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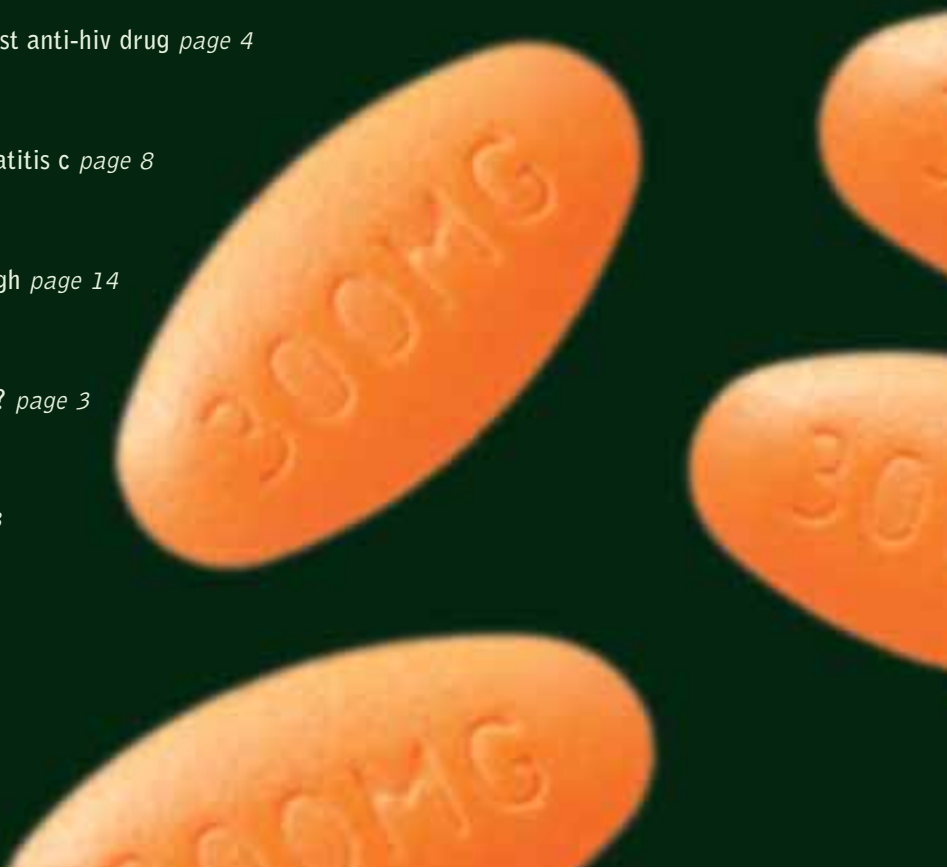
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in this issue

It's just three months into 2007, and already seismic shifts are appearing in attitudes towards anti-HIV treatment strategies from some very influential people. Experts on both sides of the Atlantic are arguing that people starting anti-HIV treatment for the first time should now be starting much earlier than has been recommended for the past six years.

They argue that anti-HIV drugs are so much easier to take than they used to be, and so the benefits of taking these drugs earlier now outweigh the risks, such as side-effects, drug resistance, and other apparent "inconveniences".

There certainly are some convincing data suggesting that untreated HIV is far more harmful than we used to think, even at CD4 counts well above 200 cells/mm³.

However, we need to remind doctors that although some people have no problems taking their anti-HIV pills, others struggle - for a vast array of reasons. Fortunately, most understand that the final decision is ours.

One thing they haven't discussed yet, however, is how the money required for earlier treatment (quantity) will affect our drug choices (quality). It's an issue that won't go away, and we'll be following it very closely in future ATUs. Watch this space!

page 3 In this month's *Upfront*, we explore why the pendulum seems to be swinging back towards starting anti-HIV treatment at higher CD4 counts.

page 4 The first new anti-HIV drug to be approved since tipranavir is finally here. Another drug purely for the treatment-experienced, it's a very welcome addition to the anti-HIV drug cabinet. Derek Thaczuk's article explains *All about darunavir*.

page 8 Treatments for people coinfecting with both HIV and hepatitis C are slowly improving - and there's some exciting breakthroughs promised soon - but more HIV-positive people are being infected with hepatitis C every week. Liz Highleyman provides this timely *HIV and Hepatitis C Coinfection Update*.

page 12 *News in Brief* takes a critical look at a recent selenium supplement study; and there's good news (about increased life expectancy) and bad news (about increased risk of bone death).

page 14 A new NAM/NAT briefing paper points out the flaws of scientific tests that have been rather too simply interpreted in criminal HIV transmission cases as 'proof' that one person infected another. However, as you will see, *HIV forensics* is a bit more complicated than that.



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ISSN 0969-4706
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charity number 1011220

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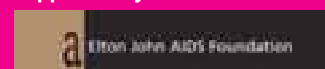
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Should we be starting anti-HIV treatment earlier?

by the NAM editorial team

It's called the 'starting treatment pendulum', and it has swung back and forth - between starting anti-HIV therapy earlier, at higher CD4 counts, and later, at lower CD4 counts - since 1996.

When the pendulum last swung back towards current recommendations - that most people starting treatment for the first time should wait until their CD4 count has fallen below 350 cells/mm³ and before they reach 200 cells/mm³ - some experts were already forecasting that it would swing back towards earlier treatment once better drugs arrived. "A more aggressive stance will re-emerge onto the scene, I think, as drugs improve," Dr Scott Hammer of Columbia University and the US AIDS Clinical Trials Group told an HIV conference in 2000: "When simple, potent, durable, non-toxic regimens become the norm, the pendulum will swing back towards aggressive early therapy".

That time appears to be now, according to some leading HIV doctors writing in the *British Medical Journal* in January. They now think that HIV treatment guidelines should be revised to recommend the initiation of antiretroviral therapy when an individual's CD4 cell count falls to 350 cells/mm³.¹

Side-effects, questions about the viability of long-term adherence, and fears about the exhaustion of HIV treatment options led to the development of treatment guidelines that favoured the postponement of HIV therapy.

However, over the past few years some doctors from the United States have begun to recommend that we consider the earlier initiation of anti-HIV therapy, following the publication of positive studies in people who have already done so. For example, a recent US study found that individuals who started anti-HIV therapy with a CD4 cell count above 350 cells/mm³ were significantly more likely than those who delayed until their CD4 cell count was in the currently recommended 350 - 200/mm³ range to experience an increase in their CD4 cell count to normal levels after six years of antiretroviral therapy.²

Last year's early closure of the SMART treatment interruption study has also led some experts to suggest that earlier is better: they cite data showing that people with CD4 cell counts between 200 - 250 cells/mm³ had a significantly greater risk of experiencing HIV disease progression. Furthermore, recent results from the D:A:D study of anti-HIV treatment side-effects found that individuals with CD4 cell counts in the region of 200 - 250 cells/mm³ had an increased risk of death from certain non-AIDS-defining illnesses, such as heart disease, liver disease and some non-HIV-related cancers.

