Open Clinical Trials

Below is a selection of currently enrolling clinical trials of antiretroviral therapy (ART), and therapies for HIV/AIDS-related conditions.

The federal government's **AIDSinfo** website includes a clinical trials section featuring 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***), a toll-free telephone service (800-448-0440; international 301-315-2816), and an interactive website.

AIDSInfo recently expanded its Live Help chat service (***www.aidsinfo.nih.gov/live_help***) to enable users to interact in real time with specialists who can assist with clinical trial searches; when navigating through the trials search page, a pop-up window will appear with a chat invitation. Live Help is available Monday through Friday, 9:00 a.m. to 1:00 p.m. Pacific Time; telephone assistance is available from 9:00 a.m. to 2:00 p.m.

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 **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 and treatment for HIV-associated illnesses. **CenterWatch** is a commercial website that includes trial listings for all diseases, including HIV/AIDS and related conditions. Trials of new drugs sponsored by pharmaceutical companies are often listed on company websites as well as ClinicalTrials.gov.

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.actgnetwork.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*

Rilpivirine Fixed-Dose Tablet

Gilead Sciences is sponsoring a study to evaluate the safety and efficacy of a single-tablet regimen containing Tibotec's new non-nucleoside reverse transcriptase inhibitor (NNRTI) rilpivirine (formerly TMC278) plus tenofovir/emtricitabine (the drugs in Truvada) among people currently on another antiretroviral regimen (see "News Briefs," page 6, for more information about rilpivirine).

This open-label Phase III trial will enroll HIV positive participants who have been on a regimen consisting of a boosted protease inhibitor plus two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) for at least six months, and have a stably suppressed viral load. They will be randomly assigned to either remain on their current regimen or switch to the rilpivirine combination tablet (25 mg rilpivirine/300 mg tenofovir/200 mg emtricitabine), administered once-daily with a meal. Investigators will assess whether the new tablet is noninferior to protease inhibitor regimens at 24 weeks. After this analysis, participants initially assigned to stay on their old regimen will switch to the new tablet.

Eligible participants must be at least 18 years of age. They must be on their first or second protease inhibitor regimen and have stable undetectable viral load (at least two undetectable HIV RNA measurements within the past

six months and below 50 copies/mL at study screening). They must be NNRTI-naive, with no previous use of any approved or experimental drugs in this class, and must have a genotypic test showing no resistance to the study drugs. People on their second regimen may not have experienced prior treatment failure. Exclusion criteria include active AIDS-defining conditions, recent malignancies, liver or kidney impairment, certain laboratory abnormalities, and use of certain other medications, including other experimental drugs. Women may not be pregnant or breastfeeding, and both women and men of childbearing potential must use effective contraception.

This study aims to enroll 420 participants at more than 100 U.S. sites (as well as sites in Canada and Europe), including Atlanta (404-876-2317 ext. 357), Austin (512-480-9660), Birmingham (205-996-5165), Boston (617-502-1700), Charlotte (704-446-1642), Chicago (four sites), Fort Lauderdale (three sites), Houston (three sites), Little Rock (501-603-0003), Los Angeles (five sites), Minneapolis (612-873-2297), Newark (973-877-2663), New York (212-420-4005), Oakland (510-437-4373), Orlando (407-647-3960 ext. 21005), Philadelphia (three sites), San Francisco (415-833-3487), San Juan, PR (787-723-5945), Seattle (206-624-1441), St. Louis (314-647-2200), and Washington, D.C. (202-745-6111). ***www.clinicaltrials.gov/ct2/show/NCT01252940*** (GS-US-264-0106, 2010-023178-37).

Shionogi-ViiV Integrase Inhibitor

The Shionogi-ViiV Healthcare collaboration has started a Phase III clinical trial for treatment-naive individuals to test its experimental integrase inhibitor GSK1349572 (or GSK572 for short; see "News Briefs," page 7, for more information).

