GMHC GAY MEN'S HEALTH CRISIS

treatment ISSUES

NEWSLETTER OF EXPERIMENTAL AIDS THERAPIES

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Five New Drugs Enter the Homestretch

By Bob Huff

It's a busy season for the folks at the FDA who approve AIDS drugs. At least five new products have passed or are soon to pass under their scrutiny on the way to your medicine shelf. And while none is expected to cause a treatment revolution, each new drug offers something that will surely improve life for someone living with HIV. The question is, "who?" Soon, with more than 20 products to choose from, it will become harder to match up the right drugs with the right people.

The U.S. Food and Drug Administration (FDA) is the federal agency charged with assuring the public that its medicines are as safe and effective as promised and that the claims made by prescription drug makers reflect what the science shows. Before the FDA approves a drug for sale in the U.S., it conducts a thorough review of all the research results that the sponsor company has submitted from human, animal and laboratory studies. After the Agency has received the data (altogether known as an NDA, for New Drug Application), it must review the application within 10 months or, as has often occurred with HIV drugs, it may decide to grant a special six-month priority review to help speed important new drugs into use.

None are revolutionary, but each has somthing that will surely improve life for someone living with HIV. But for whom?

The current crop of drugs contains a mixed bag ranging from a first-of-its-kind fusion inhibitor that blocks HIV in a completely new way, to a kinder, gentler protease inhibitor with (hopefully) fewer toxicity problems, to a couple of renovated formulations that should give a new lease on life to existing drugs. Throw in the merger of two small HIV drug developers with synergistic product lines, and the outlook looks brighter for serving people with diverse treatment needs with ever more finely tailored options. Call it the boutiquing of HIV therapy.

But while any advancement in tolerability and convenience is welcome, there is still concern that further upstream the drug pipeline is dry. Some of this concern comes from drug companies who perpetually stir fears that research will cease unless prices continue their upward march. There is also nervousness that rumored mergers between huge pharmaceutical companies such as GlaxoSmithKline and Bristol-Myers Squibb will kill the competitive drive to improve HIV treatment. But while failure to innovate and take risks will certainly hurt our chances of ever seeing another revolution like HAART, there are signs that progress continues on drugs to attack new viral targets such as integrase and that stronger and safer versions of current generation drugs are coming.

In the meantime, here's what's on the FDA's docket right now.

Zerit XR

Zerit XR is an extended-release formulation of d4T that had Champagne corks popping at Bristol-Myers Squibb (BMS or Bristol) when word of FDA approval arrived on New Year's Eve last year. The company is finalizing the label and ad copy in consultation with the agency. Next comes the advertising blitz promising a carefree world of once-daily dosing. But go slow: there are still a lot of questions that have to be answered. More convenient dosing may well be the wave of the future, but it may not be the right choice for everybody all at once.

Another block to the widespread use of Fuzeon may be its breakthrough price.

The recommended dose of Zerit XR is 100 mg once daily for individuals weighing at least 132 pounds and 75 mg once daily for individuals weighing less than 132 pounds. A comparison between extended release Zerit and conventional Zerit in a clinical trial involving nearly 800 people demonstrated comparable efficacy and tolerability. While the total amount of drug present in the blood over time obtained from Zerit XR was similar to that obtained from immediate release Zerit, the initial peak concentration that followed each dose of the drug was lower with the XR version. This may be good news if the drug's tolerability or toxicity (chiefly peripheral neuropathy) profile can be improved by smoothing out those transient peaks of overly high drug concentrations. On the worrisome side, we have yet to see what happens to blood levels of Zerit XR between 24 and 48 hours after a dose. We still don't know if a skipped dose that results in a full day of exposure to sub-therapeutic drug levels will be more likely to allow resistance than 12 hours of inadequate viral suppression.

The timing of Zerit XR is worth examining. With the first patents on conventional Zerit expiring in 2008, this improved formulation gives BMS a new lease on an old drug far beyond the six years they had left. Remarkably, BMS also introduced the EC version of their Videx product with only six years left on the original patent in 2000. Could these improved formulations have hit the market sooner? Or does "extended release" carry more meaning than we think?

Fuzeon

Fuzeon (T-20) is the Godot of HIV therapy. The long awaited, much delayed, first agent of a completely new method of suppressing HIV infection is definitely at the top of the FDA's to-do list for the New Year. Accepted for priority review in October, the Agency has to deliver a verdict by March. And despite T-20 being a difficult-to-manufacture injectable drug, with inconvenient twice-daily dosing and unpleasant injection-site reactions as a prominent side effect, its novelty and unique value for people with resistance to all available regimens means that approval of Fuzeon is virtually a sure thing.

But a green light from the FDA won't be the end of the wait for some. Because of manufacturing difficulties, Hoffman La Roche (Roche), the drug's sponsor, has announced that availability of Fuzeon will be limited during the first year following approval. Allocating the drug fairly may be a challenge since there seems to be a gap between those in greatest need and those who might expect the greatest benefit from the drug. In a large clinical trial, people who added Fuzeon to a suite of other drugs active against their virus had a much better response than those who took it on top of their worn-out regimens. The catch here is that people with other options may not want to go through the unpleasantries of twice-daily injection, while those with no other options may not find Fuzeon the life preserver they need.