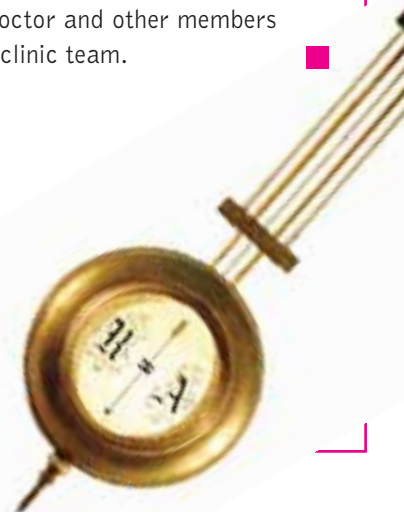
An improved understanding of what might be - and what might not be - anti-HIV drug side-effects also supports the earlier initiation of treatment, argue the authors of the *BMJ* article. The disfiguring body fat changes associated with early potent

anti-HIV regimens have been found to be caused mainly by d4T, and to a lesser extent, AZT, and the use of both is now avoided wherever possible. There is also better understanding of how to avoid the cardiovascular complications that antiretroviral treatment can cause.

HIV treatments, the authors argue, now have sufficient potency and convenience to support its earlier initiation: "We therefore suggest that guidelines should now recommend starting treatment at around 350 cells/mm³, so long as the patient is ready", they write.

UK treatment guidelines due to be produced later this year are likely to follow these recommendations. Professor Brian Gazzard, lead author of BHIVA's guidelines - who told NAM last October that the pendulum swing won't happen here - is one of the authors of the *BMJ* piece.

The most important question, though, is: are you ready to start? It's always an individual decision, and one that NAM's HIV information materials can help you make, alongside discussions with your doctor and other members of the HIV clinic team.



all about

darunavir

what we know (and don't know) about
the newest anti-hiv drug

by Derek Thaczuk



Darunavir (formerly known as TMC114) is one of the new generation of anti-HIV drugs specifically aimed at the 'heavily treatment-experienced'. Until recently, treatment options have been slim for HIV-positive people who had already been on many previous regimens, only to have had them fail due to drug resistance.

Evidence from clinical trials has established darunavir as an effective choice for such treatment-experienced people, as it appears to work against many strains of HIV that are resistant to other protease inhibitors. Dr Steve Taylor, lead consultant for HIV Services at Birmingham Heartlands Hospital, tells *ATU*: "In clinical practice we have certainly seen some very encouraging results in highly drug-experienced patients. However I would urge clinicians that in order to use the drug to obtain its maximum benefit it should be combined with at least one other agent to which the patient's virus is susceptible - based on resistance testing."

Ongoing trials are also investigating this drug's possible role for the 'treatment-naïve' - those who are beginning anti-HIV treatment for the first time - and aiming to fill in gaps in our current knowledge, such as how durable darunavir's benefits actually are, and whether it will prove to be equally effective in men, women, and all racial and ethnic groups.

darunavir 'at a glance'

generic name **darunavir** (formerly: TMC114)

trade name **Prezista**

manufacturer **Tibotec, a division of Janssen-Cilag**

drug class **protease inhibitor (PI)**

available as **300mg tablets**

Adult dose: two tablets (600mg) plus one 100mg ritonavir (Norvir) capsule, twice a day, with food.

Indicated use: only for 'treatment-experienced' HIV-positive adults who have failed more than one regimen containing a protease inhibitor, and in combination with other antiretrovirals.

Conditional marketing authorisation issued by the European Commission's European Medicines Agency (EMA) on February 16th 2007.

Darunavir, used in combination with ritonavir, interacts with many other medications and must be prescribed carefully.

Dosing: a boost from ritonavir

In terms of treatment strategy, darunavir occupies the niche of 'boosted' protease inhibitor (PI) - a phrase that might need a bit of background. To keep HIV in check, levels of anti-HIV drugs in the body have to be kept high enough at all times. Like many protease inhibitors, darunavir accomplishes this with help from ritonavir (*Norvir*). Ritonavir slows down a key chemical process in the human liver (in med-speak, the 'CYP3A enzyme pathway'), responsible for clearing many drugs out of the body. Taking any drug that relies on this pathway with ritonavir results in much higher levels of that drug in the body. Darunavir and other 'boosted' PIs turn this effect to their advantage. Small 'mini' doses of ritonavir boost darunavir to higher, more effective levels that also last longer, allowing for less frequent - twice daily - dosing. (The same ritonavir-boosting technique is used with lopinavir (*Kaletra*), atazanavir (*Reyataz*), saquinavir (*Invirase*) and several other protease inhibitors.) The downside is an extensive list of drugs that cannot be used with darunavir/ritonavir, or used only with caution: see 'Not to be taken with.' below.

The resultant adult dose of darunavir is 600mg (two tablets), plus 100mg ritonavir (one capsule), every twelve hours. This two-drug combination can essentially be treated as a single unit, referred to by the abbreviation DRV/r (the 'r' signifies the 'mini'-dose ritonavir).

How well does darunavir work?

The approval of a new drug typically hinges on the results of a few key clinical trials - large-scale studies of how safe and effective the drug is (or is not) in humans. Darunavir has performed very well in three pivotal trials conducted to date by its manufacturer, Tibotec: POWER 1, POWER 2 and POWER 3 (*Performance Of TMC114/r When Evaluated in triple-class-experienced patients with PI Resistance*). Based on 24-week data from these trials, darunavir was conditionally approved by the US Food and Drug Administration on June 23, 2006, and by the European Medicines Agency on February 16th, 2007 (in both cases, for use in treatment-experienced HIV-positive adults only).

These trials compared DRV/r to other ritonavir-boosted PIs in treatment-experienced people who were also taking an 'optimised background regimen' - other antiretrovirals chosen to provide the best 'support' to the study drugs and maximise each person's chance of treatment success. Consistently encouraging results from the POWER trials have been reported at many scientific conferences. In a nutshell, between 40% and 46% of people on DRV/r-based regimens have achieved 'undetectable' HIV viral loads (below 50 copies of virus per millilitre of blood, the current limit of viral load tests), and sustained out to 48 weeks

(the length of the trial data so far). These are impressive results for treatment-experienced people with significant PI resistance.

Naturally, the best outcomes rely on the best use of the drug. Study results have been based on combining DRV/r with other antiretrovirals carefully and specifically chosen for each individual, using resistance testing and expert medical opinion. The best outcomes have generally been seen when darunavir was paired with T-20 (enfuvirtide, *Fuzeon*) - the first of the new 'fusion inhibitor' class of antiretrovirals. This fits in with the idea that that combining darunavir with at least one new drug - ideally from a new drug class that hasn't been taken before (and, to which HIV *ought* to be totally susceptible) - will improve the outcome.

