TAGLine News about AIDS from Treatment Action Group ISSUE #1: FEBRUARY 18, 1992

THE ddC SAGA

This is a story about what happens when a pharmaceutical company refuses to provide adequate expanded access to a promising anti-HIV drug during clinical trials.

Hoffmann-La Roche's New Drug Application for ddC has been submitted to the FDA. The company seeks approval of ddC for use in AZT-intolerant people, in those failing AZT, and as a constituent in combination therapy with AZT. The available data come from three trials: ACTG114, ACTG106, and ACTG119. They show that ddC alone is inferior to AZT alone, and do not conclusively prove that AZT/ddC combination therapy is superior to AZT alone. Results are not yet available from a fourth trial, ACTG155, which may provide a more conclusive answer about AZT and ddC in combination. Activists and others have been calling for an interim analysis of ACTG155 as the best hope for a timely, informed decision by the FDA on Roche's application. The FDA's ddC Advisory Committee is not set to meet until April 20th.

Meanwhile, impatience for a decision has been exacerbated by events on the "AIDS underground," where a controversial bootleg version of ddC has been widely available for many months. Hoffmann-La Roche recently received samples of the bootleg product from an anonymous source and found them to contain as much as 300% of the dose of ddC specified on the bottle. Informed of this, the FDA visited underground buyers' clubs in Ft. Lauderdale, New York, and San Francisco and collected a second batch of samples directly from them. The FDA's analysis showed that the samples from New York contained 64 to 188% of the correct dose, while the samples from San Francisco contained 0 to 200%. Because ddC can be extremely toxic, these inconsistencies have sent waves of anxiety throughout the AIDS community. Luckily, most people who buy the drug on the underground take a low dose, which should compensate for the excess amounts of ddC found in the samples; but Derek Hodel, who runs the PWA Health Group, New York's buyers' club, has pulled bootleg ddC from his shelves, and San Francisco has done likewise.

Ft. Lauderdale gets its bootleg ddC from a different source than New York and San Francisco. The FDA found that the ddC from Ft. Lauderdale met their dosing standards, and therefore they did not ask Ft. Lauderdale to stop selling it. Ft. Lauderdale charges $25 for a bottle of 60 .5mg tablets. Call 1-800-447-9242.

Individuals with AIDS and ARC who have failed or become intolerant to AZT can call 1-800-ddC-21HI(V) to get ddC (as monotherapy) from Hoffmann-La Roche.

At a recent meeting attended by Martin Delaney (Project Inform), Derek Hodel (PWA Health Group), David Barr (GMHC), John S. James (AIDS Treatment News), Mark Harrington (ACT UP, TAG), and others, consensus was reached on four demands of the FDA: 1] A Treatment IND must be approved for combination AZT/ddC therapy in people with less than 200 CD4 cells, 2] A plan must be devised to meet the needs of people with more than 200 CD4 cells who want to take AZT/ddC in combination, 3] The ddC Advisory Committee must meet immediately, and 4] There must be an immediate, interim analysis of ACTG155.

Needless to say, FDA approval of "real," pharmaceutical grade ddC would quickly end demand for the bootleg version, provided Hoffmann-La Roche did not set an excessive price.

RIFABUTIN

In September, interim analysis of a study of Adria's rifabutin for prophylaxis of MAI showed that half as many participants taking rifabutin developed MAI as those taking placebo. All participants were immediately given rifabutin, as were those in a second trial, and both trials were stopped. Three members of the Data and Safety Monitoring Board resigned in protest, saying the trials should continue in order to produce as much information as possible. A Principal Investigators' meeting will convene late this month, at which time community activists will be apprised of all the available data. Complete analysis of both trials should be finished by March. Adria does not plan to hold a press conference about rifabutin until April.

The main toxicity of rifabutin was discolored urine. Rash and lowered white cell counts were also observed; liver toxicity, which had been feared, was not. Rifabutin may interact with AZT, reducing blood levels of the latter.

Some European data on rifabutin for tuberculosis are emerging: Fifty percent of HIV-negative people failing rifampin with positive cultures for Tb become negative when treated with rifabutin, but half of those subsequently revert to positive. In the test tube, 25 to 40% of rifampin-resistant strains of Tb respond to rifabutin. More should be known about resistance soon.

Adria only has enough rifabutin for approximately 5000 people. They hope to solve this supply problem by summer. In spite of having established a toll-free number for the purpose, the company does not expect to begin expanded access to rifabutin until March. The number, however, is already active: 1-800-552-7228. People with less than 200 CD4 cells and AIDS will be eligible.

NIH BUDGET CUTS

Thanks to budget cuts passed by Congress last year, the National Institutes of Health Division of AIDS will send only four people to the VIIth International Conference on AIDS in Amsterdam this July. The cuts were probably precipitated by Congressman William Dannemeyer, who last year succeeded in eliminating half the overall number of people attending the Florence Conference from the U.S. Public Health Service, even though their Conference registration fees and hotel deposits ($70,000 from the NIH alone) were already paid. The House subsequently cut $8 million from the PHS budget, and the Senate $5 million. The House-Senate Conference Committee then took the unprecedented step of combining both figures (instead of reconciling them) to cut $13 million, necessitating a 30% reduction in NIH travel expenditures. The cuts have also hampered the ability of NIH personnel to attend conferences and

meetings in the U.S., a more ordinary activity than attending the International Conference, but equally essential to their work.

