



# WHAT IS ANTIRETROVIRAL THERAPY (ART)?

## WHAT IS ART?

ART means treating retroviral infections like HIV with drugs. The drugs do not kill the virus. However, they slow down the growth of the virus. When the virus is slowed down, so is HIV disease. Antiretroviral drugs are referred to as ARV. ARV therapy is referred to as ART.

## WHAT IS THE HIV LIFE CYCLE?

There are several steps in the HIV life cycle. (See Fact Sheet 400 for a diagram.)

1. Free virus circulates in the bloodstream.
2. HIV attaches to a cell.
3. HIV empties its contents into the cell (infects the cell).
4. The HIV genetic code (RNA) is changed into DNA by the reverse transcriptase enzyme.
5. The HIV DNA is built into the infected cell's DNA by the integrase enzyme.
6. When the infected cell reproduces, it activates the HIV DNA, which makes the raw material for new HIV viruses.
7. Packets of material for a new virus come together.
8. The immature virus pushes out of the infected cell in a process called "budding."
9. The immature virus breaks free of the infected cell.
10. The new virus matures: raw materials are cut by the protease enzyme and assembled into a functioning virus.

## APPROVED ARV DRUGS

Each type, or "class", of ARV drugs attacks HIV in a different way. The first class of anti-HIV drugs was the **nucleoside reverse transcriptase inhibitors**, also called "**nukes**". These drugs block Step 4, where the HIV genetic material is converted from RNA into DNA. The following drugs in this class are used:

- AZT (ZDV, zidovudine, Retrovir®)
- ddI (didanosine, Videx®)
- d4T (stavudine, Zerit®)
- 3TC (lamivudine, Epivir®)
- Abacavir (Ziagen®)
- Tenofovir (Viread®) (a nucleotide)
- Combivir® (AZT/3TC combination)
- Trizivir® (AZT/3TC/Abacavir combination)
- Emtricitabine (FTC, Emtriva®)
- Truvada (combination of Emtriva and Viread)
- Epzicom (combination of abacavir and 3TC)

Another class of drugs blocks the same step of the life cycle, but in a different way. These are the **non-nucleoside reverse transcriptase inhibitors**, or **NNRTIs**. Three have been approved:

- Nevirapine (NVP, Viramune®)
- Delavirdine (DLV, Rescriptor®)
- Efavirenz (EFV, Sustiva®).

The third class of ARV drugs is the **protease inhibitors**. These drugs block Step 10, where the raw material for new HIV virus is cut into specific pieces. Ten protease inhibitors are approved:

- Saquinavir (SQV, Invirase® and Fortovase®)
- Indinavir (IDV, Crixivan®)
- Ritonavir (RTV, Norvir®)
- Nelfinavir (NFV, Viracept®)
- Amprenavir (APV, Agenerase®)
- Lopinavir (LPV, Kaletra®)
- Atazanavir (TAZ, Reyataz®)
- Fosamprenavir (908, Lexiva®)
- Tipranavir (PNU140690, Aptivus™)
- Darunavir (TMC114, Prezista™)

The newest class of ARV drugs includes **fusion and attachment inhibitors**. They prevent HIV from attaching to a cell by blocking Step 2 of the life cycle. One fusion inhibitor has been approved:

- Enfuvirtide (Fuzeon® or T-20)

## HOW ARE THE DRUGS USED?

When HIV multiplies, most of the new copies are mutations: they are slightly different from the original virus. Some mutations keep multiplying even when you are taking an ARV drug. When this happens, the drug will stop working. This is called "developing resistance" to the drug.

If only one ARV drug is used, it is easy for the virus to develop resistance. But if two drugs are used, a successful mutant would have to "get around" both drugs at the same time. And if three drugs are used, it's very hard for a mutation to show up that can resist all three drugs at the same time.

Using a triple-drug combination means that it takes much longer for resistance to develop. For this reason, using just one ARV drug (monotherapy) is not recommended.

## CAN THESE DRUGS CURE AIDS?

A blood test called the "viral load" measures the amount of HIV virus in your bloodstream. People with lower viral loads stay healthier longer. See Fact Sheet 125 for more information on the viral load test.

Some people's viral load is so low that it is "undetectable" by the viral load test. This does **not** mean that all the virus is gone. Researchers used to believe that ARV therapy could eventually kill off all of the HIV virus in the body. This is not true. The drugs do not "cure" AIDS. However, they make it possible for people with AIDS to live a long time.

## WHEN DO I START?

There is not a clear answer to this question. Most doctors will consider three things: 1) your viral load; 2) your CD4 cell count; and 3) any symptoms you've had. ARV therapy is usually started if your viral load is over 100,000, if your CD4 cell count is below 350, or if you've had any symptoms of HIV disease. See fact sheet 404 for more information on treatment guidelines. This is an important decision you should discuss with your doctor.

## WHICH DRUGS DO I USE?

Each ARV drug has side effects. Some are serious. Refer to the fact sheet for each individual drug. Some combinations of drugs are easier to tolerate than others, and some seem to work better than others. Each person is different, and you and your doctor will have to decide which drugs to use.

The viral load test is now being used to see if ARV drugs are working. If the viral load does not go down, or if it goes down but comes back up, it might be time to change ARV drugs.

## WHAT'S NEXT?

New drugs are being developed in all four of the existing classes. Researchers are also trying to develop new types of drugs, such as drugs that will block other steps in the HIV life cycle, and drugs that will strengthen the body's immune defenses. See fact sheets 460, 470 and 480 for more information on newer classes of drugs.

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