

AIDS TREATMENT UPDATE

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Mixed news on PI-sparing

New UK treatment guidelines revised after reports from San Francisco conference

BY ANNA POPPA

At a major international conference held in September, new research provided some interesting clues to a number of the unresolved questions relating to the use of non-protease inhibitor (PI)-based combinations in people new to anti-HIV treatment.

TREATMENT OPTIONS

Standard first-line treatment tends to involve taking a combination of three drugs – two from the nucleoside analogue group, and one other. A year or two ago, this would most often have been a PI. Over time, however, the use of non nucleoside (NNRTI)-based combinations has grown in popularity. In part this has happened because clinical trials comparing PIs with NNRTIs have suggested a broadly similar effect on viral load. But the perception that PIs are ‘problematic’ because pill burden is generally quite high and dosing requirements are often demanding, because the potential for negative drug interactions or variability in drug levels can be extensive, and because they have been linked with metabolic abnormalities, has also been important.

No doubt too, the allure of the new, and the marketing strategies of pharmaceutical companies who understand that their products will be most lucrative if they are used within first-line therapy where sustained effect is most likely, have also played a part.

Those in the NNRTI camp have problems of their own of course. The pills may be smaller, fewer, and can be taken less frequently, but they too have their own class-specific toxicities which can impact negatively on quality of life and adherence. They have a lower barrier to drug resistance because HIV needs make very little change to its structure in order to

escape their effects. And whilst PI-based treatment has been proven effective in extending survival and reducing illness, the later development of NNRTIs has meant that comparable data have been lacking, (See sidebar page 3).

A third option is to avoid both PIs and NNRTIs altogether by taking three nucleoside analogues. Again the availability of a new drug, abacavir, which is potent and has a low pill burden has been influential in establishing this strategy. It is the least well proven of the three regimens, however, and so is not recommended as an alternative to either PI or NNRTI-based therapy in the new British HIV Association (BHIVA) guidelines on HIV treatment.

LONGER-TERM FOLLOW-UP ON EFAVIRENZ

The landmark study in establishing NNRTI-based combinations as a viable alternative to PIs was Du Pont’s 006 study which compared efavirenz/AZT/3TC with indinavir/AZT/3TC and efavirenz/indinavir (first reported at last year’s World AIDS Conference). At the recent Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) held in San Francisco, results from the original cohort of 450 people, who have all been followed for 72 weeks on study treatment, were presented for the first time¹.

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To re-cap, participants were eligible only if they were naïve to 3TC, PIs and NNRTIs, though some experience of AZT was allowed. On entry, average viral load was around 60,000 copies, average CD4 count was 345 cells, and 80% of the cohort were drug naïve. It was an open-label study which means that participants knew which of the three regimens they had been assigned to. This is a significant limitation because these kind of studies are more open to bias than those where treatment allocation is 'blinded'. Secondly, indinavir recipients were taking 200mg capsules, rather than 400mg, which doubled their daily indinavir pill burden to twelve, compared with the six capsules they would be prescribed outside the study.

Nevertheless, the latest data show a superior effect on viral load amongst those who received efavirenz/AZT/3TC. After 72 weeks, using the most stringent intent-to-treat analysis (see sidebar page 3), which includes results from all 450 enrollees, regardless of whether they left the trial part way through, 60% of those on efavirenz/AZT/3TC had viral load below 50 copies, compared with 40% of those on indinavir/AZT/3TC and 46% of those on efavirenz/indinavir. This superiority persisted even in the sub-group of patients who began treatment with high viral load. CD4 counts have increased by around 200 cells on average in all three groups, and appear to be continuing to climb.

Overall, a high proportion of people left the study before it had finished, (24% on efavirenz/NRTIs, 41% on indinavir/NRTIs, and 35% on efavirenz/indinavir), though most of these did so for reasons other than side-effects of their treatment. The number of people discontinuing because of side-effects was higher amongst indinavir/NRTIs recipients however, at 17%, compared with 7% in the other two arms. Advocates of PI-based therapy argue that this rate is atypical compared with discontinuation rates seen in earlier studies of indinavir/AZT/3TC. 1% of those assigned efavirenz/NRTIs stopped their treatment because of central nervous system side-effects, the major toxicity associated with efavirenz.

