

# AIDS TREATMENT UPDATE

MARCH 2000

ISSUE 87

## Reaching second base

### What to do if an initial anti-HIV treatment combination fails

BY ANNA POPPA

HIV treatments fail for a number of reasons, and establishing the main cause is an important part of choosing a new regimen. Emergence of drug resistance may be a key factor, and as we report in *News in Brief*, evidence which supports the use of drug resistance testing when switching therapy is now accumulating. Sadly, however, there is no magic to these new tests and at best, they may only ever offer guidance to patients and doctors, not absolution from the need to consider the full clinical picture.

For example, people who have problems with adherence will do no better after changing treatment if they begin another regimen they are unable to adhere to, and receive inadequate support about pill-taking. The need to resolve side-effects may be another reason to consider changing treatments. On page 4 we review the latest news from studies of people who have switched from PI-containing HAART because of the metabolic abnormalities and/or fat redistribution which were initially seen as side-effects restricted to that drug class.

It is against this rather complex background that treatment experts are advocating the need to individualise treatment strategies. Given the myriad of confounding factors, interpreting the results of the limited number of trials in this area has been difficult.

#### CHANGING FIRST-LINE THERAPY

Treatment guidelines produced by and for UK doctors distinguish between changing from a first- to second-line therapy, and changing treatment after two or more different combinations have failed, (often called salvage therapy). In general, people with less drug experience are likely to have more choices available

to them. Attaining an undetectable viral load remains a key goal of second-line and subsequent therapy, but the likelihood of achieving this diminishes the more drug experienced a person is. (Editor's note: This article focuses on changing from an initial to a second-line regimen. See *AIDS Treatment Update* issue 79 and *Anti-HIV therapy: Changing therapy on aidsmap.com* for more on options for people with more drug experience).

The current wisdom is to switch to as many new drugs as possible, though this will depend on the reason for switching. If treatment has resulted in side-effects but has successfully reduced viral load to below 50 copies (currently agreed to be the virological litmus test of a first-line regimen), then it should be possible to switch only the offending drug and maintain control of HIV replication.

The table over the page summarises the British HIV Association's (BHIVA) recommendations for changing from a first-line therapy.

#### SWITCHING FROM NNRTIS

Because there is broad cross resistance between NNRTIs, retaining an NNRTI within a new combination following viral load rebound on an NNRTI-based

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## Changing therapy on first virological failure: Summary of BHIVA's recommendations

- ◆ Only consider virological failure after assessment of adherence and drug absorption.
- ◆ Diagnosis of virological failure requires two viral load tests, showing viral load above 50 copies, at least two weeks apart.
- ◆ If changes are being considered because of toxicity, changing a single agent is acceptable if viral load is below 50 copies.
- ◆ If the patient is poorly adherent, it is important to simplify the regimen and provide support and counselling.
- ◆ Testing for resistance is recommended (on stored pre-treatment sample as well if appropriate).
- ◆ If viral load is above 50 copies during the first 24 weeks of treatment, but has previously been below 50 copies, recommended action is to change all drugs.
- ◆ If the fall in viral load appears inadequate during the first 24 weeks of treatment, recommended action is to change all drugs. Alternatively, if resistance testing is available, and no resistance is found, intensifying the regimen with either abacavir or with one or two PIs is an option [depending on the regimen].
- ◆ If viral load is above 50 copies at any point after the first 24 weeks of treatment, recommended action is to change all drugs.

### Initial regimen

**2NA+PI or 2NA+2PI**

**2NA+NNRTI**

**3NA**

### Second-line options

2NA+NNRTI or 2NA+2PI or 2NA+PI+NNRTI

2NA+PI or 2NA+2PI

2NA+NNRTI or 2NA+PI or 2NA+2PI or 2NA+PI+NNRTI

*Note: Both NA should be changed. NA = nucleoside analogue; PI = protease inhibitor; NNRTI = non nucleoside reverse transcriptase inhibitor.*

regimen is not advised. However, this is an area where data are few and far between. PI-based HAART regimens have been demonstrated to have a durable effect on viral load in people with some experience of nucleoside analogues, and so may be expected to have a similar effect after an NNRTI-based HAART regimen.

### SWITCHING FROM NRTIS

The use of triple nucleoside analogue regimens as first-line therapy is still considered experimental, and how people whose viral load rebounds on these combinations should be managed, is not well understood. Theoretically, both NNRTIs and PIs should remain available for use.