Side-effects

Darunavir's most commonly reported side-effects have been mild to moderate diarrhoea, nausea, and headaches. Hardly a surprise, but the frequency and severity certainly seem no worse than with any 'typical' protease inhibitor. In the POWER trials, 40% of people taking twice-daily DRV/r had at least one drug-related side-effect, and 15% had 'serious adverse events', with 4% discontinuing treatment. Rash ('mild to moderate') has been reported in 7% of people taking DRV/r along with other drugs, and 0.3% discontinued their treatment due to rash. However,

as darunavir has only been studied in highly-treated people taking other drugs at the same time, these other medications complicate the picture: only 1.7% were thought to have serious events 'at least possibly related' to DRV/r.¹

Longer-term problems common to many protease inhibitors - lipodystrophy (increased blood fats and/or body shape changes), blood sugar elevation, and related metabolic disorders - may happen with darunavir as well. As these conditions generally emerge over time, it is still too soon to predict to what extent they might occur on DRV/r. Serious elevations in blood sugar, fats (triglycerides) and so far cholesterol have been reported in 6%, 6% and 4% of patients, respectively, in the open-label POWER 3 study.²

Not to be taken with

Adding ritonavir to an anti-HIV combination, even at the 100mg twice-daily 'mini' dose, makes for a formidable list of interactions - there are many other drugs that must not be used concurrently, or at best, used cautiously at adjusted doses. "This is true for all ritonavir-boosted PI's," notes Steve Taylor. "However, DRV/r should specifically not be taken with lopinavir or saquinavir as both of these drugs can significantly reduce darunavir levels. Furthermore, due to limited data on dose adjustments it should not be used with any other PI, except possibly with atazanavir.³ However, there are some drug interaction data to suggest that DRV/r could be used with the NNRTI's efavirenz (*Sustiva*), nevirapine (*Viramune*) and Tibotec's experimental TMC 125 (etravine)," he adds. "More studies are needed to further clarify if any dose alterations are required when coadministering DRV/r with NNRTIs. In the meantime, if at all possible, it may be prudent to measure drug levels of both darunavir and the co-administered NNRTI."

Numerous other drugs must be taken with caution, or not at all, by anyone taking DRV/r - including certain antihistamines, sedatives and sleeping



pills, anticonvulsants, herbal products (such as St. John's Wort), lipid-lowering drugs, migraine drugs (ergot derivatives), erectile dysfunction drugs (*Viagra*, *Levitra*, *Cialis*), birth control pills, and the TB treatment rifampin. This is a condensed and far from complete list^{4,5,6}. However, the all-purpose caution regarding drug interactions - check the prescribing information, check with your doctor and pharmacist, and then check again - applies to *all* PIs boosted with ritonavir. Moreover, it applies to *all* other medications: prescription, over-the-counter, legal and less-than-legal. If you indulge in 'recreational' drugs, be cautious and ask for advice from your doctor.

One last word regarding drug levels: it's recommended that DRV/r be taken 'with food'. Exactly how much food, or what kind, does not seem to matter - which is different from other PIs. Trials have studied four different types of breakfast, ranging from croissant and coffee, through 'standard', high fat, and a protein-rich nutritional drink. All had essentially similar effects, raising darunavir levels by 30% compared to no food. "Meal type not important' can be an important consideration for patients," notes Steve Taylor.

What don't we know?

Randomised studies so far have only included a few hundred participants, and results from all studies (including open-label) have extended out to 48 weeks at most. Clinical results have been very promising to this point, and there may be reason to believe that it's harder for HIV to develop resistance to darunavir than to other protease

inhibitors - based on test-tube data⁷ - which may explain its strong showing so far. However, drugs do not always perform as well as early expectations. While there's no particular call for pessimism, 'wait and see' would be a more balanced, cautious approach.

A report on a small number of 'real-world' HIV clinic patients receiving darunavir outside the clinical trial setting has in fact supported the trial findings. The report was drawn from 38 people in Houston, Texas - nearly all white men - 22 of whom had received darunavir (through a pre-approval US 'expanded access programme') for 24 weeks. Taking into account the very small numbers and short duration, results appeared to be very good - half had achieved 'undetectable' viral loads, and CD4 counts had risen by an average of 109 cells/mm³.⁸

This last report, however, highlights another shortcoming: contrary to a welcome growing trend in many clinical trials, the darunavir studies to date have not included very many women, non-white racial/ethnic groups, or people with hepatitis. The group receiving darunavir in the randomised trials included only 11% women, 19% non-whites, and 12% co-infected with hepatitis B or C. Drug levels in women have been observed to be slightly higher than in men, but since the number of women has been relatively small, conclusions can't be drawn about the possible implications. In the meantime, since there are currently no data, DRV/r should not be taken during pregnancy. Further study is now being done in larger groups of people,

POWERful outcomes

POWER 1 and 2 were randomised, controlled studies of HIV-positive participants who had extensive previous treatment, in whom resistance tests had shown resistance to protease inhibitors: 318 patients were originally enrolled in POWER 1, and 319 in POWER 2. Both groups were randomly divided in two: roughly half received 600mg darunavir and 100mg ritonavir twice daily, while the 'control arm' received a different, approved, ritonavir-boosted PI. All people in both groups also received an 'optimised background regimen' (OBR) - a combination of other antiretrovirals, including nucleoside analogues (NRTIs) and/or enfuvirtide (T-20), selected so as to give each individual participant the best chance of success.

POWER 3 was a combination of two 'open-label' studies: a non-randomised total of 324 treatment-experienced participants, all of whom received 600mg darunavir and 100mg ritonavir

twice daily, plus an OBR, with no control arm.

The main goal has been to compare DRV/r to other boosted PIs in terms of side effects and toxicities, ability to suppress viral load, and effect on CD4 counts. Pooled 24-week data from POWER 1 and POWER 2 led to darunavir's 'accelerated approval' from the US Food and Drug Administration: 131 people on DRV/r, and 124 on other PIs, had made it to the 24-week point.

Another analysis presented in San Francisco in September, showed that response rates to DRV/r therapy were essentially the same no matter whether the previous, 'failing' regimen had contained tipranavir, lopinavir or fosamprenavir. In all cases, DRV/r led to undetectable viral loads in 40% to 44% at 24 weeks. This compared with 7%-24% of participants on the comparison

PIs, depending on baseline genotypic susceptibility.¹⁰

Ongoing reports have presented longer-term data. At the 16th International AIDS Conference in Toronto (in August 2006), combined POWER 1 and 2 results showed that, at 48 weeks, 46% had reached undetectable viral loads (below 50 copies/mL) vs. an average of 10% in the comparison arms.¹¹

These results had changed very little by December, when more data were presented at the Frontiers in Drug Development for Antiretroviral Therapies (DART) conference in Mexico. Here, results from over 450 participants in all three studies showed that, after 48 weeks on DRV/r-based treatment, 45% still had undetectable viral loads (below 50 copies/mL). Over 90% who had become undetectable by the 24th week remained so at the 48-week point.^{12, 13}

including more women, different ethnic groups, children, and more people with co-infections, to see whether or not significant differences exist in the way darunavir works. (It is well established that such differences do indeed exist for several other drugs.)

Also, while the POWER studies have provided detailed comparisons of darunavir to other boosted PIs - mainly atazanavir, fosamprenavir (*Telzir*), and saquinavir - comparison with tipranavir (*Aptivus*, currently the other major contender for 'salvage PI') is very difficult as no head-to-head trial has yet been done, and the data for darunavir and tipranavir have been drawn from different groups of people.

