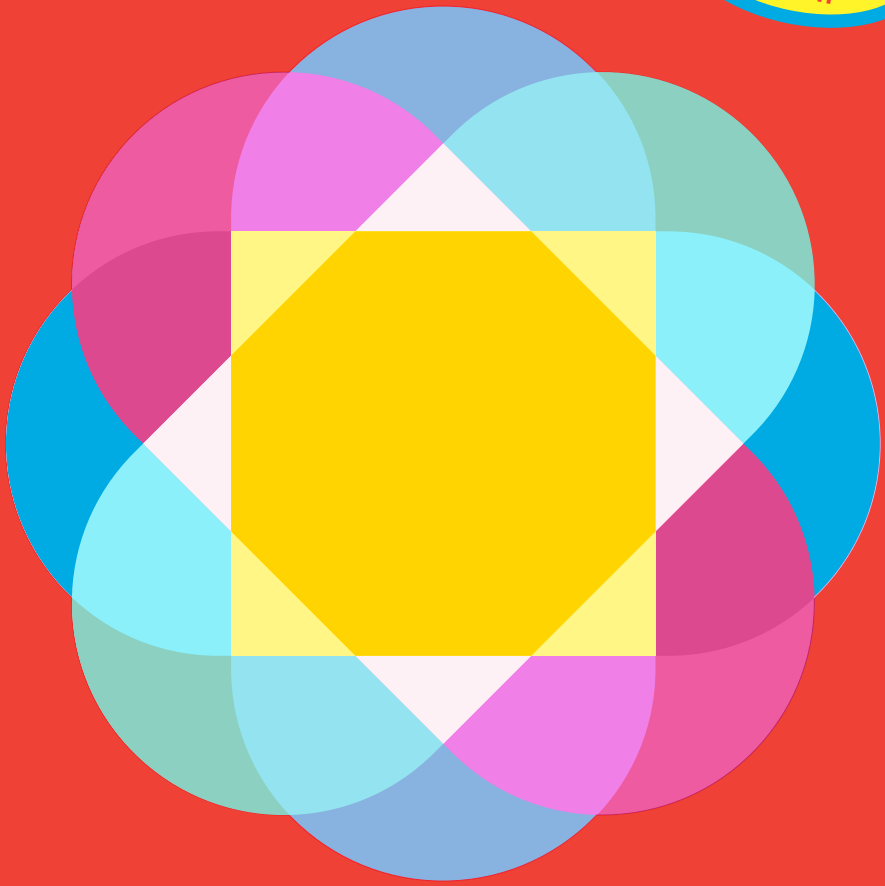
Introduction to combination therapy

July 2014

i-base
0808 800 6013

2014 edition



HIV i-Base
ISSN 1475-2077
www.i-Base.info
Watch for out-of-date information

First questions
You and your doctor
Resistance and adherence
Treatment choice

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Written and compiled by Simon Collins for HIV i-Base with thanks to an extended advisory group of HIV positive people and community advocates. Design by No Days Off. Funding thanks to The Monument Trust. Not-for-profit copying is encouraged or call for additional free copies.

HIV information dates quickly, please call to see if up-dated information is available.

If you have questions after reading this guide, i-Base runs a free treatment information phoneline for information and support on all aspects of HIV treatment.

Phoneline 0808 800 6013
Monday– Wednesday, 12–4 pm

The website also has a question and answer service where questions can be answered online and by email.

Introduction

This guide includes important information about HIV treatment.

It was written and reviewed by HIV positive people and health professionals.

If HIV is new to you, this booklet should help you feel more in control of this aspect of your life.

Information is based on latest UK guidelines (November 2013).

www.bhiva.org

When appropriate we also refer to European (2014) and US guidelines (2014).

www.eacsociety.org

www.aidsinfo.nih.gov

All guidelines stress that HIV treatment should be individualised.

This guide is updated every year because information about HIV can change.

If you are reading this after July 2015, please call i-Base for a new edition.

The main changes to this edition include:

- Minor edits throughout to improve readability.
- New information about HIV treatment and trans* people - page 13.
- New information on importance of the choice of early treatment in people who are recently infected.
- Updating the section on why treatment guidelines differ - page 18.
- Updating the section on treatment as prevention (TasP) to include results from PARTNER study - page 19 and throughout.
- Updating the section on choice of drugs to reflect latest guidelines and newly approved drugs - pages 30-38.
- Updating the section on NHS changes - new page 39.

Updates to the 4-page ARV chart in the centre pages include:

- New integrase inhibitors: dolutegravir, elvitegravir, and a four-in-one pill that includes elvitegravir (Stribild).
- New booster: cobicistat.
- Moving some of the least used ARVs to the back page of the insert.

First questions: what, when, why?

What is combination therapy?

Combination therapy is the term for using three or more drugs to treat HIV. It is also called triple therapy or ART (antiretroviral therapy).

HIV drugs are called antiretrovirals (ARVs) because they work against HIV which is a type of virus called a retrovirus.

Do the drugs really work?

In every country that uses ARVs, there has been a dramatic drop in HIV-related deaths and illnesses.

Treatment works for adults and children, for women, men and trans* people. It works no matter how you were infected. Whether this was sexually, through injecting drug use, at birth, or by blood or blood products.

Taking meds exactly as prescribed will reduce the virus in your body to tiny amounts. But some cells will always contain HIV and you will still be HIV positive.

Does everyone need treatment?

HIV infection progresses at very different rates in different people.

Nearly everyone who is HIV positive will need treatment at some time.

This includes people whose HIV progresses very slowly.

Based on starting treatment when the CD4 count is around 350:

- At least 1 in 5 people progress quickly and need treatment within 2 years of infection.
- Up to 50% of people could take 2-10 years (average of 5 years).
- About 1 in 4 people keep a CD4 count above 350 for 10 years without treatment.
- Less than 1 in 20 people keep a CD4 count above 350 for 15-20 years without treatment.
- Only 1 in 10,000 people keep a high CD4 count without treatment for more than 20 years.

However, many people start treatment at higher CD4 counts for other reasons, including to reduce the risk of transmission.

You and your doctor will discuss the best time to start treatment. This will usually take place over several visits.

It is a good idea to know about treatment even if you are not planning to use it yet.

Two essential blood tests: CD4 and viral load

Your CD4 and viral load are the main blood tests used to monitor your health.

CD4 count

- The CD4 count tells you about your immune system. Results are given as cells per cubic millimetre (cells/mm3).
- The range for HIV negative people is from about 400 to 1600, but anything above 500 is considered “normal”.
- Your CD4 count is important for deciding when to start treatment.
- Even with a very low CD4 count, treatment can boost your immune system to much stronger levels.
- UK guidelines recommend starting treatment before your CD4 count falls below 350.

Viral load

- Viral load tests tell you how much virus is in a small sample of blood. Results are given as copies/mL.
- If you are on treatment, viral load tests show how well your treatment is working. The aim of treatment is to get an ‘undetectable’ viral load. This means less than 50 copies/mL.
- Getting undetectable and staying there shows that the drugs are still working.
- If viral load doesn’t become undetectable or it increases later, the drugs may not be working or you may not be taking them correctly.
- Changing treatment may be necessary, but first, check the unusual result.

Your CD4 count and the risk of becoming ill

Your CD4 count is closely related to your risk of becoming ill. Your CD4 count and how it changes over time is used to decide when to start treatment.

Above 350, you still have a very good immune system but still are at higher risk of TB. As it drops below 350, the risk of skin or digestion problems increase.

Below 200 there is an added risk of a pneumonia called PCP.

Below 100 you become vulnerable to other very serious illnesses.

Below 50 the risks are higher still, including from a virus called CMV that can cause permanent sight loss. A CD4 count this low requires special eye checks.

HIV meds are much easier to take than drugs used to treat these HIV-related problems.

Although you may be worried about treatment, HIV is still a very real and life-threatening illness.

Deciding when to start treatment is discussed in more detail on page 14.

Figure 1: When not on treatment, your immune system works in overdrive

1. HIV infects CD4 cells and uses them to make more virus.

2. Your body makes more CD4 cells to fight the new HIV.

3. The new CD4 cells are targets for HIV to infect and replicate again.

4. Each cycle gradually weakens your immune system.

5. After treatment, when viral load becomes undetectable, your body stops over-producing CD4 cells and this cycle is stopped.

Your immune system can then take time to repair itself and grow stronger.

How do HIV drugs work?

HIV drugs work by stopping the virus from making copies of itself.

This brings viral load down to tiny levels. Your immune system (including your CD4 cells) then has a chance to become stronger again.

When not on treatment, your immune system is working in overdrive. HIV infects CD4 cells to make more virus. Your body produces new CD4 cells to fight the virus but HIV just uses these cells to keep reproducing. It is like a dog chasing it's own tail. (See Figure 1).

This cycle of immune activation is also thought to lead to other health complications. It is one of the reasons that people are now using treatment earlier. Effective treatment stops this harmful activation.

There are now over 26 drugs that work in at least six stages of the HIV life cycle. (See Figure 5 on page 31).

How long will the drugs work?

How long a combination works depends on not developing resistance.

As long as your viral load is undetectable (less than 50 copies/mL) you are unlikely to develop drug resistance as long as you keep taking your meds properly. This includes taking them at the right time, not missing doses and following any dietary advice.

Regular monitoring using blood tests will check that the drugs are working and that they continue to work.

Around 95% of people whose viral load stays undetectable for the first year, will continue to be undetectable for each following year.

There is no built-in time when treatment will stop working. If you take your meds as they are prescribed, you can use them until we get a cure!

"I was diagnosed in Feb 2014 after one low-risk experience. I knew immediately that I wanted to start treatment and I wanted to be less infectious to any future partners, even if we are using condoms.

I also learned from my support group that because I was diagnosed soon after I was infected, there may be additional benefits from early treatment.

When my first doctor didn't offer me treatment, I asked for a second opinion and I changed my doctor. This led to me starting treatment when I was still within six months of infection, which may be important.

Since then, my experience of HIV - both at the clinic and from support organisations - has been really positive. And it was great when my viral load became undetectable.

I knew I was really unlucky in catching HIV but learning and understanding how the treatment works and then deciding to use it has been an important part of how I chose to move forward."

Lenny, London

Can I take a break in my treatment?

