HIV Treatment Update

Atripla No Longer Recommended as First-Line HIV Therapy

Late this spring, the Department of Health and Human Services (DHHS) made some key changes to first-line HIV treatment recommendations. The DHHS recommendations are a guide for clinicians as they decide which antiretrovirals to prescribe. Among other revisions, one significant change was that the NNRTI-based regimen in the widely-used combination pill Atripla (efavirenz/tenofovir/emtricitabine) was downgraded from a “recommended” regimen to an “alternative” regimen for people just beginning antiretroviral therapy (ART).

Atripla is a combination pill containing the NNRTI efavirenz plus the NRTI backbone of tenofovir/emtricitabine that has been widely prescribed since its approval by the FDA in 2006. As the first one-pill, once-daily complete HIV treatment regimen to hit the market, Atripla quickly became one of the most commonly prescribed and used drugs to treat HIV because of its ease of use. This is also due to efavirenz’s benefits: The drug provides robust viral suppression for many, works relatively well even when doses are missed and is less costly than many other HIV medications on the market. A study published in 2010 reported that almost a third of people with HIV in the U.S. taking ART were using Atripla. In 2011, global sales of Atripla reached $3.2 billion.

But “virtually everyone” who starts taking efavirenz experiences some kind of central nervous system side effect such as dizziness, abnormal dreams, depression or grogginess when they start the medication, which may or may not continue long-term, says Paul Sax, MD, clinical director of the HIV Program and Division of Infectious Diseases at Brigham and Women’s Hospital, professor of medicine at Harvard Medical School, and a member of the DHHS panel that revamped the treatment guidelines. With many other good HIV treatment options out there, it’s now easier to prescribe regimens that require less side effect management. The updated list of recommended first-line therapies now includes five regimens. One is a boosted protease inhibitor regimen and four others contain an integrase inhibitor with an NRTI backbone.

Read more at: http://bit.ly/1OAJJJE

Health and Wellness

Weight Gain, Inflammation and HIV

Two new studies reveal the impact that weight gain and abdominal obesity may have on the health of people with HIV. Even for people who are successfully treating HIV with antiretrovirals and have controlled viral loads, weight gain and mid-section obesity appears to heighten immune activation and inflammation—and may ultimately result in poorer health outcomes including mortality and neurocognitive impairment.

In the Prospective Evaluation of Antiretrovirals in Resource Limited Settings (PEARLS) study, researchers measured changes in body mass index (BMI) in 246 HIV-positive people for 48 weeks. They also measured markers of inflammation such as soluble CD14 (sCD14). Among those who were overweight or obese, each incremental gain in BMI was associated with an increase in sCD14, and this association held true even when participants were on antiretroviral therapy (ART) and the researchers adjusted for baseline viral load. sCD14 is associated with poorer survival outcomes during HIV treatment, so these results suggest that weight gain, especially for people who are already overweight, may increase risk of mortality.

A second study, called CNS HIV Antiretroviral Therapy Effects Research (CHARTER), assessed changes in abdominal obesity and inflammatory markers along with neurocognitive function in 152 HIV-positive people on ART. This study hypothesized that inflammation and immune activation link abdominal obesity to neurocognitive impairment—and that this relationship exists even when HIV infection is well-controlled. This is precisely what the study found. Neurocognitive impairment was significantly greater for participants who were abdominally obese, and this relationship was mediated by two inflammatory proteins called IL-6 and soluble CD40L. The researchers speculate that determining the source of IL-6 and soluble CD40L “will be important in unraveling the mechanism linking obesity and NCI [neurocognitive impairment] in HIV+ and possibly HIV- populations.”

Reducing abdominal obesity may be key to reducing inflammation and neurocognitive impairment that some people living with HIV may experience, the researchers conclude. Preventative measures like healthier diet and exercise could help, and hormone-releasing agents that reduce abdominal fat and other anti-inflammatory drugs may also be helpful in reducing inflammation.
Clinical Research Opportunities

Studies are listed with brief descriptions only. Additional inclusion and exclusion criteria may apply. For more information, please contact the study site directly.

