Colorado AIDS Clinical Trials Unit
SCHOOL OF MEDICINE
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

Studies Open to Enrollment

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HIV Prevention

***GS2055—DISCOVER*: A Phase III, Randomized, Double-blind Study to Evaluate the Safety and Efficacy of Emtricitabine and Tenofovir Alafenamide (F/TAF) Fixed-Dose Combination Once Daily for Pre-Exposure Prophylaxis in Men and Transgender Women Who Have Sex with Men and Are at Risk of HIV-1 Infection**

This is a double-blind study comparing the safety and efficacy of F/TAF versus F/TDF administered orally once daily (QD). All participants will remain on blinded treatment for at least 96 weeks, after which participants will be unblinded and offered the option to remain on open-label F/TAF in an open-label extension (OL). Those who chose to continue on study in the OL phase will take F/TAF for 48 weeks. This study intends on enrolling 5,000 MSM and TGW (male at birth) at risk of HIV-1 infection through sexual exposure with other men.

Requirements to Enter Study:

- HIV-1 negative
- MSM or TGW (male at birth) who have at least one of the following:
    - Condomless anal intercourse with at least two male partners in the past 12 weeks (partners must be either HIV-infected or of unknown HIV status), **or**
    - Documented history of syphilis in the past 24 weeks, **or**
    - Documented history of rectal gonorrhea or chlamydia in the past 24 weeks
- ≥18 years of age
- No history of HBV or HCV

New Antiretroviral Strategies

***GSK First Long-Acting Injectable Regimen--FLAIR:* A Phase III, Randomized, Multicenter, Parallel-Group, Open-Label Study Evaluating the Efficacy, Safety, and Tolerability of Long-Acting Intramuscular Cabotegravir and Rilpivirine for Maintenance of Virologic Suppression Following Switch from an Integrase Inhibitor Single Tablet Regimen in HIV-1 Infected Antiretroviral Therapy Naïve Adult Participants.**

This study will be carried out over 120 weeks in 570 individuals (285 per arm). All participants will begin ABC/DTG/3TC regimen for 20 weeks prior to enrollment. Those with a VL <50 c/mL at week 4 will be randomized to either continue ABC/DTG/3TC or to begin CAB 30mg + RPV 25mg once daily upon enrollment. For the CAB + RPV arm, at week 4, the regimen will switch to long-acting IM injections. Two more IM injections will occur at week 8 and 12.

Requirements to Enter Study:

- HIV-infected
- ≥18 years of age
- Antiretroviral treatment naive

***GSK 205543—GEMINI*: A Phase III, randomized, double-blind, multicenter, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of dolutegravir plus lamivudine compared to dolutegravir plus tenofovir/emtricitabine in HIV-1 infected treatment-naïve adults**

This study is being conducted to compare a simplified two-drug regimen of dolutegravir plus lamivudine with a standard three-drug first-line regimen in HIV infected, ART-naïve adults. The study is designed to demonstrate the non-inferior antiviral activity of DTG + 3TC once daily compared to DTG + TDF/FTC fixed dose combination once daily at 48 weeks. This study will characterize the long-term antiviral activity, tolerability, and safety of DTG + 3TC through week 148. The study aims to enroll 700 HIV-infected, ART-naïve participants; 350 participants will be in each arm.

Requirements to Enter Study:

- HIV-infected
- ≥18 years of age
- Treatment naive
- Screening VL must be 1000 to ≤ 500,000 c/mL

Finding a cure for HIV

A5315 – Safety and Tolerability Study with a single dose of Romidepsin (RMD) for people taking antiretroviral drugs with an undetectable viral load

This study is designed to look at a one-time infusion of Romidepsin (RMD) to make sure it is safe, easy to take, and to see if it can wake up the hidden or sleeping HIV virus so that it will come out of hiding and be attacked or wiped out in an attempt to decrease the HIV reservoir. Each person will go into one of three groups (depending on when you enter this study) that will be assigned to one of three doses. Each group will enroll 15 subjects: 12 will receive RMD and 3 will receive a placebo (salt water solution) that does not contain RMD. Neither you nor the study staff will know whether you will receive RMD or the placebo (salt water solution). It is important to have placebos in this study to help us better understand any changes in viral load that may be seen. During this study, you will be seen in the clinic up to 8 times. Study staff will let you know the requirements and length of each visit. You will be admitted to the hospital for one to two nights to measure the amount of drug in your blood over time and to measure your viral load.