Unless there is a medical reason to do this, taking a break in treatment is not usually recommended.

Staying on treatment is better for your long term health. It keeps your CD4 count high and stops HIV from doing more damage.

Treatment protects against damage that HIV may do to your heart, liver, kidneys and other organs and lowers the risk of some cancers. This is compared to either not being on treatment or starting and stopping treatment.

- Stopping treatment is not generally recommended.
- Your viral load is likely to increase within days. Each interruption has a risk of developing drug resistance.
- Your CD4 count is likely to drop and it will be more difficult to recover when you restart treatment.

If you really want to take a break, talk to your doctor first. If this is because side effects are too difficult there could be alternatives that are easier to use.

Does treatment always work?

HIV meds work for nearly everyone. If you do not get a good response if could be due to the following reasons.

- Adherence - this means checking you are taking the right dose at the right time each day.
- It might mean you are not following food recommendations.
- Potency - is the combination strong enough. Some combinations are not recommended with a viral load over 100,000 copies/mL. Also, the higher you start, the longer it may take to come down.
- Resistance - your HIV may have been resistant to one or more of the drugs you used. UK guidelines recommend a resistance test before starting treatment to check for this.
- Interactions and absorption - some medicines, including supplements and vitamins, can affect how you ARVs work. Speak to your doctor and pharmacist about all medicines and supplements you take.
- Side effects - you have to be able to tolerate your meds and they have to be easy for you to take.

Trial results never show a 100% response. But if you have a good doctor and you follow your regimen carefully, anyone starting treatment for the first time should be able to get an undetectable viral load.

Can I change treatments?

Initial side effects usually improve during the first few weeks. But, if your first combination is too difficult you can change the drug or drugs that are causing the problem.

If you are not getting on with your therapy, its important that you don't stop taking it without speaking with your doctor first. Book an earlier appointment to see your doctor, or ring or email them.

If this is your first combination, you have many choices. You should not put up with difficult side effects for months on end.

Some people use one combination to get their viral load undetectable, and then change to an easier combination afterwards.

A few people may change quickly, occasionally after days. Everything in HIV care is individual.

What is 'treatment-naive'?

'Treatment-naive' or 'drug-naive' refers to someone who has never used HIV drugs.

Someone who has taken HIV drugs before is called 'treatment-experienced'.

Should I enter a study?

Many hospitals are also research centres and you may be asked to join a study.

If you are interested in the study, take time to find out about the details.

If you are only just finding out about treatment, you should not feel pressured into taking part.

Ask about the alternatives to the treatment in the study. Ask what advantages or risks the study offers over existing treatment. You can ask for advice from i-Base or other HIV organisations.

Your future care will not be affected if you decide not to join a study.

However, well-planned research can often offer more comprehensive monitoring and care than you would normally receive at your regular clinic. This may mean a few more clinic visits.

Research is essential to improve how we use both new and existing drugs.

What about alcohol and recreational drugs?

Some HIV drugs interact with recreational and street drugs, methadone and some complementary medicines.

The interactions can be complex and can increase or decrease levels of HIV meds or other drugs.

It is therefore important that your HIV doctor and pharmacist know about other drugs or supplements that you take, even if you use them rarely. Your doctor will treat this information in confidence.

Alcohol does not interact with HIV medications. However, alcohol use, as with recreational drug use, may lead to missing doses.

Low adherence has been linked to how much alcohol someone drinks and the risk of treatment failure. This is something else that is good to discuss with your doctor.

What else do I need to know?

Ongoing research changes how we think about and use treatment. The meds that your doctor prescribes today may be different from last year. And they may be different again next year.

This isn't just because there are newer drugs available. It relates to a better understanding of:

- How the drugs work;
- Why meds sometimes stop working;
- Drug resistance; and
- The impact of HIV when not on treatment.

Are the drugs a cure?

The current drugs are a treatment, but they are not a cure. They stop the progression of HIV. They let your immune system start to repair itself and your CD4 count increase. But you will still be HIV positive.

Even people who have an undetectable viral load for years, still have small amounts of HIV in their bodies. This HIV is mainly in cells that are resting.

Most of your immune cells are sleeping or inactive – like books in a library. They become active in response to an infection – like someone taking a book off the shelves.

These sleeping cells are one of the reasons that it is difficult to find a cure for HIV. Some of these cells can sleep for 50 years, but they can also wake up at any time. This is why you need to continue taking treatment.

Exciting research is trying to cure HIV but this is still likely to be many years away.

This is still a good goal though. Whether from treatment or a cure, there is a good chance that eventually you could die of old age, rather than from HIV.

"I was caught just in time, in 1996, when the first effective combinations became available. I did not think that it would make a difference. Now that I understand how the drugs work, I know that they are active, whether I believe in them or not.

Recently, I've found out that ART protects my partner. I like feeling less infectious - it helps to normalise HIV.

Ask questions about anything you don't understand. You can then take responsibility for whatever you decide.

Look at treatment as something you have to be really committed to for the next few years. Take this new aspect of your life more seriously than anything else until you get it right."

Simon, London

Age, heart disease, gender and pregnancy

How do children use HIV treatment?

HIV treatment for children is similar to adults, but there are a few differences.

The immune system and drug absorption can be different in babies, children and adults. Expert paediatric HIV care is therefore recommended for children of all ages.

CD4 counts are higher in children than adults. A baby, for example, can have a CD4 count that is 3000. Because of these differences, children are usually monitored by their CD4 percentage (CD4%).

This is the percentage of white blood cells (lymphocytes) that are CD4 cells. The CD4% of an HIV negative person is around 40% (with a wide normal range of 25-55)

A CD4% of 12-15% is similar to an adult CD4 count of about 200 (22% is about 350 and 25-30% is about 500).

There are separate treatment guidelines for children. However, they tend to be updated less frequently than adult guidelines. It is therefore important to be aware of changes in adult care that may be just as relevant for children.

For more information about children and HIV, visit the Children with HIV Association (CHIVA) and PENTA web sites:

www.chiva.org.uk

www.penta-id.org

Is age an important factor in adults?

As you get older, it becomes more important to be on ART.

The UK treatment guidelines (www.bhiva.org) include a useful table on the risk of AIDS illnesses at different CD4 and viral load levels.

Importantly, this includes separate tables for ages 25, 35, 45 and 55. All risks increase with age.

Many researchers are looking at HIV and ageing. This is becoming a specialised subject and HIV services are changing to reflect this. New services are being developed for older patients.

Ageing is linked to many health problems. This is why lifestyle factors (diet, exercise, smoking etc) are just as important if you are HIV positive.

Age, HIV drugs and heart disease

The biggest risks for heart disease are smoking, poor diet and low exercise.

Other factors include age (over 45 for men and over 55 for women), sex (male), family history of heart disease, alcohol use, high blood pressure and diabetes.

High cholesterol is an independent risk. This is also related to diet and exercise.

As some HIV drugs can cause cholesterol and triglycerides to increase, you will be monitored for this.

HIV itself may be a risk for heart disease if you are not on treatment.

In the SMART study, people who stopped treatment were more likely to develop heart, kidney or liver disease than people on continuous treatment. This study showed that the benefits of HIV treatment generally outweigh any additional risk of heart disease.

The largest study looking at heart disease and HIV treatment (called D:A:D), showed that most HIV meds are not linked to heart disease.

The two exceptions are lopinavir/r (Kaletra) and abacavir.

It is important to know your underlying risk of heart disease before you use either of these drugs.

Checking your risks for heart disease is recommended when you are first diagnosed, before starting HIV treatment and then every year.

BHIVA recommend several online risk calculators:

http://hivpv.org

http://www.qrisk.org

http://www.qintervention.org

The q-intervention calculator also looks at risk for type-2 diabetes.

As in the general population, making lifestyle changes to reduce your risk of heart disease is good advice if you are HIV positive.

This becomes even more important if you have other risk factors as these add up to a higher overall risk.

What about treatment in pregnancy?

HIV meds are very effective during pregnancy. In addition, having an undetectable viral load reduces the risk of transmitting HIV to your baby to almost zero.

Treatment during pregnancy is a specialised area. For more information see the i-Base guide: *HIV, Pregnancy and Women's Health*.

Is gender important in response to treatment?

HIV treatment works in a similar way for people of all genders.

A few side effects may affect women differently to men, but most are similar.

At the same CD4 count, women can have a slightly lower viral load, so this may be a reason for women to start treatment slightly earlier (at a higher CD4 count) than men.

However, social factors affect women, men and trans* people differently and this can include access to care and support.

Trans* people and HIV treatment

HIV meds are safe and effective for trans* people.

The main caution is to not use HIV meds that interact with hormone treatment. Your doctor needs to understand these important potential interactions.

CliniQ is a leading centre to support trans* people's sexual health and wellbeing, and is based at 56 Dean Street in central London.

www.cliniq.org.uk

Deciding when to start treatment

When should I start treatment?

If you are not yet on treatment then deciding when to start will be an important one.

This will depend on many things:

- Your CD4 count, CD4% and viral load, and how fast they are changing.
- Your current health, including whether you have other complications such as TB or hepatitis coinfection.
- Your age and how long you have been HIV positive.
- Whether you are pregnant.
- Current guidelines and available drugs.
- Whether you want to use ART to reduce the risk of transmission to your partner.

As long as there is not a medical urgency (such as pregnancy or a very low CD4), it also depends on whether you are ready to start treatment.

You are the person who has to take the meds and in the UK, you have a choice over when to start and the drugs you use.

Discuss this with your doctor before you need treatment.

- Ask about the different drugs. You need to know the good and bad things about each of them.
- Take time to think about what you want to do. Do not feel rushed or pressured into doing something you don't understand.

CD4 count and guidelines

Most guidelines recommend starting treatment based on your CD4 count.

The lower your CD4 count, the more important it is to be on treatment. UK guidelines recommend ART before the CD4 count drops below 350 and at higher levels if there are other complications.

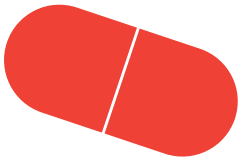
With a count below 350, you can still take time to understand your choices. This is true even just below 200 when a few weeks either way will not make much difference.

Below 200, the risks from delaying treatment become more serious.