**Bridge HIV**
San Francisco Department of Public Health
25 Van Ness, Suite 100
San Francisco, CA 94102

- Pre-Exposure Prophylaxis (PrEP) study for women: Study testing a vaginal ring containing 2 different HIV meds. Vaginal rings that slowly release HIV meds could be an effective alternative to oral PrEP or vaginal gels. Participants wear the vaginal ring for 28 days with 13 visits over 5 weeks. Must be female, HIV negative, ages 18–45. Compensation up to $250/visit. Visit www.joinprep.org or call 415-437-7485. NS
- Pre-Exposure Prophylaxis (PrEP) study: Study testing the safety of a pill and a long-acting injectable (a shot). Must be HIV negative, healthy, & age 18–50. May be male, female, or transgender. Compensation is $50–$75/visit. Visit www.sfsready.org or call 415-437-7485.
- HIV Vaccine: Study evaluating the safety and dosage of HIV vaccines. Must be HIV negative, healthy, and age 18–50. May be male, female, or transgender. Compensation is $50–$75/visit. Visit www.SFisReady.org or call 415-437-7485. You cannot get HIV from the study vaccine.
- DOT-DBS: Study evaluating if dried blood spots can be used to accurately measure medication adherence. Truvada doses taken for 2, twelve-week periods. Office visits are daily Mon-Fri with video-messaging dosing visits on weekends. Compensation for each visit when hair & blood samples are collected. Visit www.joinprep.org or call 415-437-7485.

**Optimus Medical**
870 Market Street, Suite 870
San Francisco, CA 94102
415-423-4055 / sfelsot@studyoops.com

- Study to evaluate switching from a regimen consisting of efavirenz/emtricitabine/tenofovir disoproxil fumarate to emtricitabine/rilpivirine/tenofovir alafenamide in virologically suppressed, HIV+ people. $50/visit and $50/travel.
- Study to evaluate the safety and efficacy of emtricitabine/rilpivirine/tenofovir alafenamide in HIV+ people who are virologically suppressed on emtricitabine/rilpivirine/tenofovir disoproxil fumarate. $50/visit and $50/travel.

**East Bay AIDS Center (EBAC)**
3100 Summit Street, 2nd Floor
Oakland, CA 94609
www.altabates.com/clinical/aids_scvs.html
510-863-0021

- Connecting Resources for Urban Sexual Health (CRUSH): For people age 18-29 to review (and treat) sexual health needs; providing either PEP or PrEP to HIV-negative participants if they need it. For HIV+ or HIV-negative men who have sex with men, trans men or woman, or with a known HIV+ partner. A small stipend for completing a questionnaire four times and STD testing and treatment provided.
- GS-US-366-1216: Switch study to evaluate the safety and efficacy of emtricitabine/rilpivirine/tenofovir alafenamide in HIV+ people who are virologically suppressed on emtricitabine/rilpivirine/tenofovir disoproxil fumarate. $75/visit. miki.mettinger@kp.org. 415-833-3223.
- MK-1439-024: Study to evaluate a switch to MK-1439A in HIV+ people virologically suppressed on a ritonavir-boosted PI and two NRTIs. $75/visit. miki.mettinger@kp.org. 415-833-3223.

**California Pacific Medical Center - St. Luke’s**
1580 Valencia Street
San Francisco, CA 94110

- HCV geno 2 and 3: new AbbVie combination: protease inhibitor + NSSA inhibitor for 12 weeks. Call Juliana at 415-600-1368 or Angela at 415-641-5430. NS
- Harvoni for 24 weeks in HCV geno 1 patients with poor kidney function (GFR < 30 ml/min). Call Juliana at 415-600-1368 or Angela at 415-641-5430. NS

**Kaiser Clinical Trials Unit**
4141 Geary Boulevard, Suite 219
San Francisco, CA 94110
415-833-3487

- GS-US-366-1160: Study to evaluate switching from efavirenz/emtricitabine/tenofovir disoproxil fumarate fixed dose combination to emtricitabine/rilpivirine/tenofovir alafenamide in virologically suppressed, HIV+ people. $75/visit. brooke.anderson@kp.org. 415-833-3487.

