OPEN Clinical TRIALS FOR HIV/AIDS TREATMENTS

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Below is a partial listing of currently enrolling U.S. clinical trials gathered from various sources. Two of the main clinical trial resources have recently undergone significant changes. In the summer of 2002 HIV InSite's Trials Search database of clinical trials was replaced with TrialScope, a directory of organizations that conduct HIV/AIDS-related research. It provides contact information for each research site, the types of research each site conducts, links to organizational web sites, and any affiliations with major multicenter research groups. TrialScope is available at hivinsite.ucsf.edu (enter "TrialScope" in the search field); users select their desired state from a scroll-down list.

AIDSinfo, a new web site of the U.S. Department of Health and Human Services (DHHS), allows users to search for HIV/AIDS-related studies in a database maintained by ClinicalTrials.gov, a clinical trial listing for all diseases. The database may be accessed at either www.aidsinfo.nih.gov or www.clinicaltrials.gov. AIDSinfo also offers a toll-free telephone help line at 800-448-0440 (TDD/TTY 888-480-3739; international callers should dial 301-519-0459). Specialists are on hand Monday through Friday from 12:00 pm to 5:00 pm ET (9:00 am to 2:00 pm PT) to help locate trials and answer questions.

The AIDS Community Research Initiative of America (ACRIA) maintains a directory of HIV/AIDS clinical trials in New York state, New Jersey, Connecticut, and Philadelphia, and may expand to other areas of the country in the future. The ACRIA directory is available at www.criany.org/acria.html.

Call the telephone numbers below for more information about specific trials and a listing of study sites. Protocol (study) numbers, if available, are provided in parentheses at the end of each trial description.

Antiretroviral Therapy

Salvage Therapy: Dual vs Triple PIs

This study will compare a salvage (or "rescue") regimen containing three protease inhibitors (PIs) with two different combinations containing two PIs. The study will examine safety, tolerability, effectiveness, and blood drug levels, and will look at whether "boosting" PI drug levels with ritonavir (Norvir) can improve treatment response. Participants will be randomized to receive lopinavir plus ritonavir (Kaletra); ritonavir plus GW433908, GlaxoSmithKline's new PI candidate; or lopinavir, ritonavir, and GW433908. All participants will also take one or two nucleoside reverse transcriptase inhibitors (NRTIs) and tenofovir DF (TDF, Viread); the NRTIs are not provided by the study. Blood will be drawn and tested for drug levels at weeks 12, 24, and 48. A substudy (A5174S) will conduct more intensive sampling of blood drug levels; the first 20–25 participants enrolled in each arm will also be enrolled in the substudy.

Participants must be at least 18 years of age, have been on antiretroviral therapy for a total of at least one year, and have a viral load above 500 copies/mL within 60 days of prestudy screening despite being on a stable (unchanged) anti-HIV regimen for at least 12 weeks. Exclusion criteria include previous use of both lopinavir and amprenavir (Agenerase) for more than seven days each; untreated serious illnesses; or use of other experimental drugs, cancer chemotherapy, or immune-modulating drugs within 30 days of study entry. Women must not be pregnant or breast-feeding.

There are over 30 study sites including Atlanta (404-616-6313), Boston (617-726-3819), Chapel Hill (919-843-8761), Chicago (312-942-5865), Cleveland (216-844-8051), Denver (303-372-5535), Los Angeles (323-343-8283), New York City (212-305-2665), San Francisco (415-514-0550 ext. 362), and Seattle (206-731-8877). (ACTG A5143/A5147S)

