

# aids treatment update

## AIDS in America & new drug options

This month we fix our gaze across the Atlantic, to look more closely at the American HIV epidemic. After almost twenty years of AIDS, the new administration inherits responsibility for leading an effective response to the global pandemic, both via scientific advancement and through socio-economic solutions to the problems faced by the world's worst affected regions. At home, the domestic epidemic, fuelled by the same kind of social inequalities which are propelling HIV in 'the developing world', continues to overwhelm the resources which have been dedicated to its management. George Bush Junior has a very senior task ahead of him – based on current estimates, his first term of Presidency is likely to see the total number of HIV-infected Americans reach one million.

In our second article, we take one of our regular looks into the HIV drug pipeline, with an assessment of the current progress of the next generation of antiretrovirals. One or two are expected to be hitting UK clinics by the time this edition goes to press, earmarked particularly for those with a lot of drug experience and few other options.

**a question of colour** 2

**new drug review** 6

**news in brief** 10

# a question of colour

## 2 alarm bells ring as HIV prevalence rates in American Black gay men mirror those seen in the world's worst affected nations by robert fieldhouse

At the opening session of the 8<sup>th</sup> Annual Retroviruses Conference, held recently in Chicago, Kevin de Cock of the US Centres for Disease Control (CDC), and veteran HIV epidemiologist, posed a rhetorical question. If the USA were facing HIV prevalence rates of 25% – as is the case in several sub-Saharan African countries – would the US government, and the American people, respond with the same near indifference they show for the plight of infected Africans?<sup>1</sup>

An answer to de Cock's question would be offered in the form of new data, presented the next day. These data illustrate that in fact the US is hosting dramatic prevalence rates among certain sub-groups of its population. Relative safety may be afforded to some Americans, but others, Black gay men in particular, face an entirely different scenario.

### Race and risk of infection: New York

The data came from a recent survey of 542 gay male New Yorkers, aged 23 to 29, who were identified at gay bars, clubs and social centres between March 1999 and July 2000. The survey found that whilst 2% of gay White men were HIV-positive, this compared to 14% of gay Latinos and 33% of gay Black men<sup>2</sup>.

How could such a wide variation in HIV prevalence have arisen? The study found that Black men who have sex with men were no more likely to exchange sex for money or drugs; no more likely to have a history of sexually transmitted diseases; no more likely to have had anal sex in the past six months; no more likely to have had unprotected anal sex with a serodiscordant partner; no more likely to

have tested for HIV; and were significantly less likely to report more partners, than men in other ethnic groups.

However, the study did reveal that Black men were more likely to believe themselves to be HIV-positive or perceive themselves as more likely to become HIV-positive in the future. This kind of fatalistic attitude to HIV acquisition has been well documented among gay men in the past by psychosocial researchers, yet it has never been so clearly linked to such a high prevalence rate.

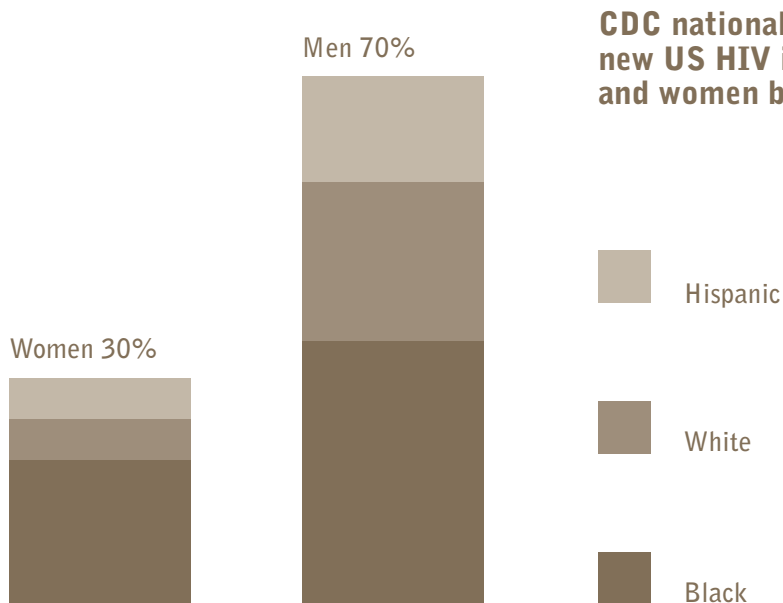
Additionally, though Black men were less likely to report having had receptive anal sex in the past six months, they were less likely to have used a condom when they did so.

