

## RESEARCH STUDY

OPTIMA is a study to find the best way to treat people who have taken a wide range of anti-HIV drugs in several different combinations and who now have a viral load above 5,000 on their current combination. Doctors have several ideas about what to do in this situation, but it is not clear which approach is best. It is for this reason that a randomized study is needed. People will be randomly assigned (by the flip of a coin, for example) to one of four treatment groups. Randomly assigning people to treatment groups reduces the possibility that doctors or patients influence the results of the study by their personal opinions; therefore, the results of the study are more reliable.

The different approaches are detailed on the centerfold of this leaflet. Anyone joining this study must be willing to follow the treatment group given to them at randomization. Everyone entering the study will be carefully monitored and their health will come first. However, where possible and safe, you will be encouraged to stay in the treatment group you were given at randomization. If people change treatment groups, it will be more difficult to prove whether one treatment strategy is better than another.

If you are satisfied with the current treatment you are receiving or do not want to be in any one or more of our proposed treatment groups, then you should not join this study.

## QUESTIONS & ANSWERS

**Q. What happens if I don't get a good response to the treatment?**

A. If you become more ill or your treatment continues to fail then you can change to whatever treatment is felt to be best for you.

**Q. Where do the ideas for this trial come from?**

A. Doctors in clinics have been seeing more and more people who have been experiencing problems with resistance and drug failure. They were unsure of the best way to treat their patients and, after consultation with other professionals, they formulated this study.

**Q. Can I stay off treatment for longer than three months?**

A. Yes, if you are doing well (in terms of CD4 count, viral load, no illnesses, etc.) the period off treatment can be varied under your physician's guidance.

**Q. Who chooses the actual drugs and will I get a voice in this?**

A. The choice of drugs you take are decided by you and your doctor. OPTIMA only decides the treatment group. If, for example, you are randomized to treatment group 1 you can take any drugs as long as you only have a combination of four or less anti-HIV drugs. Your doctor's choice will be guided by the resistance test taken when you join the study.

**Q. I am worried I will get the treatment strategy that is proven to be the worst one.**

A. This is a possibility; however, all the treatment strategies being looked at in this study are valid ways of treating people whose current treatment is failing. The study will find out if one is any better than the others, though it is possible that they will all be found to be as good as each other. If, during a study, one treatment strategy is found to be dramatically better than any other, it is usual for this to be made public and everyone is then given the opportunity to change to this treatment.

**Q. What happens if I get randomized to a group that I do not like?**

A. If you are not happy to be in any one of the treatment groups then this is not a study for you.

**Q. Will taking part in this study prevent me from getting new drugs?**

A. The organizers of this study will not prevent you joining other studies of HIV drugs under Expanded Access Protocols, and are working with drug companies to ensure you have access to new drugs. The choice of drugs is up to you and your doctor. However, some trials of new drugs will not allow you to be in other studies. You always have the right to withdraw from a study for any reason. For example, you might decide at some point in the future that this would be your best option to access a new drug.

## WORKING TOGETHER

Research studies try to answer important questions about HIV treatment. OPTIMA is more complex than some as it asks two questions. It is only by working with people with HIV, doctors, nurses, researchers and, in the case of OPTIMA, international partners, that we can answer these questions.

OPTIMA would not be possible without people like you. It is true that the best treatment might not be the approach that you are randomized to, but if the doctors and researchers knew which one of the four ideas was the best one we would not be doing this study. Your support is vital to help everyone for whom current HIV treatments are failing.

The OPTIMA study is being run in four countries. The Medical Research Council – Clinical Trials Unit manages the study for the United Kingdom and Ireland. The Department of Veteran Affairs manages and offers the study through its network in the United States of America. In Canada, the study is managed by the Canadian HIV Trials Network with funding from the Canadian Institutes of Health Research.



The website for the study is [www.optimatrial.org](http://www.optimatrial.org)

Canadian HIV Trials Network (CTN): [www.hivnet.ubc.ca](http://www.hivnet.ubc.ca)

**HIV/AIDS websites for patients**

Canadian AIDS Treatment Information Exchange (CATIE): [www.catie.ca](http://www.catie.ca)

AIDS Education Global Information System (AEGIS): [www.aegis.org](http://www.aegis.org)

The Body: [www.thebody.com](http://www.thebody.com)

**CATIE hotline:** 1-800-263-1638

**CTN toll-free information:** 1-800-661-4664

**Thank you for your time**

**Optima**  
OPTIONS IN MANAGEMENT  
WITH ANTIRETROVIRALS

## HIV RESEARCH STUDY

Is this  
leaflet  
for me?

Is your CD4 count below 300  
and your viral load over 5,000?

Have you already used  
several anti-HIV drug  
combinations?

Are you unsure what the  
options are now?

Yes to all  
of these?

Then this  
leaflet is  
for you!

## Treatment group 1

### Standard Care – up to 4 anti-HIV drugs

There is a belief that if minor changes are made to the drugs you take, the decline in the CD4 count and rise in viral load may be slowed. The changes to drug therapy would be made with the results of a resistance test to guide the choice.