Salvage Therapy: Indinavir plus Ritonavir

This randomized, open-label study will examine the safety and tolerability of indinavir (Crixivan) plus ritonavir as salvage therapy in participants who have experienced treatment failure with amprenavir, nelfinavir (Viracept), or

saquinavir (Fortovase or Invirase). The study will look at the pharmacokinetics (absorption, metabolism, and excretion) of indinavir and ritonavir, and assess the side effects of the two drugs. Researchers hope to determine whether "boosting" indinavir levels with ritonavir can allow indinavir to be taken twice rather than three times daily and at lower doses. Participants will be randomized to receive one of two different doses of indinavir with ritonavir for 24 weeks; all will also take two NRTIs (not provided by the study). Viral load and other measurements will be assessed at weeks 1, 2, 4, 8, 12, 16, 20, and 24. The week 2 evaluation will include an extensive pharmacokinetics analysis and will require a 12-hour hospital stay. Participants who experience virological failure during the trial may elect to either remain on treatment and be followed for 24 weeks, or else discontinue treatment.

Participants must be at least 18 years of age and have a viral load between 500 and 100,000 copies/mL within 45 days of study entry. They must have taken an antiretroviral regimen that includes two NRTIs plus nelfinavir, saquinavir, or amprenavir for at least 12 weeks before study entry. There must be at least one NRTI that has not been taken for more than 14 days, or never taken at all in the case of 3TC (lamivudine, Epivir). Exclusion criteria include taking any PIs other than those listed above or having HIV that is resistant to indinavir or ritonavir. Subjects must not have taken non-nucleoside reverse transcriptase inhibitors (NNRTIs), experimental drugs, or immune-modulating drugs within 30 days of study entry. Subjects also must not have had any active opportunistic illnesses (OIs), infections that require treatment, or fever within 14 days of study entry, or any cancers that require chemotherapy. Women may not be pregnant or breast-feeding. Finally, subjects must be willing and able to drink 1.5 liters of water or other fluids each day.

Study sites include Baltimore (410-955-4370), Birmingham (205-975-7925), Indianapolis (317-274-8456), New York City (212-420-4432), Philadelphia (215-349-8092), and San Francisco (415-476-9296 ext. 350). (ACTG A5055)

Salvage Therapy: T-20 and STI

This randomized, open-label study will compare immediate salvage therapy using combination antiretroviral therapy plus T-20 (enfuvirtide, Fuzeon) with a 16-week structured treatment interruption (STI) followed by combination therapy plus T-20. The study will examine whether STI helps improve the chances of successful treatment in people who have HIV that is resistant to multiple drugs. Virological response will be measured at weeks 16, 32, and 48. All participants will receive T-20 either immediately or after 16 weeks; T-20 is administered by subcutaneous (under the skin) injection twice daily. The other drugs in each subject's regimen should be the strongest antiretroviral combination available.

Participants must be at least 18 years of age and have used NRTIs, NNRTIs, and PIs. They must have been on continuous antiretroviral therapy for the 24 weeks before study entry, with no regimen changes in the preceding 12 weeks (except for substitutions within the same drug class due to toxicity). Participants must have experienced failure of at least one highly active antiretroviral therapy (HAART) regimen before study entry, and must have had a viral load greater than 500 copies/mL within the four months preceding the study. Those who experienced virological failure on their first HAART regimen are not eligible. Recent genotypic resistance testing must show at least two major mutations conferring resistance to NRTIs or PIs; participants must also show evidence of current or prior NNRTI resistance. Exclusion criteria include previous use of T-20 or T-1249; unstable HIV disease that increases risk of disease progression during the STI; an active, untreated OI or unexplained fever; active hepatitis C requiring treatment; cancer requiring chemotherapy; or other severe illness. Women must not be pregnant or breast-feeding.

This study is offered through the University of California at San Francisco (UCSF). For information contact Anna Smith, RN, at 415-476-9296 ext. 330.

