

AIDS TREATMENT UPDATE

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Interleukin-2

Major trials of immune-boosting treatment planned for the UK

BY ANNA POPPA

Interleukin-2 is a naturally-occurring substance involved in the working of the immune system, which stimulates the production and maturation of CD4 cells. Often called IL-2 for short, it is one of a group of immune system 'communication chemicals' which are collectively referred to as cytokines.

Levels of IL-2 tend to fall over time in HIV infection, and low levels are associated with an increased risk of disease progression. Research into the effects of giving an artificial form of IL-2 to people with HIV has been conducted for well over a decade, but this immune therapy is not yet unlicensed for use in HIV.

Early studies identified two key problems. Firstly, intravenous administration of IL-2 at high doses was associated with significant side-effects which many users were unwilling to tolerate, particularly those with advanced disease. Secondly, we now know that the immune reconstitution which therapies such as IL-2 should contribute towards is greater when viral load is suppressed to very low levels. The availability of more potent combination therapy therefore offers a greater opportunity for IL-2's potential benefits.

IL-2 has to be injected into the body, either directly into a vein (intravenous administration), or under the skin (subcutaneous administration). The injections tend to be given over a period of a few days, every few weeks or months, and these short treatment periods are called cycles. IL-2 is being studied at varying doses, and these are measured in millions of international units, abbreviated to MIU. A modified form of IL-2 has also been studied in the hope that it might lessen side-effects. This version is called PEG IL-2 (short for pegylated), and is given intravenously.

Over the summer a series of research papers involving IL-2 have been published. More recently,

new treatment guidelines from France have recommended that IL-2 be made available to anyone whose viral load on treatment is undetectable, but whose CD4 count remains below 200.

HOW SHOULD IL-2 BE GIVEN?

A French study called ANRS 048, was published in the *Lancet* in June¹. This study, which began recruiting participants in 1995, aimed to compare different ways of administering IL-2 amongst people receiving dual nucleoside analogue therapy.

In ANRS 048, 94 people with no previous experience of anti-HIV treatment were randomised to receive AZT/ddI plus one of four treatment options:

- ♦ IL-2 given as an intravenous infusion, 12 MIU per day for 5 days
- ♦ IL-2 given as a subcutaneous injection, 3 MIU/m² twice daily for 5 days
- ♦ PEG IL-2 as an intravenous bolus, of 2 MIU/m²
- ♦ no IL-2 (the control group)

The study was open to people with CD4 counts between 250 and 550 at entry and the average count was 384 cells. The median viral load was 36,725 copies. Antiretroviral treatment began two weeks before the IL-2 cycles began. The IL-2 cycle was given

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every two months from week two to week 50, making a total of seven cycles in all.

After 56 weeks of follow-up, the average CD4 count increase was higher amongst those who had received any form of IL-2 compared with those on AZT/ddl alone. However, these increases were greatest in those receiving either subcutaneous (up 564 cells on average) or intravenous IL-2 (up 676 cells on average). Around 70% of participants in these two groups saw their CD4 count rise by 80%, and half restored their CD4/CD8 cell ratio (another marker of immune function which is disrupted in HIV infection) to a normal value.

All those who received IL-2 reported at least one mild to moderate side-effect during cycles, most often 'constitutional symptoms' such as fever, weakness, nausea or vomiting. These are the same symptoms experienced when the immune system releases naturally occurring IL-2 in response to an infection. The most common severe side-effects were fever and asymptomatic liver abnormalities. Over the course of the study, the average total dose per cycle administered in the intravenous and subcutaneous groups was reduced because of side-effects, whereas the dose in the PEG IL-2 group remained 3.7 MIU throughout. The average daily dose during IL-2 cycles was 8.8 MIU in the subcutaneous group, and 9.9 MIU in the intravenous group.

Overall, the group receiving subcutaneous IL-2 had the best results, combining a good immunological response with fewer side-effects than in the intravenous group, and with the additional convenience of being able to receive their treatment at home rather than in hospital. Whilst PEG IL-2 was also relatively well-tolerated, it had a poor effect on CD4 counts (at least at the dosage studied here).