Risk-taking was high across the whole sample, with 58% acknowledging anal sex without a condom in the previous six months. The high prevalence rate among Black gay men therefore poses particular dangers for this group. However, if risk-taking remains the same, sexual mixing patterns among Black, Latino and White men will be a decisive factor in whether such high prevalence among Black men might fuel a resurgence of HIV among gay men of other races.

### East Coast, West Coast: same story

A separate study of high-risk behaviour and HIV prevalence among gay men aged 23-29 in six US cities suggests this disparity extends far beyond New York<sup>3</sup>.

The survey was carried out between 1998 and 2000 at public venues in Baltimore, Dallas, Los



Angeles, Miami, New York City and Seattle, and involved a total of 2,401 gay men. HIV prevalence increased with age. Again, however, it was race and not age that was the biggest predictor of HIV status. Infection rates among Latino and Black men mirrored those found in New York City, at 15% and 30% respectively.

This multi-centre study illustrates the fact that prevention efforts across the whole of the USA have failed to adequately target men of colour, given that all of these men grew up in a time of active education around HIV.

### The changing US epidemic

Data reporting in the USA is incomplete. By 1993 only 25 states had adopted HIV surveillance systems. Approximately 900,000 people in the USA are estimated to be living with HIV, but around one third are unaware of their status. New HIV incidence has remained stable since 1992 at an estimated 40,000 new infections each year.

HIV has always disproportionately affected Black and ethnic minority communities in the USA and this disparity has become even clearer since the introduction of new and more effective antiretroviral combinations in 1996. In the US, more deaths from AIDS occurred in 1993 than in any other year, when over 40,000 were recorded. Deaths from AIDS declined in

1996, but there were significant variations between racial groups and genders. Whilst deaths declined 21% amongst Whites that year, they declined only 2% amongst Black Americans, and actually increased 3% among women during the same time period.

Black gay men account for at least 40% of all AIDS cases among Black men in the USA. 70% of all AIDS cases in the US now occur among ethnic minorities. Additionally over half of all new HIV infections occur among Black people. (Figure above illustrates racial breakdown of new US infections).

### The heterosexual epidemic

New HIV infections among women make up one third of total new US infections. Black and Latino women account for 82% of all new infections among women. Concurrent partnerships, (those that overlap in time), facilitate the spread of HIV, and according to new data presented at the Retroviruses Conference, may be important in establishing and maintaining the high rate of infections in these groups.

Researchers from North Carolina interviewed 207 newly diagnosed Black American men and women, all of whom who denied male-male sexual contact and injection drug use, (and were therefore assumed to have contracted

## a question of colour continued

HIV heterosexually). Their responses were compared to a control group of 234 Black Americans who were not newly diagnosed. HIV-positive women were more likely to have participated in concurrent partnerships than the control group. 59% of HIV-positive women reported concurrent partnerships during the preceding three years, compared to 32% of the control group<sup>4</sup>.

### Access to HIV treatments

Uptake of HAART among adults receiving care in the USA has dramatically increased since 1996. The Adult/Adolescent Spectrum of Disease Project recorded data from 16,989 patients, in eleven US cities, who were eligible for HAART<sup>5</sup>. The proportion of patients prescribed HAART increased from 19% in the first half of 1996 to 68% in the first half of 1999. However, Black Americans and Latinos were found to be much less likely to be receiving therapy than White people.

### Inner city care

In a lecture on the reality of HIV care in US inner cities, Carlos del Rio presented an analysis of the role of the Emergency Room (Accident and Emergency Department), as a key provider of care for people living with HIV. Of 227 patients admitted to the Emergency Room during January to March 1997, 84% were Black Americans, 46% were injecting drug users and 14% were gay men. The majority of patients had dropped out of routine care services and used the Emergency Room to 'crisis manage' their care<sup>6</sup>.

### Transmission of drug resistant HIV

Data on the prevalence of HIV drug resistance mutations among recently and chronically infected Americans, who had not been exposed to HIV treatment, shows that White gay men are more likely than Black men to carry HIV strains which are resistant to antiretrovirals<sup>7</sup>.

The data were compiled between 1997 and 1999 in ten US cities. Overall, 10% of participants had HIV mutations associated with decreased drug susceptibility. A total of 16% of White gay men had resistance mutations, compared to 7% of Black American gay men, and 3% of Black American heterosexual men.

People with partners who were taking antiretrovirals were the most likely to have resistance to anti-HIV drugs before beginning therapy. It's hardly surprising then that the level of resistance was lowest among Black people, as they are less likely to be in touch with health care services, or to be on HAART.