We'll know more as time goes on. Tibotec is currently comparing DRV/r to *Kaletra* as a second-line treatment option in 300 men and 300 women (the TITAN trial); and in 700 treatment-naïve people at a once-daily dose of 800 mg darunavir + 100 mg ritonavir (the ARTEMIS trial).⁹ There

is also the open-label Grace (Gender, Race And Clinical Experience) study, where 70% of the 420 participants will be women. And the DUET 1 and 2 studies, which combine DRV/r with Tibotec's investigational NNRTI, TMC125 alongside other anti-HIV drugs in heavily treatment-experienced adults, are also ongoing.

Finally, Tibotec has announced a UK price for darunavir that is well below tipranavir (and much cheaper than T-20), although higher than the other PIs. This represents a welcome reversal in the pricing of new anti-HIV drugs. "It is reassuring that Tibotec has priced *Prezista* less than other currently available therapy options for highly treatment experienced patients," notes Professor Margaret Johnson, Chair of the British HIV Association (BHIVA) Executive Committee and Director of HIV/AIDS Services at London's Royal Free Hospital "Cost is becoming an ever more important consideration in HIV prescribing," notes Steve Taylor, who

also welcomed the UK price. "As doctors we want to be able to prescribe the best meds for our patients depending on need - not cost." ■



Whilst vaccination can prevent infection with hepatitis A and B, there is currently no effective vaccine for hepatitis C. However, with recent advances in hepatitis C virus (HCV) therapy and a better understanding of how HCV and HIV interact, prospects have improved for coinfecting individuals. Just as HIV treatment, research increasingly suggests that 'a la carte' therapy^{3,4} with drug doses and treatment durations adjusted based on individual factors such as HCV genotype, pre-treatment HCV viral load, and body weight - is more effective for people infected with both viruses than 'one size fits all' regimens.

On the other hand, new HCV infections in people with HIV are a growing concern - particularly (but not exclusively) for HIV-positive gay men who are choosing to have unprotected sex with other HIV-positive gay men. A recent study of HIV-positive patients at seven British clinics¹ found that 8% - or about one in twelve - also had HCV and we are hearing anecdotally from HIV clinics in London and Brighton that every week more new HCV infections are being diagnosed in (primarily, but again not exclusively) HIV-positive gay men.

How is HCV transmitted?

HIV and HCV are both blood-borne viruses and are transmitted in similar ways. Direct blood contact is the most common route of HCV transmission, and the coinfection rate reaches as high as 90% in some groups of people who share needles or 'works' whilst injecting recreational drugs.

Studies among monogamous heterosexual couples - where one of the partners had HCV alone - suggested that the risk of sexual transmission of HCV was low with less than 3% of the partners contracting HCV. Recent 'outbreaks' of acute (recently-acquired) hepatitis C in the UK and Europe have shown that sexual transmission is more common than previously believed, especially among HIV-positive gay men.

Although HCV might not be transmitted as easily as HIV through vaginal sex, the combination of anal sex, and being HIV-positive as well, appears to increase the chances that HCV is both passed on and acquired. Sexual HCV transmission amongst HIV-positive gay men has been linked to fisting, unprotected anal intercourse, multiple sex partners, recreational drug use (notably, the sharing of 'straws' or notes when snorting drugs), and infection with other sexually transmitted infections, like syphilis.^{2,3}

What can HCV do to the liver?

As anti-HIV therapy has become more effective at keeping people well, liver disease has become a significant cause

of illness and death in people with HIV. Whilst this may be partly due to liver toxicity caused by some of the drugs used to treat HIV and other illnesses, the bigger issue is that improved HIV treatment has kept coinfecting people alive long enough to suffer the long-term consequences of hepatitis.

Chronic hepatitis C can cause severe liver disease including fibrosis (growth of fibrous tissue), cirrhosis (scarring), steatosis (fat accumulation), and a form of liver cancer called hepatocellular carcinoma. In a worst-case scenario, it can lead to end-stage liver failure requiring a transplant.

Severe liver disease usually develops over 10-40 years, but progression appears more rapid in HIV-positive people. In one study, the average time from HCV infection to the development of liver cirrhosis was about ten years less in coinfecting individuals compared to those with HCV alone.⁴ But recent research suggests that coinfecting people on anti-HIV treatments with 'undetectable' HIV viral loads and good CD4 counts may fare as well as HIV-negative people.

Treatments for HCV infection

Treatment for hepatitis C has improved dramatically over the past decade with the development of new drugs and a better understanding of how to use them. The current standard-of-care is a combination of pegylated interferon-alpha (*Pegasys* or *PegIntron*) plus ribavirin. Interferon

hiv and hepatitis c coinfection update

stimulates the immune system's response to HCV, whilst ribavirin helps prevent relapse. Pegylated interferon works better than the older conventional interferon, and combination therapy works better than interferon alone.

Not everyone with hepatitis C needs to be treated. Treatment is indicated for individuals who show signs of liver disease progression, usually determined by a liver biopsy, although specialised liver function tests alone, or in combination with a *Fibroscan* machine, are increasingly becoming non-invasive alternatives. Because liver disease can develop more rapidly in HIV-positive people, many experts believe that everyone with HIV and HCV should be

treated and that coinfecting people should receive more frequent monitoring. In addition, the British HIV Association (BHIVA) recommends that coinfecting individuals should consider early treatment.

However, side-effects are a major concern with hepatitis C treatment. Interferon can cause flu-like symptoms, depression, and neutropenia (decreased white blood cell count), whilst ribavirin can cause anaemia (decreased red blood cell count). Fortunately, specialised coinfection clinics have been set up at some of the larger HIV clinics, with experts trained to help people handle these side-effects better. Studies have shown, for example, that taking antidepressants can alleviate or

even prevent interferon-related depression, and that erythropoietin (*Procrit*) can be used to treat anaemia.

Treating acute HCV

Acute hepatitis C refers to the first six months after infection with HCV. Most people have no noticeable symptoms - they can often mistake it for the flu - although a few do experience some typical hepatitis-like symptoms like jaundice (yellowing of the skin but most noticeable in the whites of the eyes) and itching. So, unless you are having your liver function monitored regularly, HCV infection is unlikely to be detected during its initial acute phase.

BHIVA recommends that all people with HIV should be screened for

can hcv be cured?

