

# PrEPared in Primary Care: Putting PrEP into Practice

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OSHP Annual Seminar

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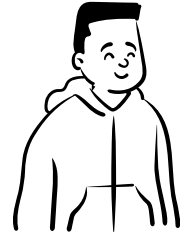


# Disclosure Statement

- Dr. Jessica Potter has no relevant financial relationship(s) with ineligible companies to disclose.



# Meet TJ



33-year-old male presenting with acute HIV seroconversion symptoms – fever, rash, lymphadenopathy

While reviewing the chart you see the patient had:

- Two ED visits in the past year for STIs
- A primary care visit documenting “inconsistent condom use”
- Negative HIV testing six months earlier
- No records of HIV PrEP ever discussed



# Pharmacist Objectives

1. Identify individuals who may benefit from HIV PrEP

2. Compare and contrast the two long-acting injectable therapies that are indicated for HIV PrEP

3. Identify key counseling points when prescribing lenacapavir subcutaneous injection therapy

4. Given a patient case, recommend monitoring requirements while on HIV PrEP therapy



# Pharmacy Technician Objectives

1. Describe dosing schedule for the two long-acting injectable therapies that are indicated for HIV PrEP

2. Compare and contrast the two long-acting injectable therapies that are indicated for HIV PrEP

3. Describe key monitoring and follow-up needs for patients receiving HIV PrEP

# Abbreviations



Term	Abbreviation
Cabotegravir	CAB
Care Coordinated Organization	CCO
Estimated creatinine clearance	ECrCl
Doxycycline postexposure prophylaxis	Doxy PEP
Emtricitabine/tenofovir alafenamide	FTC/TAF
Emtricitabine/tenofovir disoproxil fumarate	FTC/TDF
Long acting injectable	LAI

Term	Abbreviation
Lenacapavir	LEN
Men who have sex with men	MSM
Preexposure prophylaxis	PrEP
Persons who inject drugs	PWID
Sexually transmitted infection	STI
Transgender men	TGM
Transgender women	TGW

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# Pre-Test Questions

## Pharmacist Only:

Which of the following are potential indications for HIV PrEP for TJ?

Which of the following are counseling points for lenacapavir?

## Pharmacist and Pharmacy Technician:

Which of the following pairs of statements are correct?

Which of the following lab tests should be completed at least every 6 months while on lenacapavir?

## Pharmacy Technician Only:

Which long-acting injectable must be administered with an oral dose on the first and second day of therapy?



# Ending the HIV Epidemic Initiative



**Diagnose** all people with HIV as early as possible.

**Treat** people with HIV rapidly and effectively to reach sustained viral suppression.



**Prevent** new HIV transmissions by using proven interventions, including pre-exposure prophylaxis (PrEP) and syringe services programs (SSPs).

**Respond** quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them.



# Key Considerations for PrEP in Primary Care



Identify a PrEP champion to help with workflow and logistics



Assign staff roles for obtaining medication and storing medication



Develop protocols for insurance approval, drug procurement, and involvement of specialty pharmacist



Train clinicians and staff in injection protocols



Develop a script for patient education, especially for LAI PrEP regimens



Monitor patients, including tracking for injections and appointments for laboratory testing

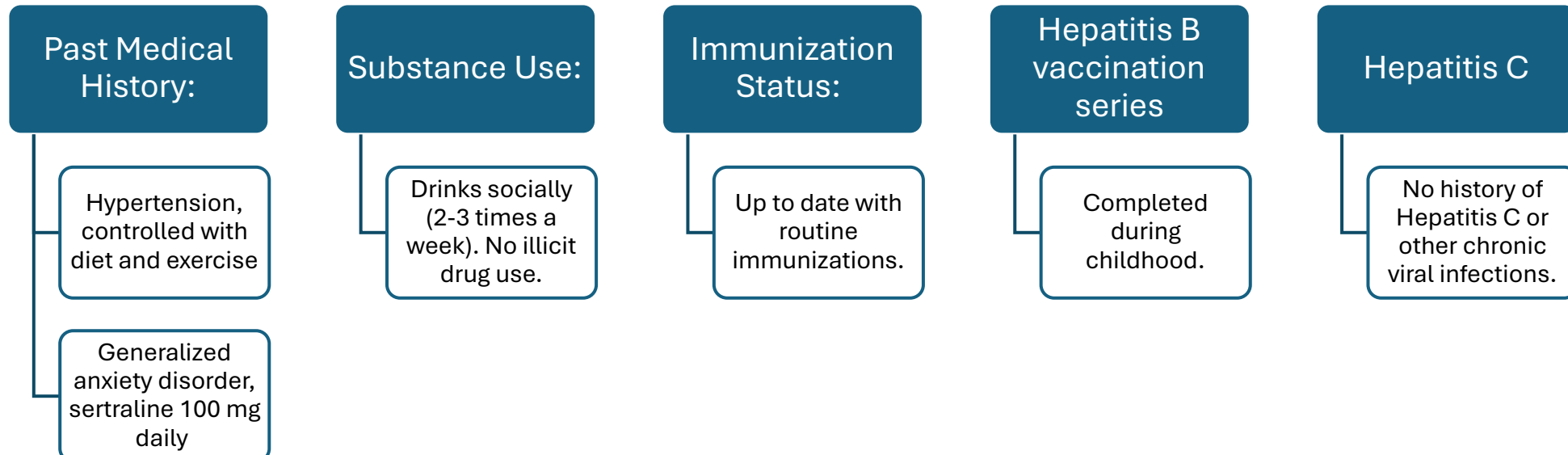


Determine how to handle interval HIV and STI testing via telehealth or nurse visits

# Meet TJ



- TJ is a 33-year-old cis male (he/him), 80 kg, presenting to his clinic pharmacist to discuss starting PrEP therapy.
- He has heard about PrEP from friends and news outlets, but unsure about the details and how it might fit into his lifestyle
- He is not interested in injectable therapy options
- He has commercial insurance with a deductible, notes he often has high copays for brand name medications



# Interviewing Patients



## Partners

- Number and gender of patient's sex partners, new partners
- Their partner's risk factors (concurrent partners, drug use, etc)

## Practices

- Asking about sex practices will guide the assessment of patient risk, risk-reduction strategies, and determination of anatomical sites from which to collect specimens for STI testing

## Protection from STIs

- Explore the subjects of condom use, patient's perception of their own risk and their partner's risk

## Past History of STIs

- A history of prior STIs may place your patient at greater risk now

## Pregnancy Intention

- Based on information obtained from above, you may determine that the patient could become pregnant.
- Questions should be focused on determining pregnancy intention/family planning



# Possible Dialogues

May I ask you a few questions about your sexual health and sexual practices? I understand that these questions are personal, but they are important for your overall health.

Are you currently having sex of any kind – so, oral, vaginal, or anal – with anyone?  
In recent months, how many sex partners have you had?  
What is/are the gender(s) of your sex partner(s)?

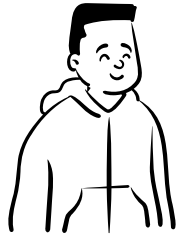
If you use prevention tools, what methods do you use? (e.g. external or internal condoms)

What parts of your body are involved when you have sex?  
Are you a top and/or bottom?

Have you been diagnosed with an STI in the past?  
When? Did you get treatment?

Do you think you would like to have (more) children at some point? When do you think that might be? How important is it to you to prevent pregnancy (until then)?