### Race and viral load

Analysis of a database of 601,352 HIV viral load tests has provided information on trends in viral load levels among Americans on HIV treatment since 1996. The database includes 286,873 individual patients, of whom 41,536 have had more than four viral load test results included in the analysis<sup>8</sup>.

Among patients from areas where Whites exceeded 60% of the population, the rate of undetectable viral load rose to 47% by the end of 1999. In areas where Whites comprised less than 25% of the population, only 33% of the sample had undetectable viral load. Differences in treatment failure rates, defined as a viral load rebound over 10,000 copies, were also found to be associated with race.

### CDC unveils new prevention plan

The CDC has set itself the goal of eliminating racial health disparities in six major areas by 2010. At last month's Retroviruses Conference, the CDC announced a new strategy to reduce new US HIV infections by 50%<sup>9</sup>. Known as SAFE, or Serostatus Approach to Fighting the HIV Epidemic, the approach aims to increase

the number of infected individuals who know their status; promote entry into health care and prevention services; increase the number of individuals living with HIV who are receiving appropriate care and treatment services; increase adherence to prescribed antiretroviral therapies; and support the adoption and maintenance of HIV risk reduction behaviour.

### Issues to consider in the UK

The epidemic among Black communities in the UK is concentrated in African communities who have contracted HIV heterosexually whilst abroad. There is little evidence of a heterosexual spread from high-risk communities (i.e. injecting drug users and bisexual men), in White or Black communities.

However, in the UK, the unlinked anonymous HIV prevalence survey of attendees at sexually transmitted disease clinics does not record information on ethnicity, but rather on the country of origin. Therefore it is difficult to clearly identify how many Black people in the UK are HIV-positive.

A new method of data reporting implemented in the past year will provide additional information to UK surveillance agencies, such as country of birth, country of infection and year of arrival in the UK. This will help to track the epidemic among Black Africans or others born outside the UK, but it will not shed light on infections among British-born Black people.

According to data from the Survey of Prevalent Diagnosed HIV Infections, of a total of 10,650 gay men seen for care in 1999 in England, Wales and Northern Ireland, 88% were White, compared to 5% who were Black, about half of whom were Black Caribbean<sup>10</sup>.

Dr Kevin Fenton of the UK Public Health Laboratory Service told *ATU*, "Whilst it's difficult to extrapolate the differences witnessed in the US to the UK, since the racial and ethnic groups have different historical contexts and socioeconomic profiles, the differences highlight the importance of poor access to care, poverty, and lack of education as major determinants of HIV disease progression and transmission".

Surveillance data suggest that the majority of UK HIV-positive Black Caribbean men have been infected homosexually. Whilst data on undiagnosed HIV infections among Black gay men in this country are lacking, the report *What are you like?* from HIV prevention group, Big Up, highlighted significant health promotion needs among Black men who have sex with men.

Bacterial sexually transmitted infections, which may facilitate HIV transmission, disproportionately burden Black Caribbean heterosexuals. It is therefore important to monitor and be vigilant, as well as invest in HIV prevention work with these communities.

### key conclusions

- HIV continues to disproportionately affect non-White communities in the US, and HIV prevalence among American, urban Black gay men is particularly alarming.
- Racial minorities, women and youth account for a growing number of AIDS cases in the US.
- Declines in AIDS incidence and mortality among Americans are not evenly distributed across racial groups, probably due to differences in access to treatments.
- The failure of HIV prevention programmes has contributed to the spread of HIV within non-White communities in the US.
- UK surveillance systems do not record the ethnicity of people with undiagnosed HIV infection, which prevents tracking of HIV within Black people in this country. HIV prevention work in the UK must target all affected communities.

### Big Up

Big Up is a sexual health organisation for Black men who have sex with men. Telephone 020 7501 9264. <http://www.bigup.co.uk>

### references

- Abstracts from the 8<sup>th</sup> Annual Retroviruses Conference, Chicago, 2001:
- 1 De Cock K, abstract L2.
  - 2 Torian L, abstract 212.
  - 3 Valleroy L, abstract 211.
  - 4 Adimora A, abstract 215.
  - 5 McNaughten A, abstract 494.
  - 6 Del Rio C, abstract S21.
  - 7 Weinstock H, abstract 265.
  - 8 Faruki H, abstract 495.
  - 9 Janssen R, abstract S20.
  - 10 Public Health Laboratory Service 1999.



