



# HIV Therapy in the Indian Context - Cheaper the Better?

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## ABSTRACT

The focus of treatment of HIV infection in developing countries is shifting from supportive treatment and prevention of opportunistic infections, to aggressive antiretroviral therapy (ART). Considering the unique circumstances prevalent in India and the financial constraints faced by the population, it is essential that the interested patient be explained the pros and cons of antiretroviral therapy, and not just the price consideration. Without being defeatist, it is our humble desire to raise these issues for discussion, so that a consensus can evolve, and the patient will get the best treatment possible. In the absence of clear-cut Indian guidelines for initiation and maintenance of ART, it is the duty of the treating physician to ensure that the patient has a complete idea of what he is getting into. While the intention of the Government to provide free antiretroviral therapy is noble, the problem of patient adherence and drug resistance must be kept in mind, in addition to cost. Thus, a certain degree of individualization is imperative, at least at a later stage in the treatment. Hence, the tendency to consider cheaper ART as better should be considered critically.

### INTRODUCTION

The approach to management of HIV disease is slowly undergoing a transformation. Until a few years back, the focus of treatment in the developing countries was supportive therapy. This included regular medical examination for early diagnosis of opportunistic infections, as well as continuation of chemoprophylaxis. Antiretroviral therapy was considered the privilege of the affording class and its initiation was considered at a later stage since the therapy had to be life-long.

However, the dramatic reduction in the cost of antiretroviral drugs (ART), the introduction of triple drug combinations, and the focus of the government and the WHO on the '3 by 5' initiative, has made ART more accessible to the lower income groups. However, a word of caution is advised. The treatment of HIV disease is lifelong and good response to antiretroviral therapy depends on the type of infecting virus, the right combination of drugs, and complete adherence to the drug regimen. Also, the treatment should ideally be based on clinical, virologic, biochemical and immunologic characteristics of the individual patient. In which case, it is futile to compare costs. Thus, cheaper may not always be better.

### ANTIRETROVIRAL THERAPY; AIMS AND OBJECTIVES<sup>1</sup>

The patient has to be explained that eradication of HIV infection is not possible due to the presence of latently infected CD4 T cells during the very early stages of acute HIV infection, which persist with an extremely long half-life.

- Clinical Goal: Prolongation of life and improvement of quality of life.
- Virologic Goal: To achieve maximal and durable suppression of viral load (< 50 copies / ml) so as to halt the disease progression.
- Immunologic Goal: To achieve immune reconstitution that is quantitative (CD4 count in normal range) and qualitative (pathogen-specific immune response).
- Therapeutic Goal: Rational sequencing of drugs not only achieves virologic goals, but also (1) maintains therapeutic options; (2) is relatively free of side effects; (3) achieves greater degree of adherence.
- Epidemiological Goal: To reduce HIV transmission.

### INDICATIONS FOR ANTIRETROVIRAL THERAPY<sup>2</sup>

The indications for starting antiretroviral therapy have been listed in Table 1. The use of highly active antiretroviral therapy

**Table 1 : Indications for Antiretroviral Therapy.**

Clinical category	CD4 + cell count	Plasma HIV RNA	Recommendations
Symptomatic HIV diseases (wasting, unexplained fever for > 2 weeks or thrush) including patients with AIDS	Any value	Any value	Start HAART
Asymptomatic	< 200 / mm <sup>3</sup>	Any value	Start HAART
Asymptomatic	200 - 350 / mm <sup>3</sup>	Any value	Offer HAART
Asymptomatic	> 350 / mm <sup>3</sup>	> 55,000 (by RT-PCR or bDNA- version 3)*	Some experts recommend starting HAART
Asymptomatic	> 350 / mm <sup>3</sup>	< 55,000	Most defer HAART

**Table 2 : Cost of Currently Available Antiretroviral Drugs**

Regimen	Approximate cost per month (Rs.)
Zidovudine + Lamivudine + Nevirapine	1350.00
Stavudine + Lamivudine + Nevirapine	1300.00
Zidovudine + Lamivudine + Efavirenz (Should not be used in women of child-bearing age)	3300.00
Zidovudine + Lamivudine + Nelfinavir	7600.00
Zidovudine + Lamivudine + Ritonavir + Indinavir	6400.00
Zidovudine + Lamivudine + Ritonavir + Saquinavir	10,500.00
Zidovudine + Lamivudine + Ritonavir + Lopinavir	10,500.00

(HAART) has been successful in reducing morbidity in HIV patients and improving the quality of life. The term HAART indicates use of two NRTIs along with an NNRTI or a boosted PI, so as to achieve the goals elucidated above.

### EVALUATION BEFORE INITIATING HAART<sup>3,4</sup>

This includes the following:

- Complete history and physical examination.
- Fundus examination.
- Complete blood count, biochemistry profile and lipid profile.
- CD4 / CD8 T cell counts and ratio.
- Plasma HIV-1 RNA measurement (viral load).
- Other tests including VDRL, Mantoux test, toxoplasma IgG serology, chest x-ray and serology for hepatitis C and B.

