

## Editorial

# HIV Drugs: The Silver Lining in the Dark Clouds

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## Introduction

The reporting of *Pneumocystis carinii* (now known as *Pneumocystis jirovecii*) pneumonia in 4 otherwise healthy homosexual individuals by a General Practitioner Dr. Merle A. Sande in 1981, opened the Pandora's box, letting the World know about Acquired Immunodeficiency syndrome (AIDS). Luc Montagnier with his colleagues from France discovered Lymphadenopathy Associated Virus (LAV) in 1983 and Robert Gallo with his group isolated and characterized Human T lymphotropic virus-III (HTLV-III) in 1984. Both LAV and HTLV-III were known to cause AIDS and presently known as HIV-1 as per regulations of International Council for Taxonomy of viruses (ICTV). In 1985, Montagnier also isolated a new virus from sera of prostitutes in Senegal, West Africa, which is now known as HIV-2.

Then, whole world observed how man became the victims of AIDs. The HIV infected individuals were progressing to full blown AIDS and embracing death. WHO declared AIDS as Global Public Health Problem.

Dr. Robert Yarchoan played a pivotal role in development of first effective drug against AIDS and along with his colleagues and conducted the first clinical of Zidovudine (AZT), Didanosine (DDI), Zalcitabine (DDC) and Lamivudine. He also conducted the first clinical trials of combination anti HIV therapy.

So, the journey of treating patients with Anti retroviral drugs began and presently almost 7 groups of Food and Drug Administration (FDA) approved anti HIV drugs have been available for use to treat People Living with HIV/AIDS.

These 7 groups of FDA approved anti HIV drugs are –

- Nucleoside reverse transcriptase inhibitor (NRTIs)
- Nucleotide reverse transcriptase inhibitor (NtRTIs)
- Non-nucleoside reverse transcriptase inhibitor (NNRTIs)
- Protease inhibitors (PIs)
- Fusion inhibitors (FIs)
- Co-receptor inhibitors (CRIs)
- Integrase inhibitors (INIs)

The HIV life cycle is very short 1.5 days (approx) from viral entry

to release of progeny virus. Along with short life cycle HIV mutate very rapidly. Because of mutation, the progeny virus may be superior to parent virus in survival and the daughter virion may be resistant to Anti HIV drugs. Kozal M in 2009 has reported that resistance occurs in all antiretroviral therapy. Hence, the present trend is to use 3 antiretroviral drugs from at least 2 different classes. This 3 drug combination therapy is commonly known as Triple Cocktail. The rationale behind this is if a mutation cause resistance to one drug, the other drugs can suppress the replication of resistant mutant progeny virus. Presently simpler formulas have been developed called fixed dose combinations, where there is combination of 3 drugs into one pill taken once daily in varied options. The combination therapy also leads to adherence or consistency to the regime and thereby development of resistance or making the process slower. The combination of drugs that can act on different viral targets is called highly active Antiretroviral Therapy (HAART).

In this combination therapy, HIV really has become a chronic disease now commented by Brad Hare, MD, Medical Director of HIV/AIDS Division at San Francisco General Hospital. He told, 'it's like diabetes or high blood pressure. If it is managed well, a long healthy life can be expected.'

But the most important point is the aim of HAART is to get the viral load so low that the person does not get symptoms, though HIV is still there and HIV can be transmitted to other person while on medication.

On 1st May, 2014 the US Department of Health and Human Services (DHHS) recommended ART for all HIV infected individual to slow the risk of disease progression. But WHO guidelines published on 30th June, 2013 recommended to initiate ART if CD4 count are  $\leq$  500 cells/ml.

A new antiretroviral drug called Cabotegravir has been developed which requires only 4 doses in a year i.e. injection once every 3 months. This new drug also belongs to an integrase inhibitor that can be active for months before being given again.

Center for Disease Control (CDC) had many clinical trials for Pre-exposure prophylaxis (PrEP) for HIV prevention. Clinical trials for several HIV vaccines are also going on in different countries in different phases.

Though the newer anti retrovirals are in pipeline and can be more beneficial with fewer side effects, lower drug resistance and less frequent dosing several issues have been arisen regarding ethical, social and economical aspect with respect to clinical trials for newer ART. Recently, the post-study issues or post-trial obligations for the participants are a major global concern as most of the clinical trials for newer ART are sponsored or conducted by researchers of economically developed countries and the participants are from economically underdeveloped countries.