# TJ – 5 P's



## Partners

- TJ is sexually active with multiple male partners, estimates 7 in the last 3 months
- He is unaware of any known risk factors of STIs or HIV in partners

## Practices

- TJ has oral and anal sex. He participates in both insertive and receptive anal sex (top and bottom)

## Protection from STIs

- He practices condom use some of the time, but notes that when alcohol is involved, he may not use protection

## Past history of STIs

- He has been treated for gonorrhea and chlamydia in the last year

## Pregnancy Intention

- Not applicable, TJ is a cis male



# Patients to Consider for HIV PrEP

- Health care professionals should provide all sexually active adult and adolescent persons with information regarding HIV PrEP
- The specific indications for HIV PrEP, as recommended in the 2021 CDC PrEP Clinical Practice Guideline, are outlined as follows:

## Sexually Active Adults and Adolescents ( $\geq 35$ kg)

- Anal or vaginal sex in the past 6 months AND any of the following:
  - Sex partner with HIV
  - STI within the past 6 months
  - History of inconsistent or no condom use with sexual partner(s)

## Persons who inject drugs

- Injecting partner who has HIV
- Sharing injection equipment
- Have sexual risk for acquiring HIV

# Patient Case/Learning Check (Pharmacist ONLY)



Which of the following are potential indications for HIV PrEP for TJ?

- a. Multiple sex partners
- b. Inconsistent condom use
- c. Patient is inquiring about HIV PrEP
- d. All the above

# Patient Case/Learning Check (Pharmacist ONLY)



Which of the following are potential indications for HIV PrEP for TJ?

- a. Multiple sex partners
- b. Inconsistent condom use
- c. Patient is inquiring about HIV PrEP
- d. All the above**

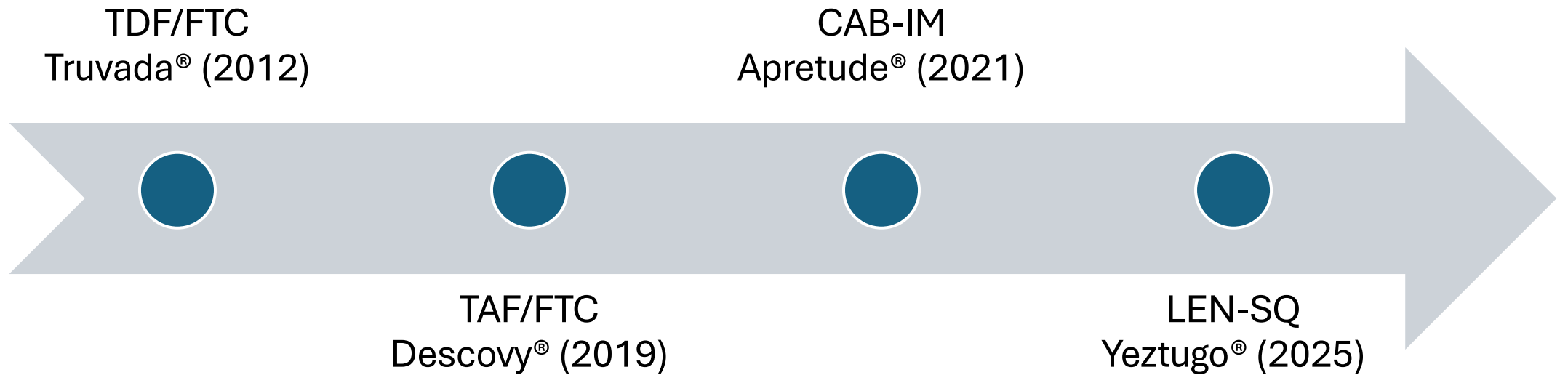


# Counseling for HIV PrEP

- HIV PrEP does not prevent bacterial STIs
- Importance of other risk modifying activities
- Importance of adherence to regimen
- Regular lab monitoring and anticipated follow-up schedule
  - HIV testing
  - STI testing at pertinent anatomical sites

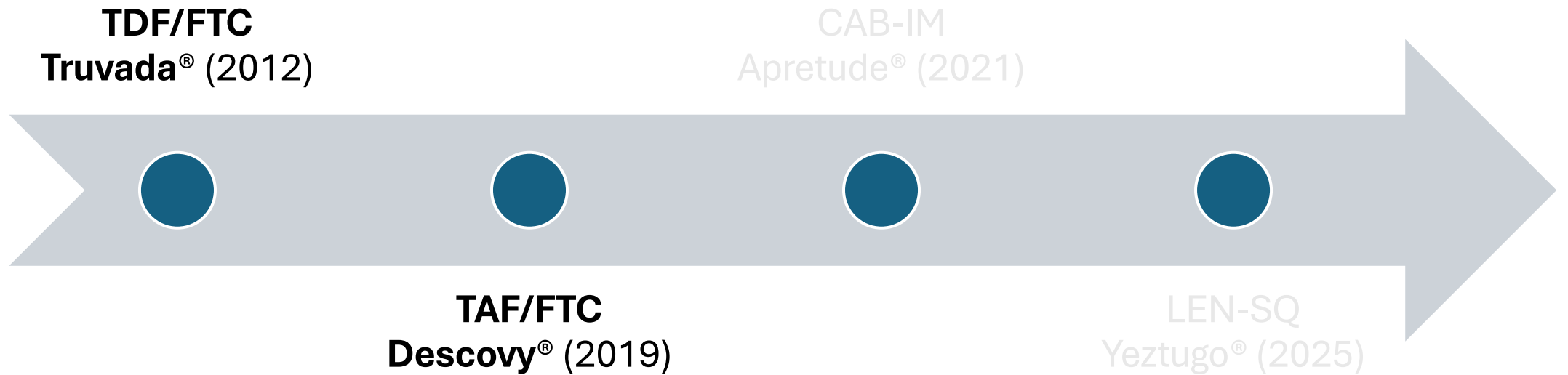


# HIV PrEP Options





# HIV PrEP Options





# Baseline Monitoring

HIV-1/2 Ag/Ab  
test with reflex  
confirmation

HIV RNA  
Assay\*

STI Testing\*\*

Hepatitis C  
serology (MSM,  
TGW, PWID)

Renal Function

Lipid Panel

Hepatitis B  
Serologies

\*Oral PrEP: For those with reported HIV exposure-prone event in last 4 weeks and signs/symptoms of acute HIV infection in the last 4 weeks

\*\*Syphilis, gonorrhea, chlamydia at appropriate anatomical sites (rectal, urogenital, pharyngeal)



**If the patient has not taken oral PrEP or PEP medication in the past 3 months  
AND  
has not received a cabotegravir injection in the past 12 months**

HIV antibody/antigen plasma test laboratory (preferred) with reflex confirmation  
OR blood rapid test

Nonreactive (negative)      Indeterminate Differentiation Assay      Reactive (positive)

**HIV+ (if laboratory test)  
(pending supplemental confirmatory testing, if non-laboratory rapid test)**

Reported HIV exposure-prone event in prior 4 weeks  
AND  
Signs/symptoms of acute HIV infection any time in prior 4 weeks

HIV- **No**      **Yes**

Send plasma for HIV antibody/antigen assay

Reactive (positive) **HIV+**  
Nonreactive (negative) **HIV-**

±

Send plasma for quantitative or qualitative HIV-1 RNA assay

HIV-1 RNA  $\geq 200$  copies/mL **HIV+**  
HIV-1 RNA detectable but  $< 200$  copies/mL  
HIV-1 RNA  $<$  level of detection no signs/symptoms on day of blood draw **HIV-**  
HIV-1 RNA  $<$  level of detection with signs/symptoms on day of blood draw  
Retest in 2-4 weeks  
Defer PrEP decision, consider nPEP

Draw new plasma specimen  
Defer PrEP decision until false positive ruled out

**Legend**

HIV- Eligible for PrEP
HIV+ Not eligible for PrEP
HIV status unclear Defer PrEP decision

# Oral HIV PrEP Options



PrEP Regimen	Indication	Dosing	Administration	Renal Dosing	Side effects	Long-term Concerns	Time to Protection
TDF/FTC Truvada®	Men, women, TGW, TGM, PWID	200/300 mg oral daily  Generic available	With or without food  2-1-1 off label dosing for select MSM	Do not use if CrCl <60	Headache, nausea, abdominal discomfort (“start-up syndrome”)	Renal dysfunction  Decreased bone mineral density	7 days (receptive anal sex) 21 days (receptive vaginal sex or drug use)  Unknown for insertive anal or vaginal sex
TAF/FTC Descovy®	Only approved in men and TGW	200/25 mg oral daily	With or without food  2-1-1 dosing efficacy has not been established	Do not use if CrCl <30 unless on dialysis	Start-up syndrome, weight gain and increased cholesterol and triglycerides	Less bone and renal impacts compared to FTC/TDF	Unknown

Gilead Sciences, Inc. Truvada (emtricitabine and tenofovir disoproxil fumarate): Prescribing information.