In India, the cost factor may preclude performance of all the above investigations in a patient, so a judicious decision is required.

### ANTIRETROVIRAL THERAPY IN RESOURCE-POOR NATIONS<sup>5</sup>

The '3 by 5 initiative' of the WHO proposes that there should be at least 3 million people on ART by the end of 2005, so as to make an impact on the prevalence and transmission of HIV infection. This goal is not achievable in the absence of a clear public health policy, which promotes the rational and safe use of antiretroviral agents. Drug access to the poor can be improved by a set of guidelines for the same, and by providing accessibility to competent health services and cheaper drugs. Fortunately, at

**Table 3 : Strategies to Improve Adherence: Patient and Medication-Related**

1. Inform patient regarding side effects.
2. Anticipate and treat side effects.
3. Simplify food requirements.
4. Avoid adverse drug interactions.
5. If possible, reduce dose frequency and number of pills.
6. Negotiate a treatment plan that the patient understands and to which he/she commits.
7. Spend time and multiple encounters to educate and explain goals of therapy and need for adherence.
8. Establish readiness to take medication *before* writing first prescription.
9. Recruit family and friends to support the treatment plan.
10. Develop concrete plan for specific regimen by considering meals schedule, daily routines, and side effects.
11. Develop adherence support groups or add adherence concerns to agenda of other support groups.
12. Develop link with local community-based organizations regarding adherence combined with educational sessions and practical strategies.

present most of the ARV drugs are available in India and the cost of these drugs has reduced remarkably over the past 2-3 years. Another limiting factor is the high cost involved in repeated viral load estimations and CD4 T cell counts.

### INDICATIONS FOR INITIATING ART IN RESOURCE-POOR SETTINGS

The WHO recommends that in resource-poor settings, HIV infected people should be offered treatment when they have:

1. WHO stage IV disease (clinical AIDS) regardless of CD4 + cell counts.
2. WHO stage I, II, or III of HIV disease, with a CD4 T cell count below 200 / mm<sup>3</sup>.
3. WHO stage II or III of HIV disease, with absolute lymphocyte count < 1200 / mm<sup>3</sup>.

CD4 T cell counts are used, instead of viral load in monitoring the patients. If facilities to count CD4 T cells are not available, total lymphocyte count may be used to make decision regarding initiation of ART. In a number of patients, however, there may be a discordance between the CD4 and total lymphocyte counts. Thus, a degree of caution is required.

### First-Line Regimens<sup>5</sup>

Antiretroviral treatment should be standardized in a developing nation. A single first-line ART regimen should be proposed, along with a limited number of second-line regimens, so that large number of patients can be treated.

The treating doctor should carefully evaluate its potency and side effects, anticipate adherence, effects of co-existing conditions in the population (e.g. infections particularly tuberculosis and HBV), potential drug interactions, cost, and the availability of healthcare facilities. Based on these considerations, the preferred first-line ARV regimens and their costs are listed in Table 2. Use of only two NRTI combinations is not recommended since these regimens do not suppress viral replication adequately and are likely to produce resistance rapidly.

Currently, the government is providing certain triple drug combinations to HIV-infected patients. However, it is the duty of the treating physician to inform the patient about the probability of treatment failure, and the need to change the drug regimens in such cases. The onus of continuing ART would lie with the patient, thus placing tremendous financial constraints on the poorer classes. The government would be hard-pressed to pay for second-line regimens in patients. So, hope aroused in the patient has to be tempered by reality.

### Second-Line Antiretroviral Regimens

In a resource-limited setting where viral loads are difficult to perform, treatment failure is evaluated primarily on the basis of clinical response and where possible, by CD4 T cell counts. The second-line regimens generally include a Ritonavir-boosted PI combination. NFV can be considered as alternative for PI component, if RTV boosted PI is not available. The NRTI component in the regimen should also be changed depending on the clinical profile of the patient, the side-effect profile, and the probability of cross-resistance.

It is recommended that countries planning to implement ART programmes should simultaneously also implement HIV drug resistance surveillance programmes, so as to detect potential drug resistance at the population level and modify the recommendations as and when required.

### CONCLUSIONS

The recent advances in the field of antiretroviral therapy (ART) as well as the reduction in prices of antiretroviral drugs has made treatment of HIV disease an achievable goal to the millions of Indians affected by it. The recent initiative of the government to provide free ART to patients deserves fulsome praise. However, a word of caution is advised. Cheaper antiretroviral drugs made accessible to the poorer classes are only one facet of the treatment. Patient education and adherence, along with access to competent health care form the other prongs of the strategy. Thus, cheaper ART is not the only situation. A holistic approach integrating the above facets is the need of the hour.

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