The authors reported extended follow-up on 34 people from the subcutaneous and intravenous groups. 24 of these received subcutaneous IL-2, and ten received only anti-HIV therapy. Five people in the IL-2 group started a protease inhibitor in this period, compared to one person in the other group. The median extended follow-up time was 52 weeks (i.e. 104 weeks after the study began), and the IL-2 recipients received a median of four cycles in this period, at a median dose of 4.1 MIU twice daily. An 80% increase in CD4 counts from baseline values was seen in 22 of 24 people in the IL-2 group at week 56 of the extended follow-up period.

IL-2 PLUS DUAL THERAPY

Though dual nucleoside analogue therapy is considered sub-optimal therapy in the age of HAART, the results of this French study suggest that IL-2 may be an attractive prospect to the sub-group of people who are unable to tolerate more than two drugs, or who have maintained a stable response on long-term dual therapy.

IL-2 AT HIGH CD4 COUNTS

In a study published in the April 1999 issue of the *Journal of Infectious Diseases*, a team at the US National Institutes of Health (NIH) compared high dose and low dose IL-2, given subcutaneously to people on stable anti-HIV therapy, all of whom had CD4 counts above 500 cells².

Participants were randomised to receive IL-2 twice daily in 5 day cycles at doses of either:

- ♦ 1.5 MIU, cycled every 4 weeks
- ♦ 1.5 MIU, cycled every 8 weeks

FLUSHING OUT HIV WITH IL-2

Researchers are also looking at whether IL-2 can be used to 'awaken' the reservoir of 'resting' HIV-infected CD4 cells among people receiving anti-HIV combination therapy, since these cells are only susceptible to HAART once they are activated. A study conducted by the US National Institute of Allergy and Infectious Diseases (NIAID) reported that researchers were unable to culture HIV from these T-cells in six of 14 people who received antiretroviral therapy plus IL-2. Lymph node biopsy in three of these people could not detect any HIV in the lymph nodes either.

Despite the encouraging results, researchers at NIAID urged caution, suggesting HIV might still be present in other reservoirs, or may be present in T-cells at levels too low to be detected with current technology.

At the recent 'Gallo Meeting', a small scientific workshop organised by HIV's co-discoverer, Robert Gallo, NIAID Director Anthony Fauci updated the ongoing flushing story. Participants had stopped their therapy and all experienced a rebound in viral load and loss of CD4 cells. However, the virus which re-grew was different to that found in the resting pool of infected blood lymphocytes. This suggests that this new virus had come from another, as yet undiscovered reservoir. The rebound in viral load also caused the resting lymphocyte pool to become re-populated with HIV, even in those people whose use of HAART and IL-2 appeared to have successfully 'flushed out' the virus. Though this is a further blow to attempts to use HIV treatments to eradicate the virus, research in this area continues.

- ◆ 7.5 MIU, cycled every 4 weeks
- ◆ 7.5 MIU, cycled every 8 weeks

After an initial cycle given in hospital, participants were taught to self-administer their IL-2 at home. They were also instructed to drink adequate fluids so as not to become de-hydrated, and to take either paracetamol or ibuprofen on a scheduled rather than as-needed basis to limit side-effects.

Three quarters of the participants either began or continued taking dual nucleoside analogue therapy in the first six months of IL-2 therapy. A fifth either began or continued three drug therapy including a protease inhibitor in this period.

After six months, CD4 increases were greater amongst those receiving the higher dose of IL-2, though there was no significant difference according to the frequency of dosing. On average, CD4 counts increased 30 cells per month in the four weekly low dose arm; 23 cells per month in the eight weekly low dose arm; 146 cells per month in the four weekly high dose arm and 85 cells per month in the eight weekly high dose arm. This represents a 95% rise in average CD4 counts after six months in the high dose group and a 19% rise in the low dose group.

Side-effects (mostly fatigue, malaise and muscle and joint aches) during cycles were common, but none were severe. They were more frequent, however, amongst those on high doses of IL-2 though these generally did not require the dosage to be lowered.