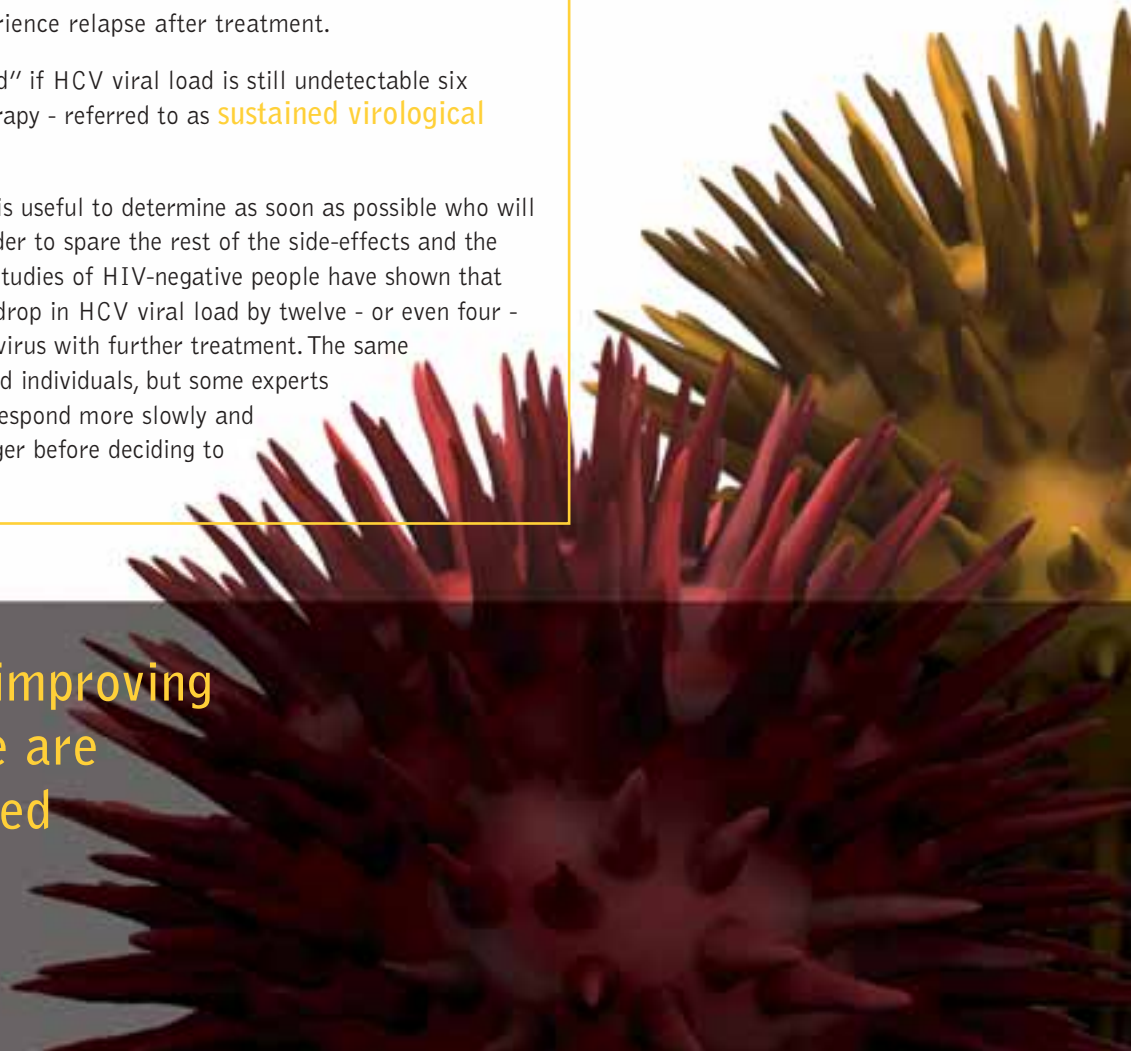
Unlike HIV, HCV can be eradicated from the body. Response to hepatitis C treatment is measured in various ways. **Rapid virological response** refers to an HCV viral load decrease of at least 2 logs after four weeks of treatment, while **early virological response** is a similar decrease after twelve weeks. **End-of-treatment response** is undetectable HCV viral load at the end of therapy. But some people experience relapse after treatment.

Hepatitis C is considered "cured" if HCV viral load is still undetectable six months after completion of therapy - referred to as **sustained virological response** (SVR).

Once treatment is underway, it is useful to determine as soon as possible who will go on to achieve an SVR, in order to spare the rest of the side-effects and the expense of additional therapy. Studies of HIV-negative people have shown that those who do not experience a drop in HCV viral load by twelve - or even four - weeks are unlikely to clear the virus with further treatment. The same appears to be true for coinfecting individuals, but some experts believe coinfecting people may respond more slowly and therefore should be treated longer before deciding to stop therapy.

treatments are improving
but more people are
becoming infected

by Liz Highleyman



hepatitis C antibodies, and people at higher risk of acquiring HCV are screened regularly. But since people with compromised immune systems may not produce enough antibodies to measure, BHIVA recommends HCV viral load testing for HIV-positive people with unexplained liver problems.

Experts disagree about whether to treat acute hepatitis C, since about one in four people spontaneously clear the virus without therapy. On the other hand, early treatment is highly successful. One study of HIV-negative people showed that 98% had undetectable HCV 24 weeks after the end of treatment⁵, whilst studies of coinfecting individuals have found success rates of around 60%.⁶ However, because the chances of complete treatment success are higher during acute infection, BHIVA recommends that treatment of acute hepatitis C should be considered, but says that it is prudent to wait twelve weeks to see if the virus goes away on its own.

Treating chronic HCV

Chronic hepatitis C is infection that lasts longer than six months. The standard length of pegylated interferon/ribavirin therapy is 48 weeks for genotype 1 and 24 weeks for genotypes 2 or 3. Several recent studies have looked at treatment in HIV/HCV-coinfecting individuals. Response rates are generally lower among coinfecting patients than those with HCV alone. As a basis of comparison, SVR rates for HIV-negative individuals using pegylated interferon plus ribavirin are around 50% overall (45% for genotype 1 and 80% for genotypes 2 or 3).

In the international APRICOT study, which included 860 coinfecting participants receiving HCV treatment for the first time, 40% of patients treated with pegylated interferon plus

ribavirin achieved SVR overall (29% for genotype 1 and 62% for genotypes 2 or 3).⁷ Sustained response rates were somewhat lower in the US ACTG 5071 trial, which included more individuals of African descent: 27% overall (14% for genotype 1 and 73% for genotypes 2 or 3).⁸ In the French RIBAVIC trial, which included more participants with advanced liver disease, 26% overall achieved SVR (11% for genotypes 1 or 4 and 43% for genotypes 2 or 3).⁹

Factors that predict response

Treatment success depends on what HCV genotype a person has. Genotype 1 is hardest to treat. People with genotypes 2 or 3 respond better to therapy (less is known about genotype 4 although it is generally treated like genotype 1). Genotypes 1 and 3 are seen most frequently in the UK.¹⁰

In people with all genotypes, having a higher HCV viral load (more than 400,000 copies) before starting treatment predicts poorer response. Treatment is also more difficult in people with more advanced liver disease.

In addition, women tend to respond better than men, younger people do better than older people, and white people tend to respond better than people of African descent. Obesity is linked with liver disease progression and poorer treatment response, since being overweight can lead to steatosis. Heavy alcohol use can also lead to worse treatment outcomes.

To achieve the best results, coinfecting patients should have a healthcare team that has experience with both HIV and HCV, ideally in a specialised coinfection clinic. Along with good health habits such as eating a balanced diet, getting moderate exercise, and limiting alcohol and recreational drug use, regular medical monitoring, good adherence,

and management of side-effects are the keys to successful treatment.

Treatment modification

Researchers have tried to determine which factors contribute to successful treatment, and whether various modifications - such as higher drug doses or longer duration - can improve outcomes.