EFFECT OF EFAVIRENZ IN LYMPH NODES

The lymph nodes play a key role in the interaction between immune cells. In untreated HIV infection, the virus quickly establishes itself in lymphoid tissue and the lymph nodes deteriorate. It is suggested that anti-HIV therapy which reduces the amount of virus in the lymph nodes will allow the regeneration of lymphoid tissue, and so restore lost immune function. It has been reported previously that people treated with PI-containing three drug

combinations have a lower viral burden in their lymph nodes than people receiving two nucleoside analogues.

At ICAAC, researchers from the US National Institutes of Health presented further evidence of the potency of efavirenz-based combination therapy². HIV genetic material could not be detected in lymph node biopsies from a small number of patients receiving efavirenz, the first time this compartment has been assessed in NNRTI-treated patients.

Nine people who had not taken anti-HIV drugs before, began treatment with efavirenz/d4T/3TC and all responded well, seeing viral load in their blood fall below 50 copies. Lymph node biopsies were performed on all nine after eight months treatment, and compared with a control group of four people treated with d4T or AZT, plus 3TC and either nelfinavir or indinavir. Cell-associated virus could not be detected in the lymphoid tissue in either group. Patients also had unusually low levels of replication-competent virus; five of eight efavirenz recipients and three of four PI recipients had less than one infectious unit per million cells.

“The three main things that determine my choice of regimen are compliance, compliance and compliance.”

– Dr Barry Peters.

LESS GOOD NEWS ON EFAVIRENZ

As we have previously reported in *AIDS Treatment Update* (see issue 80), recent news on the lipodystrophy syndrome suggests that initial moves to link this adverse effect exclusively with PI treatment may have been premature – several researchers have since reported body fat changes in people who have never received PIs.

Researchers from Du Pont Pharmaceuticals have now assessed the extended 1,266 patient cohort enrolled in their 006 study (from which virological data was noted above)

FURTHER INFORMATION
AIDS Treatment Update issues 76 and 68 provide further coverage of PI-sparing combinations. These articles are relevant for people considering anti-HIV treatment for the first time. The NAM/BHIVA website www.aidsmap.com news section offers more detailed coverage of the latest research from the 39th ICAAC, including news on future treatment options for people with drug experience.

for reports of lipodystrophy³. Bearing in mind that duration of treatment has been associated with the development of lipodystrophy, it is important to note that most of this extended cohort had been receiving their assigned treatment for just six months (664 people). 379 had been followed for close to a year, and 142 for a year and a half.

Cases of lipodystrophy which had been clinically recognised and reported occurred in three of 422 participants on efavirenz/AZT/3TC, eleven of 429 people taking efavirenz/indinavir, and six of 415 people on indinavir/AZT/3TC. Without a statistical analysis it is not possible to say definitively whether lipodystrophy occurred more or less frequently on one regimen compared to another. However, the most important message is that lipodystrophy was reported in all three arms, which counters the idea that 'PI-sparing' combinations are a risk-free alternative for people concerned about this problem.

THE ATLANTIC STUDY

Two more 'PI-sparing' regimens are under investigation in the international Atlantic study⁴. This open-label study randomised treatment-naïve patients to receive d4T/ddI plus either indinavir, the NNRTI nevirapine, or a third nucleoside analogue 3TC. 235 people have completed 48 weeks on study drugs.

Participants in this trial generally had lower viral load than other studies discussed in this article. The median baseline viral load was around 23,000 copies, and median CD4 count was 408 cells.

At 48 weeks, there was no significant difference in the proportions with viral load below either 500 or 50 copies in the intent-to-treat analysis, (59% and 57% for indinavir, 55% and 51% for nevirapine, and 57% and 49% for 3TC respectively). Again, there is no significant difference between these values. All arms experienced a median gain in CD4 cells of between 140 and 170 cells by the end of the 48 week period.

