HIV treatment 2000

Predictions for forthcoming developments in HIV medicine

BY ANNA POPPA

As this is traditionally a time for looking forward and considering change, in this article we consider some of the issues which those affected by HIV should expect to hear much more about in the coming year.

TREATMENT STRATEGIES

Three large and long-term studies, the international INITIO trial, and ACTG 384 and FIRST in the US, have now begun recruiting participants. All three are designed to help people with HIV and their doctors decide whether it is better to start anti-HIV treatment with a regimen containing an NNRTI, or with one containing a protease inhibitor, or with one containing both. It is unlikely, however that either of these important studies will provide preliminary findings until late in 2000 or 2001.

During 1999, concern over the lipodystrophy syndrome and treatment adherence were influential in establishing a trend for switching off protease inhibitor-based combinations in favour of either NNRTIs, or to a combination of three nucleoside analogues. There are now a sizeable number of studies – both large and small, randomised and uncontrolled – which are gathering information on these patients, and will report their findings throughout the year.

PenPact 1 is a trial similar to INITIO which will investigate treatment strategies in children. This joint European/US study will run over four years, and was discussed in AIDS Treatment Update issue 81.

Structured treatment interruptions, the PC term for drug holidays, will continue to be a ‘sexy topic’ at AIDS conferences, though it seems that most new information will come from small case studies. Interest in immunological treatment approaches also continues to grow. A large international study of interleukin-2 plus HAART, ESPRIT, is expected to start recruiting participants in the UK early in 2000, and initial results from the Vanguard study of IL-2 without anti-HIV therapy should be available by the summer.

LONG-TERM SIDE-EFFECTS

As we report elsewhere in this issue, research into the mechanisms causing the abnormal fat redistribution and metabolism seen in people taking anti-HIV therapy continues to point the finger at a range of possible culprits. Though it may be unrealistic to expect dramatic shifts in our understanding of this syndrome within the space of a year, observers have expressed the need for agreement over case definitions. The use of treatments to lower lipid levels by people also taking HAART is another key area.

The list of potential toxicities which may affect people taking anti-HIV drugs appears to be growing, which is not so surprising as more people take HAART for longer periods of time. As interest grows in lactic acidosis, a seemingly rare side-effect of nucleoside analogues, a small number of case studies have been reported.
reported another potential complication, bone density abnormalities in people taking HAART.

NEW DRUGS
A series of hitches have affected the availability of several experimental anti-HIV drugs. Glaxo Wellcome’s new PI amprenavir and the NNRTI delavirdine both failed to gain European Union approval despite having been licensed for some time in the US. A few weeks before, American regulatory authorities refused a licence to Gilead’s adefovir, a new type of anti-HIV drug. As lipodystrophy has provided a nasty reminder of the potential pitfalls in fast-tracking new drugs, and cross-resistance appears a significant threat within all drug classes, it now seems the drug approval process may demand more from new antiretrovirals than it has in the past. Drugs which appear to offer few clear advantages over those already licensed may face a rocky future.

So where is the good news coming from on drug development? The table accompanying this article summarises information on drugs in the pipeline. One of the most pressing issues facing the HIV community is the possibility that several of these experimental treatments may offer little to those who have already taken a number of different combinations. The arrival of T-20, a truly novel drug with a unique mode of action, is therefore particularly awaited. Limited UK trials of this new compound should begin early in the year.

ACCESS TO NEW TESTS
The UK’s Medical Research Council (MRC) is planning three studies which will assess the role of new monitoring tests in routine patient care. As we reported last month, the ERA trial (Evaluation of Resistance Assays) aims to recruit 480 people in the UK who need to switch their treatment regimen because it is no longer suppressing viral load. Participants will be entered in either Part A or Part B depending on how easy it is for a new three drug combination to be selected. In Part A, where a new combination can be selected, individuals will be randomised to have or not have a genotypic resistance test. People for whom the selection of a new regimen is more problematic will enter Part B, where they will be randomised to have either a genotypic resistance test or a genotypic test plus a phenotypic resistance test.

Several treatment centres are now set up to begin recruiting participants to ERA, and more will be added as they receive approval from their local ethics committees. However in the meantime, an increasing number of centres are beginning to offer resistance tests as part of their standard patient care package, on a limited basis.

