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EDITORIAL

Since our last HTB there have been some significant steps forward in terms of treatment access in resource poor settings including the announcement from the Clinton Foundation of a price of as low 36 cents per day for triple combination therapy - covered in the treatment access news.

Closer to home, we report from the 9th European AIDS Conference (EACS), held this Autumn in Warsaw.

FTC has been approved in Europe, and ataznavir received a positive opinion from the CPMP but only for treatment of experienced patients and only when boosted with ritonavir.

Even closer, CHIVA and i-Base organised a workshop to discuss the transition of HIV-positive adolescents from paediatric to adult care. We will be producing a report from the meeting that will be available in early 2004...

This issue of HTB is a double issue, so may we take the opportunity to wish all our readers a very happy Christmas and new Year...

The next issue of HTB will be dated February 2004 and distributed in the last week of January.

CONFERENCE REPORTS

9th European AIDS Conference (EACS)

25-29 October 2003, Warsaw, Poland

The European AIDS Conference, organised by the European AIDS Clinical Society (EACS) every two years, was formally linked this year with a new resistance and pharmacology workshop. Prior to the meeting the organisers also provided an intensive training programme for clinicians.

Abstracts from the conference are available as a pdf file from the Aegis website:

http://www.aegis.org

Other reports from this meeting are included on the following sites.

HIVandHepatitis.com

http://www.hivandhepatitis.com

The Body.com

http://www.thebody.com

NATAP

http://www.natap.org

Medscape (requires one-time free registration)

http://www.mescape.com

Lower doses of d4T produce similar efficacy and reduced side effects

Simon Collins, HIV i-Base

The first approach to the management of d4T-related peripheral neuropathy or lipoatrophy is to switch to alternative drugs that do not cause this side effect. Patients without other options and whose previous treatment history makes them reliant on d4T (stavudine, Zerit) have been managed, often successfully, by dose reduction. A poster at the International AIDS Society meeting in Paris this year reported that dose reduction of d4T in a group of Thai patients improved or resolved lipoatrophy without virologic failure. [1]

Two posters at the meeting presented further data on this approach.

Koegl and colleagues from private practice in Munich performed a retrospective analysis by chart review of 508 patients starting with d4T between 1995 and 2003. [2]

Standard doses (30mg BID if <60kgs and 40mg BID if >60kgs) were used by 369 patients and reduced doses (20mg BID if

<60kgs and 30mg BID if >60kgs) by 139 patients. Although d4T dosing is based on patient weight, the median dose in the low dose group was 0.857 mg/kg compared to 1.073 mg/kg in the standard dose group (p<0.0001).

Although both groups had similar characteristics (median age 41, range ~25-70+; CD4 230-250; VL 4.5 logs) there were proportionally more women in the low dose group (30% vs 14%). Forty-five per cent of women compared to 23% of men received the low dose regimen.

During the seven-year observation period there was no difference in CD4 or viral load response between the two groups.

Around 70% of each group discontinued d4T and incidence and reason for discontinuation was also similar: 18% vs 20% for virological failure, 26% vs 27.4% for side effects and 20% vs 25% for other reasons, in the low and standard groups respectively.

However, incidence of peripheral neuropathy was 50% lower in the low-dose group, reported in 13% vs 26% patients (p=0.001). Patients in the low dose arm were also reported as using d4T significantly longer (p=0.02; log rank test) and Kaplan Meier probability of remaining on d4T was 84% vs 74%, 67% vs 55% and 52% vs 41% after one, two and three years in the low-dose vs standard dose arms respectively.

In a second study, Delpierre and colleagues from Tropical and Infectious Disease Unit in Toulouse assessed the virological impact of reduced dose d4T on 43 patients who had been stable on regular dose treatment for a median of 14 months. [3]

Thirty-nine patients reduced from 40mg BID to 30mg BID and four patients reduced from 30mg BID to 20mg BID. The main reasons for dose reduction were lipoatrophy in 46%, neuropathy in 23% and hepatic disease in 14% of patients.

Viral load, CD4 and % undetectable were assessed at initiation of full-dose regimen, at the time of reduction and six and 12 months follow up. Median duration on lowered dose at assessment was 15 months.

Although 13 patients (30%) discontinued the study this was largely due to poor resolution of the original side-effects that led to the original dose reduction (seven for lipoatrophy, two for PN). Two left as 'patient decision' one for unrecorded reasons and only one for virologic failure.

From the data presented in the poster, it appears that patients remaining in the study maintained a similar level of viral suppression (79% at dose reduction and 75% at 12 months were <200 copies/mL in on-treatment analysis). Median CD4 count continued to rise from 575 at reduction to 638 at month 12, in on-treatment analysis.

This short study did not find evidence of reduced viral suppression as a result of the change to a reduced dose. The effect of the reduction on side effects was not presented.

COMMENT

Although the easiest way to avoid d4T-associated side effects is to not use d4T, not all patients have this option. If a lower dose produces similar efficacy and reduced toxicity then results from larger studies may provide evidence for wider use of d4T.

This would be particularly important if low dose d4T reduced levels of apoptosis, differentiation and other dysfunction at a cellular level in adipose tissue and this may be the most useful research for BMS to conduct on its once-daily extended release formulation.

The study from Thailand also reported that earlier intervention produced more effective results and even further dose reductions to 50% of standard dose in patients with poor response.

Paediatricians need to pay attention to these findings.

The routine dose of d4T for children has been 1mg/kg/dose administered BID, which is double the total daily dose generally used in adults. For younger children, in whom body surface area is a more appropriate gauge for drug dosing than weight, this is probably okay. For older children it may be that we are using higher doses than they need.

Lipoatrophy is being increasingly reported in children on d4T. With improved assays to study intracellular levels of the triphosphates and metabolites, it would be very helpful to review the pharmacokinetics in children in more detail and dose reduce them also if levels appear high.

References:

1. Hanvanich M et al. Reduction of d4T dosage improves lipoatrophy without virologic failure. 2nd IAS Conference, Paris 2003. Abs 749. http://www.ias.se/abstract/show.asp?abstract_id=10293
2. Koegl C, Wolf E, Postel N et al. Low dose stavudine: as effective as standard dose but less side effects. 9th EACS, Warsaw. 25-29 October 2003. Abstract 9.8/5.
3. Delpierre C, Cuzin L, Alvarez M et al. Lowering stavudine dosages does not compromise anti-viral efficacy in HIV-infected patients. 9th EACS, Warsaw. 25-29 October 2003. Abstract 9.4/1.

Switching from efavirenz to nevirapine to avoid CNS side effects

Simon Collins, HIV i-Base

Although guidelines widely recommend use of efavirenz (EFV, Sustiva, Stocrin) plus two nucleosides for initial therapy a percentage of patients find the associated CNS side effects substantially reduces their quality of life.

Ward and colleagues from a private practice in Washington DC performed a retrospective review of 34 patients with undetectable viral load <50 copies/mL, and three patients with 50-1000 copies/mL, who switched from efavirenz to nevirapine due to CNS-related side effects or lipid problems. The two viral load tests prior to the switch were compared to most results in October 2003.

In the absence of data on the interaction between the two drugs, and the specific effect on the pharmacokinetic induction of metabolism, nevirapine was started at a dose of 200mg once-daily for two weeks, overlapping efavirenz therapy. Efavirenz was then stopped and nevirapine increased to the 200mg twice-daily dose.

All patients who were undetectable at the switch have remained <50 copies after a median of 25 months (range 6-59). Two of the intermittently detectable patients have remained between 50-1000 copies/mL and one has become persistently <50 copies/mL.

Patients who previously reported psychiatric problems (depression, anxiety or fatigue, with or without sleep disturbance) all resolved or significantly improved. Four patients with previous isolated sleep disturbance all had significant improvement in quality of sleep.

Mean cholesterol, triglycerides and LDL cholesterol all decreased significantly by 0.5, 0.90 and 0.2 mmol/L respectively and HDL cholesterol increased by 0.1 mmol/L.

One patient, the only woman in the cohort, switched to nevirapine in order to become pregnant, had artificial insemination and delivered a healthy HIV-negative baby boy. One patient had acute hepatic toxicity and changed to acabavir/AZT/3TC.

Ref: Ward DJ, Curtain JM. Substitution of nevirapine for efavirenz in virologically controlled patients intolerant of efavirenz. 9th EACS, Warsaw. 25-29 October 2003. Abstract 7.5/1.

Interruption of treatment is safe for those who started too early

Simon Collins, HIV i-Base

Although treatment guidelines now recognise that patients who started treatment with higher CD4 counts than currently recommended, may safely discontinue therapy, especially if they are experiencing toxicity from treatment, there is still a reluctance from some doctors to suggest this option to their patients. Several studies at Warsaw provided additional support for this option.

Cotte and colleagues from Hôtel-Dieu Hospital in Lyons assessed virological and immunological response in 41 asymptomatic patients who had started treatment with CD4 counts >350 cells/mm^3, with a range of treatment histories, all of whom had undetectable viral load <50 copies/mL for the previous 12 months. The protocol recommended that patients restart treatment after two consecutive CD4 counts <350 cells/mm^3. [1]

Mean CD4 count prior antiretroviral treatment (some patients started with mono- and dual-therapy) was 489 +/–132 cells/mm^3 and 541 +/–155 cells/mm^3 prior to HAART. Mean duration of ARV treatment was 4.3 +/–1.6 years.

Mean duration of treatment interruption is currently 16 +/–14 months with nine patients restarting treatment when their CD4 count dropped below 350 cells/mm^3. One patient developed acute seroconversion symptoms three weeks after the interruption and restarted treatment two months later. One patient restarted HAART after a herpes zoster infection at month seven. All patients restarting treatment achieved viral load <50 copies/mL and CD4 count >300 cells/mm^3 by three months after the reintroduction of therapy.

Mean viral load was just over 4.5 logs and CD4 count around 650 cells/mm^3 (from a baseline of just under 800 cells/mm^3) after 24 months off-treatment.

