

AIDS TREATMENT UPDATE

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When to start?

Cohort evidence stimulates debate on what is meant by 'Hitting early'

BY KEITH ALCORN

It is perhaps a reflection of the growing concern about the longer-term use of anti-HIV therapy that the issue of when to start treatment has once again become a talking point amongst HIV researchers. Though UK treatment guidelines propose a CD4 count of 350 to be a reasonable prompt to begin therapy, whilst US advice suggests 500, it remains the case that the best time to begin is unknown.

Since the Concorde study found – a full five years ago – that people who began treatment with AZT before they developed symptoms of HIV disease fared no differently in the long-run to those who waited until symptoms appeared, there has been no further exploration of this issue on such a scale. Whilst protease inhibitor-containing three drug regimens have been shown to improve health and survival when begun in symptomatic disease, the recommendation to begin HAART at higher CD4 counts is based on theory and not data.

However, according to a review of several large cohort studies presented at the British HIV Association (BHIVA) Autumn meeting in London in October, starting therapy at a CD4 count above 200 may not offer the advantages some suppose.

Professor Andrew Phillips, a statistician at the Royal Free Centre for HIV Medicine in London, analysed four cohorts (or very big groups) of people with HIV in order to assist the development of UK treatment guidelines, and help people with HIV and their doctors decide when to start treatment. These included the 7,000 strong European cohort known as EuroSIDA, the German Frankfurt HIV Clinic Cohort, the Italian ICONA group, and the Royal Free Haemophilia Cohort. Information on participants in each of these cohorts is gathered at regular clinic appointments and

then stored on a central database. This collected data can then be used to help researchers understand more about how HIV disease progression is changing over time and, for example, the impact of treatments.

RISK OF VIROLOGICAL FAILURE

Professor Phillips reviewed four key questions which may influence decisions about starting treatment. Firstly, do people who start HAART at higher CD4 counts have a better viral load response?

To answer this question, Professor Phillips looked at 560 treatment-naïve patients from the Frankfurt Clinic Cohort, and assessed rates of virological failure according to their CD4 counts at the time of beginning HAART. HAART was defined as a combination of at least three drugs, including at least one PI or NNRTI. In the main, treatment involved the use of PI-containing HAART, and so the conclusions may be different for NNRTI-containing HAART.

The definition of virological failure used was failure to achieve viral load below 500 copies at 24 weeks, or the time to virological rebound after achieving viral load below 500 copies at 24 weeks.

Individuals who started treatment when their CD4 count was below 200 failed treatment more quickly

Contents

When to start?	1
Resistance tests	4
News in brief	6
Glossary	8

than those with CD4 counts above 200. However, there was no apparent difference between time to treatment failure in those who started treatment with CD4 counts above 350 and those who started treatment with CD4 counts between 200 and 350.

This same pattern was also apparent in over 400 treatment-naïve patients from the EuroSIDA study, and in 536 treatment-naïve patients from the ICONA cohort. An individual's viral load at baseline had no independent effect (i.e. independent of CD4), on the durability of treatment in the Frankfurt and EuroSIDA cohorts, but it exerted a small effect which was of borderline statistical significance (meaning it may have been due to chance) in the ICONA cohort.

RISK OF SIDE-EFFECTS

Next Professor Phillips looked at whether starting therapy at a higher CD4 count reduces the risk of developing side-effects which may lead to a change in treatment.

Amongst 805 people in the ICONA cohort, where the median treatment experience was 41 weeks, 35% (281) had stopped at least one drug. The most common reason for doing so was drug-related toxicity (21%), followed by non-adherence (7%). Only 5% stopped a drug because of virological failure. There was no significant relationship between baseline CD4 count and the subsequent risk of stopping a drug due to toxicity.