UK guidelines recommend earlier treatment at CD4 counts above 350:

- When there are HIV-related symptoms.
- With hepatitis B or C. or TB coinfection.
- To reduce the risk of transmitting HIV to sexual partners.

US guidelines recommend starting treatment at any CD4 count, especially if under 500. They also include being older than 50 years old as a reason to start treatment.



Late diagnosis and low CD4s

In the UK, half of all new diagnoses are in people whose CD4 count is already less than 350. This is the threshold to start treatment in this country.

25% of people are diagnosed even later with a CD4 count of less than 200.

Late diagnosis can be related to:

- Fear of testing.
- Denial: 'it will never happen to me'.
- Fear of stigma and prejudice.
- Lack of up-to-date information about HIV and treatment.

Some people, across all age ranges, only find out they are HIV positive when they become ill and are admitted to hospital.

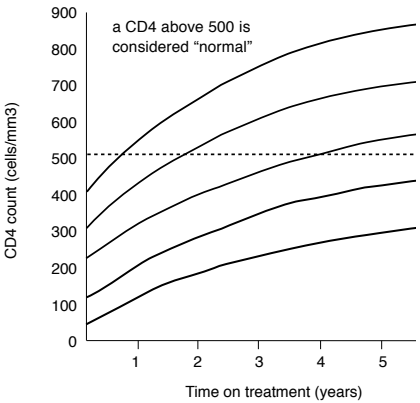
This often means starting treatment straight away, especially when the CD4 count is below 100.

Even with a very low CD4 count, even below 10, if you follow your treatment very carefully, you have a good chance that treatment will work. Your viral load will drop and your CD4 count will rise to safer levels.

This should not be seen as an option to delay treatment. Starting with a very low CD4 count can cause some infections to activate, such as TB or CMV.

This is called Immune Reconstitution Inflammatory Syndrome (IRIS) and is usually easy to treat.

Figure 2: CD4 increases on ART



The higher your CD4 count when you start treatment, the more likely that it will increase to normal levels (over 500).

This may be important over 20, 30 or 40 years because your CD4 count gradually declines as you get older.

This graph shows average levels - some people respond better or worse than average.

Nearly everyone starting above 350 with get above 500.

Early diagnosis and primary infection

If you are recently diagnosed you can find out whether you are likely to have been infected in the previous six months.

This can be done using an HIV test called STARHS or RITA (or sometimes an 'avidity' test).

Knowing when you were infected can help you know how quickly HIV progresses.

Public Health England (PHE) has recommended this test for all HIV diagnoses since 2011.

The results are still only a rough guide though.

UK guidelines only recommend treatment in primary infection in a few circumstances.

- When there are serious HIV or AIDS-related symptoms.
- If CD4 is confirmed less than 350.
- As part of a research study.
- To reduce the risk of HIV transmission.

However, US guidelines include the option to start treatment in primary infection for potential health benefits, though the data supporting this is short-term.

If you want to use very early treatment in the UK, you can say that you want to reduce the risk of transmission (see pages 18 and 19).

Using treatment at higher CD4 counts: the START trial

A large international study called START is looking at whether it may be better to start when your CD4 count is above 500.

This is a very important study. No other randomised trial has answered this question.

This study is now fully enrolled (over 4600 participants) and results are expected in late 2016.

Advantages of earlier treatment include:

- HIV drugs are effective and tolerable. They have few side effects and require few daily pills and doses.
- By starting treatment at a higher CD4 count, you will keep it higher. This increases the chance of reaching or keeping 'normal' levels (CD4 over 500). (See Figure 2).
- Treatment will make you less infectious to sexual partners.
- Treatment may have other health benefits.

Disadvantages include the potential for side effects and drug resistance, and the need to make a few lifestyle changes (for adherence).

This is why this study is so important.

"I got a shock diagnosis in January 2002 and immediately worried about dying. I pictured myself as a person in the media adverts for African people with AIDS who were just bones and skin.

My viral load was 650,000 and my CD4 was less than 10. Therefore I had to start ART immediately.

I read the leaflets and could not believe I was on treatment for HIV!

Because my CD4 count was so low when I started, the increase in CD4 cells caused TB to activate. So I started on TB treatment. I asked the pharmacist to have the TB meds as an oral solution as I couldn't swallow the large tablets.

Now, 14 years later, I take my HIV medication every day and at the right time. I would love to go back home, but a lot of people in my country have no access to ARVs."

Memory, London

Why are treatment guidelines different?

All treatment guidelines agree that ART is safe and effective.

However, some guidelines differ on the best time to start treatment.

- UK guidelines recommend ART before the CD4 count falls below 350.
- In France, Australia and some other countries this cut-off is now 500.
- US guidelines recommend treatment at any CD4 count, including when higher than 500.

This is because different experts interpret research in different ways - and there is currently not good evidence on when to start.

The START study will provide much better evidence on earlier treatment.

"When to Start" - early or late

For most of the last 15 years, UK and US guidelines have disagreed on when to start ART.

- In general, UK guidelines have recommended later treatment, with a greater caution about resistance and side effects.
- US guidelines have generally preferred earlier treatment. They now think that treatment is so safe that everyone should take ART.

Potential benefits from earlier treatment include keeping a higher CD4 count, reducing immune activation (see Figure 1) and having a smaller reservoir of sleeping cells that contain HIV.

You will also be significantly less infectious to sexual partners.

These are key factors are behind the US guidelines.

UK guidelines recognise these benefits but are more cautious about limited data on the risks.

This is because the analysis from some large databases have not shown fewer serious complications in people who started at 350 compared to at higher CD4 counts.

What if I want to start earlier

If you are more convinced by the US approach, then in the UK you can still start treatment earlier.

- UK guidelines include the option to start treatment at any CD4 count if you want to reduce the risk of transmission.

  So, although there is limited evidence that with a high CD4 count you need treatment for your own health, you can still get ART.
- To do this, you have to say that you want to be less infectious to your sexual partners.

  You need to say that this will reduce your anxiety for youself and your partner and that it will improve your quality of life.

Treatment as Prevention (TasP)

Having an undetectable viral load on ART dramatically reduces the ability to transmit HIV. This doesn't mean the risk is zero, but it becomes very low.

- Most of the data on reduced risk comes from a European study called PARTNER, which reported early results in March 2014.
- Final study results are still needed to know how low the remaining risk is likely to be.
- Although PARTNER included gay men, longer follow-up is needed to have better confidence in these results.
- So it is still good advice to use condoms. However, knowing that even if a condom breaks, the chance of transmission is so low will make many people less anxious.

These results should improve the quality of life both for HIV positive people worried about transmitting HIV and for HIV negative people worried about catching HIV.

Treatment as a choice

UK guidelines recommend that HIV positive people can use HIV treatment at any CD4 count to reduce the risk of transmitting HIV.

Whether your decision to start treatment is based on your own health or wanting to reduce infectiousness - or a combination of both - it is important that this is your own decision.

Talk to your doctor about the risks and benefits of ART to reduce HIV transmission.

Public health and private health

TasP is changing the way HIV treatment is being used.

Together with increased testing, earlier treatment could help stop new infections.

But it is important to understand the difference between public and personal benefits of ART.

- Many HIV positive people do not put others at risk. This relates to their choice of sexual activity including condom use or they have partners who are also positive.
- Most new infections are likely to currently come from people who are not yet diagnosed. This is related to people being most infectious in early infection, or having a high viral load in later infection.
- People who know that they are HIV positive are often much less likely to transmit HIV compared to someone who has not yet been diagnosed.
- Many HIV positive people on ART like the feeling that they are less infectious. This is an increasingly important factor in the discussion about starting treatment.
- For example, an undetectable viral load can reduce the anxiety and worry even when you are using condoms. It can also reduce your partner's anxiety, even when this is something that they are generally okay with.

What about side effects?

All medicines have some risk of side effects. This is a real and common concern.

However:

- Most side effects are usually mild.
- They can often be reduced with other medication that is easy to use, or by switching to other drugs.
- There is only a small risk of serious side effects. It they occur, they should be picked up by routine monitoring.
- Within a few weeks most people find that taking HIV treatment is much easier than they expected. It usually becomes an ordinary and manageable part of daily life.
- If you need to modify your combination, there are other meds that may be better for you.

Ask your doctor, nurse or HIV pharmacist about the most common side effects of the drugs that you might use.

- Ask how likely they are to occur.
- Ask how many people stop treatment because of them (usually very few).
- Even rough estimates will give you a good idea of what to expect.

Common side effects

Side effects like nausea (feeling sick), diarrhoea and tiredness, are less common with modern treatments. If they occur, they usually become easier after the first few weeks.

Very rarely, nausea and tiredness can be a symptom of another illness. This is why you should talk with your doctor about any problems.

If the first anti-nausea or diarrhoea medications do not help, ask for more effective drugs.

One of the most used drugs (efavirenz) can affect sleep patterns and change your mood. You need information about this before starting treatment.

Efavirenz side effects usually reduce during the first few weeks. If they continue, it may be better to use another drug.

Some people who manage efavirenz for many years are surprised at the difference when they eventually switch.

"I started treatment on a once-daily pill containing tenofovir, emtricitabine and efavirenz. I had nightmares the first night, but these went away. What I couldn't get used to though was feeling dizzy a few hours after taking my pill.

Even though I took the pill at night, I could not sleep properly. Perhaps because of poor sleep I felt agitated during the day. Sometimes I need to work late into the night, but the dizziness after taking my pill would prevent me from doing so.

I continued for a few weeks, but was unhappy with the effect the pill was having on my life. So I switched the efavirenz to raltegravir.

My life quickly came back to normal. I am sleeping properly. No sweats, no tossing and turning, no insomnia, no weird dreams, no dizziness, no falling over when I go to the bathroom!

I am much happier, even though this means I take a twice daily treatment."

Nathan, Cape Town

Metabolic changes: how your body processes fat and sugar

Changes in fat cells and the distribution of body fat were a side effect of the first HIV combinations. Luckily, this is now much less common with newer meds.

Changes in blood fat (cholesterol and triglycerides) are more common however, and it is important to also monitor blood sugar levels (linked to a risk of diabetes).

If you are worried, your doctor should take your concerns seriously and act on this.

Changes in fat (cholesterol and triglyceride) and sugar (glucose) levels are linked to many drugs and will be monitored by routine blood and/or urine tests.