After the initial six month period, all participants were able to continue IL-2 therapy if they wished, with an option to raise their dose or the frequency of cycles. 39 of the original 49 participants have now been followed for an average of 28 months. At month 18, the average CD4 cell count was 1,381 cells. The average IL-2 dose in this extended follow-up period was 5.8 MIU twice daily, with an average interval of 12 months between cycles. Thus even those who began at lower doses, were able to benefit from scaling-up their dose later, as CD4 response across the original four arms was comparable by month 18. On the other hand, those who began at higher doses benefited from less frequent cycles subsequently.

IL-2 IN ADVANCED DISEASE

In a third study, led by a research team from Barcelona, the use of IL-2 in people with more advanced disease was explored³. People whose CD4 counts are already low are clearly in greatest need of immune restoration, but pre-HAART study of IL-2 suggested that this patient group were less likely to benefit from its use than people with higher CD4 counts. Participants in this Spanish trial had been

taking a protease inhibitor-containing three drug combination for at least six months which had kept their viral load below 500 copies throughout this period. Prior to this current regimen, all had taken nucleoside analogue therapy. They were randomised into two groups, one of which received IL-2 (at a dose of 3 MIU twice daily for five days every four weeks for six cycles) plus their current HAART, and the other, HAART alone.

Amongst the 25 people randomised, the average CD4 count at baseline was 129 in the HAART alone group, and 165 in those receiving IL-2 plus HAART. After six months of treatment, there was no change in CD4 in the control arm, whereas the average rise in CD4 was 105 cells in the IL-2 group. This rise was sustained over an additional three months of follow-up after the last IL-2 cycle.

Although seven people left the study part way through, they were divided between the study groups, and just two refused to continue IL-2 after the first cycle. However, because 80% experienced high fevers and severe constitutional symptoms after this first cycle, the dose was subsequently halved to 3 MIU once daily to improve tolerability. 75% of the IL-2 group experienced mild constitutional symptoms subsequently, which were controlled by taking either aspirin or paracetamol one hour after injection of IL-2.

EFFECT ON VIRAL LOAD

A potential hazard of using IL-2 is that by stimulating the activation and proliferation of T-cells, one also risks stimulating further production of HIV as inactive but infected cells are encouraged to replicate. Because of this, there is a view that IL-2 should only be used alongside effective anti-HIV therapy, (though this is not proven and the use of IL-2 without anti-HIV treatment is also under investigation). Even then, it is still a concern for some that IL-2 may cause 'spikes' in viral load which could lead to a loss of virological control. On the other hand, it is possible these 'blips' may stimulate an immune response to the virus.

There was little evidence from the studies discussed in this article that people receiving IL-2 fared worse in this respect than people on HAART alone.

In the ANRS study, there was no difference in viral load response across all four arms throughout the duration of the study, with between 44% and 60% of participants achieving viral load below 500 copies after 56 weeks. Small 'blips' in viral load were seen in only a minority of cases. During the period of extended follow-up, 13 of 24 (54%) maintained viral load below 500 copies.

Similarly, in the Spanish study involving people with advanced disease, all participants

REFERENCES

- 1 Levy Y et al. *Lancet* 353(9168):1923-1929, 1999.
 - 2 Davey RT et al. *Journal of Infectious Diseases* 179:849-858, 1999.
 - 3 Arno A et al. *Journal of Infectious Diseases* 180:56-60, 1999.
- For more on flushing out HIV with IL-2 see:
Chun TW et al. *Nature Medicine* 5(6): 651-655, 1999.
Fauci A. International Meeting of the Institute of Human Virology, Baltimore, oral abstract 2, August 28-September 2, 1999.

except one kept their viral load below 500 copies throughout the study, and the rise in this one individual was transient. In the US study there was no difference in viral load response between the groups, all of whom experienced a decline.

DO CD4 RISES EQUAL BETTER HEALTH?

While these three trials, and several others, suggest that the use of IL-2 results in large rises in CD4 cells, this may not necessarily translate into better health and longer survival. Though these studies were not intended to provide conclusive answers to this question, they included some preliminary investigation into the quality of the immune response seen.