RISK OF LOST IMMUNE FUNCTION

One of the key arguments for starting treatment early is that this offers the best hope of preserving immune function. This seems to make intuitive sense if there is a threshold below which immune function which has been lost cannot be re-gained using available treatment. However, because we don't know where this threshold lies, or even if it exists, Professor Phillips analysed the immunological response to treatment when begun at a range of CD4 levels.

In the Frankfurt Clinic Cohort, in which treatment-naïve individuals have been followed for two years after starting treatment, the average increase in CD4 count has been approximately 200 cells, regardless of the CD4 count when treatment began. It should be noted, however, that CD4 count is just one – albeit an important – measure of immune function. It's possible that other aspects of lost immunity may be restored at different rates, or perhaps not at all. Moreover, it is clear that some people do not get this typical response.

Amongst those with CD4 counts below 20 at baseline, there was a higher death rate while the CD4 count remained below 20 cells

(32 in 123 person years), than after the CD4 count had risen to between 20 and 49 (four in 44 person years), or between 50 and 199 (six in 178 person years), or to greater than 200 (one in 78 person years).

This indicates that the rises in CD4 count experienced were associated with reduced risk of AIDS-related diseases. This supports other studies which have found evidence of meaningful immune reconstitution in those starting therapy even at very low CD4 counts, as long as this count rises.

RISK OF DISEASE PROGRESSION

Finally, Professor Phillips discussed how we might expect HIV disease to progress if therapy is begun later. "If we look at the delay between a CD4 count of 500 and a decline to 200 cells, the median delay is four to five years. In other words, half of individuals with CD4 counts which first fell below 500 in 1994 would only have reached 200 cells in 1999. Viral load had a slight effect on the rate of CD4 cell count decline."

Looking at the risk of developing lymphoma, which does not appear to be arrested or prevented by HAART-related immune reconstitution, there was no evidence that HAART reduced the risk of developing lymphoma at CD4 counts greater than 200. The incidence in untreated individuals with CD4 counts greater than 200 was one per 300 person years in the EuroSIDA cohort; there was no significant difference in incidence compared with those on HAART.

Closing his presentation to the BHIVA meeting, Professor Phillips concluded, "Given the current evidence, there would appear to be no compelling case for starting therapy with a CD4 count above 200 unless the patient is particularly committed to starting therapy or is experiencing symptomatic illness".

However, it seems UK guidelines are likely to continue to recommend that treatment begin when the CD4 count falls below 350. Professor Brian Gazzard, Chairman of BHIVA, said "I wouldn't change the guidelines on the basis of these data alone. However, it is reassuring that you don't get progressively greater responses if you start therapy at 500 or above, indicating that 350 is a reasonable starting point."

PROFESSOR PHILLIPS TALKS TO ATU

AIDS Treatment Update invited Andrew Phillips to discuss his intriguing presentation further.

ATU: You found that the fall from a CD4 count of 500 to a count of 200 took an average of four to five years. How long might it take to fall from 350 to 200?

Andrew Phillips: We haven't specifically done this analysis, but it's probably not unreasonable to halve the four to five years, so two to two and a half years [to fall from 350 to 200].

ATU: You considered the risk of lymphoma at CD4 counts above 200. What's the risk of other infections?

AP: Natural history data suggest that the risk of an AIDS disease before the CD4 count had fallen below 200 is about 5%. My point is that occurrence of most of these diseases would be undesirable and certainly inconvenient but, given that HAART could then be initiated, [this is] only a really serious problem if the AIDS disease is fatal and not reversible with HAART. Most clinicians I have spoken to seem to agree with this logic.

ATU: How have other people in the field responded to your presentation at BHIVA?

AP: There has been a lot of interest from UK physicians. It's clear that many already tend to wait for CD4 counts approaching 200 before starting therapy.

ATU: What are the limitations of your data given that they're derived from observational cohort studies?

