



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 **HIV InSite** Web site, provided by the **University of California at San Francisco (UCSF)**, features **TrialScope**, a database of organizations that conduct HIV/AIDS-related research.

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. **The Community Research Initiative of New England (CRINE)** offers a searchable database of trial listings for the Northeast.

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 more information about specific trials. Protocol numbers, if available, are provided in parentheses at the end of each trial description.

ACTG: www.aactg.org

AIDSinfo: www.aidsinfo.nih.gov

CenterWatch: www.centerwatch.com

ClinicalTrials.gov: www.clinicaltrials.gov

CRINE: www.crine.org/searchable_open_trial_database.html

HVTN: www.hvtn.org

NCCAM: www.nccam.nih.gov/clinicaltrials

TrialScope: www.hivinsite.org/tscope

TrialSearch: www.acria.org/clinical_trials/index.html

GRACE: Gender Differences in Response to Darunavir

Tibotec's non-peptide protease inhibitor (PI), darunavir (Prezista, formerly TMC114), was approved in June 2006 for use by treatment-experienced individuals.

The company recently announced the initiation of a new open-label Phase IIIb trial called GRACE (Gender, Race and Clinical Experience), which will study sex- and race-related differences in the drug's efficacy and tolerability. While HIV treatment trials have historically included a majority of men, GRACE will enroll 70% women. "Women who participate in GRACE will play a very important role in advancing the understanding of HIV treatment in women," said treatment advocate Dawn Averitt-Bridge.

Eligible participants must be at least 18 years of age, have a viral load of at least 1000 copies/mL, and have experienced intolerance or treatment failure on previous regimens containing PIs or non-nucleoside reverse transcriptase inhibitors (NNRTIs). Exclusion criteria include active opportunistic illnesses (OIs), abnormal laboratory results, and use of certain other medications. Women may not be pregnant or breast-feeding. All subjects will receive 300 mg twice-daily darunavir boosted with 100 mg ritonavir (Norvir) plus optimized background therapy (OBT) for 48 weeks. Follow-up visits will take place at weeks 4, 8, 12, 16, 24, 36, 48, and 52.

The GRACE trial aims to enroll 420 subjects at some 50 sites in **Canada, Mexico, and the United States**, including **Atlanta, Baltimore, Birmingham, Boston, Chicago, Dallas, Durham, Fort Lauderdale, Los Angeles, Miami, Nashville, Newark, New Orleans, New York City, Philadelphia, Salt Lake City, Seattle, St. Louis, and Washington, DC**. For details and other study sites, call 866-512-7943 or email GRACEstudy@wilm.ppd.com. www.clinicaltrials.gov/show/NCT00381303 (CR011869).

New CCR5 Inhibitor: INCB9471

Incyte Corporation recently initiated a Phase II trial to assess the safety, pharmacokinetics, and antiviral efficacy of INCB9471, an orally available CCR5 antagonist. CCR5 antagonists are a new class of antiretroviral agents that block HIV entry into cells (see "Drug Watch," page 15).

Eligible participants must be 18–65 years of age and either antiretroviral-naïve or off treatment for at least three months. They must have a CD4 count above 350 cells/mm³,

a viral load greater than 10,000 copies/mL, and HIV that uses only the CCR5 coreceptor (viral tropism will be assessed at study entry). Exclusion criteria include certain illnesses (including hepatitis B or C and heart conditions), laboratory abnormalities, and use of certain medications (including herbal supplements). Women may not be pregnant or breast-feeding, and participants must agree to use effective barrier contraception. Subjects will be randomly assigned to receive 200 mg INCB9471 or placebo once daily with food for 14 days. Virological and safety assessments, including electrocardiograms, will be conducted regularly throughout the study.

This trial will enroll participants in **Annandale, Boston, Los Angeles, Orlando, Vero Beach,** and **Washington, DC**. For more information, call 302-498-6781 or email ksolomon@incyte.com. www.clinicaltrials.gov/ct/show/NCT00393120 (INCB 9471-201).

Monoclonal Antibody CCR5 Inhibitor: CCR5mAb004

Another CCR5 inhibitor, a monoclonal antibody known as CCR5mAb004, is currently being studied in a Phase I randomized, placebo-controlled dose-escalation trial.