In the French ANRS study, a number of markers suggest that gains in CD4 cells corresponded with improved immune function. Firstly, the cells gained comprised both memory and naïve cells. Both types are usually lost as HIV progresses untreated. The loss of naïve cells (cells which are 'blank' and have not yet been programmed to recognise a particular foreign body) reduces the body's ability to respond to new infections. A reduction in memory cells leaves gaps in the immune system's 'memory bank' against certain types of infections.

Secondly, the CD8 cells (which are another type of T-cell) of those receiving IL-2 carried a molecule called CD28 on their surface, which is understood to inhibit HIV replication. Thirdly, test-tube studies found that immune responses to common infections such as tetanus toxoid improved in both the subcutaneous and intravenous IL-2 recipients.

The other two studies similarly found that the new CD4 cells included both naïve and memory cells. Furthermore, when the Spanish researchers looked for CD8 cells which carried CD28 on their surface, they found an increased number amongst IL-2 recipients, and a gradual loss in the control group.

LARGER STUDIES ON THE WAY

Though these findings suggest that the immune response to IL-2 appears to be one of quality as well as quantity, this question will not be answered without longer and larger studies. In the US, one such study, SILCAAT, has already begun, and an international trial called ESPRIT, funded by the NIH and involving the UK's MRC is planned (see sidebar on this page for more details).

CURRENT ACCESS TO IL-2

One small study is currently recruiting at the Chelsea and Westminster Hospital, London, which is looking into the effects of IL-2 plus

HAART and a second experimental immune therapy *Remune*[™] (see the August 1998 issue of *AIDS Treatment Update* for more details). The Vanguard study investigating the effects of IL-2 in people who are not on anti-HIV therapy has now closed to recruitment.

IL-2 is manufactured by Chiron as *Proleukin*[™] for the treatment of renal cancer, but is not licensed for use in HIV infection. However, because it is licensed for another indication, it can be administered to people with HIV so long as their doctors are willing to undertake full responsibility for its use. According to Chiron, outside the two UK trials, only a handful of people are currently accessing IL-2 this way in this country.

Key conclusions:

- ◆ IL-2 is produced in the body to stimulate the growth of T-cells. A 'man-made' version is being studied as a treatment for people with HIV.
- ◆ IL-2 is taken in five day cycles, repeated every month or so. Doses and frequency of cycles are varied to make the drug more tolerable, but the drug may still cause unpleasant 'flu-like' symptoms during these cycles.
- ◆ Giving IL-2 by injection under the skin appears to cause less side-effects than an infusion directly into a vein, and allows the drug to be taken at home.
- ◆ Higher doses appear to produce bigger CD4 rises but at the cost of more side-effects.
- ◆ Preliminary studies show that people taking anti-HIV therapy gain more CD4 cells if they also take IL-2. This has happened in people who began treatment with both low and high CD4 counts.
- ◆ People who take IL-2 with effective anti-HIV therapy tend not to lose control of their viral load.
- ◆ These gains in CD4 cells appear to reflect a genuine improvement in immune function, but bigger and longer studies are needed to confirm if IL-2 leads to healthier and longer life in people with HIV.

SILCAAT & ESPRIT

SILCAAT will study the effects of IL-2 on a relatively advanced group of people over a period of four to six years. All participants will be on stable antiretroviral therapy involving at least three drugs for at least six months, and should have a CD4 count between 50 and 300, and viral load below 10,000 copies at entry. They will be randomly assigned to receive either IL-2 or no additional treatment. ESPRIT will randomise 4,000 people in total, with CD4 counts above 300, who are on anti-HIV therapy, to receive IL-2 or no IL-2. The trial will last for five years and is planned to begin around the new year. Twenty sites in the UK will participate and 350 UK patients will be recruited.

Getting on your nerves

Neuropathy trial opens in the UK while new studies underway in US

BY ANNA POPPA

Neuropathy, or nerve damage, is one of the most common causes of pain in people with HIV, and one of the hardest to treat. It usually affects the feet, and though descriptions of neuropathic pain vary between individuals, it may feel like numbness, tingling, 'pins and needles', aching, or a burning or freezing sensation. Severity also varies – just the briefest of scans through HIV community press coverage of the subject throws up numerous stories of extreme pain and a significant impact on mobility and quality of life.

