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aids treatment update

special 150th issue

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in this issue

Welcome to the redesigned 150th issue of *AIDS Treatment Update*, NAM's monthly newsletter for individuals with HIV who would like to be able to talk knowledgeably with their HIV doctor about all aspects of HIV-positive health.

ATU would not have its strong reputation for providing accessible, authoritative and balanced articles on HIV treatment and other aspects of HIV-positive health if it weren't for the groundwork of its previous editors, Edward King and Anna Poppa; our small team of expert contributors; and the invaluable support provided by both the Medical Advisory Panel and the Peer Review Panel.

We would not have been able to build upon that reputation, however, without the support of both the Elton John AIDS Foundation and the Derek Butler Trust, whose generous contributions allowed us to take the time that we needed in order to make the right decisions about how and why we have redesigned *ATU*.

We hope that we can continue to be a valuable resource for those who are already loyal readers, as well as find a new audience of people living with HIV who are, or would like to become, experts in making choices about their health and treatment options.

page 3 In our new *upfront* section, which in future will focus on the month's most important piece of treatment news, we take a look back at 150 issues of *ATU*, and discover that much of what was important for UK treatment information in 1992 continues to be important today.

page 4 The theme of this month's issue is 'Starting treatment', and in this major article we discover the ideal time to start, and provide information to help make the choice of treatment options less bewildering for people who have never taken anti-HIV therapy before.

page 10 In 'Making an informed choice', Paul Clift, a member of our Peer Review Panel, explains how he approached starting treatment, providing some very helpful tips as well as great insight into how patient power works.

page 12 Amongst the items in *News in Brief*, we discover that a major CCR5 inhibitor trial has been halted, and preview NAM's news weekly email news bulletin, *HIV Weekly*.

page 14 'Does Cost Matter?' examines how changes in the way the NHS will fund its services may result in some painful choices for people living with HIV as well as the professionals who care for us.

“ *ATU* is the definitive source of up-to-date information not just for patients but for clinical staff and for many of us in the MRC CTU! I'm sure the redesign will make it more accessible to a broader readership without losing its value to its original audience. Congratulations to the team for a tremendous achievement and best wishes for the next 150! ”

Professor Janet Darbyshire
Head, Medical Research Council
Clinical Trials Unit



aids treatment update

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Going back to our roots

Looking back at the early issues of *ATU* points the way forward

by Edwin J Bernard

When NAM founder Peter Scott and *ATU*'s first editor, Edward King, launched *AIDS Treatment Update* in November 1992, they had three aims for the newsletter:

- to help individual readers become familiar with their treatment options and confident about their rights
- to encourage productive communication between people with HIV, doctors and the pharmaceutical industry
- to provide the basis for well-informed and constructive activism.

Peter and Edward (along with treatment writer Keith Alcorn, now NAM's Senior Editor, and longest-serving staff member) were true visionaries, but during the dark days of the early- and mid-1990s, even they might not have envisaged a time when people living with HIV had the relative luxury of once-daily dosing, had anxieties about body shape changes or increased heart-attack risks, or needed to be concerned about the costs of drugs. They probably also couldn't have imagined the changing face of the UK HIV epidemic.

Thirteen years and 150 issues on, *ATU* continues the spirit of its founding principles and returns to its

roots after three extensive redesigns and a necessarily intense period of focusing on rapid drug development.

And so, *ATU* will continue to focus on subjects relating to treatment and HIV-positive health, and in fact, anything that affects the physical, mental, and sometimes even the spiritual aspects of living well with HIV.

The newly-redesigned *ATU* will also include regular first-person experiences of living with HIV and its treatment regimes, a concept which began with the fifth issue in March 1993.

And, as the definition of what constitutes HIV-positive health continues to broaden to include areas that affect both quality-of-life and quality-of-treatment, we will continue to feature occasional articles about legal and policy issues,

treatment activism and other pressing concerns that may - directly or indirectly - affect our health.

If you have any comments about our redesign, or ideas for future content, please drop me an email (edwin@nam.org.uk). As Peter Scott wrote in the very first issue of *ATU*, this newsletter is "a partnership with our readers... We hope that you can [continue to] help us make this newsletter a valuable source of information and advice for everyone living with HIV in this country."



starting treatment

Summary

- Most people should start treatment if they are unwell, or when they feel well but have between 200-350 CD4 cells/mm³.
- Today's choices affect choices later, so plan ahead.
- Combine either a NNRTI or a boosted PI with two NRTIs.
- Consider potential side-effects and drug interactions, how often pills are taken, number of pills, lifestyle, and/or pregnancy plans.
- Success of treatment depends on taking the pills, day in, day out.
- You can take any recommended treatment, regardless of cost, if you think you will stick with it.

by Edwin J Bernard

In terms of first-time drug choices, there has never been a better time for someone to begin anti-HIV therapy (also known as HAART - highly active antiretroviral therapy). Although there are no perfect drugs, some of the more recent developments in HIV medicine have allowed for less toxic drugs, less pills and once-daily dosing: something that was only a pipe dream when *ATU* launched in 1992.

However, the absolute best regimen choice is still not clear-cut, and today anti-HIV therapy in the UK has become about individual choice, taking into account the number and size of pills to be taken each day, how often the pills need to be taken, and the potential side-effects, both in the short- and long-term. Other factors have to be taken into consideration too: whether or not you have acquired HIV that is already resistant to some drugs; whether or not you have hepatitis B or hepatitis C co-infection; your risk for cardiovascular disease (like heart attack or stroke) and/or diabetes; whether you have previously been diagnosed with a psychiatric illness, like depression; whether you are, or plan to become pregnant; and any other drugs you are currently taking.