In order to prevent relapse (especially in people with HCV genotype 1), it is important to use enough ribavirin. Unlike APRICOT, in which all participants received a standard dose of 800mg/day, the ongoing Spanish PRESCO trial used weight-based ribavirin; those who weighed less than 75kg received 1000mg/day, whilst heavier patients received 1200 mg/day. In this study, which included 389 coinfecting participants, 50% overall achieved SVR (36% for genotype 1 and 72% for genotypes 2 or 3).¹¹

PRESCO also looked at whether longer treatment could improve response rates. Participants continued therapy for 48 or 72 weeks if they had genotype 1 or 4, and 24 or 48 weeks if they had genotype 2 or 3. Prolonged treatment led to a greater likelihood of achieving SVR (31% with 48-week therapy compared to 53% with 72-week therapy for genotype 1 or 4 patients), but many participants stopped early due to side-effects. But in another study, extending treatment to 72 weeks did not improve sustained response rates in coinfecting patients who still had detectable HCV after twelve weeks of therapy, and 68% of



those assigned to longer treatment stopped early.¹²

HIV treatment for coinfecting people

Most HIV/HCV-coinfecting people can be successfully treated for HIV. Whilst coinfecting individuals experience similar HIV suppression after starting anti-HIV treatment, their CD4 cell recovery tends to be delayed or "blunted." One study, for example, found that coinfecting patients gained an average of 50 CD4 cells after 18 months on antiretroviral therapy, compared with 190 CD4 cells in those with HIV alone.¹³

HIV/HCV coinfection presents some challenges with regard to anti-HIV treatment. Some anti-HIV drugs are known to cause liver toxicity, and although people with pre-existing liver disease are more likely to develop drug-related liver toxicity, the overall risk is low. Another complication is the potential for additive (referred to as 'synergistic') side-effects of drugs used to treat HIV and HCV. As noted, interferon and ribavirin can cause blood cell deficiencies, and therefore these medications should be used cautiously with anti-HIV drugs such as AZT (*Retrovir*, also in *Combivir*) than can cause similar problems.

On the whole, though, the benefits of anti-HIV therapy for coinfecting individuals outweigh the risks, since it can slow liver disease progression by preserving immune function. But there remains some disagreement about whether to treat HIV or HCV first. Some experts recommend starting anti-HIV therapy first, since once HIV is under control and CD4 cell counts rise, people respond better to interferon and are more able to tolerate its side-effects. In 2004, an international panel recommended that coinfecting people starting HCV treatment ideally should have

anti-hcv agents in the pipeline

hcv polymerase inhibitors	hcv protease inhibitors	novel agents
valopicitabine (NM283)	telaprevir (VX-950)	CPG 10101 (toll receptor antagonist)
HCV-796	SCH-503034	bavituximab (monoclonal antibody)
R1626	ITMN 191	statins (used to manage high blood cholesterol, these drugs have shown activity against HCV in laboratory studies).

CD4 cell counts above 350 cells, noting that treatment does not work well in those when they are below 200 cells.¹⁴ On the other hand, people with much higher CD4 counts may benefit from treating hepatitis C first, since this can improve liver function and make it easier to tolerate anti-HIV drugs. The latest (2006) BHIVA guidelines now suggest that coinfecting people may benefit from starting anti-HIV treatment at higher CD4 counts than recommended for people with HIV alone.

Hope for the future

Coinfecting people who do not respond completely to current anti-HCV therapies can take encouragement from the fact that anti-HIV therapy itself can slow the development of liver damage, and that there are several promising agents in the development pipeline. While some represent refinements to existing therapies (such as new forms of interferon), the most excitement comes from oral agents that directly target various steps in the HCV lifecycle, much like antiretroviral drugs attack HIV - a new approach

dubbed "specifically targeted antiviral therapy for HCV," or STAT-C.

According to US hepatology expert Dr Ira Jacobson, STAT-C is "a leap forward of the magnitude of HAART." As with anti-HIV therapy, these new agents are expected to work best in combination, which should slow the emergence of resistance. Most experts predict new oral antiviral drugs will be used with interferon for the foreseeable future, but they could help shorten treatment duration and reduce side-effects.



news in brief

life expectancy

HIV still not quite 'just like diabetes'

An average 25 year-old diagnosed with HIV today can expect to live to 64, according to a recent Danish study. In contrast, the average 25 year-old who remains HIV-negative can expect to reach 76 years of age.

The study also found that HIV-positive individuals who were coinfecting with hepatitis C virus, and people who were older at the time of HIV diagnosis could expect to have poorer survival than younger, hepatitis C-uninfected HIV-positive individuals.

A total of 3,990 HIV-positive individuals treated in Danish HIV clinics from January 1995 until May 2005 were compared with 380,000 HIV-negative people from the general population of Denmark.

Survival among HIV-positive people increased significantly during the study period. In the five-year period from 2000 to 2005, the median survival rate for HIV-positive people rose to 33 years. Survival was even better (39 years) when they the 16% of HIV-positive people who were coinfecting with hepatitis C virus.

Chronic HIV infection is often compared to diabetes, but when the investigators compared the mortality among patients with type 1 diabetes with mortality amongst HIV-positive individuals, they found higher mortality rates amongst people with HIV.

"Our study suggests that most young people with HIV infection can expect to survive for more than 35 years, but an ongoing effort is still needed to further reduce mortality rates amongst infected people," conclude the investigators.

However, it's important to remember that estimates and averages are just that. Some people (including *ATU's* editor) who were diagnosed with HIV or AIDS in the early 1980s are still alive and well today, despite experts estimating that they would not live more than a few years.



hiv and illness

Bone death risk 100 times higher if HIV-positive



People with HIV have about a 100-times greater risk of developing osteonecrosis (literally, 'bone death') than the general population, according to a US study. Osteonecrosis occurs when the blood supply to the bone is disrupted, leading to painful bone decay and loss, usually at the ends of bones such as those in the hip joint. Eventually, osteonecrosis of the hip joint will usually require hip replacement surgery.

In 2002, doctors at a large US HIV clinic found that just over 4% of 339 HIV-positive patients with no symptoms actually had osteonecrosis of the hip, confirmed by MRI scan. A further 239 patients who did not have osteonecrosis then had a second MRI scan two years later and another three were found to have asymptomatic osteonecrosis - an incidence rate of 0.65 cases per hundred people per year.

It is thought that you can reduce the risk of future bone problems if you stop smoking, reduce your alcohol intake and increase weight-bearing exercise. Also if you are underweight or very overweight, talk to your HIV dietician about ways to normalise your weight, which can help prevent future bone problems.

anti-hiv drugs

GSK halts development of new PI, brecanavir

Development of the experimental protease inhibitor, brecanavir, was halted late in December by GlaxoSmithKline due to problems in developing an oral formulation of the drug.

The drug had reached phase II trials and early results in treatment-naïve and treatment-experienced patients had appeared promising.

complementary therapy

Cannabis may help peripheral neuropathy

A long-anticipated study on the effects of 'medical marijuana' on HIV-related nerve pain in the hands and feet has found that smoking up to three cannabis-containing cigarettes a day may help relieve the pain. However, the benefits should be weighed against the short-term side-effects, which can include sedation, disorientation and confusion, as well as the possibility of an increased risk of lung infections in the long term. In addition, cannabis is an illegal 'Class C' drug in the UK.

