Anti-HIV therapy

Therapy for the treatment of HIV infection (human immunodeficiency virus) involves a combination of drugs. These drugs interfere with the process in which the virus tries to replicate itself in specific cells of the immune system such as T CD4 lymphocytes or macrophages (See *Infovihtal #02 Immune system cells*).

Although they cannot eliminate HIV completely, they are able to reduce the capacity of infected cells to produce new viruses that in turn may infect human cells even further.

The anti-HIV drugs currently available come in five main categories:

1. Protease inhibitors. Blocking the protease enzyme inhibits the production of new viral proteins in infected cells. Non-functional viruses are thus produced.

- Protease inhibitors are: Aptivus® (tipranavir), Crixivan® (indinavir), Invirase® (saquinavir), Kaletra® (lopinavir+ritonavir), Norvir® (ritonavir), Prezista® (darunavir), Reyataz® (atazanavir), Telzir® (fosamprenavir), Viracept® (nelfinavir).

2. Nucleoside/nucleotide analogue reverse transcriptase inhibitors. IThese prevent this enzyme from ensuring the cell (T CD4 lymphocyte or macrophage) is infected with the HIV virus.

- Nucleoside/nucleotide analogues are: Combivir® (AZT+3TC), Emtriva® (FTC), Epivir® (3TC), Kivexa® (abacavir+3TC), Retrovir® (AZT), Trizivir® (abacavir+3TC+AZT), Truvada® (tenofovir+FTC), Videx® (ddI), Viread® (tenofovir), Zerit® (d4T), Ziagen® (ABC) and the generic Zidovudine and Lamivudine. Atripla® contains Truvada® (and Sustiva®).

3. Non-nucleoside reverse transcriptase inhibitors. These also stop reverse transcriptase from working to complete cell infection by the HIV virus, although their mechanism is different.

- Non-nucleosides are: Intelence® (etravirine), Sustiva® (efavirenz) and Viramune® (nevirapine). Atripla® contains Sustiva® (and Truvada®).

4. Entry inhibitors. These prevent HIV from entering the cell to be infected (T CD4 lymphocyte or macrophage). They prevent HIV from entering the cell to be infected.

In accordance with their operating mechanism, they are divided into:

- **Fusion inhibitors:** Fuzeon® (T-20).
- **CCR5 co-receptor antagonists**: Celsentri® (maraviroc).

5. Integrase inhibitors. These block the action of integrase, an enzyme that inserts HIV genetic material into the nucleus of the infected cell. If the virus does not reach the nucleus, it can neither replicate nor spread the infection.

- Isentress® (raltegravir) is the only drug in this family.

If you wish to know in which moment HIV replication operates in each of the drug types, please read *InfoVIHtal #07 The HIV life cycle*.

Anti-HIV treatment is also known as combination therapy or HAART (Highly Active Antiretroviral Therapy) and consists of a combination of three or more drugs, usually of at least two different kinds. The best therapy is one that adapts to each specific individual, is effective in reducing or keeping viral load at undetectable levels, is well tolerated and yields no side effects that may significantly reduce a person's quality of life or place his or her health at risk. The best therapy for one person may therefore not be the most appropriate for another. As the number of drugs available increases, treatments are tending to become tailored for each individual.

A person with HIV may not necessarily need treatment for a time. Treatment is started to prevent damage a person's immune system, which would leave the organism exposed to infections or other complications that endanger life. The degree of damage to the immune system is measured in this case by the number of T CD4 lymphocytes per millimetre of blood. Treatment is recommended for a count of below 350 CD4. If the count ranges from 350 to 500 CD4, treatment may be started if the viral load is very high and/or following the onset of an AIDS-related illness. Treatment is not usually started for cell counts of above 500 CD4.

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Side effects

Like all medicines, anti-HIV drugs may have side effects. Make sure your your HIV doctor or pharmacist explains the side effects you may expect from any drugs you decide to take, including mild ones that may wear off and serious side effects that you should report to your doctor as soon as possible.

Resistance

Resistance can develop whenever HIV continues to reproduce whilst treatment is being followed. Although HIV may be resistant to one drug, there remains a great likelihood that other antiretroviral drugs will be effective. Sometimes, however, the development of resistance to a specific drug also means the development of resistance to other drugs of the same kind, which may result in fewer treatment options in the future.

Failing to take doses or not taking them at recommended times may help cause resistance. Treatment should therefore be started when you are sure you can keep to the established times for doses. If you think it will be difficult to follow the recommended treatment, please consult your doctor (See *InfoVIHtal #46 Resistance development*).

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