

## Patient Handout – Immunodeficiency Clinic PGIMER, Chandigarh

The following information is intended to supplement, not substitute for, the expertise and judgment of your physician. It is based on the kind of information given to patients who use this medication in other parts of the world.

### **Treating HIV Infection**

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### **How HIV makes new viruses**

- HIV contains nine genes that carry all the information needed to make new viruses.
- When HIV locks onto a CD4 positive cell its genetic material is absorbed into the cell.
- HIV then makes a copy of its genetic information. It uses an enzyme (chemical) of its own called reverse transcriptase to do this.
- Drugs called reverse transcriptase inhibitors can stop the virus from making these copies. Zidovudine (AZT), Didanosine (ddI), Lamivudine (3TC) and Stavudine (d4T) are reverse transcriptase inhibitors. Efavirenz and nevirapine are also reverse transcriptase inhibitors, but work in a different way (NNRTI's).
- When the cell receives appropriate instructions, it makes another copy of the virus that's bound up in its genetic material, and this copy is then used to generate the production of new viruses from materials supplied by the cell. So, in effect, the cell has been hijacked by HIV and turned into a virus factory. Each cell can produce dozens, if not hundreds, of virions.
- The new viral building blocks need to be chopped up and assembled. An HIV enzyme called protease is produced to do this job. Drugs called protease inhibitors can stop this process. Indinavir, ritonavir, saquinavir and nelfinavir are protease inhibitors.
- All drugs mentioned above are available in India.

### **Combination therapy**

- HIV makes lots of mistakes when it copies itself. Unlike human cells it can't spot the errors or get rid of them. Many of these copies are so faulty that they cannot infect other cells, or they will only reproduce very slowly. But some will develop genetic changes that allow them to make copies even when antiretroviral drugs are around. This is called resistance.
- Every antiretroviral drug works against a slightly different part of HIV's protease or reverse transcriptase enzymes. Each enzyme is made up of many pairs of chemicals called amino acids. Sometimes these amino acids will be placed in different positions as a result of faulty copying, and this gives the virus the ability to carry on making copies even when high levels of a drug are present.
- However, another drug, which also stops reverse transcriptase from working, may work on this 'mutant' virus, because its target is a different set of amino acids.

- This is why 'combination therapy' is more effective than using one drug to fight the virus.
- Combination therapy can use different drugs that attack the same enzyme, or it can use a combination of drugs that attack several different enzymes at once. It's not known which approach is best in the long term.
- Combinations of two or more drugs have been shown to substantially reduce the risk of disease progression and death. The best results are usually seen with combinations that include a protease inhibitor or an NNRTI.

Cost is obviously the most significant single obstacle to provision of antiretroviral therapy. The cost of antiretroviral medication using drugs like Nevirapine and combining them with two other reverse transcriptase inhibitors can be between Rs 1000 to 1200 each month, while those with Efavirenz can be Rs 3200 or so. Those requiring protease inhibitors will be much more expensive costing more than Rs 7,000 each month. These medications are now available free of cost from ART centers all over India. PGIMER is one of the centers. These medications can reduce the incidence of opportunistic infections and can to a great extent avoid the need of use of anti-infectious agents in the long run.

Many of these drugs available in India have the required three drugs in a single tablet so compliance becomes easier and in non-protease inhibitor based regimens one may need to take only 2-3 tablets a day. This is a privilege that even the West does not enjoy.

Therapy is recommended for any asymptomatic person with a CD4 count below 350 cells/mm<sup>3</sup>. In asymptomatic person, with a CD4 count above 350, treatment may be considered when viral load is above 50,000 copies/ml (TR-PCR assay). The strength of the recommendation should be based on the readiness of the patient to adhere to treatment and the outcome based on CD4 count, CD4 cell rate of decline and viral load.

The goals of treatment are:

- maximal and durable suppression of viral load
- restoration and/or preservation of immunologic function
- improvement of quality of life
- reduction of HIV-related morbidity and mortality.

As with any drug, antiretroviral medication carries with it a number of side effects, a cost that must be borne till such time, as better drugs are available.

It must be remembered that there is no curative therapy for HIV infection and medications for HIV can only continue to keep the virus suppressed for long periods of time. In that sense this becomes similar to high blood pressure or diabetes mellitus where one needs to take regular medication in order to remain healthy.