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Mega-HAART

Are multi-drug combinations the best option for salvage therapy?

BY ANNA POPPA

Mega-HAART is the term being used to describe a relatively new approach to the use of HIV drugs in people who have a lot of experience of taking antiretrovirals. Treatment involves taking a large number of drugs, typically six or more and sometimes as many as nine, a strategy which coined the alternative nickname, kitchen-sink therapy.

Lowering viral load to undetectable levels is easiest in people who are new to treatment. As subsequent drug combinations fail to keep HIV suppressed, drug resistant virus populations can emerge to become the dominant strains in the body. Because all currently available classes of drugs are affected by cross-class resistance (where resistance to one drug causes resistance to others in the same class), compiling effective regimens becomes more and more difficult as more treatments are used, because fewer and fewer viable options remain.

CONFLICTING OPINIONS

Proponents of mega-HAART suggest that in these circumstances even a viral population which is resistant to several different drugs is still likely to retain a degree of vulnerability to others. If potency is great enough (because such a large number of drugs are being taken at once) then it should be possible to overcome partial resistance. Interactions between the different components – it is assumed – will result in blood levels being boosted beyond the norm.

However, mega-HAART is not without its critics. In their view, the extent of prior drug experience means a recipient of a seven drug regimen may be exposed to the toxic effects of all seven drugs but gain a benefit from only two or three. And as we report on page 4 of

this issue, large drug combinations can throw up unforeseen interactions which may result in a net loss of anti-HIV activity rather than a gain.

EARLY RESULTS FROM UK STUDY

The greatest success using mega-HAART regimens has been reported by Dr Mike Youle in a study involving patients at London's Royal Free Hospital and the Royal Sussex County Hospital, Brighton¹. Preliminary results were presented at a salvage therapy conference in Toronto in May.

This observational, open-label study included participants who had taken a protease inhibitor (PI)-containing regimen for at least six months. 85% began a mega-HAART regimen following a drug holiday off all antiretroviral treatment for at least 4 weeks. Everyone received a backbone of efavirenz, and the majority hydroxyurea, two PIs (usually ritonavir and indinavir), and nucleoside analogues (usually 3TC and ddI), and were observed closely, with both viral load and CD4 testing plus monitoring for side-effects (especially lipid levels) every 2 to 4 weeks.

Results were presented from 63 people, followed for 27.5 weeks on average. On entry, the average

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Salvage therapy

viral load across the group was 63,300 copies (though half were above 750,000), and average CD4 count was 128 cells. Participants in this study were less drug-experienced than in other mega-HAART studies. The average number of drugs which had been taken previously was 5, but the majority (54 of 63) had not taken an NNRTI before, which means they would be expected to respond well to efavirenz, at least over the short-term.

Over 28 weeks follow-up, 13 people stopped all treatment, 3 of these restarting within a month. Of all the reasons for stopping, the most common were desire on the part of the patient to interrupt or stop therapy (in 10 cases), and central nervous system (CNS) side-effects (also in 10 cases). The latter is known to be a common side-effect of efavirenz and 8 of those affected switched this drug for nevirapine with no subsequent CNS symptoms. Aside from this, the most common side-effect seen was nausea. Toxicity related to the use of hydroxyurea was mild, causing 4 people to stop that drug, and 4 to reduce their dose. (Further information on this study is found in the sidebar on this page).

MORE ON UK STUDY

In a sub-analysis including 30 people, the effect of treatment on levels of fats in the blood was investigated. Higher levels were seen at higher doses of ritonavir, and this was managed by lowering the ritonavir dose and raising the dose of indinavir. Emphasis has been placed on the 'Therapy Support Package' offered to all participants, (though Mike Youle described it as "what should be offered to all patients"). This involved a combination of intensive monitoring, access to a dedicated salvage clinic nurse, pharmacists, patient advocates, an emergency telephone service, written information, and additional medicines such as anti-nauseants, anti-diarrhoeals, sleeping tablets and an anti-psychotic to manage possible side-effects, (all prescribed before treatment started).