STOP: Predictors of Progression during STI

Current federal HIV treatment guidelines recommend that therapy be started when CD4 cell counts fall below 350 cells/mm^3. Recent research suggests that people with CD4 cell counts above this level may be able to safely discontinue antiretroviral treatment. This prospective, observational study will look at predictors of immunological and clinical disease progression in participants with CD4 cell counts above 350 cells/mm^3 who stop antiretroviral therapy. In step 1, participants will discontinue anti-HIV therapy when they enter the study, for a maximum of 96 weeks. Viral load, CD4 cell counts, immunological function, neurocognitive (mental) changes, metabolic measurements, anthropomorphic (body shape) changes, health-care utilization, and quality of life will be assessed over the course of the study. Participants and their primary care providers will decide if and when to restart anti-HIV therapy; those who do so will be followed for an additional 24 weeks or until week 96 (step 2). This study does not provide any medications.

Participants must be at least 13 years of age and have been taking stable antiretroviral treatment for at least six months before study entry. They must have had a pretreatment CD4 cell count above 350 cells/mm^3; in addition, they must have had a CD4 cell count above 350 cells/mm^3 and a viral load below 55,000 copies/mL within 45 days of study entry.

Study sites include Dallas (214-590-0414), San Francisco (415-514-0550 ext. 354), and Stanford (650-723-2804). (ACTG A5170)

OPTIMA: Mega-HAART and STI

This study, conducted jointly by researchers in the U.S., the UK, and Canada, will examine the benefits of

"mega-HAART" regimens in people for whom treatment with NRTIs, NNRTIs, and PIs has failed. It will also look at whether a three-month break from treatment can help reduce drug resistance and allow people to better tolerate therapy. Some participants will be randomized to receive mega-HAART regimens containing five or more anti-HIV drugs, while others will take standard HAART regimens of up to four drugs. Drugs will be selected by a participant's own provider, guided by genotypic resistance testing. In addition, some subjects will be randomized to undergo a three-month antiretroviral drug-free period. Outcomes to be measured will include viral load, immunological function, time to serious side effects, time to AIDS-defining illness, and survival time. Subjects will be followed for an average of two years.

Participants must be at least 18 years of age, have been on continuous HAART for at least three months, and have experienced failure of at least two different multidrug regimens. Their two most recent test results while on therapy must have shown a CD4 cell count below 100 cells/mm^3 and a viral load above 5,000 copies/mL, or a CD4 cell count below 200 cells/mm^3 and a viral load above 10,000 copies/mL. Exclusion criteria include currently taking a regimen of five or more anti-HIV drugs, inability to tolerate multiple drugs, or current serious OIs. Women may not be pregnant or breast-feeding.

In the U.S., the study will be conducted at 30 Veterans Administration medical centers, including Baltimore (410-605-7199), Boston (617-232-9500 ext. 4669), Cleveland (216-791-3800 ext. 4788), Dallas (214-857-0410), Durham (919-286-0411 ext. 7308), Los Angeles (310-268-3015), Miami (305-324-4455 ext. 4800), New York City (212-951-3348), Palo Alto (650-493-5000 ext. 63408), Philadelphia (215-823-5847), Phoenix (602-277-5551 ext. 6796), Portland (503-220-8262 ext. 57140), and San Diego (858-552-8585 ext. 2626). (CTN 167)

Therapeutic Drug Monitoring

This study will examine whether increased doses of PIs are more effective than standard doses. It will also look at the benefits of using therapeutic drug monitoring (TDM, or measuring drug levels in individuals) and drug resistance testing to guide drug selection and dose adjustment. Participants who have experienced treatment failure on their second, third, or fourth HAART regimen will receive drug resistance testing while still taking their failing therapy. At study entry subjects will begin a salvage regimen using drugs selected by their own physicians based on the results of the resistance tests. Two weeks later blood will be drawn to assess drug levels, and a "normalized inhibitory quotient" (NIQ) will be calculated for each subject. Those with an NIQ of 1 or less will be randomized to receive either standard antiretroviral therapy (arm A) or adjusted doses of PIs based on TDM test results (arm B). Those with an NIQ greater than 1 will be randomized either to an observational arm (arm C) or to discontinue the study. Subjects in any arm who experience virological failure after the first week will be eligible to receive a second resistance test.