While no dramatic changes are expected for participants in this group, there may be benefits as the regimen should be more stable and easier to follow than treatment groups two and four. There is some evidence that this approach may still have some benefit.

Some of the other treatment groups have high amounts of risk associated with them and increases in the number of drugs to take.

#### Pros and Cons

- ✓ Not much change.
- ✓ Fewer drugs to take (than some other treatment groups).
- ✓ Less risk of opportunistic infections if no HIV-drug-free period.
- ✗ Less chance of a dramatic positive change.
- ✗ Using up to four drugs may not be as potent as using six anti-HIV drugs.
- ✗ May continue to develop resistance to existing drugs.

## Treatment group 2

### Mega ART – 5 or more anti-HIV drugs

The resistance test that will be done when a person is screened for this study is likely to show resistance to many drugs. Where little or no resistance is shown to a drug, it will be chosen (unless the person has been unable to tolerate it before and does not want to give it another try).

The thinking behind this treatment group is that even if the virus is slightly resistant, each drug is still doing something against HIV. So if you get several small bits of work from several drugs you may get more effect and less virus. A doctor may suggest more than five drugs—some have tried up to 11 with favourable results in the reduction in HIV viral load.

#### Pros and Cons

- ✓ A fall in viral load has been seen in some smaller studies.
- ✓ Less risk of opportunistic infections with constant anti-HIV drugs.
- ✓ This approach is successful in other areas such as cancer treatment.
- ✗ More drugs can theoretically increase risk of side effects.
- ✗ Difficulty taking large combinations at different times.
- ✗ It is unknown how long the effect will last.

## Treatment group 3

### Stop anti-HIV drugs for 12 weeks, then restart with up to 4 drugs

Another idea is to stop all drugs for up to 12 weeks, then restart with up to four drugs. The choice of drugs for the new regimen will be guided by the results of the resistance test. The thinking behind this is that changes, which make the virus less resistant to drugs, have been seen in the virus when HIV drugs are not taken for around 12 weeks. The changes to the virus make the virus easier to kill by the anti-HIV drugs that had almost stopped working before. Twelve weeks is chosen because in tests most of the changes in the virus happen around 10 weeks after stopping drugs.

People are carefully monitored during the drug-free period for early detection of any dangerous drop in CD4 counts or opportunistic infections, and if this occurs you will be able to restart treatment immediately.

#### Pros and Cons

- ✓ A harder hit to the virus when drugs are restarted.
- ✓ The HIV drug-free period gives you and your body a rest from the side effects of anti-HIV drugs.
- ✓ Gives a chance for the resistant virus to reduce.
- ✗ You may worry about not being treated when on the HIV-drug-free period.
- ✗ Your CD4 count may fall and may not come back to the same level when drugs are restarted.
- ✗ Viral load is expected to rise and may take time to (or may never) fall again once drugs have been restarted.
- ✗ Increased risk of opportunistic infections and the need to take drugs to prevent them.
- ✗ Unknown how long the hard hit (the effect of the drug-free period) will last for and whether this makes a difference in the long run.

## Treatment group 4

### Stop anti-HIV drugs for 12 weeks, then restart with 5 or more anti-HIV drugs

This idea combines the effects of the drug-free period and the enlarged hitting power of Mega-ART (more than five anti-HIV drugs). It is thought that this might have the potential for substantial benefit but also a number of disadvantages.

#### Pros and Cons

- ✓ In small studies this approach has produced better results than other approaches.
- ✓ Harder hit to virus when drugs are restarted.
- ✓ The HIV-drug-free period gives you and your body a rest from the side effects of anti-HIV drugs.
- ✓ Combination of many drugs may reduce the viral load.
- ✓ Gives a chance for the resistant virus to reduce.

- ✗ You may worry about not being treated during the HIV drug-free period.
- ✗ Your CD4 count may fall and may not come back to the same level when drugs are restarted.
- ✗ Viral load is expected to rise and may take time to (or may never) fall again once drugs have been restarted.
- ✗ Increased risk of opportunistic infections and the need to take drugs to prevent them.
- ✗ Unknown how long the hard hit (the effect of the drug-free period) will last for and whether this makes a difference in the long run.
- ✗ More drugs can theoretically increase risk of side effects.
- ✗ Difficulty taking large combinations at different times.

Participants are randomly assigned to one of the four treatment groups detailed on the left.

#### You may be included if

- You are aged 18 years or older
- You have HIV infection
- You have had failure of at least two different multi-drug combinations that included drugs of all three classes, or are resistant to all three classes of anti-HIV drugs
- You've been taking the same HIV drugs continuously for at least three months
- You have a CD4 count below 300
- You have a viral load above 5,000

#### You may be excluded if

- You are pregnant, or intend to become pregnant
- In the opinion of your doctor, *Mega-ART* of five or more anti-HIV drugs is unsafe for you to take
- You currently have a serious, uncontrolled opportunistic infection (OI)
- You have a serious non-HIV-related illness

Participating clinics will be able to give you more detailed information and help if you decide that this study is right for you. You can also visit the **OPTIMA** website for the full patient information sheet or contact the independent advisory groups.

OPTIMA website: [www.optimatrial.org](http://www.optimatrial.org)

#### Local Contact Information