PREDICTING RESPONSE

After 36 weeks, 62% of the group had viral load below 50 copies, with a further 21% above 50 copies but below 400. The average rise in CD4 was 120 cells, which seems a little low given the extent of viral load suppression, and is probably the result of hydroxyurea's tendency to slow T-cell production.

For each additional log of viral load on starting treatment, the chance of falling below 400 copies fell by 40%, and for each additional month off treatment before starting therapy, the likelihood was increased by 15%.

IS THIS RESPONSE TYPICAL?

Researchers from Canada presented new information about a group of 82 people receiving mega-HAART who had been followed for an average of 12 months². In this group, prior use of treatments had involved 7 drugs on average, taken for an average duration of 45 months. The new, multi-drug regimen included up to 9 drugs: up to 4 nucleoside analogues, hydroxyurea, 2 PIs, and 2 NNRTIs.

Average viral load at entry was 50,000 copies and average CD4 count was 185 cells. After 30 weeks treatment, 45% sustained viral load below 400 copies. The results of phenotypic resistance testing are available for 60 people and suggest that better viral load responses were seen in those who were sensitive to at least three drugs in their mega-

HAART regimen when beginning treatment, and in those who began with lower viral load. Note that in this study, participants did not take a drug holiday. Side-effects were not well described but were referred to as frequent by the study investigators.

RESULTS WITH MORE DRUG EXPERIENCE

Further data were presented by researchers from New York, who observed 35 people on mega-HAART³. Treatment experience was greatest in this cohort: average prior number of antiretrovirals was 9, taken for an average duration of 73 months. 9 were NNRTI naïve.

Participants took between 6 and 8 drugs, including 2 or 3 nucleoside analogues, hydroxyurea, 2 PIs, and 1 NNRTI. Average viral load on starting treatment was 21,016 and average CD4 count was 153 cells.

One person stopped his medication after two weeks because of low white cell count (probably due to hydroxyurea) and intolerance of ritonavir. Of the remaining 34, 39% sustained viral load below 40 copies for a follow-up period of 7 months. CD4 counts rose by around 100 cells.

Overall, treatment was reported to be well tolerated, though all participants experienced diarrhoea. Other than ddl, which had to be taken as a separate dose, all other drugs were dosed twice daily. Mega-HAART pill burdens can be rather high, however – up to 35 per day in this study.

Though most had no break in treatment, 8 people had a drug holiday of between 1 and 3 months before starting their multi-drug regimen. This is a small number, but no difference in response was seen between those who took a break and those who did not, despite baseline viral load being slightly higher in the holidaying group.

Those who began with prior experience of NNRTIs actually did better in terms of effect on viral load and CD4 than those who had not taken an NNRTI before. This is an atypical finding, however, and may be due to the small numbers involved in the analysis.

THE GERMAN COHORT

The fourth mega-HAART cohort is in Frankfurt. Their experiences were reported at a conference in Glasgow last November⁴. 37 people, most of whom took 6 or 7 drugs, were followed for an average of 8 months. Average viral load at baseline was 320,000 copies and average CD4 count was 110. 29 of the 37 achieved viral load below 500 copies, though 7 subsequently rebounded to detectable levels. CD4 rose by 95 cells on average.

A separate analysis involving 20 people was performed to investigate the relationship

between phenotypic resistance at baseline and response to therapy. Unsurprisingly, those sensitive to the greatest number of drugs were most likely to achieve undetectable viral load. However, partial responses were seen even in people with high levels of drug resistance

The group also observed that a small group of people who took a drug holiday before starting mega-HAART experienced a switch in their viral phenotype during this period from highly drug resistant to drug sensitive⁵.

MORE ON DRUG HOLIDAYS

At the meeting in Toronto, the same researchers presented further new information on this subject⁶. 94 people who received mega-HAART consisting of more than 6 drugs were followed for an average of 12 months. Two thirds of those who achieved viral load below 500 copies were found to be sensitive to at least 4 drugs in their regimen at baseline, whereas a little over two thirds of those who did not reach this cut-off were sensitive to no more than three drugs.