**Metropolis Medical Group**
815 Hyde Street, Suite 301
San Francisco, CA 94109
www.metropolismedical.net

Studies provide free blood work-up, study drugs, and compensation between $500-$750.

- Sword: Switch study to a "nuc-sparing" regimen, containing Tivicay® and Edurant®, once/day. HIV+ people qualify if they are on their 1st or 2nd HIV treatment with an undetectable VL. Compensation is $75/visit; study ongoing for 3 years with HIV meds provided.
- Amber: Switch study for HIV+ people with undetectable viral load on a boosted PI regimen (i.e.Prevista*/Norvir® or Reyataz*/Norvir®) and Truvada®. Switch to an investigational once-daily regimen containing darunavir, cobicistat, emtricitabine and tenofovir alafenamide (TAF) or darunavir/cobicistat and Truvada. Compensation is $75 per study visit. NS
- Striving: A switch study for people with an undetectable VL to Triumeq® (one tablet containing Dolutegravir/Abacavir/Lamivudine). Participants need to be on their 1st or 2nd HIV regimen. 48 week study. Compensation is $75 per study visit.
- TMC114IFD3013: People with HIV, but never treated (“treatment-naive”) and detectable VL will start Reyataz*/Norvir®, and Truvada® or an investigational once-daily regimen containing darunavir, cobicistat, emtricitabine and tenofovir alafenamide (TAF). $75 per study visit.

**ABBREVIATIONS**

| NS | New study in this issue, or changes to an existing study |
| ARV | Antiretroviral |
| > | Greater than |
| < | Less than |
| VL | Viral Load |
| PI | Protease Inhibitor |
| II | Integrase Inhibitor |
| NRTI | Nucleoside/Nucleotide Analog |
| NNRTI | Non-nucleoside Analog |
**San Francisco Veterans Affairs Medical Center**
4150 Clement Street
San Francisco, CA 94121

- A prospective, randomized, placebo-controlled, double-blind clinical trial to evaluate whether injected tesamorelin (Egrifta), 2 mg once daily, increases the risk of development or progression of diabetic retinopathy in HIV-positive people with abdominal lipohypertrophy (excess deep-belly fat) and type-2 diabetes. Compensation is $50 per study visit (15 visits over 3 years). Call 415-683-9895.

**Stanford Clinical Trials Unit**
1000 Welch Road, Suite 202
Palo Alto, CA 94304
650-723-2804
http://actu.stanford.edu

Compensation is provided for travel and meals for most studies.

- AS332: The main purpose of this clinical trial is to see if pivastatin can prevent heart disease and heart disease-related deaths in people with HIV infection who are taking HIV medications. Participants must be HIV infected, between the ages of 40 and 75 years, on ARVs for at least 6 months, CD4>100, no history of cardiovascular disease and not currently using a statin drug.

**Substance Use Research Unit**
San Francisco Department of Public Health
525 Van Ness, Suite 500
San Francisco, CA 94102

- M2.0: Study testing if taking a medication (mirtazapine) reduces meth use in men who have sex with men. Study includes weekly substance use counseling. Compensation is $5 to $45 per study visit. To see if you are eligible, please call us at 415-437-6319. Email: m2.study@sfdph.org; Website: www.m2study.org
- TREX: Study testing if a monthly injectable medication (naltrexone) reduces meth use among men who have sex with men. Includes weekly substance-use counseling. Compensation is $10–$50 per visit. 415-554-9013. Email: trex.sf@sfdph.org; Website: www.trexsf.com.
- Single-Session Intervention Project (SIP): A project for gay and bisexual men who drink alcohol. A one-time intervention that involves a conversation with a counselor about your alcohol use and how it relates to your general wellbeing and sexual health. Open for HIV+ or negative people. Compensation is a $40 gift card for your time. Please call: 415-437-6314.