# new drug review

## 6 Chicago Retroviruses Conference hears new data on experimental anti-HIV drugs & their performance against drug resistant HIV by anna poppa

At last month's 8<sup>th</sup> Annual Retroviruses Conference in Chicago, new data were unveiled on a host of prospective therapeutic candidates for use in the treatment of people with HIV. These drugs will, in most cases, be of greatest interest to people who have lots of treatment experience and who are in need of new treatment options.

### T-20

Fusion inhibitors have solicited considerable interest from the HIV community because they are an entirely new class of antiretroviral, and therefore offer a new option to people with broad experience of currently available drugs. They target an early stage in HIV's reproductive cycle, fusion between the viral 'envelope' proteins and entry molecules on the surface of human immune cells.

Trimeris, an American Biotech company, has entered into a partnership with Roche

Products, who have a long experience of the HIV therapy field, to bring their two fusion inhibitors T-20 and T-1249 to market. The first of these, T-20, has entered Phase III study in the US, and is expected to do so in Europe soon. This study will recruit patients at a limited number of centres in the UK. An expanded access programme is unlikely this year.

Forty-eight week data from a study investigating the use of T-20 in a group of highly treatment experienced people were reported at last summer's Durban International AIDS Conference, (see *AIDS Treatment Update* 92). Early results from a second pilot study were presented in Chicago.

Study T-20-206 is an open-label, dose-comparison study involving people who have previously taken PIs but not NNRTIs. Seventy-one people were randomised to receive either a four drug 'salvage' regimen consisting of

abacavir, amprenavir/ritonavir and efavirenz (the control group); or the four drug regimen plus T-20, given as a twice daily subcutaneous injection of either 50mg, 75mg or 100mg.

At entry, median viral load was 4.27 logs (around 18,000 copies) and median CD4 was 232 cells. After 16 weeks, 37% of the control group and 48% of the T-20 recipients had viral load below 50 copies; and 58% and 71% were below 400 copies respectively. These are intention to treat analyses, where participants whose results were missing were counted as failures. CD4 responses were also improved in the T-20 arms.

This trial is ongoing and a protocol amendment has shifted all T-20 recipients to the 100mg twice daily subcutaneous dose. Injection site reactions such as swelling, redness and pain are common unwanted effects of administering treatments in this way, and these occurred in two thirds of T-20 recipients. Most were mild to moderate, and only two people withdrew from the study as a result.

## T-1249

T-1249 is a second generation fusion inhibitor, which has been 'rationally designed' by Trimeris as a follow-on drug for T-20. Its molecular structure is intended to produce activity against HIV which has developed resistance to T-20. Though test-tube studies support this concept, it has yet to be proven in people. Several companies are now looking at testing combinations of fusion inhibitors with a view to developing regimens which don't require use of any of the current therapies. This strategy, if successful, is at least three or four years away.

Study T-1249-101 is the first study to pilot this drug in humans, and results were presented at the Retroviruses Conference. Seventy-two people were recruited to this dose-ranging, monotherapy study. All were treatment experienced with viral load over 5,000 copies. After a two week antiretroviral wash-out period, volunteers were randomised to one of six dosing arms:

- 6.25mg once or twice daily
- 12.5 mg once or twice daily
- or 25mg once or twice daily.

Of 72 individuals enrolled, 63 received at least one dose of T-1249, and 61 completed the fourteen day study period. Mean viral load was in the range of 4.95-5.54 logs, mean CD4 was from 84-146 cells, and the prior number of antiretrovirals which participants had been exposed to was ten. Of 194 treated-related adverse events, just two were considered serious: one case of hypersensitivity and one neutropenia. Aside from these, common side-effects were injection site reactions (40%); headache (11%); dizziness (8%); fever (8%); and diarrhoea (6%).

Viral load responses, and average trough concentrations of T-1249 in the blood stream were dose dependent (and that's what studies of this type expect to observe), though at the 6.25mg dose there was no measurable virological effect. At the other end of the spectrum, those who received the twice daily high dose experienced an average viral load fall of 1.3 logs between ten and fourteen days after treatment began.

## BMS-232632

BMS-232632 is a protease inhibitor in development from Bristol-Myers Squibb. It is dosed once daily with food, and the pill burden is expected to be low, perhaps one tablet a day. In test-tube studies, BMS-232632 remains active against HIV which is resistant to a single PI, but virus with reduced sensitivity to several PIs also has reduced sensitivity to the BMS drug. So far, clinical trial data is available on its use in people who are new to treatment only and so its usefulness to people with drug experience is unclear.