The AIDS Clinical Trials Group recompetition process is almost complete. Attempting to divide a smaller pie, the ACTG has reduced the number of adult trial sites from 38 to 27. Some sites advocated by activists have been added, including hospitals in Brooklyn, Galveston, Philadelphia, and New Haven; but others, such as New York's St. Luke's, have been cut, and New York's Cornell and NYU sites may, in effect, be scaled back by half.

Congress is partly responsible for these reductions, having mandated a disproportionate figure ($20 million) for pediatric sites.

"Minority infrastructure" grants were awarded some months ago to sites in Puerto Rico, Hawaii, and at Howard University to help insititutions serving minority populations to prepare for the ACTG recompetition. One of these sites, Puerto Rico, has been funded. It will be a pediatric unit.

HYPERICIN

Synthetic, intravenous hypericin is the property of VIMRx Pharmaceuticals. It was developed by that company as a substitute for natural hypericin, which eradicates HIV in the test tube and in mice. People with HIV have long attempted to use natural hypericin by taking St. John's Wort tablets, but the tablets contain an insufficient amount of hypericin to achieve antiviral concentrations in blood.

In a recent press release, VIMRx revealed preliminary information about the AIDS Clinical Trials Group (ACTG) study of its synthetic hypericin, VIMRxyn. The Phase I, dose-ranging trial at NYU Medical Center and two other sites (Boston and Minneapolis) has temporarily stopped enrolling new participants. VIMRxyn did not show any systemic toxicity, but some people dropped out of the trial when their skin became painfully sensitive to light, necessitating an adjustment in the dosing schedule of the drug. Those who remain will continue to receive VIMRxyn, and enrollment will resume when the new dosing schedule has been approved.

VIMRx is working on an oral formulation of VIMRxyn at the University of Iowa in collaboration with the National Institutes of Health.

SELECTOR BOX

Applied Immune Sciences has recently completed a Phase I trial of its "selector box" in a small number of people with AIDS. The selector consists of multiple chambers which can be lined with monoclonal antibodies to various immune system cells, in this case cytotoxic T cells (CD8 cells). The selector was used to harvest CD8 cells from each PWA. The cells were then treated with IL-2, to make them proliferate, and returned to the body. Each person was subsequently given a continuous, low-dose infusion of IL-2 for three days, to render the new CD8 cells more active.

The treatment was given at sites in Pittsburgh and Miami in five to seven escalating, monthly doses. Allegedly: No toxicity was observed. Two people with chronic wasting gained weight and developed no OI's during the course of treatment. Hairy leukoplakia resolved in three. Two with KS who had failed chemotherapy experienced improvement in their lesions.

The researchers believe that activated CD8 cells secrete a factor that inhibits HIV and other antigens. Other companies are now attempting to isolate that factor. Applied Immune Sciences is preparing its Phase I data for submission to the FDA. They particularly want to develop the treatment for KS, and envision a Phase II trial at the University of California at San Francisco and in Miami.

TAG

We are proud to announce the birth of a new AIDS activist organization, Treatment Action Group (TAG). Our Mission Statement is as follows:

> The Treatment Action Group fights to find a cure for AIDS and to ensure that all people living with HIV receive the necessary treatment, care, and information they need to save their lives. TAG focuses on the AIDS research effort, both private and public, the drug development process, and our nation's health care delivery systems. We meet with researchers, pharmaceutical companies, and government officials and resort, when necessary, to acts of civil disobedience. We strive to develop the scientific and political expertise needed to transform policy. TAG is committed to working for and with all communities affected by HIV.

TAG grows directly out of ACT UP/NY's Treatment + Data Committee and draws upon the long experience of its members in that group. Despite rumors to the contrary, no one in TAG has renounced ACT UP or T+D membership, but on January 22nd Charles Franchino resigned his long-held post as T+D facilitator, and *T+D Digest* writers Rich Lynn and Chris DeBlasio ceded their responsibility for T+D's weekly newsletter to the floor of T+D. TAG members continue to attended T+D meetings to pursue their work as members-at-large.

TAG's current long-term projects include an assessment of the state and direction of research on AIDS pathogenesis—how HIV actually causes disease—and a report on extramural grant system of the National Institutes of Health and other organizations.

An affinity group, Treatment Action Guerrillas, also part of TAG, has carried out a number of actions to date, including civil disobedience at the home of Senator Jesse Helms, at Daiichi Pharmaceuticals (makers of the preclinical anti-KS drug, SP-PG), and at the U.S. headquarters of Astra (makers of the anti-CMV drug, foscarnet). Collaborators in these actions have included Greenpeace, Women's Health Action Mobilization (WHAM!), and ACT UP/Boston.

TAG plans to hold either a community forum or an open meeting every six weeks. *TAGLine* will be available at TAG's community forums and at ACT UP general meetings.

TAG's first Community Forum: Wednesday, March 18th, 8PM, at the Gay and Lesbian Community Services Center, 208 W. 13th St.

Questions about this issue of TAGLine can be addressed to Chris DeBlasio, 212-675-7828.