C O M M E N T

Discontinuation of treatment in any asymptomatic individual is likely to lead to improved quality of life - that could potentially last for several years. Caution should be taken when stopping drugs that have long half-life and low resistance threshold such as 3TC, nevirapine and efavirenz. BHIVA guidelines suggest switching the NNRTI in a regimen to nelfinavir for the last two weeks of therapy.

Ref: Cotte L, Lebouche B, Miailhes P et al. HAART interruption in virologically controlled patients who started treatment at an early stage of HIV-infection. 9th EACS, Warsaw. 25-29 October 2003. Abstract 7.6/1.

T20 is cost effective for UK purchasers

Simon Collins, HIV i-Base

One of the controversial aspects of T20 (enfuvirtide, Fuzeon), the new entry inhibitor recently approved in both the US and Europe, is its cost. At over £14,000 per year it costs more than three times that of the most expensive currently available antiretrovirals.

Prior to licensing, the cost as much as the need to take the drug by twice-daily subcutaneous injection, had the potential to limit widespread use of T20, even among patients with drugs resistant virus for whom it could effectively contribute to sustained virological suppression.

Since licensing, use of T20 has been more limited and certainly much less than predicted by Roche. In support of the treatment a cost-economics model has been developed to demonstrate that additional costs of T20 as a life-saving therapy are still well below that of many other National Health Service treatments that are routinely prescribed.

The model used estimated costs of NHS therapy and healthcare together with efficacy results from 24-week results from the TORO Phase 3 studies. Wider benefits such as increased productivity from HIV-patients using T20 were not included.

The incremental cost per year of life and cost per quality adjusted life year (QALY) gained were estimated using the formula:

$$C/E = \frac{TC\ (B) - TC\ (A)}{Q\ (B) - D\ (A)}$$

C/E represents the incremental cost-effectiveness ratio and for T20+optimised background regimen (B) and optimised background alone (A), TC represents the total discounted cost of the intervention and Q represents the effectiveness measure (either life expectancy or QALY).

Projected longer life from using T20 plus optimised background therapy and reduced risk of new AIDS defining events produced cost-effectiveness per life year gained of £18,859 and per QALY gained of £23, 200. In a sub-group analysis based on genotypic sensitivity score (GSS) for number of susceptible additional drugs used in the regimen, cost per QALY gained was £36,128, £24,094 and £14,949 for a patient with GSS score of 0, 1 and >/=2 drugs respectively.

C O M M E N T

The London Commissioners Group has already issued guidance for prescribing T20 for doctors, health trusts and patients, based on recommendations in the July 2003 BHIVA guidelines. [2]

This recommends that all patients currently receiving T20 as part of an active combination should continue to do so. Also that patients with high risk of short term disease progression with CD4 counts <50 cells/mm^3 should be able to use T20, even without optimal sensitive background therapy.

In order to optimise the chance of long-term benefit, and minimise the risk of resistance, all other patients are recommended only to use T20 supported by one or two drugs to which their virus is still sensitive. Highly treatment experienced patients with multiple drug resistance who are virologically and immunologically stable with little risk of short-term disease progression, are advised to wait until they have sufficient sensitive drugs to use alongside T20, perhaps waiting until tipranavir is available.

This strategy will limit the risk of developing resistance to T20 and T1249, the pipeline successor, which can occur in as little as six months when T20 is used as virtual monotherapy.

Within the annual NHS budget, the additional costs for a limited number of people using T20 are dwarfed in comparison to the increased budget required for standard HAART and routine monitoring for the increasing number of newly diagnosed individuals.

References

1. Hornberger J, Youle M, Beck EJ et al. Cost-effectiveness of enfuvirtide from UK health payer perspective. 9th EACS, Warsaw. 25-29 October 2003. Abstract 19.5/1.
2. London HIV Consortium: HIV Drugs and Treatments Group. Clinical guideline for use of enfuvirtide (T20). October 2003.

Intrauterine exposure to efavirenz

Polly Clayden, HIV i-Base

In pre-clinical studies, efavirenz showed teratogenic effects in 3/13 exposed foetal monkeys, including severe neural tube defects in one. Efavirenz was given to the pregnant monkeys early in pregnancy in the period analogous to the human first trimester. As a result this drug is contraindicated in pregnancy.

A report from a French database survey of patients attending four hospitals in Seine-Saint-Denis, evaluated the effect on 10 pregnancies (out of 349 followed in this study since 1999), in which women inadvertently received efavirenz in the first trimester, including three that resulted in abnormalities.

Of the 10 pregnancies, six women delivered: there was one spontaneous abortion at eight weeks gestation, one voluntary abortion at six weeks and four days - and two therapeutic abortions at 24 weeks and 18 weeks and four days of pregnancy.

Abnormalities were observed in three infants: one had facial dysmorphy, another facial dysmorphy and severe hypotrophy and a third lung segmentation abnormalities, bicuspid pulmonary valves and severe accelerated skeletal maturation. The exposure periods to efavirenz were the first three weeks, the first six weeks and four days and the first 18 weeks and four days of gestation respectively.

The investigators reported that in this small study: "It is not certain that there is a relationship between efavirenz exposure and the described abnormalities." Nevertheless inadvertent exposure to efavirenz in pregnancy is not uncommon and the investigators stress the importance of pharmacovigilance notification in all possible foetal or childhood abnormalities possibly related to intrauterine exposure to efavirenz.

Ref: Khoung-Josses MA, Jeantils V, Delassus JL et al. Abnormalities and intrauterine exposure to efavirenz. 9th EACS, Warsaw. 25-29 October 2003. Abstract 4.5/1.

C O M M E N T

It would be unwise to read too much into this abstract. Facial dysmorphism in infants is not easily defined, and no details were given in the poster. Rubinstein et al originally described a syndrome of facial dysmorphism that they ascribed to 'congenital HIV infection' which has been convincingly refuted in subsequent studies.

It has frequently been pointed out that no other antiretroviral drug has been tested in the foetal monkey, thus efavirenz may have acquired an unfair reputation for teratogenicity. Data from the international Antiretroviral Pregnancy Registry have not suggested any adverse fetal effects from exposure to efavirenz. Prospective pharmacovigilance notification of all pregnancies in which antiretrovirals are used is essential in order to evaluate potential toxicities in human fetuses and young infants.

All physicians prescribing antiretrovirals to pregnant women are encouraged to report prospectively to the Registry which can be accessed at www.apregistry.com

African patients and adherence in the UK

Polly Clayden, HIV i-Base

In order to assess whether there is any evidence to support the widely held view that Africans living in the UK are less likely to accept and adhere to HAART, a small retrospective study from Newham General Hospital evaluated adherence levels and virological response in African vs non-African patients.

The investigators performed a case note review of all HIV positive persons diagnosed between October 1998 and October 2001, allowing a minimum follow up period of 15 months. Pregnant women or those diagnosed through antenatal testing and people who were antiretroviral experienced were excluded from the analysis.

Of a total of 142 eligible patients, 117 were African and 25 non-African. African patients were more likely to be women compared to non-Africans (58% vs 28%). They were also more likely to present with a lower CD4 count (197 vs 245 cells/mm^3).

The investigators reported no difference in achieving undetectable viral load results of <50 copies/mL (one or more measurement during the study period) – 83% in both groups. At six and 18 months the proportion of patients with an undetectable viral load was 76% and 59% for African and 67% and 44% for non-African. They also reported that despite lower initial CD4 counts, African patients achieved similar increases in CD4 counts over time.

The investigators concluded that this study suggests in this London clinic: "The uptake and adherence in African patients is similar to non-African patients."

Ref: Wheeler H, Leventis P, Chilton D et al. Do African patients accept and adhere to HAART? 9th EACS, Warsaw. 25-29 October 2003. Abstract 10.1/9

Five-year results of Kaletra-based therapy in treatment-naïve HIV patients

Antiretroviral regimens have demonstrated potent virologic and CD4 responses, but longer-term data are needed to evaluate the durability of these responses.

One hundred antiretroviral-naïve patients received one of three doses of Kaletra (lopinavir/ritonavir, LPV/r) with d4T and 3TC twice-daily. After 48 weeks, all patients received LPV/r 400/100 mg twice-daily with d4T and 3TC.

Median baseline HIV viral load and CD4 count were 4.9 log10 copies/mL and 338 cells/mm3 respectively. Prior to week 252, 32 patients discontinued study therapy due to adverse events (13%) or other reasons [loss to follow-up, nonadherence, personal reasons (19%)].

At year five (week 252), 67/68 (observed data, 99%) and 67/100 (intent-to-treat, 67%) had viral load <400 copies/mL. The only HIV RNA measurement >400 copies/mL at year five occurred during a lengthy treatment interruption.

Through five years, no PI-associated mutations have been observed in patients with virologic failure.

Median CD4 increase from baseline to week 252 was 505 cells/mm^3 among patients continuing therapy. The most common drug-related moderate/severe side effects through week 252 were diarrhoea (28%), nausea (16%), abdominal pain (10%), and asthenia (9%).

Sixteen and 13 patients initiated lipid-lowering agents (LLA) with total cholesterol >240 mg/dL or triglycerides >400 mg/dL (measured without regard to fasting); from LLA initiation to the final value available through week 252, total cholesterol and triglycerides decreased by a median of 24% and 32%, respectively.

The statins used were pravastatin in 11 patients, atorvastatin in nine, and four received both; nine patients used a fibrate, eight of them fenofibrate. Three patients used both a statin and a fibrate. Initiation of lipid-lowering therapy was at the discretion of the investigator and was not study defined.

“Lipid elevations are relatively common with lopinavir/ritonavir,” commented Dr Hicks, “but the most important piece of information here is that standard lipid-lowering therapy can have a pretty good impact, at least in this small subset of patients.”

LPV/r-based therapy demonstrates sustained antiretroviral activity and is generally well tolerated in ARV-naïve patients through five years of therapy. Decreases in total cholesterol and triglycerides were observed in patients initiating lipid-lowering agents.