Study AI424-007 randomised volunteers to receive either nelfinavir, or one of three doses of the BMS PI for a two week monotherapy period. After that, d4T and ddI were added to make a three drug HAART regimen. 98 people completed 48 weeks of treatment, and an additional 322 began the three drug phase subsequently. Average viral load at entry was 4.75 logs.

After 24 weeks on three drug therapy, 63% of nelfinavir recipients, and 65-68% of BMS-232632 recipients had viral load below 400

## glossary

### adherence

Taking a treatment exactly as prescribed.

### antiretroviral

A substance that acts against retroviruses ,e.g. HIV.

### CD4

A molecule on the surface of some cells onto which HIV can bind. The CD4 cell count roughly reflects the state of the immune system.

### cholesterol

A waxy substance, mostly made by the body and used to produce steroid hormones, associated with hardening and narrowing of arteries.

### double-blind

A trial where neither the researchers nor participants know which assigned treatment an individual participant is taking.

### HAART

Highly Active

Antiretroviral Therapy, a term used to describe anti-HIV therapy with three or more drugs.

### lipid

A general term for fats.

### monotherapy

Taking a drug on its own.

### mutation

A single change in gene sequence.

### neutropenia

A shortage of white blood cells called neutrophils.

### NNRTI

Non nucleoside analogue reverse transcriptase inhibitor. Antiretroviral family which includes efavirenz, nevirapine.

### NRTI

Nucleoside analogue reverse transcriptase inhibitor.

### nucleoside analogue

Antiretroviral family which includes AZT, ddI, ddC, 3TC, d4T, abacavir.

copies. In this study, nelfinavir was dosed three times daily, and both it and the BMS PI are taken with food. ddI, on the other hand is taken on an empty stomach, which is likely to have presented a greater adherence challenge for the nelfinavir recipients than those on the BMS PI. Whilst this is only an early look at the data, one might therefore have expected the viral load responses to the BMS drug to have been somewhat better.

Diarrhoea affected 51% of those receiving nelfinavir and 17% of BMS-232632 recipients. The BMS PI has been associated with raised bilirubin levels, which may lead to jaundice if drug levels are not reduced. There was an early and sustained rise in total cholesterol in the nelfinavir arm, and a minimal increase in the BMS PI arm, and triglycerides rose on nelfinavir and remained unchanged on BMS-232632. A structured assessment of body fat changes has not been incorporated into the study at this point, and so claims that the BMS PI is a 'lipid-safe' option should be treated with caution.

### Tipranavir

Tipranavir belongs to a new class of PIs called dihydropyrones or non-peptidic PIs. Originally developed by Pharmacia & Upjohn, tipranavir was bought by Boehringer Ingelheim when Pharmacia left the HIV field last year. Whilst test-tube studies indicating that tipranavir retains activity against HIV which is resistant to multiple PIs have made this drug look promising, its development seems to have slowed during 2000 and there have been little new data for some time. Dosing the drug with ritonavir seems the likely way forward as this reduces what was an unattractive pill burden.

Two clinical trials have been reported. In study 0015, 31 treatment naive individuals were

randomised to receive either 1200mg tipranavir twice daily, or either 300mg or 1200mg tipranavir with 200mg ritonavir twice daily for fourteen days. Viral load fell by more than 1.5 logs in those who received tipranavir with ritonavir, compared to a fall of around 0.8 logs in the tipranavir group. Nausea occurred more frequently in those on the 1200/200mg regimen, but otherwise no substantial differences in side-effects were reported.

In study 006, 38 NNRTI naive individuals with experience of at least one PI were randomised to receive either 1200mg or 2400mg tipranavir with 200mg ritonavir, along with efavirenz and one nucleoside analogue. After 12 weeks, the average viral load reduction in the high dose group was 2.29 logs, compared with 2.72 logs in the low dose group. Similar proportions had viral load below 400 copies at week 12 (71% versus 75%).

Phase II/III studies of tipranavir are ongoing in the USA and Europe, though not in the UK. Expanded access during 2001 is a possibility. A paediatric formulation is being developed.

### DMP 450

DMP 450 (mozenavir) is a PI which was discovered by DuPont Pharma and is now being developed by Triangle Pharmaceuticals. A Phase I/II comparison of DMP 450 with indinavir, in combination with d4T and 3TC in people new to treatment, found no difference in viral load suppression after twelve weeks. Those receiving indinavir were more likely to experience an increase in total cholesterol, but again these are very preliminary data. DMP 450 is not available in the UK.