This randomized, double-blind study will assess whether 50 mg once-daily GSK572 is noninferior to 400 mg twice-daily raltegravir (Isentress, the sole approved integrase inhibitor), both used in combination with a dual NRTI fixed-dose combination pill (abacavir/lamivudine [Combivir] or tenofovir/emtricitabine [Truvada]). Efficacy will be compared at 48 and 96 weeks.

Participants must be at least 18 years of age and be starting antiretroviral therapy for the first time. They must have a viral load of at least 1,000 copies/mL. Exclusion criteria include active AIDS-defining conditions, malignancies, liver impairment, serious laboratory abnormalities, and recent use of certain other medications or vaccines. Women may not be pregnant or breastfeeding and must use effective contraception.

The study aims to enroll nearly 800 participants in the U.S., Europe, and Australia. U.S. sites include Atlanta, Austin, Charlotte, Dallas, Denver, Fort Pierce, Hillsborough (NJ), Houston, Little Rock, Long Beach, Los Angeles, Phoenix, St. Louis, and Washington, D.C. For all sites, contact the U.S. GSK Clinical Trials Call Center (877-379-3718) or email info@clinicaltrialsforgsk.com. ***www.clinicaltrials.gov/ct2/show/NCT01227824*** (ING113086).

When to Start ART

The INSIGHT START (Strategic Timing of Antiretroviral Treatment) trial—cosponsored by the U.S. National Institutes of Health, the European AIDS Treatment Network, and other agencies—aims to provide further information about the optimal time to initiate ART. Investigators will assess whether the risk of serious illness or progression to AIDS is lower if participants start taking ART when their CD4 cell count is still relatively high, instead of waiting until it falls to the level at which there is currently good evidence for starting treatment. (See "When to Start Antiretroviral Treatment: A Changing Equation," *BETA*, Summer 2008).

In this open-label Phase IV study, participants with well-preserved immune function, indicated by a CD4 cell count above 500 cells/mm^3, will be randomly assigned to either start ART immediately or defer treatment until their CD4 count falls below 350 cells/mm^3 or they show signs of progression to AIDS. ART regimens will be selected by study physicians in accordance with national treatment guidelines and may include any approved drugs. The study is expected to continue for 4.5 years, with follow-up visits every four months. 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 cell count above 500 cells/mm^3. Exclusion criteria include clinical events indicating HIV disease progression, recent use of certain drugs, and certain recent illnesses, including cardiovascular events, non-AIDS-defining cancer, and serious liver or kidney impairment. Women may not be pregnant or breastfeeding and must agree to use approved contraception.

START aims to enroll 4,000 participants worldwide. U.S. study sites include Bethesda (301-319-8673), Boston (617-505-1711), the Bronx (718-901-6346), Chicago (312-413-8966), Denver (303-602-8712), Detroit (313-916-2570), Fort Sam Houston (210-916-7843), Minneapolis (612-873-7678), Newark (973-972-1268), New Haven (203-785-3557), New Orleans (504-988-1971), New York (212-939-2957), Orlando (407-647-3960 ext. 2136), 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, D.C. (202-745-8000 ext. 7558). ***www.clinicaltrials.gov/ct2/show/NCT00867048***

or ***http://insight.ccbr.umn.edu/start*** (0603M83587, U01AI068641, 2008-006439-12).

Acute HIV Infection

A study sponsored by the University of North Carolina at Chapel Hill will investigate the safety and tolerability of combination antiretroviral therapy started during acute HIV infection. Findings will inform the ongoing debate about "test-and-treat," a strategy of voluntary universal HIV testing followed by prompt treatment initiation for everyone found to be infected. Prior research indicates that people treated during very early infection may have a lower viral load set-point and slower disease progression.

People enrolled in this single-arm, non-randomized Phase IV pilot study will take the once-daily Atripla combination pill (tenofovir/emtricitabine/efavirenz) and will participate in a treatment adherence support program. Investigators will evaluate safety parameters and antiviral efficacy (viral load in plasma, cerebrospinal fluid, and semen or vaginal secretions) over two years. They will also assess the prevalence of genotypic and phenotypic drug resistance mutations.

