SALVAGE THERAPY

WHAT IS SALVAGE THERAPY?

Antiretroviral therapy (ART) sometimes needs to be changed. This usually happens when the viral load (see fact sheet 125) increases instead of staying very low. This treatment failure almost always means that HIV has developed resistance (see fact sheet 126) to the antiretroviral drugs (ARVs) someone is taking. Then HIV can multiply even when someone is taking ART. Treatment failure is also often caused by skipping doses (poor adherence, see fact sheet 405).

Before the use of triple combinations of antiretroviral drugs (ARVs) many health care providers changed ART at the first sign of an increase in viral load. Patients were given just one new ARV at a time. This approach is called "sequential monotherapy" or "virtual monotherapy." The goal was just to keep the patient alive for a few more months.

We now know that this is not the best way to control viral load. If the virus is only exposed to one new drug, it's much easier for the virus to develop resistance.
As a patient's virus accumulates more and more resistance mutations, it becomes harder to choose ARVs that can control it. When there are no good treatment options, ART for these patients is referred to as "salvage therapy." The number of people with HIV in the US who need salvage therapy is unknown, but is estimated to be between 20,000 and 40,000.

HOW CAN YOU AVOID SALVAGE THERAPY?

The best way to avoid salvage therapy is to make each regimen of ART last as long as you can. Be sure to miss as few doses as possible. Learn about the pattern of resistance of your virus. Ask your health care provider about any changes in your ART.

If possible, you should always have two or more "active drugs" in your ART regimen. An active drug is one that is expected to work against HIV based on the mutations in your virus. Your health care provider will need to review the results of a resistance test (see fact sheet 126). This can be a genotypic test or a phenotypic test.

Remember, the best way to get into trouble is to just add one new drug at a time to failing ART. That will set you up for resistance to the new drug in a very short time.

WHEN DOES SOMEONE NEED SALVAGE THERAPY?

Once HIV has acquired several resistance mutations, the chances of serious HIV disease are higher. This is especially true for patients with low CD4 counts (see fact sheet 124.) You may need to make immediate changes if:

- you are losing weight
- your CD4 count is dropping
- you have serious side effects
- you have increasing symptoms

However, if your health and CD4 count are stable, you can go onto a "holding regimen" while you wait for new drugs to be developed. **Do not stop taking medications to prevent opportunistic infections (OIs, see fact sheet 500).** The drugs you need to take to prevent OIs are based on your CD4 count.

WHAT IS A "HOLDING REGIMEN"?

If you don't have at least two active ARVs to use, you need to preserve your CD4 count and keep your viral load as low as possible. You also want to preserve your treatment options. This normally means stopping any ARVs that are only partly effective so that your virus doesn't develop more resistance to them. This would make them totally ineffective. However, stopping all ARVs can be harmful.

On the other hand, stopping NNRTIs (delavirdine, nevirapine, or efavirenz) does not lead to increases in viral load or drops in CD4 cells. There's no benefit to keeping an NNRTI in a holding regimen. It appears that stopping protease inhibitors is less risky than stopping nukes (reverse transcriptase inhibitors.)

It can be scary to wait until you have two active ARVs available. The alternative is to "use up" a new ARV and lose its benefits quickly due to viral resistance.

GETTING ACCESS TO NEW DRUGS

You may not have to wait until new drugs are approved before you can use them. You may have access to a clinical trial (see fact sheet 105) of a drug in development. Some ARVs become available through an expanded access program long before they are approved. Currently the NNRTI etravirine (TMC125) and the integrase inhibitor raltegravir (Isentress) are available in expanded access. Sometimes these programs continue after approval for patients with special needs.

Remember that you want to be able to combine a new drug with at least one other active drug. You should review clinical trials carefully with your health care provider to make sure you're not exposed to sequential monotherapy. This is most likely if you get assigned to a "placebo" arm and don't receive the new drug being studied. More information on clinical trials is available at the following web site:
http://www.salvagetherapies.org/clinical.html
http://www.acria.org/clinical_trials/index.html
or http://www.clinicaltrials.gov/

The best option is being able to use a drug in a new class. Your virus will almost certainly not have any resistance mutations to a fusion or attachment inhibitor, or an integrase inhibitor. Right now, you might have access to T-20 (Fuzeon, enfuvirtide) which is a fusion inhibitor (see fact sheet 461.) There are also clinical trials of attachment inhibitors (see fact sheet 460) and integrase inhibitors and other ARVs (see fact sheet 470).

THE BOTTOM LINE

There are more options today for people with advanced HIV disease than at any time in the past. Treatment can have excellent results, even for people whose virus is resistant to most existing ARVs. An experienced health care provider is very important in helping you decide when to change treatment and when to wait.