AP: I didn't intend to give the impression that my findings are definitive and answer the

question once and for all. I don't feel that this is the case. The data I presented only indirectly address the issue [of when to start treatment]. A randomised trial which allocates people with high CD4 counts to immediate versus delayed HAART is what is really needed. However, there is a great reluctance to carry out such randomisation. Besides which, the trial would have to be very large and long-term, and there would be a danger that the results were 'out-of-date' by the end of it. It will be difficult, but I would certainly support efforts to embark on such a trial if there were sufficient interest from clinicians. Ultimately, there is no way of knowing whether today it is right to start therapy in a person with a high CD4 count. The answer depends on how effective newly developed therapies are in the future and whether their effects are compromised in pre-treated patients.

There is another issue that has been raised. This is the concern that CD4 rises in HAART are slow and perhaps even with full suppression of virus, normal CD4 counts may never be attained. Some rare patients get only small CD4 rises on therapy. While CD4 counts of over 300 seem sufficient to avoid any serious infections, some patients or clinicians may be particularly concerned to maintain a "normal" CD4 count. Patients with CD4 counts above 350 or so who feel this way may wish to start therapy. This emphasises how different patients will make a different decision based on the same evidence, according to what their main concerns are.

COMING SOON: DECEMBER 1999 HIV & AIDS TREATMENTS DIRECTORY

A new edition of the acclaimed HIV & AIDS Treatments Directory, a comprehensive guide to all medical aspects of HIV, will be published in late December. Order now to ensure you get your copy as soon as it is published.

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Resistance tests

Funding & problems with interpretation slow move from lab to clinic

INTERVIEW BY ANNA POPPA

With access to tests for drug resistance widening, and a new UK study evaluating their role in patient care in the offing, *AIDS Treatment Update* discussed issues raised by the introduction of these new monitoring tools with two experts; one a virologist and the other an HIV clinician. Dr Deenan Pillay (DP) works at the Public Health Laboratory Service Antiviral Susceptibility Reference Unit, and Dr Graeme Moyle (GM) at the Chelsea and Westminster Hospital.

ATU: What are the key problems which may count against the use of resistance testing in routine patient care at present?

DP: Firstly, many HIV clinics have not yet secured extra funding for these assays, and therefore are reluctant to purchase them from laboratories. Second, the number of laboratories currently offering genotypic assays is limited, although those that are, may be providing a service for a number of different clinics around the country. There remains little standardisation of assays. Although commercial kit-based assays are available, they still have limitations. Thirdly, interpretation of genotypic assay results is complex. There will be many HIV clinicians very familiar with genotypic drug resistance data, but equally there will be some who are less familiar, and support is required to ensure that patients benefit from current state-of-the-art knowledge of resistance data.

All genotypic assays will have a limit of detection of around 1,000 copies/ml, so it may be difficult to amplify the relevant viral genes at a lower copy number. Nevertheless, in practice it may be difficult to generate a result with higher viral load. These assays demand a high level of technical skill which is not necessarily available currently within diagnostic laboratories.

The sequencing techniques involved in genotypic assays have previously only been available within a research environment, without the need for routine provision of information back to the clinician. The criteria for providing any laboratory test for direct patient management include formal systems for receipt and storage of specimens, well validated tests with standard operating procedures and quality control, fully trained staff (a range of staff able to undertake any one assay in order to ensure continuity of the service), adequate facilities, and an

interpretative service. All these aspects of any routine laboratory are covered in the accreditation programme for which all UK diagnostic laboratories have to apply.

Thus, the problem is to move new complex and experimental techniques such as genotypic sequencing into this diagnostic arena [in a way that] ensures the continual availability of a high quality assay service. This transition requires heavy investment. In my view, this represents the major problem facing us with regard to widely available genotypic assays. I have no doubt that the situation will change, however, at present, many laboratories are struggling with all these issues. From the perspective of a user of these services, I think the major question to be asked is whether the laboratory providing the assay result is accredited to undertake molecular biological (such as viral load assays, genotyping etc.) diagnostic assays.