Ref: Hicks C, Da Silva B, King KR et al. 5-year results of lopinavir/ritonavir (lpv/r)-based therapy in antiretroviral-naive HIV-infected patients. 9th EACS, Warsaw. 25-29 October 2003. Abstract 7.3/16.
http://www.hivandhepatitis.com/2003icr/EACS_9/documents/1105/110503_a.html

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IL-2 effectively increases CD4 count in people with low CD4 nadir

Graeme Moyle MD, NATAP.org

Two large ongoing investigator led studies are evaluating the role of interleukin-2 (IL-2) as an immune modulator in persons with treated HIV infection. The studies, known as SILCAAT and ESPRIT, are not simply evaluating CD4 numbers but are also looking for clinical endpoints (such as new HIV related infections, AIDS defining events and deaths). IL-2 is administered subcutaneously twice-daily for “cycles” of five days with subsequent cycles being given every eight weeks.

During the administration of IL-2 the majority of individuals reported flu-like symptoms and some experienced rashes or fluid retention. The symptoms generally resolve a few days after the completion of the cycle.

As with the administration of enfuvirtide (T-20) some patients administering IL-2 experience injection site reactions. In general, the severity of the symptoms declines with each cycle. IL-2 is a messenger normally produced by CD4 cells which affects both the activation of CD8 cells and causes expansion of CD4 numbers. Evidence from the pre HAART era suggested that the use of IL-2 was associated with a modest reduction in the risk of opportunistic disease events.

The SILCAAT study is an international, randomised, controlled trial of IL-2 in patients with current CD4 50-300 cells/mm^3 and viral loads <10,000 copies/mL. The study is fully enrolled with 1,970 patients participating from across 142 sites in 11 countries. Patients were scheduled to receive 4.5 MIU IL-2 BID subcutaneous every eight weeks for six cycles. Data presented at the 9th EACS conference focused on the CD4 response in individuals who received IL-2. At entry, patients had a median CD4 count of 201 cells/mm^3 (interquartile range (IQR) 150-252 cells/mm^3). The median nadir CD4 count was just 60 (IQR 24-108) cells/mm^3. For the 449 patients for whom data are available at one year, the median increase in CD4 count was 123 cells/mm^3. Increases were more substantial in patients with higher baseline counts (142 vs 98 cells/mm^3 for patient with baseline

counts of >200 cells vs baseline counts of 50-199 cells/mm^3); and for patients who received more cycles (139 vs 80 cells for six cycles vs <3 cycles).

The data certainly indicate that even in individuals with low CD4 counts meaningful rises in CD4 cell numbers can be achieved. The study will now continue looking at clinical events to see whether these substantial rises in CD4 numbers converted into a reduction in the number of clinical events in patients who received IL-2 relative to the control population in this study of individuals who have not received IL-2.

Ref: Levy Y, Mitsuyasu R, Tambusi G, et al. CD4 count increases in patients with CD4 counts of 50-300 treated with intermittent IL-2: immunologic results from the Study of IL-2 in Combination with Active Antiretroviral Therapy (SILCAAT) Trial. 9th EACS, Warsaw. 25-29 October 2003. Abstract F14/3

Hepatitis coinfection: incidence in Europe and response to transplant

Simon Collins, HIV i-Base

Several studies presented at the conference covered issues related to hepatitis coinfection.

In Europe, 9% of HIV patients have hepatitis B and more than 30% hepatitis C: link to higher mortality

The EuroSIDA study is a large collaborative study involving mainly European national cohorts and two studies looked at the incidence and implications for coinfection with hepatitis B or C.

Dr Stephane DeWit presented the results of coinfection with hepatitis B. [1]

An analysis of the databases in this cohort showed an incidence of 9% HBV coinfection across the cohorts, but that this also included large national differences. Of 5,883 patients tested for HbsAg at time of recruitment in EuroSIDA, 530 patients were positive. The highest prevalence was found in Argentina (17.8%) vs Northern (9.7%), Central (9.2%), Southern (9.1%) and Eastern Europe (6%).

Median CD4 count at recruitment was lower in HbsAg-positive persons (234 cells/mm3) vs HBsAg-negative (274 cells/mm3, p<0.0001). Coinfection with HCV was found in 158 HbsAg-positive (29.8%) and 1,363 HBsAg-negative patients (25.5%) (p=0.023).

Although incidence of any new AIDS diagnosis was higher for HbsAg-positive subjects, this was not significant after adjustment for CD4, age, AIDS diagnosis, HAART, risk group, gender, ethnic origin, region of Europe, date of recruitment, and HCV status (Poisson regression model).

The incidence of global and liver-related mortality was significantly higher in HbsAg-positive patients (12 vs 2.6 and 0.5 vs 0.2 /100 person-years respectively), and remained significantly higher in multivariate analysis (including HCV status) with incidence rate ratios of 1.55 (global;95%CI:1.24-1.93) and 3.77 (liver-related mortality;2.07-6.87).

HbsAg status did not influence virological or immunological response among the 1,752 subjects starting HAART.

Jurgen Rockstroh presented the results of hepatitis C (HCV) coinfection. HCV serology was available from almost 5,000 patients in EuroSIDA and was positive in 34% of cases (75% IVDU). There was a higher incidence and wider variation between cohorts than with hepatitis B.

The highest HCV-prevalence was found in Southern and Eastern Europe with 44.9% (623/1,387) and 47.7% (412/864) vs 22.9% (280/1,221) in Central and 24.5% (346/1,410) in Northern Europe. The higher incidence of AIDS or death in HCV-positive versus HCV-negative patients (5.6 vs 4.2 per 100 PYFU p<0.0001) was not significant after adjustment for CD4, age, prior AIDS, HAART, recruitment date, hepatitis B status, gender and ethnic origin (incidence rate ratio 0.92; 95% CI 0.79 - 1.07, p = 0.27).

In further multivariate analyses, there was an increased risk of liver-related deaths in HCV-positive vs HCV-negative patients (IRR 3.18, 95% CI 1.23 - 6.18, p = 0.014) but not of AIDS (p = 0.061) or global-mortality (p = 0.4).

As with HBV, no significant difference was found in the response to treatment. Median time to viral load <400 copies/mL or time to 50% increase in CD4 count was found between HCV-positive and negative individuals.

The authors concluded that one in three HIV-infected patients in the EuroSIDA Cohort are coinfected with HCV. While HCV-coinfection did not influence virological and immunologic response to HAART, HCV-positive patients experienced a higher mortality rate due to liver disease related causes.

Response to liver transplant higher when not coinfected with HCV

Norris and colleagues from Kings College Hospital in London reported responses to liver transplant in 12 HIV-positive patients (10 men, two women, age range 26-59 years) carried out between January 1995 and March 2002. [3]

Indications for transplant were HCV (n=5), HBV (n=4), ALD (n=2), and NonANonB (n=1); three patients presented with acute liver failure. Mean CD4 count at transplant was 267 cells/mm^3 (range 124 - 500), and HIV viral load ranged from <50 to 197,000 copies/mL. Only seven patients used HAART prior to transplant.

All patients in the non-HCV group (n=7) are alive, with five patients surviving more than 365 days (range 4 - 67 months). No patient experienced HBV recurrence, and graft function is normal in all seven recipients.

However, despite some initial responses, all HCV patients have died, with median survival post-transplant of 161 days (range 95-784 days). Four of these patients died of complications due to recurrent HCV infection and sepsis, despite antiviral therapy in three. Three patients experienced complications relating to HAART therapy.

C O M M E N T

This is a comprehensive look at the prevalence of HBV and HCV co-infection in the EuroSIDA cohort. As with other cohort studies in 'low' prevalence areas for HBV, co-infection as assessed by HbsAg positivity is at around 10%, implying higher rates of infection and chronicity in patients infected with HIV.

The reasons for higher prevalence rates in Argentina are not obvious but may be due to low HBV vaccine coverage or possibly a selection bias in terms of the HIV population reported to EuroSIDA. More importantly, this cohort study shows higher rates of liver-related mortality in both the HBV and HCV co-infected patients and has implications for the management of co-infections in these patients.

There is still some debate about the impact of HCV on virological and immunological response to HAART. The Swiss Cohort study demonstrated a clear reduction in CD4 response to HAART in patients co-infected with HCV, although this was certainly not the case in the EuroSIDA cohort. More data is needed.

The poor outcomes associated with liver transplantation in HCV/HIV co-infected patients in the Kings College Hospital cohort have not been duplicated in the recently reported Miami and Pittsburgh cohorts from the USA (Neff et al. Liver Transplantation 2003). As HAART improves survival in HIV-infected patients, there may be an increase in morbidity and mortality from hepatic disease in these patients and the demand for liver transplantation may increase. In the post-HAART, there is an urgent need to re-visit the concept of solid organ transplantation in HIV-infected patients. HIV infection should no longer be a relative contra-indication to solid-organ transplantation. National and International databases need to be established to share the transplant experience and delineate factors associated with poor outcomes.

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Rituximab plus CDE for HIV-related Non-Hodgkins Lymphoma (NHL)

Simon Collins, HIV i-Base

Spina and colleagues from the Italian Cancer Centre presented results from a phase-II study (started in June 1998) of the monoclonal antibody rituximab given with CDE therapy plus HAART in 64 HIV-positive patients with NHL. Sixty-nine percent of patients had advanced stage (III-IV) disease and 52% had B symptoms. Median baseline CD4 count was 161 cells/mm3 (range 3-691).

CDE was administered by continuous intravenous infusion for four days every four weeks (cyclophosphamide 187.5 mg/m2/day, doxorubicin 12.5 mg/m2/day and etoposide 60 mg/m2/day) and rituximab 375 mg/m2 i.v. on day one of each cycle. HAART was given concomitantly with CT.