In a sub-group of 39 people who took a drug holiday prior to mega-HAART, resistance tests were performed before and after the holiday, and showed that in the majority (26 of the 39), the viral population shifted from drug resistant to wild-type (the name given to virus seen in people who've taken no anti-HIV drugs), during this period. After 8 weeks treatment, the drop in viral load was greater in those who had a shift from resistant to wild-type (2.9 log) than those without a shift (0.78 log). After 24 weeks, 18 of 25 shifters had viral load below 500 copies compared to 2 of 11 who had no shift.

Whilst off treatment, those with a shift to wild-type virus saw their viral load rise faster, and their CD4 count fall more rapidly, than those whose viral population remained predominantly resistant. While this supports the proposition that resistant viruses tend to grow more slowly than wild-type and cause less depletion of CD4, it also suggests that people who stop their treatment should be very closely monitored.

Biologically, it seems unsurprising that viral populations switch from drug-resistant to drug-sensitive during a break from treatment – without the 'selective pressure' which the drugs exert on the virus, resistant strains will lose their competitive advantage over wild-type strains which tend to be more virulent. Resistant viruses will be 'archived' however, as minority sub-groups which might grow back once drugs are re-introduced. These mega-HAART studies should eventually provide more information about whether this happens.

There may be other factors which make drug holidays attractive however. Dr Graeme

Moyle of London's Chelsea and Westminster Hospital said "Drug holidays are used quite a lot at the Chelsea and Westminster. They allow the P450 system [which is involved in the metabolism of many antiretrovirals] to cool down a bit so the new regimen won't be hyper-metabolised."

VIEWS OF UK DOCTORS

All of the mega-HAART studies reported so far are observational rather than comparative. The data are preliminary and it is not known whether this approach will prove better, worse, or no different from other current salvage options in the short or long term. Other alternatives, such as regimens involving fewer drugs, or remaining on a regimen which is failing to suppress viral load are discussed elsewhere in this issue.

Amongst members of *AIDS Treatment Update's* Medical Advisory Panel, we found a range of opinion. Professor Brian Gazzard of London's Chelsea and Westminster Hospital said, "Salvage studies are extremely difficult to interpret. They are heterogeneous in terms of patients entering the study, some of whom are resistant to drugs, some of whom are not. Others have taken very few drugs in terms of being compliant, and others have had sub-optimal doses and so have never really been exposed to the drug. Therefore it is hardly surprising that the outcome from these studies is very different."

With the use of resistance tests he continued, "It would have been possible to predict which agents were likely to work. Instead of having to use 7 or 8 drugs, 2 or 3 could have been used with equal effect."

Professor Tony Pinching from St Bart's Hospital, London, agreed on the need to consider these studies in the light of information on resistance, adherence and drug level monitoring. At present, he said, they "lack the individualised approach to treatment that a lot of the resistance and adherence data seems to be steering us towards".

This was echoed by Dr Barry Peters, of St Thomas' Hospital, London, who emphasised the importance of drug level monitoring in people whose drugs are failing, saying "There are a lot of issues to sort out before deciding if they really are a salvage patient".

Dr Mike Youle, lead reporter on the UK mega-HAART study felt, "There is a paucity of understanding of the benefits of salvage therapy by both purchasers and providers. There is too much focus on drug costs and an assumption that multi-drug combinations carry unacceptable tolerance or toxicity. Surrogate marker improvements and lack of clinical progression show the potential benefits and appear to be sustained."

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KEY CONCLUSIONS

- ◆ Mega-HAART combinations, which include large numbers of anti-HIV drugs, are being used to manage rising and high viral load by people with a lot of experience of different antiretrovirals. Short-term studies suggest these multi-drug regimens offer a reasonable chance of reducing viral load to below detectable levels.
- ◆ Some mega-HAART studies appear to have produced better responses than others, and it's unclear why this is so. Possible contributing factors include the extent of prior antiretroviral exposure, taking a drug holiday prior to mega-HAART, and the availability of support when treatment begins.
- ◆ Mega-HAART will only be suitable for people who are motivated to manage a demanding pill-taking schedule. Side-effects occur frequently amongst mega-HAART recipients, though these may be managed by switching components of the regimen. An individualised approach to treatment failure is important.
- ◆ The effects of taking a break from treatment before starting a new regimen are not well understood. Their impact on quality of life is likely to be an important consideration for some people.

