



Open Clinical Trials

Below is a list of selected currently enrolling clinical trials gathered from various sources.

The federal government's **AIDSinfo** website 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 advice about clinical trial participation via email (ContactUs@AIDSinfo.nih.gov), an interactive website (www.aidsinfo.nih.gov/live_help; specialists available Mon.–Fri. 9:00 am–1:00 pm PST), and a toll-free telephone service (800-448-0440, international 301-315-2816; specialists available Mon.–Fri. 9:00 am–2:00 pm PST).

Most U.S. government HIV/AIDS treatment trials are conducted by the **AIDS Clinical Trials Group (ACTG)**. HIV prevention trials fall under the auspices of the **HIV Prevention Trials Network (HPTN)**, the **HIV Vaccine Trials Network (HVTN)**, and the **Microbicide Trials Network (MTN)**. The other two trials networks funded by the National Institutes of Health are the **International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT)** and the **International Network for Strategic Initiatives in Global HIV Trials (INSIGHT)**. The **National Center for Complementary and Alternative Medicine (NCCAM)** conducts trials of complementary therapies for all conditions, including HIV/AIDS.

TrialSearch, operated by the **AIDS Community Research Initiative of America (ACRIA)**, is a searchable online database of clinical trials related to HIV/AIDS. **CenterWatch** is a commercial website that includes trial listings for all diseases, including HIV/AIDS and related conditions.

Call the telephone numbers listed for each study or see the indicated websites 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/trials/current-drug-trials

ACTG: www.aactg.org

AIDSinfo: www.aidsinfo.nih.gov

CenterWatch: www.centerwatch.com

ClinicalTrials.gov: www.clinicaltrials.gov

HIV Prevention Trials Network: www.hptn.org

HIV Vaccine Trials Network: www.hvtn.org

IMPAACT: www.impaactgroup.org

INSIGHT: www.insight-trials.org

Microbicide Trials Network: www.mtnstopshiv.org

NCCAM: www.nccam.nih.gov/research/clinicaltrials

When to Start ART

The **INSIGHT START (Strategic Timing of Antiretroviral Treatment)** trial aims to inform the debate about optimal time to initiate antiretroviral therapy (ART). (See “When to Start Antiretroviral Treatment: A Changing Equation,” *BETA*, Summer 2008).

In this open-label Phase IV study, participants with a CD4 cell count above 500 cells/mm³ will be randomly assigned to either start ART immediately or defer treatment until their CD4 count falls below 350 cells/mm³, in accordance with current U.S. and European treatment guidelines. ART regimens will be selected by study physicians and may include any approved drugs. Follow-up visits will take place every four months and the study is expected to continue for 4.5 years. Investigators will compare incidence of AIDS-defining events and serious non-AIDS-related disease in the two groups. Other outcomes, including neurocognitive and blood vessel function, will be assessed in smaller subgroups.

Participants must be at least 18 years of age, treatment-naive, and have a CD4 count above 500 cells/mm³ within 60 days prior to study entry. Exclusion criteria include previous use of antiretroviral drugs or interleukin 2, prior diagnosis of clinical AIDS-related events, and recent illness, including cardiovascular events, cancer, or kidney dialysis. Women may not be pregnant or breastfeeding and must agree to use approved contraception.

START will initially enroll 900 individuals, with a planned expansion to 4,000 participants. U.S. study sites include Bethesda (301-319-8673), Boston (617-505-1711), the Bronx (718-901-6346), Chicago (312-413-9793), Denver (303-602-8743), Detroit (313-916-2570), Fort Worth (817-321-4812), Houston (713-500-6751), Minneapolis (612-626-8049), Newark (973-972-1268), New Haven (203-785-3557), New Orleans (504-988-1971), New York (212-939-2957), Orlando (407-647-3960 ext. 2148), Philadelphia (215-707-8846), Portland, OR (503-229-8428), Richmond (804-828-2477), San Diego (619-532-5889), Tampa (813-307-8015 ext. 6460), and Washington, DC (202-745-8000 ext. 7558). www.clinicaltrials.gov/ct2/show/NCT00867048 or <http://insight.cabr.umn.edu/start> (0603M83587, 09-I-0108).

GSK Integrase Inhibitors

GlaxoSmithKline (GSK) is sponsoring several clinical trials of two investigational integrase inhibitors it is developing in conjunction with Shionogi and Co. Early data indicate that the drugs, GSK1349572 (GSK-572) and GSK1265744 (GSK-

744), have potent antiviral activity and are generally well tolerated (see “News Briefs,” page 4).

The first study is a Phase IIb dose-ranging trial of GSK-572 in combination with two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) in treatment-naïve HIV positive individuals. Participants will be randomly assigned to receive GSK-572 at once-daily doses of 10 mg, 25 mg, or 50 mg, or else efavirenz (Sustiva) as a control drug; they will also take either abacavir/lamivudine (Epzicom) or tenofovir/emtricitabine (Truvada). Pharmacokinetic parameters will be assessed at weeks 4, 12, and 24; safety and efficacy evaluation will continue through week 96.