### Tenofovir

Tenofovir is an experimental, once daily nucleotide analogue, a class which targets

HIV's reverse transcriptase enzyme. Tenofovir is currently on trial in the UK and elsewhere, and Gilead Sciences have recently announced a limited expanded access programme which is expected to open in the UK in the near future.

In study 907, tenofovir was used to intensify HAART among people with detectable viral load. At entry, average viral load was around 3,000 copies, and average CD4 count was 427 cells. 94% had evidence of resistance to nucleoside analogues; 58% to PIs; and 48% to NNRTIs.

In this randomised, double-blind, placebo-controlled study, the addition of 300mg tenofovir to stable background therapy produced an average viral load decline of 0.59 logs after 24 weeks of treatment. Forty-five per cent (155/346) of tenofovir recipients had viral load below 400 copies at this point compared to 13% (23/172) of those on placebo.

Tenofovir's development was preceded by adefovir, whose study in HIV disease was terminated due to the high level of kidney toxicity observed in people taking it. Fears that tenofovir may be similarly affected have been assuaged by data thus far. No kidney complications were reported over 48 weeks follow-up.

Virological response to tenofovir is related to prior nucleoside analogue use (drugs which also target reverse transcriptase), appearing greater in people with 3TC resistant virus, and poorer in people with a resistant strain called T215F/Y, which is associated with resistance to AZT and d4T. The multi-nucleoside resistant Q151M strain remains sensitive to tenofovir, but sensitivity to the T69SS mutant, also multi-nucleoside resistant, appears related to the presence or absence of 3TC resistance.

## FTC

FTC is a new once daily nucleoside analogue from Triangle, in Phase II study and not yet widely available. Two new studies which compared the drug with 3TC, were presented at the Retroviruses Conference.

Study FTC-303 randomised 440 people with viral load below 400 copies on a 3TC-containing three drug regimen to either remain on that regimen, or switch from 3TC to FTC. After 48 weeks follow-up, there were no differences in the number of virological failures between arms.

Study FTC-302 compared FTC and 3TC with d4T plus either efavirenz or nevirapine amongst 468 people who were new to treatment. The study found a greater number of virological failures in the FTC arm. Adverse events related to FTC were uncommon.

## New formulations

Sustained release formulations of both d4T and AZT are in development and should reduce daily dosing. Pill burdens should be reduced by the successful future development of a 200mg delavirdine tablet, a 600mg efavirenz capsule, and a 625mg nelfinavir tablet.

## Failed or suspended drugs

No review of the HIV drug pipeline can be complete without a cautionary reminder that the development process necessarily produces successes and failures. In recent memory a number of candidates have been abandoned, or suspended due either to unforeseen side-effects or poor anti-HIV activity. These include lovirodine, FddA, dOTC, GW420867X, adefovir, SC-52151, MK944A, PD178390, and of late capravirine, an NNRTI which was in fairly late stage development, but whose future is currently uncertain.

### open-label

Clinical trial where both the researcher and participants know who is taking the experimental treatment.

### PI

Protease inhibitor.

### placebo

A pill which looks and tastes exactly like a real drug but contains no active substance.

### protease inhibitor

Antiretroviral family which includes saquinavir, indinavir, ritonavir.

### randomisation

The process of selecting by chance the treatment that a trial participant will receive.

### regimen

A drug combination and the way it is taken.

### resistance

A drug-resistant HIV strain is one which is less susceptible to the effects of one or more anti-HIV drugs.

### triglycerides

The basic 'building blocks' from which fats are formed.

### viral load

Measurement of the amount of virus in a sample. HIV viral load indicates the extent to which HIV is reproducing in the body.

### access to new drugs

Several drugs mentioned here are available in the UK through trials or special access schemes. See [aidsmap.com](http://aidsmap.com) for the most up-to-date news.

### further reading

In next month's *AIDS Treatment Update* we will be looking in more detail at the choices available to people with lots of drug experience.

## Adherence predicts future health

According to new research from the University of California at San Francisco (UCSF), people who experience problems adhering to HAART progress to AIDS or severely compromised immunity more quickly than those with better adherence. Though previous research has linked poor adherence with viral load rebound and treatment failure, this is the first study to associate adherence with disease progression.

The UCSF team followed people who had been taking three or more anti-HIV drugs for at least one month. Their adherence was measured using MEMS, an electronic device which registers whenever a medication container is opened, and by conducting a series of unannounced home pill counts. The two key events which study participants were to be monitored for were the development of an opportunistic infection, or a CD4 count below 200 cells. Those who missed more doses of their medication were found to have a higher risk of disease progression.