Gilead Sciences, Inc. Descovy (emtricitabine and tenofovir alafenamide): Prescribing information.

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# Monitoring on Oral PrEP

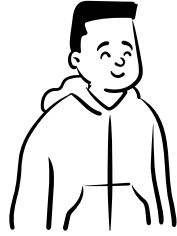
Test	Baseline	Q 3 months	Q 6 months	Q 12 months	Upon Discontinuation
HIV	X	X			X
eCrCl	X		If age $\geq 50$ or CrCl $< 90$ at initiation	If age $< 50$ and CrCl $> 90$ at initiation	X
Syphilis	X	MSM/TGW	X		MSM/TGW
Gonorrhea	X	MSM/TGW	X		MSM/TGW
Chlamydia	X	MSM/TGW	X		MSM/TGW
Lipid panel (FTC/TAF)	X			X	
Hepatitis B	X				
Hepatitis C	MSM, TGW, PWID			MSM, TGW, PWID	



# Monitoring HIV RNA on PrEP

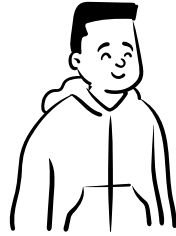
Guideline	Recommendation
2021 CDC Guidelines	"Send plasma for HIV antibody/antigen AND HIV-1 RNA assay"
International AIDS Society – USA	"RNA testing as part of routine monitoring for PrEP failure is not recommended due to low positive predictive value and false positive results have significant negative sequelae"
NY State/AIDS Institute	"Perform... HIV RNA test in individuals who present with or report symptoms or signs of acute HIV infection" "Perform... HIV RNA test in individuals who report inconsistent adherence to or an interruption of oral PrEP of more than 1 week"
CDC 2025 Update	HIV antigen/antibody testing is recommended ... with follow-up injections"

# TJ: Initial Visit



- You discussed basic PrEP counseling with TJ, as well as risk reduction methods for HIV and STIs
- Reviewed that oral PrEP is ~99% effective when taken daily
- He understands he will need to undergo follow-up and lab testing every 3 months
- You discuss oral PrEP therapy options and plan to initiate FTC/TDF #90 tablets based on patient's insurance formulary
- You obtain baseline lab work prior to writing prescription