**UFC/San Francisco General Hospital**
SCOPE Study Group
1001 Potrero Ave, Ward 5B & 995 Potrero Ave, Building 80, Ward 84
San Francisco, CA 94110
http://hiv.ucsf.edu/research/scope.html

- Lymph node biopsy study: A study seeking to measure and analyze the HIV viral reservoir in lymph nodes. Study involves an inquinal lymph node biopsy and blood draw. Enrolling newly infected and/or treatment-naive, ART-suppressed >12 months, or HIV-negative. Other criteria apply. Compensation provided. Call 415-476-4082, ext 144; email: Marianna.Kerbleski@ucsf.edu.
- DARE: A study to identify how & where HIV persists in the body. Multiple visits to measure HIV viral reservoirs; may include blood draws, leukapheresis, and tissue biopsies. Enrolling newly infected and/or treatment-naive or continually ART-suppressed >10 years. Compensation provided. Call 415-476-4082, ext 139, or ext 144; email: Rebecca.Hoh@ucsf.edu or Marian.Kerbleski@ucsf.edu
- Fecal Microbial Transplantation (FMT): Study to determine if the transfer of intestinal microbial communities is safe and can improve immune function and reduce inflammation in HIV+ patients on ART. Must have CD4 count > 200, undetectable viral load. Compensation provided. Contact Montha Pao at 415-476-4082 x140 or email montha.pao@ucsf.edu.
- RADL: A study to assess ARV levels in lymphoid tissues by drug regimen and if ARV drug levels are associated with the amount of HIV in the body. 2-3 visits with questionnaires, blood draws, flexible sigmoidoscopy or colonoscopy procedure (with biopsies) and optional lymph node biopsy procedure. Must be on first & only ARV regimen of Truvada OR Epzicom plus Istentress OR Reyataz and Norvir OR Prezista and Norvir. On ART for > 1 year with undetectable VL. Compensation provided. Call 415-476-4082 ext 155 or email Lauren.Reed-Guy@ucsf.edu.
- SCOPE Study: Study recruiting: (1) elite controllers (HIV+ with VL <2,000 copies/mL & not taking ARVs), (2) individuals with no prior ART, (3) long-term non-progressors (HIV+ for >10 years with a CD4 count >500 cells/mm3 with no ARVs), and (4) HIV-negative controls. Study involves interviews & blood draws every 2–4 mos. Compensation provided. Call 415-476-4082, ext. 139 or ext 144, Rebecca.Hoh@ucsf.edu or Marian.Kerbleski@ucsf.edu

- LIFE-HIV: Study to see if blood pressure medication losartan with current ART decreases inflammation & improves immune function. Must be over 50 years, taking ART for 2 years with undetectable viral load for 1 year, and CD4 <600. Compensation provided. Call 415-476-4082, ext. 155, or email Lauren.Reed-Guy@ucsf.edu

- Observational SCOPE study assessing immune response to flu vaccine. 3 visits for blood draw and questionnaire. Can either be 1) HIV+, age 50-65 years with documented undetectable VL & >3 years on current ART or 2) HIV-negative, age 50-80. Flu vaccine not provided. Compensation provided. Call 415-476-4082, ext. 330 or ext 139, Mollie. Hudson@ucsf.edu Rebecca.Hoh@ucsf.edu

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**UCSF/Adult AIDS Clinical Trials Unit**

995 Potrero Ave, Building 80, Ward 8
San Francisco, CA 94110
415-476-4082 ext. 358
http://php.ucsf.edu/rsrch_trials.shtml

- A5332: Study to see if pitavastatin can prevent heart disease and related deaths. Participants must be HIV+, 40-75 years, on ARVs for at least 6 months, CD4 >100, no history of cardiovascular disease, and not currently using a statin drug. NS

- A5314: Study to evaluate the effect of low dose methotrexate on markers of cardiovascular disease and inflammation. Participants must be >40 years old, on ART, HIV RNA undetectable ≥24 weeks, CD4 cell count >400, with cardiovascular disease risk. Compensation is $20-$50 per visit.