HOW IS IT CAUSED?

People with HIV can experience neuropathy for many different reasons, either because of:

- ♦ the direct effects of the virus on the nervous system (which can occur at any stage of infection)
- ♦ side-effects of some antiretrovirals (the 'd' drugs – ddC, d4T and ddI), and other prescription drugs, including vincristine and thalidomide
- ♦ opportunistic infections and tumours which may affect the nervous system
- ♦ over-use of alcohol, heroin, cocaine or amphetamines (speed)
- ♦ nutritional problems such as vitamin B12 or folate deficiency.

It seems that these different causes may interact, so that people with mild symptoms might find these worsen if they begin an antiretroviral such as d4T.

Before the use of antiretrovirals, neuropathy was reported in around a third of people with symptomatic HIV infection, and was more common at lower CD4 counts. The incidence of peripheral neuropathy, (peripheral means that the damaged nerves are in the limbs), as a side-effect of ddC or d4T is approximately 20%, and around 10% for ddI. Though symptoms generally improve once the drug is stopped, this may take several months. Some people – particularly those who have been on higher doses – experience a worsening of pain for a month or two off treatment, which is sometimes called 'coasting'.

CURRENT TREATMENTS

Neuropathy which results from nutritional deficiencies should be treated by correcting the deficiency with supplements and dietary changes. Mild symptoms may be manageable with painkillers such as coproxamol.

In cases where neuropathy is more severe, the following treatments may be used:

- ♦ tricyclic antidepressants, e.g. amitriptyline, nortriptyline. These are usually prescribed to treat depression, but at higher doses than usually used for neuropathy.
- ♦ anticonvulsants, which are used to manage epilepsy, e.g. carbamazepine, sodium valproate, phenytoin. These drugs interact with protease inhibitors however, so either cannot be used with them, or require a dose adjustment.
- ♦ antiarrhythmics used to treat irregular heartbeat, e.g. mexiletine.

Where these options fail, the anaesthetic ketamine or opiates such as methadone may also be used. People with a history of opiate use may find it particularly hard to get adequate pain control, and will usually require higher doses.

Which of these treatments are most effective in people with HIV is not known, and most have not been adequately studied for this purpose. This means that individuals may need to try various different options before they get relief from their symptoms. Doctors advise that finding an effective treatment is best attempted by trying one drug at a time, beginning at the lowest dose, and only raising the dose after several days treatment have not brought satisfactory pain relief. A potential hazard with the various treatment options listed above is the frequency of side-effects, which are more common and more severe the higher the dose used.

OTHER OPTIONS

At last year's World AIDS Conference, early results of an American study called ACTG 291 were reported¹. They found the use of a 'man-made' version of nerve growth factor (a naturally occurring bodily substance which repairs damaged nerves), improved neuropathic pain compared with a placebo. The only significant side-effect was pain at the injection site, and while other treatment options can only relieve symptoms, this drug may actually repair damaged nerves. However, despite these promising findings, manufacturer Genentech has since closed its nerve growth factor development programme following the drug's poor performance as a remedy for diabetic neuropathy – potentially a far more lucrative market.

AIDSMAP.COM

For more detailed information on research into peripheral neuropathy see www.aidsmap.com. Go to 'Symptoms and Illnesses' on the aidsmap.com.

REFERENCES

¹ MacArthur J et al. 12th World AIDS Conference, Geneva, abstract 32454, 1999.

Chelsea and Westminster Hospital AIDS Care Handbook, ed. Brian Gazzard. Mediscript Limited, 1999.

Over the course of this year, two new peripheral neuropathy studies have opened in the US within the ACTG network. In fact both of these involve drugs which are already approved anticonvulsants in both the UK and the US; gabapentin and lamotrigine. Although these treatments are available to people with HIV now (so long as their doctor is willing to take responsibility for prescribing them 'off-label'), these studies should provide welcome evidence on their usefulness, and on appropriate dosages.

NEW UK STUDY

Nucleoside analogues are known to damage the tiny energy-producing machinery of cells called mitochondria. This may have many negative effects on the body (and has recently been proposed as a cause of lipodystrophy), one of which may be peripheral neuropathy.

