Open Clinical Trials

Below is a list of selected currently enrolling clinical trials gathered from various sources. **TrialSearch,** operated by the **AIDS Community Research Initiative of America** (ACRIA), is an extensive online database of clinical trials related to HIV/AIDS.

The federal government's **AIDSinfo** Web site includes a clinical trials section that features an introduction to HIV/AIDS research and study listings from the National Institutes of Health's **ClinicalTrials.gov** database. AIDSinfo also offers personalized advice about clinical trial participation via email (ContactUs@AIDSinfo.nih.gov), an interactive Web site (*www.aidsinfo.nih.gov/live_help;* specialists available Mon.-Fri. 9:00 am-1:00 pm PT), and a toll-free telephone service (800-874-2572, international 301-874-2572; specialists available Mon.-Fri. 9:00 am-2:00 pm PT). **CenterWatch** is a commercial Web site that includes trial listings for many diseases, including HIV/AIDS and related conditions.

Most U.S. government-sponsored HIV/AIDS trials are conducted by the adult and pediatric **AIDS Clinical Trials Group** (ACTG). The **National Center for Complementary and Alternative Medicine** (NCCAM) conducts trials of complementary therapies for conditions related to HIV and its management. The **HIV Vaccine Trials Network** (HVTN) is an international collaboration testing preventive vaccines.

Call the telephone numbers listed for each study or see the indicated Web sites for further information about specific trials. Protocol numbers, if available, are provided in parentheses at the end of each trial description.

ACRIA TrialSearch:
www.acria.org/clinical_trials/index.html
ACTG: *www.aactg.org*
AIDSInfo: *www.aidsinfo.nih.gov*
CenterWatch: *www.centerwatch.com*
ClinicalTrials.gov: *www.clinicaltrials.gov*
HVTN: *www.hvtn.org*
NCCAM: *www.nccam.nih.gov/clinicaltrials*

Etravirine plus Darunavir/Ritonavir in Patients with Enfuvirtide Side Effects

This Tibotec-sponsored study will examine the safety, tolerability, and effectiveness of switching to the PI darunavir/ritonavir (Prezista) plus TMC125—the combination studied in the DUET trials—in individuals who have achieved full viral suppression on a regimen containing PI(s), NNRTI(s), and enfuvirtide (Fuzeon; T-20), but who can no longer tolerate enfuvirtide. Backbone NRTIs will remain unchanged. In this open-label Phase IIIb study, investigators will regularly assess HIV viral load, as well as adverse events, blood lipid changes, drug resistance, adherence, and quality of life, during a 48-week treatment period.

Eligible participants must be at least 18 years of age and must be on a stable (at least four months) PI-containing regimen that includes enfuvirtide with a viral load below 400 copies/mL for at least six months. They must have a history of drug resistance or treatment failure while receiving the three major antiretroviral classes (PIs, NNRTIs, and NRTIs). They should intend to stop using enfuvirtide due to injection site reactions that persist despite optimal injection technique. Exclusion criteria include current use of darunavir, genotypic resistance tests showing three or more darunavir resistance-associated mutations, use of any drug contraindicated with darunavir (see package insert at *www.prezista.com*), and abnormal liver enzyme levels or reduced creatinine clearance (an indicator of impaired kidney function).

The study aims to enroll 40 participants at five sites. It is currently enrolling in **Los Angeles** (323-954-1072). *www.clinicaltrials.gov/ct2/show/NCT00460746* (CR011866).

CCR5 Antagonist Vicriviroc

Schering-Plough has initiated two Phase III trials to evaluate the safety and efficacy of the experimental CCR5 co-receptor blocker vicriviroc in treatment-experienced individuals. In these twin double-blind studies, participants with CCR5-tropic HIV will be randomly assigned to receive either 30 mg once-daily vicriviroc or placebo in combination with an optimized background antiretroviral regimen for 48 weeks. Background therapy will be selected by study investigators on the basis of resistance tests, treatment history, and drug toxicity, and will include a ritonavir-boosted PI. If vicriviroc proves safe and effective, participants who successfully complete 48 weeks of treatment will be offered the drug free of charge until it becomes commercially available.