Participants must be at least 18 years of age and starting antiretroviral therapy for the first time. They must have a viral load of at least 1,000 copies/mL and a CD4 count of at least 200 cells/mm³. Those receiving abacavir must have a negative HLA-B*5701 hypersensitivity test. Exclusion criteria include recent use of certain other medications and vaccines, active AIDS-defining conditions, and various other diseases and laboratory abnormalities; asymptomatic hepatitis C that does not require treatment is not exclusionary. Women may not be pregnant or breastfeeding and must use effective contraception.

The study aims to enroll 200 participants in the U.S. and Europe. U.S. sites include Bakersfield, Baltimore, Fort Lauderdale, and San Francisco. www.clinicaltrials.gov/ct2/show/NCT00951015 (ING112276).

A second Phase IIb study will evaluate GSK-572 in treatment-experienced patients who have developed resistance to the sole approved integrase inhibitor, raltegravir (Isentress). Laboratory data indicate that the new drug is active against raltegravir-resistant virus. In this open-label study, all participants will receive 50 mg once-daily GSK-572 while remaining on their current background drugs. After ten days on “functional monotherapy,” they will switch to an optimized background regimen and continue through at least week 24.

Prospective participants must be at least 18 years of age and have a viral load of at least 1,000 copies/mL. They must be treatment-experienced, have been on stable ART for at least two months, and have current or prior virological failure while taking raltegravir. In addition, resistance testing must demonstrate documented resistance to raltegravir and at least one drug from three or more approved antiretroviral classes. Exclusion criteria include current or anticipated use of several specific antiretroviral drugs, including efavirenz, boosted fosamprenavir (Lexiva), or boosted tipranavir (Aptivus); recent use of certain other medications and vaccines; active AIDS-defining illnesses and certain other diseases (again, asymptomatic, untreated hepatitis C is permitted); and various laboratory and electrocardiogram (ECG) abnormalities. Women may not be pregnant or breastfeeding.

This trial will enroll 30 participants in the U.S. and

Europe. U.S. sites include Fort Lauderdale and Santa Fe. www.clinicaltrials.gov/ct2/show/NCT00950859 (ING112961).

Finally, a third study will evaluate the safety and efficacy of GSK-744. This compound, which the company considers a backup to GSK-572, has similar characteristics overall, but a longer half-life in the body. In this small Phase IIa trial, currently untreated HIV positive participants will be randomly assigned to receive either GSK-744 monotherapy or placebo for ten days.

Participants must be 18–65 years of age and have a CD4 count of at least 200 cells/mm³. They may be either treatment-naïve or treatment-experienced if they have been off ART for at least three months and have adequate treatment options to construct a regimen of at least three active drugs. Exclusion criteria include recent use of certain other medications and vaccines, use of recreational drugs or regular alcohol consumption, active AIDS-defining illnesses, and various other diseases and laboratory or ECG abnormalities. Women may not be pregnant or breastfeeding. In addition, because less is known about GSK-744, women of childbearing potential are excluded (sterilized and postmenopausal women are permitted) and men must use approved contraception.

This study will enroll 14 participants in Charlotte, Ft. Lauderdale, Orlando, and Vero Beach. www.clinicaltrials.gov/ct2/show/NCT00920426 (ITZ112929).

For further information or to enroll in any of these trials, contact the U.S. GSK Clinical Trials Call Center at 877-379-3718.

CNS-Targeted ART

The CIT2 study, sponsored by the National Institutes of Health and the University of California at San Diego, will evaluate the effectiveness of ART that penetrates the central nervous system (CNS). As described in “HIV and the Brain” on page 16, it is not clear whether antiretroviral drugs that enter the brain can prevent or improve HIV-related cognitive impairment.

In this Phase II/II trial, patients with HIV-associated neurocognitive impairment who are planning to initiate ART or change their current regimen will be randomly assignment to receive either a CNS-targeted ART regimen designed to maximize brain penetration or a comparator regimen intended to fully suppress plasma viral load but not expected to have significant CNS penetration. The primary outcome, change in global neuropsychological performance, will be evaluated at 16 weeks. Plasma and cerebrospinal fluid (CSF) viral load will also be assessed.

Participants must be at least 18 years of age, have measurable neurocognitive impairment, and have a viral load of at least 2,000 copies/mL within 60 days of enrollment. They may be either treatment-naïve or treatment-experienced, and must be willing to undergo three lumbar punctures (spinal taps) for CSF testing. Exclusion criteria include serious

illness such as active AIDS-related opportunistic infections, severe psychiatric disorders, and recent use of certain medications and vaccines. Women may not be pregnant.

The study aims to enroll 120 participants in Baltimore (443-287-8341), San Diego (619-543-8080), and St. Louis (314-747-1096). www.clinicaltrials.gov/ct2/show/NCT00624195 (CIT2, 060154, R01-MH5807).