COMPARING ABACAVIR WITH INDINAVIR

The use of triple nucleoside analogue combinations is also under investigation in a study called CNA3005 which compares abacavir/AZT/3TC with indinavir/AZT/3TC⁵. AZT/3TC was given as the combined pill *Combivir*[™], and because this was a blinded study all participants were taking three active drugs plus one inactive placebo. This gives a total of sixteen pills per day and a three times daily dosing regimen, whereas the actual dosing regimen for abacavir/*Combivir*[™] outside this study would be two tablets twice a day. Again, the discontinuation rate was quite

high; around 40% of the 562 people randomised did not complete 48 weeks on their allocated treatment. Roughly 19% of discontinuations in both arms were due to side-effects.

Participants in the study had not taken any anti-HIV therapy before. Average viral load at baseline was around 68,000 copies and average CD4 count was 360 cells. After 48 weeks on treatment, using an intent-to-treat analysis, there was no significant difference in the proportions achieving viral load below either 400 copies (51% in both arms), or 50 copies (46% and 40%). CD4 counts at this point had risen by around 145 cells on average in both arms.

TRIPLE NUKES AT HIGH VIRAL LOAD

A key criticism which has been levelled at triple nucleoside analogue regimens has been the weakness of data showing their effectiveness in people who begin treatment with high viral load. Results of the studies discussed in this article tend to reinforce this concern rather than refute it.

Amongst the sub-group of people in CNA3005 who began therapy with viral load over 100,000 copies, a greater proportion of indinavir recipients achieved viral load below 50 copies after 48 weeks by intent-to-treat analysis (45%, or 23 of 52 people) than in the abacavir arm (31%, or 14 of 46 people).

Atlantic study participants were divided at entry into four sub-groups according to their viral load. In the upper quarter who began with viral load above 51,000 copies there was no difference between arms with respect to suppression of viral load below 500 copies. However, using a below 50 copies cut-off there was a suggestion that the triple nucleoside analogue arm performed less well than the other two. This difference did not reach significance but the numbers of patients in this analysis were small.

DELAVIRDINE: ANOTHER OPTION

A third NNRTI, delavirdine, is unlicensed for use in the European Union at present, but has been available on named patient basis for some time. A key delavirdine study called protocol 0021-part II, which was a placebo-controlled comparison of delavirdine/AZT/3TC versus AZT/3TC and versus delavirdine/AZT, has now reported final 52 week data⁶.

Of the 124 people assigned to the three drug arm, 80% were drug naïve and the remainder had less than six months AZT experience. Average viral load was 31,000 copies and average CD4 count was 355 cells. After 52 weeks, 67% of 61 people receiving all three drugs had viral load below 50 copies

NNRTIS IN LATE DISEASE

The lack of data on the use of NNRTIs in advanced disease may be as much the product of historical factors as anything else. The introduction of PI-containing triple drug therapy led drug licensing authorities to begin approving antiretrovirals on the basis of their short-term effect on viral load and CD4 counts, rather than on 'harder' evidence of their ability to reduce illness or death. In large part, this change was due to pressure from activists who asserted that so-called 'body count' trials were unethical, given the weight of evidence suggesting viral load and CD4 counts were surrogate markers for risk of illness and death.

INTENT-TO-TREAT ANALYSIS

See *AIDS Treatment Update* issue 73 for more information on how different ways of analysing data can affect a trial's results.

by on treatment analysis, and CD4 counts had risen by 115 cells on average.

A RANGE OF OPINION

The current consensus within BHIVA, the UK's professional body for HIV doctors, is that there is no clear advantage or disadvantage of PIs versus NNRTIs for initial therapy, and that the pros and cons of each should be considered with each individual patient. This position encompasses a range of prescribing practices, however. In particular, it seems clear that a proportion of doctors continue to see PI-based treatment as the most appropriate option for people with advanced or symptomatic disease.