LARGEST SALVAGE STUDY SO FAR

At the recent salvage therapy workshop, held in Toronto in May, the preliminary results of the largest prospective, randomised study of 'salvage therapy' so far were reported. This American study, code-named ACTG 359, involved 277 people who had previously taken nucleoside analogues and indinavir, and experienced a rebound in viral load. At entry, the average period of prior indinavir use was 14 months. Average viral load level was 31,476 copies and average CD4 count was 229 cells. All were NNRTI naïve. Participants were allocated at random to one of these arms:

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

Treatment allocation was partially blinded. Though participants knew which protease inhibitors (PIs) they were receiving, they were unaware of whether they were receiving delavirdine, adefovir, or both alongside. (A major side-effect of adefovir is kidney damage, and all participants took an additional treatment, L-carnitine, to protect against this.)

The viral load results observed after 16 weeks were disappointing. Overall, 30% of participants had viral load below 500 copies at this point, and CD4 counts increased just 19 cells on average. When the researchers compared responses across the six arms, they found no significant difference between the ritonavir-containing and the nelfinavir-containing arms.

In a pooled analysis of the triple drug arms, delavirdine recipients fared better than those who received adefovir instead – not so surprising given that participants were new to NNRTIs (so would be expected to respond well to delavirdine), but had experience of nucleoside analogues (which can produce a poor response to adefovir, see *AIDS Treatment Update* 72).

However, the four drug arms did not perform

any better than those where delavirdine was taken without adefovir. Subsequent drug interaction studies found a negative interaction between the two drugs, with adefovir causing delavirdine levels to fall by half. This decrease affected saquinavir absorption, which is normally boosted by the presence of delavirdine.

KEY CONCLUSIONS

Despite its disappointing outcome, this study has provided some useful lessons:

- ◆ It seems the combination of delavirdine with adefovir should be treated with caution for the time being, and may require a dose adjustment at the very least. Both are used relatively infrequently in the UK at present because of their experimental status.
- ◆ People whose viral load on indinavir rebounds to a level similar to that seen in this trial (30,000 copies) are unlikely to see their viral load fall back to undetectable levels by switching to new PIs plus one or two other new drugs. A combination containing a larger number of drugs (termed mega-HAART) may provide a greater chance of achieving this goal at present. (People who switch off their failing regimen earlier, as soon as viral load begins to rebound, may do better).
- ◆ First-line use of NNRTIs by people with PI and nucleoside analogue experience may be problematic if the other components of the regimen provide only weak anti-HIV activity. In these circumstances, the loss of benefit from a further drug class seems the most predictable outcome.
- ◆ Pharmacokinetic studies, which evaluate how drugs are processed in the body, may have an important role in the future selection of multi-drug regimens. In ACTG 359, complex and unexpected drug interactions contributed to treatment failure, but were not identified until after failure had occurred.

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Viral fitness & resistance

What are the implications for the immune system?

BY KEITH ALCORN

Harvard Institute researchers have discovered that HIV which develops resistance to the protease inhibitor nelfinavir is significantly slower to replicate than HIV which has never been exposed to drugs before. It is also slower to replicate than virus which has developed resistance to other protease inhibitors such as ritonavir and indinavir.

Dr Richard D'Aquila and colleagues tested viruses with specific mutations known to be associated with drug resistance to see how quickly they replicated in the test tube¹. They found that virus with the mutation called D30N, which is usually the first sign of nelfinavir resistance, grew 30% more slowly than virus not exposed to any drugs – termed wild-type virus. In comparison, viruses with the common saquinavir resistance mutation L90M grew only slightly less slowly than wild-type virus, and mutants resistant to indinavir grew at the same rate as wild-type.