Eligible participants must be 18–64 years of age and off antiretroviral therapy for at least 60 days prior to the start of the study. They must have a viral load greater than 5000 copies/mL, a CD4 count above 250 cells/mm³, and HIV that uses only the CCR5 coreceptor (to be assessed at study entry). Exclusion criteria include certain illnesses (including cancer and hepatitis B or C), laboratory abnormalities, and use of certain medications. Women may not be pregnant or breast-feeding and must agree to use effective contraception. Participants will be randomly assigned to receive either a single intravenous infusion of one of four doses of CCR5mAb004 or else a placebo infusion, and will be followed for 56 days.

This trial aims to enroll 40 participants at about ten U.S. sites, including **Baltimore, Cleveland, Columbus, Fort Lauderdale, Los Angeles, Orlando,** and **San Francisco**. For more information, call 866-447-9749 or email Thomas_Platek@hgsi.com. www.clinicaltrials.gov/ct/show/NCT00114699 (CCR5-HV01).

Elite Controller Study

The Elite Controller Study is a collaborative effort to understand factors associated with long-term non-progression of HIV disease. The study defines “controllers” as individuals able to maintain low HIV viral loads (below 2000 copies/mL) without treatment, and “elite controllers” as those able to maintain undetectable HIV RNA levels (below 50 copies/mL). The investigators will assess multiple viral and host char-

acteristics, including genetic variations such as the CCRΔ32 mutation, which is associated with resistance to HIV infection and slow disease progression (described in “Drug Watch,” page 15).

Eligible participants must be HIV positive adults 18–75 years of age. They must not be on antiretroviral therapy and must have viral loads below 2000 copies/mL and asymptomatic infection. Candidates will first undergo a one-time blood draw by their local provider. The sample will be sent to the study coordinators and analyzed to determine eligibility. The coordinators will then arrange for further participation.

This collaborative study is coordinated by Bruce Walker, MD, of Partners AIDS Research Center at Massachusetts General Hospital in **Boston**, and includes participating researchers and community advocacy groups in **Chicago, Durham, Los Angeles, Nashville, New York City, San Diego, San Francisco, Seattle,** and in cities in **Canada, Europe,** and **Australia**. The researchers hope to identify 700–800 HIV controllers worldwide; individuals who believe they may qualify need not live in one of these cities. For more information or to discuss eligibility, contact Rachel Rosenberg (617-726-5536; rosenberg2@partners.org) or Florencia Pereyra (fpereyra@partners.org). www.mgh.harvard.edu/aids/hiv_elite_controllers.asp.

FOTO: Five Days On, Two Days Off Therapy

Recent studies have shown that interruption of antiretroviral therapy based on CD4 cell count is a potentially risky strategy (see “News Briefs,” page 6); less is known, however, about treatment using fixed-length cycles. The Phase IV FOTO study, sponsored by CRINE, will compare continuous therapy against a five-days-on/two-days-off schedule of efavirenz (Sustiva), tenofovir (Viread), and emtricitabine (Emtriva).

Eligible participants must be 18–65 years of age, have a CD4 count of at least 200 cell/mm³, and an undetectable HIV viral load (below 50 copies/mL). They must be on a stable regimen containing efavirenz, tenofovir, and emtricitabine or 3TC (Epivir) for at least 90 days. Subjects will have six clinic visits after randomization; those assigned to continuous therapy will cross over to cyclical therapy at 24 weeks if viral load remains undetectable.

This study aims to enroll 60 participants in **Boston** (617-778-5454 ext. 267), **Miami** (305-856-2171), **Orlando** (407-647-3960), **Vero Beach** (772-978-9556), **West Springfield** (413-734-2264), and **Washington, D.C.** www.clinicaltrials.gov/show/NCT00414635 (06-156).

Genetic Marker for Abacavir Hypersensitivity

Several recently reported studies have shown that a specific genetic variation known as HLA-B*5701 is associated with hypersensitivity to abacavir (Ziagen). Abacavir

manufacturer GlaxoSmithKline is evaluating whether this genetic marker can be used to predict which patients will develop the reaction.