Discussing practice at London's Chelsea and Westminster Hospital, Dr Graeme Moyle told *AIDS Treatment Update*, "The standard of care here has tended towards NNRTIs as a first-choice regimen and that's been almost exclusively efavirenz. The area where the level of evidence is lacking for efavirenz, and all NNRTIs, is in individuals with a low CD4 count and symptomatic disease."

Asked how he saw triple nucleoside analogue regimens, Graeme said "My feeling is that we shouldn't use [them] for initiation". Virological response in those with high baseline viral load at 48 weeks "is where we separate the men from the boys", he continued, arguing that data from the Atlantic study and CNA3005 raise questions about the potency of these regimens.

Dr Mike Youle of the Royal Free Hospital, London, said "I still prefer to start using PIs and am impressed with the initial results with ABT-378. If a patient really wants an easy regimen I would go for efavirenz/*Combivir*[™] or efavirenz/3TC/abacavir. I worry about the initial risk of failure with an NNRTI, and there are still a lot of CNS side-effects with efavirenz. For high viral loads I favour the same approach."

Professor Tony Pinching of St Bart's Hospital, London, shared Mike's concern about NNRTI failure. "I am amused to see the pendulum swinging to and fro. PIs were over-egged at the outset, even though [nevirapine data from] INCAS looked just as good at Vancouver. Now the new kids on the block are getting over-cooked with the worries about PIs. Is this wise, given the way resistance data we are now seeing suggest NNRTIs get readily squeezed out by mutations? As always, all the pros and cons of potential regimens need to be assessed on the balance of all the accumulated evidence, shaped by and chosen with the patient, based on their perspective and priorities."

BHIVA Chairman, Professor Brian Gazzard felt "Although there are concerns about the low genetic barrier [against resistance] of

NNRTIs, these don't seem to have been borne out in practice so far and this same worry would apply whenever such treatments were given. It's much more difficult to think of a regimen which would be totally suppressive if NNRTIs are not used first-line."

Dr Ray Brettle of the Western General Hospital, Edinburgh, said "It's important to remember the entry criteria for many of these studies [discussed in this article] excluded those with low CD4 counts. Whilst I might consider a non-PI regimen for a well patient, mostly because of the ease of taking the pills, at present I tend to use PI regimens for those who have serious disease."

He continued, "NNRTIs have been less popular in Edinburgh because of interactions with opiates. This is a major turn-off."

Dr Barry Peters of St Thomas' Hospital, London, felt "Currently the differences between the different combinations are small in terms of efficacy and the three main things that determine my choice of regimen for patients with a high viral load or symptoms are compliance – what regimen will lead to the best compliance for each individual, compliance and compliance."

James Deutsch, Chief Executive of Crusaïd and one of two HIV community representatives on the writing committee for the new BHIVA guidelines felt "The reasonable consensus seems to be that no triple nucleoside regimen has yet demonstrated close enough equivalence to warrant standard prescription for first-line therapy. Concerning NNRTIs versus PIs as first-line therapy, my view is that both are acceptable but that most patients with low to moderate viral loads will probably choose to start with efavirenz. Patients with high viral loads may choose a double PI combination, or they may choose efavirenz because of its apparent potency."

Key conclusions:

- ◆ There is no clear evidence which of the currently available drug combinations is best for people starting HIV treatment.
- ◆ Several trials suggest a combination of one NNRTI and two nucleoside analogues is as effective in reducing viral load below 50 copies as a combination containing a PI and two nucleoside analogues. One NNRTI, efavirenz, appears more effective than a PI-based combination in this respect.
- ◆ A combination of three nucleoside analogues is another option, but this appears less satisfactory therapy for people with high viral load.

REFERENCES

All abstracts are from the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy, held San Francisco, September 26th-29th, 1999.

- 1 Staszewski S et al, abstract 507.
- 2 Dybul M et al, abstract LB-15.
- 3 Tashima K et al, abstract 1304.
- 4 Murphy RL et al, abstract LB-22.
- 5 Staszewski S et al, abstract 505.
- 6 Para M et al, abstract 1979.