Another block to the widespread use of Fuzeon may be its breakthrough price. Rumors are rife that Roche will set a new record when pricing T-20. Because of budget shortfalls in many states' AIDS Drug Assistance Programs (ADAPs), it seems increasingly likely that coverage of Fuzeon may be limited to those with private insurance willing to pay for it. Some states have adopted a "budget neutral" policy about adding new drugs to their formularies and if plugging T-20 into the typical regimen means significantly boosting the cost of treating HIV, then people dependent on state assistance may be out of luck. Roche has promised that no one who truly needs Fuzeon will go without, but details of their plan to patch over access problems remain to be seen.

Atazanavir

Atazanavir is a nearly next generation protease inhibitor from BMS making a big claim that may revitalize the class. The worrisome cholesterol and triglycerides abnormalities that have hit most long-time users of PIs seem blessedly absent in those who've received atazanavir in clinical trials. Going straight for the competition, atazanavir took on Sustiva (efavirenz), the once and future PI alternative, in a nearly yearlong head-to-head comparison involving over 800 people starting HIV therapy for the first time. Of course, since BMS subsequently bought Sustiva when it acquired DuPont Pharmaceuticals, it has

been in competition with itself, and the company clearly hopes to find itself holding the premier agents in both the non-nuke and PI classes of therapy. But that's not all. As the first daily-dosed PI, atazanavir will climb aboard Bristol's unstoppable once-a-day juggernaut, joining Sustiva, Videx EC and Zerit XR. Bristol filed the paperwork for FDA approval in December and if they made a good case for priority approval, atazanavir could be commercially available by June.

In the trial, atazanavir proved comparable to efavirenz in its ability to bring down viral load below 400 copies in most trial participants. There are also some tantalizing early indications that atazanavir may retain activity after resistance to other PIs has developed—and even a suggestion that resistance mutations to atazanavir may possibly increase viral sensitivity to other PIs. While much more data is needed before making definite claims, it may behoove people with extensive resistance who are considering Fuzeon to wait a bit longer and add atazanavir at the same time. For those who can't wait, see the sidebar about early access programs.

Atazanavir holds no breakthrough in potency, since only about half of those who had viral load suppressed below 400 copies also went below 50 copies. And there is an apparently benign but unpleasant side effect that raised bilirubin levels and turned some people yellow with jaundice. Stopping the drug got the yellow out, but that's a poor justification for treatment interruption. These may be quibbling points in light of evidence that people with elevated cholesterol due to HIV therapy saw numbers normalize after going on atazanavir. Although long-term follow up must be conducted to be sure, the promise alone that atazanavir might dramatically lower the risk of heart disease or diabetes in people taking lifetime HIV therapy could mean eager acceptance after approval. Still, one nagging question returns, "What's up with that bilirubin?"

Fosamprenavir

On the same day in December that Bristol filed for FDA approval of atazanavir, GlaxoSmithKline (GSK or Glaxo) submitted data to support the approval of their PI hopeful, fosamprenavir (also known simply as "908"). Although Glaxo surely petitioned the Agency for priority review of 908, gaining that favor doesn't seem likely, which would mean approval by as late as October.

Why the lack of enthusiasm? To begin with, fosamprenavir isn't so much a new drug as it is a tricked-up version of Glaxo's Agenerase with a VIP pass to get into the bloodstream more efficiently. Agenerase (amprenavir) was approved by the FDA in 1999, but hasn't found many converts, mainly because of the need to gag down eight big fat pills twice a day. The problem is that very little of the drug in the pill gets from the intestines into the blood. But fosamprenavir is specially designed to be taken up by the gut and then immediately processed into amprenavir before being sent to the bloodstream. The "fos" means the difference between 16 pills a day and only two pills a day. Factor in improved tolera-

Expanded Access Program for Atazanavir

Bristol-Myers Squibb is currently enrolling patients in an Early Access Program (EAP) to provide the investigational protease inhibitor, atazanavir, to eligible patients infected with HIV. An EAP provides medicines to patients in need of alternative therapy prior to the medicine's approval. Atazanavir is in Phase III clinical development as a product to treat HIV infection in combination with other antiretroviral agents.

HIV-infected patients who have experienced treatment failure with other available antiretroviral agents and who require alternative antiretroviral agent in order to construct a new treatment regimen may be eligible to participate in the atazanavir EAP. Reasons for treatment failure may also include antiretroviral resistance, intolerance or adherence problems. Physicians must use atazanavir in combination with two or more new or recycled antiretroviral agents. In addition, patients must meet other protocol-specified eligibility criteria. Pharmacokinetic interaction and safety data on the use of atazanavir with other antiretroviral agents (i.e., protease inhibitors, non nucleoside reverse transcriptase inhibitors) are outlined in the protocol.

Patients may be enrolled in the atazanavir EAP through physicians only. U.S. physicians may call 1-877-7-BMS-EAP (1-877-726-7327) or visit www.atveap.com for more information on the atazanavir EAP.