A further complication, which so far hasn't affected many of us in the UK (unlike much of the rest of the world), but which is becoming an increasingly urgent issue, is the cost of anti-HIV

therapy. This year's updated British HIV Association (BHIVA) guidelines discuss the cost of therapy for the first time, suggesting that doctors consider the cost of equally effective drugs that have different side-effects or dosing schedules. Whilst the BHIVA guidelines are purely voluntary, there are growing fears over the Department of Health's plans to issue much more stringent guidelines across-the-board, which might force HIV clinicians to prescribe anti-HIV therapy on the basis of cost.

Fortunately, at the moment, few doctors in the UK would expect an individual with HIV to consider the cost of a particular drug or anti-HIV regimen when making the often bewildering decisions that accompany starting therapy. Nevertheless, you may currently attend an HIV clinic where the cost of drugs is already an issue. In those circumstances, you should be aware that you are entitled to discuss – and access – all BHIVA-recommended drug options: after all, every HIV doctor should want their patient to adhere to their anti-HIV regimen, and you are more likely to do so if you choose a regimen that you can live with.

When starting treatment you should also think ahead. The best responses to anti-HIV treatment are generally seen with the first drug combination, so starting too early, or with the wrong drug combination may be a waste. Allowing for more choice in your second-line and third-line options can

Deciding when and which anti-HIV therapy to take for the first time remains one of the most challenging episodes in an HIV-positive individual's life, but new treatment guidelines can lead us through the maze.



“ Any HAART regimen should be individualised in order to achieve the best potency, adherence and tolerability; to minimize potential long-term toxicity and to avoid any likely drug–drug interactions. The cost of the regimen should also be considered. ”

BHIVA Guidelines 2005

make life a lot easier in the future. Starting anti-HIV therapy for the first time is rarely urgent, and it is possible for you to take the time to make the decision that works out best for you.

When do I start?

There are several clear events that make when to start treatment a no-brainer: if you are ill because of HIV, or have an AIDS-defining illness; and/or if your CD4 cell count is at or below 200 cells/mm³. We also know that if you are feeling well and have a CD4 count above 350 cells/mm³, and a CD4 percentage above 17% (see below), that the likelihood of short-term HIV disease progression is considered to be very low, and there is no need to start just yet.

But what if you have between 200 and 350 CD4 cells mm³? Well, looking at how fast your CD4s are

dropping, and how high your viral load is, can help figure this out: if your CD4 count is falling by more than 80 cells per year and/or if your viral load is above 100,000 copies/ml, you are at a higher risk of getting sicker quicker, and might want to start anti-HIV therapy before your CD4 count drops much further.

If you are still unsure, and your viral load is under 100,000 copies/ml, a new study^[1] suggests that looking at your CD4 percentage may help you figure out whether it is best to consider starting treatment now as opposed to waiting until later. It found that a CD4 percentage below 15% is as significant in terms of the risk of disease progression as having a viral load above 100,000 copies/ml.

You may wish to consider starting treatment closer to 350 cells/mm³ if you are also infected with hepatitis C

virus (HCV), as liver disease becomes worse when the CD4 cell count is lower. And since a recent study^[2] found that individuals with more than 350 cells/mm³ but a CD4 percentage below 17% had a risk of disease progression three-and-a-half times higher than those with a CD4 percentage above 17%, you may want to consider beginning anti-HIV therapy at a higher threshold than current guidelines suggest, if your CD4 percentage is lower than 17%.

If you are advised to start treatment but choose not to, then you should review your decision regularly and have your CD4 count (and CD4 percentage) and viral load monitored more frequently than usually recommended, for example every two months.

What should I take?

For someone starting anti-HIV therapy in the UK in 2005, the aims are to

starting treatment

suppress HIV replication to 'undetectable' levels, restore immune function (reflected by CD4 count and other immunological tests), and improve both your quality and quantity of life.

Standard anti-HIV treatment for people who begin taking it for the first time will involve a combination, or 'regimen', of three antiretrovirals. BHIVA have made the choices easier by recommending preferred and alternate regimens and setting up a 'choose one from columns A, B and C' situation.

BHIVA recommend starting with **either** a non-nucleoside reverse transcriptase inhibitor (NNRTI), **or** a 'boosted' – i.e. taken with an additional small amount of ritonavir – protease inhibitor (PI) [choose one from table 1] **plus** two nucleoside reverse transcriptase inhibitors (NRTIs), one of which should be 3TC or FTC. The NNRTI or PI in the combination is thought to pack the most punch against HIV, supported by two NRTIs; these NRTIs are sometimes called the 'backbone' drugs.

Unboosted PIs, like indinavir (*Crixivan*) and nelfinavir (*Viracept*), are no longer recommended for individuals starting treatment for the first time, and taking three NRTIs together, for example as the single triple-drug combination pill, *Trizivir*, is also not recommended, although combining *Trizivir* with tenofovir (*Viread*) is an option in the unusual situation when boosted PI- or NNRTI-based HAART cannot be taken.

NNRTIs or PIs?