Requirements to Enter Study

- Taking combination antiretroviral therapy (ART) that does not include a protease inhibitor (PI)
- HIV-1 RNA (viral load) < 50 copies/ml or undetectable for past 24 months
- CD4+cell count $\geq$ 300 cells/mm^3
- Men and non-pregnant women age $\geq$18 years
- Agree to follow birth control requirements, as needed

A5336 – A Randomized, Pilot Study of Ruxolitinib in Antiretroviral-Treated HIV-Infected Adults

Ruxolitinib is an FDA-approved medication to treat myelofibrosis, a disorder not related to HIV-1 infection in which bone marrow is replaced by scar (fibrosis) tissue. Many of the cytokines (regulators of the body's reaction to infection, immune response, and inflammation) affected by myelofibrosis are also affected by HIV-1. Because ruxolitinib reduce these cytokines in people with myelofibrosis, it is proposed that it may also reduce inflammation in the bodies of people living with HIV-1 in whom the virus is suppressed by ART. Laboratory experiments have also shown that ruxolitinib may reduce the ability of HIV-1 to produce more copies of itself. This purpose of this study is to learn about the safety and tolerability of the use of ruxolitinib in people with HIV-1 infection who have an undetectable viral load. We want to learn whether ruxolitinib will decrease inflammation and immune activation in the body, whether it will affect the level of HIV in your blood, and how it

interacts with ART in the blood. This is a 12 week study which will randomize participants to either 5 weeks of ruxolitinib or no study treatment.

Requirements to Enter Study:

- HIV+ men and women between the ages of 18 and 75
- Be on continuous HIV-1 treatment for the last 2 years with undetectable viral load, and no plans to change medications for the duration of the study
- CD4+ count ≥350
- No other medical conditions or taking any medications that would be contraindicated for individuals taking study medication

A5321 – Decay of HIV-1 Reservoirs in Subjects on Long-Term Antiretroviral Therapy: The ACTG HIV Reservoirs Cohort (AHRC) Study

AHRC (pronounced "ARC") is a study of differences and changes over time in HIV reservoirs (groups of HIV infected cells that 'hide' from anti-HIV medications). Participants will attend visits twice a year for about 7 years. At these visits, blood and a small amount of hair will be collected from all participants. Some participants who meet additional criteria may be asked to participate in an additional spinal tap procedure. This study is being done to try to answer questions about the ways that HIV infection is controlled. This may have to do with a person's viral load and CD4 count, when they started their anti-HIV medications, and genetic factors.

Requirements to Enter Study:

You must be in one of the following three groups:

- Group 1: Participated in ACTG study A5276s or A5001. If you were a part of A5001 you must have also participated in one of these other studies: ACTG 384, A5095, A5142, A5202, or A5257.
- Group 2: Began your anti-HIV medications during the very early part of your HIV infection
- Group 3: Had a viral load less than 500 copies/mL prior to starting any anti-HIV medications.

Additionally, you must:

- Be a HIV-infected man or woman, ≥ 18 years of age
- Be taking anti-HIV medications that have been controlling your viral load for 1-2 years (depending on which Group you will be in).
- Have never stopped your anti-HIV medications for greater than 3 weeks.
- Have no active Hepatitis B or C infection, an autoimmune disorder or a condition requiring steroid therapy.