Eligible participants must be at least 16 years of age and must have exclusively CCR5-tropic virus. (For an explanation of HIV coreceptor tropism, see "Drug Watch" in the Winter 2007 issue of *BETA*). They must have a viral

load of at least 1,000 copies/mL and must either be on a stable regimen of at least three antiretroviral drugs or off therapy for at least four weeks. In addition, they must have documented resistance to at least two of the initial antiretroviral drug classes (PIs, NNRTIs, and NRTIs), or at least six months experience with NRTIs, NNRTIs, and/or two PIs. Exclusion criteria include CXCR4-tropic or dual/mixed-tropic HIV, a history of cancer (except for cutaneous Kaposi's sarcoma), and seizure disorders. Women may not be pregnant or breastfeeding and must use effective contraception.

Both studies have a target enrollment of 375 participants. VICTOR-E3 is recruiting at sites in **Puerto Rico** and **Central America.** VICTOR-E4 is recruiting at about 25 North American sites, including **Boston, the Bronx, Columbus, Dallas, Ft. Lauderdale, Houston, Indianapolis, Little Rock, Los Angeles, Miami, Newark, New York City, Orlando, Rochester,** and **Tampa.** For more information about either study, contact the Schering-Plough Clinical Trial Registry Call Center at 888-772-8734.
www.clinicaltrials.gov/ct2/show/NCT00523211 (VICTOR-E3; P04405; 3553293);
www.clinicaltrials.gov/ct2/show/NCT00474370 (VICTOR-E4; P04889; 3547030).

In a related randomized Phase III trial, investigators will assess the safety and efficacy of vicriviroc versus placebo with optimized background therapy in patients with dual/mixed CCR5/CXCR4-tropic HIV. The study design is the same as that of the previous two studies, and—with the exception of co-receptor tropism—eligibility requirements are also similar.

VICTOR-E2 aims to enroll 210 participants, and is currently recruiting in **Vero Beach, FL,** and **Ponce, Puerto Rico.** For more information, contact the Schering-Plough Clinical Trial Registry Call Center.
www.clinicaltrials.gov/ct2/show/NCT00551330 (VICTOR-E2; P05057; 3555431).

Finally, Schering-Plough is planning to conduct a randomized, open-label Phase II/III trial of vicriviroc versus tenofovir/emtricitabine (Truvada) plus ritonavir-boosted atazanavir (Reyataz) in treatment-naive individuals with CCR5-tropic virus. This trial is not yet recruiting; check the Web site for updates.
www.clinicaltrials.gov/ct2/show/NCT00551018 (P04875).

AMICI: Enfuvirtide plus Experimental Integrase Inhibitors

Roche and Trimeris have initiated a study of enfuvirtide in combination with experimental integrase inhibitors. Drugs in this class prevent HIV from integrating its genetic material into the host cell's DNA, thereby halting viral replication.

The current open-label, randomized Phase IV study will evaluate the safety and efficacy of enfuvirtide plus an integrase inhibitor available through an expanded access program plus optimized background therapy in patients who are treatment-experienced but have never used enfuvirtide or an integrase inhibitor. Patients will initially receive 90-mg twice-daily enfuvirtide injections until response is confirmed, then will be randomly assigned to continue 90 mg twice-daily or switch to 180 mg once-daily enfuvirtide; non-responders will be discontinued.

The first integrase inhibitor, raltegravir (Isentress), was available through expanded access but recently was granted marketing approval (see "News Briefs," page 5). Gilead's experimental integrase inhibitor, elvitegravir (GS-9137), is now the furthest along in the development pipeline.

Eligible study participants must be at least 18 years of age with a viral load greater than 1,000 copies/mL and triple-class (PI, NNRTI, NRTI) treatment experience. Exclusion criteria include severe clinical or laboratory adverse events, untreated infections, and cancer requiring chemotherapy or radiation.

The AMICI study aims to enroll about 250 participants at more than 50 sites, including **Annandale, Atlanta, Berkeley, Boise, Boston, Chicago, Dallas, Ft. Lauderdale, Houston, Kansas City, Long Beach, Los Angeles, Miami, Newark, New York City, Orlando, Philadelphia, Phoenix, Ponce (PR), Stanford, Tampa,** and **Washington, DC.** For further information, call 800-526-6367 or 973-235-5000.
www.clinicaltrials.gov/ct2/show/NCT00488059 (ML20837).