Choosing between an NNRTI or a PI remains largely a matter of personal opinion since no studies have concluded that one is superior to the other. However, there are some important differences between the two classes of drugs. ▶

Table 1 BHIVA-Recommended PIs/NNRTIs















Drug Name	Drug Class
Preferred regimens	
 efavirenz (<i>Sustiva</i>)	NNRTI
 lopinavir/ritonavir (<i>Kaletra</i>)	PI (boosted with ritonavir*)
Alternative regimens	
 saquinavir (<i>Invirase</i>)	PI (boosted with ritonavir**)
 fosamprenavir (<i>Telzir</i>)	PI (boosted with ritonavir**)
Other options for specific groups	
 nevirapine (<i>Viramune</i>)	NNRTI
 atazanavir (<i>Reyataz</i>)	PI (unboosted)
 atazanavir (<i>Reyataz</i>)	PI (boosted with ritonavir**)
* Ritonavir included in each capsule. ** Ritonavir capsules taken separately.	
Please note: pill/capsule sizes are not shown at their actual size	

Table 2 BHIVA-Recommended NRTI 'Backbone' Drugs

Drug Name	Usual Prescription
Choose Either One of these Fixed Dose Combination NRTIs	
 <i>Combivir</i> (300mg AZT/150mg 3TC)	1 pill twice daily
 <i>Kivexa</i> (600mg abacavir/300mg 3TC)	1 pill once daily
 <i>Truvada</i> (300mg tenofovir/200mg FTC)	1 pill once daily
Or two of these single NRTIs	
One of these four	
 AZT (zidovudine, <i>Retrovir</i>)	250mg/1 capsule twice daily
 abacavir (<i>Ziagen</i>)	300mg/ 1 pill twice daily
 tenofovir (<i>Viread</i>)	300mg/1 pill once daily
 ddI (didanosine, <i>Videx EC</i>)	400mg/1 capsule once daily on empty stomach
And one of these two	
 3TC (lamivudine, <i>Epivir</i>)	150mg/ 1 pill twice daily 300mg/ 1 pill once daily
 FTC (emtricitabine, <i>Emtriva</i>)	200mg/1 pill once daily

to select your combination
**choose one drug from table one
 and one option from table two**

Usual Prescription	Daily Pill Count	Common Side-effects	Other Side-effects
600mg/1 pill once daily	1	Short-term rash; vivid dreams, sleep and mood disturbances, drowsiness.	Rarely, depression, suicidal thoughts, Stevens-Johnson Syndrome (1-in-1000 risk).
133.3mg/3 capsules twice daily with food	6	Diarrhoea, raised blood fats.	Long-term risk of central fat gain, cardiovascular disease, diabetes.
500mg/2 capsules twice daily after meals (+ 100mg ritonavir/ 1 capsule twice daily)	6	Diarrhoea, raised blood fats.	Long-term risk of central fat gain, cardiovascular disease, diabetes.
700mg/1 pill twice daily (+ 100mg ritonavir/ 1 capsule twice daily)	4	Diarrhoea, raised blood fats.	Long-term risk of central fat gain, cardiovascular disease, diabetes.
200mg/1 pill twice daily or 2 pills once daily ***	2	Short-term rash; liver problems.	Rarely, Stevens-Johnson Syndrome (3-in-1000 risk).
200mg/2 capsules once daily ****	2	Increased bilirubin levels, jaundice.	Rarely, haematuria (red blood cells in the urine).
150mg/2 capsules once daily with food (+ 100mg ritonavir/ 1 pill once daily) ****	3	Increased bilirubin levels, jaundice.	Rarely, haematuria (red blood cells in the urine).
<p>*** Women with CD4 counts below 250 who plan to become pregnant; men with CD4 counts below 400; people with previous psychiatric history who want to avoid efavirenz. once-daily dosing possible but may worsen liver side-effects</p> <p>**** Not yet approved for first-time HAART in Europe, but BHIVA suggests boosted or unboosted atazanvir might be useful where cardiovascular risk factors are high and a PI needs to be used.</p>			

Daily Pill Count	Common Side-effects	Other Side-effects
2	See individual drugs.	See individual drugs.
1	See individual drugs.	See individual drugs.
1	See individual drugs.	See individual drugs.
2	Nausea, fatigue, anaemia.	Rarely, long-term facial, limb fat loss, severe muscle pain, skin pigmentation changes in non-Caucasians.
2	Nausea, fatigue.	Rarely, life-threatening hypersensitivity reaction.
1	Nausea, diarrhoea, low-grade kidney dysfunction.	Rarely, rash, kidney toxicity.
2	Peripheral neuropathy, diarrhoea.	Rarely, pancreatitis, lactic acidosis.
1 or 2	Short-term nausea, diarrhoea.	Rarely, peripheral neuropathy, neutropenia, rash.
1	Short-term dizziness, headache, diarrhoea, nausea, rash.	Rarely, skin pigmentation changes in non-Caucasians, liver toxicity.

starting treatment

glossary

AIDS-defining illness

a list of various illnesses, or opportunistic infections, that result in an AIDS diagnosis, rather than being 'just' HIV-positive. Examples include PCP pneumonia, tuberculosis and some cancers.

CD4 cell count

the absolute number of CD4 T-cells, which reflect the state of the immune system.

CD4 percentage

the number of CD4 T-cells within every 100 lymphocytes, the subset of white blood cells that includes T-cells and B-cells.

HAART

highly active antiretroviral therapy, a term used since 1996 to describe anti-HIV combination therapy with three or more drugs.

NNRTIs appear to present fewer problems with side-effects like lipodystrophy than protease inhibitors. This, together with the potential for easier adherence, are the main reasons why NNRTI-based combinations are the most popular in the UK for people starting anti-HIV treatment. If you think you are someone who can't take pills exactly on time or worry about occasionally missing a dose, NNRTIs are also considered more 'forgiving' than PIs due to their longer half-lives (i.e. they linger longer in the body). Their major disadvantage is that it is very easy for HIV to develop drug resistance to an NNRTI drug if you regularly miss doses or stop the drugs without a doctor's help; if this happens, it is unlikely that you will benefit from any other currently-approved NNRTI.

Efavirenz (*Sustiva*) is BHIVA's preferred NNRTI, but should be avoided by women considering pregnancy, due to its association with birth defects, and individuals with a history of psychiatric illness may prefer to stay away from the drug too.

