

AIDS TREATMENT NEWS

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Statement of Purpose:

AIDS Treatment News reports on experimental and standard treatments, especially those available now. We interview physicians, scientists, other health professionals, and persons with AIDS or HIV; we also collect information from meetings and conferences, medical journals, and computer databases. Long-term survivors have usually tried many different treatments, and found combinations which work for them. *AIDS Treatment News* does not recommend particular therapies, but seeks to increase the options available.

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Tenofovir Approved: Broad Indication

by John S. James

On October 26 the FDA approved Viread (tm) - generic name tenofovir disoproxil fumarate, or tenofovir DF. The approval was expected; less expected was the broad indication, which both the company and treatment activists wanted, but which some of the advisory committee had questioned (see "Tenofovir: FDA Hearing on Important New Antiretroviral," *AIDS Treatment News* #372, October 19, 2001). From the package insert:

"INDICATIONS AND USAGE

"VIREAD is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection. This indication is based on analyses of plasma HIV-1 RNA levels and CD4 cell counts in a controlled study of VIREAD of 24 weeks duration and in a controlled, dose ranging study of VIREAD of 48 weeks duration. Both studies were conducted in treatment-experienced adults with evidence of HIV-1 viral replication despite ongoing antiretroviral therapy. Studies in antiretroviral naive patients are ongoing; consequently, the risk-benefit ratio for this population has yet to be determined.

"Additional important information regarding the use of VIREAD for the treatment of HIV infection:

"* There are no study results demonstrating the effect of VIREAD on clinical progression of HIV.

"* The use of VIREAD should be considered for treating adult patients with HIV strains that are expected to be susceptible to tenofovir as assessed by laboratory testing or treatment history."

A patient-oriented description of the drug appears at:
<http://www.aidsmeds.com/drugs/tenofovir.htm>

The Medscape drug-interaction calculator, recently updated to include tenofovir, is at:
<http://hiv.medscape.com/Medscape/HIV/DrugInteractions/index.cfm>

An FDA Talk Paper is at:
<http://www.fda.gov/bbs/topics/ANSWERS/2001/ANS01111.html>

And the complete package insert can be found on the Gilead site at:
http://www.gilead.com/prod_pdf/viread_pi.pdf.

T-20 Small Program, CD4 < 50, Will Enroll November 27 at 3:00 P.M.

by John S. James

A small and difficult T-20 expanded-access program will begin receiving phone calls from U.S. physicians on November 27 at 3:00 p.m. Eastern time. The first 56 eligible physicians will be accepted. Each physician must have exactly 3 patients who qualify for this program when they call. The 168 patients accepted will be eligible to receive T-20 when the program starts -- in the first quarter of 2002, depending on drug supply.

T-20 is the first member of a new class of anti-HIV drugs called fusion inhibitors, which block the entry of HIV into cells. Because it works by a different mechanism than any approved drug, virus resistant to the approved drugs is not expected to be resistant to T-20. However, T-20 resistance can develop when the drug is used, as with the other antiretrovirals.

Patients must have a CD4 count under 50, a viral load over 10,000, and be at least 16 years old. Physicians are asked to give preference to patients "who have had an AIDS defining opportunistic infection, neoplasm or condition AND CD4 lymphocyte count <50 cells/mm³, both while on HAART within the last 90 days."

T-20 is being developed jointly by Roche Pharmaceuticals and Trimeris, Inc., and is currently in phase III clinical trials. This new program is called Protocol T20-305, "Open Label Safety Study of T-20 in Patients with Advanced HIV Disease who are Unable to Construct a Viable Antiviral Regimen."

Physicians interested in this program should

make sure that they have a November 2 Dear Doctor letter from Trimeris and Roche, which was sent to 2,000 AIDS-treating physicians on November 2; currently it is on the Web at <http://www.hivandhepatitis.com/recent/resistance/110701a2.html>. Also, a physician or patient with questions about T-20 can call Professional Product Information at Roche, 1-800-526-6367, 8:00 a.m. to 6:30 p.m. Eastern time Monday through Friday, either before or after November 27. (Note: This is NOT the number to call starting November 27 at 3:00 P.M.; see the physician letter for complete information.)