Encouragingly, a 10% increase in the level of adherence reduced the risk of developing an OI, or progressing to a CD4 level below 200, by between 21-28%, which demonstrates the substantial health benefits to be gained through the provision of effective adherence support measures to people on HAART. Whilst adherence levels above 90% were deemed necessary for ongoing viral load suppression, the UCSF team concluded that lower levels of adherence, between 50-90%, may still delay disease progression over the short-term.

*Reference: Bangsberg DR et al. 8th Annual Retroviruses Conference, Chicago, abstract 483, 2001.*

## Treatment response in non-Europeans

Doctors from two of London's leading HIV treatment centres have presented conflicting information on treatment outcomes in people infected with non-B HIV subtypes. These subtypes are predominantly carried by people who acquired HIV infection outside Europe and North America.

At the Royal Free Hospital, 50 people infected with non-B subtypes were compared with 50 matched subtype B patients from the Free's patient database. All had started HAART and had subsequent CD4 and viral load results recorded over a minimum of 24 weeks. There were no differences between the two groups in their average baseline viral load, the proportions who were treatment naïve, or in the regimens used. The groups differed only with respect to gender – women were found more frequently in the non-B group than the subtype B group.

After an average follow-up period of 75 weeks, there were no differences in the proportions whose viral load fell either below 400 or below 50 copies, or in the speed at which these two markers were reached. Similarly, there was no difference in the average fall in viral load, in the average duration of response, or in the proportions who maintained a virological response after 48 weeks of treatment.

However, a comparison between European and non-European patients at St Mary's Hospital found that non-Europeans were less likely to have undetectable viral load twelve months after starting HAART than European patients. Eighty-nine people with non-B subtypes, most of whom were Ugandan, were matched with

248 people infected with subtype B. The non-B group included a greater proportion of women than the subtype B group. After six months of HAART, viral load responses were similar across the two groups, with 81% having an undetectable viral load. However, by twelve months the groups had diverged: while 84% of the subtype B group had undetectable viral load at this point, only 56% of non-B patients were undetectable.

The St Mary's group suggest the differences they observed cannot be explained by differences in subtype response to anti-HIV drugs, given the similarity of viral load responses at the six month mark. Instead, they propose that poor adherence may explain the poorer response amongst non-B patients (though this was not measured within this study), and that there may be a need to reconsider the applicability of available adherence support measures to Africans and other non-Europeans.

*References: Frater AJ et al. 8th Annual Retroviruses Conference, Chicago, abstract 493, 2001. Loveday C et al, abstract 526.*

## US guidelines updated

Newly updated antiretroviral treatment guidelines from the US Department of Health and Human Services (DHHS), released to coincide with last month's 8<sup>th</sup> Annual Retroviruses Conference, reflect growing conservatism amongst HIV doctors on that side of the Atlantic. According to the DHHS guidelines, the US is to follow UK practice and recommend that anti-HIV treatment need not begin until an individual's CD4 cell count has fallen below 350 cells. The prior version of these guidelines advocated earlier intervention with anti-HIV therapy, beginning at CD4 counts below 500.

The new DHHS guidelines have swung into line with the 2000 British HIV Association (BHIVA) guidelines on HIV therapy as a result of increasing concern over long-term side-effects, and recognition that there is currently no evidence of a greater clinical benefit to starting treatment at higher CD4 counts.

BHIVA's yearly revision of the UK's treatment guidelines is currently underway, and it is anticipated that the question of when to start anti-HIV therapy will be scrutinised no less closely here than in the US. According to some BHIVA members, there is still scope to lower the CD4 threshold at which treatment initiation may be recommended.

*Reference: The US DHHS guidelines are available on the web at <http://www.hivatis.org>. UK guidelines are available at the NAM/BHIVA website <http://www.aidsmap.com>*

## Rising Irish infections

Doctors at St James' Hospital, Dublin, have documented a rising rate of new HIV diagnoses among injection drug users (IDUs) in Dublin. Most of these newly diagnosed infections have occurred in people under 25.

Newly diagnosed infections amongst IDUs had been declining since 1989, when 121 cases were diagnosed. An all-time low of twelve new cases were diagnosed in 1998. However, this increased five-fold between 1998 and 1999, and there were 96 new cases between January 1999 and June 2000.

The average age of those people diagnosed between 1999 and 2000 was 25, and 40% of new diagnoses occurred in people under 22 years of age. Three quarters were also found to be infected with hepatitis C.