Nevirapine (*Viramune*) is BHIVA's second-choice NNRTI, mainly due to the fact that potentially serious liver problems can occur with this drug, particularly in women with CD4 counts above 250 cells/mm³, men with CD4 counts above 400 cells/mm³, and those with active hepatitis B or C.

If a protease inhibitor is used, the BHIVA guidelines suggest that it should always be 'boosted' by the addition of a small dose of ritonavir with the exception of atazanavir (*Reyataz*, see next page). Boosting increases PI blood levels, allowing for both fewer pills and fewer doses, and may result in the PI becoming less vulnerable to the risk of drug resistance. The main disadvantages of PI-based combinations are that, with the exception of atazanavir, they present a higher risk of longer-term side-effects, like lipodystrophy (which includes body shape changes, heart disease, stroke and diabetes), and because there are still more pills to take than NNRTIs, they may be less easy to adhere to. The ritonavir boost also means that PIs can interact with a greater number of other drugs, medicines and herbs than NNRTIs. They are also less 'forgiving' than PIs if you are more than an hour or so late or occasionally miss a dose, due to their much shorter half-lives.

Boosted lopinavir (*Kaletra*) is BHIVA's preferred choice, because there are more data on its short- and long-term effectiveness than other boosted PIs. In addition, out of the relatively few people who fail to keep their viral load 'undetectable' on *Kaletra*, even fewer appear to acquire resistance to the drug, theoretically leaving more options open for the next combination.

side-effects glossary

anaemia

low red blood cells, causing tiredness

bilirubin

blood by-product; too much can cause jaundice, or yellowing of skin or eyes

lactic acidosis

rare, sometimes life-threatening build-up of lactate, a blood sugar

neutropenia

low white blood cells, increasing infection risks

pancreatitis

inflammation of the pancreas, a digestive system organ

peripheral neuropathy

nerve pain in hands, legs and feet

Stevens-Johnson Syndrome

rare, life-threatening skin-eating rash

Fosamprenavir (*Telzir*), a new formulation of amprenavir that requires fewer pills each day and makes more of the drug available in the blood to suppress HIV, is BHIVA's alternative PI regimen, with a lower pill burden than *Kaletra*. It is also the only PI that can be taken with or without food.

Saquinavir (*Invirase*) is another alternative choice. It is now available in a new easier-to-take formulation, consisting of 500mg tablets, and a recent study³ found that the few (4%) people that failed to keep viral load suppressed below 500 copies/ml after 30 weeks on the combination didn't appear to acquire resistance.

non-nucleoside reverse transcriptase inhibitor (NNRTI)

anti-HIV drugs with a particular biochemical structure that target an HIV protein called reverse transcriptase; considered as potent as PI's.

nucleoside reverse transcriptase inhibitors (NRTIs)

anti-HIV drugs with a particular biochemical structure that also target reverse transcriptase; at least two are needed to back-up NNRTIs or PIs.

protease inhibitor (PI)

anti-HIV drugs which target an HIV protein called protease; considered as potent as NNRTIs.

peripheral neuropathy

nerve damage to the lower legs, feet and hands.

undetectable

the lowest limit of detection of the viral load test used, usually below 50 copies of HIV per millilitre of blood.

viral load

measurement of the amount of virus in a blood sample, roughly indicating the extent to which HIV is reproducing in the body.

Atazanavir (*Reyataz*) is not currently approved in the UK for people starting treatment for the first time, although it is in the United States. Nevertheless, BHIVA says that unboosted or boosted atazanavir could be used here in certain circumstances, because not only does it have the advantage of once-daily dosing, but it also does not appear to cause lipodystrophy. People who need to use a PI, but have established risks for heart disease, for example, might well benefit from this drug.

Which nucleoside backbone?

Although there are eight drugs in this class (including the NtRTI, tenofovir), BHIVA recommends that you only consider the following six when taking anti-HIV therapy for the first time: AZT, abacavir, tenofovir, or ddI, plus either 3TC or FTC.

AZT, abacavir and tenofovir are now available in a fixed-dose combination pill with either 3TC or FTC: *Combivir* combines AZT and 3TC, *Kivexa* combines abacavir and 3TC and *Truvada* combines tenofovir and FTC. Currently there are not enough data to decide between them, so, again both doctor and patient preference count here.

Although AZT has been used for longer than any other anti-HIV drug, and is known to be effective, it is now coming to light that AZT might be implicated in lipodystrophy-associated

fat loss. In addition, AZT may damage the bone marrow, the substance in the body which produces blood cells. Short-term side-effects can include nausea, vomiting, fatigue, headache and insomnia.

Abacavir has not been implicated in lipodystrophy-associated fat loss. Its short-term side-effects can include nausea and vomiting, headaches, weakness, diarrhoea, insomnia, dizziness, and abdominal pain. However, of greater concern is a potentially life-threatening allergic reaction (often involving fever and rash) that occurs in 3% - 8% of people taking abacavir, usually within four weeks of starting the drug. Fortunately, many clinics now conduct a genetic test to see if a person is likely to have this allergic reaction to abacavir. Liver problems can also be a rare side-effect of the drug.

Tenofovir has also not been implicated in lipodystrophy-associated fat loss. Its short-term side-effects can include diarrhoea and nausea. It is also suspected to cause mild – and occasionally severe – kidney damage.

Although studies have shown that ddI is well-tolerated and effective, it is now likely to be a less popular choice because it requires a two-hour fast before and after taking the drug, making adherence more difficult. It is also associated with peripheral neuropathy.