Participants must be at least 18 years of age and have a viral load of 2,000 copies/mL or more at study screening and at least one viral load measurement of 400 copies/mL or more within 60 days of study entry. Subjects' failing HAART regimens must consist of at least three but fewer than six drugs; at least one failing regimen must have included a PI. Participants must have been taking their current regimen for at least 12 weeks before study entry. Exclusion criteria include having an acute illness requiring treatment within 21 days of study entry, cancer requiring radiation or chemotherapy, or a history of pancreas problems. Subjects should not have recently received experimental drugs, immune-modulating drugs, or HIV vaccines, and may not have used a previous mega-HAART regimen containing more than six drugs. Women must not be pregnant or breast-feeding.

Study sites include Boston (617-632-0785), Chicago (312-572-4545), Denver (303-372-5535), New York City (212-263-6565), Pittsburgh (412-647-0771), Rochester (585-275-2740), San Francisco (415-514-0550 ext. 362), and Seattle (206-731-8877). (ACTG A5146).

Interrupted vs Continuous Treatment

This randomized study will examine the benefits of short cycles of intermittent HAART vs continuous treatment. It will attempt to determine whether intermittent treatment suppresses viral replication and reduces drug side effects. Participants in one study arm will continue to receive their current HAART regimen on an ongoing basis, while those in the other arm will stop treatment every other week (seven days on followed by seven days off therapy) for 72 weeks. Blood will be drawn at the end of off-treatment cycles every month, or else every other month.

Participants must be at least 18 years of age and have been taking anti-HIV therapy (at least two NRTIs plus either an NNRTI or a PI) with an undetectable viral load for at least one month. They must have a CD4 cell count of at least 175 cells/mm^3 within 30 days of study entry. Viral load must have been below 500 copies/mL for at least one month, and below 50 copies/mL at least once within 30 days of enrollment. Exclusion criteria include evidence of drug-resistant HIV, symptomatic OIs, hepatitis B, or serious conditions such as heart or kidney disease. Subjects may not be taking nevirapine (Viramune) or abacavir (Ziagen). Women must not be pregnant.

For more information and a list of study sites contact Diane Rock Kress, RN, at 301-435-8003 or 800-772-5464 ext. 58003. (M77-02-I-0013)

SMART: Drug Conservation vs Viral Suppression

The SMART study is a large trial comparing two HIV treatment strategies to determine whether participants at low risk of disease progression can safely reduce their use of anti-HIV therapy, thus staving off drug resistance and conserving treatment options until they are most needed. The drug conservation strategy involves episodic use of antiretroviral treatment for the minimum time necessary to maintain a CD4 cell count of at least 250 cells/mm^3. The viral suppression strategy will attempt to keep viral load at undetectable levels regardless of CD4 cell count. Participants will be seen at months 1, 2, 4, 6, 8, 10, and 12 after study entry, and then every four months thereafter. For those in the drug conservation arm, treatment will be stopped upon enrollment. Therapy will be restarted (or started for the first time) if the CD4 cell count falls below 250 cells/mm^3 and will be continued until there are two consecutive CD4 cell count measurements above 350 cells/mm^3. For those in the viral suppression arm, current treatment will be continued (or treatment will be initiated) and modified as necessary to keep viral load as low as possible. Some 6,000 participants will be followed for an estimated 6–9 years, until 910 primary events (disease progression or death) occur. Selected groups of participants will be followed with more intensive data collection for secondary outcomes related to cost, health-care utilization, metabolic complications of treatment, and quality of life.

Participants must be at least 13 years of age and have a CD4 cell count above 350 cells/mm^3. Subjects may be using any available antiretroviral and immune-modulating drugs at study entry. Women must not be pregnant or breast-feeding.

