

AIDS TREATMENT UPDATE

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Which drugs first?

More light shed on starting treatment with 'protease-sparing' combinations

BY ANNA POPPA

Last summer, *AIDS Treatment Update* reported on an emerging HIV treatment strategy – the use of 'protease-sparing' drug combinations as first-line therapies.

Regimens which do not include a protease inhibitor (PI) have come under the spotlight for several reasons. Though PIs are known to be very potent suppressors of HIV, they are perceived to be demanding in terms of adherence. They have become closely linked with an unexplained syndrome of body and blood fat changes being seen in some people, though it is far from proven that they are the cause of it. Consequently, the timely appearance of new drugs such as efavirenz and abacavir has rekindled interest in other classes.

At the Sixth Conference on Retroviruses and Opportunistic Infections held in Chicago in February, a number of trials investigating the use of NNRTI-based and triple nucleoside analogue combinations reported new information. Though the question of how to start antiretroviral therapy has not been answered conclusively by these studies, they have shed light on some of the controversial areas raised in our earlier coverage in issue 68.

LATEST TRIAL RESULTS

The table which accompanies this article (on page 3) summarises data from several key trials, all of which involve participants who have very little or no prior experience of treatments. In brief, these are:

- ♦ DMP 266-006, which is a head-to-head comparison of efavirenz/AZT/3TC versus indinavir/AZT/3TC versus efavirenz/indinavir
- ♦ Altantic, a head-to-head comparison of d4T/ddI plus either nevirapine or 3TC or indinavir
- ♦ CNA 3005, a head-to-head comparison of

abacavir/AZT/3TC versus indinavir/AZT/3TC

- ♦ CNA 3003, which compares abacavir/AZT/3TC with AZT/3TC alone
- ♦ Virgo, which investigates the use of nevirapine in combination with d4T/ddI
- ♦ An EU/South African study of AZT/3TC with or without delavirdine.

HEAD-TO-HEAD COMPARISONS

The DMP 266-006 study has been important in establishing the value of NNRTI-based combinations. After 48 weeks on treatment, those who received efavirenz with AZT/3TC were more likely to have undetectable viral load, than those who received either of the indinavir-containing combinations.

This benefit was observed regardless of how the data were analysed, i.e. whether data from those who stopped their allocated treatment part way through were included (called an intent to treat analysis) or excluded (an observed data analysis). An intent to treat analysis provides an unbiased measure of a drug's efficacy (see *AIDS Treatment Update* 73).

With consideration of the data from this trial, and from other efavirenz studies, the European drug licensing body, the Committee for Proprietary Medicinal

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Products (CPMP), have recently recommended marketing approval for efavirenz within the European Union. It is likely that efavirenz will become available on prescription within the next few months.

As the table shows, the preliminary report from the Atlantic trial did not include a statistical analysis of the data. This means that it is not yet known whether the differences in viral load or CD4 response between people who began treatment with a triple NRTI regimen, an NNRTI-based regimen, or a PI-based regimen, are significant or could instead be due to chance. Participants will be followed for three years, with structured switches in therapy allowed if the initial combination fails.

Glaxo Wellcome's CNA 3005 trial is a blinded study where all participants follow food and fluid requirements for indinavir and receive 16 tablets per day. (The blinding means all participants take both regimens; one is active drug and the other placebo). After the first 24 weeks of treatment there was no difference between the two arms, with two thirds of participants below 400 copies at that point.

HIGH VIRAL LOAD

One of the key criticisms that has been levelled against PI-sparing combinations is that they are less potent than regimens that contain a PI, and that they should not therefore be used in people who begin treatment when their viral load is quite high, for example above 100,000 copies.

In the 006 trial, however, efavirenz/AZT/3TC continued to outperform the other two arms when the data were separated to look at responses in those who began with viral load above or below 100,000 copies. In fact this study found that both indinavir-containing combinations were less effective when used at higher viral load. As Dr Graeme Moyle, of London's Chelsea and Westminster Hospital points out, several studies have suggested that all drugs are less effective at higher viral loads. For example, the SPICE trial, (which compared a four drug dual PI combination with two three drug PI-containing combinations, and with a combination of two PIs), found the four drug regimen studied to be more effective than either three drug regimen it was compared against in people with higher viral load.