**references**

Full references for this article can be found on page 14.

further information**For comprehensive information on individual drugs, search NAM's website, aidsmap.com**

NAM's booklet *Anti-HIV Drugs* provides more details on all the drugs mentioned here, including dosing, side-effects, interactions and resistance. NAM's award-winning booklet *HIV Therapy* provides an overview of the latest BHIVA guidelines. Both are available as free downloads from aidsmap.com. For printed copies (free to HIV-positive individuals in the UK) call or email NAM on 020 7840 0050 or info@nam.org.uk





Earlier this year, after nearly 17 years of diagnosis, I took my first dose of anti-HIV drugs. Why so long? Well, partly because I was a 'slow progressor' – unlike several of my friends and contemporaries who fell ill soon after being diagnosed, many of whom died. Secondly, I went through a painful period soon after combination therapy was introduced in 1996 of wanting nothing to do with it – if my friends had not been able to benefit from it what right had I to it? Lastly, my own efforts at keeping broadly fit seemed to be working – my CD4s were high enough to keep opportunistic infections at bay, so why tamper with anything?

how to make the right decisions for yourself

- Do your own research.
- Listen to other people's experiences but remember side-effects vary with the individual.
- Discuss your concerns with your doctor.
- Consider the options.
- Make your choice.

However, without meds the virus cannot be held back indefinitely. Over the last eighteen months or so, my CD4s were in definite decline. At the same time, my viral load was consistently high (around 100,000) and the CD4 percentage was dropping steadily to dodgy levels, around 10%. My doctor first suggested, then **recommended** that I start, but still I held out.

So we compromised. I would keep off anti-HIV drugs but start preventative treatment for PCP, the AIDS-defining pneumonia that can occur when CD4s are below 200 cells/mm³. First I tried *Seprin* (co-trimoxazole or *Bactrim*), but that gave me a skin rash, so I switched to another PCP preventative drug, dapson, which gave me an even worse rash, so I finally switched to pentamidine (*NebuPent*). This gets a bad press, and it's easy to see why. But it gave me no trouble, and I came to prefer the monthly inconvenience of breathing nebulised Pentamidine to taking daily pills.

But reality catches up, and even I could not sustain my opposition much longer, not with CD4s down to 200 and no sign of levelling off. Even though it felt like handing control to the doctors and meds, I decided to take the plunge. Making the decision to start is one thing, what to start with is quite another. Over the years since combination therapy was introduced I saw and

read enough to be concerned about side-effects, worried about the complications of taking a complex regimen of many pills on time every time, and the fact that we are still in a relatively unknown territory. HIV and its associated medications are relatively new to medical science; we still do not know all the long-term effects, or effectiveness, of these treatments. Starting HIV meds is the start of a long-term, possibly lifelong, option and is not to be undertaken lightly. So, what to do?

As someone involved in HIV for some time, I felt fairly well-informed about the drugs in theory, from NAM info booklets and other reputable sources. But

yes, we *can* ask our doctor questions

with 'theory' about to move on to 'practice' I sought out other people's experiences of actually taking the various meds, focusing on those which seemed most likely to be prescribed as a first-line regimen. At the clinic I go to this is usually *Combivir* plus efavirenz. However, different clinics tend to have their (i.e. the doctors') favoured first-line therapy.

Making an informed choice

What happens when a well-informed individual with strong opinions starts treatment for the first time? Paul Clift, Patient Representative at Brighton's Lawson Unit HIV clinic, shares his experiences.

After the homework I had a few questions and conditions to lay down to my doctor. And yes, we *can* ask our doctor questions! HIV is a new discipline in the history of medicine, and has been shaped from its earliest days by patient activism. This in turn has shaped a tendency for HIV clinicians to be open to discussion. This is not to say that *all* doctors are relaxed about discussion with patients, but enough of them are for this to be a defining feature of HIV medicine.

My main concerns were about side-effects, followed by ease - or otherwise - of taking the drugs and adhering to the regimen.

First, the side-effects. I told my doctor that I was not prepared to take anything that is associated with lipodystrophy, or with psychological side-effects. I knew that this would throw a spanner in the works, because *Combivir* contains AZT, now associated with the fat loss component of lipodystrophy and efavirenz can have a range of psychological side-effects, from mild to wild! But I was firm on this. We had a long discussion about the relative merits of efavirenz and the alternative nevirapine. The first leads, in most cases, to psychological experiences in various degrees, the second leads to skin

and liver problems in some cases, very seriously in a very few cases. On balance I preferred to chance nevirapine. And although I did experience a mild rash towards the end of week one, it gradually disappeared through week two.

To have the least possibility of lipodystrophy my doctor suggested *Truvada* (FTC + tenofovir in one pill). Then there's the cost issue. Although *Truvada* is more expensive than *Combivir*, it wasn't an issue for me, but if the costs of a combo that you find best suited to you are brought up, it is still worth digging in your heels and insisting on your informed choice. If we take a combo of our choice, we are more likely to adhere to it and therefore get the most out of it; in spite of higher initial cost, this may be the most cost-effective in the long run.

As for ease of taking the meds, *Truvada* is one pill once a day, nevirapine is one pill once a day for two weeks then one pill twice a day thereafter (although I subsequently got the go-ahead to take nevirapine as two pills once a day, but

only after discussing it with my doctor). And there are no dietary restrictions. There is also a generous window in dosing schedule allowing a certain flexibility; so although I aim to

efavirenz can have a range of psychological side-effects, from mild to wild

take the pills on time, there is just enough room to feel relaxed if I'm, say, an hour late with a dose.

So far, it's working well. My viral load is now 'undetectable' and my CD4 count is a very respectable 450 cells/mm³, which is fine on paper, but how do I actually feel? More awake! I used to sink into a fatigue almost every afternoon and had to take an hour's nap, but that is past now. So overall, although I did have some serious concerns, they seem to have been dispelled through talking things over with my doctor to find the combination that suits me.