This retrospective Phase IV case-control study will enroll 40 black and 40 white individuals with abacavir hypersensitivity and 200 black and 200 white abacavir-tolerant control subjects (the gene occurs with varying frequency in different racial/ethnic populations). Eligible participants must be at least 18 years of age.

The trial will be conducted at more than 70 sites, including **Akron, Albany, Atlanta, Austin, Baltimore, Birmingham, Chapel Hill, Chicago, Dallas, Denver, Detroit, Fort Lauderdale, Houston, Jacksonville, Lexington, Little Rock, Los Angeles, Memphis, Miami, Nashville, New York City, Oakland, Orlando, Philadelphia, Portland, Rochester, San Francisco, Seattle, Spokane, St. Louis, Tucson, and Wichita**. For more information, call 877-379-3718. www.clinicaltrials.gov/ct/show/NCT00373945 (ABC107442; SHAPE).

Protease-Sparing Regimens for Adolescents

This open-label Phase III trial, sponsored by National Institute of Allergy and Infectious Diseases (NIAID), will compare the effectiveness of antiretroviral drug regimens with or without a PI in HIV positive adolescents, and will also assess whether drug level monitoring and individualized dose adjustment can improve the efficacy of therapy. Participants will be randomly assigned to receive either lopinavir/ritonavir (Kaletra) or efavirenz, both with two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs); at the same time, they will be independently randomized to receive or not receive therapeutic drug monitoring.

Eligible participants must be 13–23 years of age, weigh at least 35 kg (77 lbs), and have an HIV viral load of at least 10,000 copies/mL. They may be either treatment-naïve or treatment-experienced, but the latter group must have HIV that is susceptible to lopinavir. Exclusion criteria include prior use of lopinavir or any NNRTI, active OIs, clinical depression, and certain abnormal laboratory results. Female subjects may not be pregnant or breastfeeding, and participants must agree to use effective contraception.

The trial is still recruiting participants at about a dozen sites, including **Baltimore** (410-955-9749), **Chicago** (312-572-4554), **Houston** (832-824-1339), **Los Angeles** (323-669-2390), **Memphis** (901-495-3490), **Miami** (305-243-4445), **New Orleans** (504-586-3804), **Philadelphia** (215-427-5284), **San Juan** (787-759-9595), and **Worcester** (508-856-1692). www.clinicaltrials.gov/show/NCT00075907 (PACTG P1034).

Interactions between Lopinavir/Ritonavir and Contraceptives

Because certain antiretroviral medications and hormone-based oral contraceptives are metabolized by the same pathways, these agents can interact, potentially lowering hormone levels enough to cause contraceptive failure resulting in unintended pregnancy. Such interactions may be less likely using a transdermal contraceptive patch that delivers hormones through the skin.

This non-randomized, open-label Phase II pharmacokinetic study, sponsored by NIAID, will assess interactions between lopinavir/ritonavir and two contraceptive methods—the Ortho-Novum 1/35 pill and the Ortho Evra patch—in women with HIV. Eligible participants must be at least 13 years of age with a CD4 count of at least 200 cells/mm³ and a viral load less than 55,000 copies/mL. Subjects must either be taking a stable regimen containing lopinavir/ritonavir or else be off treatment or receiving only NRTIs. Exclusion criteria include pregnancy, certain medical conditions, and use of hormonal therapies within 60 days of study entry. Women must agree not to consume caffeine or alcohol for portions of the study, and smokers over age 35 are ineligible. All patients will receive a single dose of Ortho-Novum 1/35 on day 1 and will start using the Ortho Evra patch on day 3.

This study aims to enroll 54 participants at about a dozen sites, including **Baltimore** (410-706-1476), **Chicago** (773-257-5717), **Denver** (303-372-5535), **Honolulu** (808-737-2751), **Indianapolis** (317-274-8456), **Jacksonville** (904-244-5331), **Los Angeles** (323-226-2226), **New York City** (212-746-4393), and **Seattle** (206-731-8877). www.clinicaltrials.gov/ct/show/NCT00125983 (ACTG A5188).

Protease Inhibitors and Glucose Metabolism

Several recent reports have focused on the relationship between HIV and its treatment and abnormal glucose metabolism (see “News Briefs,” page 11).