The MRC is also planning the OPIUM trial (Optimising Protease Inhibitors Using Monitoring) which is awaiting funding approval. If funded, this study will assess the use of tests to measure drug levels amongst 400 people starting a new regimen which contains a protease inhibitor. Participants may be drug naive or experienced, and in this randomised study will have a fifty-fifty chance of being allocated to receive or not receive a protease inhibitor blood level test. OPIUM will run in collaboration with the Department of Pharmacology at Liverpool University, which is internationally renowned in this field.

Finally, the MRC is also planning a study to investigate resistance testing in children with HIV who are switching anti-HIV treatments.

CHANGING NEEDS
Alarming statistics on the spread of hepatitis C (HCV) infection were presented at a recent infectious diseases meeting in the US. 170 million people world-wide are estimated to be HCV-positive by the World Health Organisation; some 3% of the world’s population. One in five Egyptians and 2% of Americans are believed to be HCV-positive. Amongst the US HIV-positive population, a third are thought to be co-infected with HCV.

In the UK it is predicted that increasing emphasis will be placed on the problems faced by people with HIV from African communities, including access to treatments and disclosure of status.

KEY PREDICTIONS
- How to start HIV treatment may become clearer.
- When to start will not, but may be influenced by the availability of effective ways of managing HAART’s long-term side-effects.
- There will be growing pressure to understand, define and manage treatment failure better.
- The trend towards using simpler regimens will continue, but will not be a panacea for problems with treatment adherence.
- The use of structured treatment interruptions will be a key research focus.
- Resistance tests will be used much more often by people changing treatment in the UK, and healthcare commissioners will be under pressure to ensure access is equitable.
- Drug level tests may be used more often by people taking a protease inhibitor.
# The drug pipeline

## Anti-HIV drugs in current development

**BY ANNA POPPA**

<table>
<thead>
<tr>
<th>What is it called?</th>
<th>Who is it made by?</th>
<th>Stage of development</th>
<th>Access in the UK</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protease inhibitors (PIs)</strong></td>
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<tr>
<td>Amprenavir (Agenerase)</td>
<td>Glaxo Wellcome</td>
<td>Phase IV</td>
<td>Trials, expanded access for people with limited options</td>
<td>Approved in US, recent application turned down by EU</td>
</tr>
<tr>
<td>ABT-378 (Lopinavir, Aluviran)</td>
<td>Abbott Laboratories</td>
<td>Phase III</td>
<td>Trials, very limited expanded access for salvage therapy</td>
<td>Co-formulated with ritonavir to boost blood levels. Strong viral load data in naïve patients, and in PI-experienced</td>
</tr>
<tr>
<td>Tipranavir (PNU-140690)</td>
<td>Pharmacia &amp; Upjohn</td>
<td>Phase II</td>
<td>Not available, but trials expected before summer</td>
<td>First non-peptidic PI, may be effective against PI-resistant strains, but heavy pill burden in current formulation</td>
</tr>
<tr>
<td>BMS 232632</td>
<td>Bristol-Myers Squibb</td>
<td>Phase I</td>
<td>Not available, but trials expected early in 2000</td>
<td>Possible once daily PI</td>
</tr>
<tr>
<td>L-756, 423</td>
<td>Merck Sharpe &amp; Dohme</td>
<td>Phase I</td>
<td>Not available</td>
<td>‘Second-generation indinavir’, possible once daily PI</td>
</tr>
<tr>
<td>DMP 450</td>
<td>Triangle</td>
<td>Pre-clinical</td>
<td>Not available</td>
<td>New ‘cyclic urea’ PI</td>
</tr>
<tr>
<td>AG-1776</td>
<td>Agouron Warner-Lambert</td>
<td>Pre-clinical</td>
<td>Not available</td>
<td>‘Second generation amprenavir’ designed to have lower pill burden</td>
</tr>
<tr>
<td>GW433908</td>
<td>Glaxo Wellcome</td>
<td>Pre-clinical</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td><strong>Non-nucleoside reverse transcriptase inhibitors (NNRTIs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delavirdine (Rescriptor)</td>
<td>Agouron Warner-Lambert</td>
<td>Phase IV</td>
<td>Named patient basis</td>
<td>Approved in US, recent application turned down by EU</td>
</tr>
<tr>
<td>Emivirine (MKC-442, Coactinon)</td>
<td>Triangle</td>
<td>Phase III</td>
<td>Not available</td>
<td>Unimpressive early data, unlikely to work in NNRTI-experienced, twice daily dosing, negative interaction with nelfinavir</td>
</tr>
</tbody>
</table>