Treatment News from Recent Conferences: Finding Web Reports

by John S. James

Much treatment information came out at several conferences in October and early November. It did not get major press attention because there was no big headline story or single coherent message. Unless you know someone who was there, the best way to learn about these conferences shortly after they happen is through Web reports by researchers, physicians, or other experts. While few will read all this material, patients and medical professionals can scan to find information about problems they are having, treatments they are using, or relevant leads.

You can scan the lists of major topics, below, to decide what you want to see, then go to the Web sites to read the selected summaries. Note that these reports are written mainly for medical professionals, and some are more difficult than others.

These conference Web reports provide quick, accessible treatment education updates in areas you choose. This article lists major topics reported (as of mid November 2001, when we went to press).

Recent Conferences

* IDSA 2001 (annual conference of the Infectious Diseases Society of America), October 25-

28 in San Francisco;

* The 3rd International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV, October 23-26 in Athens, Greece;

* The 8th European Conference on Clinical Aspects and Treatment of HIV Infection (EC-CATH), October 28-31 in Athens, Greece (by the European AIDS Clinical Society);

And for reports on liver diseases,

* 66th Annual Scientific Meeting of the American College of Gastroenterology, October 19-24, Las Vegas;

* AASLD (American Association for the Study of Liver Diseases), will be held November 9-13, Dallas.

Web Sites with Conference Coverage

The following four sites have extensive reporting on these conferences (though only The Body covered all five of them).

Note the more specific Web addresses for some of the conference coverage, further below. But if one of these addresses does not work (perhaps because the site has been reorganized), use the address here to get to the home page, and then look for the conference coverage on the site. Some sites take down their conference reports after one year.

* The Body, <http://www.thebody.com>, has the most extensive conference coverage.

* HIV and Hepatitis.com, <http://www.hivandhepatitis.com> has perhaps the most extensive coverage of AIDS and hepatitis treatment news on the Web.

* Medscape, <http://www.medscape.com> has many excellent medical resources. (You need to register and choose a password to use this site, but the registration is free.)

* NATAP (National AIDS Treatment Advocacy Project), <http://www.natap.org> has valuable information, though some of it has been technical and hard to read.

While these Web sites are credible, nothing is perfect. These rapid Web reports, often online within days of a meeting, sometimes within a day, do not always leave time for thorough fact checking. And the pervasive "spin" throughout the entire U.S. medical field, especially pharmaceuticals, makes all treatment reporting difficult. The trials conducted and results published reflect complex, often secret negotiations between corporate, professional, regulatory, organizational, personal and other interests. There is no way to cover a field as complex as AIDS and even be aware of all of the important spin.

Approved HIV Drug Names

We use generic drug names in this article -- or the more familiar abbreviations AZT (generic name zidovudine), ddI (didanosine), d4T (stavudine), and 3TC (lamivudine). Generic names are usually but not always used on the sites. For those more familiar with the brand name, here is a table of the brand names and generic names of the anti-HIV drugs currently approved in the U.S. Since all antiretrovirals are patented in this country, there is only one brand name here for each generic (except for saquinavir, which has an earlier, weaker formulation named Invirase).

Agenerase	amprenavir
Combivir	[AZT+3TC]
Crixivan	indinavir
Epivir	lamivudine (3TC)
Fortovase	saquinavir
Hivid	zalcitabine (ddC)
Kaletra	lopinavir/ritonavir
Norvir	ritonavir
Rescriptor	delavirdine
Retrovir	zidovudine (AZT)
Sustiva	efavirenz
Trizivir	[abacavir+AZT+3TC]
Videx	didanosine (ddI)
Viracept	nelfinavir
Viramune	nevirapine
Viread	tenofovir DF
Zerit	stavudine (d4T)
Ziagen	abacavir

Major Topics Covered

Here are some of the most important topics on each site, as of November 14. New reports may still be added. If we have missed other sites that should be included, please let us know.

Also note that the same research is often presented at more than one conference. So the same Web site can have different writeups on the same research.

We wrote the title lines below to give a less technical view of the contents of each summary. You can usually spot the corresponding writeup by following the link provided to reach a table of contents for that conference Web report. Many of the summaries are short, a page or less; a few are considerably longer.