The Atlantic trial on the other hand, does not provide useful information on this question. Amongst those recruited to the study, average viral load was around 15,000 copies, a relatively low value. Indeed, several observers have commented that people with viral load and CD4 in this range (average CD4 was 450) might be better off starting treatment later.

In CNA 3005, there was no difference between the efficacy of the PI-containing and PI-sparing combinations in people with baseline

viral load above or below 100,000 copies. However, in another trial investigating abacavir plus AZT/3TC this was not the case.

In the CNA 3003 study, abacavir/AZT/3TC suppressed viral load to less than 400 copies in 61% of recipients after 48 weeks of treatment. In a subset of 18 people who began this combination with viral load above 100,000 copies, the response was less good – a third had viral load below 400 copies after 48 weeks. Though the study was not able to reach a clear conclusion on this issue given the small number of participants from which the data are derived, some commentators have nonetheless cautioned against the use of this particular PI-sparing combination with high viral load until more data are available.

Amongst participants in the Virgo study, the subset who began treatment with viral load above 100,000 copies is again very small (13 people). The likelihood of having viral load below 50 copies after 24 weeks appears lower in this group than that seen in the study overall, though the difference may be due to chance – no firm conclusions can be drawn.

As we reported in issue 68 however, other studies of nevirapine-containing combinations, (e.g. the UK named patient programme), have not found a clear association between high baseline viral load and poorer viral load response. The results of an Italian study, ISS 047, have recently been published. It looked at the efficacy of AZT/ddl with or without nevirapine in untreated people with advanced disease. Those who received two drugs were very unlikely to have viral load below 400 copies after 48 weeks treatment if their starting value was above 250,000 copies. This was not the case for those with high viral load who received all three drugs.

Similarly for delavirdine, the last trial which features in our table largely supports an earlier study which investigated the combination of delavirdine/AZT/3TC in (mostly) untreated people called Protocol 0021 Part II (see issue 68). The rather high median baseline viral load amongst participants in this second study (200,000 copies), suggests that this combination too can be considered for use at viral load levels in this range.

IMMUNE RESTORATION

The majority of data on the ability of anti-HIV therapies to restore lost immune capacity concern PI-containing regimens. In comparison, relatively little is known about the effect which treatment with PI-sparing regimens might have on the immune system, apart from changes in absolute CD4 levels.

In the Virgo study, the use of nevirapine with d4T/ddl was associated with a rapid increase in both naïve and memory CD4 cells, followed by

DELAVIRDINE ACCESS

Delavirdine was recently considered for accelerated approval in Europe by the CPMP. Approval was not given because the panel required more information on the use of the drug with protease inhibitors. It is expected that Pharmacia and Upjohn will re-apply in September. Until then, a named patient programme continues to provide delavirdine free of charge to applicants who meet the inclusion criteria.

WHAT'S KNOWN ABOUT PI-SPARING COMBOS?

Six trials which have reported new information about 'PI-sparing' combinations are summarised here. Almost all the people who took part in these trials had no prior experience of taking anti-HIV drugs, and so the results cannot be applied to people who have taken treatments before. For each trial we list its name (Column 1); the drug combinations studied (Column 2); key characteristics of the trial participants, including the average starting viral load and CD4 values (Column 3); the length of time for which participants had been followed for which results were reported (Column 4); and the outcomes reported (Column 5) – these are expressed respectively with regard to Column 2, i.e. results are listed arm by arm in the order written in Column 2.