### STAGE OF DEVELOPMENT

**Pre-clinical** – describes studies undertaken in test tubes (in vitro) or in animals, and occurs before trials in humans.

**Phase I** – these trials test the treatment in only a few people, (sometimes healthy volunteers who are HIV-negative, or people with HIV who are not taking other medications), to learn whether it is safe to take, and to find the maximum safe dose.

**Phase II** – describes studies which assess whether the treatment is active against the disease in the short-term by looking for changes in certain markers, such as viral load or CD4 count, and assess its risks, i.e. side-effects.

**Phase III** – these further test the treatment in a larger group of people, to assess the balance of risks and benefits.

**Phase IV** – also called post-marketing studies, these trials evaluate the longer-term safety and efficacy of a treatment.
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</thead>
<tbody>
<tr>
<td>AG-1549 (S-1153)</td>
<td>Agouron Warner-Lambert</td>
<td>Phase I/II</td>
<td>Not available, but trials expected before summer</td>
<td>Appears unlikely to work after a previous NNRTI</td>
</tr>
<tr>
<td>GW420867X</td>
<td>Glaxo Wellcome</td>
<td>Phase I/II</td>
<td>Not available</td>
<td>Once daily, no food restrictions</td>
</tr>
<tr>
<td>Calanolide A</td>
<td>Sarawak Pharmaceuticals</td>
<td>Phase I</td>
<td>Not available</td>
<td>Derived from a plant found in the Malaysian rain forest</td>
</tr>
<tr>
<td>DMP 961 and DMP 963</td>
<td>DuPont Pharma</td>
<td>Pre-clinical</td>
<td>Not available, but trials expected before summer for DMP 961</td>
<td>‘Second generation efavirenz’</td>
</tr>
</tbody>
</table>

**Nucleoside analogue reverse transcriptase inhibitors (NRTIs)**

<table>
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<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lodenosine (FddA)</td>
<td>US Bioscience Inc</td>
<td>Development suspended</td>
<td>Not available</td>
<td>Phase II studies suspended after reported liver toxicities</td>
</tr>
<tr>
<td>Emtricitabine (FTC, Coviracil)</td>
<td>Triangle</td>
<td>Phase II/III</td>
<td>Not available</td>
<td>Similar to 3TC in structure and likely to be cross-resistant, also active against hepatitis B, possible once daily dosing</td>
</tr>
<tr>
<td>dOTC (BCH-10652)</td>
<td>BioChem Pharma</td>
<td>Phase I/II</td>
<td>Not available</td>
<td>Possible once daily, active in the brain</td>
</tr>
<tr>
<td>DAPD/DXG</td>
<td>Triangle</td>
<td>Phase I/II</td>
<td>Not available</td>
<td>Possibly active against multi-NRTI resistance, and against hepatitis B</td>
</tr>
</tbody>
</table>

**Other drug classes**

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<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Adefovir dipivoxil (Preveon, PMEA) – Nucleotide reverse transcriptase inhibitor</td>
<td>Gilead Sciences</td>
<td>Phase III</td>
<td>Trials, rollover access scheme</td>
<td>Future uncertain, US development terminated after US approval rejected due to weak potency and high level of kidney side-effects</td>
</tr>
<tr>
<td>Tenofovir (PMPA) – Nucleotide reverse transcriptase inhibitor</td>
<td>Gilead Sciences</td>
<td>Phase II/III</td>
<td>Not available, but trials expected before summer</td>
<td>Second generation nucleotide, unclear as yet whether kidney toxicities will be a problem</td>
</tr>
<tr>
<td>T-20 – Fusion inhibitor</td>
<td>Trimeris/Roche</td>
<td>Phase II/III</td>
<td>Not available, trials expected early in 2000</td>
<td>Currently given by injection, under investigation in salvage patients</td>
</tr>
<tr>
<td>T-1249 – Fusion inhibitor</td>
<td>Trimeris/Roche</td>
<td>Phase I</td>
<td>Not available</td>
<td>‘Second generation T-20’</td>
</tr>
</tbody>
</table>
ATU reader survey ‘99