### SWITCHING FROM PIS

Because most people who started HAART in the early days of three drug therapy began with a PI-based regimen, there is now more information on how these people have fared on subsequent combinations than exists for other regimens. A number of studies have indicated, unsurprisingly, that being NNRTI naïve is advantageous in these circumstances because it allows the addition of a new drug class when changing regimens.

ACTG 359 was an American study designed for people who had previously taken

nucleoside analogues and indinavir, but had not taken an NNRTI before<sup>1</sup>. Everyone who joined had viral load between 2,000 and 200,000 copies, though the average value on entry was 32,000 copies. Evidence suggests that 'early' virological failure is more likely to involve the development of resistance to the NRTI components of a HAART regimen rather than to the PI. However, as viral load continues to increase, PI resistance mutations are likely to accumulate, reducing the potential for a favourable response to a second PI in many cases. Phenotypic resistance testing on a subset of 93 of the 277 people enrolled in this study found that half were resistant to indinavir.

Participants were randomised to one of six treatment arms. All received two PIs plus at least one other drug (either the NNRTI delavirdine, the nucleotide analogue adefovir, or both). Therefore the arms were:

- ◆ ritonavir/*Fortovase*/delavirdine
- ◆ ritonavir/*Fortovase*/adefovir
- ◆ ritonavir/*Fortovase*/delavirdine/adefovir
- ◆ nelfinavir/*Fortovase*/delavirdine
- ◆ nelfinavir/*Fortovase*/adefovir
- ◆ nelfinavir/*Fortovase*/delavirdine/adefovir

After an initial 24 weeks of therapy, participants were eligible for an extension phase if their viral load at 12-16 weeks had fallen below 5,000 copies, or had fallen by at least one log. 52% completed this second

**NEW PIs**  
Amprenavir and tipranavir are experimental PIs which may prove beneficial to some people with PI experience, according to test-tube studies. This has not yet been fully assessed in clinical trials.

phase, and at 48 weeks, 55% had viral load below 500 copies by intent-to-treat analysis. There was no difference in response between those receiving ritonavir compared to nelfinavir, but those who received delavirdine, either with or without adefovir, fared better than those whose two PIs were supported only by adefovir. Also, those who had been taking indinavir longest before joining the study, had the worst response. Duration of indinavir use in this context is likely to be a surrogate for the development of indinavir resistance, though there has been no direct assessment at present of indinavir resistance at baseline and subsequent response to therapy.

### ABT-378/R WITH NEVIRAPINE

Lopinavir is the new name for the experimental PI, ABT-378/r. (The r is for ritonavir, a small amount of which is co-formulated with the drug in order to boost blood levels). A recently reported study investigated the use of the drug in 70 NNRTI naïve people with viral load rebound on a PI-containing regimen<sup>2</sup>. Patients were randomised to receive 400mg of ABT-378 and either 100mg or 200mg of ritonavir, and after fifteen days added nevirapine and changed at least one nucleoside analogue. After 48 weeks, 76% had viral load below 50 copies using an as treated analysis, 60% by intent-to-treat analysis.

Because there is no control arm of people who did not take nevirapine, it's impossible to say how much the inclusion of an NNRTI, or the new NRTI(s), added value to the new regimen. The response rate observed in this study is high compared to other second-line therapy trials however, suggesting the combination of three new drugs offered a potent antiviral effect.

The effect of the ritonavir component of ABT-378/r allows blood levels to remain thirty times higher than the critical level needed to control viral replication. This has led some to suggest that some loss of sensitivity to the drug, as measured by phenotypic resistance testing, may have no clinical relevance. This trial provides some evidence that this may be true. At entry, eleven patients had evidence of significantly reduced sensitivity to ABT-378/r. However after 48 weeks treatment, seven of these eleven had viral load below 400 copies.

Two studies involving patients from San Francisco have reported similar findings regarding the inclusion of an NNRTI in regimens designed for people with viral load rebound on a PI. The first, an observational study, involved 99 people, most of whom had previously taken indinavir<sup>3</sup>. The response to a change in therapy was fairly poor; just 22% had undetectable viral load 24 weeks after

switching. A successful response, however, was reported to be "common" amongst those who were NNRTI naïve and who began a drug from that class in their new combination.