No expanded access programs for Coviracil or fosamprenavir have been announced. An expanded access program for Fuzeon has closed to enrollment.

bility and fewer side effects and it could be that amprenavir is finally ready for prime time. But is this too little, too late?

On its own, fosamprenavir given twice a day can produce viral suppression comparable to nelfinavir without the troublesome rise in triglycerides. But once-a-day is all the rage, and 908 can go that route too—with a little boosting from ritonavir. Unfortunately, ritonavir brings more pills, elevated triglycerides and tolerability problems. And with atazanavir looming, nelfinavir is no longer the benchmark PI. Still, there may be benefits for some people lurking within amprenavir's resistance profile, although what that might be remains murky. There have been a few suggestions about a lack of cross-resistance between atazanavir and amprenavir. If so, then the possible benefit of using the two together should be explored for people with extensive and complicated treatment histories. This drug may not be for everyone, but those it helps will be happy to have it.

Stopping atazanavir reversed the jaundice, but that's a poor justification for treatment interruption.

Coviracil

Coviracil (FTC) is another drug wending its way through the FDA. Its maker, Triangle Phamaceuticals, filed for approval in September and, under standard review, the drug should become available by summer. But in a surprise, what went in as a Triangle drug is going to come out under the brand of Gilead Sciences, the makers of recently approved Viread, who announced the acquisition of Triangle in December.

Coviracil is difficult to distinguish from Glaxo's Epivir (3TC) although some have detected a possible resistance advantage, and in comparison with Zerit, Coviracil was shown more potent and less toxic. But the exciting potential for Coviracil under Gilead's roof is as part of a new once-a-day, all-in-one-pill alternative to Glaxo's Combivir as the nucleoside analog backbone of choice. In other words, no AZT.

The approval of Coviracil is step one. Already Gilead is said to be working on performing the necessary studies that the FDA will want to see when they are asked to approve a coformulated Viread/Coviracil. Hopefully, this data will be in the Agency's in-box by next year.

Next Steps

Gaining FDA approval for this bundle of drugs will be a nice step forward, but the story won't end there. We will have to wait to see how doctors and people with HIV will actually use these new drugs. Big budget ad campaigns in magazines and on bus shelters will certainly have their say, but personal experience and the constantly shifting consensus about therapy usually prevails. First, though, more data from clinical trials are needed to develop our understanding of these new options, and the next wave will come at February's Retrovirus Conference in Boston. The conference halls will be buzzing with opinions, but nothing is as convincing as research well done. In the years ahead, as these newcomers become established, we can expect them to be knocked down by newer—and merely newly tweaked—drugs to come. One question still begging an answer is, with twenty-plus HIV drugs to choose from in the U.S., what does our embarrassment of riches mean to the 90 percent of HIV-positive people in the world who have access to none?

First Wave of Cuts Hits NewYork's ADAP

The following is the text of a letter being sent to health care providers in New York State concerning the first wave of cutbacks to New York State's AIDS Drug Assistance Program (ADAP).

New York State's Uninsured Care Programs (ADAP) has grown rapidly since 1996, with increasing enrollment, higher numbers of participants using program services and increasing drug prices. The Program is primarily funded with federal money. To make the best use of limited resources available, we must take steps to make sure that the Program is cost-effective and meets the highest priority needs.

The Uninsured Care Programs (ADAP) is making some changes that will allow us to continue new enrollments and maintain core services. The following changes are effective February 15, 2003.

Mandatory Generics—ADAP will stop paying for brand-name drugs when there is an A-rated generic equivalent for a brand-name drug. If you get a prescription that is Dispense as Written (DAW), the participant will need to get a new prescription. There will be no exception process for these medications (see the list of affected medications enclosed with this mailing).

Maximum limit of 5 refills per prescription—ADAP will pay for the first prescription and then five (5) refills. This step will help ADAP reduce waste and save money by not refilling prescriptions that have been discontinued. To assure that funding is maximized for all participants, pharmacies should not automatically refill and bill for medications without assurances from the participant that they are still taking the medication.

New limit on nutritional supplements—The maximum amount of nutritional supplements that ADAP will pay for will be no more than three (3) cans per day or the equivalent amount in other forms (e.g., powders, bars).

Maximum number of clinic visits each year—ADAP will pay for up to thirty (30) clinic/threshold visits each year. Enhanced fee visits (that have their own limits) are not counted toward this 30-visit limit (e.g., annual comprehensive exam, mental health visits and dental visits).

Maximum number of dental visits—ADAP will pay for no more than eight (8) dental visits per year.

Formulary Reduced—ADAP will no longer pay for the following drugs.

Oxandrolone
Androgel
Octreotide
Famotidine (Pepcid)
Nizatidine (Axid)
Loratidine (Claritin)
Famciclovir

Quantity Restrictions on Zolpidem (Ambien)—ADAP will pay for only 15 tablets of Ambien per month.

Prior Approval for atovaquone (Mepron)—ADAP will require prior authorization through a physician to pay for atovaquone (Mepron). Participants currently taking atovaquone will receive a separate letter with the authorization form to bring to their doctors.

We are sorry that we have to limit these services, but ADAP only has the funds allocated to it each year and must adjust our services to match our funding.