Starting with PIs

Much of the key data which have supported the ascendancy of non-PI based regimens for first-line therapy have come from head-to-head studies which have pitted them against indinavir plus a dual nucleoside analogue backbone. Whilst the latter is a well-established combination it seems unlikely that many in the HIV community would consider it to be the 'standard of care' today, or even the most desirable way of prescribing indinavir.

The creative use of drug-drug interactions has been one of this year's key developments in the search for more tolerable anti-HIV regimens. In particular, the discovery that taking ritonavir with indinavir could not only turn the latter from a three times a day to a twice daily drug, but could also relax the need for dietary restrictions, has been important given the demand for simplified regimens. (See *AIDS Treatment Update* issue 77).

ONCE DAILY PROTEASE INHIBITORS?

Ritonavir's potent effect on enzymes involved in the metabolism of indinavir, and a number of other antiretrovirals, slows down the clearance of indinavir from the body when the two are taken together. This allows for less frequent dosing. Now preliminary experiments in HIV-negative volunteers suggest there may be scope for these dual PI combinations to be prescribed as once daily therapies in future.

Researchers from the Netherlands, and from Merck, conducted pharmacokinetic studies of once daily indinavir plus ritonavir, at multiple doses, in HIV-negative volunteers^{7,8}. A number of dosages were found to result in comparable peak and trough levels to those seen when indinavir is given three times daily as a sole PI. However, it is unclear which regimen is best, and what the effect might be on the frequency of the kidney toxicities associated with indinavir. Dr Graeme Moyle expressed the concern that "What you may gain in adherence you may lose in tolerance".

Roche have similarly assessed so-called 'baby dose' ritonavir in combination with the soft-gel formulation of saquinavir⁹. Again, pharmacokinetic study suggests the potential for once daily dosing, though the optimal regimen is not yet defined. At this early stage, it would be inadvisable to experiment with once daily dosing of dual PIs outside these research settings.

IN THE PIPELINE I: ABT-378

Of the newer, unlicensed PIs, ABT-378 continues to appear a potent option in people new to treatment. A small trial investigating a range of doses, each given with a 100mg dose of ritonavir, in combination with d4T/3TC has now reported results to 36 weeks¹⁰. Average viral load amongst the 100 participants was 100,000 copies at entry and average CD4 counts were in the range of 300-400 cells. After 36 weeks, 75-81% had viral load below 50 copies by intent-to-treat analysis. CD4 counts had risen by around 200 cells on average.

Generally, treatment was well tolerated, and the most common side-effects were diarrhoea, nausea, weakness and headache. Five people had stopped treatment by week 36, and none of these were due to side-effects. An earlier report from this study had found increased blood levels of triglycerides, a type of fat, in a minority of participants. This is a recognised side-effect of PI therapy, (and to a lesser extent of treatment with other antiretrovirals), which has been linked with the lipodystrophy syndrome.

IN THE PIPELINE II: AMPRENAVIR

Amprenavir is another unlicensed PI, at present not available for people needing first-line therapy, (other than via a trial for people with primary infection). 48 week data from a study comparing amprenavir/AZT/3TC with AZT/3TC in naïve patients was reported at ICAAC¹¹. Baseline median viral load was 50,000 copies and median CD4 count was 425 cells.

Discontinuations were high in this study, with just over half (52%) of the 116 amprenavir recipients stopping treatment before 48 weeks. A third of these discontinuations were due to side-effects, of which nausea was the most common. Amprenavir may be better tolerated if combined with nucleoside analogues (e.g. d4T, 3TC) which are themselves associated less frequently with this side-effect.

At week 48, 41% of the three drug arm had viral load below 400 copies by intent-to-treat analysis. This same analysis using a lower limit of 50 copies is not yet available, but the on treatment analysis at 48 weeks showed 59% (42 of 71) amprenavir recipients below 50 copies.