Eligible participants must be at least 18 years of age and be diagnosed with acute HIV infection. Exclusion criteria include active AIDS-defining illness, serious medical conditions, acute hepatitis, certain laboratory abnormalities (including evidence of kidney impairment), use of kidney-toxic drugs and certain other medications, and recent use of experimental therapies or immune-modulating agents. Women may not be pregnant or breastfeeding and must use two effective forms of contraception.

The study will enroll 90 people in Chapel Hill and Durham, at sites participating in the Duke-UNC Acute HIV Infection Study Consortium (919-966-8533). ***www.clinicaltrials.gov/ct2/show/NCT00924898*** (CID 0805, PHI 02).

CNS-Targeted ART

Despite the widespread use of effective ART, many people with HIV continue to develop neurocognitive problems. This may be due in part to antiretroviral drugs that fail to penetrate the blood-brain barrier and enter the central nervous system (CNS), or brain and spinal cord (see "HIV and the Brain," *BETA,* Summer/Fall 2009).

This Phase II/III study, sponsored by the University of California at San Diego, will evaluate the effectiveness of CNS-targeted ART regimens compared with non-targeted therapy. While smaller studies have observed better neurocognitive outcomes with targeted therapy, this randomized clinical trial will provide the level of evidence needed to formulate ART guidelines that take into account neurocognitive impairment.

The targeted strategy will involve initial selection of drugs known to penetrate the brain, with modification of the regimen if pharmacokinetic testing shows low drug exposure. People in the control arm will receive standard ART intended to suppress plasma viral load.

Eligible participants must be at least 18 years of age and have measurable HIV-related neurocognitive impairment. They must be willing to undergo at least three lumbar punctures (spinal taps) to collect cerebrospinal fluid. Exclusion criteria include serious illness, neurological disorders that could cause neurocognitive impairment, severe psychiatric disorders, and recent use of immune-modulating agents or experimental drugs or vaccines. Women may not be pregnant.

The study aims to enroll 120 participants in Baltimore (443-287-8341), New York City (212-241-0352), San Diego (619-543-8080), San Francisco (415-206-4328), and St. Louis (314-747-1096). ***www.clinicaltrials.gov/ct2/show/NCT00624195*** (060154, R01 MH58076).

Vitamin D Supplementation

Several recent studies have shown that people with HIV often have low vitamin D levels and are at risk for bone loss and subsequent fractures (see "News Briefs," page 11).

This non-randomized, uncontrolled study, sponsored by the University of California at Los Angeles, will assess the prevalence of vitamin D deficiency in HIV positive people on ART, and will evaluate the safety and efficacy of supplementation.

All participants will receive 50,000 IU of vitamin D twice weekly for five weeks, followed by a 2,000-IU once-daily maintenance dose through week 12. At that point, vitamin D levels will be measured, and patients who remain deficient may undergo a second period of supplementation through week 24. Investigators will measure HIV viral load, CD4 cell count, cholesterol, glucose, and other metabolic parameters at baseline and after six months of vitamin D supplementation.

Eligible participants must be 18 to 90 years of age and on suppressive ART with viral load below 200 copies/mL. They will have received vitamin D screening within 90 days of study entry. Exclusion criteria include current use of vitamin D supplements (above the 400 IU dose in a standard daily multivitamin).

The study aims to enroll 140 participants receiving primary care at the UCLA CARE Center in Los Angeles (310-557-9062). ***www.clinicaltrials.gov/ct2/show/NCT01250899.***

Tesamorelin and Growth Hormone

Human growth hormone and growth hormone–releasing factor have both been shown to reduce abdominal fat ac-

cumulation in people living with HIV. Tesamorelin (Egrifta), a synthetic growth hormone-releasing factor, was recently approved by the U.S. Food and Drug Administration (see "News Briefs," page 6, for information on the approval, and "Drug Watch: Tesamorelin Update," page 16, for background information).

This open-label Phase II trial, sponsored by Massachusetts General Hospital, will examine the short-term effects of two different doses of growth hormone, compared with tesamorelin, on brain secretion of growth hormone and glucose metabolism, testing the hypothesis that tesamorelin will have a less detrimental effect on insulin sensitivity. Participants will be randomly assigned to receive once-daily injections of recombinant growth hormone (6 mcg/kg or 2 mg regardless of body weight) or tesamorelin for two weeks.