Treatment of Recent HIV Infection

Research to date has produced conflicting evidence about the benefits and drawbacks of treatment during primary (acute) or recent HIV infection. In the SETPOINT study, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) and the ACTG, researchers will assess whether a nine-month course of antiretroviral therapy during early infection can alter the eventual viral "set point."

In this open-label study, newly infected participants will be randomly assigned to either start immediate treatment with twice-daily lopinavir/ritonavir (Kaletra) plus once-daily tenofovir/emtricitabine or undergo observation without treatment for 36 weeks. At that point, all subjects will be offered treatment continuation or initiation based on virological, immunological, and clinical criteria. Viral load in the two groups will be compared periodically through 96 weeks; investigators will also collect data on CD4 cell count, AIDS-related events, symptoms of acute retroviral syndrome, and serious or treatment-limiting adverse events.

Eligible study participants will be at least 18 years of age and recently infected with HIV. They must have a viral load greater than 500 copies/mL, a CD4 count of at least 350 cells/mm^3, and a CD4 cell percentage of at least 14% within 21 days prior to study entry. Exclusion criteria include previous use of antiretroviral drugs (not including postexposure prophylaxis more than one year ago), receipt of an experimental HIV vaccine, known allergy or resistance to study drugs, advanced HIV disease, history of pancreatitis, serious medical or psychiatric illness, and recent use of certain medications, including corticosteroids, chemotherapy, and immunomodulators. Women may not be pregnant or breastfeeding and must agree to use effective contraception.

The study aims to enroll 150 participants at nearly 40 sites, including **Atlanta** (404-616-6313), **Boston** (617-724-0070), **Chapel Hill** (919-843-8761), **Chicago** (312-695-5012), **Columbus** (614-293-8112), **Denver** (303-372-5535), **Detroit** (313-916-2570), **Greensboro** (336-832-7888), **Indianapolis** (317-274-8456), **Miami** (305-243-3838), **New York City** (212-327-7281), **Philadelphia** (215-349-8092), **Providence** (401-793-4971), **Rochester** (585-275-2740), **San Diego** (619-543-8080), **San Francisco** (415-476-9296 ext. 318), **Seattle** (206-731-8877), and **St. Louis** (314-454-0058). *www.clinicaltrials.gov/ct2/show/NCT00090779* (ACTG A5217; AIEDRP AIN503).

A related study, also sponsored by NIAID, will assess whether a one-year course of antiretroviral therapy administered during acute infection or early seroconversion can slow HIV disease progression. In this open-label trial, participants will be randomly assigned to receive combination antiretroviral treatment or undergo observation without treatment. Viral loads and CD4 cell counts will be compared 24 and 36 months after initial presentation.

Eligible participants must be at least 18 years of age and have documented acute or recent HIV infection (within the past 12 months). They must have a CD4 cell count of at least 350 cells/mm^3. Exclusion criteria include prior use of antiretroviral drugs (except postexposure prophylaxis), serious illness, and recent use of investigational agents, cancer chemotherapy, corticosteroids, immunomodulators, and experimental HIV vaccines. Women may not be pregnant or breastfeeding and must agree to use effective contraception.

This study has a target enrollment of 180 participants at Johns Hopkins University in **Baltimore** (410-614-7796), CHUM-Hotel-Dieu in **Quebec, Canada** (514-890-9000), **Sunnybrook Health Sciences Center in Toronto, Canada** (416-465-7936), and **University of British Columbia in Vancouver, Canada** (604-642-6429). *www.clinicaltrials.gov/ct2/show/NCT00106171* (1R01AI056990-01A1).

HIV and Cardiovascular Risk

Much remains to be learned about how HIV infection and antiretroviral therapy influence cardiovascular disease risk. Patients taking antiretroviral therapy often experience metabolic abnormalities, including elevated blood lipid levels, insulin resistance, and body composition changes; initial studies suggest increased carotid intima-media thickness and endothelial (blood vessel) dysfunction. However, traditional risk factors such as lipid elevation do not fully predict cardiovascular disease risk in this population, and other factors, including increased inflammation and cytokine changes, may play a critical role.

To explore these issues, the National Institute of Diabetes and Digestive and Kidney Diseases is sponsoring a natural history study to investigate the relationship between adipocytokines (cytokines produced by fat tissue) and subclinical atherosclerosis in HIV positive patients on antiretroviral therapy compared with HIV negative individuals.