A group of twenty NNRTI naïve people with viral load rebound on indinavir or ritonavir were switched to a new regimen containing nelfinavir, saquinavir, abacavir plus either nevirapine or a new nucleoside analogue<sup>4</sup>. Though this is a small study and treatment was not randomised, those who received nevirapine had a better virological response after 24 weeks than those who did not.

### DO YOU REALLY NEED THE NNRTI?

A number of small, often uncontrolled studies have provided conflicting evidence on the possibility of switching to a second PI-based combination which does not include an NNRTI (see *AIDS Treatment Update* issue 69 and *Anti-HIV therapy: Changing therapy on aidsmap.com*). The difference between these two strategies – whether to include an NNRTI or not – probably lies in access to reliable resistance test results. Because resistance tests cannot be performed at viral loads below 1,000 copies, people who want to switch treatment at lower levels of viral rebound than this will need to do so without the possible guidance such a test may provide. Whilst available evidence suggests that susceptibility to PIs should have been retained at low but detectable viral load levels, some people may feel that including an NNRTI and a PI in the new combination provides additional security. At present there is no clear evidence to indicate which course of action will prove best in the long run.

## Key conclusions:

- ◆ Treatment failure occurs for several reasons and all possible causes should be considered before changing to a new combination.
- ◆ People switching from a PI-based HAART regimen because of viral load rebound may do better if their next combination includes an NNRTI (so long as they have not taken one before).
- ◆ What to switch to from PI-sparing combinations has been less well studied.
- ◆ The use of resistance tests may help exclude treatment options.

#### REFERENCES

- 1 Gulick RM. 7th Conference on Retroviruses and Opportunistic Infections (CROI), San Francisco, Jan 30 - Feb 2, abstract 235, 2000.
- 2 Deeks S. 7th CROI, abstract 532, 2000.
- 3 Deeks S. *AIDS* 13:F35-F43, 1999.
- 4 Deeks S. *Journal of Infectious Diseases* 179(6):1375-1381, 1999.

# Lipodystrophy update

## Switching from PIs to NNRTIs for metabolic problems & fat redistribution

BY KEITH ALCORN

Australian data suggest that length of time on protease inhibitor (PI) therapy increases the risk of developing body fat changes, with people who had been taking PIs for two years or more at four times greater risk of having developed the changes. Are these data a justification for switching from a PI, even if you don't have any body fat changes yet, or if the changes are relatively minor?

Dr Mark Nelson of the Chelsea and Westminster Hospital says: "At the moment I would advise people with minor changes to wait and see. The data presented in San Francisco were disappointing. We need longer term studies. In my clinical experience people do not go back to normal when they switch, although there is some improvement."

Longer-term follow-up of patients with body fat changes who have switched from a protease inhibitor to a PI-sparing combination shows that body fat maldistribution does not improve after six to twelve months in the vast majority of cases, according to presentations at the 7th Retroviruses Conference in San Francisco in February.

Studies reporting on switches from PIs to efavirenz or nevirapine all showed that by and large, fat distribution was not significantly affected by the therapy switch, even though all studies showed improvements in cholesterol and triglyceride levels, and little evidence of viral rebound after the switch.

However, switching to abacavir did result in improvement in just over half of individuals in one study, and one Spanish study showed some improvement in central obesity after a switch to efavirenz.

There was little further information about the effect of dropping d4T from a regimen. A number of studies have linked d4T use to fat wasting in the limbs and face, but there is little evidence on the effect of dropping d4T, because people tend to change more than one drug when switching.

So if people on protease inhibitors are unhappy with body fat changes that have occurred since they started HAART, should they consider switching drugs at the moment?

"If people are unhappy I would advise switching to an NNRTI, although there is the danger with patients who have taken lots of NRTIs that they will have resistance to 3TC. In the case of someone taking, say, d4T/3TC/indinavir, I would advise switching to efavirenz and intensifying with abacavir to overcome the 3TC resistance," Mark Nelson said.

This is similar to the strategy used in an Australian study in which people with undetectable viral load and body fat changes were randomised to stay on their PI or switch to abacavir/adefovir/hydroxyurea/nevirapine.

The strategy may be problematic however, because of the potential for nevirapine to cause a rash soon after starting treatment (rash is less frequently a problem with efavirenz). This is because abacavir can also cause a rash that may be an early sign of a life-threatening hypersensitivity reaction that affects about 3% of people who start abacavir.