GM: Anytime you do a test in medicine you have to interpret the results with a grain of salt. For example if I have a patient with three undetectable viral loads in a row who hasn't had anything wrong with them, says that they've been completely compliant, and has a viral load of let's say 100, then I will simply repeat the test and not do anything about that because nine times out of ten it will be a technical error. That's one of the difficulties with resistance testing in that it's certainly likely that there's a degree of under-estimation of the extent of resistance present.

In the same way that a few years ago it was said that people who received their HIV care from inexperienced physicians who looked after few HIV patients tended to do less well, it's possible that people who receive their resistance tests from non-commercial labs who are doing a relatively low through-put may be getting less good value from their money than if they were to go through a commercial organisation.

The technology is fairly similar technology therefore it gets down to the experience and training of the person who is reading the outputs. The outputs are checked manually from a computer read-out so it depends on how good the computer is and how good the technician is at assessing those.

Interpretations that are provided by laboratories are very much a mixed bag. A lot of the reason why physicians are anxious about doing resistance tests at other clinics is

WHICH TEST?
Genotypic resistance tests look for changes in HIV's genes which are associated with the development of resistance. Phenotypic tests measure the amount of a drug needed to stop HIV reproducing. The amount increases as drug resistance develops.

MORE INFO
A booklet in NAM's Information Series for Positive People, *Resistance*, provides a useful introduction to some of the issues discussed in this article. Copies are available free to people directly affected by HIV by contacting NAM on 020 7627 3200.

if they get a result back that doesn't have an interpretation provided with it they don't know what to do with the result, and if they do get an interpretation back, one of the problems is that it might be rather mediocre.

That doesn't mean that I know what to do with the results of most of the tests that come back. I can provide as much evidence as I am able to from keeping up with the literature, but for example, the d4T issue – I don't know how to interpret someone who has got three AZT mutations; whether one should call them d4T resistant or not. If they have the L90M mutation do you say that they are resistant to all protease inhibitors or not? There's a lot of difficult interpretations even though particular mutations are associated with resistance in vitro it still doesn't make it guaranteed that one can provide an accurate interpretation in vivo. So there are quite a lot of challenges to it in that regard.

There's the other problem that most of the tests are designed for clade B strains and so in particular amongst African patients there may be a substantial under-estimate of the extent of resistance.

ATU: There seems to be a particular lack of data about the use of resistance testing to guide therapy choices in naive patients. Are there circumstances in which this might be beneficial?

DP: There are two situations in which testing of drug naïve patients can be undertaken – in seroconverters/primary infection or in drug naïve individuals. Testing in primary infection is more likely to pick up transmitted resistant virus. Following this transmission, in the absence of therapy, further evolution of the virus may occur such that "wild type" virus emerges. Thus, testing someone later in infection may not detect these resistant variants. This does not mean to say that resistant virus has been cleared from the body – indeed, it may be present as proviral DNA within latently infected cells – only that it is not the majority virus within the plasma. For this reason, transmission of resistance is more likely to be detected by genotypic assays the earlier a patient is tested following initial infection. It follows that the absence of any drug resistance mutations in a drug naïve individual tested some years after infection may not exclude the presence within the body of transmitted resistant virus.

GM: At the moment there is no purchaser as far as I know which is providing money for that to be done. There are reports from large urban areas in the United States that give an idea that there may be a, let's say, 5% maximum incidence of non-AZT mutations

involving protease inhibitors and NNRTIs circulating in those areas at the present time. Is 5% enough to change your practice? Well, in genitourinary medicine if there's a more than 5% incidence of penicillin resistant gonococcus in the population most GU clinics move over to using non-penicillin based therapy. It does raise the issue that it may shift practice patterns. Interestingly, those figures may well shift patterns back to using protease inhibitors because there seems to be a lower level of resistance to those drugs.

For those individuals who present with chronic infection rather than primary infection, your pick-up rate is going to be much less than that 5%. You're going to occasionally pick up polymorphisms [i.e. naturally occurring mutations] which you don't know how to interpret that may cause some physicians to choose drug combinations which are less evidence based, or not necessarily the right thing for the patient. Certainly, the benefit hasn't been demonstrated for testing in those circumstances.