There are 20 study sites, including Boston (617-778-5456), Chicago (773-244-5802), Denver (303-436-7195), Fort Lauderdale (954-467-3006 ext. 223), Los Angeles (310-478-3711 ext. 40272), Minneapolis (612-347-7678), New Orleans (504-584-1971), New York City (212-939-2917), San Francisco (415-476-9554 ext. 23), and Washington, DC (202-745-8301). (CPCRA 065)

Shortstop: Resistance Testing

This study will evaluate the effectiveness of resistance tests in assessing whether specific drugs in an antiretroviral regimen are active against HIV. The trial is for people who have a detectable viral load despite treatment with d4T (stavudine, Zerit), ddI (didanosine, Videx), or efavirenz (Sustiva). Subjects will discontinue one of these drugs for two (d4T or ddI) or three (efavirenz) weeks, then the drug will be restarted. Blood will be drawn several times for viral load and genotypic and phenotypic resistance tests before, during, and after the discontinuation.

Participants must be at least 18 years of age, have a viral load between 5,000 and 100,000 copies/mL within six weeks prior to prestudy screening, and have a CD4 cell count above 50 cells/mm^3 within four weeks of enrollment or above 100 cells/mm^3 within eight weeks of enrollment. They must have been on stable anti-HIV therapy containing d4T, ddI, or efavirenz for at least six months. Subjects must not have had an acute infection or received a vaccine within the previous four weeks. Certain anti-HIV and other drugs are excluded. Women may not be pregnant.

For more information and study sites, contact 800-772-5464 ext. 57689 or 800-411-1222. (01-I-0004)

ESPRIT: Interleukin 2

This randomized, open-label trial will evaluate the benefits of subcutaneous interleukin 2 (IL-2, Proleukin) in people receiving antiretroviral therapy. IL-2 is a protein produced by certain white blood cells that stimulates the production of CD4 cells. Past studies have shown that IL-2 can increase CD4 cell counts in people with HIV, but it is not clear whether this has any clinical or survival benefit. The goal of this trial is to determine the effect of IL-2 therapy on the rates of AIDS-related illness and death. Participants will be randomly assigned to receive IL-2 or no IL-2 (there is no placebo). Those receiving IL-2 will have twice-daily injections for five-day cycles every eight weeks. Clinic visits will take place at least every four months. The study is expected to last five years.

Participants must be at least 18 years of age and have a CD4 cell count of at least 300 cells/mm^3. They must currently be taking anti-HIV therapy or be willing to start treatment. Exclusion criteria include any AIDS-defining illness in the past year, or current cancer or major heart, lung, kidney, central nervous system, or immune system disorders. Participants must not have taken IL-2 in the past, or corticosteroids or other immune-suppressing drugs or cytotoxic (cell-killing) agents within 45 days of study entry. Women must not be pregnant or breast-feeding.

There are over 30 study sites, including Atlanta (404-321-6111 ext. 3298), Berkeley (415-476-9554 ext. 22), Bethesda (301-435-7689), Detroit (313-343-7351), Houston (713-500-6751), Los Angeles (310-478-3711 ext. 42745), Miami (305-323-3267), Newark (973-483-3444 ext. 33), and San Francisco (415-476-9554 ext. 22).

Side Effects

Fat Irregularities and High Insulin Levels: Metformin and Rosiglitazone

This randomized, double-blind, placebo-controlled trial will evaluate the effect of metformin (Glucophage) and rosiglitazone (Avandia), taken alone or in combination, on high insulin levels and fat accumulation in the abdomen and other areas of the body. Metformin and rosiglitazone are currently approved by the Food and Drug Administration (FDA) for these indications in people without HIV. High

insulin levels and intra-abdominal obesity, both symptoms of HIV-related lipodystrophy syndrome, are risk factors for heart disease.

Several clinical measurements will be performed at study entry. Participants will be randomized to receive either metformin plus rosiglitazone placebo (arm A), rosiglitazone plus metformin placebo (arm B), metformin plus rosiglitazone (arm C), or placebos of both drugs (arm D). After 16 weeks participants who remain in the study will be switched to an open-label phase and all will receive metformin plus rosiglitazone for an additional 16 weeks. Clinic visits will take place at weeks 2, 4, 8, 12, 16, 18, 20, 24, 28, and 32. Insulin and glucose levels will be assessed; blood must be drawn after fasting overnight. In addition, visceral (internal) fat, subcutaneous fat, and thigh size will be measured.

