Antiretroviral Therapy (ART)

WHAT IS ANTIRETROVIRAL THERAPY (ART)?

Antiretroviral therapy (ART) is a group of medications that treat HIV. The drugs do not kill the virus or cure HIV. However, when taken in combination they can prevent the growth of the virus. When the virus is slowed down, so is HIV disease. Antiretroviral drugs are referred to as ARVs. Combination ARV therapy is referred to as highly active ART (HAART).

WHAT IS THE HIV LIFE CYCLE?

There are several steps in the HIV life cycle.

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 material (RNA) is used by the reverse transcriptase enzyme to build HIV DNA.
5. The HIV DNA is inserted into the cell's chromosome by the HIV 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.

Nucleoside reverse transcriptase inhibitors (NRTIs) block step 4, where HIV genetic material is used to create DNA from RNA. NRTIs bind to and block reverse transcriptase. HIV uses reverse transcriptase to convert its RNA into DNA (reverse transcription). Blocking reverse transcriptase and reverse transcription prevents HIV from replicating. Some drugs in this class are:

- lamivudine (Epivir)
- abacavir (Ziagen)
- tenofovir DF (Viread)
- emtricitabine (Emtriva)

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) also block step 4 but in a different way. Some drugs in this class are:

- efavirenz (Sustiva)
- etravirine (Intelence)
- rilpivirine (Edurant)
- doravirine (Pifeltro)

Protease inhibitors (PIs) block step 10, where the raw material for new HIV virus is cut into specific pieces. PIs block protease (an HIV enzyme). By blocking protease, PIs prevent new (immature) HIV from becoming a mature virus that can infect other CD4 cells. The drugs in this class are:

- atazanavir (Reyataz)
- darunavir (Prezista)

Entry inhibitors prevent HIV from entering cells by blocking step 2 of the life cycle. Some drugs in this class are:

- maraviroc (Selzentry)
- ibalizumab-uiyk (Trogarzo)
- fostemsavir (Rukobia)

Integrase inhibitors prevent HIV from inserting its genetic code into the human cell's code in step 5 of the life cycle. Some

drugs in this class are:

- raltegravir (Isentress, Isentress HD)
- dolutegravir (Tivicay, Tivicay PD)
- elvitegravir (Vitekta)
- cabotegravir (Vocabria)

Pharmacokinetic Enhancers (PK Enhancers) are used to boost the effectiveness of another drug. When the two drugs are given together, the PK enhancer interferes with the breakdown of the other drug, which allows that drug to remain in the body longer at a higher concentration. PK enhancers are included in some HIV treatment regimens. The drugs in this class are:

- ritonavir (Norvir)
- cobicistat (Tybost)

Combination HIV medicines contain 2 or more ARVs from 1 or more drug classes. The drugs in this class are:

- Kaletra
- Epzicom
- Truvada
- Atripla
- Complera
- Stribild
- Triumeq
- Prezcobix
- Evotaz
- Genvoya
- Descovy
- Odefsey
- Juluca
- Biktarvy
- Symfi and Symfi-Lo
- Cimduo
- Delstrigo
- Symtuza
- Dovato
- Cabenuva

HOW ARE THE DRUGS USED?

ARVs are usually used in combinations of 3 or more drugs from more than 1 class. This is called combination therapy. Combination therapy helps prevent drug resistance.

Manufacturers of ARVs keep trying to make their drugs easier to take and have combined some of them into single tablet regimens.

WHAT IS DRUG RESISTANCE?

When HIV multiplies many of the new copies have mutations, which means they are slightly different from the original virus. Some mutant viruses keep multiplying even when you are taking ARV drugs. When this happens, the virus can develop resistance to the drug and ART may stop working.

If only 1-2 ARV drugs are used, it is easy for the virus to develop resistance. For this reason, using just 1-2 ARVs is not recommended. But if 3 drugs are used, a successful mutant would have to get around all of the drugs at the same time. Using combination therapy means that it takes much longer for resistance to develop. Read more about HIV drug resistance.

CAN THESE DRUGS CURE HIV/AIDS?

ARVs reduce the viral load, the amount of virus in your bloodstream, but are not a cure. A blood test measures the viral load.

Some people's viral load is so low that it is undetectable by the viral load test. People with undetectable viral loads stay healthier longer. They are also less likely to transmit HIV infection to others. Having an undetectable viral load does **not** mean that all the virus is gone, however, and it does not mean a person is cured of HIV infection.

WHEN TO START ART

Current U.S. guidelines recommend that all people with HIV should start ART, regardless of how long they have had the virus or their current health status. This is an important decision you should discuss with your healthcare provider.

The recommendation for all people with HIV to start ART includes the following groups:

- People in the early stages of HIV
- People who are pregnant or breastfeeding
- People with stage 3 HIV
- People with HIV-related infections or cancers

Ideally, you should begin ART on the day you receive a diagnosis of HIV, or as soon as possible after this. This gives you the best chance of reducing your viral load and risk of complications.

If you do not receive effective ART, the virus typically develops into the most advanced stage, stage 3 HIV, within 10 years. At this stage, the immune system is badly damaged, which can lead to opportunistic infections (OIs) or certain types of cancer. Research shows that receiving prompt treatment reduces the risk of transmission, disease progression, and complications. However, it can be challenging to follow a daily treatment plan consistently for many reasons. These include:

- Access to and affordability of medications
- Stigma and discrimination in the healthcare system
- Mental health and substance use issues
- Pill fear or pill fatigue

If you are having trouble following your ART regimen consistently, it is best to talk to your healthcare provider as soon as possible to work out a plan to stay healthy.

HIV.gov provides information about covering the costs of HIV treatment and tips for following an ART regimen.

WHICH DRUGS DO I USE?

ARVs are chosen on the basis of treatment guidelines, HIV drug resistance, your health (for example, kidney or liver disease) and lifestyle factors. While ARV regimens are usually well tolerated, each ARV drug can have side effects. Some may be serious. Refer to the fact sheet for each individual drug for more information. Each person is different and you and your healthcare provider will have to decide which drugs to use.

Adherence to ARVs is very important for treatment to work. The viral load test is used to see if ARV drugs are working.

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.

THE BOTTOM LINE

Antiretroviral therapy (ART) is a group of medications that treat HIV. The drugs do not kill or cure the virus. However, when taken in combination they can prevent the growth of the virus.

Each type, or class, of antiretroviral drugs (ARVs) attacks HIV in a different way. ARVs are chosen on the basis of treatment guidelines, HIV drug resistance, your health (for example, kidney or liver disease) and lifestyle factors. While ARV regimens are usually well tolerated, each ARV drug can have side effects. Some may be serious.

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MORE INFORMATION

HIV.info.NIH.gov: FDA-Approved HIV Medicines

US Food & Drug Administration (FDA): HIV and AIDS: Medicines to Help You

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