Eligible participants will be 18–65 years of age, and may be either HIV positive or negative. HIV positive participants must have a CD4 cell count greater than 350 cells/mm^3 and have been on a stable antiretroviral regimen (e.g., PI or NNRTI plus two NRTIs, or triple NRTIs) for longer than six months. Exclusion criteria include certain abnormal laboratory values (including low hemoglobin and elevated liver enzymes), recent use of anabolic agents or other medications that affect glucose or body composition, recent weight loss of more than ten pounds, active substance abuse, cancer, acute infections, and pregnancy or breast-feeding.

This study has a target enrollment of 150 participants at Massachusetts General Hospital in **Boston** (617-724-8015). *www.clinicaltrials.gov/ct2/show/NCT00465426* (DK49302-10AR).

Crofelemer for HIV-Related Diarrhea

The ADVENT trial, sponsored by Napo Pharmaceuticals, will assess the safety and efficacy of crofelemer, an experimental therapy for HIV-associated diarrhea. Crofelemer is derived from a common South American plant that has long used by local people for medicinal purposes. Based on earlier trials, crofelemer has been granted "fast track" status by the U.S. Food and Drug Administration (FDA).

In this double-blind Phase III study, the first 200 participants will be randomly assigned to receive one of three doses (125, 250, or 500 mg) of oral crofelemer twice daily or placebo; this stage will determine the optimal dose of the study drug. Then, 150 participants will be randomly assigned to receive either the selected dose of crofelemer or placebo, focusing on effectiveness. Patients will initially receive randomized therapy for 31 days; if results are

promising, all will receive crofelemer for up to five months in an extension phase. Participants will be required to use a daily phone diary to report diarrhea symptoms such as number and consistency of bowel movements, severity of abdominal pain, and need for antidiarrhea medication.

Eligible participants will be 18 years of age, on stable (at least four weeks) therapy for HIV disease, have persistent diarrhea lasting at least one month, and be willing to stop all antidiarrhea medications and certain other drugs for the first six weeks of the trial. Exclusion criteria include a CD4 count below 100 cells/mm^3, fever, certain current or past gastrointestinal medical conditions or surgery, certain laboratory abnormalities, and use of certain medications, including opiates. Women may not be pregnant or breastfeeding and must agree to use effective contraception.

ADVENT aims to enroll 350 participants at nearly 50 sites, including **Atlanta, Baltimore, Boston, Chicago, Columbia, Dallas, Detroit, Ft. Lauderdale, Houston, Iowa City, Kansas City, Los Angeles, Miami, New York City, Oakland, Orlando, Phoenix, Portland (OR), San Antonio, San Francisco, Seattle, Spokane, St. Louis, Tampa,** and **West Hollywood.** For further information, contact 513-345-1837 or 760-476-3592.
www.clinicaltrials.gov/ct2/show/NCT00547898 (NP303-101).

Mindfulness-Based Stress Reduction

The Staying Well study is a controlled trial of mindfulness-based stress reduction (MBSR) for people with HIV who are not taking antiretroviral treatment. The study aims to determine whether stress reduction through meditation is associated with reduced HIV disease progression, less depression, and improved quality of life; it will also assess the mechanisms by which stress and mood may influence immune function.

In this Phase II study, subjects will be randomly assigned to participate in either MBSR or general education on health and well-being for HIV positive individuals. Both groups will attend eight weekly sessions (each lasting 1.5–3 hours) at UCSF's Osher Center for Integrative Medicine. Participants will have blood drawn and will complete psychological questionnaires at study entry and at months 3, 6, and 12; they will receive compensation for each completed assessment. Those initially assigned to the education group may participate in the MBSR program for free after 12 months.

Eligible participants must be at least 18 years of age and able to speak English. They must not have taken antiretroviral therapy for the past 120 days, and must have an HIV viral load greater than 100 copies/mL and a CD4 cell count above 250 cells/mm^3 at study entry. They should not plan to start treatment during the 12 months following enrollment, but may do so if medically necessary and remain in the study. Exclusion criteria include previous MBSR training or current practice, use of chemotherapy or immunomodulator drugs, and recent initiation of psychiatric medications. The study has a target enrollment of 330 participants in **San Francisco** (415-353-9745).
www.clinicaltrials.gov/show/NCT00271856 (AT002024).