IDSA (39th Annual Meeting of the Infectious Diseases Society of America), October 25-28, San Francisco

The Body

<http://www.thebody.com/confs/idsa2001/idsa2001.html>
(click "Conference Summaries")

- * Can short-term changes in viral load predict long-term response?
- * Transmission of drug-resistant HIV;
- * Lopinavir/ritonavir in heavily pretreated patients;
- * Starting therapy at a T-cell count of 350;
- * Simplifying protease-inhibitor treatment by switching to abacavir;
- * Nevirapine and liver toxicity in HIV patients with hepatitis C;
- * Nevirapine vs. protease inhibitors -- long-term cohort study;
- * Using amprenavir after nelfinavir use;
- * Amprenavir+abacavir+3TC, 48-week data;
- * Abacavir+efavirenz+AZT+3TC, preliminary 48-week results;
- * Four-drug study, efavirenz+abacavir+AZT+3TC;
- * Hepatitis G co-infection and HIV treatment;
- * EPO (erythropoietin, Epoetin Alfa) in anemic HIV patients;
- * Prior antiretroviral therapy and genotype testing;
- * How well can patients predict their T-cell and viral load test results?

*** Cutting-Edge Issues in HIV Medicine (symposium)**

- Challenges of Antiretroviral Therapy in the Developing World;
- Future Horizons in Antiretroviral Drugs;
- Structured Treatment Interruption: Panacea or Pandora?
- HIV and HCV Co-Infection -- Current Status and Future Directions.

HIVandHepatitis.com

<http://www.hivandhepatitis.com/2001conf/39idsa/main.html>

"Report on Salvage Therapy from the 39th Annual Meeting of the IDSA," by Daniel R. Kuritzkes, M.D. This essay looks at real-world experience in very heavily pretreated patients with: lopinavir/ritonavir (Kaletra); indinavir+ritonavir; delavirdine strategy to boost protease inhibitor levels; and amprenavir use after nelfinavir.

Medscape

<http://hiv.medscape.com/Home/Topics/AIDS/directories/dir-AIDS.ConfSummaries.html>

(then select **39th Annual Meeting of the Infectious Diseases Society of America**)

These are the HIV-related titles now on the site:

- * Antiretroviral Agents and Response to Therapy
- * Optimizing Long-term HIV Treatment Strategies Through a Greater Understanding of Disease Pathogenesis
- * Metabolic Complications and Adverse Drug Reactions in HIV
- * Update: Incidence, Diagnosis, and Clinical Manifestations of HIV-Related Opportunistic Infections
- * PI vs. Boosted PI vs. Efavirenz: And the Winner (Again) Is?
- * Switching from a Protease Inhibitor: The Answers Are Known, It's Time to Move On
- * Four-Drug HAART Regimen in Patients with Advanced HIV Disease
- * HIV Evolution Limited by Successful HAART
- * A New and Simple Way to Diagnose Pneumocystis carinii Pneumonia
- * Evidence for Increased Risk of Heart Disease in Treated HIV Infection
- * Myocardial Infarction: A Consequence of HIV Disease, Treatment, or Both?
- * Has HAART Really Improved Mortality in Patients with Advanced HIV Disease?
- * Rates of Most HIV-Related Diseases No Longer Falling

Note: Bioterrorism, and other infectious diseases, have separate sections in this Web report from the IDSA conference.

8th European Conference on Clinical Aspects and Treatment of HIV-Infection

The Body

<http://thebody.com/confs/eccat2001/eccat2001.html> (click "Conference Summaries")

* TMC-125, experimental NNRTI, produced 2-log HIV reduction in volunteers; [Note: "NNRTI" is an abbreviation for "non-nucleoside reverse transcriptase inhibitor," a class of anti-HIV drug. Two drugs in this class are currently approved, nevirapine and efavirenz.]

- * Indinavir/ritonavir vs. saquinavir/ritonavir;
- * NNRTI use and lipodystrophy study;
- * Nevirapine and HDL cholesterol ("good cholesterol");
- * Tipranavir, a new kind of protease inhibitor;
- * Tenofovir intensification study;
- * Cardiovascular risk factors, association with antiretroviral therapy;
- * First-line treatment choice and lipid metabolism;
- * Switching from protease inhibitors to NNRTIs;
- * Tenofovir, antiretroviral activity regardless of baseline demographics, CD4, viral load;
- * Long-term followup of switching from protease inhibitors to NNRTIs with undetectable viral load;
- * Lack of drug interaction between tenofovir and several other anti-HIV drugs;
- * Once-daily treatment with experimental drug emtricitabine (FTC, brand name Coviracil), ddI, and efavirenz, 2-year followup;
- * Atazanavir (experimental protease inhibitor) 48-week data on lack of lipid elevation;
- * Nevirapine, ddI, and d4T long-term followup;
- * Minor interaction between efavirenz and saquinavir/ritonavir.

