeficiency virus positive patients.

## CONCLUSION

Second line ART of regime that is considering in the study was most effective in treatment of subject treated after treatment failure of first line ART. CD4 count increase and viral load decrease clinical feature improve after treatment of ART. Clinical symptoms in our study was decrease in subject at the start of second line ART and after 1 year of second line ART treatment and also opportunistic infection improve in study subject it mean second line ART is effective. It is also continuously scrutinized the adherence of ART2 medications.

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