Forty-five out of 64 patients (71%) achieved a complete remission (CR), 4/64 (6%) had a partial remission and 15 patients progressed. Seven of the CRs have since relapsed and 44/64 patients are still alive. Grade 3-4 neutropaenia, anaemia and thrombocytopaenia were observed in 78%, 36% and 25% of patients respectively. One quarter of the patients developed bacterial infections during neutropenia. The actuarial overall survival and time to treatment failure (TTF) at two years were 65% and 63% respectively.

The study concluded that the combination of rituximab and CDE treated concomitantly with HAART is safe, feasible and active and that the clearance rate (71%) and TTF at two years (63%) are comparable to those observed in high grade NHL of the general population.

Ref: Spina M, Simonelli C, Vaccher E et al. Rituximab and infusional cyclophosphamide, doxorubicin and etoposide (CDE) in combination with HAART: a safe and highly active regimen in HIV-related Non-Hodgkins Lymphoma (NHL). 9th EACS, Warsaw. 25-29 October 2003. Abstract F9/1.

TREATMENT ACCESS

Access to treatment – some progress…

Polly Clayden, HIV i-Base

- On 23 October, in an agreement with generic antiretroviral manufacturers Aspen, Cipla, Ranbaxy and Matrix, the Clinton Foundation HIV/AIDS Initiative announced a price of just 36 to 38 cents a day (less than $140 per year) for triple combination therapy in South Africa, Mozambique, Rwanda, Tanzania and the Caribbean - around half the current price for antiretrovirals in the developing world.

- On 19 November, the South African cabinet approved the long awaited Operational Plan for Comprehensive Treatment and Care for HIV/AIDS. Unsurprisingly the Treatment Action Campaign (TAC) welcomed the cabinet's decision stating: "This is a wonderful day for all in South Africa" but remind us "…the hardest work is ahead of us."

- Brazil negotiated a 76.4% discount on the US price of $13.80 for the protease inhibitor atazanavir making it a still rather costly but infinitely more affordable $3.25 per capsule.

- The draft 2003 revision of the WHO treatment guidelines for resource-limited settings – final version due to be published on 1 December – recommends NNRTI-containing triple regimens for first line therapy - either efavirenz or nevirapine plus 3TC plus either d4T or AZT, and stresses the advantages (besides price) of generic manufacturers' fixed dose combinations (FDCs). Notably WHO discuss the question of whether single dose nevirapine prophylaxis compromises subsequent NNRTI containing HAART, which it describes as one of "…the most pressing operational research questions facing the field."

WHO approves combination pills

Fiona Fleck, BMJ

The World Health Organisation will soon formally approve three new combinations of three antiretroviral drugs in fixed doses for use in patients with HIV in sub-Saharan Africa. The approval could have a major impact on antiretroviral treatment for patients all over the world.

The fixed dose combinations, whose endorsement WHO hopes to announce on 1 December, World AIDS Day, is part of a drive by the organisation to get antiretroviral drugs to three million people with HIV or AIDS in the world's poorest countries by 2005.

Fixed dose drugs have proved successful in treating malaria and tuberculosis. Whether in the form of a single pill or a "blister" pack containing three pills, the triple combinations are expected to be easier and cheaper than other drugs to deliver and simpler for patients to take and could be prescribed by nurses and paramedics. WHO plans a massive training programme to boost the number of non-doctor medical staff who can prescribe the drugs.

"We're trying to come up with a shortlist of three preferred drug combinations based on published evidence and clinical experience," said Jonathan Quick, WHO's head of essential medicines. He added: "By 1 December we will know which are clinically preferred combinations, then it's a matter for the companies to develop the product."

Dr Quick said Ranbaxy and Cipla, two Indian companies that make generic drugs, were already producing triple fixed dose combinations that needed to be fully evaluated, while another possibility was for GlaxoSmithKline, Ranbaxy, or Cipla, to convert their current combinations of two fixed dose drugs that are already on WHO's list of recommended drugs to triple combinations.

The International Federation of Pharmaceutical Manufacturers Associations said it was not opposed to the triple fixed dose combinations but argued that some drugs under consideration had not been properly clinically tested in Africa.

"The developing world is awash today in substandard and fake medicines, and as we all work to expand the treatment of people with HIV/AIDS we should use tested affordable treatments and not encourage use of alternatives of unproven safety, efficacy, and quality," said Eric Noehrenberg of the Geneva based association.

Mr Noehrenberg said that the triple fixed dose combinations were unlikely to violate patents - for several reasons. Under a World Trade Organisation agreement India is not due to abide by patent law until 2005, and the patents that will then come into force are not retrospective.

Many countries in Africa do not have patents - because drug companies do not bother to file patents in countries that do not have their own drugs industry, as there is no danger of infringement. There are no international patents, only national patents, and very few patents are in force in sub-Saharan Africa.

Mr Noehrenberg said that it had not yet been announced where the triple combinations will be manufactured.

Generic drug manufacturers in countries such as India are already ahead in the race to produce triple fixed dose antiretrovirals - because they can copy patented drugs produced by different companies and combine them. Drug companies in the United States would need special agreement among themselves to combine their products in this way.

For a list of proposed simplified treatment for public consultation:
http://www.who.int/hiv/pub/prev_care/draft/en/

Source: BMJ 2003;327:1067 (8 November)

South African Competition Commission finds GSK and BI responsible for 'excessive pricing' and 'abuse of market position'

The South African Competition Commission has found that pharmaceutical firms GlaxoSmithKline South Africa (Pty) Ltd (GSK) and Boehringer Ingelheim (BI) have contravened the Competition Act of 1998. The firms have been found to have abused their dominant positions in their respective anti-retroviral (ARV) markets.

In particular the Commission has found the firms have engaged in the following restrictive practices:

1. Denied a competitor access to an essential facility
2. Excessive pricing
3. Engaged in an exclusionary act

The Commission has decided to refer the matter to the Competition Tribunal for determination.

Menzi Simelane, Commissioner at the Competition Commission, said: "Our investigation revealed that each of the firms has refused to license their patents to generic manufacturers in return for a reasonable royalty. We believe that this is feasible and that consumers will benefit from cheaper generic versions of the drugs concerned. We further believe that granting licenses would provide for competition between firms and their generic competitors."

"We will request the Tribunal to make an order authorising any person to exploit the patents to market generic versions of the respondents' patented medicines or fixed dose combinations that require these patents, in return for the payment of a reasonable royalty. In addition, we will recommend a penalty of 10% of the annual turnover of the respondents' ARVs in South Africa for each year that they are found to have violated the Act."

Simelane said these practices violate the Competition Act of 1998's prohibitions against excessive pricing (section 8(a)), refusing access to essential facilities (section 8(b)) and exclusionary acts that have an anticompetitive effect that outweighs technological, efficiency or other pro-competitive gains (section 8(c)).

"Indeed the very goals of our Competition Act - promoting development, providing consumers with competitive prices and product choices, advancing social and economic welfare and correcting structural imbalances - have been made difficult in this context by the refusal of the respondents to license patents."

The original complaint in this matter was filed by Hazel Tau and others alleging that GSK and BI were charging excessive prices to the detriment of consumers for their patented ARV medicines.

GSK and BI hold patents on certain antiretroviral (ARV) medications used to treat HIV/AIDS. GSK holds patents in South Africa on AZT (Retrovir), lamivudine (3TC) and AZT/lamivudine (Combivir). BI holds patents in South Africa on nevirapine (NVP, Viramune).

Source: South Africa Competition Commission PR, 16 October 2003

ANTIRETROVIRALS

FTC (emtracitabine, Emtriva) approved in Europe

On 28 October 2003 the European Commission granted Marketing Authorisation for FTC (emtricitabine, Emtriva) 200 mg hard capsules and 10 mg/mL oral solution in all 15 member states of the European Union. FTC will be available in individual European countries as local reimbursement approvals are obtained.

FTC is a nucleoside reverse transcriptase inhibitor (NRTI) for the treatment of HIV infection, and is dosed as a single capsule

taken once a day as part of combination therapy.

FTC is indicated for the treatment of HIV-infected adults and children in combination with other antiretroviral agents. This indication is based on studies in treatment-naïve patients and treatment-experienced patients with stable virological control. There is no experience with the use of FTC in patients who are failing their current regimen or who have failed multiple regimens. When deciding on a new regimen for patients who have failed an antiretroviral regimen, careful consideration should be given to the patterns of mutations associated with different medicinal products and the treatment history of the individual patient. Where available, resistance testing may be appropriate.

FTC is dosed once daily and can be taken with or without food. More than 2,000 HIV-infected adults have been treated with FTC for periods of 10 days to 200 weeks in phase I, II and III clinical trials. Assessment of adverse drug reactions is based on data from three studies in adults (n=1,479) and two paediatric studies (n=114). In the adult studies, 1,039 treatment-naïve and 440 treatment-experienced patients received FTC (n=814) or comparator medicinal product (n=665) for 48 weeks in combination with other antiretroviral medicinal products. In the paediatric studies, treatment-naïve (n=83) and treatment-experienced (n=31) paediatric patients aged four months to 18 years were treated with Emtriva in combination with other antiretroviral agents.

The most common adverse reactions observed in the studies described above include headache, diarrhoea, nausea and elevations in creatine kinase. Additionally, as outlined in the US prescribing information, skin discoloration was observed at a higher frequency in FTC versus control groups. Skin discoloration, manifested by hyperpigmentation (excess pigmentation) on the palms and/or soles, was generally mild and asymptomatic. The mechanism and clinical significance of this adverse event are unknown.

FTC is available as a 200 mg capsule for use in adults and as a 10 mg/mL oral solution for use in infants older than four months, children and patients who are unable to swallow hard capsules and patients with renal insufficiency who require dose reduction. Please refer to the Summary of Product Characteristics for Emtriva 10 mg/mL oral solution.