Trial	Combination	Participants	Follow-up	Outcome
DMP 266-006	EFV/AZT/3TC vs IND/AZT/3TC vs EFV/IND	Baseline VL 58,884. Baseline CD4 345. 3TC, NNRTI, PI naïve. 148-154 people per arm.	48 weeks	71%; 48%; 54% below 400 and 65%; 43%; 48% below 50 (ITT NC=F). 98%; 86%; 84% below 400 and 90%; 79%; 74% below 50 (OD). CD4 rise 175-200 cells per arm.
Atlantic	IND/d4T/ddl vs NVP/d4T/ddl vs 3TC/d4T/ddl	Baseline VL 15,849. Baseline CD4 450. Treatment naïve. 68-88 people per arm.	24 weeks	74%; 69%; 71% below 500 and 71%; 67%; 56% below 50 (ITT). 91%; 89%; 80% below 500 and 83%; 85%; 64% below 50 (OD). CD4 rise 100-150 cells per arm.
CNA 3005	ABC/AZT/3TC vs IND/AZT/3TC	Baseline VL 63,000. Baseline CD4 360. Treatment naïve. Approx. 187 people per arm.	24 weeks	65%; 65% below 400 and 45%; 42% below 50 (ITT). 85%; 87% below 400 and 63%; 61% below 50 (OD). CD4 rise 100 cells per arm.
CNA 3003	ABC/AZT/3TC vs AZT/3TC	Baseline VL 31,623. Baseline CD4 450. Treatment naïve. Approx. 62 people began on 3 drugs.	48 weeks	61% of those who began on 3 drugs below 400 and 56% below 50 (ITT). CD4 rise 150 cells per arm.
Virgo	NVP/d4T/ddl	Baseline VL 31,623. Baseline CD4 415. Treatment naïve. 60 people.	24 weeks	85% below 500 and 66% below 50 (ITT). 90% below 500 and 70% below 50 (OD). CD4 rise 162 cells.
N/A	DLV/AZT/3TC vs AZT/3TC	Baseline VL 199,526. Baseline CD4 211. Treatment naïve. 73-76 people per arm.	54 weeks	72% below 400 in 3 drug arm. CD4 rise 134 cells in 3 drug arm.

KEY:

ABC = abacavir, DLV = delavirdine, EFV = efavirenz, IND = indinavir, NC=F = non completer equals failure analysis, NVP = nevirapine, OD = observed data analysis, ITT = intent to treat analysis, VL = viral load

NOTES:

Allocation of treatment was blinded in CNA 3005 and in the delavirdine study (bottom row), so neither investigators nor participants knew who was taking which regimen. In the other trials, participants did know which treatments they were taking. Blinded studies are less open to bias. In DMP 266-006, there were more discontinuations for IND/AZT/3TC (rates were 25%; 42%; 35%). In Atlantic, NVP and ddl were given once daily. Statistical analysis has not yet been performed. In CNA 3005, AZT/3TC was given as *Combivir*. Differences in outcome are not significant. In CNA 3003, open-label ABC was offered to dual NRTI arm after 16 weeks. In Virgo, there is no comparison arm.

NAM FORUM

The Information Forum on Monday, April 26th is on 'Starting anti-HIV treatment', and will feature a panel of doctors and people with HIV who will discuss different approaches to beginning treatment.

The venue is the Palms Room, 4th Floor, University of London Union, Malet Street, London WC1, and the forum runs between 7pm and 9pm. Entry is free, all are welcome and a sign language interpreter will be available.

a plateau in the number of memory cells and a continued, slower increase in naïve cells. (The pattern typically seen in HAART-treated patients is an initial rise in memory cells and a slower rise in naïve cells).

A team of French researchers have reported on the recovery of immune function in 35 people who have been successfully treated for 1-3 years with a combination containing either one PI and 2RTIs, or 3RTIs. (The authors do not specify whether this means NNRTIs or nucleoside analogues). However, they found no difference in the extent of the increase in CD4, or the ability of the immune system to mount a response to a range of antigens, between the two types of treatment.

A recent report in the medical journal *AIDS* has added some less positive findings on this subject. The INCAS study compared nevirapine/AZT/ddl with nevirapine/AZT and with AZT/ddl. Subsequent follow-up of a subset of 29 participants from the Netherlands, who were divided between the trial arms and had comparable baseline viral load and CD4 levels, found that increases in the number of memory and naïve CD4 cells occurred only over the first eight weeks of treatment. After two years, the number of naïve cells was not significantly above the starting value even in those receiving triple therapy.

Those whose viral load was suppressed to undetectable levels for the two year period were more likely to see an increase in both memory and naïve CD4 cells compared to those with detectable viral load. However, the relationship between maximally suppressed viral load and an increase in both CD4 subsets was not easy to predict. With so few data, conclusions can only be speculative. It seems likely that more robust comparisons between different regimens will not be possible until we have data on immunological response from some of the larger 'strategy trials' currently being planned (see *AIDS Treatment Update* 73).