Although central fat accumulation did improve somewhat in those who switched treatment in this study, there was no improvement in the peripheral fat wasting of the arms, legs and face, and they actually lost muscle mass. There were also high levels of discontinuation because of side-effects from hydroxyurea, chiefly nausea, vomiting and diarrhoea, and Dr Andrew Carr, presenting the study, said that these side-effects may have put people off eating, leading to weight loss.

### SUBJECTIVE CHANGES

Mark Nelson notes that in his experience, "People often report feeling better about their bodies after switching. I don't know to what extent this is true and to what extent it's perception, but [in the Carr] study people who switched perceived that their body shape had improved, even though objective measures showed little or no improvement."

Another study showed a similar finding. Spanish patients switched from a PI to nevirapine showed no improvement in body fat changes after 48 weeks, but did report a better quality of life due to a reduced number of pills. Most had been taking indinavir prior to switching, which involved taking tablets every eight hours on an empty stomach.

Alison Gray, Executive Director of AIDS Treatment Project, says that quality of life issues of this sort should not be dismissed.

"Even if objective measurements of fat redistribution don't show improvements, surely patients feeling better is reason enough to consider switching. Doctors often don't look at psychological aspects of treatment. As a woman I feel bad because I've had to wear trousers and a loose top because of body fat changes, and I know gay men with facial wasting often report feeling very self-conscious going into bars or social situations."

#### EDITOR'S NOTE

The cause of the fat abnormalities discussed in this article remain unclear. Though this syndrome was initially associated with PIs, other drug classes have since been implicated. For background reading on the issues raised in this article, see *AIDS Treatment Update* issues 80, 75, 68 and 67. More information can also be found on [aidsmap.com](http://aidsmap.com) in *Body fat and metabolic changes whilst on treatment in Anti-HIV therapy*.

## SUMMARY OF SWITCHING STUDIES

Study	Drug switch/ length of follow-up	Numbers followed/ randomised study?	Body fat improvement?	Lipids improvement?
Saint-Marc (SF 52)	d4T to other NRTI(PI-naïve)/ 9 months	36/NO	Peripheral fat YES: 11/36 reported near normalisation, 21/36 partially improved	Triglyceride YES Cholesterol, glucose, insulin NO
Tebas (SF 45)	PI to NVP/24 weeks	40/NO	NO (got worse)	Triglyceride YES Cholesterol NO
Gharakanian (SF 46)	PI to EFV/10 months	33/NO	NO	NO
Bonnet (SF 49)	PI to EFV /24 weeks	43/NO	NO	NO
Martinez (SF 50)	PI to EFV/24 weeks	24/NO	11/24 reported central fat improved; peripheral fat NO	Triglyceride YES Cholesterol NO
Viciana (SF 48)	PI to EFV/24 weeks	39/NO	Patients reported improvement, but no significant difference when measured	Triglyceride and cholesterol increased slightly
Moyle (ICAAC 1288)	PI to EFV/24 weeks	8/NO	Weight increased by 3.5kg	Triglyceride and cholesterol rose at 12 weeks but normal at 24 weeks; glucose tolerance YES
Gatell (San Diego 40)	PI to NVP/14 months	23/NO	Subjective improvements	YES to all metabolic parameters
Carr (SF 205)	PI to NVP/ABC/HU/ADF/ 24 weeks	49/YES	Lean muscle reduced, no significant improvement in fat despite patient perceptions	Triglyceride, cholesterol YES Insulin resistance NO
Rozenbaum (SF 47)	PI to ABC/12 weeks	32/YES	Some patients reported improvement, but no improvement overall	Both groups declined slightly, no significant difference between the two
Goebel (SF 51)	PI to ABC/24 weeks	210/YES	No significant improvement (N=31; sub-study)	Cholesterol, insulin sensitivity YES Triglyceride NO

### KEY TO TABLE

NVP = nevirapine; EFV = efavirenz; ABC = abacavir; HU = hydroxyurea; ADF = adefovir; SF = Seventh Retroviruses Conference, 2000; ICAAC = 39<sup>th</sup> ICAAC, 1999; San Diego = First Workshop on Adverse Drug Reactions and Lipodystrophy in HIV Infection, 1999.

However, Dr Mark Nelson remarks that different people will have different priorities. "I saw one patient today with a big increase in abdominal fat who is not interested in changing therapy. She is perfectly happy to stay on her protease inhibitor because her

viral load is undetectable and her CD4 count has gone up from 3 to above 500. She doesn't want the risk of viral rebound."