Please assist our participants in securing other health care coverage options such as public entitlement programs that cover more drugs and services than ADAP. These include Medicaid, Medicaid Spenddown, Family Health Plus and Veterans Health Care Coverage. These programs offer more comprehensive coverage.

As always, the New York State ADAP hotline staff are available (1-800-542-2437) Monday to Friday 8:00 A.M. to 5:00 P.M. to answer questions about the Program.

State ADAPs with waiting lists, client expenditure caps and/or drug access restrictions:

Alabama—175 people waiting
Guam—4 people waiting
Idaho—Program closed to new enrollees
Indiana—4 people waiting
Kentucky—62 people waiting
Montana—2 people waiting
Nebraska—Program closed to new enrollees
North Carolina—60 people waiting
Oregon—18 people waiting
Puerto Rico—64 people waiting
South Dakota—43 people waiting
Texas—ARV restrictions
Wyoming—Program closed to new enrollees
Washington—Program restrictions

Source: www.ATDN.org

Message to Congress: SAVE ADAP!

Dear Senator/Representative:

The undersigned organizations serving the needs of people living with HIV write to ask that Congress provide a minimum of $162 million in additional federal funding for AIDS Drug Assistance Programs for FY 2003.

This year, 13 state AIDS Drug Assistance Programs (ADAPs) have been forced to take steps to limit access to life-saving HIV medications for uninsured and underinsured Americans due to inadequate funding. Texas, for example, has recently announced that in order to close its deficit, it will retroactively lower its income limits from 200% of the federal poverty level (300% with spend downs) to 140%. That action will require the removal of 2500 presently enrolled ADAP clients from the program by June 1, 2003.

New York must also address a $16 million structural deficit in 2003 and a projected $50 million deficit in 2004 if either state/and or federal funding is not increased by that amount.

According to the most recent National Alliance of State and Territorial AIDS Director's (NASTAD) Report, the following states have also initiated waiting lists as of 12/5/2002: Alabama (175), Indiana (34), Kentucky (62), Montana (2), North Carolina (60), Oregon (18) and South Dakota (43). Idaho, Nebraska and Wyoming have closed to new enrollees. In addition to New York and Texas, Colorado, Florida, Georgia, Nevada and South Carolina have projected the need to impose access restrictions in early 2003.

One major factor driving increased ADAP need is enrollment growth, which is due to the success of the new drugs in decreasing deaths and slowing progression to AIDS. Since the introduction of effective combination HIV therapies in 1996, America's death rate from AIDS has fallen by over 50%. Because people are staying alive longer, they need ADAP longer and so enrollment continues to climb. While this should be taken as a sign of the program's success, resources flowing to ADAPs are not being increased to take care of the swelling numbers of people that are being kept alive.

Ironically, attempting to save money in the short term may cost taxpayers more money in the long term. Recent data presented by the University of Alabama at Birmingham at the International AIDS Conference in Barcelona demonstrates that the average cost of care for a person with early HIV disease is approximately $14,000 a year while waiting to treat that person until they are disabled costs about $34,000 a year.

Fears of particularly serious problems for FY 2003 are exacerbated by the expected arrival of new drugs that few programs in crisis are likely to be able to afford. Fuzeon (T-20), the first fusion inhibitor to reach the market, could provide urgently needed support for patients whose anti-retroviral options have run out when it is approved in early 2003, but the drug is expected to be expensive, which could force ADAPs to ignore the need for the drug.

The second class of drugs that most ADAPs are unlikely to be able to afford are those to treat HCV. While HCV has become the number one cause of death among people with HIV, most states are resistant to adding new classes of treatment when resources are scarce.

Finally, in order to make best use of ADAP funding we ask that you fund required services provided under the Ryan White CARE Act at the highest possible levels. Without the support services provided by the CARE act, many ADAP clients would have no realistic access to the medical care and auxiliary services they require to maximize the usefulness of anti-HIV medical regimens.

We believe that it is imperative to provide life-extending AIDS drugs to all Americans in need. We hope that you will agree.

Sincerely,

Partial listing: ADAP Working Group • African Services Committee, New York, NY • AIDS Action • AIDS Action Baltimore • AIDS Coalition of Texas Now! (ACT Now!) • AIDS Council of Northeastern, NY • AIDS Foundation of Chicago • AIDS Rochester • AIDS Services of Dallas • AIDS Treatment Data Network AIDS Vaccine Advocacy Coalition • Alianza of New Mexico • AMASSI, Inc. • Bailey House, New York, NY • Betances Health Center, New York, NY Boulder County AIDS Project • CARE Resource, Miami, FL • Catholic Social Services of Mobile, Alabama • Center for Community Alternatives Families Connecting for Kids, The Adoption Exchange • Florida AIDS Action • GMHC • Hepatitis C Action & Advocacy Coalition, San Francisco Hepatitis C Advocate Network, Inc (HepCAN) • HIVandHepatitis.com • IDC Research Initiative, Orlando, FL • International AIDS Empowerment, El Paso, Texas • International Foundation for Alternative Research in AIDS • Long Island Association for AIDS Care (LIAAC) Los Angeles County Office of AIDS Programs and Policy • Los Angeles Family AIDS Network (LAFAN) • Los Angeles Gay and Lesbian Center Miami Beach Community Health Center, Inc. • Milwaukee Lesbian, Gay, Bisexual, Trangender Community Center • Montrose Clinic, Houston, TX National AIDS Treatment Advocacy Project • New York AIDS Coalition • New York City AIDS Housing Network • North Carolina Council for Positive Living Nova Southeastern University, College of Dental Medicine • Physicians' Research Network • POZSeattle • Project AZUKA, Inc. • Project Inform Provincetown AIDS Support Group • San Mateo County AIDS Program • Search for a Cure • Sierra Foothills AIDS Foundation • Staten Island HIV C.A.R.E. Network Tarzana Treatment Centers • Tennessee AIDS Support Services, Inc. • The Center for AIDS: Hope & Remembrance Project Title II Community AIDS National Network • Treatment Action Group • Tucson Interfaith HIV/AIDS Network (TIHAN) • United Foundation for AIDS Vermont People with AIDS Coalition • Williamsburg/Greenpoint/Bushwick HIV CARE Network