LIPODYSTROPHY & METABOLIC DISORDERS

Last month we reported on the possible causes of the metabolic disturbances and body fat alterations being reported in people taking PIs. A pertinent question for those considering taking a PI-sparing combination and feels influenced by this issue, is whether alternative combinations might also have similar effects.

Anecdotally, doctors report that this syndrome does occur, albeit less commonly, in people taking combinations which do not include a PI, but relevant data from current trials are sparse. The research team behind the 006 study have previously reported preliminary information on lipid levels amongst study participants, but these were analysed in a non-fasting state and so were inconclusive. Their report of 48 week

data in Chicago contained no mention of subsequent follow-up of this issue.

Similarly, the CNA 3005 comparison of an abacavir versus an indinavir-containing combination reported preliminary data on non-fasting cholesterol levels only, and no data have been reported from Atlantic's lipid sub-study.

ANOTHER STRATEGY: INTENSIFICATION

Of course, the choices available to those starting treatment are more complex than whether the drug to be added to a double NRTI 'backbone' should be a PI or not. This might include considering whether three drugs are enough, or whether NNRTIs might be best used with PIs rather than as alternatives.

A further option is to 'intensify' an antiretroviral combination by adding another drug if a first viral load test suggests the initial regimen is unlikely to lower viral load to undetectable levels. The most intriguing data on this issue has come from CNA 3009, in which abacavir was added to the treatment of 52 people who had been receiving AZT/3TC for at least 12 weeks. At the time that abacavir was added, participants' median viral load was around 800 copies, and almost a third were below 400 copies. After 48 weeks on all three drugs, this proportion had increased to 72%. Using an ultrasensitive test, 6% were below 20 copies when abacavir was added, and almost half were by 48 weeks.

Starting treatment with two nucleoside analogues is considered inadvisable today. Nonetheless, this trial supports the principle that abacavir might be considered for intensification of a three drug regimen. The success of this strategy may well be dependent on the level of viral load at the time of intensification, and on whether this level is stable or is part of a pattern of rebound from a lower level.

CONCLUSION

Since our previous coverage of 'PI-sparing' combinations last summer, some observers continue to feel that much of the reason for beginning treatment with these regimens is related to anxiety about the side-effects and pharmacokinetics of PIs rather than confidence in alternatives. For a proportion of British doctors, and for the authors of US treatment guidelines, efavirenz merits being seen as a 'special case' – particularly in regard to the vexed question of which combination is best for those who start therapy when their viral load is high. How anti-HIV therapy might restore immunity, and effect virus found outside the blood are important new areas of research. Current understanding of how PI-sparing treatments fare in this respect remains less complete than our equivalent knowledge of PIs.

- REFERENCES**
Abstracts from 6th Conference on Retroviruses and Opportunistic Infections, Chicago, 1999: Tashima, LB-16
Katlama, 18
Staszewski, 20
Fischl, 19
Raffi, 632
Wood, 624
Johnson, 389
Carvelain, 324
Rozenbaum, 377.
Also Florida M et al, *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 20(1):11-19, 1999, and Pakker NG et al, *AIDS* 13(2):203-212, 1999.

HIV treatment in the UK

Largest ever survey of people with HIV in Britain: an exclusive report

BY WILL ANDERSON

In August 1998, *AIDS Treatment Update* readers were sent a small green questionnaire with their copy of the newsletter. The questionnaire was part of a national survey exploring the impact of combination therapy on the lives of people with HIV, focussing principally on use of treatment and treatment services. The report from this survey has just been published and is available free from Sigma Research. This article summarises some of the key findings from the study.

The most important feature of the study is its sheer size: 2,367 people returned usable questionnaires, making this one of the largest surveys of people with HIV ever undertaken. The Communicable Diseases Surveillance Centre (CDSC), which monitors the prevalence of HIV, estimates that there are over 16,000 people living with diagnosed HIV infection in the UK. Hence this study included up to 15% of this population. Furthermore, this was a genuinely national study: the response from different parts of the country was comparable to the CDSC's data on regional prevalence, with a slight under-representation of Londoners. Thanks are therefore due to everyone who filled in and returned a questionnaire and to the 144 organisations throughout the UK who helped to distribute and promote the survey.