This randomized Phase IV study, sponsored by the Department of Veterans Affairs, will attempt to determine how PIs contribute to the development of diabetes in people with HIV—in particular, whether PIs impair insulin secretion and increase the production of glucose by the liver. In order to separate out the effects of PIs from those of HIV itself, this study will enroll HIV negative volunteers. Participants will be randomly assigned to receive either a single dose of a PI or placebo. Insulin secretion will be assessed using the hyperglycemic clamp technique. Somatostatin, growth hormone, and glucagon will be infused before and during the clamp study. Liver glucose

production will be measured in the fasting and hyperinsulinemic (excess insulin) states.

This study aims to enroll 80 healthy, HIV negative participants 18–72 years of age. Volunteers may not have medical conditions associated with insulin resistance, such as obesity or elevated blood fat levels, and may not be taking glucocorticoids, growth hormone, niacin, or antipsychotic medications. Women may not be pregnant. This study will take place at the **San Francisco Veterans Affairs Medical Center** (415-221-4810 ext. 2118 or ext. 3395). www.clinicaltrials.gov/ct/show/NCT00259727 (RCD-005-05S; H574-23263).

Project T: Tenofovir to Prevent HIV Infection

Use of antiretroviral agents as pre-exposure prophylaxis (PrEP) to prevent HIV infection was a prominent topic at the recent International AIDS Conference in Toronto (see “New Approaches to HIV Prevention,” page 29). The Centers for Disease Control and Prevention (CDC), in conjunction with the San Francisco Department of Public Health (SFDPH), the AIDS Research Consortium of Atlanta, and the Fenway Community Health Center in Boston, is conducting a double-blind Phase II trial to assess whether tenofovir can help prevent infection, as suggested by animal studies.

Participants will receive either daily oral tenofovir or placebo, and will be followed every three months for two years. This phase of the study will focus on the safety of the drug and whether use of a potentially protective agent will lead to an increase in high-risk sexual behavior. Because it is not yet known whether tenofovir can prevent HIV infection—and because some subjects will receive placebo—participants should continue to practice safer sex, and will receive risk-reduction counseling and free condoms. If any participants become infected, SFDPH will facilitate referrals for HIV care and treatment.

Eligible participants must be sexually active HIV negative men aged 18–60 years who have sex with men or transgender (male-to-female) women. Exclusion criteria include certain medical conditions (including impaired kidney or liver function and bone disease) and use of certain drugs (including nephrotoxic medications). The study is enrolling participants in **San Francisco** (415-554-8888; www.helpfighthiv.org/projt.htm), **Atlanta** (404-876-2317; www.aidsresearchatlanta.org/TheT), and **Boston** (617-927-6450). www.clinicaltrials.gov/show/NCT00131677 (CDC-NCHSTP-4323).

ACE: Acyclovir for HIV Prevention

Treatment of sexually transmitted infections (STIs) also serves as a strategy for preventing HIV transmission.

This randomized, placebo-controlled Phase III study, sponsored by NIAID, will assess the effectiveness of acyclovir (Zovirax)—a commonly prescribed anti-herpes drug—in preventing HIV infection in people with herpes simplex type 2 (HSV-2).

Eligible participants must be HIV negative and HSV-2 positive; there are no age restrictions. Subjects will be randomly assigned to receive either 400 mg twice-daily acyclovir or placebo. Follow-up visits will occur monthly for one year; participants will be tested for STIs at each visit and treated as necessary.

This study aims to recruit more than 3600 participants worldwide. Women will be enrolled in **Africa**, while men who have sex with men will be enrolled in **Peru** and in the **United States**, in **New York City** (212-388-0008), **San Francisco** (415-437-4782; www.helpfighthiv.org/cestudy.htm), and **Seattle** (froehle@u.washington.edu). www.clinicaltrials.gov/ct/show/NCT00076232 (HPTN 039).

Rectal Microbicides

Large-scale studies of microbicides for HIV prevention primarily involve vaginal use in women, and most are taking place in developing countries. But there are a few preliminary studies concerning microbicides for rectal use during anal sex.