Truvada PrEP for Men

The aim of this Phase III study, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), is to evaluate whether daily use of tenofovir plus emtricitabine (the drugs in the Truvada combination pill) can be used as pre-exposure prophylaxis (PrEP) to help prevent HIV infection among men who have sex with men (MSM). (For more on PrEP, see “Is HIV Treatment HIV Prevention?” on page 30.)

HIV negative men at risk for HIV infection will be randomly assigned to receive either once-daily oral tenofovir/emtricitabine (300/200 mg coformulation) or placebo. All participants will receive counseling, free condoms, and treatment for sexually transmitted infections. The primary outcome will be HIV seroconversion after three years. Changes in risk behavior, drug resistance, and safety endpoints—including kidney function, bone mineral density, body fat distribution, and hepatitis flares in people with hepatitis B virus coinfection—will also be assessed.

Eligible participants are HIV negative gay, bisexual, or other MSM at least 18 years of age who are at high risk for HIV infection (e.g., having had unprotected anal intercourse with an HIV positive or unknown-status male partner during the past six months or exchanging anal sex for money, gifts, shelter, or drugs). Exclusion criteria include serious active infections, clinically significant medical problems (including heart disease or diabetes), hepatitis B requiring treatment, and certain laboratory abnormalities.

This study plans to recruit 3,000 participants worldwide. In the U.S., the trial is being conducted by the San Francisco Department of Public Health (415-554-9070 or 415-554-9104) and the Fenway Community Health Center in Boston (617-927-6400 or 617-927-6021). www.clinicaltrials.gov/ct2/show/NCT00458393 (5U01AI06400202, U01-AI064002).

Tenofovir Gel and Tablets for Women

A related trial, sponsored by NIAID and MTN, will evaluate tenofovir (Viread) tablets and vaginal gel as a PrEP strategy for women. This Phase II study will assess acceptability, adherence, pharmacokinetics, blood drug levels, changes in risk behavior, and safety parameters. However, it is not large enough to determine efficacy in preventing infection.

In this open-label crossover trial, participants will be randomly allocated to receive various regimens of tenofovir in oral (300 mg once-daily tablet) and gel (100 mL of 1%

gel applied daily) formulations for 20 weeks. Individuals will receive a regimen for six weeks, followed by a one-week “washout” period (during which no tenofovir is used), then switch to a second regimen, followed by a second washout period and a third regimen. Participants will have multiple study visits that include counseling, physical examination (including pelvic exams), behavioral assessment, and urine and blood sample collection.

Eligible participants are sexually active HIV negative women 18–45 years of age who are in generally good health, have normal menstrual cycles, and have had a normal Pap smear within the 12 months before enrollment. Exclusion criteria include latex allergy, more than three sexual partners in the month prior to screening, recent injection drug use, and certain illnesses or laboratory abnormalities. Participants may not be pregnant or breastfeeding and must use effective contraception.

The study will enroll 144 participants in the U.S. and Africa. U.S. sites include Birmingham (205-975-8699), Cleveland (216-844-8786), and Pittsburgh (412-647-0771). www.clinicaltrials.gov/ct2/show/NCT00592124 (MTN-001, 1-U01-AI068633-01).

HVTN 505 Vaccine Study

The HVTN 505 study, sponsored by NIAID’s HIV Vaccine Trials Network, will evaluate whether a two-part vaccine regimen can reduce the viral load “set-point” of participants who become infected with HIV. In this Phase II trial, HIV negative volunteers will first receive three immunizations with a recombinant DNA plasmid primer vaccine over the course of eight weeks, followed by a single dose of a recombinant booster vaccine using a weakened adenovirus type 5 (Ad5) vector carrying HIV proteins.

Eligible participants are healthy, sexually active, HIV negative MSM aged 18–45 years. Volunteers must be circumcised and test negative for Ad5 antibodies. These requirements were added because the STEP trial found that among uncircumcised men with Ad5 antibodies, vaccine recipients had a higher rate of HIV infection than those receiving placebo injections (see “News Briefs,” *BETA*, Summer 2008). Exclusion criteria include participation in previous HIV vaccine trials, recent use of antiretroviral drugs for pre-exposure or postexposure prophylaxis, use of certain other medications, and various illnesses.

The study aims to enroll 1,350 participants in 12 U.S. cities, including Atlanta (877-424-4673), Boston (617-525-7327 or 617-927-6450), Bethesda (301-451-8715), Birmingham (205-975-2839), Chicago (312-413-5897), Los Angeles (310-358-2429), Nashville (615-322-4673), New York (212-388-0008 or 212-305-2201), Philadelphia (215-746-7346), Rochester (585-756-2329), San Francisco (415-554-9068), and Seattle (206-667-2300). www.clinicaltrials.gov/show/NCT00865566 or www.hopetakesaction.org (HVTN 505).