Diet, exercise, changing treatment or using lipid lowering drugs can all help.

Fat accumulation to the stomach or breasts and/or across the shoulders or neck has been linked to all combinations. It is not understood why some people are affected.

Mild symptoms may reverse if you switch to different HIV meds. Exercise and dietary changes can also help.

Fat loss (from arms, legs, face and buttocks) was due to d4T and AZT, which are no longer used in the UK.

Other side effects

Serious side effects can occur with any medicine, but these are rare. Any rash should always be reported to your doctor. Each drug has its own side effect profile.

Ask about the potential side effects for all the drugs in your combination, before you start treatment.

The i-Base booklet: *HIV and your quality of life: a guide to side effects and other complications* includes information for each drug:

www.i-base.info/guides

It also contains useful information about long-term health issues that may be related to both HIV and some of the drugs used in treatment.

Your routine monitoring should also include heart disease and bone health.

For a free copy please call 020 7407 8488.

The i-Base website also includes information on each drug and links to other sources.

You and your doctor

A good relationship with your doctor and health workers can help your health in the long-term.

Nurses and pharmacists can give you support and advice on all aspects of your treatment. This includes adherence and side effects.

They can make referrals to other professionals, including dieticians, psychologists and social workers.

Both you and those involved in your care have certain rights and responsibilities. The following lists include some of your rights and responsibilities as a patient.

Your rights as a patient

- To be fully involved in all decisions about your treatment and care.
- To be seen within 30 minutes of your appointment. If they are running late, you should expect an explanation.
- To be treated with respect and confidentiality.
- To have different options for treatment explained to you. This should include the risks and benefits of each option.
- To have your doctor or nurse explain any test results.
- For your records to be kept securely. They should be made available for you to see if you ask.
- To choose whether to take part in research trials. This should not affect your current and future care.
- To be able to make a complaint about your treatment. Any complaint must be fully investigated. Again, this must not affect your future care.
- To have a second opinion from a suitably qualified doctor.
- If you write to your hospital or clinic, you should have a written response within 14-28 days.

- To change your doctor or treatment centre without it affecting your future care. You do not have to give a reason for changing doctors or clinics. However, if there has been a problem, then giving a reason can sometimes help resolve the problem.
- To have test results and a summary of your treatment history forwarded to your new doctor or clinic.

Things you can do to help

- Find a clinic that is convenient to you and that you feel comfortable with.
- Find a doctor who you like. If you are a woman and want to see a female doctor then ask for this.
- If you are a gay man and want to see a gay doctor, this may be available and may affect your choice of clinic.
- Turn up for your appointments on time. Tell the clinic if you can't make it. Then they can give your slot to another patient.
- Make a list of things you want to discuss with your doctor. Remember to take it to your appointment!
- Ask to see the same doctor at each visit at least until you are settled with your care. This is important. It's difficult to develop a good relationship if you always see a different doctor.

  Once you are more settled, one advantage of sometimes seeing a different doctor is to get a second opinion and different perspective.
- Treat all people involved in your care with the same respect you would wish to receive yourself.
- Have your routine bloods taken 2-3 weeks before your regular clinic visits so the results are ready for your appointment.
- Listen carefully to the health advice that you are given, and act upon it.
- If you don't understand something, ask your doctor to explain it again or in a different way.
- Be honest with those caring for you. Tell them about any other drugs that you are taking. This includes alcohol, legal and illegal drugs and complementary treatment.
- Be honest about your level of adherence (see page 25). If the people managing your care don't know you are having problems, they can't help.

Adherence and why it is so important

What is adherence?

Adherence is a word used to describe taking your drugs exactly as prescribed. This includes taking them at the right time. It also includes following any special diet restrictions.

Adherence is the most important thing you have to think about when you start treatment. It makes sure that all the drugs in your combination are at high enough levels to control HIV for 24 hours a day. If these levels drop too low it increases the risk of resistance.

Adherence can be a challenge. You may need some support to get used to the changes treatment makes in your life. A routine or daily schedule can really help.

- Pick a time to start treatment when you have a few unstressed days to adjust to the changes.
- During the first few weeks nothing else should take priority over getting your treatment right.
- Some treatment centres have a health advisor who can help you.

How much is enough?

Unfortunately, 'almost 100%' is still the best goal... Even missing one or two doses a week can cause some meds to fail, especially when starting treatment.

However, a window period of about an hour either side is likely to be okay for most drugs and most people.

Some drugs (and some people) have a wider window period than others.

Because of this variation it is better to aim for the same time each day.

Once your viral load becomes undetectable you may have a bit more flexibility, but it is still important to take adherence seriously.

Diet restrictions are important too. Ignoring these can be like only taking half a dose. You will not absorb enough of the drug for it to work properly.

Tips to help

- Choose a treatment you think you can manage.
- Find out what is involved before you choose your treatment: How many tablets? How big are they? How often do you need to take them? How exact do you have to be with timing? Are there food restrictions? Are there easier options?
- Plan your timetable (see page 27). For the first few weeks mark off each dose and the time that you take it.
- Contact your doctor if you have difficulties with side effects. S/he can prescribe additional meds to help or change the treatment if necessary.
- Use a daily or weekly pill box. Then you can see if you miss a dose.
- Set up an alarm for all doses using your mobile phone or watch. It can be better to set this just after the right time, so it is a reminder and not something you rely on.
- If you go away, take a few extra meds with you. Be prepared in case flights or other travel arrangements change.

- Keep a supply where you may need them in an emergency. This can be in your car, at work or at a friend's house.
- Ask a friend to help you remember difficult dose times.
- Ask a friend to remind you when you are out at night.
- Ask friends how well they are managing and if they have tips. Most clinics can arrange for you to talk to someone who is already taking the same treatment.
- Many combinations are taken once-daily. This usually means taking them every 24 hours. Twice-daily drugs need to be taken every 12 hours.
- Completely missing a once-daily combination may be more serious than forgetting a twice-daily dose. Adherence is especially important with once-daily combinations.
- Ask your doctor for a small prescription for meds to control nausea and diarrhoea. These side effects are more common when starting therapy.

What if I forget to take my pills?

Almost everyone will forget or be late with their drugs at some time.

There is a difference though between occasionally missing a dose and regularly forgetting on a daily or weekly basis.

- Be strict with yourself in assessing how adherent you are.
- If your adherence is not good, you need more support. It is available but you will need to ask.

If you regularly take your HIV meds late or miss doses completely, talk to your doctor, nurse or pharmacist about other options.

There may be an easier combination.

You need a regimen that you can follow everyday. This includes both during the weekend and in the different situations involved in life.

There are always things that can help improve adherence, whatever your lifestyle.

Taking days off treatment is a risky way to use HIV meds.

If you realise you have missed a dose, take it as soon as you remember.

BUT, if you only realise when you're going to take your next dose, do not take a double dose.

Adherence diary

Use the table below to mark when you take each drug in the first few weeks of your combination. This will help you know if you have just taken a dose - or if you are late or miss a dose. Getting everything right from the start is important.

Date at start of week _____

	Drugs & times (morning)	Drugs & times (evening)
Monday		
Tuesday		
Wednesday		
Thursday		
Friday		
Saturday		
Sunday		

Date at start of week _____

	Drugs & times (morning)	Drugs & times (evening)
Monday		
Tuesday		
Wednesday		
Thursday		
Friday		
Saturday		
Sunday		

Drug resistance

What is resistance?

Drug resistance occurs when the genetic structure of HIV changes in a way that stops a drug from working. These changes are called drug mutations.

- The risk of resistance increases when drugs levels in your body drop below a minimum active level. This usually only occurs if you miss doses or stop treatment. (See Figures 3 and 4).
- Resistance only develops if you are on treatment or in the short period after stopping treatment.
- You can be infected (or reinfected) with drug resistant HIV.

About 8% of new infections in the UK have resistance to at least one med.

This is why in the UK everyone should have a resistance test when they are diagnosed and before starting treatment. But you may need to ask for this test, so it is important to check.

How does resistance occur?

Mutations that lead to drug resistance are generally only produced if you continue taking a treatment when your viral load is still detectable.

If your viral load is still above 500 copies/mL after 2-3 months, or above 50 copies/mL after 6 months, you may have developed resistance and may need to change drugs.

Your doctor should look for why your results are not as good as they could be.

Your doctor will also want to discuss adherence and side effects. This may include tests for resistance and possibly drug levels.

A viral load test is recommended four weeks after starting or changing treatment. This should then be monitored every 3–4 months when on treatment.

Get the results when they are ready, usually within two weeks. Don't just wait until your next routine visit.

Some clinics let you get your blood tested 2-3 weeks before you see your doctor. Then you will have the results back for the appointment.

Resistance can develop even at viral load levels between 50 and 500 copies/mL.

What happens if my viral load rebounds?

If your viral load increases, you should get a second viral load test. This should be when you get the first results.

Often slight increases are due to errors in the test. Small increases that go back down again that are called 'blips'.

The second test will check what is happening. If the combination is failing then you reduce the risk of further resistance by checking this straight away.

You will get a better response to a second treatment if you change when viral load levels are still low.

See the i-Base *Guide to changing treatment and drug resistance* for more information:

www.i-base.info/guides

How do I avoid resistance?

The best way to avoid resistance is to take your meds every day and on time. But you also need to be using a combination that is strong enough to control the virus.

Avoiding resistance is more important than increasing in your CD4 count. Avoiding resistance will let your treatment work long-term.

If your viral load becomes undetectable (less than 50 copies/mL) you dramatically reduce the risk of resistance. If you are starting treatment and are adherent this is a realistic goal.

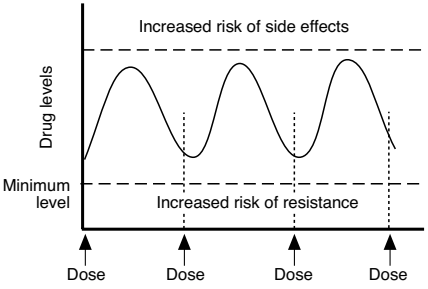
What is cross-resistance?

Cross-resistance is when resistance to one drug causes resistance to other similar drugs, even if you have never taken them before.

This is particularly true of drugs in the same class.