Improving the health of people on antiretroviral therapy

A5332 – Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE)

HIV causes inflammation inside the body, which can contribute to diseases such as heart disease. HIV medications can lower inflammation somewhat, but levels of inflammation can remain higher compared to people who are not infected with HIV. Statins are used to lower cholesterol and levels of triglycerides, but some clinical trials have shown that statins may have other benefits. Pitavastatin is a statin used to treat high cholesterol and lowers triglyceride levels in the blood. The purpose of this study is to see if pitavastatin can prevent heart disease and heart disease related deaths in people with HIV infection who are taking HIV medications. This is a 6 year study with participants randomized to pitavastatin or a placebo.

Requirements to Enter Study:

- HIV+ men and women between the ages of 40 and 75 (women cannot be pregnant)
- On ARTs for at least 6 months prior to study entry
- CD4+ cell count >100

- No history of cardiovascular disease (history of heart attack, stroke, etc.)
- No history of cancer in the last 3 years
- Not currently using statins

A5324 – A Randomized, Double-Blinded, Placebo-Controlled Trial Comparing Antiretroviral Intensification with Maraviroc and Dolutegravir with No Intensification or Intensification with Dolutegravir Alone for the Treatment of Cognitive Impairment in HIV

A5324 is a study for HIV-infected individuals with undetectable HIV viral load who have mild neurocognitive impairment. Subjects will be randomized to one of three study arms to add either placebo for maraviroc (MVC) and placebo for dolutegravir (DTG) (Arm A), DTG active drug and placebo for MVC (Arm B), or MVC and DTG active drugs (Arm C) to their existing antiretroviral therapy (ART). The main purpose of the study is to see if intensification with MVC and DTG will improve neurocognitive performance and functioning in subjects who have at least mild neurocognitive impairment and have an undetectable viral load. Safety and tolerability of MVC and DTG when added to a stable ART regimen and the effect of the study drugs on markers in the blood and spinal fluid will also be studied.

Requirements to Enter Study:

- HIV-1 infected men and women at least 18 years of age
- On current ART for at least 12 months
- Undetectable HIV viral load (<50 copies/mL)
- No more than one viral load between 50 and 200 copies/mL (only one "blip") in the past 6 months
- At least mild HIV-associated neurocognitive impairment on neurocognitive tests done at screening
- Able to complete the neuropsychological tests in English
- No medical condition not related to HIV that may cause cognitive impairment
- No current hepatitis C
- No prior or current use of any integrase inhibitor or MVC
- No active syphilis or treatment for syphilis

COPD and HIV: **Immunosuppressive effects of smoking and HIV-1 on the development of lung disease**

This study plans to learn more about pulmonary (lung) complications and disease in HIV/AIDS. The study consists of 2-4 clinic visits, with visits 2-4 testing for COPD (if not previously completed) which can include 6-minute walk, chest CT scan, lung function tests and questionnaire completion. All participants will be asked to undergo a bronchoscopy and donate a single stool sample.

Requirements to Enter Study:

- Volunteers between the ages of 30 and 70 years old
- Both HIV-negative and HIV-positive individuals with and without chronic obstructive pulmonary disease (COPD)
- If HIV-positive, on a stable three-drug ART regimen with undetectable viral load for past 6 months

HIV and Lipodystrophy: Factors mediating gut microbiota dysbiosis and metabolic disease in HIV patients

This study aims to determine whether the development of lipodystrophy syndrome is related to changes in the types of bacteria that live in the gut(stool) that occur in HIV-infected individuals. The study will consist of 2-3 clinic visits which will include a physical exam, screening for lipodystrophy, blood collection, and a diet questionnaire. All participants will be asked to donate a single stool sample.

Requirements to Enter Study:

- Non-obese HIV-positive people between the ages of 18-70

- Exhibiting the symptoms described above, indicating the possibility of lipodystrophy

Diet Modification Study: Diet/Gut Microbiome Interaction and Influence on Inflammatory Disease in HIV Patients

This study plans to learn more about the short-term effects of consuming either a Western-style diet or an Agrarian-style diet (a diet low in fat and high in fiber/carbohydrates) on inflammatory and metabolic markers in people with and without HIV. The study will consist of 4 clinic visits which will include a physical exam and blood collection at each visit. At entry, participants will be asked to answer two dietary questionnaires and will be randomized to a 2-week supplied diet (Agrarian vs. Western). Visit 3 will supply each participant with dietary counseling and recipes to continue study diet for the following two weeks. All participants will be asked to donate 3 stool samples. Participants have the option to undergo a flexible sigmoidoscopy/mucosal biopsy at visits 2 and 4.