The study, from California, enrolled 50 people experiencing peripheral neuropathy, many of whom were already taking other pain-relief medications. All participants had prior experience with smoking

cannabis, and people with any other "current substance abuse" (including smoking tobacco) were excluded.

Half the participants smoked up to three pre-rolled cannabis-containing cigarettes over five days, and the other half smoked a placebo (similar-looking cigarettes without THC – the active component of cannabis). No-one knew who had been assigned to which group until the trial ended.

On average, smoked cannabis doubled the pain relief: pain was reduced by 34%, compared with 17% on placebo. But it wasn't effective for everyone: only half of those smoking the cannabis cigarettes reported a significant reduction in pain; and even a quarter of those smoking the placebo reported significant pain reduction.

complementary therapy

Is selenium supplementation necessary?

Daily supplementation with 200micrograms of selenium might be a useful, non-harmful additional therapy for people who have not yet started anti-HIV treatment, or for people who are taking anti-HIV therapy but do not have an 'undetectable' viral load. It is not a replacement for anti-HIV drugs.

That's the consensus following the results of the first randomised, placebo-controlled clinical trial examining the effects of selenium. The trial found that the supplement stabilised - but did not reduce - viral loads and modestly increased CD4 cell counts in a group of HIV-positive people who took the supplement regularly over nine months.

Selenium is a mineral essential for human health. It has been thought for decades that it may improve the health of HIV-positive people because several early studies showed that selenium deficiency can predict an increased risk of death from AIDS. However, there had been no randomised studies comparing the supplement with a placebo until now.

Researchers from the University of Miami, who have extensive experience of investigating the relationship between HIV disease and micronutrient deficiencies, recruited 262 HIV-positive adults, three quarters of whom were already receiving anti-HIV therapy.



One hundred and forty-one were randomised to receive 200mcg of selenium a day and 121 received a placebo.

After nine months only 174 participants remained in the study (91 on selenium, 83 on placebo). Fifty of the 91 on selenium had significantly higher levels of selenium compared to those on placebo and were classified as 'responders'. The 41 'non-responders' did not take their selenium regularly, or else did not have high enough levels of selenium in their blood because of gastrointestinal problems that prevented them from absorbing it. These people had the same results as the placebo group.

Whereas non-responders had a small viral load increase over nine months, responders had no significant change in viral load. And whereas non-responders lost an average of 25 CD4 cells over nine months, responders had an average increase of 27 CD4 cells.

Although the differences were statistically significant, in practice CD4 cells and viral load can easily fluctuate on a daily basis by these amounts, and so the clinical significance is uncertain. However, since selenium appears to be beneficial and has no negative side-effects or drug interactions, there appears to be no harm in taking it as an additional, complementary therapy.



hiv forensics

why scientific evidence alone is not 'proof' enough in criminal hiv transmission cases
by Edwin J Bernard

This month a new briefing paper aimed at both scientific experts and people working in the criminal justice system outlines how and why scientific evidence known as *phylogenetic analysis* cannot be used as the main, or only, proof that one person infected another in prosecutions for HIV transmission.

Published jointly by NAM and the National AIDS Trust (NAT), the briefing paper includes the legal background to criminal HIV transmission prosecutions; how phylogenetic analysis has been used in other cases around the world; the weight that 'expert witness' testimony has in English and Welsh courtrooms; and a detailed analysis of the pitfalls as well as the acceptable standards of phylogenetic analysis when presented in a court of law as forensic evidence.

Not guilty verdict

The paper is co-authored by two internationally esteemed virologists, one of whom is Dr Anna Maria Geretti, from London's Royal Free Hospital, who served as an expert witness for the defence in the first - and so far only - criminal HIV transmission trial to end with a 'not guilty' verdict.

Last August, a trial at Kingston Crown Court collapsed after Dr Geretti explained the limitations of the phylogenetic analysis evidence presented by the prosecution as 'proof' that the defendant infected the complainant.

In this case, the complainant believed that the defendant had infected him with HIV, and had done so without

disclosing his HIV-positive status before they both agreed to have unprotected sex during their short relationship. Dr Geretti testified that although the two men's viruses were genetically similar, phylogenetic analysis was unable to answer questions of timing or direction, nor rule out the possibility that a third party with genetically similar virus may have been responsible.

Using evidence from the complainant's sexual health clinic notes, the defence then argued that since the complainant had engaged in high-risk sexual activities with other men between testing HIV-negative in 1999 and HIV-positive in 2004, it was possible that he had been infected by a third party during this period. During his summing up, Judge Benning told the jury that this was a "clear possibility...[and] I have to be of the view that the evidence is a safe foundation for a decision. Therefore I am duty bound to direct you to acquit."

No witnesses

Since there are no witnesses at the time of a viral infection, criminal HIV transmission cases must rely on a combination of scientific and other evidence (such as GP, sexual health, or HIV clinic notes - none of which are exempt from being used as evidence in a court of law) to attempt to reconstruct the chain of events under investigation.

A common misconception based on press releases or media reports regarding HIV transmission prosecutions - which necessarily simplify

the science to its most basic level - is that if the complainant and defendant shared the same HIV subtype (e.g. subtype A, subtype B, subtype C etc.), then the defendant must have infected the complainant.

Since even the rarest HIV subtypes have been found in more than two people in the UK (and subtypes A, B and C have been found in hundreds, if not thousands of people in the UK), sharing the same HIV subtype does not 'prove' anything.

However, each individual can be infected with a variety of related but slightly different genetic versions of the same HIV subtype, known as *quasispecies*. These can be examined in much greater detail by analysing HIV's genetic code (RNA). By examining very small differences in different parts of HIV's RNA (known technically as *gene sequencing*), scientists are able to estimate how these HIV strains are genetically related.

What is phylogenetic analysis?

Phylogenetic analysis requires the use of complex computational tools to create a hypothetical diagram (known as a phylogenetic tree) that helps estimate how closely related two samples of HIV are likely to be. However, this method is unable to create a definitive 'match'. This is because HIV, unlike human DNA samples or fingerprints, is never unique and is ever-changing.

No current method of phylogenetic analysis can be considered 100% accurate, although there are a variety of methods by which scientists can improve their ability to be confident that the two viruses are, at least, very closely related.

But very closely related viruses are seldom - if ever - found only in the defendant and the complainant. Highly similar HIV strains may be found in many more people than simply the two individuals under investigation if they are both part of a wider transmission network (i.e. individuals that share sex partners, at some point, whether they

know it or not). The majority of HIV-infected people are part of such networks. For example, phylogenetic analysis of HIV gene sequences obtained in 1999-2003 from British gay men found six large clusters, each comprising of between 26 and 62 men who shared very closely-related virus strains.¹

Acceptable standards

The briefing paper makes several recommendations about the way that experts should carry out phylogenetic analysis for HIV forensic purposes, as well as how the results are interpreted.

One of the key points is that it is vitally important that phylogenetic analysis for HIV forensic purposes compares the complainant's and the defendant's viruses with the right kind of comparison samples (known as *controls*), otherwise this could exaggerate how related they appear to be.

To provide scientists with the highest level of confidence, these comparison samples should come from other

HIV-positive people in the area where the defendant and complainant live and/or socialise, and should be collected around the time of the alleged transmission event.