- A5325: Study to evaluate Isotretinoin on immune activation. Participants must be HIV+, on ART therapy for >12 months, HIV RNA undetectable, CD4 <350, no active hepatitis B or C infection. Compensation is $20 per visit.

- A5315: Safety and tolerability study of Romidepsin for people taking ARVs with an undetectable viral load. Participants must be taking ART that includes raltegravir, deltaritgravir, or efavirenz-based regimen, viral load <50 for past 12 months, CD4+ cell count >300, men and non-pregnant women >18 years. $20/visit, $150-$300 per procedure completed.

- A5336: 12-week study evaluating if ruxolitinib will reduce inflammation. HIV+ patients on HIV treatment, CD4 >350, undetectable VL for 2 years, willing to be randomized to 5 weeks of treatment or no study drug at all. NS

- A5337: Evaluation of sirolimus to reduce inflammation and the HIV latent reservoir. HIV-infected patients, with CD4 cell counts of >400 & HIV RNA <75 or less for at least 24 months, will receive 20 weeks of open label, oral sirolimus, an inhibitor of T cell activation that has been used as an antirejection drug in organ transplantation. Cannot be on an ART regimen containing an HIV protease inhibitor or cobicistat. Active HCV or HBV prohibited. NS

- A5342: Vaccine study. Phase I study of monoclonal antibody to evaluate impact on HIV reservoir: HIV+ patients, well controlled on ART x at least 2 years with HIV RNA < limit of detection, CD4 > 200, will receive 2 IV infusions of monoclonal antibody and 2 infusions of placebo (4 infusions total). Active viral hepatitis is exclusionary. NS

- A5327: Acute HCV treatment study in HIV/HCV coinfected: All oral sofosbuvir/ledipasvir x 8 weeks for acute HCV infection (6 months or less from first lab abnormalities) in HCV genotype 1 or 4. NS

- Three, all oral, interferon-free triple therapy studies for HIV/HCV coinfected patients with HCV genotypes 1 & 4. Will enroll both treatment naive and experienced (including prior sofosbuvir failures). Liver biopsy not required. ART permitted includes darunavir/r, atazanavir/r, and can be on an ART regimen containing an HIV protease inhibitor or cobicistat. Active HCV or HBV prohibited. NS

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**UCSF/Anal Neoplasia Clinic**

1701 Divisadero Street, Suite 480
San Francisco, CA 94115

- Anal cancer rates are rising among people living with HIV. The ANCHOR study’s goal is to find the best way to prevent anal cancer among HIV+ men and women ≥35 years old. Study visits are every 6 months for at least 5 years. Participants are compensated $100 per visit. For more info go to anchorstudy.org or call 415-353-7443.

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**UCSF Memory and Aging Center HIV Research Group**

675 Nelson Rising Lane
San Francisco, CA 94115
415-476-1688
HIVOver60@memory.ucsf.edu

- UCSF HIV Elders Study: A new behavioral intervention study examining the usefulness of Mindfulness Based Stress Reduction (MBSR) to alleviate symptoms of attention, executive functioning, stress, and anxiety in older (aged 60 and above) HIV-infected individuals. Study includes an 8-week MBSR course, cognitive testing, blood draw, and MRI; eligible subjects will be followed for up to one year. Must demonstrate mild to moderate cognitive impairment and have controlled viral load. Other criteria apply. Compensation is $15-$50 per visit study. (www.valcourlab.ucsf.edu)