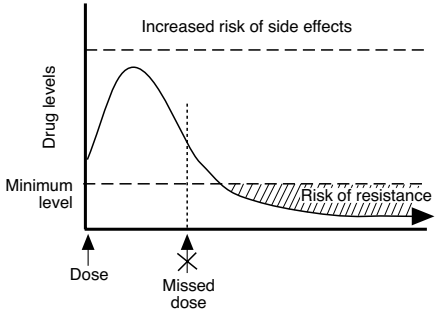
So if you develop resistance to one NNRTI such as efavirenz then you may also have resistance to some other NNRTIs such as nevirapine.

Figure 3: Drug levels with good adherence



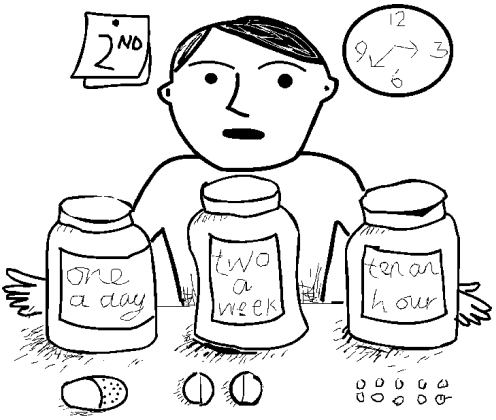
Drug doses are calculated so that average drug levels are high enough to be active against HIV for 24 hours a day. They are also low enough to minimise the risk of side effects.

Figure 4: A missed or late dose increases the risk of resistance



Missing or being late with a drug lets the drug levels fall to a level where resistance can develop. The more often you are late, the greater the chance of resistance.

Which drugs, which combination?



Main types of HIV drugs

There are six main types (or classes) of drugs that work at different parts of the HIV life cycle. (See Table 1 and Figure 5).

Table 1: Main types of HIV drugs

Abbreviation	Full name (s)
NRTIs/NtRTIs ("nukes")	Nucleoside/tide reverse transcriptase inhibitors or nucleoside/tide analogues
NNRTIs ("non-nukes")	Non-nucleoside reverse transcriptase inhibitors
PIs	Protease inhibitors
INIs (or INSTIs)	Integrase (strand transfer) inhibitors
CCR5 inhibitors	CCR5 inhibitors are a type of entry inhibitor
Fusion inhibitors	Fusion inhibitors are a type of entry inhibitor

There are more than 25 HIV drugs and formulations. However, only a few combinations are commonly used.

What is the best combination?

There isn't one best combination because different drugs can affect people differently.

Any combination should be:

- Strong enough to reduce your viral load to undetectable levels.
- Easy to tolerate and adhere to, including any dietary restrictions.

Guidelines recommend preferred combinations but also include alternatives. The most commonly used ones are discussed on the next few pages.

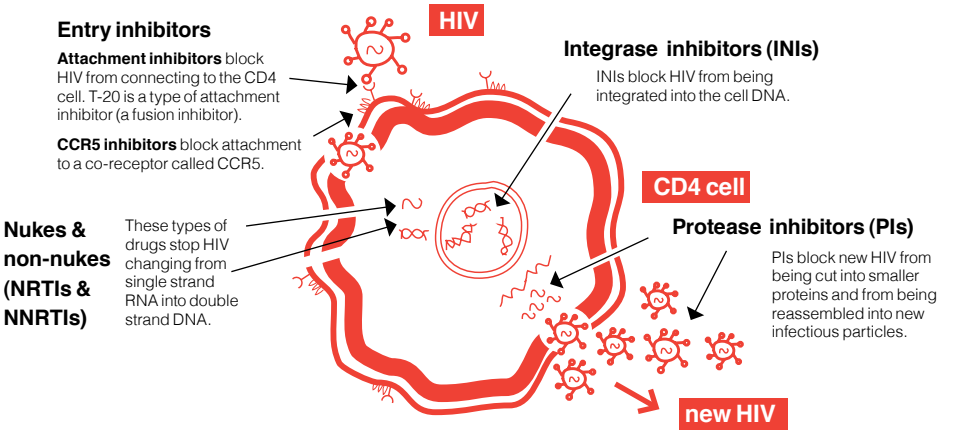
You and your doctor should discuss which combinations you can choose from.

If you have taken HIV drugs before, or have drug resistance, this will affect your choice.

Ask for information about dosing, pill size and side effects. This will help you pick a combination that is right for you.

Figure 5: HIV lifecycle - how drugs work in different ways

If a CD4 cell is infected by HIV, this cell is used to produce hundreds of new copies of HIV. Different drugs block different parts of this HIV life cycle.



First combination meds

UK guidelines include starting treatment with two nukes plus a third componant (see Table 2).

The two nukes

Nukes were the first type of HIV drugs to be developed. They are still the basis of most HIV combinations.

Table 2: Summary recommendations for choice of ART in the UK

	Preferred	Alternative *
Two nukes	tenofovir + emtricitabine (Truvada)	abacavir + lamivudine (Kivexa)
Plus a third component	efavirenz (NNRTI) ***or*** atazanavir - boosted (b/PI) ***or*** darunavir - boosted (b/PI) ***or*** raltegravir (integrase inhibitor) ***or*** elvitegravir/cobicistat (boosted integrase inhibitor)	nevirapine (NNRTI) ***or*** rilpivirine (NNRTI) ***or*** lopinavir/r (boosted PI) ***or*** fosamprenavir/r (boosted PI)
	dolutegravir ** (integrase inhibitor)	

Adapted from BHIVA guidelines (November 2013).

* Alternative drugs can only be used in specific situations. ** Dolutegravir was expected to receive NHS approval as we went to press. This is likely to be a preferred option in the 2014 BHIVA guidelines.

Two widely-used formulations include two nukes in the same pill. One is called Truvada (tenofovir + emtricitabine) and the other Kivexa (abacavir + lamivudine).

UK guidelines recommend Truvada as a better choice for most people. They suggest Kivexa is an alternative.

These meds are once-daily drugs. They both generally have a low risk of serious side effects.

None of these drugs cause fat loss (lipoatrophy), nerve pain (neuropathy) or damage red blood cells (anaemia).

Tenofovir is processed by your kidneys. This means your kidney function will be monitored if you use this drug.

You also need to be careful of other drugs that can affect the kidneys.

Tenofovir also causes a small reduction in bone density during the first six months. This does not appear to increase bone loss more than other HIV meds after six months.

This means that tenofovir may not be recommended if you already have kidney or bone problems.

Emtricitabine (FTC) is generally very easy to tolerate.

A mild rash on the palms of the hands was reported in about 10% of people who are black. This is now thought to be less common.

FTC is very similar to 3TC, but it may have slight advantages for adherence as drug levels stay higher for longer.

Lamivudine (3TC) is very similar to FTC. If nukes are prescribed separately rather than a combined pill, then either FTC and 3TC can be used.

3TC was approved in the 1990s and generic versions may make this less expensive than FTC.

Abacavir should not be used if your viral load is over 100,000 copies/mL (unless this is with dolutegravir).

Some studies showed that it increased the risk of a heart attack **in people who had a high risk of heart problems**. This was not reported in people who have lower risks for heart disease.

Abacavir can cause a hypersensitivity reaction. If you are negative on a HLA B*5701 test your risk of this reaction is dramatically reduced.

Hypersensitivity symptoms include fever, rash, headache, sore throat, diarrhoea, abdominal pain, tiredness, nausea, vomiting and flu-like aches that get worse each day.

Anyone who gets these symptoms must seek urgent medical advice with a view to stopping the abacavir.

Once stopped, abacavir must not be used by that person again.

Other nukes: d4T, ddI and AZT

d4T (stavudine), ddI (didanosine) and AZT (zidovudine) and Combivir (AZT+3TC) are no longer recommended and rarely used.

"Seeing people get better on combination therapy is without a doubt the most extraordinary thing I have ever seen. It made me become an activist."

Polly, London

"My first reaction was to put off starting therapy for as long as possible. I tried to improve my immune system by stopping smoking and using supplements, until I realised that my best bet was to use ARVs. They are the only way to ensure my long-term survival.

After 8 months of resisting treatment I eventually started ARVs. I do not say that I gave in but that I became more clever!"

Vladimir, St Petersburg

"No-one wants to take drugs every day and I certainly didn't. I put it off til the last possible moment. Looking back I wish I had started sooner.

I still wonder whether the three years I spent waiting for my CD4 count to fall would have been happier and more active ones if I had started treatment at a higher CD4 count, when my doctor recommended this."

Matt, Brighton

Triple-nuke combinations

Triple-nuke combinations are no longer recommended.

Nukes that don't mix

Although one nuke can often be switched for another, Table 3 shows some combinations that should never be used.

Table 3: Nukes that don't mix

AZT and d4T *	At any time
3TC and FTC	At any time
ddI and tenofovir	Especially with an NNRTI
abacavir and tenofovir	Not in a 3-drug combo
d4T and ddI	Never during pregnancy
Triple-nuke combinations	Only two combinations: AZT+3TC+abacavir or AZT+3TC+tenofovir, can be used. Others have a high risk of failure.

* d4T (stavudine) is a nuke that has not been used in the UK for many years because of the higher risk of side effects. It is still used in some countries.

Choice of the third component

The choice for the third component can be an NNRTI, a boosted PI or an integrase inhibitor (boosted or unboosted), see Table 2.

- efavirenz (NNRTI) ***or***
- atazanavir/r (boosted PI) ***or***
- darunavir/r (boosted PI) ***or***
- raltegravir (INI) or
- elvitegravir/cobicistat (boosted INI) ***or***
- dolutegravir (INI; expected 2014)

The first five options all produced roughly similar results in research studies. Dolutegravir results were slightly better, but was still undergoing final stages of NHS approval as we went to press.

All combinations are very effective against HIV. Small differences are mainly related to side effects, but these are also generally mild.

Some need to be taken with food and some have more cautions for drug interactions. Raltegravir is the only twice-daily option but also has some of the fewest side effects.

These differences show why you need to be personally involved in the choice of drugs, especially as recommended options may vary depending on where you life in the UK.

If you have problems with drug though it is easy to switch to another.

Efavirenz - an NNRTI

Efavirenz is once-daily NNRTI. It is also in a single pill (with tenofovir and emtricitabine) called Atripla.