In 1997, Italian researchers reported that people who developed neuropathy on nucleoside analogues had low levels of a substance called acetylcarnitine, whereas levels were normal in those without neuropathy. Acetylcarnitine is an amino acid, or protein, which is involved in the processing of fatty acids for energy production by

mitochondria. Carnitine is naturally produced by the body, but is also taken in to the body through eating red meat, (and is sold in gyms and health food stores as a 'body-building' supplement). While acetylcarnitine is also being touted as a treatment for lipodystrophy, the first randomised, placebo-controlled study to investigate its use for peripheral neuropathy is due to begin in early October in London and Brighton.

This study will recruit 80 people with painful peripheral neuropathy on stable antiretroviral therapy, at the Royal Free Hospital and St Mary's in London, the Royal Sussex and County Hospital, Brighton, as well as in the Netherlands. Participants will receive twice daily injections of either acetylcarnitine (500mg) or placebo for 14 days. Treatment will be blinded so neither you nor your doctor will know which injection you are receiving. Injections are self-administered at home, and there is an eight week follow-up period after they finish.

Further information on this study is available from Dr Mike Youle or Debbie Wilson at the Royal Free on 0171 830 2242, from Tracey-Ann Doggett at the Royal Sussex on 01273 664532, or from Ken Legg at St Mary's on 0171 725 6790.

NEWS IN BRIEF

Death rates falling

New mortality data from the US Centers for Disease Control and Prevention (CDC) suggest the numbers of Americans dying from AIDS continued to fall in 1998. However, the rate of decline was considerably slower than that seen in 1997.

Though the absolute number of deaths was lower in '98 than for the previous year (down to 17,047 from 21,222), this represents a 20% decline in the mortality rate between 1997 and 1998, compared with a 47% reduction between 1996 and 1997. The tumbling death rates seen in this period have been linked with the use of protease inhibitors.

While close monitoring will be required to fully determine the reasons for this slowing decline, public health researchers believe a combination of factors are likely to be contributing. It's possible that those people with a diagnosed HIV infection who might benefit from treatment have already been reached by the US healthcare system, and that treatments themselves are beginning to fail,

whether through the emergence of resistance, toxicities, or other causes.

Looking at UK figures, a similar picture emerges. The total number of deaths in HIV-positive people fell 54% in 1997, (from 1,374 to 634), compared to 1996. The decline in 1998 was 36% (to 405 deaths). According to Janet Mortimer of the Public Health Laboratory Service, "It's not too unexpected that the decline should slow because [new] treatments more or less came into use at one time. However, there are still likely to be fewer deaths in 1998 than in 1997".

Drug interactions

In a letter to US doctors, Glaxo-Wellcome has revealed that adding a 200mg (two tablets) dose of ritonavir to the normal amprenavir dosage (1200mg) cancels out the negative effects of efavirenz on amprenavir blood levels. 1250mg of nelfinavir twice daily (five tablets twice daily) had a similar effect.

Researchers at the US National Institutes of Health looked at a group of 17 individuals

participating in a salvage study of amprenavir, efavirenz and abacavir who added either ritonavir or nelfinavir. Efavirenz reduces the minimum concentration of amprenavir by 49%, resulting in weakened anti-HIV potency which may leave users of the combination at risk of resistance. However, those who added ritonavir increased their minimum amprenavir concentration six-fold compared with others who did not add ritonavir. Adding nelfinavir increased the minimum concentration of amprenavir three-fold.

This means that NNRTI-naïve individuals may be able to assemble a viable salvage regimen composed of amprenavir, efavirenz and another drug if they use a booster dose of ritonavir. The nelfinavir dose used in this study is the standard therapeutic dose, but may not be effective for people with previous protease inhibitor experience because of cross-resistance, (and involves taking a slightly higher number of pills per day compared to adding ritonavir). Amprenavir is the only protease inhibitor currently available which appears to be active against virus already resistant to indinavir, ritonavir and saquinavir in the majority of individuals.

Amprenavir is currently available through an named patient scheme in the UK. The drug is already licensed for twice daily use in the US.

