

# DIVISION OF CLINICAL SCIENCES



The Department of Clinical Sciences at NARI has been carrying out research related to the improving the clinical management of HIV infected individuals. NARI has been identified as an ART Link Centre by the National AIDS Control Organization to provide Anti-Retroviral Therapy (ART) to NARI research study participants. During the last one year from April 2006 to March 2007, 64 participants have been enrolled in the free ART programme at the NARI Clinic located at NIV. A total of 191 subjects have been receiving free ART from the NARI clinic located at the National Institute of Virology by the end of March 2007. In the study on the efficacy of DOTS in treatment of tuberculosis in HIV infected and HIV uninfected individuals, a total of 289 subjects were enrolled. These included 164 HIV seronegative and 125 HIV seropositive pulmonary tuberculosis patients. The results indicate that there was a significant mortality seen in HIV associated TB patients as compared to that in HIV uninfected tuberculosis patients. These results indicate that studies are needed to determine when to start ART to reduce the mortality in HIV associated TB patients. In the ACTG 5175 study, where once daily and twice daily administered ART regimens are being studied for their efficacy, 106 subjects have been enrolled and another 14 subjects are to be enrolled to complete the target number of study subjects to be enrolled for the study at NARI.

### **A. Efficacy of DOTS in the Management of HIV-1 Seropositive and HIV-1 Seronegative Tuberculosis patients :**

*[Principal Investigator: Dr.S.P. Tripathy]*

This was a collaborative project between NARI, Pune and TRC, Chennai. At Pune, the work was done in collaboration with the Talera Hospital in the Pimpri-Chinchwad area. The objectives of this project were to evaluate the efficacy and safety of RNTCP (intermittent short course) regimens in patients with HIV and TB, to study the relationship between stage of HIV disease and response to anti-TB treatment and to study the relapse rates and their clinical presentation in detail.

Of the 164 HIV seronegative tuberculosis patients enrolled, 129 (78.7%) were male, while among the 125 HIV seropositive tuberculosis patients, 106 (84.8%) were male. In both groups, majority of the study volunteers were males.

The enrolment in the study has been completed but the follow up of the enrolled subjects is ongoing at present. Of the 27 deaths observed during treatment, 23 (85%) deaths were seen in the HIV seropositive group. In the HIV seropositive tuberculosis patients, 12.9% of the sputum AFB positive patients died while in the sputum AFB negative group, 23.8% of the patients died. The corresponding figures in the HIV seronegative TB patients were 1% and 4.8%. The difference in the mortality in the HIV seropositive and HIV seronegative TB patients was statistically significant ( $p < 0.001$ ). The mortality associated with HIV associated TB could be decreased by initiating suitable anti-retroviral treatment in this group of patients.



**Table 2.1: Treatment Outcome**

	HIV Positive		HIV Negative		Total
	Sputum Positive	Sputum Negative	Sputum Positive	Sputum Negative	
Cured / Treatment Completed	42	40	91	44	217
Defaulted	6	1	6	0	13
Expired During Treatment	8	15	1	3	27
Treatment Failure	1	0	2	1	4
Treatment Outcome Awaited	3	2	1	15	21
Transfer Out	2	5	0	0	7
Total	62	63	101	63	289

**B. AACTG 5175 Study: A phase IV, randomized, open label evaluation of the efficacy of once daily protease inhibitor and once daily non-nucleotide reverse transcriptase inhibitor containing therapy for initial treatment of HIV-1 infected subjects from diverse areas of the world.**

*[Lead Investigators: Dr. S.P. Tripathy, Dr. R.R. Gangakhedkar, Dr. S.V. Godbole, Dr. M.V. Ghate]*

This is a multicentric collaborative study initiated by the AIDS Clinical Trials Group (ACTG) and funded by the National Institutes of Health (NIH), USA. The primary objective of the study is to demonstrate the non-inferiority of a once-daily PI- and a once-daily NNRTI-containing regimen as compared with standard twice-daily ARV therapy for the initial treatment of subjects infected with HIV-1 from diverse areas of the world.