This combination has been widely used for many years.

The main side effects of efavirenz relate to the Central Nervous System (CNS). This can include mood changes such as anxiety, euphoria and depression, and sleep disturbance that includes vivid dreams and nightmares.

Nearly everyone will get some side effects, but these usually get easier after a few days or weeks. About 10-20% of people stop efavirenz because of this.

Severe side effects are more rare. Less than 3% of people get severe psychiatric symptoms, but using a different drug is important if this occurs.

Before starting efavirenz, your doctor should give you information about the side effects.

UK guidelines say that efavirenz can be used during pregnancy and when trying for a baby, even though the information that comes with efavirenz does not say this.

Boosted PIs

Only two PIs are now widely used: atazanavir and darunavir. Both need to be boosted.

Usually, the booster is ritonavir, but a new option called cobicistat was recently approved and may be used more in the future.

Currently, ritonavir or cobicistat are given as a separate pill. However, single pill formulations of both atazanavir/cobicistat and darunavir/cobicistat are in development.

The booster gives you better and more constant drug levels of the PI. This reduces the risk of resistance. It also reduces the number of pills and dietary requirements compared to unboosted PIs.

Ritonavir and cobicistat seem to have similar side effects. These include stomach upset, diarrhoea, nausea and increases in cholesterol and triglycerides.

Atazanavir is a once-daily PI.

The recommended daily dose is 300 mg (taken as one 300 mg or two 150 mg capsules), boosted by 100 mg of ritonavir.

Atazanavir is generally very well tolerated but the main side effect is increases levels of bilirubin.

This is not a concern unless levels become more than five times the upper normal limit (more than 70 mmol/L).

This can cause your skin or whites of your eyes to look slightly yellow, which can be disconcerting. About 1 in 10 people switch to an alternative.

Sometimes the booster may not be needed and a higher atazanavir dose (400 mg) is used. But drug levels need to be checked using therapeutic drug monitoring (TDM).

Unboosted atazanavir should not be used in a combination with tenofovir.

Atazanavir interacts with some antacids ("proton pump inhibitors" or PPIs).

Darunavir is a PI that is mainly used once-daily (800 mg) plus 100 mg ritonavir or 150 mg cobicistat.

If your HIV has some drug resistance, darunavir is usually dosed twice-daily (600 mg plus 100 mg ritonavir).

Darunavir is generally easy to tolerate and fewer people switch than with atazanavir. Side effects include rash, nausea, diarrhoea and lipid changes.

Integrase inhibitors

Raltegravir is an integrase inhibitor that is taken twice-daily.

It probably has fewer side effects compared to other first line options. It has no CNS side effects that affect sleep or moods. It also has fewer ritonavir-related side effects like nausea, diarrhoea and lipid changes.

In the past, raltegravir was less widely used because it was more expensive than other options. This changed recently and raltegravir is recommended as the preferred alternative to efavirenz in some parts of the UK, including London.

Elvitegravir is a once-daily integrase inhibitor that needs to be boosted by cobicistat

Both drugs are included in a 4-in-1 single combination pill (with tenofovir and emtricitabine) called **Stribild**.

Stribild is approved by the NHS. However, if it continues to be more expensive than alternative combinations it is likely to be less used in the UK.

Dolutegravir is an integrase inhibitor that is mainly used once-daily and that doesn't need boosting. Dolutegravir was approved in Europe in January 2014.

As this booklet went to press, dolutegravir was in late stages of the NHS review. However, based on the results from clinical trials, approval is very likely, with access in the UK then becoming dependent on the price.

Dolutegravir is notable for study results that found it was at least as good as current preferred options and was often significantly better. This included studies in first-line treatment, second-line treatment and in people with more extensive drug resistance. The differences were largely due to fewer side effects than the comparison drugs.

In people with drug resistance to other integrase inhibitors, dolutegravir is taken twice-daily.

Dolutegravir results were also good in people who started treatment with viral load above 100,000 copies/mL, including if they used abacavir/lamivudine as background nukes.

"I was diagnosed with HIV in 1997 and had to start on treatment when I was still in shock. I discussed the pros and cons of each drug with the nurse but most of it went in one ear and out of the other.

I needed time to find out about the different drugs and side affects, but with a low CD4 count I needed to start treatment soon. The information I got from the clinic was detailed and complex.

I was lucky. I had a good network of positive friends and got sound advice in terms I could understand.

Over the past 17 years, I have seen treatments become easier to take with far less side effects.

HIV treatment is not rocket science. You can easily learn about it. I am sure I get better treatment for my HIV because I understand what is going on. This gives me the confidence that I should live a long and happy life, just with a manageable illness.

I talk with my doctor and I take an active role in my choice of treatment. I always say if I have problems with side effects or adherence."

Paul, London

This might make dolutegravir-based combinations less expensive that currently used combinations, especially when abacavir and lamivudine are both off-patent and available as generics.

A single pill of dolutegravir/abacavir/lamivudine is already in studies.

Alternative first-line options

Drugs listed as alternatives in UK guidelines have been widely used in the past and can still be good options.

Nevirapine is an NNRTI that is rarely used because of a slightly higher risk of very serious side effects.

This includes a rash called Stevens-Johnson Syndrome (SJS) and liver toxicity (both can be fatal).

The risk of liver toxicity means that nevirapine is not recommended in people with hepatitis C.

Side effects usually occur in the first two months of treatment. In people who do not get these reactions nevirapine is generally easy to take.

Nevirapine use is limited by CD4 count to only starting in women whose CD4 is less than 250 or less than 400 in men.

Nevirapine is started at 200 mg once-daily for the first two weeks, and then, only if you do not have a rash, the dose increases to 200 mg twice-daily. **Any rash should be promptly reported to your doctor.**

A once-daily 400 mg formulation of nevirapine is available for use after the two week lead-in period.

Lopinavir/r (Kaletra) and **fosamprenavir/r** are alternative PIs that are sometimes used if you cannot tolerate other options.

Kaletra includes ritonavir in the same pill.

Rilpivirine is a once-daily NNRTI that is approved as a first-line drug, but only when viral load is less than 100,000 copies/mL.

Rilpivirine needs to be taken with a meal (about 500 kcal). It has similar side effects to efavirenz but they are less common. It has cross-resistance with efavirenz and nevirapine.

A 3-in-1 combination of rilpivirine plus tenofovir/emtricitabine called **Eviplera** is a single once-daily pill. In this formulation, the food requirement is about 400 kcal.

Other meds that are sometimes used

Maraviroc (a CCR5 inhibitor) is usually only used in second-line treatment or in studies. To use maraviroc you need to check that your HIV uses the CCR5 co-receptor.

Etravirine is used if you have resistance to efavirenz or nevirapine. It has also been studied and used as an alternative for people who have side effects to efavirenz.

Tipranavir/r and **T-20 (enfuvirtide)** are only used by people with extensive drug resistance.

Non-standard combinations

Alternative combinations to two nukes plus either an NNRTI or boosted PI are sometimes used. This is only in specific circumstances or in research.

Some studies do not use nukes. These include using boosted darunavir only, or a boosted-PI plus either an NNRTI, an integrase inhibitor or lamivudine.

If you are already using an unusual combination that is working well, you do not need to change treatment unless there are reasons to do so. Ask your doctor about your current drugs if you are unsure.

HIV in the UK: NHS changes and generics

In the UK, the NHS provides a very high quality of HIV care.

Even if you have problems with your clinic, the provision of testing, monitoring and treatment, that is all free at the point of care, makes this one of the best in the world.

This high level of care will continue in the future. This is helped by community and healthcare organisations producing guidelines on best standards of care. See for example the British HIV Association Standards of Care for People Living with HIV (2013):

http://www.bhiva.org/standards-of-care-2013.aspx

During 2014, the NHS is being restructured. HIV will continue to be a specialist commissioned service, but in the UK this will now be managed by seven regions: four for England (North, South, Midlands and London) plus Scotland, Wales and Northern Ireland.

Standards should remain high wherever you access treatment and you will still be able to choose your clinic. However, as each region negotiates drug prices, there may be differences in guidelines for ARV prescribing.

All drugs should still be available in every area. If there are problems, then as a last resort you can choose where you receive treatment.

For the last three years, the NHS has also been under financial pressure from government-imposed budget restrictions.

The same funding has to stretch further and more people need treatment each year.

Drug cost and treatment choice

UK guidelines make clear that the choice of HIV treatment should be based on the most appropriate medical treatment.

- HIV care is not based on the cheapest drugs but on the most effective.
- However, when two similar drugs have very different prices, the least expensive is likely to be used first.
- If there are clinical reasons to use more expensive drugs, these will continue to be available.

For example, if the first drugs cause side effects, then switching to alternatives should be easy.

Generic ARVs

Generic versions of widely-used drugs may be important to help the NHS save costs.

When drugs are first approved, the company that developed them gets a license to be the only manufacturer. This usually provides 10-15 years to profit from the investment costs.

After the patent ends, other companies can make the same drugs. These are called generic drugs.

- In the UK, 60-85% of all NHS prescriptions are for generic medicines.
- These savings enable the NHS to continue to provide free health care.
- Some of the HIV drugs that are still widely used are now off-patent and more will follow. This includes lamivudine, nevirapine and efavirenz.

Just like in other health areas, the NHS is likely to move to generic HIV versions unless the original manufacturers also lower their prices.

- Generic drugs are just as carefully regulated as the originals. They are the same high production quality with the same active ingredients.
- Generic drugs are just as effective as brand name originals.
- Generic drugs will usually be a different shape and/or colour pill to the brand name drugs. They use different packaging and also have a different manufacturer and brand name but the active ingredients are the same.

Your doctor and pharmacist should always explain when you are changing to a generic drug.

Impact of generic drugs on single pill combinations

The availability of generic options may reduce use of combination pills like Atripla, Eviplera, Kivexa and Truvada.

This means that individual drugs may be prescribed rather than the single pill combinations.

This would increase the daily pill count by one or two pills, depending on the combination. Although this is less convenient, the savings will enable other important HIV services to continue.

However, currently (July 2014) this has not yet been needed in the UK.

Please talk to your doctor if you are worried about these issues.

Your personal treatment history

The next few pages include space to record important information about your own treatment and treatment history.