Similar findings were reported by two teams at the Chicago Retroviruses Conference in February. A joint Franco-American team reported that virus highly resistant to saquinavir did not cause T-cell depletion in mouse experiments after 28 days study, despite low level viral replication². In two mice with the same viral load, the only factor which was significantly associated with the size of the CD4 count was the fitness of the virus, not the level of the viral load.

Beyond animal models, another French team reported on the loss of viral fitness (the ability to replicate) in 14 people receiving protease inhibitors who experienced viral rebound whilst maintaining high CD4 counts³. During average follow-up of 20 months, viral fitness declined by 28% despite an average viral load increase of 1.4 log copies. The degree of decline in viral fitness showed a strong inverse association with CD4 increase; in other words, the less fit the virus after 20 months, the bigger the CD4 increase.

These finding suggests that rebounding viral load levels might not always give an accurate prediction of the long-term risk of CD4 decline and illness, and this theory is borne out by several large studies of people on HAART, which show that a significant proportion of people who experience viral rebound will maintain high CD4 counts for long periods, despite rising viral load.

They also suggest that some protease mutations make HIV less harmful to CD4 cells even when viral load is rising, and that rather

than restricting depletion of CD4 cells or lengthening their lifespan (as suggested by other research groups), protease inhibitor therapy may preserve CD4 cell populations by reducing the pathogenicity (virulence) of HIV.

Another drug-associated mutation which has been shown to reduce HIV's replicative fitness is the M184V mutation seen with 3TC resistance. The Colate study is investigating the effects of maintaining 3TC after virological failure (see *AIDS Treatment Update* 77).

IMPLICATIONS FOR CURRENT PRACTICE

These findings highlight the discordance between virological and immunological responses to HAART that has been widely reported. They also raise questions about which events should trigger changes in therapy, and how to manage such changes.

For example, if you are taking nelfinavir, is it necessary to switch from the drug immediately upon virological failure? The D30N mutation is almost always the first to appear in the emergence of nelfinavir resistance, and does not commonly confer cross-resistance to other PIs. If that is the case, it might be beneficial to remain on nelfinavir despite rebounding viral load, in order to maintain a viral population which is less fit than the wild-type virus which would be expected to return in the absence of nelfinavir. A less fit virus population may result in longer maintenance of any CD4 increase which was gained whilst viral load was suppressed. This option may be attractive to some people who find that a nelfinavir-containing combination suits them.

Some doctors suggest that maintaining nelfinavir and 3TC after loss of viral suppression may be as valid an approach to salvage therapy as any of the other strategies currently in use (discussed in the other articles in this issue). However, there are no long-term data to support this approach. It may be safer to assume that any virological rebound should be treated in the same way, i.e. with an early switch to a new regimen, regardless of the drugs involved.

In the context of salvage therapy on the other hand, where other options are extremely limited, early switching may be impractical. Remaining on an existing regimen despite a rising viral load may be a useful alternative for some until drug combinations involving new kinds of antiretrovirals are in closer reach.

FUTURE THERAPIES

The NAM/BHIVA website aidsmap.com contains updated information on all experimental antiretrovirals, including a number of drugs from new classes which target HIV in novel ways.

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ddl news

Two alternative formulations of ddl are now available on named patient basis in the UK for people who can't tolerate standard ddl tablets. Reduced mass 200mg tablets, which contain less of the buffer solution responsible for diarrhoea and other gastrointestinal side-effects often experienced with ddl, will be made available to anyone having problems tolerating four 100mg tablets daily. This formulation is unlikely to be licensed in Europe until the last quarter of 1999.

A powdered form of ddl for making an oral solution, previously available only for use in children, is also available for adults who have difficulty in tolerating the tablet form of ddl. In both cases, doctors should contact the Medical Department at Bristol-Myers Squibb.