Participants must be 18 to 60 years of age and on a stable ART regimen for at least 12 weeks. They must show evidence of body shape changes during HIV treatment, including increased abdominal girth, loss of limb fat, or facial lipoatrophy. Men should have a waist circumference of at least 95 cm and waist-to-hip ratio of at least 0.94; for women, 94 cm and 0.88, respectively. Exclusion criteria include severe chronic illness or cancer, carpal tunnel syndrome (a potential side effect of growth hormone), certain laboratory abnormalities, and recent use of anti-diabetic drugs, steroids, or hormones (including hormonal contraceptives). Women may not be pregnant.

The study aims to enroll 36 participants at Massachusetts General Hospital in Boston (617-726-5312). ***www.clinicaltrials.gov/ct2/show/NCT00795210*** (DK63639A, R01DK063639).

Atorvastatin for Atherosclerosis

HIV positive people on ART have been shown to be at greater risk for cardiovascular disease compared with the general population. This study will assess whether using a statin drug reduces development and progression of atherosclerosis ("hardening of the arteries") and its associated inflammatory changes (for more information see "Inflammation, Immune Activation, and HIV," *BETA,* Winter/Spring 2010).

The study, sponsored by Massachusetts General Hospital, will enroll participants with early coronary artery disease. They will be randomly assigned to take atorvastatin (Lipitor) or placebo once-daily for 12 months. Investigators will measure coronary and aorta plaque inflammation, function of the endothelial lining of blood vessels, lipid and fat hormone levels, and C-reactive protein (an inflammation biomarker).

Participants must be 18 to 60 years of age and on a stable ART regimen for more than six months. They must have signs of subclinical coronary artery disease, defined as a CT scan showing one or more plaques, but no clinically significant artery blockage or history of cardiac symptoms (such as angina) or events (such as heart attack or stroke); in addition, they must have an LDL ("bad") cholesterol level of 70–130 mg/dL. Exclusion criteria include acute coronary conditions, recent infections, current statin use, certain laboratory abnormalities, and recent significant radiation exposure. Women may not be pregnant or breastfeeding.

The study aims to enroll 40 participants at Massachusetts General Hospital in Boston (617-724-9109). ***www.clinicaltrials.gov/ct2/show/NCT00965185*** (2008-P-000257, R01HL095123, HL 095123).

Acute Hepatitis C

A substantial proportion of people with HIV are coinfected with hepatitis C virus (HCV), including gay and bisexual men with apparently sexually transmitted HCV. Studies show that liver disease progression may be faster in people who acquire acute HCV infection when they are already HIV positive (see "News Briefs," page 14), and coinfected individuals tend to respond more poorly to hepatitis C treatment.

This non-randomized, open-label Phase IV trial, sponsored by the University of California at San Francisco, will assess the benefits of hepatitis C treatment started during the first six months after acquiring HCV. Participants will start combination therapy using 180 mcg/week pegylated interferon alfa-2a (Pegasys) plus 1,000–1,200 mg/day weight-adjusted ribavirin. Pegylated interferon will be taken for 24 weeks; ribavirin will be used for either 12 or 24 weeks, depending on early response. Investigators will evaluate sustained virological response (SVR), or undetectable HCV RNA, 24 weeks after completion of therapy.

Participants must be at least 18 years of age and HIV positive. They must have newly acquired HCV within the past six months and have detectable HCV RNA at study entry. Exclusion criteria include uncontrolled depression (which may be worsened by interferon) and other serious liver disease. Women may not be pregnant.

The study will enroll 20 participants at San Francisco General Hospital (415-476-4082 ext. 313 or 556). ***www.clinicaltrials.gov/ct2/show/NCT00845676.***

EraMune: HIV Eradication

A cure for HIV—either total viral eradication or a "functional cure" that allows people to stop taking ART—has been a topic of increased attention this year. The EraMune02 trial (a collaboration between the U.S. National Institute

of Allergy and Infectious Diseases, the French vaccine research group ORVACS, and others) will evaluate whether an intensified combination ART regimen along with an immune-modulating vaccine can eliminate HIV from the body, including hidden reservoirs.