If I was seroconverting I'd want to have my virus tested and want to know what drugs my partner was taking at the time. But in chronic infection it's probably a waste of time. You may pick up an AZT mutation because AZT resistant viruses have been reported to stay around for considerable periods of time, certainly more than one year. But if you got something like 184 [associated with 3TC resistance] at the time of seroconversion, almost certainly, it will fade into the background very quickly.

ATU: Imagine a wealthy man with HIV whose first-line PI containing regimen is failing despite good compliance, with viral load confirmed around 1,000 copies. He would like a resistance test to help plan his next regimen but his treatment centre is not funded to provide it. He has £1,000 to spend on the right tests. What would be the best use of his money?

DP: My view would be that the success of second-line protease inhibitor therapy is dependent upon the array of resistance associated mutations that have emerged on first-line PI. On this principle, the earlier one changes following failure of first-line PI, the more likelihood of success. This is dependent upon the number of mutations present, and their position. For this reason, I think a genotypic assay would be useful at this early stage of failure. I do not see any major advantage of doing a phenotypic assay over a genotypic assay in this specific scenario.

GM: Where one is observing virological rebound on a protease inhibitor containing

NEW STUDY

The UK Medical Research Council is about to launch a randomised study called ERA (Evaluation of Resistance Assays).

The trial is in two parts. First, individuals who are not heavily pre-treated will be randomised to receive or not receive genotypic resistance testing at baseline and at subsequent treatment failure to help guide the selection of a new regimen. Second, individuals who are heavily pre-treated will all receive genotypic resistance testing and will, additionally, be randomised to receive phenotypic resistance testing. Follow-up will be according to routine clinical practice for a minimum of one year.

Participating centres will be posted on aidsmap.com in early 2000.

Resistance tests

regimen the important thing not to do is throw the baby out with the bath water. He could be failing because while he says he taking every dose he's not following the food requirements of the drug. It could be that he's had poor exposure to protease inhibitors and is therefore failing because of [poor blood levels]. It could that he's forgotten to tell the doctor about something his GP has prescribed for him. He could have had a diarrhoeal illness and not bothered to report to the doctor that his diarrhoea got a little bit worse for two weeks at the time that they did that test. So I think the advantage of doing a resistance test in those circumstances is it finds out whether you're getting rebound related to resistance to multiple components of the regimen, or to one component, or that you're getting rebound which is wild-type, i.e. the combination that you started with is insufficiently potent to control their virus. It could be that he was an individual who started with a very high viral load, managed to get a nadir below 50 but has rebounded because it was 49 copies and not 0 copies.

So, yes I think it would be reasonable to have a resistance test performed. I suppose the next question is whether he should also invest a little money in measuring the pre- and post-dose blood level for his protease inhibitor to see if he's getting sufficient exposure to the drug. I suspect that there may be people who would advocate that that may be a worthwhile thing in the future.

I think the important thing is that you don't look at that individual and say "He's been taking AZT/3TC/nelfinavir; we can never use any of those drugs again because we've got resistance to all of them", when he might actually only have resistance to 3TC.

I think that probably getting a commercially available genotype would be the best thing to do. My personal bias, having no financial arrangement with any resistance testing programme, would be that VIRCO would probably be the most reliable place at the present time in Europe and the UK to get that test done.

Editor's note: VIRCO is one of two commercial organisations providing high throughput genotypic and phenotypic HIV resistance tests, and have built up a very large database by which specific genotypes can be matched to a phenotype. They currently provide resistance tests to the Chelsea and Westminster Hospital, on the basis of a pharmaceutical company funded research protocol.