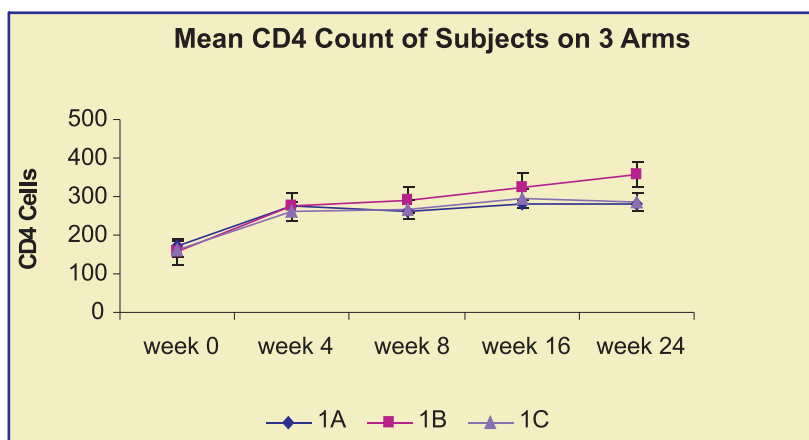
**At entry into the study, subjects are randomized (1:1:1) to one of the following three treatment arms:**

1. Arm 1A: Lamivudine (3TC) / Zidovudine (ZDV) 150 / 300 mg 1 tablet BID + Efavirenz (EFV) 600 mg QHS
2. Arm 1B: Emtricitabine (FTC) 200 mg QD + Aatazanavir (ATV) 400 mg QD + Didanosine Enteric-coated (ddI-EC) 400 mg orally QD for subjects who weight > 60 kg and 250 mg QD for subjects who weight < 60 kg
3. Arm 1C: FTC 200 mg QD + Tenofovir (TDF) 300 mg QD + EFV 600 mg QHS

So far, 106 subjects have been enrolled in the study and the remaining 14 subjects would be enrolled by May 2007.

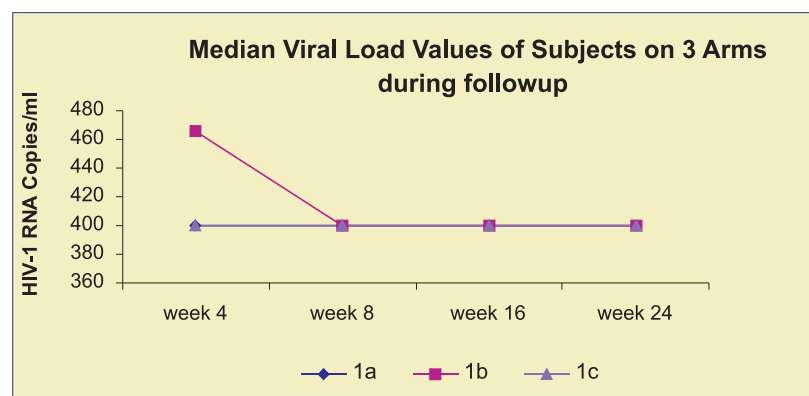
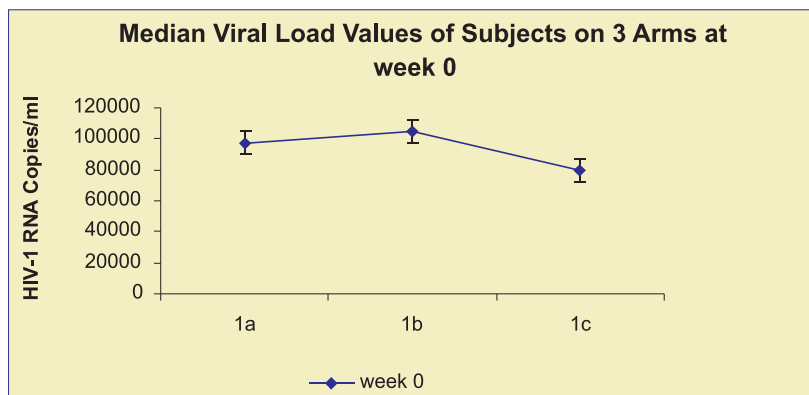


Figure 2.1: Mean CD4 Count of Subjects on 3 Arms



Participants of all Arms show **increase in CD4 count** from baseline. The differences in the CD4 counts across the three arms were not statistically significant.

Figure 2.2: Median Viral Load of Subjects on 3 Arms at baseline and follow-up



Participants of all three Arms showed decrease in HIV-1 viral load values from baseline. In all three arms, the HIV-1 Viral load was <400 HIV-1 RNA Copies/ml. by 8 weeks in all three arms. There was virologic failure in one study subject. Eleven study participants developed adverse events which included asymptomatic hyperbilirubinemia in 5 (all in arm 1B and did not warrant any intervention), anemia in 2, subacute intestinal obstruction in 1, pulmonary TB with pneumothorax in 1, left palatal palsy in 1 and death due to suicide in 1.