Results now in from NAM’s yearly barometer of readers’ views

BY ANNA POPPA

In August of last year we mailed a short questionnaire to all AIDS Treatment Update readers who have a free subscription. This yearly task allows NAM to plan for the future, creating new additions to our portfolio of resources, and to make changes to existing publications according to the feedback we receive from our readers.

Our initial concern that after a year in which several other HIV agencies had already undertaken similar exercises, many of our readers would simply be ‘surveyed-out’, turned out to be unwarranted. Of just under 7,000 questionnaires distributed, 18% were returned, a good response rate.

In brief, just under half the respondents were living in London. 93% had an HIV-positive diagnosis. 90% were White, which means that White people were over-represented in the sample relative to epidemiological information. Black Africans, on the other hand, were under-represented. One of NAM’s operational priorities this year is to work in partnership with other agencies to develop a new information resource which will target Black Africans, and we intend that this project will help us reach, and serve, more members of those communities.

Overall, the verdict of AIDS Treatment Update readers is that the newsletter provides a highly valued service. The vast majority of respondents read the whole issue, describe the language employed as ‘about right’, and find the information provided helpful in making decisions about HIV treatments. The message from this majority is “Don’t go changing”.

The challenge for NAM, and for myself as Editor, is to find appropriate ways to respond to the minority of readers who are less happy with AIDS Treatment Update, without straying too far from what many people already see as a winning formula. We have always positioned AIDS Treatment Update at the higher-tech end of the spectrum, and given the breadth of HIV publications available in the UK now, we do not plan to venture down market. That said, a significant number of readers sometimes find articles too long and are put off by too much medicales. These criticisms have not fallen on deaf ears, and we will continue to think about how we can best use the full range of publications NAM produces to assist the greatest number of people.

LOOKING FORWARD

This month, Robert Fieldhouse joins NAM as a fully-fledged staff member and will contribute to AIDS Treatment Update regularly. Robert will be well-known to readers of BP Newsletter and Axiom already, and we plan to add more new contributors over the course of the year.

Our plans to update AIDS Treatment Update’s appearance is another exciting development, which we hope to bring you before the summer. Our emphasis will be on accessibility, and we’ll be trying hard to find ways to incorporate the graphics and diagrams which many of you have asked for.

To finish, I would like to register my gratitude, and that of NAM, to everyone who gave their feedback and encourage you to do so again in future. It continues to be an absolute honour to edit AIDS Treatment Update, and to work on a publication which is so well thought of.

www.aidsmap.com

Questions about treatment? Find out your options at aidsmap.com

FREE booklet: HIV Treatment Information on the World Wide Web. A practical guide to help you get to grips with the growing range of HIV-related treatment information on the World Wide Web, and make the most of the wealth of resources available on NAM’s acclaimed website www.aidsmap.com. To order your free booklet telephone 020 7627 3200, email info@nam.org.uk, or write to NAM Publications, FREEPOST LON277, London SW4 7YY.
Adefovir stumbles
Gilead Sciences have shelved the development of their anti-HIV drug adefovir dipivoxil (Preveon™) for the treatment of HIV disease in the US. This follows the recent decision of the US regulatory authorities to refuse Gilead’s application for marketing approval for adefovir. Gilead say they will continue to pursue the development of the drug for the treatment of hepatitis B.

Gilead applied for adefovir’s approval within the European Union in September, and the company were anticipating an initial decision from the European drug approval agency, the Committee for Proprietary Medicinal Products (CPMP) by the end of December. Gilead’s plans for adefovir in Europe are dependent on that decision. As this issue goes to press, the outcome is difficult to predict, though most observers would suggest that historically, the approach of European drug licensing bodies has been more conservative than that of their US counterparts rather than less.