ACCESS TO TREATMENT

The study's most encouraging results concern access to treatment. Hardly anyone (0.5%) reported that they had been refused treatment in the previous six months, and almost everyone who was taking antiretroviral therapy was on a combination: only 0.6% of those taking antiretroviral therapy were on monotherapy. These results suggest that combination therapy is established at the heart of the clinical care of people with HIV throughout the UK.

Furthermore, the great majority of respondents (87.0%) said that they were satisfied with their clinical services; only 4.4% said they were dissatisfied and 8.6% said that they were 'not sure'.

These results would be less impressive if there was evidence that people with HIV are having to travel great distances to get treatment and/or a satisfactory service from their clinic. Happily, other results from the study demonstrate that such journeys are the exception rather than the rule: only 3.0% said that they took more than two hours to get to their clinic. Most people with HIV are getting a

satisfactory clinical service relatively near to where they live.

Overall, these results indicate that the medical profession has responded swiftly and effectively to the challenge of combination therapy. The problems that remain largely concern the organisation of services for continuous treatment provision: the minority (6.1%) who said they had problems getting HIV treatments (including the 0.5% who had been refused treatment) mentioned interruptions in the supply of drugs at the clinic, difficulty getting to clinic to renew prescriptions, difficulty getting appointments and professional insensitivity to individual needs.

There also appears to be a lack of equity in the provision of treatment as there is lower take-up of combination therapy among women, injecting drug users, homeless people and young people (but there are no regional or ethnic differences).

TAKING COMBINATION THERAPY

Seven out of ten respondents (71.0%) were taking antiretroviral therapy. This leaves 21.1% who had never taken therapy and 7.8% who had taken therapy in the past but had stopped.

Among those who had never taken antiretroviral therapy, the most common reason by far for not doing so was simply 'no need'. Some were worried about the implications of taking the drugs, such as having to endure the side-effects or reducing options for the future, but only a small minority said that they did not trust the drugs. It seems that the widespread suspicion of antiretroviral treatment that characterised the pre-combination therapy era has disappeared, though this does not mean that everyone is confident about the success of the new treatments. Only a quarter of all respondents agreed with the statement 'there will always be new anti-HIV treatments to replace the ones that fail', whilst half said they were 'not sure'. In addition, almost everyone (95.7%) agreed that 'HIV is still a very serious medical condition'.

Among those who were not taking antiretroviral therapy but had done so in the past, half had stopped because of side-effects or treatment failure – equivalent to one in twenty-five (3.9%) of all respondents. We do not know from this study how many of these people had run out of options and how many were taking a break from treatment before starting again. However, it is clear that the

SIGMA RESEARCH

The full report is available from Sigma Research, Unit 64, Eurolink Centre, 49 Effra Road, London SW2 1BZ.

management of side-effects is key to sustaining combination therapy. In contrast, very few people said they had stopped because of difficulties integrating the pill-taking regimen into daily life.

Those who were taking antiretroviral therapy at the time of the survey described the numbers of antiretroviral medications, pills and doses of pills they took every day. The average number of antiretroviral pills taken every day was 13 with one in ten respondents taking more than twenty per day. On top of these drugs, further burdens were borne by the two thirds who were also taking preventive treatments and also by people with haemophilia, hepatitis C or other chronic diseases.

The range of possible combination therapy regimens is striking – some people are having to cope with far more demanding daily schedules than others. Not surprisingly, those who had to take more drugs, more pills or more doses were more likely than others to find their regimens difficult. Overall, however, 43.6% of those taking combination therapy said their regimen was ‘easy’ or ‘very easy’. This compares with only 14.8% who said it was ‘difficult’ or ‘very difficult’, although the choice of ‘it varies’ by 41.6% must have encompassed a range of personal difficulties with the daily round of pill-taking.