In a separate development, the European Union has approved the use of the standard formulation ddl as a once daily treatment. Though this dosing schedule has been in use for some time, ddl was formally licensed as a twice a day medicine. This approval makes ddl the first once daily nucleoside analogue to receive European approval.

Lipid news

Doctors from St George's Hospital in London have reported on the occurrence of lipodystrophy in a small group of people being treated with a nevirapine-containing combination. Lipodystrophy is the name given to the changed body fat distribution which has emerged as a side-effect of anti-HIV treatment, most commonly involving protease inhibitors. Their letter appeared in the 7th May issue of the medical journal *AIDS*.

The group interviewed 58 people in their clinic who were receiving nevirapine (an NNRTI) with two nucleoside analogues for at least six months. Nine (16%) either self-reported or were assessed by clinic staff as having experienced changed body shape consistent with lipodystrophy. The most common manifestation was central obesity. All nine had sustained undetectable viral load as a result of their treatment.

At April's 3rd International Conference on Nutrition and HIV Infection in Cannes, a number of researchers presented data suggesting that the use of some nucleoside analogues is a significant risk factor in the development of lipodystrophy, particularly d4T

and 3TC. A summary report of the meeting is available on Medscape's HIV website at <http://www.medscape.com/Medscape/HIV>.

Efavirenz licensed

On June 1st, efavirenz was given formal approval for marketing in the European Union and is now available on prescription for use in combination with other antiretrovirals. Efavirenz is a once daily drug from the NNRTI class. For more on efavirenz in people new to treatment, see *AIDS Treatment Update* 76. Issue 72 reviewed the use of the drug in people with prior treatment experience.

Manufacturers DuPont Pharma have priced efavirenz (an NNRTI) at a level equivalent to the protease inhibitor indinavir, and significantly above the cost of the only other licensed NNRTI, nevirapine.

Viagra news

In a letter to the medical journal the *Lancet*, doctors at the Royal Bolton Hospital have reported the death of a man who was being treated with protease inhibitors and the anti-impotence drug *Viagra* (June 12, 1999 issue).

The case involved a 47 year old man (a heavy smoker for 30 years) treated with ritonavir and saquinavir for over a year, who had been prescribed *Viagra* for erectile dysfunction. Having experienced no untoward effects on eight prior occasions, the man was admitted to hospital suffering severe chest pain soon after taking a 25mg dose of *Viagra*. He had a heart attack and died the next day.

As we reported in our last issue, just two months ago, Pfizer issued new information concerning potential interactions between *Viagra* and other drugs. They advised a dose reduction to 25mg if taken alongside protease inhibitor treatment, and that a single 25mg dose should not be exceeded in any 48 hour period. Similar advice applies when the drug is taken with the anti-fungals ketoconazole, itraconazole or with erythromycin.

Protease inhibitors and *Viagra* are metabolised through a common enzyme in the liver, P450 3A4. Consequently, PIs can cause blood levels of *Viagra* to rise, increasing the risk of potentially serious side-effects. It is not known if a drug interaction played any role in the death of this man, and it should be remembered that heart attacks are not uncommon amongst smokers of his age.

NAM FORUM

On July 26th, Dr Graeme Moyle from London's Chelsea & Westminster Hospital will speak at a NAM Information Forum on 'Fat Changes and Lipodystrophy', presenting the latest information from the First International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV held in San Diego in late June. The venue is the Palms Room, 4th Floor, University of London Union, Malet Street, London WC1. Admission is free and forums run from 7pm to 9pm. A sign language interpreter is available.

NAM & how it's funded

Frequently asked questions answered by NAM's director, Colin Nee

What is NAM and what does it do?

NAM's overriding aim is to support the fight against AIDS and HIV with relevant, accurate, independent and comprehensive information. We're a registered charity, all our funds being used to support that main aim. In the UK, we're probably best known for our information on HIV treatment issues but we create and disseminate resources on all aspects of HIV for organisations throughout the world.

What does NAM's treatments information programme consist of?