# TJ: Initial Visit



HIV-1/2  
Ag/Ab test

Nonreactive

HIV RNA  
Assay

Undetectable

STI testing

Syphilis bloodwork is  
negative

C/G testing at all  
sites (anal,  
pharyngeal,  
urogenital) are  
negative

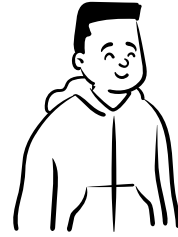
Renal  
function

CrCl >60

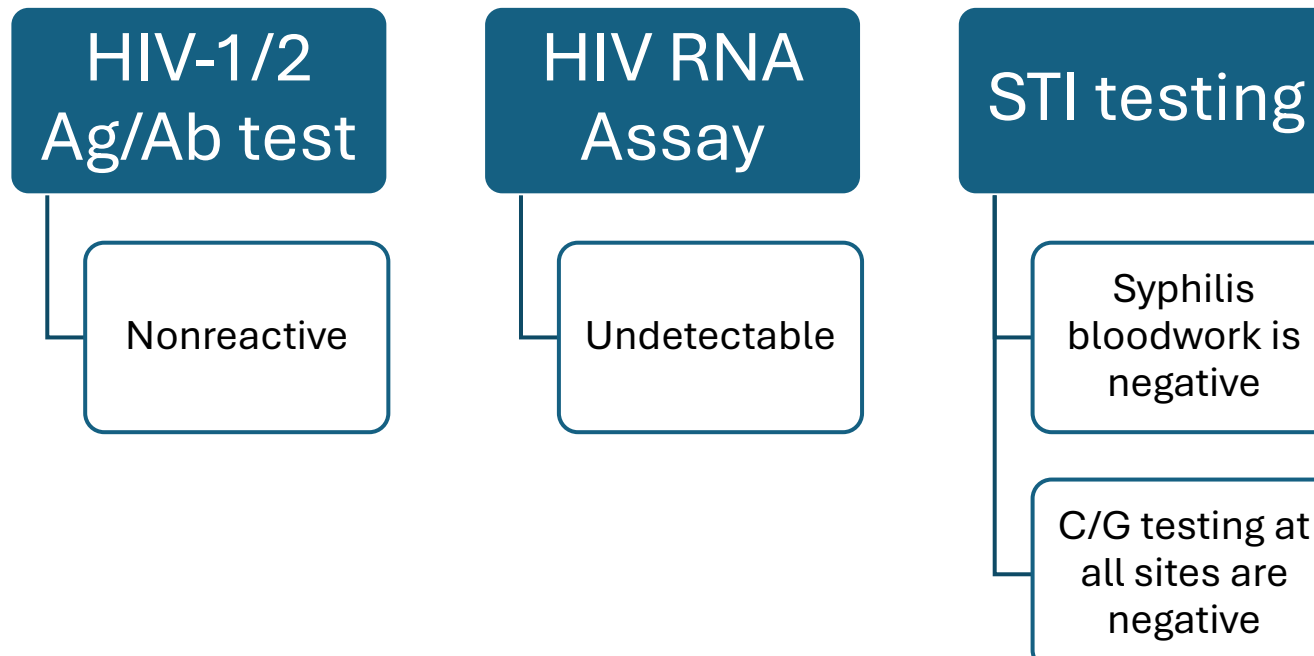
Hepatitis B  
serologies

Show immunity from  
vaccination

# TJ: Follow-up Visit



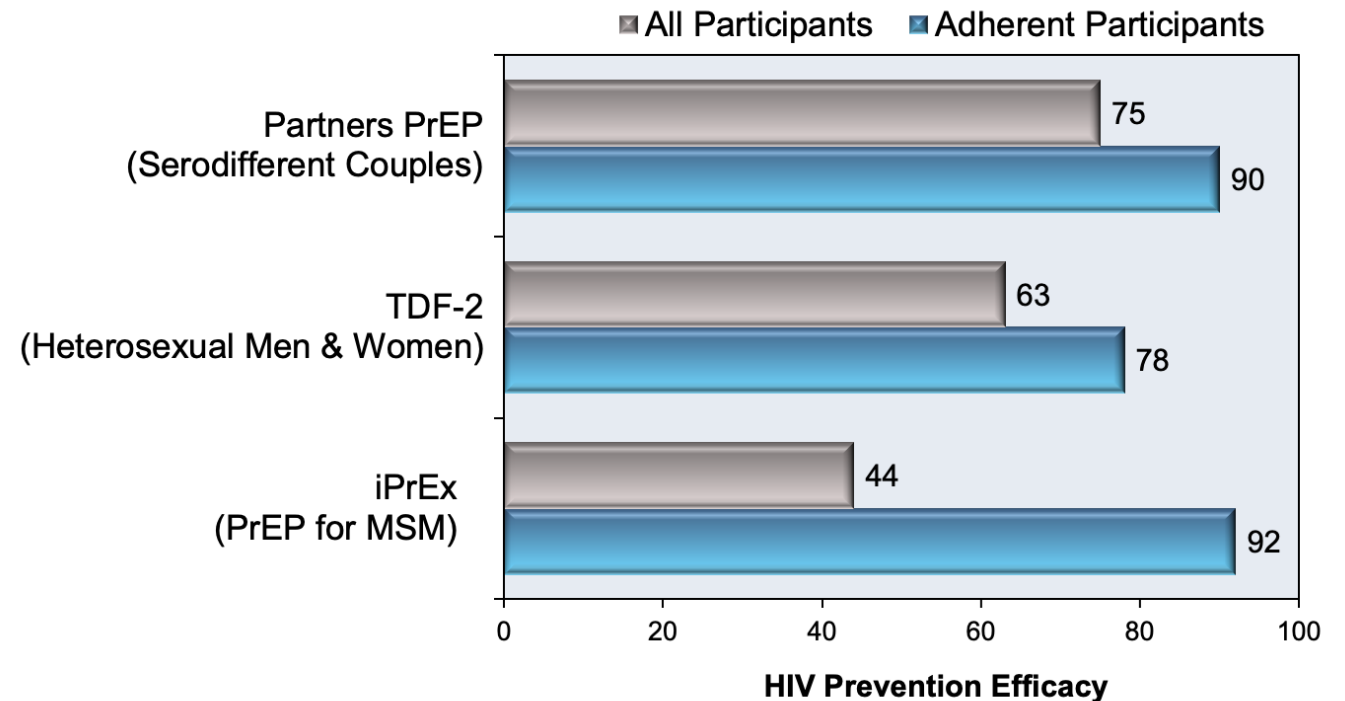
- TJ presents 2.5 months later to discuss tolerability and barriers to adherence
- He is taking TDF/FTC but wonders about importance of taking it daily





# Adherence to PrEP

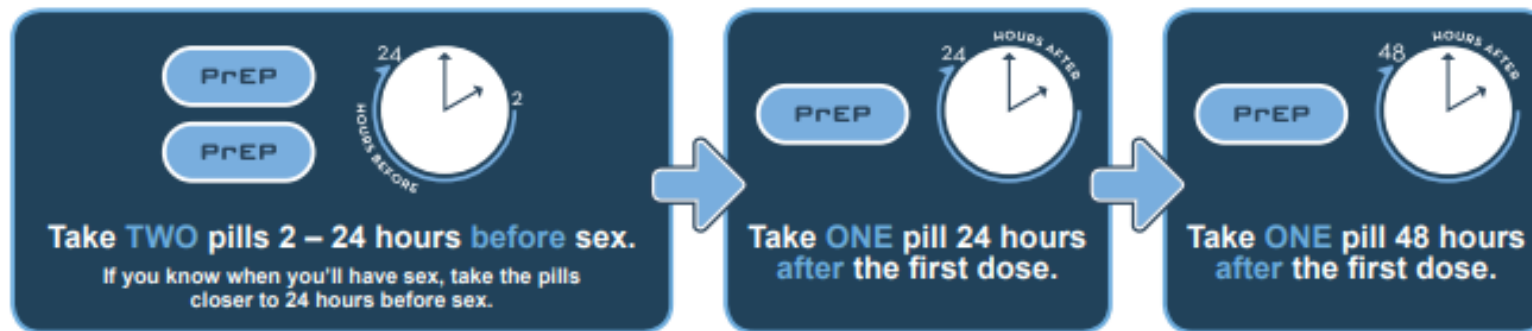
- Adherence is critical for efficacy
- HIV risk reduction is estimated to be:
  - 99% with 7 doses/week
  - 96% with 4 doses per week
  - 76% with 2 doses per week
- Can consider 2-1-1 method (off-label)



# 2-1-1 Dosing

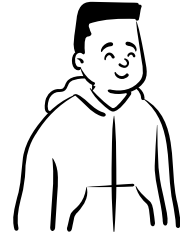
- Also known as on-demand, intermittent, event-driven PrEP
- 2-1-1 dosing has not been approved by the FDA, but studies have evaluated its use in MSM
- Studies show HIV prevention of 86% or more with 2-1-1 dosing strategy
- Consider in MSM who request non-daily dosing, have sex infrequently ( $\leq 1x/week$ ), and can anticipate sex or delay it until TDF/FTC can be taken at least 2 hours before activity
- Possibility of "start-up" symptoms with infrequent dosing

PrEP 2-1-1 starts by taking **TWO** pills between 2 and 24 hours before sex. Taking the pills closer to 24 hours before sex is better but you can use PrEP 2-1-1 up to 2 hours before sex. After sex, you take **ONE** pill 24 hours after the first pills, and **ONE** pill again 24 hours after that. That's PrEP 2-1-1, get it?



**Important Note:** The PrEP 2-1-1 dosing schedule changes if you are going to have sex within seven days of your last PrEP dose. Start by taking just **ONE** pill between 2 and 24 hours before sex. You still take **ONE** pill 24 hours after the first pill, and **ONE** pill again 24 hours after that.

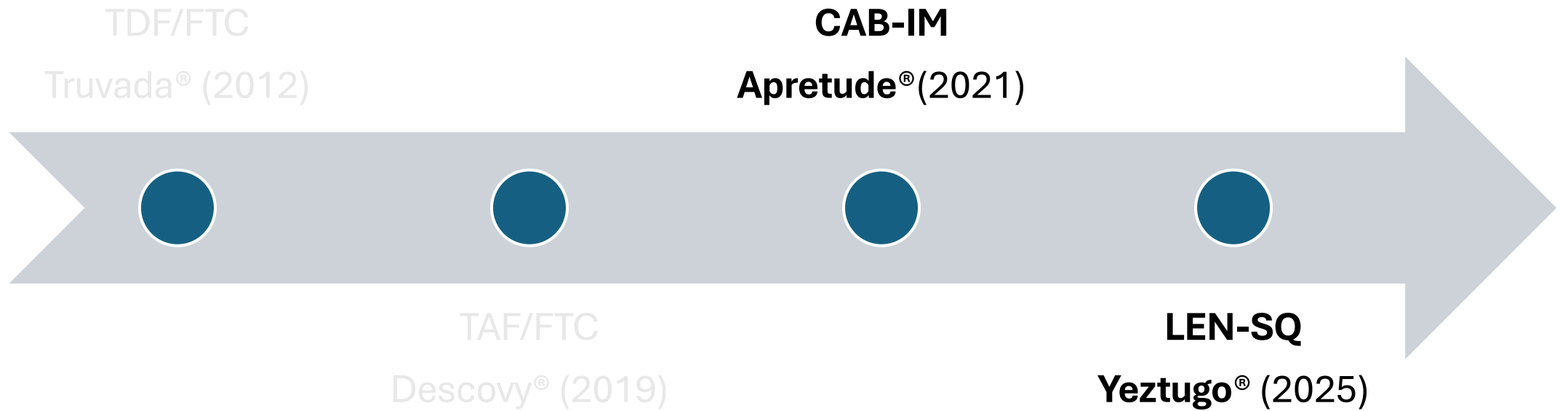
# TJ: Follow-up Visit



Patient presents 3 months later. He continued to try oral therapy and tried shifting to the 2-1-1 method but is finding he is missing doses frequently and couldn't follow 2-1-1 method reliably, he is now interested in possible injectable therapy options