However, even with the appropriate comparison samples, phylogenetic analysis cannot 'prove' that HIV transmission occurred directly between two individuals.

Other possibilities may include:

- the complainant was infected with a similar viral strain by someone from the same transmission network
- both the complainant and the defendant were independently infected with similar viral strains by people from the same transmission network.

Even if phylogenetic analysis suggests that the two viruses are very closely related, this does not provide enough information to know the direction or timing of the alleged transmission (i.e. who might have infected who; or who

might have been infected first). Additional detailed samples and very costly and time-consuming complex analysis - neither of which have yet been used in criminal HIV transmission cases - would be necessary to produce data relevant to this question.

Nevertheless, if phylogenetic analysis is carried out rigorously it is reliable enough to show that the virus from the defendant and the complainant are *not* closely related to each other. In other words, phylogenetic analysis can exonerate the person being investigated.

The NAM/NAT Briefing Paper, *HIV Forensics: The use of phylogenetic analysis as evidence in criminal investigation of HIV transmission* is available to download from www.aidsmap.com or www.nat.org.uk.

references to all articles

upfront [page two]

1. Phillips AN et al. *When should antiretroviral therapy for HIV be started?* BMJ 334: 76 – 78, 2007
2. Moore RD et al. *CD4+ cell count 6 years after commencement of highly active antiretroviral therapy in persons with sustained virologic suppression.* Clin Infect Dis 44 (online edition), 2007.

all about darunavir [page four]

1. Tibotec *Prezista* prescribing information, June 2006.
2. Saag M et al. *Efficacy and safety results of DRV/r in treatment-experienced patients: POWER 3.* 44th IDSA, Toronto, abs 957, 2006.
- 3,4 See 1.
5. US DHHS Guidelines, *Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*, 2006.
6. Sekar V et al. *Pharmacokinetic interaction between TMC114 and lopinavir/ritonavir...ethinyl estradiol and norethindrone,....and.sildenafil.* 46th ICAAC, San Francisco, abs A-0367, A-0368, A-0369, 2006.
7. Gazzard B. *Predicting response? Phenotypic and genotypic determinants of resistance to TMC114.* 8th Congress Drug Therapy HIV Infection, Glasgow. abs SS2.6, 2006.
8. Gathe J et al. *Single-center experience of DRV in 38 HIV-infected adults enrolled in US expanded access program.* DART, Cancun, abs 65, 2006.
9. Tibotec press release, Dec 2006.
10. Lefebvre E et al. *Impact of use of TPV, LPV and (f)APV at screening on TMC114/r virologic response in treatment-experienced patients in POWER 1, 2 and 3.* 46th ICAAC, San Francisco, abs H-1387, 2006.
11. Lazzarin A et al. *TMC114 provides durable viral load suppression in treatment-experienced patients: POWER 1 and 2 combined 48 week analysis.* 16th IAC, Toronto, abs TuAb0104, 2006.
12. Ruane P et al. *Safety and efficacy of darunavir in combination with low-dose ritonavir: 48-week results from the POWER studies.* DART, Cancun, abst 74, 2006.

13. Gathe J et al. *Examination of factors influencing response to darunavir combined with low-dose ritonavir in POWER 1, 2, and 3: pooled 48-week analysis.* DART, Cancun, abs 66, 2006.

hiv and hepatitis coinfection update [page eight]

1. Turner J et al. *Hepatitis C virus coinfection and HIV-infected patients in the UK collaborative HIV cohort.* HIV Med 7 (suppl 1), abs 014, 2006.
2. Danta M et al. *Evidence for sexual transmission of HCV in recent epidemic in HIV-infected men in the UK.* 13th CROI, Denver, abst 86, 2006.
3. Turner JM et al. *Behavioural predictors of subsequent hepatitis C diagnosis in a UK clinic sample of HIV-positive men who have sex with men.* Sex Transm Infect 82: 298-300, 2006.
4. Mohsen AH et al. *Impact of human immunodeficiency virus (HIV) infection on the progression of liver fibrosis in hepatitis C virus infected patients.* Gut 52: 1035-1040, 2003.
5. Jaeckel E et al. *Treatment of acute hepatitis C with interferon alfa-2b.* NEJM 345: 1452-1457, 2001.
6. Vogel M et al. *Treatment of sexually transmitted acute HCV-infection in HIV-positive individuals.* 46th ICAAC, San Francisco, abs H-1060, 2006.
7. Torriani FJ et al. *Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients.* NEJM 351: 438-450, 2004.
8. Chung R et al. *Peginterferon alfa-2a plus ribavirin versus interferon alfa-2a plus ribavirin for chronic hepatitis C in HIV-coinfected persons.* NEJM 351: 451-459, 2004.
9. Carrat F et al. *Pegylated interferon alfa-2b vs standard interferon alfa-2b, plus ribavirin, for chronic hepatitis C in HIV-infected patients: a randomized controlled trial.* JAMA 292: 2839-2848, 2004.
10. Mann A. *Hepatitis C in England: An update 2006.* Health Protection Agency, Dec 2006.
11. Nunez M et al. *The PRESCO trial: role of extended duration of therapy with pegylated interferon alfa-2a*

plus weight-based ribavirin dose in 389 HCV/HIV co-infected patients. 8th Congress Drug Therapy HIV Infection, Glasgow, abstract PL13.1, 2006.

12. Fuster D et al. *Results of a study of prolonging treatment with pegylated interferon-alpha2a plus ribavirin in HIV/HCV coinfecting patients with no early virological response.* Antiviral Therapy 11: 473-482, 2006.
13. Braitstein P et al. *Impact of hepatitis C virus on CD4+ response post-initiation of HAART among a population-based cohort.* 2nd IAS Conf, Paris, abs 214, 2003.
14. Soriano V et al. *Care of patients with hepatitis C and HIV co-infection: consensus panel recommendations.* AIDS 18: 1-12, 2004.

news in brief [page twelve]

HIV still not quite 'just like diabetes'

1. Lohse N et al. *Survival of persons with and without HIV infection in Denmark, 1995-2005.* Annals of Internal Medicine 146: 87-95, 2007.

Bone death risk 100 times higher if HIV-positive

1. Morse CG et al. *The incidence and natural history of osteonecrosis in HIV-infected adults.* Clin Infect Dis 44: online edition, 2007.

Is selenium supplementation necessary?

1. Hurwitz BE et al. *Suppression of human immunodeficiency virus type 1 viral load with selenium. A randomised controlled trial.* Arch Int Med 167: 148-154, 2007.

Cannabis may help peripheral neuropathy

1. Abrams DI et al. *Cannabis in painful HIV-related sensory neuropathy: a randomized placebo-controlled trial.* Neurology 68: 515-521, 2007.

hiv forensics [page fourteen]

1. Hué S et al. *Genetic analysis reveals the complex structure of HIV-1 transmission within defined risk groups.* Proc Natl Acad Sci USA 102(12): 4425-4429, 2005. (www.pubmedcentral.nih.gov/articlerender.fcgi?artid=555492)

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NAM would also like to acknowledge the generous support of individual donors, and in particular Gavin Hay and Tim Cohen

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