



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.
4. The HIV genetic code (RNA) is used by the reverse transcriptase enzyme to build HIV DNA.
5. The HIV DNA is inserted into the cell's DNA by the integrase enzyme. This establishes the HIV infection in the cell.
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 NRTIs or "nukes".) These drugs block Step 4, where the HIV genetic material is used to create DNA from RNA. The following drugs in this class are used:

- Zidovudine (Retrovir, AZT)
- Didanosine (Videx, Videx EC, ddl)
- Stavudine (Zerit, d4T)
- Lamivudine (EpiVir, 3TC)
- Abacavir (Ziagen, ABC)
- Tenofovir, a nucleotide analog (Viread, TDF)
- Combivir (zidovudine/lamivudine combination)
- Trizivir (zidovudine/lamivudine/abacavir combination)
- Emtricitabine (Emtriva, FTC)
- Truvada (combination of emtricitabine and tenofovir)
- Epzicom (combination of abacavir and lamivudine)

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**, also called **non-nukes** or **NNRTIs**. Four have been approved:

- Nevirapine (Viramune, NVP)
- Delavirdine (Rescriptor, DLV)
- Efavirenz (Sustiva or Stocrin, EFV)
- Etravirine (Intelence, ETR)

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

- Saquinavir (Invirase, SQV)
- Indinavir (Crixivan, IDV)
- Ritonavir (Norvir, RTV)
- Nelfinavir (Viracept, NFV)
- Amprenavir (Agenerase, APV)
- Lopinavir/ritonavir (Kaletra or Aluvia, LPV/RTV)
- Atazanavir (Reyataz, ATZ)
- Fosamprenavir (Lexiva, Telzir, FPV)
- Tipranavir (Aptivus, TPV)
- Darunavir (Prezista, DRV)

A newer class of ARV drugs is **entry inhibitors**. They prevent HIV from entering a cell by blocking Step 2 of the life cycle. Two drugs of this type have been approved:

- Enfuvirtide (Fuzeon, T-20)
- Maraviroc (Selzentry or Celsentri, MVC)

The newest type of ARV drug is the integrase inhibitor. It prevents HIV from inserting its genetic code into the human cell's code in step 5 of the life cycle. The first drug of this type is:

- Raltegravir (Isentress, RGV)

HOW ARE THE DRUGS USED?

Antiretroviral drugs are usually used in combinations of three or more drugs from more than one class. This is called "Combination Therapy." Combination therapy works better than using just one ARV alone, it also helps prevent drug resistance.

Manufacturers of ARVs keep trying to make their drugs easier to take, and have combined some of them into a single pill. See Fact Sheet 409 for more information on combination medications.

WHAT IS DRUG RESISTANCE?

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 ARV drugs. 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. For this reason, using just one ARV drug (monotherapy) is not recommended. 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 the right mutations 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.

CAN THESE DRUGS CURE AIDS?

At present, there is no known cure for HIV infection or AIDS. ARVs reduce the viral load, the amount of HIV in your bloodstream. A blood test measures the viral load. People with lower viral loads stay healthier longer. They are also less likely to transmit HIV infection to others.

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, and it does not mean a person is cured of HIV infection. See Fact Sheet 125 for more information on viral load.

WHEN DO I START?

There is not a clear answer to this question. Most doctors will consider your CD4 cell count and any symptoms you've had. ARV therapy is usually started if your CD4 cell count is dropping to near 350, if you are pregnant, need treatment for hepatitis B, or have symptoms of HIV-related disease. See fact sheet 404 for more information on treatment guidelines. This is an important decision you should discuss with your health care provider.

WHICH DRUGS DO I USE?

Each ARV drug can have side effects. Some may be 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 health care provider will have to decide which drugs to use.

The viral load test is 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 studied in all 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 470 and 480 for more information on newer classes of drugs.

Revised April 24, 2009