In the meantime, Gilead plan to open an expanded use programme in Europe early in the New Year. This is expected to provide the drug on a rollover basis to participants in the ADHOC study, which recently closed to recruitment. It is not expected that this scheme will provide adefovir to people who have not used it previously.

Adefovir is the first of a new class of anti-HIV drugs called nucleotide analogues. Gilead are now expected to concentrate their HIV research efforts on a sister drug, tenofovir. Tenofovir (also known as PMPA) is in Phase II/III study and is available in the US through a small expanded use scheme. No such scheme exists in Europe, nor is tenofovir available through clinical trials at present, though these are scheduled to begin this year.

Pancreatitis risk
Bristol-Myers Squibb (BMS), manufacturer of ddl, d4T and hydroxyurea, has written to US doctors warning them to be on the lookout for cases of pancreatitis (inflammation of the pancreas) in patients with high CD4 counts taking ddl. The warning comes after a number of reports to the US Food and Drug Administration of pancreatitis cases in people taking ddl with hydroxyurea and d4T, and four deaths from pancreatitis in clinical trials where these drugs were being tested. Pancreatitis was identified as a potential side effect of ddl in early trials of the drug, but appears to occur less frequently with current doses and in individuals with less advanced HIV infection.

While BMS are concerned that use of ddl with hydroxyurea (to boost ddl levels) may result in an increased risk of pancreatitis, the company stresses that three out of the four individuals who died in clinical trials had other risk factors for pancreatitis, such as severe obesity, very high levels of triglycerides (a type of fat) in the blood, and gall stones (cholelithiasis). High alcohol consumption is also a serious risk factor for pancreatitis.

The symptoms of pancreatitis include nausea, vomiting and abdominal pain, often through to the back, and can develop suddenly. Individuals taking ddl who experience these symptoms are advised to seek medical advice immediately, and clinicians are advised to discontinue ddl treatment permanently if pancreatitis is diagnosed.

GW three-into-one
Glaxo-Wellcome is moving ahead with plans to combine its three nucleoside analogues AZT, 3TC and abacavir into one tablet called Trizivir™. The company has now submitted applications to EU and US licensing authorities, and UK studies were beginning as this issue went to press.

At the moment, AZT and 3TC can be taken as a single combined tablet (Combivir™) twice a day, and abacavir is taken as a single tablet twice a day. The three drug dose will also fit into one tablet, which will be taken twice daily. The use of triple nucleoside analogue combinations was discussed in AIDS Treatment Update issue number 83.

Ritonavir approved
Abbott Labs have received final confirmation that they may begin marketing their soft capsule formulation of ritonavir in the UK and other EU member states. These capsules had been available through a special access scheme begun when the regulatory agency gave an initial positive indication in August.
New lipo theory

Disrupted production of the steroid hormones cortisol and DHEA may be involved in the body fat and metabolic changes seen in people taking anti-HIV treatment, according to French researchers. The team suggests that steroid hormone production may be disrupted by the effects of protease inhibitors on cytochrome p450, a liver enzyme involved in both the production of the steroid hormones, and the metabolism of protease inhibitors.

The group tested 37 men on HAART and 20 HIV-negative patients for a variety of immunological, metabolic and body fat changes, and found:

- 23 of the 37 HAART recipients had body fat changes (lipodystrophy), though these were not related to particular drugs or drug classes
- CD8 cells were significantly higher in those with lipodystrophy, and were likely to have increased further after starting therapy
- Very low density lipoprotein (VLDL) cholesterol (high levels of which are linked with increased risk of heart disease) was significantly higher in the lipodystrophy group, as were all triglyceride measurements (but the latter were also elevated in those on HAART without lipodystrophy)
- Insulin concentration was significantly raised compared with the control group
- Cortisol levels were significantly higher in those on HAART, but there was no difference between those with and without lipodystrophy
- DHEA levels were significantly lower in the lipodystrophy group, and the ratio of cortisol to DHEA was markedly higher, compared to the other groups. An elevation in this ratio was significantly associated with lipid ratios suggesting increased risk of heart disease.

What might these findings mean?