Experience of side-effects was common, with a majority (60.2%) of those taking combination therapy reporting one or more current side-effects. The most common side-effects were diarrhoea (reported by 22.7%) and nausea/sickness (18.7%) followed by peripheral neuropathy (14.2%), fatigue (12.3%) and gastro-intestinal problems (8.4%). Most of those who had only recently started their current combination were experiencing side-effects, and over half of those who had been taking combination therapy for a year or more reported continued side-effects. Hence for a substantial number of those taking combination therapy, side-effects are a chronic as well as a short-term problem.

ADHERENCE TO COMBINATION THERAPY

A great deal of stress has been placed on the importance of treatment adherence to the success of combination therapy, although the level of adherence needed will always vary between different people and between different drug regimens.

The results from this survey indicate that most people with HIV have listened to what their doctors (and many others) have said, and are largely coping with this issue very well. Half of those taking combination therapy said they had not missed a single dose in the previous month

and three-quarters had not missed a dose in the previous week.

Compared to adherence to medications in other chronic diseases, these results are extremely good. This may be because, as reported above, almost everyone still considers HIV to be a very serious condition – a clear motivation for getting the most from treatment. However, the unusually harsh implications of non-adherence may also help to explain the high levels of adherence reported. Knowledge of these implications was almost universal, demonstrated by the finding that 94.1% of those taking combination therapy knew that ‘HIV can become resistant to treatments, especially if they are not taken properly’.

Living with HIV entails much more than the medical management of a viral infection.

There is further evidence of the commitment made by people with HIV to sticking to their treatment regimens in their reasons for the last missed dose of therapy. Very few people chose not to take a dose and no-one said ‘they couldn’t be bothered’. Although most respondents intended to take the planned dose, they typically forgot. Some forgot because of a change of routine, such as the start of a weekend or being on holiday; some forgot because they had gone out without their pills; some failed to anticipate how long they were likely to be asleep. But many gave no more reason than simply ‘I forgot’. Forgetfulness does not reflect a lack of will, but a failure to plan for all the disruptions and unexpected events of day-to-day life. Although just about everyone knows that they must not forget, they still do. This is after all, the nature of forgetting.

The only other prominent reason for missing a dose was sickness or nausea, reported by one in ten of the respondents who gave a reason for missing their last dose. In three-quarters of these cases, they had been too sick at the time of the dose or the prospect of taking the pills had made them feel nauseous; the rest had vomited the pills after taking them.

It is widely assumed that non-adherence increases as the number of drugs, pills or doses in a regimen increases. This assumption proves

EDITOR'S NOTE
NAM Publications would like to join SIGMA in thanking all those who shared their experiences by completing this important survey. We are especially pleased to have been voted a close second to respondent's doctors as ‘Most helpful’ source of HIV treatment information. Feedback from anyone who uses our services on how we can best meet your needs is always welcome – see page 8 for contact details.

to be unfounded – those who were taking more complicated regimens were no more likely to miss doses than those on simpler regimens. However the study did not look at the implications of special dietary requirements on taking combination therapy, for which other recent research has found a strong link with non-adherence.

Hardly any respondents (0.5%) identified a need for more information about adhering to therapy. However, 11.8% of those taking combination therapy had not been told anything about how to take the drugs when they had first started, and over a quarter (28.7%) had not been given any written information. As more missed doses were reported by those who did not know about the link between non-adherence and viral resistance, the importance of these basic interventions is clear.

REFERENCES

Anderson W and Weatherburn P. "Taking heart? The impact of combination therapy on the lives of people with HIV (phase 2)". Sigma Research, 1999.

Anderson W and Weatherburn P. "The impact of combination therapy on the lives of people with HIV". Sigma Research, 1998.

LIFE CHANGES

This survey is the second phase of a larger research project exploring the impact of combination therapy on the lives of people with HIV. The first phase, published in March 1998, drew attention to the differences between clinical change and personal and social change, stressing that the commitments and expectations of any individual's life will be shaped by much more than the state of their health and the immediate effects of therapy.

The survey followed up this theme by asking respondents a series of questions about the changes in their lives which had occurred over the previous six months. These questions related both to changes in clinical/physical health – viral load, CD4 count, physical health and mobility – and to broader personal and social changes – in quality of life, mental health, personal confidence, social life, relationships, sex life and hopes for the future.