Participants must be between 18 and 65 years of age and have a viral load below 10,000 copies/mL within 30 days of study entry. They must have specific blood insulin levels and meet physical restrictions based on height, weight, and amount and location of body fat. Subjects must have been taking a stable anti-HIV regimen for at least 60 days before study entry. Exclusion criteria include diarrhea, nausea, vomiting, or heart disease; previous use of drugs to control blood sugar; and use of immune-modulating drugs within six months of study entry. Participants may not be taking ritonavir with either simvastatin (Zocor) or lovastatin (Mevacor); there are also restrictions regarding use of hormones. Women must not be pregnant or breast-feeding.

Study sites include Birmingham (205-975-7925), Boston (617-726-3819), Chicago (312-695-5012), Cincinnati (513-584-8373), Honolulu (808-737-2751), Los Angeles (310-206-8029), New York City (212-420-4432), San Francisco (415-514-0550 ext. 362), and Washington, DC (202-687-5378). (ACTG A5082)

Women

Human Papillomavirus

This observational study will attempt to determine whether use of antiretroviral therapy affects the incidence of human papillomavirus (HPV) infection in women with HIV. HPV is associated with cervical, genital, and anal dysplasia (abnormal cell growth) and cancer. Researchers hypothesize that as anti-HIV treatment improves immune system function, women may be less likely to contract HPV or may experience less aggressive HPV disease. Participants will receive a pelvic exam and Pap smear at baseline, at weeks 24 and 48, and then every 48 weeks. Those with abnormal Pap smear results will receive a colposcopy (a procedure in which the cervix is examined with a lighted magnifying instrument). Blood will be collected to monitor HIV viral load, CD4 cell counts, and the presence of HPV antibodies.

Participants must be at least 13 years of age and intend to start antiretroviral treatment within 14 days of study entry, either as part of another clinical trial or under the care of their own physician. Exclusion criteria include previous use of antiretroviral therapy for more than 14 days, or use of certain immune-modulating, anti-HPV, or experimental drugs. Subjects may not have a history of cervical cancer and may not have participated in previous HPV trials.

Study sites include Baltimore (410-614-4487), Birmingham (205-975-7925), Boston (617-632-0785), Los Angeles (323-343-8283), Miami (305-243-2154), New York City (212-420-4432), San Francisco (415-514-0550 ext. 362), and San Juan (787-759-9595). (ACTG A5029)

Alternative Therapies

Peripheral Neuropathy: Medical Marijuana

This study will evaluate the short-term safety and efficacy of smoked marijuana to relieve pain related to peripheral neuropathy. The study will consist of four stages: a seven-day outpatient period during which pain will be measured, a two-day inpatient lead-in stage, a seven-day inpatient intervention stage during which participants will smoke marijuana cigarettes three times per day, and a seven-day outpatient follow-up stage. A heat/capsaicin (hot pepper) pain test will be administered on days 1 and 7. Participants who complete all study stages will receive $600.

Participants must be at least 18 years of age, have HIV-related painful neuropathy, have been taking stable anti-HIV therapy for the past eight weeks, and have used marijuana at least six times in the past. There are no CD4 cell count or viral load requirements. Exclusion criteria include use of smoked marijuana within 30 days of study entry; current tobacco smoking; active substance abuse; history of heart, lung, kidney, or liver disease; and active OIs requiring treatment. Women must not be pregnant or breast-feeding.

The study will take place in San Francisco (415-476-9554 ext. 21). (00018269)

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Lifestyle Habits That Contribute to Optimal Health

- Eat a low-fat diet based on fruits, vegetables, and whole grains
- Exercise daily for at least 30 minutes
- Sleep at least eight hours every night
- Avoid smoking and second-hand smoke
- Reduce alcohol intake