We are trying to reach as wide an audience as possible by creating a range of differently pitched materials, in different media from hi-tech to no-tech. With one exception, all of these services are free to people in the UK who are directly affected by HIV:

- ♦ free subscriptions to *AIDS Treatment Update* and the monthly *Factsheets* to over 6,000 people with HIV throughout the UK; about 12,000 people read it
- ♦ ATU and factsheets on audiotape for people with sight or reading problems
- ♦ our website, aidsmap.com, run in partnership with the British HIV Association
- ♦ booklets on viral load, nutrition, clinical trials, anti-HIV drugs, treatments information on the world wide web, resistance and introduction to HIV therapy for African communities
- ♦ treatments workshops throughout the UK
- ♦ monthly information forums in London
- ♦ the *HIV & AIDS Treatments Directory*, the world's most comprehensive information resource on the medical aspects of HIV. We sell it to individuals affected by HIV at the subsidised price of £9.95 (almost £50 less than professionals have to pay and well below what it costs to produce). This is the only exception to our policy of providing treatments information materials free of charge to those most affected
- ♦ training and consultancy for organisations
- ♦ before the end of the year, we hope to publish a new treatments training manual for organisations, self-help groups and healthcare professionals.

How do people get the free subscription?

All they need to do is to telephone us on 020 7627 3200 and we will put them on our strictly confidential mailing list. If you know people affected by HIV who don't already get our information, please let them know.

Who funds NAM?

We need to raise £700,000 this year to fund what we believe are vital information services. This is undoubtedly a lot of money and our board of trustees is there to ensure NAM is managed effectively and spends its funds wisely. Of course, we'd love to be able to raise more because there is so much more we could do to expand access to the highest quality information materials, empowering individuals to make the treatment choices that are right for them.

Roughly 35% of NAM's income comes from the fees that professionals and agencies pay to subscribe to our publications and for the training and consultancy. There are four other sources of funding: the Department of Health and London health authorities (31% of the total); pharmaceutical companies (21%); other companies and charitable trusts such as Crusaid and Hysteria (9%) and finally the European Commission (4%).

Doesn't raising money from drug companies compromise your independence?

We receive these grants gratefully but definitely on a no-strings basis. There is no question of companies being allowed to interfere with our editorial stance or influence us in any other way which undermines our independence. Our coverage of treatment issues will remain impartial and fair regardless of whether a particular company does or doesn't fund us. Our medical advisory panel which brings together a cross section of medical opinion underpins this approach. We also make sure this funding is completely out in the open. All our funders are listed on the back of this issue and every issue of ATU.

Is NAM one of the HIV sector giants?

No, I don't think anyone would accuse us of that. NAM is about a sixth of the size of the UK's biggest HIV charity. We rent an office above a restaurant in south London and wedge 12 people into it. We aim to be low on cost but big on impact.

Do you accept donations from individuals?

Absolutely! We welcome support from individuals. Anyone who would like to discuss how to support our work through a single donation or through setting up a covenant or legacy should telephone me on 020 7627 3200. Individual giving can make a huge difference in helping NAM provide better services to more people who need them.

GLOSSARY OF TERMS

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

CNS Central nervous system. The brain, spinal cord and its coverings

comparative study Trial which compares the effects of an action, e.g. a new drug, on two or more groups

cross resistance When resistance to one drug reduces the virological response to subsequent treatment with another drug which has not been taken before

genotype The sequence of proteins which makes a gene

lipid A general term for fats in the blood

log Short for logarithm, a measurement scale often used when describing viral load

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

observational study Trial which reports on an unfolding situation

open-label A clinical trial where both the researchers and participants know who is

taking the experimental treatment. Opposite is double-blind, where neither is aware

phenotype Trait or behaviour which results from changes in genotype

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

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

salvage therapy Any treatment regimen used after an number of earlier regimens have failed

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

wild-type virus Virus found in people who have never taken anti-HIV treatments before

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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
Monday & Wednesday, 6pm - 9pm
All calls charged at local rates.

♦ Body Positive

Treatment Advice: Tue, Wed & Fri 2pm - 7pm
Call Adam, Jo or 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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