Significantly, none of the studies reported that body fat changes got worse once a switch has occurred.

## CHOLESTEROL AND TRIGLYCERIDES

Body fat isn't the only form of fat that tends to go haywire on HAART. Fats circulating in the blood (cholesterol and triglycerides) also tend to rise, sometimes to high levels. Very high levels of triglycerides can cause fatal pancreatitis, and high levels of the type of cholesterol which rises on HAART (LDL) are associated with an increased risk of heart disease. There are concerns that elevated LDL cholesterol in people with other risk factors for heart disease could lead to an increased risk of heart attack.

These increases occur in the majority of people who commence HAART, although there appear to be predisposing factors such as high baseline cholesterol and triglycerides, age and weight.

Switching studies are also confusing on the subject of lipids. The 48 week Spanish study of switching to nevirapine discussed above is one example. Whilst the people who switched to nevirapine experienced a decline in lipids after 48 weeks, so did the indinavir group, and there was no statistically significant difference between the two groups in lipid levels after 48 weeks of follow-up.

However, people in the Australian study mentioned above did experience a significant decline in lipid levels after 24 weeks.

A study of switching to efavirenz conducted by Dr Graeme Moyle at the Chelsea and Westminster Hospital showed that triglyceride and cholesterol levels actually rose when people switched drugs for the first three months, and then fell back to normal levels.

## KEY CONCLUSIONS

- ◆ It is unclear at the moment whether switching from a protease inhibitor will improve body fat redistribution, although in the majority of studies they do not seem to get worse after switching.
- ◆ It is unclear if switching before the development of visible changes will prevent the problem from occurring.
- ◆ There are still too few data to determine what contribution d4T makes to fat loss.
- ◆ There is no clear pattern of improvement in lipid levels, or in insulin sensitivity, after a switch to an NNRTI.
- ◆ Patients often say that they feel better after switching, but changes in quality of life have rarely been measured.

# NEWS IN BRIEF

## Abacavir warning

Glaxo Wellcome have issued a warning to doctors to be aware of newly identified symptoms of an abacavir hypersensitivity reaction. Anyone who has recently started abacavir (Ziagen) and who is experiencing flu-like symptoms or acute respiratory illness should notify their doctor immediately. If a hypersensitivity reaction is confirmed, treatment with abacavir will be stopped and should never be resumed. Abacavir hypersensitivity occurs in 3% of people starting the drug. Other symptoms already identified include fever, shortness of breath, sore throat or cough, skin rash (redness or itching), nausea, vomiting, diarrhoea or abdominal pain, severe tiredness, aches and a general feeling of ill-health. Less commonly reported symptoms include joint pain, conjunctivitis, mouth ulcers and low blood pressure.

## Oral sex risk

Until now oral sex has tended to be classified as a low risk activity for HIV transmission. Recent findings from a study of new HIV infections in San Francisco has attributed 7%

of new infections reported between 1996 and 1999 to oral sex. The study of 122 infections could not identify any other possible route of transmission for 8 of the 122 men who seroconverted during the period of the study. The men all considered oral sex as carrying little or no risk for HIV infection. (7<sup>th</sup> CROI, abstract 473).

## Nevirapine vs PI

24 week data from a study of 142 treatment naïve patients randomised to receive AZT and 3TC with either nevirapine or nelfinavir have shown that those receiving nevirapine had significantly better viral suppression than those receiving nelfinavir. Individuals who started therapy with a viral load greater than 100,000 copies (though not a very large group), also experienced a significantly better virological response on the NNRTI.

Responses in the nelfinavir arm appear poorer than that seen in other trials. Overall, 58% of the nevirapine group had viral load less than 20 copies at 24 weeks, compared with 33% of the nelfinavir group by intent-to-treat analysis. Among those participants who started therapy with a viral load above

### REFERENCES

Studies noted on these pages were presented at the 7<sup>th</sup> Conference on Retroviruses and Opportunistic Infections, San Francisco, January 30 – February 2, 2000. Abstract numbers are noted.

### NAM FORUM

The next NAM Information Forum will be held on March 27<sup>th</sup> at the University of London Union, Malet Street, London W1 from 7pm. Admission is free and a sign language interpreter is available.

100,000, the percentages below 20 copies were 57% of fifteen nevirapine recipients and 22% of 22 on nelfinavir.