Interview with Joep Lange

Reprinted from European AIDS Treatment News
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The International AIDS Society's (IAS) Governing Council reads like a Who's Who of the HIV world. Robert Gallo, Tony Fauci, Luc Montaigner and the late Jonathan Mann all at one time served on the Council. Today, the IAS leadership is still composed of leading scientists and physicians including Scott Hammer from the University of Columbia, Souleymane Mboup and Elly Katabira, both respected and established HIV advocates from Africa, and Helene Gayle, formerly of the U.S. Centers for Disease Control (CDC) and now with the Bill and Melinda Gates Foundation.

While the IAS may lack the gravitas of the World Health Organization (WHO), the resources of the National Institutes of Health (NIH), and the high-status prefix of UNAIDS, from an activist perspective, the IAS is respected for its world conferences and for making itself amenable and accessible to the activist community in Europe. Stefano Vella, the former IAS President, before and during his presidency, was no stranger to European AIDS treatment activists. His engagement with AIDS activism has been a personal commitment and has helped to establish an important liaison between advocates operating at pan-European and international levels.

Joep Lange is the recently appointed President of IAS. While his demeanor may be brusque and disarmingly forthright, his intellect, integrity and dedication to fighting HIV on all its geographical fronts, is without reproach. Lange is a rare individual who understands the business of governance but does not respect the insidious imposition of power. Entrenched positions of power, and abuse of it, he has long claimed, have the potential to bring nations to a halt. Whether the abuse of authority is the result of political machinations, business greed or personal lethargy, it is always reprehensible.

On the eve of his inauguration as President of IAS, Lange shared his thoughts on HIV, his presidency and what to do about AIDS in Africa.

Professor Lange, how would you describe the HIV situation in the developing world?

Well, I would begin by describing the scale of the situation. HIV has devastated individuals, communities and populations on a proportion that can only be expressed as a human tragedy. The suffering, misery and total lack of hope that I witness when I travel to Africa is beyond description. I would also illustrate the toll of HIV against the stark reality of economics—since that is, and will continue to be, the great motivator for many nations.

What specific efforts do you feel are essential to contain and adequately address HIV in the developing world?

Treatment. All our breast-beating is futile. And our efforts to date—50 patients here, 50 patients there—are negligible. Let's look at the figures, 28 million in Africa, 7 million in Asia. We are told that 30,000 people are being treated in the developing world. Well, that must be a lie—it is actually less than this. Our commitment, no matter how well meant, has been fragmented. We have not even begun to consolidate our own actions. What is needed is concerted, responsible and sustainable intervention. Let's look at it like this—we will need treatment, yes. But we will also need to devise effective strategies for speeding up drug supply, drug delivery, identify key players, develop clinical and technical expertise. The Global Access Initiative launched here in Barcelona is one way of sharing and building upon our resources and commitment. We organized ourselves against smallpox eradication. Let's do it for HIV.

People under a bad government are punished enough—let's not punish them anymore by making them suffer a disease for which we have treatment.

Who is responsible for addressing this global tragedy? Who are the key agents whose contribution will make a difference—African governments, western governments, WHO, scientists, physicians, pharmaceutical companies, international NGOs, activists?

There is so much to be done. So much intellect, resource, capital and commitment is out there, yet no one seems to be playing together. I have often said that we are fighting over Africa and Asia for our own political and career interests, duplicating efforts and obstructing real potential. Instead, let's divide the world amongst those who have the resources and thus the responsibility to treat. I proposed earlier that

the NIH could be responsible for some part of the world, the ANRS for another and so on. The WHO does have a role. It's role is to lead—but it cannot deliver alone. Bad governments impede our efforts. I have always been vocal on this issue. People under a bad government are punished enough—let's not punish them anymore by making them suffer a disease for which we have treatment. There are operational issues and supply issues to be addressed. Let's work positively and responsibly with those who have the treatment resources—the pharmaceutical industry and those who make generics. NGOs will remain essential in this process. They can support, empower and vocalize. As Paul Farmer so rightly said, "the community is part of the infrastructure."