Source: Gilead PR and EMEA website

http://www.gilead.com/wt/sec/pr_1067371563
http://www.emea.eu.int/humandocs/Humans/EPAR/emtriva/emtriva.htm

C O M M E N T

FTC is a very similar drug to 3TC. Potential advantages include a longer plasma and intracellular half-life that may provide a safer window period in the event of a missed Q24H dose. Whether patients will be able to benefit from this in the UK may depend on the negotiated price in different Health Trusts, although the list price for FTC is set just under the list price for 3TC. Use of GSK's once-daily formulation of 3TC is very low because of the relatively small additional cost over the BID 3TC formulation.

As with 3TC, physicians should be aware of anti-HBV activity of FTC, and patients coinfected with HIV and HBV should follow cautions for stopping FTC that are included in the summary of product characteristics.

Link:

EMEA summary of opinion

http://www.emea.eu.int/htms/human/opinion/opinion.htm

(Click on emtricitabine for pdf)
http://www.gilead.com/uk

EMEA recommend approval for atazanavir for treatment experienced patients

On 20 November 2003 the Committee for Proprietary Medicinal Products (CPMP) adopted a positive opinion recommending a marketing authorisation for atazanavir 100mg, 150mg, 200mg and 50mg/1.5g hard capsules and oral powder for treatment of antiretroviral experienced adults. Marketing authorisation is expected to follow within 90 days, in early 2004.

The CPMP summary opinion lists benefits of atazanavir as "its once-daily dosing, the low risk of dyslipideamia and the good gastro-intestinal tolerance in comparison to lopinavir/r". The opinion also recommends atazanavir be used at a dose of 300mg and boosted by 100mg ritonavir, although only limited data was available on this combination. Atazanavir was originally studied in treatment naïve patients at a dose of 400mg daily, without ritonavir boosting.

The opinion does not recommend or comment on use in treatment naïve patients.

Source: EMEA press release

http://www.emea.eu.int/whatsnewp.htm

C O M M E N T

In practice, once a drug is licensed and available even with a limited indication, individual doctors have flexibility to use it in any patient who they believe would benefit from that treatment. Given the US approval of atazanavir for both naïve and experienced patients, there are certainly supportive data for this.

A similar example was set with the original EMEA approval of tenofovir. US approval had included both experienced and naïve patients, while the European indication for treatment naïve patients only followed assessment of 96-week data. Tenofovir was widely used off-label for first line therapy prior to this decision and is now recommended as such in guidelines.

Fosamprenavir (Lexiva) approved in US

On 20 October the US Food and Drug Administration approved the protease inhibitor fosamprenavir (Lexiva, GW908). Fosamprenavir is a pro-drug of amprenavir (Agenerase). This new formulation requires fewer pills than amprenavir (now usually four pills a day including the ritonavir, vs. 16 pills a day for Agenerase), and no food restrictions.

European approval is expected to follow in about six months and until then fosamprenavir remains available on an expanded access programme.

Information for doctors and patients is at:

http://www.lexiva.com

Other links:

Brief review by the FDA of the pivotal clinical trials:

http://www.thebody.com/fda/lexiva.html?m18

GSK review:

http://www.gsk.com/press_archive/press2003/press_10212003a.htm

An extensive review by the activist organisation TAG (Treatment Action Group), supporting approval - but only when Lexiva is “boosted” with a low dose of ritonavir to increase blood levels of Lexiva:

http://www.aidsinfonyc.org/tag/tx/fosamprenavir.html

Combinations, adverse events, dosing, interactions, resistance:

http://www.hivandhepatitis.com/hiv_and_aids/lexiva_1.html

Source: AIDS Treatment News

http://www.aidsnews.org

US paediatric, adult and maternal-child guidelines updated

US guidelines have been updated, largely to include information on recently approved drugs (T20, atazanavir and FTC) and newly identified interactions (triple-nucleoside, atazanavir etc). The paediatric guidelines also have substantial changes in other sections.

The guidelines are now available in pdf file and html format, and very helpfully all new changes are highlighted with yellow background text in the pdf and bold text in the html versions.

http://aidsinfo.nih.gov/guidelines/

Guidelines for the use of antiretroviral agents in pediatric HIV infection

Convened by the Department of Health and Human Services and the Henry J. Kaiser Family Foundation, 22 September, 2003.

Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents panel on clinical practices for the treatment of HIV

Convened by the Department of Health and Human Services and the Henry J. Kaiser Family Foundation, 10 November, 2003.

Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States

Produced by Public health service task force on 22 September, 2003, together with a supplement 'Safety and toxicity of individual antiretroviral agents in pregnancy' published on 10 November 2003.

METABOLIC COMPLICATIONS

Polylactic acid (New-Fill) repairs facial wasting and improves quality of life

Simon Collins, HIV i-Base

Early reports from using New-Fill to safely and successfully repair facial lipoatrophy provided hope for many patients, given that the procedure was inexpensive in the context of overall HIV therapy, that it indicated few safety concerns and most importantly, when given by an HIV-experienced practitioner, produced successful and natural-looking results for many patients.

Facial lipoatrophy is the loss of facial fat especially in the buccal region that results in a progressively emaciated appearance and which is the cause of significant patient distress and reduced quality of life [1].

Concern about lipoatrophy is a reason that many patients give for delaying use of treatment, and the most recent research from Nolan et al suggests that the underlying mechanism for altered adipocyte differentiation and increased apoptosis is linked to nucleoside-related mitochondrial toxicity [2].

Results from using New-Fill were first presented at the 2nd Lipodystrophy Workshop in 2000, and have since been presented at most large meetings since then, but access to New-Fill has been limited to a restricted number of patients through National Health Service programmes or through private practice [3, 4].

It is therefore important that one of the earliest and largest studies has now been published in the influential peer-reviewed journal AIDS [5]. This together with inclusion of New-Fill as an appropriate treatment for lipoatrophy in the UK Treatment guidelines should broaden access further [6].

In the VEGA study, 50 patients from Hôpital Pitié-Salpêtrière, Paris, with severe facial lipoatrophy who had been receiving antiretroviral treatment for >3 years (median 8.9 years) and had viral load suppression <5000 copies/mL, were treated in an open label single arm pilot study. At baseline, median facial fat thickness measured by ultrasonography and colour Doppler evaluation was zero (range 0.0-2.1mm).

This careful and objective measurement of changes in the dermal, epidermal and fat thickness by the same trained radiography for all patients is an important aspect of the study and was supported by photography. Patients were evaluated at weeks six, 24, 72 and 96 and quality of life (QoL) measured at screening, at month three, and subsequently every six months out to two years.

Patients received a set of injections (one vial of New-Fill, 0.15g dry powder reconstituted with 3-4ml water) at baseline and every two weeks. A fifth injection could be given if total cutaneous thickness (TCT) was <8mm after the fourth injection. Each treatment involved up to 20 deep injections into and around the deep dermis of each cheek. Lidocaine was injected locally and thorough massaging of the treated area is essential to ensure better distribution of the solution.

Three, four and five sets of injections were provided to four, 26 and 20 patients respectively. Mean (and range) TCT increases in millimetres from baseline were +5.1 (2.2-8.6), +6.4 (3.1-9.1), +7.2 (4.2-9.6), +7.2 (3.5-9.6) and +6.8 (3.9-10.1) at weeks six, 24, 48. 72 and 96 respectively, and indicated a sustained effect over 18 months after the last injection, and also at least some level of response among all patients. Just over 40% of patients achieved primary endpoint of the study with TCT greater than an arbitrary 10mm at week 24, which was maintained out to week 96 ($p<0.001$ at both time points).

Median change in QoL, obtained from 44 patients, progressively improved from baseline to +8.0 (range, -2.9 - +10.0) at week 48 and was the secondary endpoint of the study ($p=0.021$), although this dropped to +0.4 at week 96 and lost statistical significance.

Minimal and localised oedema at injection site was seen in most patients and resolved within 24-48 hours. Fifteen patients developed minimal ecchymosis, which resolved spontaneously within 2-3 days. 22 patients reported palpable (but non-visible) subcutaneous micronodules that resolved in six patients by week 96. [Note: Further clinical experience suggests that this risk is minimised by intense post-injection massage, and that this is essential element of care].

The authors comment on the importance of these results in the absence of other effective strategies to manage facial lipoatrophy and say that the data should provide health providers and payers with sufficient efficacy and safety data to consider reimbursement. It is also notable that the journal carried an editorial comment that highlighted the importance of New-Fill being administered by a practitioner specially trained in treating HIV-associated lipoatrophy, and concluded that "at last we have something with clear results to offer to our patients".

C O M M E N T

Although the process for providing New-Fill within the NHS has been slow and protracted, several major centres are now providing this treatment at least for some patients, and commissioner funding has been forthcoming. In an overview at the Autumn BHIVA conference, Dr Simon Barton estimated that several hundred patients have probably been treated on the NHS and a similar number in private practice.

Of note, Brighton provided treatment to more than 50 patients last year and the long-expected programme at the Chelsea and Westminster Hospital in London has started evaluation and treatment of patients most affected.

At least two commissioning documents have already been produced that may be useful for clinicians obtaining this treatment for their patients [7, 8].

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CARDIOVASCULAR DISEASE

Increased risk of myocardial infarction associated with duration of protease inhibitor treatment

Simon Collins, HIV i-Base

Several large studies have addressed the concern that antiretroviral therapy could increase the risk of cardiovascular disease, and a useful analysis and summary (including the AIDS article reviewed here) was published earlier this year by the Forum for Collaborative Research and is now available online [1].

Results from the largest of these studies to date, the DAD study with almost 24,000 patients and 36,000 patient years follow-up, showed a small but significant increased risk associated with each year of antiretroviral treatment. Although the absolute risk is still very low for most HIV-positive patients, this finding is most relevant to those who already have traditional high risk factors, and the importance of lifestyle modifications such as smoking cessation, diet and exercise is as important as it is for HIV-negative individuals. Full results from this study have just been published, together with an editorial comment in New England Journal of Medicine [2].