# HIV PrEP Options





# Cabotegravir-IM (Apretude<sup>®</sup>)

*Abbreviation: CAB*



# Cabotegravir-IM

- Integrase strand transfer inhibitor which prevents the HIV complex from integrating into host DNA

## HPTN 083

- CAB vs TDF/FTC
- Men and TGW who have sex with men
- CAB superior to TDF/FTC, HR 0.31
- HIV Incidence: 0.41 per 100 person-years (CAB) vs 1.22 per 100 person-years (TDF/FTC)
- Injection site reactions

## HPTN 084

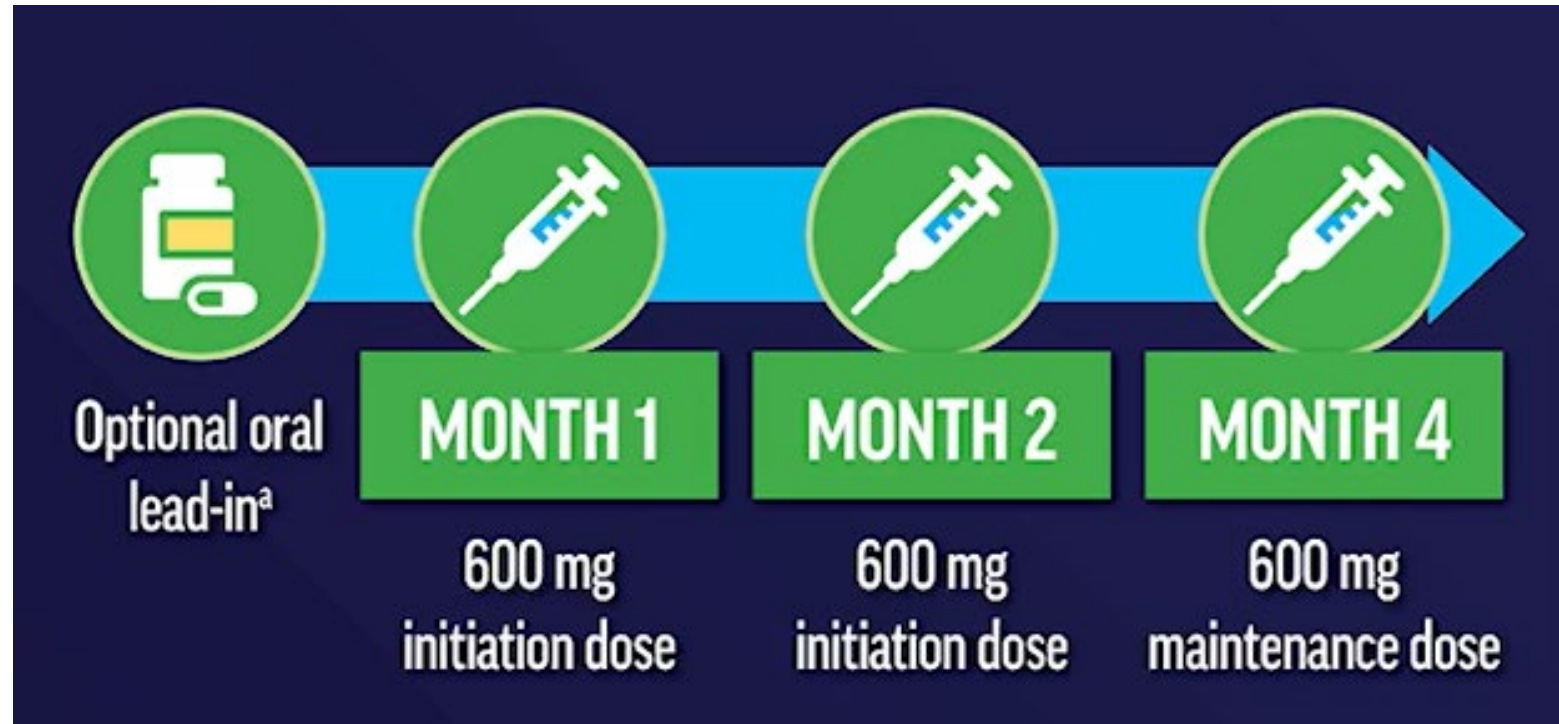
- CAB vs TDF/FTC
- Cisgender women
- CAB superior to TDF/FTC, HR 0.1
- HIV incidence: 0.21 per 100 person-years (CAB) vs 1.79 per 100 person-years (TDF/FTC)
- Injection site reactions

# Cabotegravir-IM



Cabotegravir-IM	
Indications	Adults and adolescents at risk of HIV who weigh at least 35 kg Recommended for use in PWID who have sexual exposure
Dosing	600 mg (3 mL) injection repeated 1 month after first injection, then every 2 months thereafter Optional oral lead-in dose
Administration	Administered by healthcare provider office into gluteal muscle

# Cabotegravir-IM (Apretude)



\*Optional lead-in with oral cabotegravir which may be used for approximately 1 month to assess tolerability

- If given, IM should be given on the last day of the oral lead-in or within 3 days of completing the oral lead-in
- Limited benefits as injectable therapy is typically well tolerated



# Cabotegravir-IM (Apretude)

Cabotegravir-IM	
Indications	Adults and adolescents at risk of HIV ( $\geq 35$ kg) Recommended for use in PWID who have sexual exposure
Dosing	600 mg (3 mL) injection repeated 1 month after first injection, then every 2 months thereafter Optional oral lead-in dose
Administration	Administered by healthcare provider office into gluteal muscle
Common Side Effects	Injection site reactions
Time to Efficacy	Unknown, steady state after 3 doses 95% will have protective blood concentrations 7 days after starting 50% will have it 1 day after first injection
Missed Dose	See next slide for guide



# Cabotegravir-IM (Apretude)

Dose Missed	Time since Previous Dose	Recommendation
Second Injection	≤ 2 months	Administer dose as soon as possible, then continue every 2-month schedule
	>2 months	Restart initiation dosing, followed by every 2-month schedule
Third injection or after	≤ 3 months	Administer dose as soon as possible, then continue every 2-month schedule
	>3 months	Restart initiation dosing, followed by every 2-month schedule