The results demonstrated that those who had started therapy were very likely to have seen improvements in their clinical and physical condition, but they were no more likely to report improvements in all the other variables than those who were not taking therapy at all. Changes in viral load were reflected in changes in health and mobility, but not in quality of life, personal confidence or any of the other non-clinical variables.

Overall, improvement or worsening in quality of life, etc. was experienced to the same degree, regardless of whether respondents were taking combination therapy or of the time they had spent on therapy.

This does not diminish the importance of combination therapy, but acknowledges that living with HIV entails much more than the medical management of a viral infection. Benefiting from improved health does not necessarily overcome the many possible implications of an HIV diagnosis.

NEWS IN BRIEF

Efavirenz side-effects

As reported elsewhere in this issue, the NNRTI efavirenz has recently been recommended for licensing in the EU. This drug has aroused interest not only for its potency, but also for its side-effect profile, both of which have been reported in equally sensationalist terms on occasion. What are the facts?

Manufacturers Du Pont Pharmaceuticals have recently analysed data from 15 efavirenz clinical trials. Two types of side-effects are seen most often in people who take efavirenz, nervous system symptoms (NSS) and rashes. The NSS have been reported in around half of efavirenz recipients compared with 27% of people in control arms (who did not receive efavirenz). These symptoms are usually, but not exclusively described as dizziness, lightheadedness, restlessness, feeling out of sorts, difficulty concentrating, difficulty sleeping or vivid dreams. In the main, the severity of these symptoms is reported as mild to moderate, rather than severe, and have only very rarely caused people to stop treatment.

NSS usually begin with the first two days of treatment, are improved though not resolved by taking the dose at bedtime, and generally stop within two to three weeks of treatment. Some doctors are managing this initial period by offering a course of treatment with for example, haloperidol, an anti-psychotic.

Rash occurred in 28% of efavirenz recipients compared with 18% of control patients, giving an attributable rate for efavirenz of 10%. These rashes usually occurred early, were mild to moderate and resolved within several weeks. Rash is a commonly observed side-effect of all NNRTIs. For nevirapine, the reported rate of rash which is attributable to that drug is 16%. The delavirdine-attributable rate is 18%.

BHIVA guidelines

The British HIV Association guidelines on anti-HIV treatment are in the process of being updated. The consultation process has been widened – to read and comment on the draft text via the internet, see the NAM/BHIVA website at <http://www.aidsmap.com>.

ADVISORY PANEL

We are pleased to welcome Professor Frances Gotch to NAM's Medical Advisory Panel, which comments on *AIDS Treatment Update's* content prior to publication. Frances directs the Department of Immunology at the Chelsea and Westminster Hospital.

GLOSSARY OF TERMS

antigen Something the immune system can recognise as 'foreign' and attack

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

HAART Highly Active Antiretroviral Therapy; potent combination therapy, usually including a protease inhibitor

lipid A general term for fats in the blood

metabolism The mechanisms which sustain life, including turning sugar and fat into energy

named patient programme 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

nucleoside analogue Anti-HIV drugs that include AZT, ddI, ddC, 3TC and d4T

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

pharmacokinetics How a drug is processed in the body

placebo A harmless inactive substance against which the benefits and toxicities of a treatment can be compared

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

treatment naive Someone who has not taken anti-HIV treatments

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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Free to individuals in the UK affected by HIV or AIDS. Professional/organisational rate: £69/year. Voluntary organisation rate: £50/year. Overseas rate: within EU add £10/year; outside EU add £15/year. Tel: Helen or Letitia on 0171 627 3200

Medical Advisory Panel

Dr Fiona Boag, Dr Ray Brettle, Professor Janet Darbyshire, Dr Martin Fisher, Professor Brian Gazzard, Dr Diana Gibb, Professor Frances Gotch, Professor Paul Griffiths, Dr Margaret Johnson, Dr Jacqueline Mok, Dr Graeme Moyle, Professor Tony Pinching, Dr Gareth Tudor-Williams, Professor Jonathan Weber, Dr Ian Williams, Dr Mike Youle

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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: 0645 470047
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 0171 287 8010 to make an appointment.

◆ The Terrence Higgins Trust

Helpline: 0171 242 1010 Daily 12noon - 10pm
Treatment Support: Call Sarah Porch on 0171 831 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.

Donations towards production costs are welcomed.