The study from the French Hospital Database on HIV (FHDH) published in the 21 November issue of AIDS also reports an increased risk of myocardial infarction (MI) related to use of protease inhibitor therapy [3]. The results were from records of almost 35,000 male patients starting HIV therapy between 1996 and 1999, with a follow-up corresponding to over 88,000 patient years.

Data in the FHDH includes all HIV-positive patients who have provided consent from a network of 68 French University Hospitals. Data has been collected prospectively since 1992 with a follow-up form completed at least every six months, and by 1999 more than 73,000 patients were included with a median follow-up of 32 months.

Entry to the study started from January 1996, when PI therapy was just becoming widely available in France, and patients with a previous history of MI were excluded. Women were not included in the analysis because the very low number of cardiovascular events (n=6) recorded in the database for this period would not sufficiently power the final results.

MI was diagnosed in 60 men, including 49 cases in men using PI treatment. In the Cox model, exposure to PI was associated with a higher risk of MI [relative hazard (RH), 2.56; 95%CI, 1.03-6.34]. The expected incidence in the French general male population (FGMP) was 10.8/10,000 PY. The standardised morbidity ratio relative to the FGMP was 0.8 (95% CI, 0.5-1.3) for men exposed to PI for < 18 months (G1), 1.5 (95% CI, 0.8-2.5) for men exposed for 18-29 months (G2) and 2.9 (95% CI, 1.5-5.0) for men exposed for > 30 months (G3). With G1 as reference, the standardised morbidity ratio was 1.9 (95% CI, 1.0-3.1) for G2 and 3.6 (95% CI, 1.8-6.2) for G3.

In the multivariate analysis, initial CD4 cell counts, exposure to NRTI and exposure to NNRTI did not influence the risk of MI. MI was more likely in older patients and those exposed to PI. The risk of MI increased by 42% per 10-year age increment, and more than twofold in patients exposed to PI.

In an editorial comment in the same journal Peter Reiss emphasised that this increased risk, while important to follow closely, remained very low compared to the clear benefit provided by combination therapy. He also reaffirmed the importance of lifestyle changes to modify known cardiovascular risks and "cautious use of lipid lowering and anti-diabetic agents according to available guidelines". [4]

Focusing on absolute rather than relative risk was also one of the summary recommendations from the Forum for Collaborative Research report cited earlier, which also recommended always including patients with MI risk factors including previous history of MI.

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HEPATITIS COINFECTION

UK guidelines for treating coinfection with HIV and hepatitis B or C published online

Two guidlelines from the British HIV Association (BHIVA) guidelines have been published and can be viewed online or downloaded as pdf files.

Written by the BHIVA coinfection guideline committee, one covers coinfection with hepatitis B and the other with hepatitis C.

http://www.bhiva.org

Kidney and liver transplantation in HIV-infected patients: case presentations and review

Until recently, HIV-infected patients have been excluded from consideration for solid organ transplantation. The relatively high mortality rates among HIV-infected transplant recipients observed in the era prior to the use of HAART, coupled with long waiting times for cadaveric organs, made it difficult to support organ transplantation in this patient group.

However, in response to the marked reductions in morbidity and mortality associated with HIV infection, several transplant centres have developed pilot studies or revised their clinical criteria to allow transplantation in this group of patients.

In this article from AIDS Patient Care STDS, researchers at the University of California in San Francisco describe two cases, one kidney transplant recipient and one liver transplant recipient, and review the major clinical and research issues related to this topic.

Reports of transplantations in the pre-HAART era highlight two important findings. First, some HIV-infected transplant recipients did very well with long survival periods. However, overall progression to AIDS and death appeared accelerated.

The researchers recently reported on their preliminary experience with 45 selected transplant recipients in the HAART era. One-year patient survival rates were similar to unmatched survival data from the United Network for Organ Sharing (UNOS) database.

Median CD4+ T-cell counts remained stable in the follow-up period compared to pre-transplant. HIV-1 RNA nearly uniformly continued to be suppressed below the limits of detection.

Preliminary data are promising and support the current efforts to evaluate patient and graft survival among HIV-infected transplant recipients and to explore the mechanisms underlying the many potential complications of transplantation in this population.

Source: HIVandHepatitis.com

http://www.hivandhepatitis.com/recent/transplantation/110703e.html

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Ref: Roland ME, Adey D, Carlson LL et al. Kidney and liver transplantation in HIV-infected patients: case presentations and review. AIDS Patient Care STDS 17(10): 501-507. October 2003.

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London epidemic of sexually transmitted hepatitis C

Graham McKerrow, HIV i-Base

Two studies indicate an epidemic of acute hepatitis C in London, transmitted sexually among HIV-positive men who engage in high-risk, unprotected sexual activities with other men. A high percentrage of individuals spontaneously cleared the HCV infection.

Mark Nelson et al at the Chelsea and Westminster Hospital report: "In recent months we have seen an epidemic of acute hepatitis C, probably sexually transmitted, with individuals reporting unsafe sex and a higher rate of recent syphilis infection." [1]

Fletcher at the Ian Charleson Centre at the Royal Free Hospital says that whereas major risk factors for HCV transmission have been sharing needles for intravenous drug users (IVDUs) and receiving blood and blood products, "recent findings suggest that HCV is being increasingly sexually transmitted, particularly among HIV-positive men who engage in high-risk, unprotected sexual behaviours with other men". [2]

Fletcher looked at cumulative data on patients being treated at the centre, and she reports that 16 HIV-positive patients were diagnosed with sexually acquired HCV infection – all were homosexual men with no history of IVDU "who had been involved in high-risk, unprotected sexual behaviours, which included active and passive anal intercourse, fisting, rimming and oral sex".

Six patients (37.5%) spontaneously cleared the infection. The remaining 10 were treated with pegylated interferon alpha-2b in combination with ribavirin. Three patients achieved a significant reduction in HCV RNA after 12 to 24 weeks of treatment.

Nelson and colleagues carried out a prospective evaluation of acute HCV infection between January 1997 and June 2003. Forty-four individuals were identified, 38 in the last 18 months. All were homosexual men and one had a history of recent IVDU. Fifteen were diagnosed with syphilis in the year before HCV seroconversion. Twenty did not receive treatment; 10 of them because they spontaneously seroreverted to PCR-negative. Those who spontaneously seroreverted to PCR-negative were more likely to have a CD4 count >500 (70% vs 30%) and had higher ALT at diagnosis. Tweny-four patients were treated, 15 of them have finished treatment and nine continue. One received interferon/ribavirin, one pegylated interferon alone and the rest pegylated interferon/ribavirin. Of the 15, 10 have been successfully treated to the point of testing PCR-negative, and treatment failed for five (one due to toxicity, four because of lack of response). The researchers report that treatment response to interferon was lower in the subjects than in the HIV-negative population.

References:

1. Nelson M, Browne R, Asboe D et al. Increasing incidence of acute hepatitis C in HIV positive men secondary to sexual transmission, epidemiology and treatment. 9th EACS, Warsaw. 25-29 October 2003. Abstract F12/3.
2. Fletcher S. Sexual transmission of hepatitis C and early intervention. J Assoc Nurses AIDS Care. 2003 Sep-Oct;14(5 Suppl):87S-94S.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14571563&dopt=Abstract

PAEDIATRIC CARE

Dramatic decline in mortality, disease progression and hospital admissions in children with HIV infection in the UK and Ireland

Gareth Tudor-Williams, for HIV i-Base

Dr. Di Gibb and colleagues from the Collaborative HIV Paediatric Study group have published evidence showing a dramatic decline in childrens mortality and disease progression, gathered from 944 perinatally infected children.

Mortality rates fell from 9.2 per hundred-child-years-at risk in the pre-combination ART era (before 1997) to 1.2–2.0 in the years

2000 – 2002. A 50% reduction in disease progression to Category C disease (AIDS-defining illnesses) and an 80% reduction in hospital admission rates were observed over the same period.

An obvious implication of this improved survival is that increasing numbers of children with perinatally acquired HIV are now entering their teens and are expected to survive into adulthood. Specialist adolescent services need to be developed, and GU physicians should anticipate young people with complex treatment histories making the transition to their services.

Ref: Gibb DM, et al. Decline in mortality, AIDS and hospital admissions in perinatally HIV-1 infected children in the United Kingdom and Ireland. BMJ 2003: 327; 1019-1022.

New tool for assessing risks of disease progression and death based on age, CD4 percentage and viral load in HIV-infected children

Gareth Tudor-Williams, for HIV i-Base

A revision of the 1994 CDC classification system for HIV-infected children has been long-overdue [1].

This system included immunological categories that recognised age-related changes in CD4 counts in children, but was only crudely related to clinical disease progression, especially for younger children.

Trinh Duong and her colleagues from the HIV Paediatric Prognostic Markers Collaborative Study group have analysed data from a number of cohorts of children followed prospectively in the pre-combination-ART era [2].

They have published new graphs that show the relationship between age and CD4 percentages and clinical events (disease progression and death in the next 6 or 12 months). It is striking that CD4 percentages in children provide a much more sensitive prognostic marker than viral loads. For example, across the range of CD4 percentages for a 12 month old child, the risk of disease progression or death within the next 12 months from about 10-75%. In contrast the risk based on viral loads ranging from 3.5 to 6.5 logs is only about 8-30%.

A tool has been developed based on these data that allows the risks to be calculated by entering either CD4 percentage or viral load and age for individual children. This tool can be accessed and downloaded via the Pediatric European Network for the Treatment of AIDS (PENTA) website at www.pentatrials.org

http://www.ctu.mrc.ac.uk/penta/hppmcs/calcProb.htm

It is likely that this approach will revolutionise the criteria for starting treatment in children. The PENTA Steering Committee are currently working on the next update of the European treatment guidelines, which will reflect how these data might be used.

References

1. Centers for Disease Control. 1994 revised classification system for human immuno-deficiency virus infection in children less than 13 years of age. MMWR 1994; 43 / No. RR-12: 1-10.
2. HPPMCS group. Short-term risk of disease progression in HIV-1-infected children receiving no antiretroviral therapy or zidovudine monotherapy: a meta-analysis. Lancet 2003; 362: 1605–11.