New drugs

As this newsletter went to press, Abbott Labs were expected to open a small named patient programme for their experimental protease inhibitor ABT-378. This would provide the drug to people with very low CD4 counts who have experience of protease inhibitors and have limited treatment options. The drug is also available in the UK through two clinical trials, one of which is open to people who are new to anti-HIV treatment. The other investigates the drug's use in people who have used protease inhibitors before, but have no experience of NNRTIs.

It is not clear whether ABT-378 will prove effective against strains of HIV which are resistant to other protease inhibitors. Preliminary results from a study involving people with experience of PIs, but naïve to NNRTIs, found that starting ABT-378 with nevirapine and two nucleoside analogues reduced viral load below 400 copies in three quarters of recipients after 24 weeks.

Being able to gather a number of drugs to which you may expect to benefit can be a challenge for anyone compiling a salvage regimen. Aside from ABT-378, (for which

Abbott promise a larger expanded access scheme in early 2000), the next new drug which may become available in the UK is adefovir. Manufacturers Gilead have been stalling over widening access for several months, and now say a scheme will begin early next year. Adefovir is a nucleotide analogue, the first of a new type of reverse transcriptase inhibitor. Past use of nucleoside analogues is likely to affect the benefit gained from its use. You can read more about both these drugs on the NAM/BHIVA website at <http://www.aidsmap.com>

Nevirapine for kids

Nevirapine has been licensed for use in children with HIV infection in the European Union, the first NNRTI to be approved for use in young children over two months old. The drug is available in a liquid form (as well as the standard tablet form used by adults). Boehringer Ingelheim have undertaken to provide the drug free for use in children until the end of the current financial year.

Manchester meeting

On Thursday, October 7th Body Positive North West and NAM present a Discussion on Adherence in HIV Treatment at Granada Studios. Guest speakers including Dr Ed Wilkins, Nicki Archer and Henry Grahame-Smith will talk about the challenges presented by combination therapy and answer questions from the audience. The discussion starts at 6pm with the bar open and food available from 8.30pm to 9.30pm.

This free event will take place on Granada's House of Commons, Rovers Return and Woolpack sets. Places are limited however, and booking is advised. For more information call Leon, Zoe or Gary at BP North West on 0161 873 8100.

NAM forum

At the next NAM Information Forum on Monday, 18th October, Dr Jose Catalan, reader in psychiatry at Imperial College, London, and Dr Jenny Petrak, Clinical Psychologist at St Bartholomew's and the Royal London Hospitals, London, will discuss the psychological impact of taking anti-HIV drugs, including how they may affect the brain, and how problems with mood, body image and sex drive may be supported.

The venue is Room 101, 1st Floor, University of London Union, Malet Street, London WC1. Forums are free and run from 7pm to 9pm, and a sign language interpreter is available.

NEW ON AIDS MAP.COM

The latest news from the 39th ICAAC, one of this year's most important scientific conferences is amongst this month's updates available through the NAM/BHIVA website <http://www.aidsmap.com>.

Later in October, NAM's treatments writers will be posting daily news stories to aidsmap.com direct from the 7th European Conference on Clinical Aspects and Treatment of HIV Infection in Lisbon.

HELP NEEDED

NAM is looking to recruit a team of volunteers to translate our popular *Factsheets* and *Information booklets for people with HIV* into French, Spanish, Portuguese, Italian or German. This will allow us to make these resources available in a range of languages through the NAM/BHIVA website aidsmap.com.

If you are able to help, please contact Keith Alcorn at NAM on 020 7627 3200.

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

clinical outcome The occurrence of a physical symptom

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

diabetes A blood disorder caused when the body can't use or metabolise sugar properly. Symptoms include extreme thirst, blurred vision and frequent urination

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

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

named patient basis A means of access to an unlicensed drug, where a doctor request supplies from the manufacturer on behalf of a specified person

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

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

placebo A pill which looks exactly like a real drug, but contains no active substance

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

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

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

regimen Drug or treatment combination

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

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

salvage therapy Regimens taken by people who've used other combinations in the past

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

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

Subscriptions

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 Claire on 020 7627 3200

Medical Advisory Panel

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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.

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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