”



news in brief



new drugs

Major CCR5 inhibitor study stopped

Glaxo SmithKline (GSK), one of three drug companies in the race to deliver the first class of oral anti-HIV fusion inhibitors, also known as CCR5 antagonists, has terminated a major study of its experimental drug aplaviroc (GW873140) following reports of severe liver toxicity in two out of the 250 people in the study who were new to anti-HIV therapy.

This side-effect was unexpected and has not been reported by the other drug companies developing their own CCR5 inhibitors - Pfizer's maraviroc (UK-427,857) and Schering-Plough's vicriviroc (SCH-D).

GSK is allowing treatment-experienced patients already enrolled in the study to choose whether or not to continue on aplaviroc and says that these patients will be monitored closely for signs or symptoms of liver toxicity.

latest research

Ethnicity does not affect how well anti-HIV therapy works in women

A study of HIV-positive women from the United States has found that ethnicity in itself does not affect how well a woman responds to highly active antiretroviral therapy (HAART), but that adherence and depression are worse in non-white women, and this does make a difference. The study included 961 women who started HAART between 1995 and 2003: 60% were African American, 20% were white and 20% were Hispanic. After almost eight years of follow-up, the investigators found that 70% of African American women were still alive, compared to 77% of Hispanic women and 80% of white women. White women were significantly more likely than African American women to get their viral load 'undetectable' after starting HAART, experience an increase in CD4 cell count of at least 100 cells/mm³ after initiating HIV treatment, and were less likely to experience a rebound in their viral load or die of any cause. However, ethnicity did not make a difference to the effectiveness of anti-HIV therapy for the women who took it as prescribed, suggesting that socio-economic factors, and quality of life issues, like depression, are responsible for the difference in survival rates.

latest research

Common wart virus increases cancer risks despite HAART

A San Francisco study of more than 350 HIV-positive gay men has found that over 50% had precancerous cell changes in their anus, putting them at a high risk of developing anal cancer in the absence of diagnosis and treatment. The study found that taking highly active antiretroviral therapy (HAART) did not protect against these precancerous changes.

Infection with certain strains of human papilloma virus (HPV) - the virus that causes anal and genital warts - has been strongly associated with an increased risk of developing precancerous and cancerous cell in the cervix (which can lead to cervical cancer), as well as precancerous cell changes in the anus, and this study found that 95% of the men had anal infection with HPV.

Next month, *ATU* will be focusing on HPV in detail, looking at how this virus affects people with HIV and what can be done to treat, diagnose and prevent problems.

uk services

BPNW stays open

Last month we reported the withdrawal of funding from the Manchester self-help HIV charity, Body Positive North West, by North Manchester, Salford and Stockport Primary Care Trusts, despite a high-profile campaign that included local MP Tony Lloyd, HIV consultants, service users, and the local business association. Happily, BPNW remains open with all of its services still running. "We are not closing," says Felicity Greenham, Body Positive's Chief Executive. "We are secure and, indeed, have some strong expansion plans. The issue is whether the NHS is willing to work alongside self-help organisations that HIV-positive people run to provide the services that HIV-positive people want."

new drugs

One pill once-daily HAART not likely soon

Attempts to combine tenofovir (*Viread*), FTC (emtricitabine, *Emtriva*) and efavirenz (*Sustiva*) into one pill that would mean one pill, once-a-day for a currently recommended anti-HIV therapy combo are coming unstuck, according to Gilead Sciences, the manufacturers of tenofovir and FTC, who partnered with efavirenz manufacturer, Bristol Myers Squibb, last December in an attempt to make a highly active anti-HIV regimen in one pill. Although GSK's Trizivir, which combines AZT, 3TC and abacavir in one pill is already available, this regimen is not considered to be as powerful as a combination of two nukes and an NNRTI or a boosted PI.



new drugs

Brand new anti-HIV drug looks promising

A fifth anti-HIV drug class, known as maturation inhibitors, may soon join the other better-known classes of anti-HIV drugs (NRTIs, NNRTIs, PIs and fusion inhibitors), following promising phase IIa results of PA-457 from Panacos Pharmaceuticals. PA-457 reduces HIV viral load by interfering with the production of the HIV capsid protein. If this protein is not assembled, any HIV particles that are produced will be defective and unable to infect other human cells. Panacos carried out a randomised ten day study where neither the doctors nor the participants knew who was getting one of four doses of PA-457 (25, 50, 100 or 200mg) or a placebo (inactive pill). The 200mg dose packed the most powerful punch, with viral load declines that compare favourably with the fusion inhibitors, T-20 (enfuvirtide) and maraviroc (the experimental CCR5 antagonist). It's too early to tell, however, whether there will be any short- or long-term side-effects, or other problems, including its cost, that may limit PA-457's availability in the clinics at some time in the future.

the new hiv news update from nam

news from *hiv weekly*

HIV and hepatitis B vaccination

Liver disease caused by hepatitis B and hepatitis C has become one of the major causes of illness and death in HIV-positive people since effective anti-HIV drugs became available. All HIV-positive people are recommended to receive hepatitis B vaccinations (unless they are naturally immune).

Although the hepatitis B vaccine is perfectly safe for HIV-positive people to receive, a higher proportion of HIV-positive people may not develop protection from the vaccine or may lose the protective effects of their vaccination over time.

Hepatitis B vaccination consists of three injections into muscle over a period of six months.

An international study involving American and Irish patients found a very low rate of success for the vaccination. The study involved just under 200 patients. The researchers found that an HIV viral load below 400 copies/ml predicted the success of vaccination. CD4 cell count, even a high CD4 cell count, was not associated with the vaccine providing protection.

The researchers recommend that patients who do not initially develop protection from their course of vaccination should receive boosters.

HIV and ageing

The number of older people with HIV is increasing due to a rise in new infections amongst older people and the aging of the HIV population who are living longer thanks to anti-HIV treatment.