VACCINE DEVELOPMENT

VaxGen AIDSVAX vaccine fails in Thailand

On 12 November VaxGen announced preliminary results from a randomised, double-blind, placebo-controlled phase III clinical trial in Thailand that show that the investigational preventative AIDSVAX HIV vaccine designed to work against sub-types B and E failed to protect against infection.

The trial randomised 2,546 injecting drug users at 17 clinical sites in Bangkok, Thailand, in 1:1 ratio of vaccine to placebo. During the 36-month follow-up, seven vaccine/placebo injections were administered at months 0, 1, 6, 12, 18, 24 and 30.

No difference in incidence of infection was found. One hundred and five volunteers who received placebo became infected with HIV compared to 106 volunteers who received at least one injection of the vaccine. The annual infection rate in both placebo and vaccine recipients was 3.1%.

When similarly disappointing results from the US trial of the same vaccine were released earlier this year (see HTB Vol4 No3, April 2003), VaxGen received heavy criticism for implying through scientifically flawed analysis that the vaccine may have some activity in non-Caucasian people.

Source: VaxGen, Inc.

http://www.vaxgen.com

COMMUNITY ACTIVISM

Access to HIV treatment in Eastern Europe

On 24 and 25 October 2003, the European Community Advisory Board (ECAB), a working group of the European AIDS Treatment Group mainly including members from the Eastern European states, met with four major pharmaceutical companies producing antiretroviral drugs.

This was the first time that the majority of the community members representing Eastern European NGOs had formally met with industry in a community initiated forum. It was also the first time that representatives of these pharmaceutical companies had sat in the same room as HIV-positive individuals and their advocates to address access to antiretroviral treatment in Eastern Europe.

Each company - Roche Laboratories, Boehringer Ingelheim, GlaxoSmithKline and Bristol-Myers Squibb - heard first hand about official and estimated figures for incidence of HIV/AIDS in countries from Eastern Europe and the Newly Independent States, together with current availability of either brand or generic antiretroviral therapy in these countries.

It was clear that a few countries - generally those with low incidence and who have the political will to address HIV as an important health issue, such as Estonia and Latvia - have a access to treatment as patients in Western Europe. However, for people living in Ukraine or Russia - two of the Eastern States with highest rates of HIV infection - there is little access to either treatment or monitoring tests.

In Russia unofficial estimates suggest up to two million people could be living with the virus, with less than 5,000 people on treatment. In Ukraine 300,000 people are thought to be HIV-positive, with the government providing treatment to less than 100 patients a year.

In addition to discussing cost, access to drugs and laboratory tests manufactured by each of the companies, the meeting included other subjects important for patient care, such as access to trials of new agents and importantly continued access to treatment once a trial ends.

There have been reports of trial participants not receiving access to treatment that they were promised when they first enrolled.

The HIV epidemic in Eastern Europe, which has dramatically increased over the last two years, largely affects heterosexual intravenous drug users and their partners and is complicated further by very high rates - perhaps in up to 90% HIV-infected patients - of co-infection with Hepatitis C.

Additional figures from Central and Eastern European Harm Reduction Network website are included below.

- HIV epidemic in the countries of Central and Eastern Europe and NIS (CEE/NIS) is rising faster than anywhere in the world.
- There are over 300,000 officially registered HIV cases in the region. According to evaluations of international organizations, the estimated number of people living with HIV/AIDS is around 1.2 million.
- Less than 0.3% of registered HIV/AIDS cases are receiving required antiretroviral treatment.
- Injecting drug users (IDUs) are one of the most vulnerable groups at risk of HIV/AIDS. Eight of 10 HIV cases in the region are connected with injecting drug use.
- There are 1.2 million people registered as injecting drug users in the region.
- As a response to the epidemic, in 1994 the first harm reduction projects appeared. They provided needle exchange and substitution treatment. Now harm reduction projects work in 26 countries of the region.
- Over 200 organizations in CEE/NIS provide needle exchange and counselling on HIV, blood-borne hepatitis, overdoses and vein care for IDUs. They have reached more than 40,000 individual drug users and exchanged more than 490,000 needles and syringes in 2002.
- The most effective way of drug treatment - substitution treatment - is widespread in the Southern and Central European and Baltic countries. In the other parts of the region this way of HIV prevention is not accessible because of the governmental drug policies.
- 77% of all substitution treatment services is offered in nine countries of CEE/NIS, where IDUs are less than 15% of total HIV cases.
- In the entire region, only 12 special programs work in prisons where drug use is widely spread.

- Sex work is closely connected with drug use. In Togliatti (Russia) 86% of female IDUs are involved in the sex industry.

Source: EATG Press Release and CEEHRN website
http://www.eatg.org

http://www.ceehrn.lt/index.php?ItemId=10472

For more information contact Svilen Kolev Konov: svilen.konov@aidsbg.info

ON THE WEB

A guide to the best new reports and resources posted to the internet.

Conferences and guidelines:

The European AIDS Conference 2003 abstracts are now available online.

http://www.aegis.org/Conferences/EACS2003/

This conference has also been added to the AEGiS search engine, so that you can isolate a search to the conference.

This excellent site now includes abstracts from recent Retrovirus (CROI) and IAS conferences and ensures that conference abstracts are available to people unable to attend meetings, and that they will continue to be available as a resource for future research.

Journal articles available online:

Medscape requires one-time free online registration.

The AIDS Reader

Successful treatment of Hepatitis C in a patient with advanced AIDS and decompensated cirrhosis

Frank D. Johanson, MD, Debra B. Balliram, DO

http://www.medscape.com/viewarticle/463786

AIDS

Selections from 2003 - Volume 17, Number 15

http://www.medscape.com/viewpublication/744

Risk of severe hepatotoxicity associated with antiretroviral therapy in the HIV-NAT cohort, Thailand, 1996-2001

Failures of 1 week on, 1 week off antiretroviral therapies in a randomized trial

NEJM

Combination antiretroviral therapy and the risk of myocardial infarction: the data collection on adverse events of anti-HIV drugs (DAD) study group

NEJM, Volume 349:1993-2003, 20 November, 2003, Number 21

http://www.natap.org/2003/nov/112003_1.htm

HIV Medicine

Selections from 2003 - Volume 4, Number 4

http://www.medscape.com/viewpublication/1008_index

- **Epidemiological risk factors for hypersensitivity reactions to abacavir.**
- **The prevalence of reduced zidovudine susceptibility in zidovudine-naïve, antiretroviral-experienced HIV-1-infected patients.**

- **Matched case-control study to evaluate risk factors for hyperlactataemia in HIV patients on antiretroviral therapy.**

JAIDS: Journal of AIDS

Selections from 2003 - Volume 34, Number 1

http://www.medscape.com/viewpublication/878_index

- **Factors associated with mitochondrial dysfunction in circulating peripheral blood lymphocytes from HIV-infected people.**

- **Modeling the time course of CD4 T-lymphocyte counts according to the level of virologic rebound in HIV-1-infected patients on highly active antiretroviral therapy.**

Online medical lectures:

New online essays

Serial publication of a collection of essays on important clinical issues in the treatment and management of HIV and hepatitis C, from the HIVandHepatitis.com website.

http://www.hivandhepatitis.com/

Adherence: the key to successful HAART - Brian Boyle, MD

While there are, of course, many reasons for HAART not being successful, including medication intolerance, prior ineffective antiretroviral therapy and infection with a drug-resistant strain of HIV, non-adherence and non-persistence with antiretroviral therapy is far and away the major reason most patients fail to get any benefit from and develop resistance to HAART.

HCV viral kinetics and the impact of treatment with peginterferon and ribavirin - Peter Ferenci, MD

The ability to predict either a positive or negative therapeutic response is of obvious benefit to clinicians and patients. Positive predictive evidence early in the course of treatment could be used to reinforce the importance of compliance in ensuring a successful outcome.

Conversely, negative predictive capability would allow clinicians to discontinue therapy early during the course of treatment, which would save health care resources and, more importantly, could prevent drug-related adverse events.

Women and HIV/AIDS in the United States: setting an agenda for the future, a policy forum

Watch a documentary, browse through fact sheets and read transcripts of key speeches.

Multimedia meeting highlights from the Henry J. Kaiser Family Foundation (October 23, 2003)

http://dev.kff.org/hivaids/hiv102303package.cfm

Newsletters and reports:

HIV inSite Knowledge Base

Other malignancies associated with HIV - Donald W. Northfelt, MD, FACP.

http://hivinsite.ucsf.edu/InSite.jsp?page=kb-06-04-03

Transmission of HIV by blood, blood products, tissue transplantation, and artificial insemination

Elizabeth Donegan, MD. .

http://hivinsite.ucsf.edu/InSite.jsp?page=kb-07-02-09

Hopkins HIV Report – September 2003

The Hopkins HIV Report is a bimonthly newsletter for practitioners caring for patients with HIV/AIDS. All articles are written by faculty of The Schools of Medicine, Public Health, and Nursing who practice in The Johns Hopkins AIDS Service.

http://hopkins-aids.edu/publications/report/report_toc_03.html

- Antiretroviral therapy update from the 2nd IAS conference
- Pharmacology in Paris
- Panel on clinical practices issues revised adult ART guidelines
- Basic lipids: NCEP made easy for HIV patients
- Focusing on …prevention in positives

PRN Reports

Two pre-press reports on use of 'rapid' HIV tests and on research into RNAi are posted online prior to next issue of PRN notebook.

http://www.prn.org/prn_nb_cntnt/prepress.htm

Understanding and utilizing new techniques for HIV testing - Bernard M. Branson, MD

Shooting the messenger: harnessing RNA interference to combat HIV infection - Judy Lieberman, MD, PhD

HIV and hepatitis coinfection:

Update on chronic hepatitis C in HIV/HCV-coinfected patients: viral interactions and therapy

http://www.natap.org/2003/oct/102303_2.htm

This 5,000 word report provides a nice review of key topics in HCV/HIV co-infection. It is written by Norbert Brau, treating physician at Bronx VA Hospital, NYC. Here is the list of topics covered.