These have been taken from the i-Base Treatment Passport which is available free from i-Base.

If you'd like a copy of the more detailed booklet please call 020 7407 8488 or go online:

www.i-Base.info

Why keep a treatment history?

Keeping a record of your treatment history can:

- Help you understand your health and treatment.
- Help if your doctor changes at your clinic.
- Help if you speak to other health care workers or to a treatment advocate for advice.
- Help if you ever change hospitals or clinics, if you want a second opinion, when on holiday or abroad or if you move to another country.

Any treatment choice for your future care is closely linked to your previous treatment history.

This includes results from blood tests like the CD4 count, viral load and resistance tests, as well as the history of drugs you have used and your reasons for changing them.

As treatment improves you could need this record for 20 years or more. Whether new treatments work will depend on your previous treatment history.

This record is important. If you change clinic you should ask for your medical records to be forwarded. Because this does not always happen or is delayed, make sure that you have a record of your hospital or clinic number.

These pages will help provide a useful record in all these situations.

Your doctor can provide you with details to help fill in these pages but it does not replace your medical notes.

All patients have the right to see their medical records. You can also make photocopies but you need to let the clinic know beforehand.

If you are changing clinics it is sometimes easier to take a summary copy of your notes with you.

CD4 and viral load results

These blood tests are used to monitor your health and your response to treatment.

CD4 count This blood test checks your immune system.

CD4% This is similar to the CD4 count but is often more stable.

Viral load This test measures the amount of HIV in a sample of blood.

It shows whether treatment is working, and is sometimes used when deciding to start treatment.

Even rough figures from your previous history are useful and your doctor can provide you with these.

The lowest CD4 count and highest viral load results when you were first diagnosed and before you started treatment are the most important.

	Date (month/year)	CD4 (cells/mm3)	CD4%	Viral load
e.g.	July 2010	335	21%	120,000

Date (month/year)	CD4 (cells/mm3)	CD4%	Viral load

Antiretroviral treatment history

Your choice of new and future drugs will depend on the drugs you have used in the past and the reason you stopped using them.

It is important to know whether this was because of resistance or side effects.

If you can't remember exact details, even rough dates are useful (i.e. taking AZT for 6 months in 2001 etc).

Pictures of the most common drugs with their different names are in the ARV Chart included as the centre page pull out section of this guide.

	Drugs & combination details (name & dose)	Date started	Date stopped	Reason
e.g.	Kaletra	Feb 07	Jan 09	High cholesterol

Other infections and illnesses

A record of other infections (e.g. TB) or HIV-related illnesses (PCP, shingles, etc.) is also important.

Illness or infection	Treatment & dose	Dates

Side effect and allergies

Main side effects or drug-related allergies.

Side effect or symptom	Suspected drug	Date started/stopped

"I was confused about how my clinic worked, even when I was on treatment. One day I asked the nurse to explain the tests and what a 'good' or 'bad' result might mean.

It was tremendously helpful. I used to be happy with doctors saying 'everything's okay' but now I want to know details about a few key things - my cholesterol, my bone health, my liver and kidneys."

Matt, Brighton

"I was very scared of treatment. I did not think it worked cause I had just arrived from Zimbabwe.

I came to the UK after my husband died and I needed treatment immediately. I told my doctor that I did not want to be on d4T and ddI and he laughed because these drugs were no longer in use in the UK. It is amazing what the disparity of wealth does to countries.

I never used to read about the meds I was given but after my experience with efavirenz (which I changed) I now read every detail on every drug.

Now I tell everyone that the drugs are fantastic because they have given me a new lease of life."

Hosanna, UK

Immunisation record

Keeping a history of vaccination and immunisation (hepatitis A and B, pneumovax, flu, tetanus and holiday vaccinations, etc.) can also help. HIV positive people usually need to use 'non-live' vaccinations and you may have to ask for these specially.

Date	Vaccination

Date	Vaccination

Trials and studies

Study name and treatment received	Dates

Resistance tests

Date	Results (continue summary on notes pages if necessary)

Glossary

adherence
The term to describe taking medication exactly as prescribed – at the right time and following any food advice.

antibody
A protein that is part of the immune system and which is produced to fight an infection.

antigen
A protein found on the surface of a virus or bacteria. It is recognised by the immune system which then generates antibodies.

antiretroviral (ARV)
An HIV drug (HIV is a retrovirus).

ART or HAART
A term for combination therapy (Highly Active Anti-Retroviral Therapy).

CD4 cells
A type of white blood cell that helps your body fight infections.

first-line therapy
The first combination of HIV drugs that you use.

mutation
A change in the structure of the virus. Sometimes mutations can lead to a drug to stop working.

opportunistic infection (OI)
An infection that occurs after your immune system has been damaged by HIV.

seroconversion
The time after HIV infection (usually a few weeks) when your body generates an immune response to HIV.

side effect
A secondary effect of a drug other than the reason it is prescribed. Side effects are usually negative effects.

therapeutic drug monitoring (TDM)
A test to measure the levels of a drug in your blood.

toxicity
The term for the degree to which a drug can cause harm.

treatment-experienced
Someone who has previously used HIV treatment.

treatment-naive
Someone who has never taken any anti-HIV treatments before. People who are treatment naive can have drug resistance if they were infected with a drug resistant strain of HIV.

triglyceride
A type of body fat related to cholesterol.

viral load test
A test to measure the amount of HIV in blood but which can also check levels in other compartments like genital fluid, semen or spinal fluid. Tests can only measure down to certain levels (i.e. 50 copies/mL).

viral rebound
When viral load increases above detectable levels on treatment.

wild-type virus
HIV that has not developed any mutations. This is usually, but not always, the virus that you are first infected with.

Further information

If you have questions after reading this guide or would like to talk to someone about treatment, contact the i-Base information service.

HIV i-Base

The i-Base website has other treatment guides including translations, technical bulletins, an online Q&A service, a treatment manual, information about workshops and many other resources.

It also contains information about each drug, conference reports and technical reviews of published studies.

www.i-Base.info

UK-CAB

A community network that focuses on treatment including peer-support and training.

www.ukcab.net

Community treatment information

The following community sites, most of which are based in the US, have information on individual HIV drugs, factsheets, more detailed referenced research, conference reports and treatment news.

www.aidsinfonet.org
www.aidsmeds.com
www.tpan.com
www.aidsmap.com
www.natap.org

Pipeline drugs

i-Base and the US activist organisation TAG produce a pipeline report each year.

This includes a review of new drugs in development for HIV, hepatitis and TB.

www.pipelinereport.org

HIV and ageing

A UK guide to HIV and ageing called "Coming of Age" is available from:

www.justri.org

Drug approval agencies

Detailed prescribing information in most European languages and other scientific documents are available from the European Medicines Agency (EMA). This is the European organisation responsible for drug approval and drug safety.

Use the link on their site for 'product information/human medicine':

www.ema.europa.eu

Patient rights in the UK

For information about your rights as a patient, see **'Your Guide to the NHS'** available by phoning 0800 555777 or online:

nnuh.nhs.uk/docs%5Cleaflets%5C36.pdf

Information about healthcare services including how to make a complaint are on the 'About the NHS' link on the NHS homepage:

www.nhs.uk

"Get involved in choosing your treatment. It needs to fit to your life, schedules and routines as much as possible.

Being able to share with my relatives and close friends has helped me a lot. My boyfriend always asks me if I took the pills on time.

I've been taking HIV treatment for the last 20 years. When I started, no one would had imagined the choice we have now. I now feel truly optimistic about the future.

As new drugs become available, choices will become even more individualised. A good relationship with our doctors and nurses is important: we'll probably need to see them for years!"

Xavi, Barcelona

"Part of the reason I started combination therapy was hearing the experiences of other people living with HIV and seeing how well they looked.

I now facilitate treatment workshops with African people in the UK. People want to know more about their treatments and want to learn."

Winnie, London

Feedback

Your feedback on this guide helps us develop new resources and improve this resource. All comments are appreciated.

These can be made using an online survey at:

http://www.surveymonkey.com/s/978R8F9

Comments can also be posted free to:

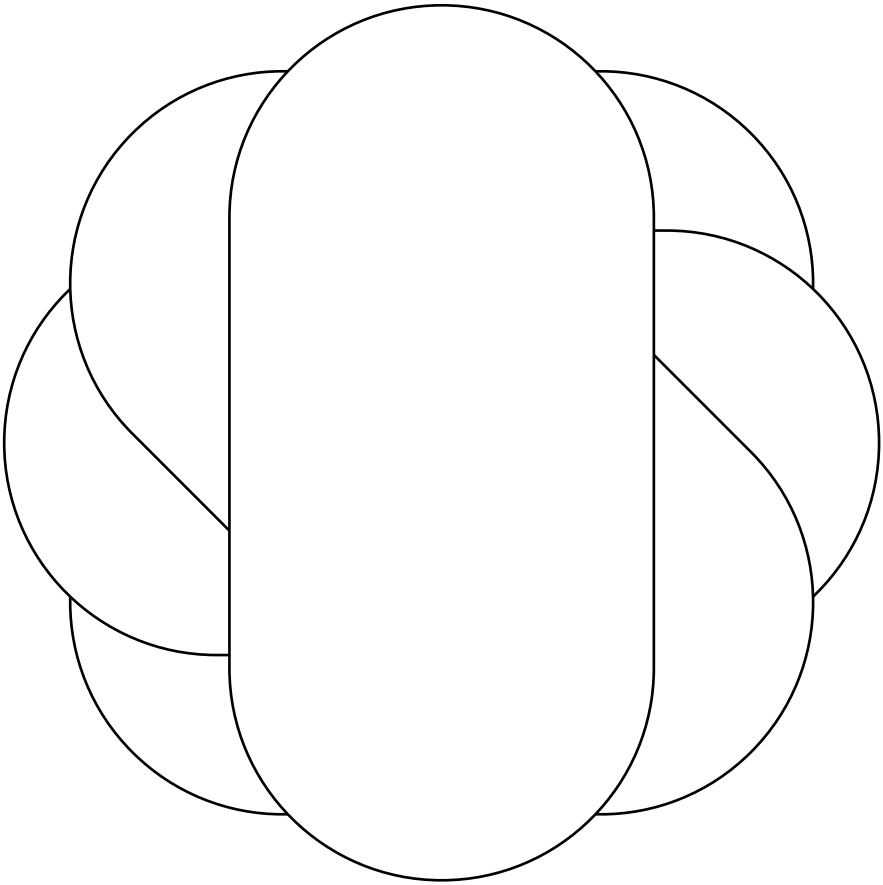
FREEPOST RSJY-BALK-HGYT, i-Base, 57 Great Suffolk Street, London SE1 0BB.