Requirements to Enter Study:

- HIV-positive and negative men and women between the ages of 18 and 65
- BMI between 21-29 kg/m^2 (non-obese)
- If HIV-positive, treated with ART for at least 12 months with no changes in ARVs over the past 6 months
- If HIV-positive, plasma HIV-1 RNA ≤50 copies/mL in preceding 6 months

Exercise for Healthy Aging in HIV-Positive and Negative Individuals

This study aims to determine the best "dose" of exercise in people aging with HIV, and whether or not the dose differs from people without HIV. Exercise sessions (cardiovascular + strength training) are 3x/week at the Anschutz Exercise Research Facility (Leprino) for 6 months.

Requirements to Enter Study:

- Men and women aged 50-70
- If HIV-positive, on ART for at least 2 years with no detectable viral load
- If HIV-positive, CD4 count >200
- No active Hepatitis B or C, or chronic infections
- If diabetic, must be well-controlled on oral medications (no insulin)
- BMI between 20 and 40

Hepatitis C co-infection

A5320 – Viral Hepatitis C Infection Long-term Cohort Study (V-HICS)

This is a five year observational study for participants who are co-infected with HIV and Hep C virus (HCV), or are mono-infected with HCV alone. Participants will begin a new Hep C treatment as part of the study (medication not provided). Blood will be collected to look at and compare the differences in each person's HCV and genetic differences in each person that may play a role in success or failure of treatments. Questionnaires will be given to measure each person's quality of life and how success/failure of treatment affects quality of life. This study will also help us understand how long resistance to new HCV medications lasts in a person and whether if affects future HCV treatment.

Requirements to Enter Study:

- HIV+/Hep C co-infected men and women who are at least 18 years of age
- **OR** HCV mono-infected men and women who are at least 18 years of age
- Completed treatment for Hep C in the last 12 months as part of a clinical trial
- Not currently on Hep C treatment

- Willingness to adhere to study visits twice a year AND a one-time visit prior to starting any new Hep C treatment study after V-HICS study enrollment

A5329 – Interferon-Free Therapy for Chronic Hepatitis C Virus Genotype 1 Infection in Persons with HIV-1 Coinfection Receiving Concurrent Antiretroviral Therapy

This study is for people coinfected with HIV and HCV, but are HCV treatment naïve. Current treatments for HCV usually consist of a combination of drugs including interferon, but new drugs are being developed that do not contain interferon. These regimens could be useful in treating people coinfected with HIV and HCV because they do not often respond well to interferon. This purpose of this study is to test if these drugs can effectively treat HCV and if they are safe and well tolerated in people who have HIV and HCV. Study drugs will be provided and participants will be treated for 12 or 24 weeks, based on randomization.

Requirements to Enter Study:

- HIV and HCV infected men and women between the ages of 18 and 70 (women cannot be pregnant or currently breastfeeding)
- No HIV genotypic resistance to any ARV medications prior to study entry
- No history of virologic failure during treatment for HIV
- HIV-1 viral load <50 copies/mL
- On one of the following HIV-1 ARV regimens:
    - Raltegravir (Isentress) 400mg twice a day **or** darunavir (Prezista) 800mg once a day administered with ritonavir (Norvir) 100mg a day **AND**
    - Tenofovir (Viread) plus emtricitabine (Emtriva) once a day (or Truvada) **or** tenofovir (Viread) plus lamivudine (Epivir) once a day
- CD4 cell count ≥200 BMI from ≥18 to ≤38 kg/m^2
- HCV treatment naïve, HCV viral load >10,000 IU/mL, HCV genotype 1
- Test to classify liver disease prior to entry
- No other causes of liver disease
- No active depression or uncontrolled mental health disorders

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