What is your personal vision and aim as President of IAS?

To be an advocate. To take the lead. To overcome the issue of infrastructure as an obstruction to treatment. Infrastructure is used incessantly as an argument for not treating HIV. We have the WHO treatment guidelines as a starting point. Let's establish treatment, scale-up and work with countries to improve existing health care delivery systems now.

The Vice-Chair of the EATG said in a press conference "scientists are turning into politicians" and "activists are getting angry again." How do you respond to that?

Unfortunately, scientists can't just stay scientists. Their resources and skills are needed to mobilize treatments on a global scale. Scientists and physicians have delivered astounding achievements in this area. But we need to push them and their talents so that research and clinical care are available and made meaningful to those who need it the most. And yes, I have observed the community getting angry again. That is a good sign. We need strong advocates from both the developed and the developing world. Activists emerging from Africa have already established historical landmarks.

My message to European treatment activists? Partner up with activists and networks in the developing world, share with them what you know, learn from them about their experiences of HIV, and build alliances that will be supportive, challenging and formidable.

Interview conducted by Y Halima and R Camp, EATG

Written by Y Halima, EATG, UK

Our thanks to Professor Lange for sharing with us his candid comments and views.

Intervention in a Village

By Maitreya

Email correspondence from the AIDS-INDIA discussion list

Dear Umesh,

This is in response to your post requesting information on village-level interventions for HIV prevention.

Your description of a village "having low literacy level, low socio-economic status and totally male dominated," fits more than 80 percent of Indian villages. Therefore we could say that strategies adopted in most villages could be applicable in your case also.

But I must say, you must start with "men as high-risk group" and address them first exclusively. Usually health projects address women first, as they are sitting ducks at home, but those projects forget about power relations in sexual matters. So if you start with women, all you will end up doing is creating more fear to go along with their already powerless existence. Women may be easy to approach and available, but make sure, as difficult it may seem, that you address the men first.

Never talk to men in the language of fear and death, for they always live dangerously in life situations and at work. Approach them first with the idea of pleasure and then health. Tell them we need health to sustain pleasure. You may encounter resistance among them about using safe sex methods, especially condoms. Tell them there are ways to wear condoms pleasurably by, say, asking your partner to put them on. Slowly build the idea of health woven strongly with the

idea of pleasure, or else they may listen stoically but will never practice.

Next, work out ways to bring up the topic of injustice in power relations that exists between genders — point out how a submissive and docile wife actually lessens the pleasure, and stress the aspect that an active partner heightens pleasure. Also mention that this is why men seek out sex workers. Under existing conditions it is men who take the initiative in all sexual matters. Thus, once you can build the idea of pleasure around all health aspects, men will start to listen.

In short, first make men responsible for their acts.

Once this part is initiated then you can ask the village heads to address the issue of HIV / AIDS broadly through awareness campaigns and meetings.

Only after this, should you address women exclusively to show the disparities in gender relations and tell them that they should ask their spouses to use safe sex methods. This way the men won't feel affronted when women dare to ask them. This way you can avoid a lot of violence and bitterness among couples.

Don't stick to "condoms are the only method" to safe sex practice. Make sure you teach them the pleasures of mutual masturbation, using thighs, etc. Tell to avoid penetrative sex as far as possible and, if need be, only then use condoms. Tell men that penetrative sex is for making babies and that they don't have to push their stick in all the encounters.

Now, we have to show that there are different sexuality groups and there is nothing to hide or be shameful about. That sex between consenting adults — between man and man, woman and woman, man and intersex person, woman and intersex person or among intersex persons — is permissible and "quite natural" also. Also say that there are bisexual persons and there are different shades of sexual orientation, and that there are confused persons with their different sexual orientations, but all is okay, if it is done on mutual agreement with respect and concern. Again show them that there are different sexual practices and all are acceptable with above agreement. What is wrong in sexual encounters is what is forced and without consent. Tell men, even if that happens between married couples, it is wrong.

In short teach sexuality in depth to bring about behavioral changes. Only in a brothel set up one can demand the use of condom in sexual encounters. All other relationships need mutual agreement, responsibility, respect and concern, in short, love.

Men will ask about sexual matters, about pleasure and other details. Talk about these in small, comfortable groups. But never create literature to explain it, for there will be "moral morons" around who will topple the apple cart. The fundamentalist business will come into action, so don't leave anything for them to chew upon. At any confrontation, deny everything, but if you leave anything written, you will be in trouble. Police and the fundamentalist mafia will make mincemeat of you. Sex and the politics of power goes together.

Make sure that condoms are available once you promote their use. Easy availability increases use.

Once you can build the idea of pleasure around all health aspects, men will start to listen.

The most neglected issue concerns the treatment given to the AIDS patients. You have to fight for the medicines with all the authorities. This you should do with other NGOs at all levels. Start a care center if there are any AIDS patients, but to treat them you need expert people.

We also have to address the stigma around PLWHAs (People living with HIV / AIDS). Make people sensitive about it. If possible include in your team an HIV+ person. If there are already HIV+ people in the village, this will help immensely. Moreover this will wipe out fear and discrimination immediately. People see what is preached as practiced.