HIV and Hepatitis.com

<http://www.hivandhepatitis.com/2001conf/8thclinical/main.html>

- * Atazanavir at 48 weeks;
- * Saquinavir/ritonavir new dosage regimen;
- * Lopinavir (Kaletra) 3-year data in treatment naive patients;
- * Switching from protease inhibitor(s) to NNRTI;

- * Once daily d4t;
- * T-20 (experimental fusion inhibitor, a new class of antiretroviral);
- * Saquinavir and efavirenz interaction corrected with ritonavir;
- * Efavirenz, ddI, and FTC (Coviracil) combination, 96-week study;
- * Nevirapine and lipid profile improvement;
- * Once daily vs. twice daily nevirapine;
- * No important drug interaction between tenofovir and indinavir, lopinavir, 3TC, or efavirenz;
- * TMC 125, experimental NNRTI;
- * Efavirenz vs. nevirapine in treatment-naive patients;
- * Switching from a protease inhibitor to efavirenz.

NATAP

<http://www.natap.org/> -- select 'Conference Reports' (on left), then '2001' (if necessary), then select the conference by name

- * Atazanavir vs. nelfinavir;
- * T-20 late phase II results;
- * Extended-release d4T;
- * Tibotec/Virco presentations, including TMC 125 (an NNRTI), and a method for predicting response to protease inhibitors;
- * T-20 data in adults and children, and T-1249 data in adults. (T-1249 is a "second generation" T-20.)
- * Indinavir/ritonavir vs. saquinavir/ritonavir, both twice daily;
- * Hepatitis C and B.

3rd International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV

The Body

<http://www.thebody.com/confs/adrl2001/adrl2001.html> (click "Conference Summaries")

- * Mitochondrial function may not be causing lactate elevation;
- * Increased lipolysis (fat destruction) in HIV, with or without fat redistribution;
- * Inhibiting lipolysis improves insulin sensitivity;
- * Lactate risk factors in antiretroviral therapy;
- * More tumor necrosis factor released from skin fat in HIV patients with lipodystrophy;
- * Lab studies comparing indinavir, nelfinavir, and amprenavir effects on fat cells -- and protection by

rosiglitazone;

* Lipodystrophy and metabolic disorders 48 weeks after switching from protease inhibitors to Trizivir, vs. not switching;

* Prospective study of lipid elevation with two antiretroviral regimens.

HIV and Hepatitis.com

<http://www.hivandhepatitis.com/2001conf/3rdlipo/main.html>

In an excellent summary of the lipodystrophy workshop, ten well-written papers by leading experts describe what happened in various areas:

By Andrew Carr, M.D.: Mitochondrial Toxicity and Lactic Acidemia; Liver Disease; Hypersensitivity; and Thyroid Disease.

By Graeme Moyle M.D., M.B.B.S.: Insulin Resistance; Adipocytes (fat cells); Clinical Data; Switch Studies; Cardiovascular Disease; and Clinical Risk.

NATAP

<http://www.natap.org/>, select 'Conference Reports' (on left), then '2001'

- * Overview;
- * Lipodystrophy;
- * Amprenavir;
- * List of conference highlights;
- * Abacavir;
- * Mitochondrial toxicity and lipodystrophy;
- * Nevirapine;
- * Thyroid abnormalities;
- * Lactic acidosis and mitochondrial toxicity;
- * Potential therapy for lipodystrophy;
- * Heart disease risk;
- * Abnormalities of glucose metabolism.

Liver Disease Conferences Coverage

The following conferences are most relevant for coverage of hepatitis or other liver-related illness.