One such study, sponsored by CONRAD and the University of California at Los Angeles, is the first-ever trial of rectal use in humans of UC-781, an investigational NNRTI gel microbicide. This Phase I study is designed to assess the product’s safety and acceptability, not its efficacy.

Eligible participants must be at least 18 years of age, HIV negative, and have experience with receptive anal intercourse. Women may not be pregnant or breast-feeding, and all participants must agree to use condoms. Exclusion criteria include certain medical conditions and laboratory abnormalities. Subjects will be randomly assigned to use a gel containing one of two concentrations of UC-781 or else placebo. During Stage 1, they will receive a single dose at the clinic. During Stage 2, they will self-administer the gel once daily for seven days. Study evaluations will include flexible sigmoidoscopy.

This study will enroll 36 participants at the UCLA Center for HIV Prevention Research in **Los Angeles** (310-825-9254 or csiboliban@mednet.ucla.edu). www.clinicaltrials.gov/ct/show/NCT00408538 (U19-AI060614:P4).

A related study called the Anorectal Microbicide Project will assess rectal health, sexual behavior, and potential acceptability of rectal microbicides. In this observational, cross-sectional study, men and women will participate in computer-assisted interviews concerning their behavioral

repertoire surrounding anal intercourse, rectal symptoms, and healthcare. Participants must be at least 18 years of age, with or without a history of receptive anal intercourse, and willing to undergo STI testing and rectal exams. This study aims to enroll nearly 900 participants in **Los Angeles** (310-358-2429) and **Baltimore** (410-502-5949). www.clinicaltrials.gov/ct/show/NCT00377221 (U19-AI060614:P3).

Vaccines for HIV Negative Individuals

As noted in the article on page 29, HIV vaccine research includes both candidates aimed at preventing HIV infection and those designed to improve immune response after infection. Below is a sample of NIAID vaccine trials currently enrolling HIV negative volunteers; for a more comprehensive list, visit www.clinicaltrials.gov and search for “HIV vaccine.”

Eligibility criteria are similar for all of the following trials. Participants must be 18–50 years of age, HIV negative, and in good general health. Exclusion criteria include participation in previous HIV vaccine trials, recent receipt of various other vaccines, certain medical conditions (including heart disease, diabetes, and hepatitis B or C), spleen removal, use of certain medications, and adverse reactions to past vaccines (and, in some cases, allergy to eggs). Women may not be pregnant or breast-feeding, and participants must agree to use effective contraception.

Phase I study testing an HIV-1 gag DNA vaccine, with

and without an interleukin-15 DNA adjuvant (at escalating doses of 100, 500, and 1500 mcg), and in combination with two other adjuvant-containing booster vaccines in some participants. Enrolling in **Boston** (617-732-5394), the **Bronx** (718-588-8900), **New York City** (212-388-0008), and **Rochester** (585-275-5744). www.clinicaltrials.gov/show/NCT00115960 (HVTN 063).

Phase I trial to determine the safety and immunogenicity of the DNA vaccine candidate pGA2/JS7, followed by the MVA/HIV62 booster. Enrolling in **Baltimore** (410-706-1289), **Birmingham** (205-975-2840), **Nashville** (615-322-5641), **Rochester** (585-275-5744), and **St. Louis** (314-268-5448). www.clinicaltrials.gov/show/NCT00301184 (HVTN 065).

Phase I study to assess an adenovirus vector booster vaccine (VRC-HIVADV014-00-VP) given after three doses of a DNA plasmid primer vaccine (VRC-HIVDNA009-00-VP). Enrolling in **Birmingham** (205-975-2840), **Boston** (617-732-5394), **New York City** (212-388-0008), and **Seattle** (206-667-2344). www.clinicaltrials.gov/show/NCT00384787 (HVTN 069).

Phase II trial to evaluate the safety and immunogenicity of a multiclade HIV-1 DNA plasmid vaccine (VRC-HIVDNA016-00-VP) followed by a recombinant adenovirus vector boost (VRC-HIVADV014-00-VP). Enrolling in **Birmingham** (205-975-2840), **Baltimore** (410-706-1289), **Boston** (617-732-5394), **Nashville** (615-322-5641), and **Rochester** (585-275-5744). www.clinicaltrials.gov/show/NCT00125970 (HVTN 204).

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