A related study, sponsored by the National Center for Complementary and Alternative Medicine, will explore the effect of an eight-week MBSR program on the experience of drug-related side effects in patients taking antiretroviral therapy. In this randomized trial, individuals receiving the intervention immediately will be compared with those on a waiting list to join the program. The primary outcome will be frequency of and distress associated with antiretroviral side effects, with secondary outcomes of quality of life and medication adherence.

Eligible participants must be at least 18 years of age and able to speak English. They must have been on antiretroviral therapy for at least 30 days, and must be experiencing significant side effect–related bother and distress as determined by standard scales. Exclusion criteria include severe cognitive impairment, active psychosis, active substance abuse, and participation in another MBSR or adherence intervention program. The study aims to recruit 100 participants in **San Francisco** (415-597-9374).
www.clinicaltrials.gov/show/NCT00312936 (R21 AT003102-01).

VivaGel Microbicide

In recent years, biomedical prevention technologies have received increasing attention as a means to stem the persistent spread of HIV/AIDS (see "New Approaches to HIV Prevention" in the Winter 2007 issue of *BETA*). Clinical trials of such methods are often conducted in resource-limited countries with high overall HIV prevalence, but a trial of one microbicide—SPL7013, or VivaGel—recently began for HIV negative young women in the United States. VivaGel received FDA accelerated review status in January 2006.

The randomized, placebo-controlled, double-blind Phase I study, sponsored by Starpharma, NIAID, and the Microbicide Trials Network, will look at the safety of 3% SPL7013 gel administered to the mucous membranes of the vulva, vagina, and cervix for 14 days; efficacy is not being assessed at this stage.

Eligible participants will be healthy, HIV negative, sexually active women 18–24 years of age. They must not be pregnant and must be willing to use effective contraception. Exclusion criteria include a history of adverse reactions to latex or sensitivity to the products under study, ab-

normal findings on a pelvic exam, sexually transmitted or reproductive tract infections, and use of antibiotic or antifungal medications

The trial aims to enroll 40 participants at the University of South Florida in **Tampa** and the University of Puerto Rico in **San Juan.** For further information, contact 310-206-3580. *www.clinicaltrials.gov/show/NCT00442910* (MTN-004; SPL7013-006).

Bupropion to Reduce Methamphetamine Use

The BUMP study, conducted by San Francisco Department of Public Health and sponsored by the National Institute on Drug Abuse, is designed to evaluate whether an antidepressant medication can help gay and bisexual men stop using or reduce their use of methamphetamine. Researchers also will assess whether this helps reduce high-risk sexual behavior, such as anal sex without a condom.

Subjects will be randomly assigned to receive either the antidepressant bupropion (Zyban, Wellbutrin)—which is also prescribed to aid smoking cessation (see "Smoking and Your Health" on page 35)—or a placebo for 12 weeks. If this approach proves feasible, the investigators plan to conduct a larger trial. Study visits will take place weekly and will include a urine test; participants will receive $10–$35 per visit.

Eligible participants must be men at least 18 years of age, either HIV positive or HIV negative, who have engaged in anal sex with men while using methamphetamine in the past three months. Exclusion criteria include acute illnesses, history of seizures, liver or kidney dysfunction, and use of certain medications. The study is enrolling participants in **San Francisco** (415-554-9013 or 415-703-7273; sf.bump@sfdph.org). *www.clinicaltrials.gov/show/NCT00318409* or *www.sfbump.com* (R21DA021090-1).

Smoking is a habit. It is often a stress-related activity. Smoking is also a risk factor for many conditions that affect people with HIV, including cardiovascular disease, bone disease, and anal cancer.

The FDA has approved bupropion (Zyban) and varenicline (Chantix) as nicotine-free medicinal quitting aids. Nicotine replacement therapies—in the form of lozenges (Commit), patches (Habitrol, Nicoderm, Nicotrol), inhalers (Nicotrol Inhaler), and gum (Nicorette)—are another means of quitting. Complementary methods include behavior modification, counseling and support, and acupuncture.

The Stop Smoking Center (***www.stopsmokingcenter.net***) is a unique Web site that offers a Quit Program, online support services, and links to a wide range of smoking cessation resources, including the American Lung Association (212-315-8700) and Nicotine Anonymous (415-750-0328).

The Tobacco Education Center of UCSF/Mt. Zion (415-885-7895) is a quitting resource for San Francisco Bay Area residents.

Learn more about the art of quitting. There is no better time than now.