Okay, these are some of the thoughts that crossed my mind. If you ask on specific matters I may be able to answer them later. Say, I may not know all the answers but all I am saying is I am ready.

Love,
Maitreya

Global Treatment Update

By Bob Huff

Developing new drugs is one thing, but finding ways to get them to the vast majority of people in the world who need them is proving a lot tougher than hoped. Of course price has been and will continue to be a problem, but the logistics of shipping, clearing customs, transporting and storing medicines need attention too. Then come issues of diagnosing, dispensing and monitoring therapy when doctors, diagnostics and skilled staff are in short supply or lacking altogether.

Gilead Sciences, the makers of Viread (tenofovir) and soon-to-be custodians of Coviracil (FTC), have announced a plan to distribute tenofovir at no profit to organizations in every country in Africa and in 15 other resource-challenged countries. Providing drugs at cost or even for free is not a new idea. Other companies have launched similar programs that have met with mixed success. Boehringer Ingelheim, for example, has a program to provide free nevirapine for prevention of mother to child transmission of HIV. Yet the required paperwork was initially so convoluted and difficult to negotiate, that few were successfully treated.

What sets the Gilead plan apart is the attention given to addressing the problems of actually distributing and dispensing the drug. First, Gilead plans to arrange for direct purchasing by treatment programs in each country. Some small treatment programs have found that drugs offered at an affordable price by a generic maker may have to pass through a third-party wholesaler who can add on significant markups or divert their shipment to another customer willing to pay more. Next, the company has indicated a willingness to provide information and technical assistance to organizations that are interested in adding treatment to their services. The intention, the company says, is to "take appropriate steps to ensure that Viread shipments reach their intended destination and, to

Short Course *Notes on HIV drugs in development*

Tipping the Scales at 500 mg—Tipranavir!

Boehringer Ingelheim has announced that they have finally settled on a dosage for their protease inhibitor, tipranavir. Now, larger Phase III clinical trials of the drug can begin. A recently completed Phase II study had compared three different dose combinations of tipranavir plus ritonavir given twice daily. A dosage of 500mg tipranavir plus 200mg ritonavir was chosen as providing the best balance of adequate viral suppression with the fewest side effects. The ritonavir acts to keep blood levels of tipranavir higher, longer, by slowing its metabolism through the liver.

The Phase II study was conducted in people with extensive experience using multiple drugs in all classes of antiretroviral therapy. Since tipranavir may be able to suppress multiple-PI resistant and wild type virus with about equal efficacy, it represents an urgently needed therapy for people who've run out of treatment options. Even though primary resistance to tipranavir itself seems to be slow to develop, people who still have an array of treatment choices probably won't choose tipranavir. Besides being a twice-a-day product, ritonavir boosted tipranavir is likely to raise blood lipid levels and cause drug interactions and tolerability problems. Unfortunately, these are factors that will also limit its use among some people who will desperately need it.

Having settled on a dose, Boehringer is now set to start up a pair of large Phase III trials. One study (RESIST 1) will be a 24-week trial in sites throughout North and South America, and Australia. A 16-week trial (RESIST 2) will be conducted exclusively in Europe. The time to approval of tipranavir will depend on how quickly the Phase III studies are enrolled, how much time the company needs to pull its data together for the FDA, and how long the FDA needs to review the application. Mid 2004 would be an optimistic guess.

As the Phase III trials get going, and with the approval of T-20 (Fuzeon) expected in March, it becomes urgent to finalize the details of a tipranavir expanded access program for people with no other treatment options. We know that T-20 has the best shot at working when it is accompanied by at least one other drug active against an individual's viral strain, and for many, tipranavir is the best candidate on the horizon. With access to T-20, tipranavir and atazanavir opening up in the next six months, things might start looking brighter for the growing number of people who critically need an effective third, fourth or fifth-line regimen.

the extent possible... monitor the recipient programs on an ongoing basis to ensure that quality care is being provided."

Realizing effective programs will depend on continued research into both the medical and the operational aspects of delivering treatment in resource-limited settings. Gilead is also a participant in the "Development of Antiretroviral Therapies" (DART) study, a 3,000-patient clinical trial sponsored by the U.K. Medical Research Council scheduled to begin this year in Uganda and Zimbabwe. DART aims to investigate ways to optimize the provision of therapy with simplified protocols and diagnostic tools.

There are more than a few stumbling blocks ahead, even with the company's willingness to smooth the way. To date, no price has been announced and it's possible that Gilead's "no profit" price will exceed what many programs can afford. Then, cheap Viread is fine, but one drug is not enough. What other drugs on what terms will be available to programs that wish to begin offering treatment? Gilead is in the process of acquiring Coviracil, which should prove nicely compatible with Viread, but that won't be available for perhaps another year—and still, the third leg is missing. If Gilead is serious about making this program work, it should plan to act as the "at-cost" middleman for a full combination, including, say, Viread plus Epivir and Viramune or Sustiva in the package. At the very least, Gilead should pledge not to disqualify or discriminate against programs that plan to use generic versions of these other drugs in their affordable combinations.