25 nelfinavir users and 23 nevirapine users left the trial early; quite a high number. The majority of discontinuations in the nevirapine group were due to elevated liver enzymes. The most commonly reported adverse event in the nelfinavir arm was diarrhoea. The findings are likely to call into question recently updated US guidelines, which depict nevirapine as a less favoured option than efavirenz, nelfinavir or indinavir. (7<sup>th</sup> CROI, abstract 510).

## PIs & osteoporosis

Early reports began to emerge over a year ago of diminishing bone density due to loss of mineral components among people treated with protease inhibitors. Researchers have now found that 21% of a group of 64 men receiving protease inhibitors had severe osteoporosis as compared with 6% of an age-matched HIV-negative control group. 50% of the PI group had some evidence of reduced bone mass, compared to 29% of the control group. The researchers failed to find any association between low testosterone and reduced bone mass. A team of Australian researchers also reported reduced bone mass in 80 patients with lipodystrophy: 28% had some signs of osteoporosis and switching to a PI sparing regimen failed to lead to improvement. (7<sup>th</sup> CROI, abstracts 207, 208).

## Re-infection

The strongest evidence so far that re-infection or 'super-infection' occurs was presented at a conference in San Francisco last month. A 40 year old gay man who had never taken anti-HIV treatment experienced a CD4 cell decline of over 400 cells and a rise in his viral load from 20,000 copies to over 100,000 copies over a period of six months in 1998. The man suggested that he could have been re-infected with drug resistant HIV during a relationship with a highly treatment-experienced man in 1997.

When virus samples from the two men were compared, along with a stored sample from 1989, it emerged that regions of their HIV genes that don't normally mutate, bore a striking resemblance to one another. The man was also found to have developed mutations associated with 3TC resistance and protease inhibitor resistance. The only antiviral he had ever taken was ribavirin in 1989 in a clinical trial. Re-infection has been demonstrated previously in chimpanzees, but many doctors and people with HIV have remained sceptical about the possibility and effects of re-infection in people. (7<sup>th</sup> CROI, abstract LB2).

## Resistance tests

Previous studies have highlighted the possible utility of genotypic resistance tests to guide a change of therapy. At this year's Retrovirus Conference, the attention switched to phenotypic resistance testing. Whilst genotypic tests look for changes in HIV's genes which are associated with drug resistance, phenotypic tests measure the amount of drug required to reduce the ability of the virus to replicate. As resistance develops, a higher concentration of a drug is required in order to prevent growth of the virus.

271 individuals with viral load rebound on a protease inhibitor, and viral load over 2,000 copies, were randomised to switch therapy either using the results of phenotypic resistance test or without. Over a short follow-up period of sixteen weeks, the use of a phenotypic resistance test improved the likelihood that an individual would have viral load below 400 copies. At week 16, 38% of those who used phenotypic resistance testing were below 400 copies, compared to 23% of those who did not, by intent-to-treat analysis.

These data are encouraging, though at sixteen weeks it may be too soon to comment on their significance in the long term. (7<sup>th</sup> CROI, abstract 237).

## PCP prophylaxis

A range of studies have shown that after a sustained CD4 cell increase to greater than 200 cells, primary PCP prophylaxis, that is therapy to prevent a first episode of PCP, may be safely discontinued. Now researchers have evaluated the safety of stopping secondary prophylaxis (therapy to prevent a recurrence of PCP) among individuals using similarly effective HAART.

Data from eight European cohorts were included in the analysis of the study. Of a total of 17,500 people taking HAART across Europe, 246 individuals had stopped secondary prophylaxis for PCP after a median of thirteen to 25 months on HAART. The median CD4 count when prophylaxis was stopped ranged between 277 and 371 cells. In the follow-up period of five to thirteen months, there were no reported cases of PCP recurrence. The researchers concluded that the risk of recurrence of PCP after the CD4 count has risen above 200 cells was as low as that for primary PCP. (7<sup>th</sup> CROI, abstract LB5).

A test-tube study found that protease inhibitors were able to stop the growth of the organism responsible for PCP, which may be part of the explanation for the protection from PCP which successful HAART seems to provide. Other types of antiretrovirals were not studied. (7<sup>th</sup> CROI, abstract 245).

### TIPRANAVIR

The worldwide rights to the novel protease inhibitor tipranavir, currently in Phase II study, were acquired by Boehringer Ingelheim at the end of January. Boehringer manufactures the NNRTI nevirapine.