In this Phase II trial, participants on standard ART with stable undetectable viral load will intensify therapy by adding the integrase inhibitor raltegravir (Isentress) and the CCR5 blocker maraviroc (Selzentry) for 56 weeks. Some will be randomly assigned to do this alone, while others will also receive an adenovirus-based therapeutic HIV vaccine. Investigators will measure plasma viral load, proviral HIV (latent HIV genetic material in resting cells), and HIV in gut lymphoid tissue; they will also look at HIV-specific immunity and T-cell activation.

Participants must be 18 to 60 years of age and on uninterrupted ART for at least three years. They must have had plasma viral load below 500 copies/mL for three years and below the limit of detection during the past year, as well as proviral DNA between 10 and 500 copies. CD4 count must be at least 350 cells/mm^3. There are additional criteria for adenovirus titers and blood cell counts. Exclusion criteria include hepatitis B or C coinfection, recent cancer, history of autoimmune disease, certain laboratory abnormalities, previous use of integrase inhibitors or CCR5 antagonists, and recent use of immune-based therapies. Women may not be pregnant or breastfeeding and all participants must agree to use barrier contraception.

EraMune02 will enroll 28 participants in the U.S. at the University of California at San Francisco (415-476-4082), Northwestern University in Chicago (312-695-5012), and Cornell University in New York City (212-746-7262). A similar study in Europe is evaluating ART intensification plus interleukin 7 (IL-7). ***www.clinicaltrials.gov/ct2/show/NCT00976404.***

CD4 Cell Gene Therapy

Another investigational approach to curing HIV is modifying CD4 T-cells to make them resistant to HIV entry. Sangamo Biosciences is conducting trials to test whether a zinc finger nuclease can be used to remove the gene for CCR5, one of the coreceptors HIV uses to enter host cells. People who naturally lack the CCR5 coreceptor are protected from HIV infection and disease progression, and studies have shown that humanized mice with CD4 cells altered in this way experience less HIV disease progression and CD4 cell loss.

Two related non-randomized Phase I trials are testing this approach in humans. Participants' CD4 cells will be obtained using a process called apheresis, in which blood is withdrawn, desired cells are removed, and the rest of the blood is returned to the body. Collected CD4 cells will be altered in the laboratory using the zinc finger (SB-728-T) technique, allowed to reproduce, and then returned to the patient. Participants will receive a single infusion containing one to three batches of 5–10 billion modified cells.

Investigators will evaluate the safety of the procedure, and measure the activity and persistence of the altered CD4 cells; some participants will be followed for as long as 10 years. A small number of participants in one trial will undergo ART interruption to see if the modified cells are protected from HIV infection.

The studies will enroll different types of patients. Some will have been on antiretroviral treatment for at least two years with continuous undetectable viral load starting six months after ART initiation, but with suboptimal CD4 cell recovery (below 500 cells/mm^3). Other participants will be on ART but still have viral load of 1,000 copies/mL or higher; some will have experienced treatment failure on two or more ART regimens.

Participants must be at least 18 years of age. Exclusion criteria include recent AIDS-defining illness, chronic hepatitis B or C coinfection, most cancers, certain laboratory abnormalities, recent use of certain drugs (including maraviroc, enfuvirtide [Fuzeon], and immune-modulating agents) or vaccines. Women may not be pregnant or breastfeeding and participants must agree to use effective contraception.

One trial aims to enroll 13 participants at the UCLA Center for AIDS Research and Education in Los Angeles (310-557-3729) and Quest Clinical Research in San Francisco (415-353-0212); ***www.clinicaltrials.gov/ct2/show/NCT01044654*** (SB-728-0902). The other will enroll 18 people at the University of Pennsylvania in Philadelphia (215-349-8091) and Jacobi Medical Center in the Bronx (718-918-3662); ***www.clinicaltrials.gov/ct2/show/NCT00842634*** (806383).