New Handbook for Organizations Seeking to Provide Treatment

Initiatives like the Viread distribution program could be an attractive solution for employers, religious missions, health clinics, clean water programs or any of a number of similar existing economic or health development projects that would like to add HIV care and treatment to the services they offer. But small community-based organizations (CBOs) and non-governmental organizations (NGOs) interested in dispensing HIV medicines have a lot to consider before taking the plunge.

The International HIV/AIDS Alliance, along with the World Health Organization (WHO) and UNAIDS, has developed a handbook entitled, "Mobilising NGOs, CBOs and PLHA groups for improving access to HIV/AIDS-related treatment." Intended as practical toolkit, the handbook contains a series of training exercises designed to prepare management and staff to deal with the full range of tasks and issues that will accompany undertaking a treatment program, including how to:

- Make decisions on involvement in treatment provision and drug supply by providing a basic understanding of the main factors involved in HIV/AIDS treatment;
- Gain access to and make use of existing local and national drug supply systems where available; explore and use alternatives to these systems and drugs where necessary and useful; understand the uses of donated drugs and the constraints associated with their management and use;
- Work with the practical issues involved in drug supply and financing, with special regard to cost, quantification, quality and sustainability in the context of the development of the epidemic and in relation to other public health needs;
- Ensure good practice in the use of HIV/AIDS-related drugs, including clinical requirements and the use of treatment protocols, technical support (such as laboratory services) and psychosocial support (such as confidentiality and counseling).

Although the Handbook is designed to build practical skills through interactive exercises, simply reading through the material gives an overview and reality check about what treatment provision can entail.

Copies of the Handbook are available at: www.unaids.org/publications/documents/health/access/NGOtoolkit/index.html.

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Ring in the New... *Now*

By Gregg Gonsalves

As the New Year begins, it's time to take stock of where we've been and where we're going. Around the world, only a fraction of the people who need AIDS treatment get it and the virus continues to spread like wildfire in Asia, Eastern Europe, and Africa. In the United States, 13 state AIDS Drug Assistance Programs (ADAPs) have already closed enrollment to new clients or limited access to antiretroviral treatments. Adding expensive new drugs like T-20 or treatments for hepatitis C are out of the question for most ADAPs.

Meanwhile, the extreme right wing within the Bush Administration continues to play politics with HIV prevention, pushing abstinence-only prevention programs—despite evidence that suggests these kinds of efforts are ineffective—and questioning the worth of condoms, despite data that confirms their central role in protecting people against HIV.

Soon, Congress, working with Draconian budget caps, the prospect of more tax cuts, and a war in Iraq, will have nothing to spend on domestic discretionary programs, including those for HIV/AIDS. Nor will there be room for any real investment in international efforts to combat the epidemic. Additionally, the doubling of the NIH budget has come to an end, forcing some hard choices about the future of AIDS research.

As Irish poet William Butler Yeats wrote 80 years ago, "the best lack all conviction, while the worst are full of passionate intensity." Since the advent of highly active antiretroviral therapy (HAART) in the late 1990s, we've seen a waning of AIDS activism here in the United States. It seems as if many of the activists who fought for the programs and policies that we rely on today—if they survived to see the drugs—considered their work done and moved on. And although many new-generation AIDS activists have focused their energies on vital international work, one wonders if and when we'll see resurgence in the activism needed here at home.

The passionate intensity of the Right is bent on destroying all we have worked for during the past twenty years, yet people with AIDS and their advocates in the U.S. seem strangely silent. Have gay men in New York City and around the country forgotten what it was like in the 1980s? Or have they decided, now that they've got HAART and health insurance, and now that the epidemic has moved into African-American and Latino communities, that HIV is not their problem? Are there still some leaders in the African-American and Latino communities practicing denial about the swath of destruction that HIV has unleashed in their communities?

A few of our readers here at *GMHC Treatment Issues* have complained that the newsletter has gotten "too political" over the past couple of years. I happen to like our focus on treatment information, policy and advocacy—it eloquently reflects the challenges and opportunities of the next decade of the pandemic. In counterpoint, I would maintain that a few of our readers have gotten "too complacent" since HAART came on the scene.

Today, I can ask: where were you when your state's ADAP program closed? Where were you when "just say no" abstinence-only programs were instituted as the only HIV prevention efforts in your teenager's high school? Soon, I'll be able to ask: where were you when public funding for AIDS programs began to slide backwards? Where were you when your local AIDS service organization started cutting back services to those most in need due to lack of funding from individuals and foundations? Where were you when the number of people in the world infected by HIV—where, for the majority, AIDS remains a death sentence—hit 70 million?

So, it's a New Year. Time to make your resolution. Pick up a pen and write to the President, your members of Congress, your governor, and your mayor. Check in with your local AIDS organization to see what needs to be done, and then get to work. If every subscriber to *Treatment Issues* did this, thousands of calls and letters would flow to Washington, D.C., to the people who make the decisions that affect our lives.

Yeats concluded his poem by asking, "what rough beast, its hour come round at last, slouches towards Bethlehem to be born?" Those of us living with AIDS don't need to ask; this terrible creature lives in our bodies, swirling in our blood, and it links our fate to all people with HIV, whether they are a subway ride away or a world apart.