HIV infection may involve additional complications in older people, partially due to the aging of the immune system. Liver and kidney function is reduced in older people and this may increase the risk of treatment-related side-effects. Bone mineral loss - osteoporosis - occurs in old age and can also be associated with some anti-HIV drugs and with HIV infection itself. Studies suggest that older age is associated with more frequent diagnosis of HIV-related dementia. It is thought that anti-HIV treatment can increase the risk of heart disease, a risk that is also increased by older age.

Kaletra and liver side-effects

Treatment with the *Kaletra* (lopinavir/ritonavir) does not involve a high risk of liver side-effects, Spanish researchers have found.

Earlier studies have suggested that as many as 11% of patients taking *Kaletra* will develop major liver-related side-effects. However the Spanish researchers found that fewer than 1% of their 755 patients who took *Kaletra* experienced side-effects affecting the liver, even though 44% of these individuals had hepatitis B or hepatitis C.

subscribe to *hiv weekly*

At the end of October, NAM is launching a new, weekly email bulletin, *HIV Weekly*, that will provide people with or affected by HIV with a concise, plain English digest of the very latest HIV news. The bulletin will be edited by Michael Carter, NAM's patient information and news editor. One of the unique benefits of *HIV Weekly* is the inclusion of hyperlinks within the stories so that you can quickly and easily access further information on NAM's website, aidsmap.com, at the click of a mouse. Information and news about the latest NAM treatment information resources will also be included in the bulletin.

To register your interest to receive your free weekly news digest from the end of October, visit www.aidsmap.com and click on www.aidsmap.com/hivweekly

■ **share the knowledge**

If this issue of *AIDS Treatment Update* includes information which you think might be useful for a friend, family member or colleague, please do share it with them. Better still, why not encourage them to subscribe themselves? *ATU* is available free to individuals in the UK affected by HIV/AIDS by filling in the form on the back, calling 020 7840 0050, or emailing info@nam.org.uk.

■ **nam forum**

On the last Monday of every month, NAM facilitates a meeting between HIV experts and people living with HIV, to provide the latest information on a variety of treatment issues in a friendly, open atmosphere. Everyone is welcome, and refreshments are provided. NAM's October forum will feature Professor Brian Gazzard of London's Chelsea and Westminster Hospital talking about the latest British HIV Association (BHIVA) treatment guidelines which were published last month. The forum will take place on Monday 31st October, from 7pm at the University of London Union, Malet Street, London, WC1. Questions from the audience are welcome, and to make sure your voice is heard you can even email your questions in advance to forums@nam.org.uk. Visit www.aidsmap.com/en/events/forums.asp closer to the event for most up-to-date details.

■ **living with hiv**

Work is currently underway on an updated edition of NAM's *Living with HIV*. The book includes short pieces written by people with first-hand experience of life with HIV.

We need your experiences to be included in the next edition. You don't have to be a brilliant writer to have your work in the book. Just write honestly about how HIV has affected you and say if you would like the work to be published under your name or anonymously.

Please email them to michael@nam.org.uk, or post them to us directly. NAM's address can be found on page two.

Everybody's experiences are valuable.

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does cost matter ?

by Edwin J Bernard

The abundant anti-HIV drug choices available in the UK today might soon be history once the NHS commences major cost-cutting initiatives.

A growing concern in HIV healthcare today is the increasing cost of the more recently-approved anti-HIV drugs. As anti-HIV drug prices plummet in the developing world (and middle-income countries like Brazil negotiate hard for reduced drug prices), someone, argue the drug companies, has to fund their profits, some which are reinvested into research and development costs for future drugs. No profits may mean no new drugs, they warn.

Not coincidentally, the latest BHIVA treatment guidelines include a section on drug pricing for the first time. According to BHIVA's figures, taking the most frequently prescribed combination in the UK, *Combivir* and efavirenz, costs £7,428 a year. At the other extreme, combining the recently-approved combination of *Truvada* with boosted atazanavir costs £10,836 a year. Since the older, cheaper combination is considered to be as potent as the latter, and isn't particularly difficult to take in pill-count and timing terms (although they do have very different side-effects), this begs the question: Why should the NHS pay for the more expensive drugs?

The object of the exercise, BHIVA hopes, is that doctors – and savvy patients – will become more cost-aware, since by 2008-9, the way HIV treatment is funded will have changed dramatically: by then, the money that 90% of hospitals receive will be linked to the amount of work they do, fixed by a national tariff. This is known as payment by results. Two top HIV doctors – Professor Brian Gazzard, lead author of the BHIVA guidelines, and Consultant Physician and Research Director of HIV/GUM, St. Stephen's Clinic, Chelsea and Westminster Hospital, London and Dr Steve Taylor, Consultant Physician and Lead for HIV Services at Birmingham Heartlands Hospital - were happy to answer some questions regarding this potentially controversial issue.

Are costs currently an issue?

Steve Taylor

The issue of cost of treatment is an ongoing debate at our unit. However, the conclusion of most recent discussions are that individualisation of therapy remains the priority over cost. We strongly believe that choice of antiretroviral drugs should be made on clinical grounds. We don't burden the patient with the cost of the various therapies; we do not believe that this is something that patients who are already making difficult life-changing decisions should have to make.

Brian Gazzard

So far costs of drugs have never been an issue within HIV care. However, my own belief is that as such care is mainstreamed, these painful choices which are already a reality for many other specialities of medicine, will become our reality too.

How will the NHS proposals change things?

Brian Gazzard

Negotiations are still continuing as to what the payment per patient should be, and also whether this tariff should vary according to the complexity of the patient's individual problems. Once these negotiations are concluded, hospitals will receive a fixed sum of money to spend on patient care for a year. This will cover drug costs as well as support service costs such as the number of pharmacists, the number of adherence nurses, the manning of outpatients, etc. Inevitably this will require that patients and their doctors make joint choices about the trade-offs between drug costs and other patient care costs.