REFERENCES

- 7 Burger DM et al, abstract 321.
- 8 Saah A et al, abstract 329.
- 9 Saag MS et al, abstract 330.
- 10 Eron J et al, abstract LB-20.
- 11 Goodgame J et al, abstract 509.

Diarrhoea remedies

Calcium tablets taken twice daily appear to have a dramatic impact on nelfinavir-related diarrhoea, doctors from Texas reported at the recent ICAAC conference in San Francisco. A small fifteen person open-label study tested the effectiveness of 500mg calcium twice daily in patients with nelfinavir-related diarrhoea which had not been controlled with standard anti-diarrhoeal medications. 87% had mild to moderate diarrhoea, and 13% severe. After a minimum of 48 hours calcium treatment, all reported significant improvement in their symptoms. 87% reported normal stools and 13% reported mild diarrhoea.

A study of psyllium husk fibre bars for the control of PI-associated diarrhoea reported similar encouraging results. Psyllium husks can absorb huge amounts of liquid. Thirteen of fourteen individuals reported improved symptoms after taking two bars one hour before bedtime; the severity of diarrhoea improved after two weeks, and the treatment was well tolerated. (39th ICAAC abstracts 1308, 1307).

GM-CSF

US and Canadian researchers have reported that adding granulocyte macrophage-colony stimulating factor (GM-CSF, sargramostim) to HAART reduced the risk of developing new illnesses or death over a 24 week follow-up period. 309 individuals on stable HAART were randomised to receive 250 microgrammes of GM-CSF or a placebo twice weekly by injection. Participants had experienced at least one AIDS-defining illness and either had CD4 counts at baseline below 100, or had a prior CD4 count below this level.

GM-CSF, a cytokine which increases the production of neutrophils (white blood cells which control bacteria and fungi), also increased CD4 counts significantly compared to a control group, and appeared to reduce the rate of viral rebound in people who began with viral load below 30,000 copies. (39th ICAAC, abstract 693).

Changed OI pattern

The incidence of AIDS-defining events (ADEs) has fallen dramatically across Europe during

the HAART era according to new research presented at ICAAC. Data from 7,200 participants of the EuroSIDA cohort show that 31 people in 100 became ill within a year in 1994, but that this rate had fallen to three people in 100 by 1998. This period was marked by the gradual introduction of HAART.

The spectrum of diseases reported in people with HIV has also changed. Whilst ADEs such as CMV retinitis and MAI, which occur at very low CD4 counts, have become less common, the relative frequency of non-Hodgkin's lymphoma has increased from 4% of all ADEs in 1994 to 16% in 1998.

Data from a large American cohort confirms that mortality following major ADEs has significantly improved since 1995. PCP, CMV, candidiasis, lymphoma and disseminated MAI were all associated with longer survival periods. However, for toxoplasmosis, AIDS dementia and visceral KS survival was unchanged, and in the case of bacterial pneumonia had actually worsened. The reasons for this are unclear – researchers had not so far compared survival rates with individual use of treatments, though this analysis is planned. It is suggested that the poor prognosis associated with bacterial pneumonia may reflect differential access to HAART by injecting drug users, the patient group most commonly affected by this ADE. (39th ICAAC abstracts 1156, 1157).

Drug resistance

Back in Europe, the prevalence of drug resistance mutations poses another challenge. A multi-centre study in mainland Europe assessed viral isolates from 415 people with experience of at least two nucleoside analogues taken for at least two months, and from 237 'controls' who had not received more than one.

The frequency of mutations associated with multi-nucleoside and nucleotide resistance was relatively low, at 2.5% for Q151M and 0.5% for T69S-SS. These multi-drug resistant patterns occurred primarily in people treated with AZT and ddI, or with AZT and ddC.

Worryingly, amongst 112 drug naive samples, 13% had AZT-related mutations (including mutants which result in high-level AZT

BHIVA GUIDELINES

Guidelines on the use of HIV treatments from the British HIV Association underwent additional revision following the ICAAC conference, and are now expected to be finalised by the end of October. Last month's NAM Factsheet: *Treatment guidelines 1999* will be updated to reflect any significant changes.