At present there are an estimated 13,000 Dubliners who have heroin addiction, and 5,000 receive a regular methadone prescription. The St James' group suggest a revised methadone treatment protocol, introduced in Dublin in 1996, may have contributed to increased HIV transmission between IDUs. The protocol moved responsibility for methadone prescription to GPs, which may have resulted in an overall reduction in methadone supplied via the illegal market, and a consequent increase in the use of street heroin.

*Reference: Clarke S et al. 8th Annual Retroviruses Conference, Chicago, abstract 217, 2001.*

### treatment interruption study

TILT has recently begun recruiting patients to a randomised trial comparing continuous anti-HIV therapy with a structured treatment interruption, or with IL-2 therapy plus a treatment interruption (see this month's Factsheet). TILT is recruiting at the Royal Free Hospital, the Mortimer Market Centre, and the Royal Sussex County Hospital, Brighton. Participants must genuinely have no opinion about stopping treatment; must have been on stable HAART with viral load below 50 copies for at least three months; must have CD4 above 300; and a CD4 nadir above 100.

### NAM forum

Hepatitis is the subject of our Information Forum on Monday March 26<sup>th</sup>, and our guest speaker is Dr Mark Nelson. Venue: Palms Room, 4<sup>th</sup> Floor, University of London Union, Malet Street, WC1, from 7pm to 9pm. A sign language interpreter will be available, and everyone is welcome. NAM forums are free.

### correction

Apologies for our error in last month's ATU. CHIPS stands for Children with HIV Paediatric Surveillance, and surveys children in both Ireland and the UK.



## credits

**editor**  
Anna Poppa

AIDS Treatment Update  
founded by Peter Scott

**copyright**  
©NAM Publications 2001  
All rights reserved

**design**  
Alexander Boxill

**printing**  
Cambrian Printers

**ISSN**  
0969-4706

**charity number**  
1011220

## 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  
Dr Barry Peters  
Professor Tony Pinching  
Dr Gareth Tudor-Williams  
Professor Jonathan Weber  
Dr Ian Williams  
Dr Mike Youle

## thanks to our funders

NAM's treatments information for people living with HIV is provided free thanks to the generosity of:

Department of Health, NHS London Region HIV/AIDS Specialist Commissioning Advisory Group, Crusaid, Levi Strauss & Co, British HIV Association, Bristol-Myers Squibb, GlaxoSmithKline, Roche Products, Roche Molecular Systems, Boehringer Ingelheim, Abbott Laboratories, Merck Sharp & Dohme, Du Pont Pharma, Visible Genetics, Virco, Surrey Social Services, and these health authorities: Barking & Havering, Barnet, Bexley & Greenwich, Birmingham, Brent & Harrow, Camden & Islington, Croydon, Ealing, Hammersmith & Hounslow, East London & the City, East Surrey, East Sussex, Brighton & Hove, Enfield & Haringey, Hillingdon, Kensington, Chelsea & Westminster, Kingston & Richmond, Lambeth, Southwark & Lewisham, Manchester, Merton, Sutton & Wandsworth, Norfolk, Redbridge & Waltham Forest, Stockport, West Pennines, West Surrey



## any questions

For an introduction to HIV treatment issues  
The booklets in NAM's Information Series for Positive People are free to people with HIV. This easy-to-read series covers six key topics: Viral Load, Clinical Trials, Nutrition, Anti-HIV Drugs, Resistance, and a Glossary.

**The HIV & AIDS Treatments Directory**  
This 600 page book, published twice a year, is a comprehensive guide to the medical aspects of HIV. Available at only £12.95 to people with HIV, £64.95 to professionals.

<http://www.aidsmap.com>  
NAM's resources are also available online at [aidsmap.com](http://aidsmap.com). These include our extensive and searchable treatments database, the latest news on treatment developments, our online directory of AIDS organisations, hundreds of links to recommended HIV-related sites, and free downloadable resources.

**Monthly NAM information forums in London**  
Each month an expert speaker discusses a treatment-related topic. Entry is free. Future forums are advertised inside this newsletter.

**AIDS Treatment Phonenumber 0845 9470 047**  
From Terrence Higgins Trust: Mon & Wed 3-9pm, Tue 3-6pm.

NAM recommends that you discuss all your treatment decisions with your doctor.



## 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.

**AIDS Treatment Update is available on audio tape, and can be emailed to you as a pdf file for viewing with Acrobat Reader. Telephone 020 7627 3200 for details.**

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.