PEP^2 Study Frequently Asked Questions (FAQs)

What is the PEP^2 study?

The PEP^2 study seeks to determine the ability of new anti-HIV agents to be absorbed by different body tissues in HIV-negative men who have sex with men (MSM). This information will be used when considering new agents for post-exposure prophylaxis (PEP) in the future.

What is PEP?

Post-exposure prophylaxis, or PEP, is an intervention that is used to prevent HIV infection up to 72 hours after a potential exposure. HIV-negative people with a possible exposure to HIV are instructed to take 28 days of a regimen of anti-HIV medications.

Who is eligible for this study?

The population being studied for this protocol will be HIV negative MSM aged 18-49 years.

What is the inclusion criteria for the study?

- HIV-negative man who reports receptive anal sex (bottoming) with another man in the last 6 months
- Aged 18-49 years
- Not currently taking PrEP and no plans to initiate during study
- Not currently taking PEP
- Able to provide informed consent in English
- No plans for relocation in the next 3 months
- Willing to undergo peripheral blood, penile swabs, urine, and rectal biopsy sampling
- Willing to use study products as directed
- Willing to abstain from receptive anal intercourse for 3 days prior to starting study product, for the duration of the study and for 7 days after any rectal biopsy procedure
- Hepatitis B surface antigen (HBsAg) must be negative (screening lab test)
- No history of renal (kidney) failure

What will happen during the study visit?

<u>Pre-drug Arm</u>

Visit 1: Eligibility screening, bloodwork

Visit 2: Bloodwork, penial and urethral swabs, urine test, rectal swabs, and biopsy

<u>Arms A, B, C</u>

Visit 1: Eligibility screening, bloodwork

Visit 2: Receive dose of Genvoya® and darunavir, bloodwork, urethral and penial swabs, and urine test

Visits 3, 4: Bloodwork, penial and urethral swabs, and urine test

Visit 5 (Arm C only): Bloodwork, penial and urethral swabs, and urine test

***Rectal swabs and biopsy will be conducted at either visit 2, 3, or 4, depending on the study arm and subgroup**

How long will the study last?

Each arm of the study will last a minimum of 1 week and a maximum of 3 months. All study visits will be conducted at the Hope Clinic of Emory University. There is no charge for parking at the Hope Clinic.

What is a rectal biopsy and what are the risks?

The study clinician will be performing all rectal biopsies with the assistance of the study coordinator. Prior to biopsy sampling, 1-2 swabs will be used to collect rectal secretions for gonorrhea and/or chlamydia. The clinician will insert a plastic tube, called a 'rigid sigmoidoscope', into the rectum. Once the scope is inserted, up to 12 biopsies will be performed in which small (less than a ¼ inch) pieces of

your bowel wall will be removed. As there are no pain nerves in the rectum (only stretch), most participants describe this process as uncomfortable, but not painful.

Rectal biopsies may cause mild irritation and the sensation of needing to pass stool, as well as limited bleeding for 2 to 3 days after the procedure. Bowel puncture and infection and bleeding are extremely rare complications of this procedure and could need treatment with antibiotics and/or surgical repair. The risk of such difficulties is less than 1 in 5,000 each time the procedure is done. There is also risk of infection and death as a result of bowel puncture. It is important to realize that the risk related to multiple biopsies is not known. Hence there may be additional risks of the biopsy procedure, which are not known at this time. Bottoming the week following the biopsies can increase your risk of sexually transmitted diseases including HIV.

Are the study drugs safe?

Darunavir is an FDA-approved drug that has been used for treatment of HIV infection. Previous clinical trials showed the drug was well-tolerated.

Genvoya® is a combination anti-HIV medication. Based on clinical trials previously conducted, the drug was shown to be well-tolerated.

What are some of the possible side effects of the study drugs?

Darunavir: The most common associated drug reactions were diarrhea, nausea, rash, headache, abdominal pain, and vomiting. These effects are not expected to occur with the 1 day dose schedule for this protocol. Darunavir should be used with caution in patients with a known sulfonamide allergy.

Genvoya®: The most common associated drug reactions were nausea, diarrhea, headache, and fatigue. This usually occurs less than 10% of the time. Over a long period of time, Genvoya® can also cause a decrease in kidney function, a buildup of lactic acid, or weakening of the bones. These effects are not expected to occur with the 1 day dose schedule for this protocol.

Is there compensation for participating?

$25 for the screening visit
$50 for each blood, swab, and urine collection visit
$125 for each biopsy visit

A $10 gift card will also be provided for the waiting period when procedures are done on the same day as the study drug. If an extra study visit is needed, participants will be compensated $20 for completion of visit.