One of DHEA’s functions is to control levels of cortisol. If DHEA levels are suppressed, the authors of the report suggest this will permit cortisol levels to rise, encouraging an increase in lipid production. DHEA is also involved in the regulation of lipid production, and has been shown to reduce blood levels of cholesterol and body fat in HIV-negative men.

DHEA also regulates insulin secretion. A decline in DHEA levels could become self-perpetuating, because such a decline will also allow increased insulin secretion, an increase in insulin resistance and the knock-on effect of a further reduction in DHEA levels.

These hormones are involved in the regulation of fat deposits in both peripheral tissues (the arms and the legs) and the central adipose tissue of the abdomen. Elevated cortisol levels could stimulate fat cells in peripheral tissue to release stored fats, while the decline in DHEA levels may block the storage of fat in peripheral tissue. Meanwhile, circulating fat is mopped up by central fat deposits, leading to the characteristic fat belly seen in some people with abnormal fat redistribution syndrome.

Cautions

However, doctors have urged people with HIV to be cautious in interpreting this new information. Changes in the relative levels of DHEA and cortisol have been observed in people with AIDS prior to HAART. Also, this study was conducted in men and hormonal changes in women may differ. Another puzzle is the relationship seen in this study between strong CD8 responses and increased lipodystrophy risk. In people whose anti-HIV therapy resulted in high levels of CD8 cells and fully suppressed viral load, one would expect DHEA levels to be high rather than low.

The need for further studies

DHEA is already used quite frequently by people with HIV as an anti-depressant, as an energy booster and as an aid to building muscle (it is a precursor of testosterone). This makes it important to tell your doctor if you are using DHEA and also taking antiretroviral therapy, so that any possible effects of DHEA can be taken into account.

These findings may encourage some people with lipodystrophy to consider experimenting with DHEA, but it should be stressed that this would be speculative and may have no effect on this condition whatsoever. To determine if DHEA supplementation has any effect on the development, severity or reduction of body fat changes, large scale trials will be needed. At present DHEA is being marketed on the internet as a ‘wonder hormone’ capable of burning fat, increasing energy and reversing ageing, and can be bought as an over-the-counter ‘health supplement’ in the US. It is unlicensed in the UK.

adherence The act of taking a treatment exactly as prescribed
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
cross resistance When resistance to one drug reduces the virological response to subsequent treatment with another drug which has not been taken before
fusion inhibitor Anti-HIV drug targeting the point where HIV locks on to an immune cell
genotypic test Resistance test which detects changes in HIV’s genes
insulin Hormone which enables body tissues to take up sugar from the blood
insulin resistance When insulin is present in the blood but unable to do its job properly
lactic acidosis High blood level of lactic acid: a rare side-effect of nucleoside analogues
lipid A general term for fats in the blood
lipodystrophy A disruption to the way the body processes, uses and distributes fat
naive Never having taken HIV treatments before
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
phenotypic test Resistance test which measures the amount of drug needed to stop HIV reproducing
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 a trial participant will receive
regimen Drug or treatment combination
resistance A drug-resistant HIV strain is less susceptible to the effects of one or more anti-HIV drugs because of its genetic make-up
reverse transcriptase An enzyme which converts genetic material from RNA into DNA, an essential step in the lifecycle of HIV
toxicity The extent or ways in which a drug is poisonous to the body
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

Glossary of Terms

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

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Nucleoside analogue reverse transcriptase inhibitors: anti-HIV drugs that include AZT, ddi, ddc, 3TC and d4T

Phenotypic test Resistance test which measures the amount of drug needed to stop HIV reproducing

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 a trial participant will receive

Regimen Drug or treatment combination

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

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

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

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

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
  Phonenumber: 0845 9470047
  Mon & Wed 3pm - 9pm, Tue 3pm - 6pm
  All calls charged at local rates.

- Body Positive
  Treatment Advice: Tue & Wed 12pm - 5.30pm
  Call Robert on 020 7287 8010 to make an appointment.

- The Terrence Higgins Trust
  Helpline: 020 7242 1010 Daily 12noon - 10pm
  Treatment Support: Call the Treatments Team on 020 7831 0330 for an appointment.

NAM recommends readers to seek treatment advice from more than one source, and to discuss all your decisions with your doctor.

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

Donations towards production costs are welcomed.