The PHLS Antiviral Susceptibility Reference Unit, in Birmingham, provides HIV genotypic tests to 25 HIV clinics across the UK. They are about to start a prospective study of resistance in primary infection, in collaboration with the UK Register of HIV Seroconverters in order to monitor the transmission of HIV drug resistance. Results will be provided back to the referring HIV clinic in "real time". There will be no charge for this service.

NEWS IN BRIEF

Amprenavir news

As this issue went to press, *AIDS Treatment Update* heard that amprenavir, Glaxo Wellcome's experimental protease inhibitor had failed to gain approval from the European Union's drug licensing authority. The application will be reviewed in six months, when more information on the use of amprenavir in salvage therapy is available.

Glaxo Wellcome recently reported 48 week data from a randomised, open-label, Phase III study. PROAB3006 compared amprenavir with indinavir in a group of 504 nucleoside analogue experienced, PI naïve patients. At entry, median viral load was around 8,000 copies, with the median CD4 count around 400. The study protocol encouraged participants to switch one of their nucleoside analogues at the same time as starting their PI, and 73% did so.

At 48 weeks, by intent-to-treat analysis, 30% of amprenavir recipients had viral load below 400 copies, compared to 46% in the indinavir arm, a statistically significant difference. A fairly high number of people discontinued their allocated study medication early. By week 48, discontinuations were 44% in the amprenavir arm and 36% in the indinavir arm, and the proportions stopping due to adverse events were 18% and 15% respectively.

Amprenavir has been associated with a relatively high drop-out rate in another Glaxo Wellcome study, PROAB3001, which was reported in last month's *AIDS Treatment Update*. Though dosed twice daily, the drug's pill burden of eight large capsules is one of the highest of currently available antivirals.

Whilst these factors count against amprenavir's use in first-line therapy, its

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resistance profile may allow its use as a second-line PI, though the efficacy of such a strategy has not been proven as yet. Similarly, amprenavir has been less strongly associated with the lipodystrophy syndrome than other PIs. Whether this may simply be a factor of its later development is unclear. Abnormal fat redistribution syndrome was reported more frequently in those in the indinavir arm of the PROAB3006 study than the amprenavir arm, (28 events versus eight, a significant difference). However, though toxicity data were gathered prospectively, the study was not designed to measure the relative risk of lipodystrophy between the two regimens. It is possible that differences may be the result of a bias in investigator reporting.

Delavirdine news

The NNRTI delavirdine has also been turned down for European licensing, after its manufacturer Pharmacia & Upjohn made a third application for approval. It's understood that the licensing committee considered that insufficient information on delavirdine's interactions with protease inhibitors had been provided by the company.

In October, Pharmacia & Upjohn sold the marketing rights to delavirdine, to Agouron/Warner Lambert. Agouron/Warner Lambert also produce the PI, nelfinavir, though the drug is marketed by Roche in Europe.

US no to adefovir

The US Food and Drug Administration's Antiviral Advisory board has voted against Gilead's application for a US licence which would have allowed their anti-HIV drug adefovir to be prescribed to people requiring salvage therapy. The committee voted against approval on the grounds of adefovir's risk of kidney toxicity (approximately 5% of people previously treated with adefovir appear to have sustained permanent kidney damage at a dose of 120mg/day), and because Gilead presented only one study which convincingly demonstrated virological efficacy. Though test-tube studies have suggested that adefovir may have an enhanced antiviral effect against 3TC-resistant virus, this was not considered an adequate reason to issue a marketing licence.

It is unclear how this decision will affect the availability of adefovir in the European Union, where Gilead have stalled on plans to open an expanded access programme. The company may now decide to shelve adefovir and concentrate on the development of their 'second generation' nucleotide analogue, tenofovir instead.

F-ddA dropped

Development of lodenosine (F-ddA), a new nucleoside analogue, has been terminated after a number of recipients developed serious liver and kidney problems on the drug, and one died. Though it is unclear that lodenosine was the cause, the drug's manufacturers US Bioscience have withdrawn the drug from further study. Lodenosine was available in the UK through participation in a clinical trial.