1. Significance of HCV in the HIV-infected population
2. Prevalence of HIV/HCV-coinfection
3. Interactions between HIV and HCV infection:
   —Influence of HIV infection on the course of chronic hepatitis
   —Influence of HCV infection on the course of HIV disease
4. Treatment of chronic HCV in HIV/HCV-coinfected patients
5. Lactic acidosis
6. Special considerations in HCV therapy for HIV-infected persons
7. Which HIV/HCV-coinfected patients should be treated for chronic hepatitis C and how?
8. Management of HIV/HCV-coinfected patients with end-stage liver disease:
   —Treatment for decompensated liver disease
   —Liver transplantation
9. Future research questions

Other news:

Update on dangerous interactions between club drugs and HAART

From Liquid X to speed, ecstasy to Special K, club drugs are growing in popularity. It's no secret that many of them cause health problems, but did you know that several can also interact dangerously with HIV meds? Sarah Biel-Cunningham, M.S.W., has the details.

http://www.thebody.com/asp/julaug03/club_drugs.html?m20

Clinton Q & A: "I knew it needed to be done"

Bill Clinton talks to TIME about his foundation and the ongoing fight for better global access to HIV medications. Article from TIME Europe (November 3, 2003)

http://www.thebody.com/redirect/updates/web031105c.html?m20

The big chill at the lab

Columnist Bob Herbert examines the recent controversy over a list of US government research grants — some of which focus on HIV/AIDS and high-risk sexual behaviour – that the National Institutes of Health has been asked to review. The list was compiled by the Traditional Values Coalition, a deeply conservative religious group.

Op-ed column from The New York Times (November 3, 2003)

http://www.thebody.com/redirect/updates/web031105e.html?m20

MEETING ANNOUNCEMENTS

Wolfson Institute International Conference on AIDS-related cancer

Saturday 17 January 2004

The first AIDS-related cancer forum in Europe will be held on Saturday 17 January 2004 at the Wolfson Institute for Biomedical Research at UCL, Cruciform Building, Gower Street, London WC1E 6BT.

The Registration Fee is £100 and attendance will be limited to 200 participants.

To register, please fill in the registration form online at:

http://www.ucl.ac.uk/wibr/HIVcancer.htm

The deadline for submission of poster abstracts is November 14th 2003.

PUBLICATIONS AND SERVICES FROM i-BASE

NEW: Introduction to Combination Therapy – in Russian

Our Introduction to Combination Therapy has been translated into Russian and is available in hard copy and on our website.

This non-technical patient guide to treatment is now available in 12 languages. It explains what combination therapy is, how well it works, who can benefit from it, when to start taking it, some differences between treating men and women, side effects, the best combinations, changing treatment, taking part in drug trials, your relationship with your doctor, the importance of adherence, and how to avoid drug resistance. Information about HIV treatment changes very quickly. You should only read information that is up to date. Be careful of information, whether printed or from the internet, that is not clearly dated.

When starting therapy it is important that you choose a combination that is going to work for you. It must also be able to fit into your lifestyle. Getting as much information as possible before you start therapy is very important. It will help you make informed decisions about your therapy.

This guide has been translated into Portuguese, Latvian and Slovak, by HIV-positive support organisations in those countries. The Portuguese version is available to download as a pdf file and reprint from the i-Base website:

http://www.i-base.info/pdf/guides/nonuk/COMBO_PORTUGUESE_jan03.pdf

For Latvian and Slovak copies please contact the i-Base office on 020 7407 8488.

Printed versions of this booklet are also available in Bulgarian, Chinese, English, French, Georgian, Italian, Macedonian and Spanish.

NEW: Updated Italian treatment guides

We have updated Italian versions of our three treatment guides: Introduction to Combination Therapy, Guide to Changing Treatment and Guide to Avoiding and Managing Side Effects. For details of what is in each guide see under the separate headings on these pages. The guides are available in a single printed publication (to order, see below) or from our website:

Intrduzione alla terapia di combinazione

http://www.i-Base.info/pdf/guides/nonuk/combo-ITALIAN03.pdf

Guida al cambiamento di terapia

http://www.i-Base.info/pdf/guides/nonuk/salvage-ITALIAN03.pdf

Como evitare e gestire gli effetti collaterali

http://www.i-Base.info/pdf/guides/nonuk/salvage-ITALIAN03.pdf

NEW: Guide to HIV, Pregnancy and Women's Health

This patient guide aims to help women get the most out of HIV treatment and care before, during and after pregnancy. It should help whether you are on therapy or not and includes information for your own health and for the health of your baby.

The guide gives information on medication, Caesarean section and breastfeeding, as well as details of other sources of help. It is aimed at people in a wide range of circumstances including positive women thinking about having children and pregnant women who have recently been diagnosed HIV-positive.

http://www.i-base.info/pub/guides/pregnancy03/index.html

Guide to Changing Treatment: second-line and salvage therapy

This is a non-technical patient guide to second-line and salvage therapy. This booklet should help patients in discussions with doctors, and covers what you can do if your viral load starts to rise, the importance of considering or finding out why your current combination failed. Other sections include monitoring your new treatment, finding out what new treatments will become available, especially through expanded access programmes, how to keep up-to-date with the latest research, treatment interruptions, new drugs in development, and what you can do if you have a very low CD4 count.

A Greek translation of the guide can be downloaded as a pdf file from our website:

http://www.i-Base.info

Guide to Avoiding and Managing Side Effects

This is a comprehensive 36-page guide that is aimed at helping anyone using HIV drugs to get the most out of their treatment, the most out of their relationships with their doctor and other health professionals, to get better medical care to improve their health and, most importantly, to enjoy a better quality of life.

It is written by people who are HIV-positive, who have been on most of the treatments, who have had many of the side effects and who have learnt to negotiate their own healthcare.

Chinese, French, Italian and Spanish translations of this booklet are also available. To order copies, see below.

Treatment information request service – 0808 800 6013

i-Base offers specialised treatment information for individuals, based on the latest research.

We can provide information and advice over the phone, and we can also mail or email copies of the latest research studies relevant to the caller.

For details, call the i-Base treatment information free phone line on 0808 800 6013. The line is usually staffed by positive people and is open Mondays, Tuesdays and Wednesday from 12 noon to 4pm.

All calls are in confidence and are free within the UK.

UK-Community Advisory Board: reports and presentations

The UK-Community Advisory Board (UK-CAB) is a network for community treatment workers across the UK. Each meeting includes two training lectures and a meeting with a pharmaceutical company.

The programme and reading material for the seventh meeting, held on 21 November, are posted to the i-Base website, and reports and presentations should be posted within 1-2 weeks.

The training sessions for this meeting was an introduction to statistics, given by Dr Caroline Sabin from the Royal Free Hospital.

In the afternoon session, the CAB met with Gilead to discuss their new nucleoside FTC and recent drug interaction data involving tenofovir.

http://www.i-base.info/ukcab/nov03/index.html

Transcriptions and slides of training sessions from previous meetings also on the site include:

Genetics, resistance and HIV - Professor Clive Loveday

Approaches to Salvage Therapy - Dr Mike Youle

Pregnancy, HIV and Women's Health - Dr Karen Beckerman

Fertility treatment and sperm-washing techniques - Dr Leila Frodsham

Access to treatment for UK visitors, refugees and asylum seekers - Linda McDonald

Resistance, Lipodystrophy and IAS Report - Simon Collins

TB and HIV coinfection - Dr Anton Pozniak

http://www.i-base.info/ukcab/index.html

Treatment 'Passports'

These popular, handy booklets are for HIV-positive people – whether newly diagnosed or positive for a long time - to keep a record of health and treatment history. Such a record is useful when talking to different health care workers, changing clinics or changing treatments.

Like all i-Base publications, they are available free as single copies, or in bulk for volunteers and professionals to distribute to clients. Copies can be ordered using the form on the back page or by visiting our website (details below).

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You can use the site to read all i-Base publications, find details of the UK Community Advisory Boards (UK-CABs), learn about the organisation, our phone service and meetings, and access our archives and an incomparable range of links. It can also be used to order publications and regular subscriptions to be delivered by post or email (as pdf files).

The i-Base site receives, on average, over 2,250 hits and 700 successful requests for pages every day.

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AEGiS.com - the longest established and largest global resource of online HIV information - includes HTB in the regular journals that it puts online. You can find us at:

http://www.aegis.com/pubs/i-base/2003/

The AEGiS daily email news service also carries i-Base conference reports.

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h-tb

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Introduction to Combination Therapy *(October 2003)*

1 ☐ 5 ☐ 10 ☐ 25 ☐ 50 ☐ 100 ☐ Other_____ _____ _____

Also available in FRENCH, ITALIAN, SPANISH, PORTUGUESE, CHINESE, and GREEK
as pdf files on the i-Base website

Changing Treatment - Guide to Second-line and Salvage Therapy *(November 2003)*

1 ☐ 5 ☐ 10 ☐ 25 ☐ 50 ☐ 100 ☐ Other_____ _____ _____

Guide To Avoiding and Managing Side Effects *(August 2002)*

1 ☐ 5 ☐ 10 ☐ 25 ☐ 50 ☐ 100 ☐ Other_____ _____ _____

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as pdf files on the i-Base website

Positive Treatment News (PTN) *from Winter 2003*

1 ☐ 5 ☐ 10 ☐ 25 ☐ 50 ☐ 100 ☐ Other_____ _____ _____

Paediatric HIV Care - March 2001 - Report from i-Base Paediatric Meeting

1 ☐ 5 ☐ 10 ☐ Other_____ _____ _____

Adherence planners and side effect diary sheets - In pads of 50 sheets for adherence support

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