### ST JOHN'S WORT

Users of the herbal antidepressant St John's Wort have been warned not to take the drug with indinavir where this is the sole PI in an anti-HIV regimen. Drug interactions may result in inadequate exposure to the PI.

### EMAIL & AUDIO ATU

ATU is also available on audio tape and as a pdf file which can be viewed using Acrobat Reader. For details contact NAM, see back page.

### CORRECTION

As we reported last month, the Western General Hospital, Edinburgh, is participating in a study of human growth hormone for wasting. We apologise for recording their phone number incorrectly. The correct number is 0131 537 2842.

## GLOSSARY

**antiretroviral** Something that attacks retroviruses such as HIV

**CD4** Molecule on the surface of some cells onto which HIV binds. CD4 cell count roughly reflects the state of the immune system

**insulin** Hormone which enables body tissues to take up sugar from the blood

**insulin resistance** When insulin is present in the blood but unable to do its job properly

**NNRTI** Non-nucleoside reverse transcriptase inhibitors: anti-HIV drugs that include nevirapine, delavirdine, and efavirenz

**NRTI** Nucleoside analogue reverse transcriptase inhibitors: anti-HIV drugs that include AZT, ddI, ddC, 3TC and d4T

**protease** An enzyme that HIV uses to break up large viral proteins into smaller ones

**protease inhibitor** Anti-HIV drugs which target the protease enzyme, e.g. saquinavir, ritonavir, indinavir, nelfinavir

**resistance** A drug-resistant HIV strain is less susceptible to the effects of one or more anti-HIV drugs because of its genetic make-up

**reverse transcriptase** An enzyme which converts genetic material from RNA into DNA, an essential step in the lifecycle of HIV

**viral load** The amount of virus in a sample. HIV viral load indicates the rate at which HIV is reproducing in the body

## FREE THIS MONTH

You will find enclosed with this issue a copy of the sixth booklet in NAM's award-winning information series: an HIV Treatment **Glossary**.

Written by NAM's Treatments Team with the help of Mike Youle & Theo Bloom, this new resource is designed to help you get to grips with the technical and scientific terms that are essential to understanding the issues involved when making decisions about treatment for HIV.

Containing both an explanation of terms and a pronunciation guide, the **Glossary** is a portable and easy-to-use reference resource for anyone who needs to master treatments terminology.

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NAM's treatments education for people living with HIV is provided free thanks to the generosity of: The Department of Health, NHS London Region HIV/AIDS Specialist Commissioning Advisory Group, Crusaid, the British HIV Association, Glaxo Wellcome UK, Bristol Myers Squibb, Pharmacia & Upjohn, Abbott Laboratories, Merck Sharpe & Dohme, Boehringer Ingelheim, Du Pont Pharma, Roche Products, Levi Strauss & Co, Enfield & Haringey Health Authority, The Hysteria Trust, Bexley & Greenwich Health Authority, Barnet Health Authority, Redbridge & Waltham Forest Health Authority, Hillingdon Health Authority, Birmingham Health Authority, Manchester Health Authority, Stockport Health Authority

## ANY QUESTIONS?

The following national agencies, all based in London, offer one-to-one advice and information about treatment options, in person or over the telephone:

- ◆ **AIDS Treatment Project**

Phoneline: 0845 9470047  
Mon & Wed 3pm - 9pm, Tue 3pm - 6pm  
All calls charged at local rates.

- ◆ **Body Positive**

Treatment Advice: Tue & Wed 12pm - 5.30pm  
Call Anthony on 020 7287 8010 to make an appointment.

- ◆ **The Terrence Higgins Trust**

Helpline: 020 7242 1010 Daily 12noon - 10pm  
Treatment Support: Call the Treatments Team on 020 7831 0330 for an appointment.

NAM recommends readers to seek treatment advice from more than one source, and to discuss all your decisions with your doctor.

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### AIDS TREATMENT UPDATE

Published monthly by



NAM Publications  
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Southside  
London SW4 7AB.  
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<http://www.aidsmap.com>

Editor:  
Anna Poppa

AIDS Treatment Update  
founded by Peter Scott  
Copyright: © NAM  
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Design:  
Positive Design Works,  
London W10

Imagesetting & Printing:  
Cambrian Printers,  
Aberystwyth

ISSN: 0969-4706