### C. National AIDS Control Organization Programme- NARI ART Link Centre

*[Lead Investigators: Dr. M.V. Ghate, Dr. S.P. Tripathy]*

On World AIDS Day 2003 (1st December) Government announced its decision to provide Anti Retroviral Treatment (ART), free of cost to people living with HIV/AIDS in the six HIV high prevalence states of TamilNadu, Andhra Pradesh, Karnataka, Maharashtra, Manipur, and Nagaland and the state of Delhi from April 2004, in keeping with WHO Guidelines on ART for resource constrained settings.

NARI has been identified as link ART center. This aims to provide treatment for as many NARI research study participants as possible. The programme has initially sanctioned for 500 participants.

#### **Criteria for starting ART therapy:**

Confirmed HIV infection and one of the following conditions

WHO Stage IV HIV disease irrespective of CD4 count

WHO Stage III disease with consideration of using CD4 counts < 350/ mm<sup>3</sup>

WHO Stage I or II HIV disease with CD4 counts < 200/ mm<sup>3</sup>

WHO Stage IV HIV disease irrespective of CD4 count

The center began enrollment on 1<sup>st</sup> December 2005. Total 211 patients were screened and 191 participants were enrolled by end of March 2007. Of these 64 participants were enrolled between April 2006 and March 2007. Out of 64 participants, 41 were ART naïve and 23 were already on ART at the time of enrollment.

The treatment regimens for participants are mentioned in Figure 2.1 The treatment adherence was more than 95%. Five patients expired, two were transferred to other centers, one stopped the treatment and four lost to follow up. Fifteen patients reported hospitalization due to various reasons. Side effects of ART were experienced by 55 patients.

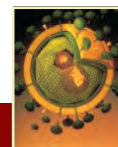


Figure 2.3: NACO ART NARI Link Center

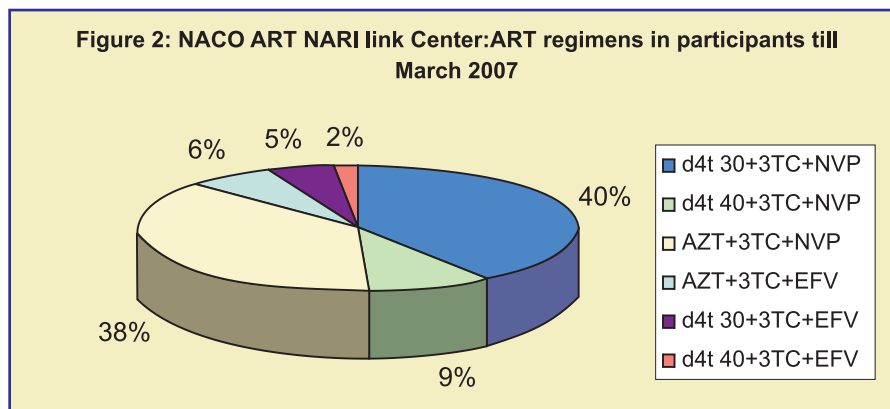
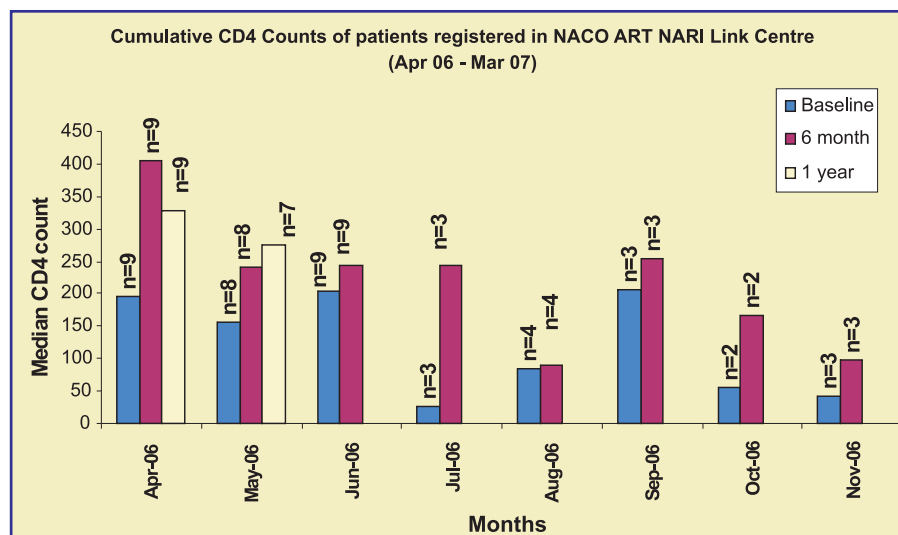


Figure.2.4: CD4 counts of the patients increased during the 6 monthly follow-up



Enrollment and follow-ups are ongoing at present.