Steve Taylor

This is going to be a difficult balance to achieve. From talking to various colleagues around the country, current attempts to save money on the drug budget in an attempt to free money for staffing has not been successful, and the money saved on drugs has not found it's way back into HIV services for reinvestment.

So, how do we balance the costs of anti-HIV drugs with other costs?

Brian Gazzard

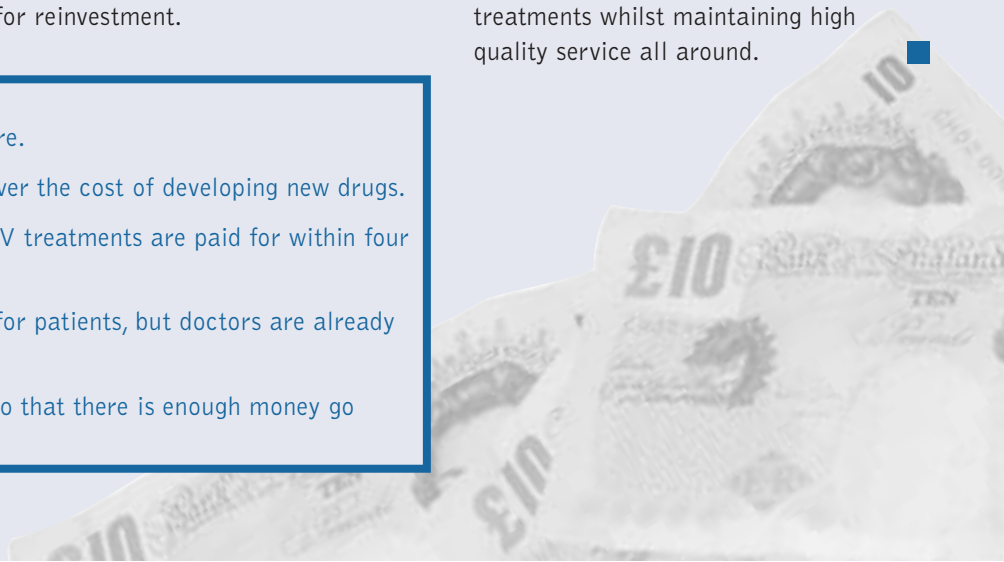
My own belief is that we should involve the HIV-positive patient population as widely as possible in such discussions. The costs of relatively similar medication varies widely and sometimes painful choices may need to be made between, for example, potential tablet burden – a slightly larger number of tablets may be associated with much reduced costs – versus other support services, like the wait for pharmacy, the wait to be seen in outpatients, the length of appointment time, the frequency of appointment times, the ability to provide support nurses such as adherence nurses, etc. Some of these decisions may be quite painful but the more we are able to provide a consensus view of the relative importance of some of these things, the better service we will be able to provide.

Steve Taylor

We would urge pharmaceutical companies to price any new compounds within the range of existing drugs so that we can access best treatments whilst maintaining high quality service all around.

Summary

- Newer anti-HIV drugs are costing more.
- Drug companies say they need to recover the cost of developing new drugs.
- The NHS wants to change the way HIV treatments are paid for within four years.
- Costs are not currently a major issue for patients, but doctors are already concerned.
- Painful choices will have to be made so that there is enough money go round for both drugs and care.



thanks to our funders

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Where to find out more about HIV

■ Find out more about HIV treatment:

NAM's factsheets, booklets, directories and website, keep you up to date about key topics, and are designed to help you make your healthcare and HIV treatment decisions. Contact NAM to find out more and order your copies.

■ Information events in London

On the last Monday of every month, an expert speaker discusses an HIV treatment related topic. Entry is free, further details are listed in this copy of *ATU*.

■ www.aidsmap.com

Visit our website for the latest news about HIV & AIDS and a fully searchable treatments database and a complete list of HIV treatment centres in the UK.

■ THT Direct Phonenumber

Offers information and support to help you take decisions about testing and treatment
0845 1221 200
Mon-Fr 10am-10pm Sat-Sun, 12pm-6pm

■ i-Base Treatment Phonenumber

A HIV Treatment phonenumber; where you can discuss your issues with a treatment expert.
0808 8006 013
Mon-Wed, 12pm-4pm



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■ How to place an order

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■ Here are just a few of NAM's resources that you might be interested in receiving

■ HIV & AIDS Treatments Directory

This is a comprehensive guide to the medical aspects of HIV and AIDS. It has A-Z listings of symptoms, illnesses, treatments and medical tests, and chapters covering the immune system, HIV's lifecycle and drugs used by people with HIV.

£12.95 to anyone personally affected by HIV. (For Professionals & Organisations: £64.95)

■ AIDS Reference Manual

This directory is a guide to the social impact of HIV and AIDS, and contains information on the origins of the epidemic, transmission, testing, prevention, vaccines, and the law and HIV.

£12.95 to anyone personally affected by HIV. (For Professionals & Organisations: £54.95)

■ Information booklets

These booklets are intended to provide introductions to key HIV topics. These booklets are also offered free of charge to certain UK-based organisations and clinics who make information available to people living with HIV.

Free to anyone personally affected by HIV.

(For Professionals & Organisations: £1 per copy, minimum order value £10)

■ Factsheets

Our monthly one page, A4 factsheets provide a basic overview on a wide range of topics relating to HIV.

Free to everyone and can be download at: www.aidsmap.com/factsheets

Please feel free to photocopy these and pass them on.

If you would like further information about any of NAM's resources, or have any questions, please call us on +44 (0) 20 7840 0050, or email info@nam.org.uk