Notes

i-base
0808 800 6013

ARV chart
2014/15

July 2014



A supplement to the i-Base Introduction to Combination Therapy

Drug names		Recommended adult dose *	Total daily pills
Fixed dose combinations			
Atripla (efavirenz 600 mg + emtricitabine 200 mg + tenofovir 300 mg)		One tablet, once-daily. Guidance as for separate drugs. Take at night and not with a high fat meal.	1
Eviplera (rilpivirine 25 mg + emtricitabine 200 mg + tenofovir 300 mg)		One tablet, once-daily, with food (390 kcal). See separate drug info.	1
Stribild (elvitegravir 150 mg + cobicistat 150 mg + emtricitabine 200 mg + tenofovir 300 mg)		One tablet, once-daily, take with food. See separate drug info.	1
Nukes: nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs)			
Dual nukes			
Truvada (tenofovir 300 mg + emtricitabine 200 mg)		One tablet, once-daily.	1
Kivexa (abacavir 600 mg + lamivudine 300 mg)		One tablet, once-daily.	1
Single nukes			
lamivudine (3TC) [++] (Epivir [pictured] - or generic)		1 x 300 mg or 2 x 150 mg (150 mg shown), (taken as a once-daily or twice-daily dose).	1 if 300 mg 2 if 150 mg
abacavir (Ziagen, Epzicom)		2 x 300 mg tablets (taken as a once-daily or twice-daily dose).	2
emtricitabine (FTC) (Emtriva)		1 x 200 mg capsule, once-daily.	1
tenofovir DF (Viread)		1 x 300 mg tablet, once-daily.	1

* Different doses and formulations are sometimes used - always check the dose with your doctor and pharmacist.

[++] Generic versions of lamivudine (3TC), didanosine (ddI), zidovudine (AZT), nevirapine and efavirenz may be a different colour and shape.

[°°] Elvitegravir is only available as a separate drug on expanded access from the manufacturer.

PK boosters: ritonavir is the most widely used pharmacokinetic (PK) booster. Cobicistat was approved in 2013 but can only be used to boost atazanavir, darunavir and elvitegravir. Some drugs are not recommended for first-line therapy. Smaller pills are for children or if larger pills are difficult to swallow. Sometimes syrup formulations are available.

Pictures approximate to actual size.

Drug names		Recommended adult dose *	Total daily pills
NNRTIs: non-nucleoside reverse transcriptase inhibitors (non-nukes)			
efavirenz ++ (Sustiva) 600 mg or 200 mg	 	1 x 600 tablet (or 3 x 200 caps) once-daily; at night, not with high fat meal.	1 tablet (or 3 capsules)
nevirapine ++ 200 mg and nevirapine 400 mg (Viramune PR)	 200 mg 	200 mg once-daily for first 14 days. Then 1 x 200 mg tablet, twice-daily or 2 x 200 mg once-daily; OR 1 x 400 mg prolonged release tablet once-daily (pic on right).	1 or 2 (based on 200 mg or 400 mg)
etravirine (Intelence)		1 x 200 mg tablet, twice daily, take with food. Dispersible in water.	2
rilpivirine (Edurant)		1 x 25 mg tablet, once-daily, take with main meal (500 kcal).	1
INIs: integrase inhibitors			
raltegravir (Isentress)		1 x 400 mg tablet, twice-daily. Take with or without food.	2
elvitegravir (Vitekta) °° (see also Stribild). Expanded access only.		1 x 85 mg or 1 x 150 mg tablet, once-daily in boosted PI. Take with food.	1
dolutegravir (Tivicay) *		1 x 50 mg tablet, once-daily (or 1 x 50 mg twice -daily). With food if twice-daily but with or without otherwise.	1 or 2
CCR5 inhibitors (entry inhibitor)			
maraviroc * (Celsentri, Selzentry)		150 mg or 300 mg or 600 mg, as directed, depending on other ARVs in the combination.	1 or 2 or 4
b/PI: boosted protease inhibitors			
atazanavir * (Reyataz)		1 x 300 mg cap + booster, once-daily. Take with food. 150 mg and 200 mg capsules also available.	1 (+ 1 booster)
darunavir * (Prezista)		1 x 800 mg + booster once-daily (or 1 x 600 mg + 100 mg booster twice-daily if resistance). Take with food.	1 or 2 (+ 1 or 2 boosters based on dose)
PK (pharmacokinetic) boosters			
cobicistat (Tybost)		150 mg tablet, once daily. Used to boost atazanavir, darunavir and elvitegravir.	depends on boosted drug
ritonavir (RTV) * (Norvir)		100 mg tablets used at different doses to boost other PIs.	depends on PI

Drugs that are used less frequently

The drugs on this page are now used more rarely or in very specific circumstances. For example, both tipranavir and T-20 are usually only when other options are not available due to drug resistance. Combivir, Trizivir, lopinavir/r and fosmprevanvir/r are no longer recommended as preferred drugs.

Drug names		Recommended adult dose *	Total daily pills
Nukes: nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs)			
Single nukes			
AZT, zidovudine (Retrovir [pictured], or generic)		1 x 250 mg capsule, twice-daily.	2
ddI (Videx, didanosine)		1 capsule, once-daily, (125, 200, 250 or 400 mg). Take on empty stomach, 2 hrs before & after food.	1
Dual nukes			
Combivir (AZT + lamivudine)		One tablet, twice-daily.	2
Triple nukes			
Trizivir (AZT + lamivudine + abacavir)		One tablet, twice-daily.	2
PIs: protease inhibitors			
lopinavir/r (Kaletra) 200/50 or 100/25 mg	 100 / 25 mg	2 x 200/50 tablets twice-daily or 4 x once-daily (or 4 x 100/25 mg tabs twice-daily). With or without food.	4 (or 8 using smaller pills)
fosamprenavir/r * (Telzir)		1 x 700 mg tablets + 100 mg ritonavir, twice-daily. Take with or without food.	2 (+ 2 ritonavir)
saquinavir/r * (Invirase)		2 x 500 mg tablets + 100 mg ritonavir, twice-daily. Take with food.	4 (+ 2 ritonavir)
tipranavir/r (Aptivus)		2 x 250 mg capsules + 200 mg ritonavir, twice-daily. Take with food.	4 (+ 4 ritonavir)
Entry inhibitors			
T-20 (Fuzeon, enfuvirtide)	 not to scale	90 mg injection under the skin, twice-daily.	2 injections daily

i-base
0808 800 6013

i-Base publications

All i-Base publications are available free

Treatment guides are written in everyday language

HTB is written in more technical medical language

Please photocopy or cut out this form and post to

HIV i-Base

4th Floor, 57 Great Suffolk Street, London, SE1 0BB

or fax to 020 7407 8489

or order online www.i-Base.info

Please send me

- **Introduction to Combination Therapy** *(this guide)* ☐
- **Changing treatment: guide to second-line therapy** ☐
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- **Guide to hepatitis C for people living with HIV** ☐
- **HIV Treatment Bulletin (HTB)** ☐

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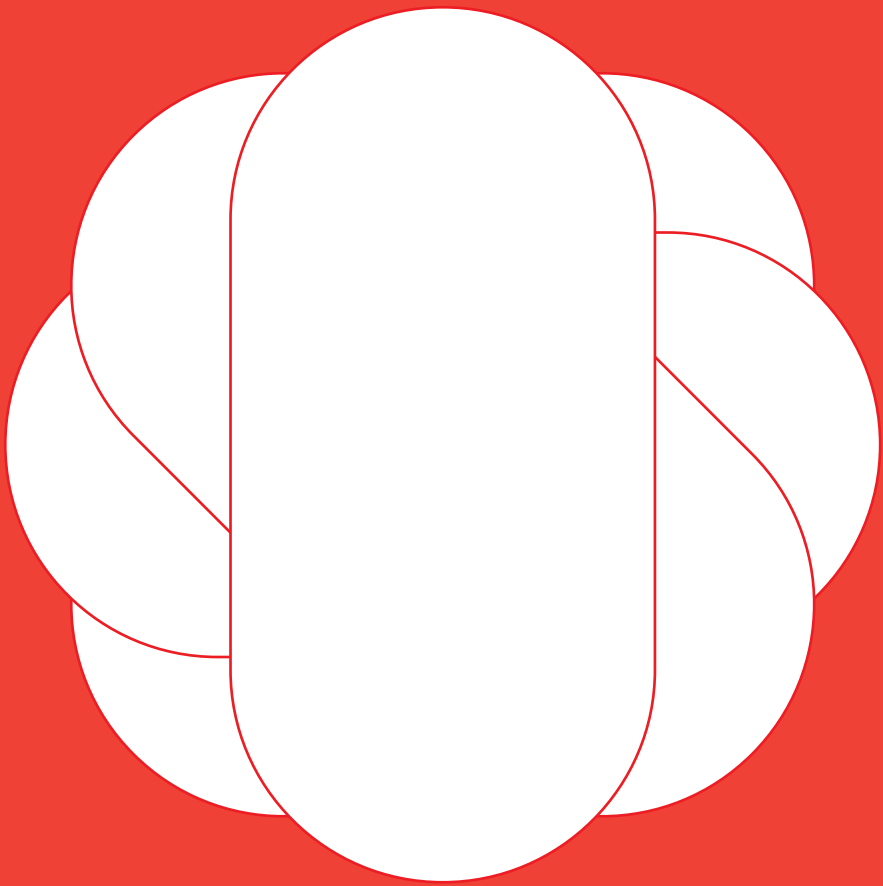
i-Base would like to thank The Monument Trust for their support in funding this publication

Call us on
0808 800 6013

i-Base Treatment Information Phoneline

Monday to Wednesday
12 noon to 4pm



i-Base can also answer your questions by email or online

questions@i-Base.org.uk
www.i-Base.info/questions