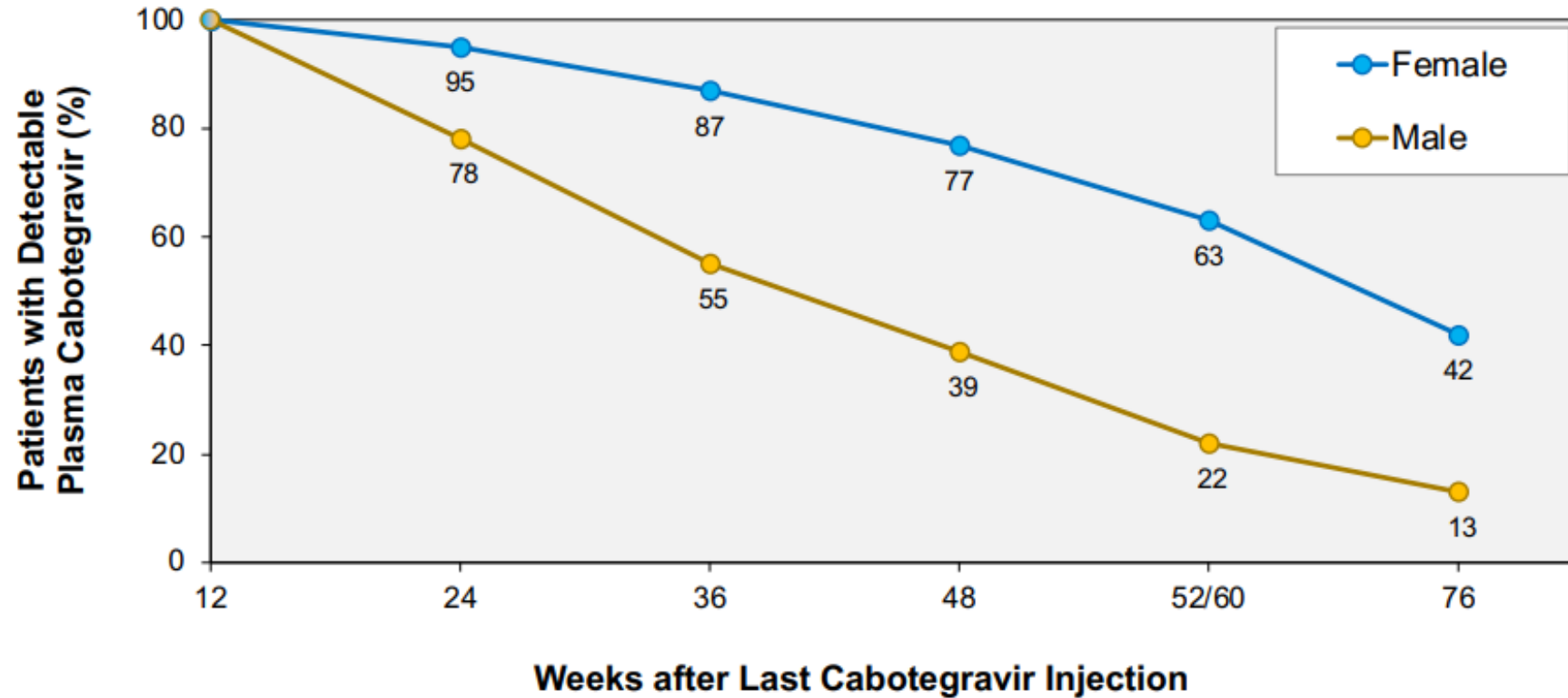
Planned missed dose by >7 days: Take oral cabotegravir daily for ≤2 months to replace 1 missed scheduled injection; if treating >2 months, use an alternative oral regimen.



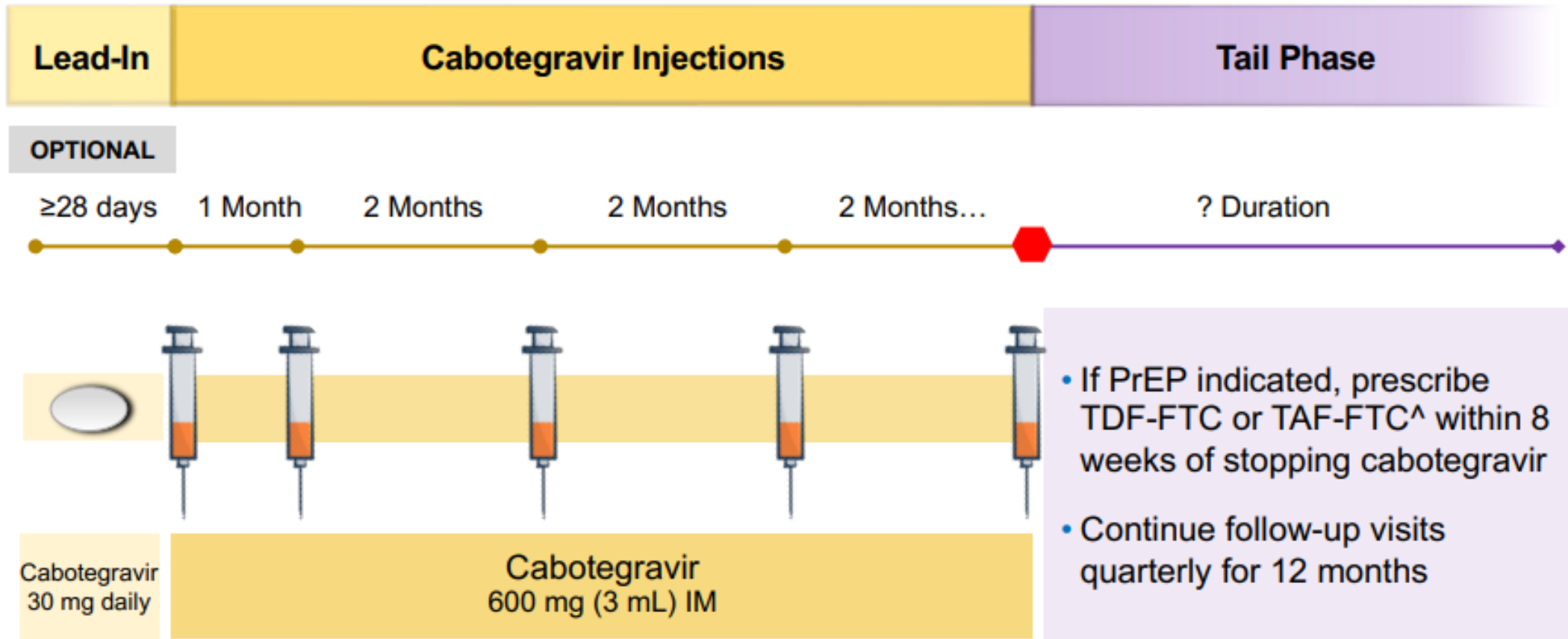
# Monitoring on Cabotegravir

Test	Baseline	1-mo visit	Q 2 mo	Q4 mo	Q6 mo	Q12 mo	At discontinuation
HIV	X	X	X	X	X	X	X
Syphilis	X			MSM/TGW	Heterosexually active women and men	X	MSM/TGW
Gonorrhea	X			MSM/TGW	Heterosexually active women and men	X	MSM/TGW
Chlamydia	X			MSM/TGW	Heterosexually active women and men	X	MSM/TGW
Hepatitis B	X						
Hepatitis C	MSM, TGW, PWID					MSM, TGW, PWID	

# Tail Effects: CAB



# Tail Effects: CAB





# CAB Drug-Drug Interactions

## Effect of Other Drugs on CAB

### Strong inducers of UGT1A1 or UGT1A9

- Expected to decrease CAB plasma concentrations, use is contraindicated for both oral and injectable
- E.g.: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine

### Polyvalent cations

- Coadministration with **oral** formulation may lead to decreased absorption

## Effect of CAB on Other Drugs

### Inhibits OAT1 and OAT3

- May increase AUC of OAT1/3 substrates by up to ~80%
- Drug interactions may persist for several months after last injection



# CAB Logistics and Cost

## Prescription benefits

- Never a local pharmacy
- Specialty pharmacy ships to office
- Insurance may specify which specialty pharmacy you can go through

## Medical benefits

- Specialty pharmacy
- Buy and bill
- Infusion center

## Alternative Sites of Care

- <https://prep.advancingaccess.com/hcp/asoc-locator>

Optional lead-in dose is restricted to TheraCom specialty pharmacy



# CAB Logistics and Cost

## Average Wholesale Price

- \$5074 per injection (~30,500 annual cost)

## ViiVConnect Patient Savings Program

- Commercially insured patients
- Payments as low as \$0 per injection
- Max annual savings of \$7,850