**66th Annual Scientific Meeting of the
American College of Gastroenterology,
October 19-24, Las Vegas**

The Body

<http://thebody.com/confs/gastroenterology/gastroenterology.html>
(click "Conference Summaries")

- * Hepatitis C;
- * Liver disease in AIDS;
- * New treatments for hepatitis C;

- * PEG-interferons: When to use them;
- * PEG-interferons: How to use them;
- * Lamivudine (3TC) for hepatitis C: When to start, when to stop.

AASLD (American Association for the Study of Liver Diseases), November 9-13, Dallas

The Body

<http://www.thebody.com/confs/aasld2001/aasld2001.html>

Check the site; coverage incomplete as we went to press.

HIV and Hepatitis.com

<http://www.hivandhepatitis.com/2001conf/52aasld/main.html>

Check the site; coverage incomplete as we went to press.

NATAP, <http://www.natap.org/>, select 'Conference Reports' (on left), then '2001'

Check the site; coverage incomplete as we went to press.

Anthrax, Bioterrorism Fears Stimulate Immune, Other Research

Comment by John S. James

A November 7 press report ("All-Purpose Drugs Are Being Tested," by Jeff Donn, The Associated Press) surveyed some of the work being done on finding drugs to treat many diseases -- the opposite of the traditional "magic bullet" approach of targeting only one particular bacterium or virus. Many of these "all purpose" potential drugs work by strengthening the immune system -- especially innate immunity, which is less well understood than the more familiar "adaptive" immunity involving T-cells (with which the body quickly produces a customized response to a particular invader, hopefully in time to cure the illness). Invertebrate animals survive and fight infection with only innate immunity.

Some of the approaches now being studied have long been used in traditional or "alternative" medical treatments. Others are far from ready for

human test.

The AP story mentions:

* Certain cytokines and peptidoglycans that may stimulate natural immunity. These approaches are being examined as possible defenses against bioterrorism, including anthrax or smallpox. If they work, they might have great impact on more routine medical practice as well.

* "Androstene steroids" to block the action of cortisone (according to the reporter's writeup, which we have not yet checked further).

* Ways to correct the immune-system damage caused by exposure to nuclear radiation. Success here might lead to ways of strengthening the immune system in HIV, malaria, and other diseases.

* A drug that acts like the popular supplement NAC (N-acetylcysteine) may help treat certain bacterial toxins, by reducing free-radical damage.

* Old remedies based on silver are now getting scientific study, after one consistently worked as well as tetracycline in laboratory tests against certain bacteria.

The new focus on bioterrorism will greatly stimulate research on immune-based treatments, neglected traditional medical approaches, and on completely new approaches as well. It will bring in new people and resources, and move with urgency and serious support -- no longer at the leisurely pace of academic medical journals, or under the commercial short-term focus on already-proven profit areas. Here is the urgency we have long sought but seldom found. The AIDS community should pay close attention.

Africa: Funding Sought for Epidemic Control

by John S. James

In the U.S. Congress, 8 Senators and more than 70 Representatives have signed a Dear Colleague letter seeking 1.2 billion dollars in emergency supplemental funding for the global AIDS crisis. The letter will soon be sent to President Bush.

Despite the great costs resulting from the September 11 attacks, the money is available, as the U.S. is now about halfway through a \$100 billion economic stimulus package. This \$100 billion needs to be spent anyway, on something, in order to stimulate the U.S. economy. Less than 2% of this money would cover the U.S. share of a good start on global control of HIV/AIDS, tuberculosis, and malaria -- and encourage serious contributions from others.

For more information, including ways you can help, see the Global AIDS Alliance, <http://www.globalaidsalliance.org>

World AIDS Day Web Page

"To help journalists and others interested in HIV/AIDS issues, the Kaiser Family Foundation has created a World AIDS Day web page, <http://www.kff.org/worldaidsday/> "

World AIDS Day is December 1. There is little central organizing; instead, local agencies and communities do their own events. As a result, there is no overall calendar. Persons interested in events in their area should check with local AIDS organizations.

The Kaiser Family Foundation page includes links to about 10 other Web pages on World AIDS Day.

Printing Error in Previous Issue, # 372

Our last issue had the inside pages out of order, due to a printing error. Each individual page is printed and numbered correctly, so the newsletter can be read as intended by following the page numbers, instead of the layout. Note that the column beginning "* Mother-to-infant transmission" goes with the Tenofovir article, not the New HIV Drugs article beginning on page 6.