NAM FORUMS

'HIV therapy at the end of the millenium' will be the subject of a panel discussion at the NAM Forum on Monday, 29th November, from 7-9pm. The venue is the Palms Room, 4th Floor, University of London Union, Malet Street, London WC1. On December 7th, NAM will be joining with Positively Women for a special Forum on antenatal testing at PW's offices from 7-9pm.

AIDSMAP NEWS

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resistance); 1% had ddC mutants; 1% had ddI mutants; and 6% had 3TC mutants. The prevalence of drug resistance mutations in drug naive patients was 16% overall. This suggests the transmission of drug resistant HIV is becoming a significant public health problem. (39th ICAAC abstracts 1170).

Delavirdine/indinavir

Delavirdine and indinavir can be combined to increase indinavir levels, thus reducing the cost of indinavir. This strategy may be especially attractive in mega-HAART where five or six drugs are being used. A study presented at ICAAC reported on a three times daily regimen of indinavir, delavirdine and AZT in which individuals were randomised to receive either 400 or 600mg of indinavir with the standard doses of AZT and delavirdine, or to receive AZT, 3TC and indinavir.

After 48 weeks on treatment, there was no significant difference between any of the treatment arms in virological response or CD4 response, although the number of participants in this study was very small at 36. Taking 600mg of indinavir with delavirdine resulted in a 400% increase in the minimum indinavir concentration, compared with a 130% improvement in the 400mg arm of the study. The disadvantage of this strategy is that it involves using a treatment from each major class of antiretrovirals which may limit future options. (39th ICAAC abstract 1985).

Hep C conference

The 4th International Hepatitis C Conference, organised by Mainliners, will take place at London's South Bank Centre on the 29th and 30th of November. This major meeting offers an opportunity for health care/social care professionals, clinicians, counsellors and health educators to discuss issues relating to policy, prevention, treatment and care for Hep C infection. The fee to attend both days is £150, and more information is available from Mainliners on 020 7582 5434.

Manchester event

Last month we told you about a special event planned to take place in Manchester, a discussion on adherence to HIV treatments arranged by Body Positive North West with NAM. Unfortunately, we advertised the wrong date and apologise for any confusion this may have caused. Looking on the bright side,

however, this means you have a second chance to go – the event will (really) happen on Tuesday, November 16th.

The venue is Granada Studios' House of Commons, Rovers Return and Woolpack sets, and guest speakers include Dr Ed Wilkins, Nicki Archer and Henry Grahame-Smith. The discussion starts at 6pm with the bar open and food available from 8.30pm to 9.30pm. Places are limited and booking is advised so call Leon, Zoe or Gary at BP North West on 0161 873 8100 for more details.

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GLOSSARY OF TERMS

antiretroviral Something that attacks retroviruses such as HIV

biopsy A small sample of tissue that can be examined for signs of disease

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

central nervous system The brain, spinal cord and its coverings

cytokine A natural chemical used to pass signals between cells

HAART Highly Active Antiretroviral Therapy: a phrase used to describe HIV combination therapy with three or more drugs

lipodystrophy A disruption to the way the body produces, uses and distributes fat

lymph nodes Special areas in the body where white blood cells and other important immune cells are found. Also called glands

named patient basis prescribing A means of access to an unlicensed drug, in which a doctor requests supplies from its manufacturer for a specific individual

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

placebo Pill which looks and tastes exactly like a real drug, but contains no active substance

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

randomisation Process of selecting by chance the treatment that a trial participant will receive

regimen Drug or treatment combination

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

toxicity The extent or ways in which a drug is poisonous to the body

treatment-naïve Never having taken anti-HIV treatments before

undetectable viral load A level of viral load that is too low to be picked up by the particular viral load test used

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

virologic response Effect of treatment on viral load

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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 Robert 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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