Nevirapine news

Persistently aired concerns about the potency of the NNRTI nevirapine in people who begin treatment with high viral load may have been finally dispelled after manufacturer Boehringer-Ingelheim presented new data at the 7th European Conference on Clinical Aspects and Treatment of HIV Infection held in Lisbon in October.

73 people were randomised to receive AZT/3TC/nevirapine in a placebo-controlled study. Mean viral load was 150,000 copies and mean CD4 count was 82 on entry to the study. After 48 weeks follow-up, 49% of nevirapine recipients had viral load below 50 copies. In a small sub-group of 24 people with viral load greater than 500,000 copies at baseline, 54% achieved viral load below 50 at this point.

HIV & pregnancy

Mother-to-baby transmission of HIV has fallen dramatically in the UK, according to a survey published in the *British Medical Journal*. The estimated transmission rate fell from a high of 20% in 1993 to 2% in 1998. Between 1995 and 1998 use of antiretroviral therapy increased each year, to 97% of live births in women known to be infected by 1998.

Lipodystrophy news

Body fat alterations (lipodystrophy) were seen just one year after people with primary HIV infection began HAART, warned Australian doctors at a European medical conference held in Lisbon in October.

Dr John Miller of Australia's National Centre of HIV Epidemiology reported that half of 38 people who began HAART shortly after HIV infection had developed self-reported body fat changes within a thirteen month follow-up period. In two cases, individuals were receiving d4T/3TC/nevirapine rather than a PI-containing regimen. These findings are likely to challenge the view that lipodystrophy may be a consequence of long-term HIV infection, low CD4 count or many years of antiretroviral therapy.

LIPO STUDY

A small pilot study investigating the effects of a physical exercise programme on the levels of circulating lipids in people with HIV-related lipodystrophy is recruiting at Liverpool's John Moores University and at a second site in Manchester. Participants must be willing to commit themselves to ten weeks of exercise. For details contact Simon Jones on 0151 283 3801.

NAM FORUM

The next NAM Forum, on Viral Hepatitis & HIV, takes place on Monday 24th January at the University of London Union, Palms Rooms, 4th Floor, Malet Street, London WC1 from 7pm to 9pm. Admission is free and a sign language interpreter is available.

AUDIO ATU

An audio tape version of this newsletter is available. Please contact Helen or Claire on 020 7627 3200 for details.

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

expanded access scheme A programme which allows access to an experimental drug outside clinical trials for people in need

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

lipid A general term for fats in the blood

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

nadir The lowest point to which viral load falls after starting anti-HIV drugs

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

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

salvage therapy Any treatment regimen used after earlier regimens have failed

treatment naive Never having taken anti-HIV treatments before

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

BARRY JACKSON

NAM's Director, Colin Nee, remembers Barry Jackson who died on 25th October 1999: When I say Barry was the epitome of a good trustee, I mean he was extremely committed, challenging, mature, supportive, funny and he really knew his stuff. As a staff member here, I found him inspiring in the sense that the pride he took in NAM and what it does really shone. To say that the staff and trustees here will miss him is an understatement. He was a trustee for over 8 years and has played a crucial role in NAM's success.

He had long been committed to promoting the arts and to developing gay rights. In terms of gay community concerns, his presence or influence was everywhere, from the London Lesbian & Gay Switchboard where he was a long-term volunteer to helping to organise funding for those victimised in the Soho bombing. He was Chair of the Mike Rhodes Trust, which runs annual awards to celebrate the promotion of greater understanding of lesbian & gay life, and in 1999 he helped raise £500,000 to create the annual London Mardi Gras, replacing Gay Pride.

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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.

The publishers have taken all such care as they consider reasonable in preparing this newsletter. But they will not be held responsible for any inaccuracies or mis-statements of fact contained herein. Inclusion in this newsletter of information on any drug or clinical trial in no way represents an endorsement of that drug or trial. This newsletter should always be used in conjunction with professional medical advice.

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