## ViiV Healthcare Patient Assistance Program

- Uninsured
- No cost to patients who qualify
- 1-844-588-3288



# Lenacapavir-SQ (Yeztugo<sup>®</sup>)

*Abbreviation: LEN*



# LEN Mechanism of Action

- First in class HIV-1 capsid inhibitor that inhibits HIV-1 replication by interfering with multiple essential steps of the viral lifecycle
  - The capsid core contains and protects viral RNA and enzymes for HIV replication
  - The HIV-1 viral life cycle is dependent on the function of the capsid during nuclear transport, virus assembly and release, and capsid core formation
  - LEN disrupts each of the above stages, resulting in abnormal structure of the virus and inhibiting HIV-1 replication

# LEN Studies: PURPOSE 1

- Evaluated safety and efficacy of LEN or FTC/TAF in parallel compared to active internal control group receiving daily FTC/TDF for HIV prevention
- Included adolescent girls and young women (16-25 years of age) sexually active with male partners

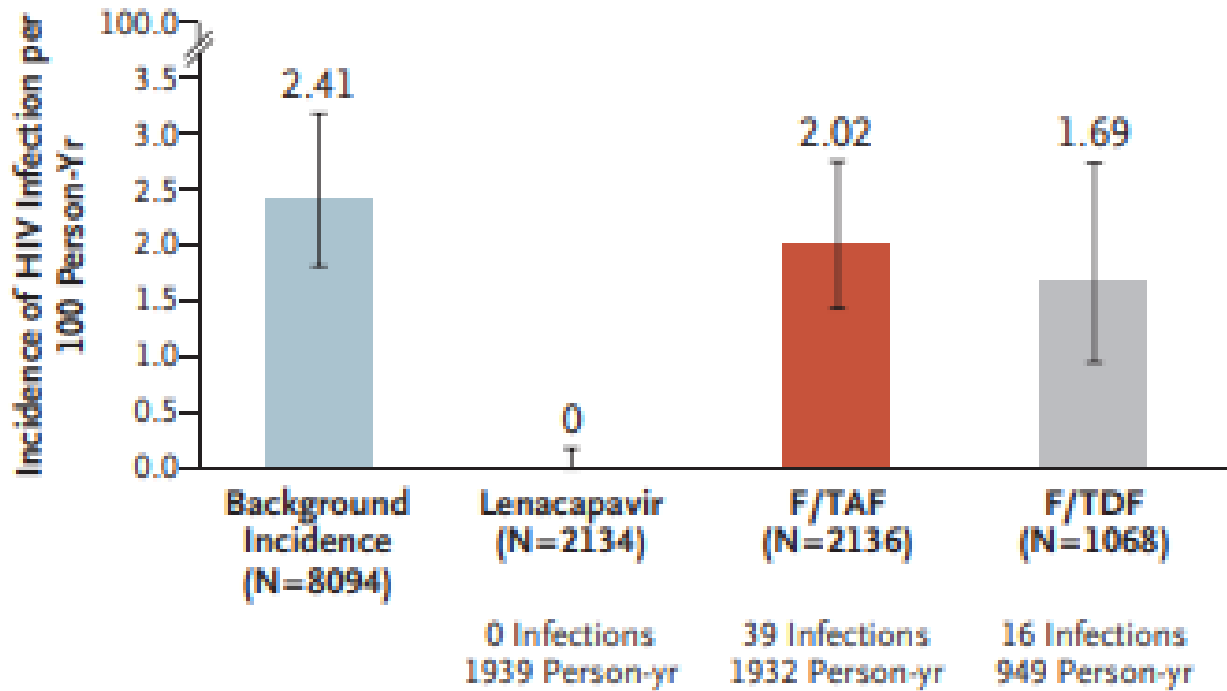


## Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

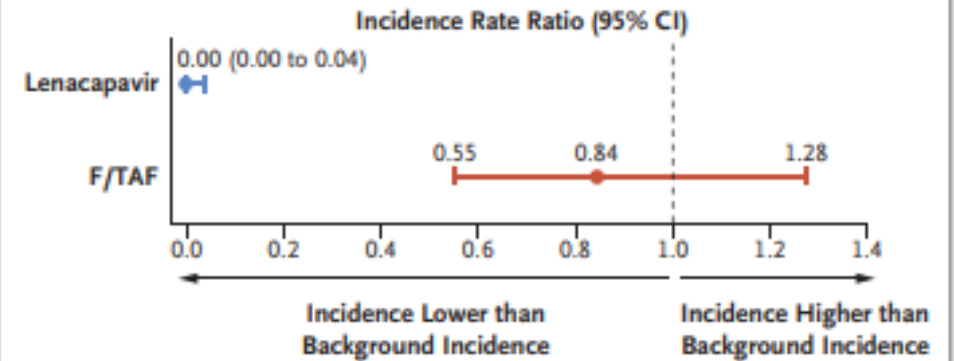
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# PURPOSE 1 Results

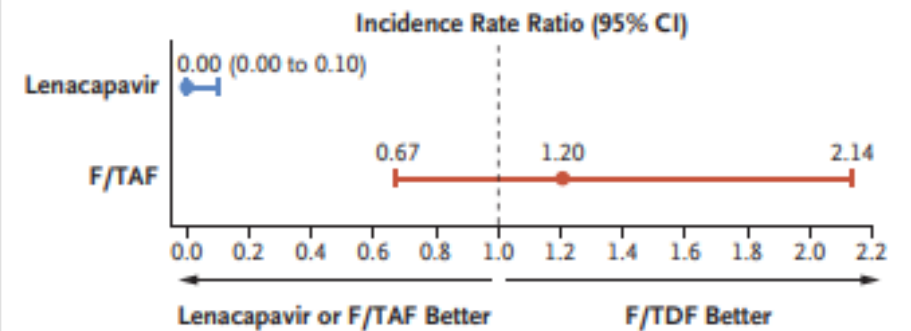
**A Background HIV Incidence and HIV Incidence in Lenacapavir, F/TAF, and F/TDF Groups**



**B Incidence Rate Ratio Comparing HIV Incidence in Lenacapavir and F/TAF Groups with Background HIV Incidence**



**C Incidence Rate Ratio Comparing HIV Incidence in Lenacapavir and F/TAF Groups with Incidence in F/TDF Group**



**Figure 2. Incidence of HIV Infection.**

In Panel A, the I bars indicate 95% confidence intervals.

# LEN Studies: PURPOSE 2

- Evaluate efficacy and safety of LEN in gender-diverse population compared to active control group on FTC/TDF
- Recruited subpopulations disproportionately affected by HIV



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### Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons

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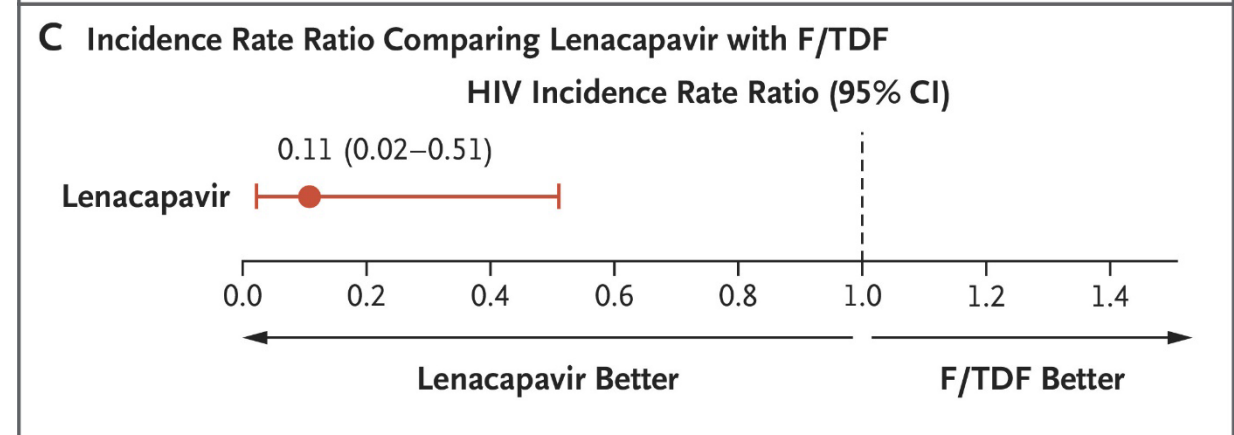
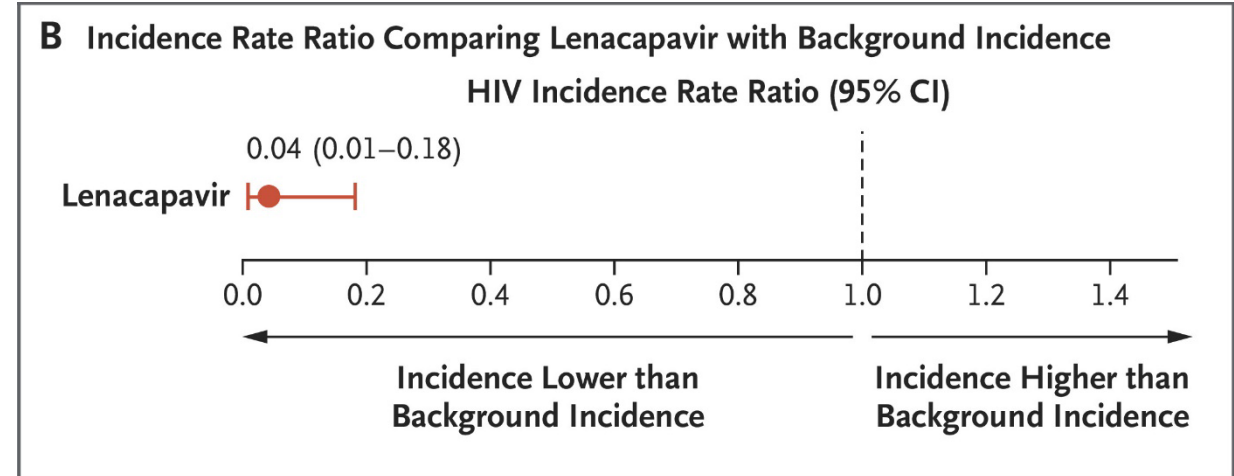
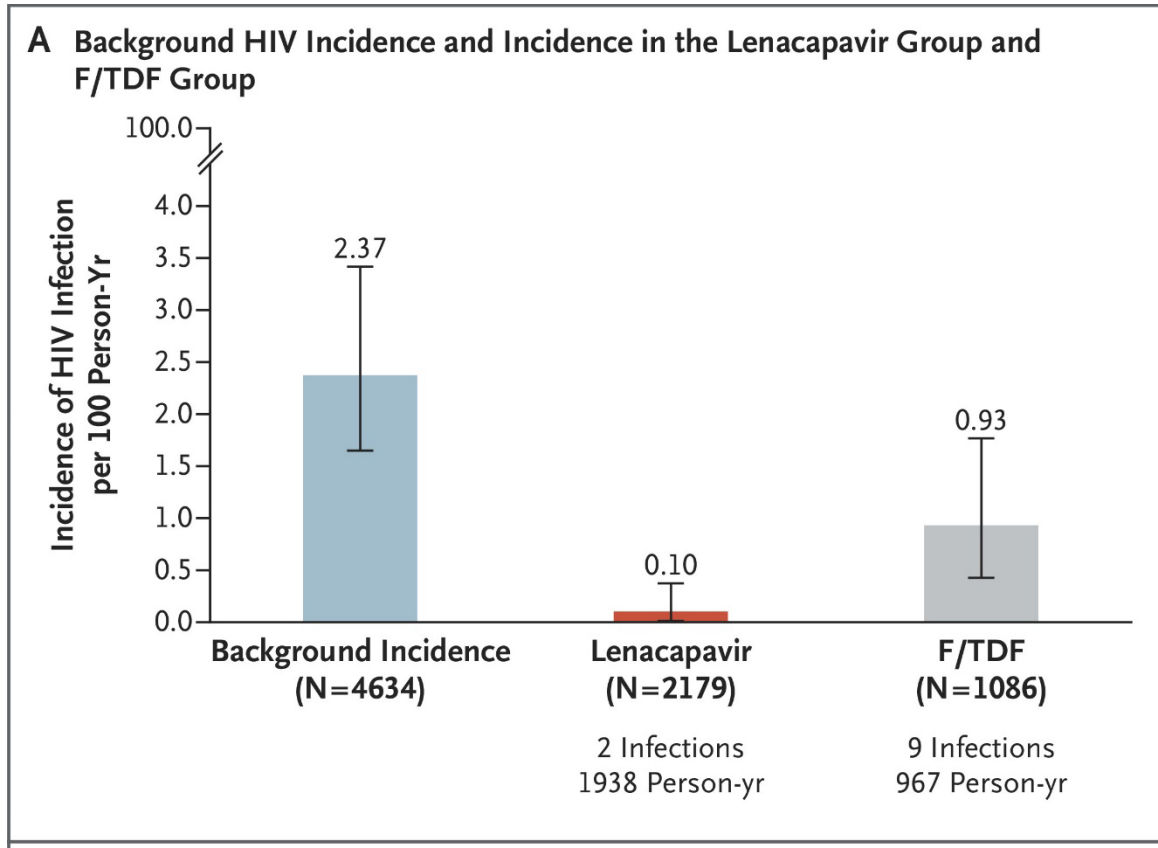
# LEN Studies: PURPOSE 2

- Evaluate efficacy and safety of LEN in gender-diverse population compared to active control group on FTC/TDF
- Recruited subpopulations disproportionately affected by HIV

**Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.\***

Characteristic	Lenacapavir (N=2183)	F/TDF (N=1088)
<b>Gender identity — no. (%)</b>		
Cisgender man	1697 (77.7)	846 (77.8)
Transgender woman	315 (14.4)	161 (14.8)
Transgender man	29 (1.3)	14 (1.3)
Gender nonbinary‡	136 (6.2)	63 (5.8)
Other§	6 (0.3)	4 (0.4)
<b>Sexual orientation — no./total no. (%)</b>		
Straight or heterosexual	148/2168 (6.8)	66/1079 (6.1)
Gay	1634/2168 (75.4)	806/1079 (74.7)
Bisexual	322/2168 (14.9)	166/1079 (15.4)
Other¶	64/2168 (3.0)	41/1079 (3.8)

# PURPOSE 2 trial Results





# LEN – Guideline Directed

## CDC

- Strongly recommends subcutaneous LEN every 6 months as a PrEP option

## World Health Organization

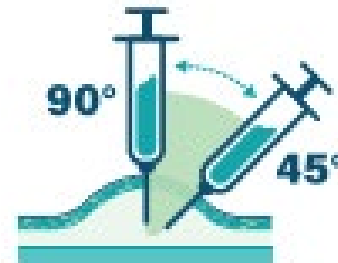
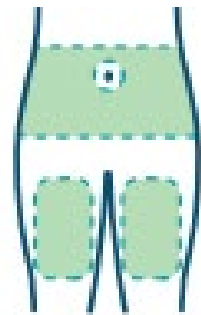
- Long-acting injectable lenacapavir should be offered as an additional prevention choice for people at risk of HIV

## International Antiviral Society - USA

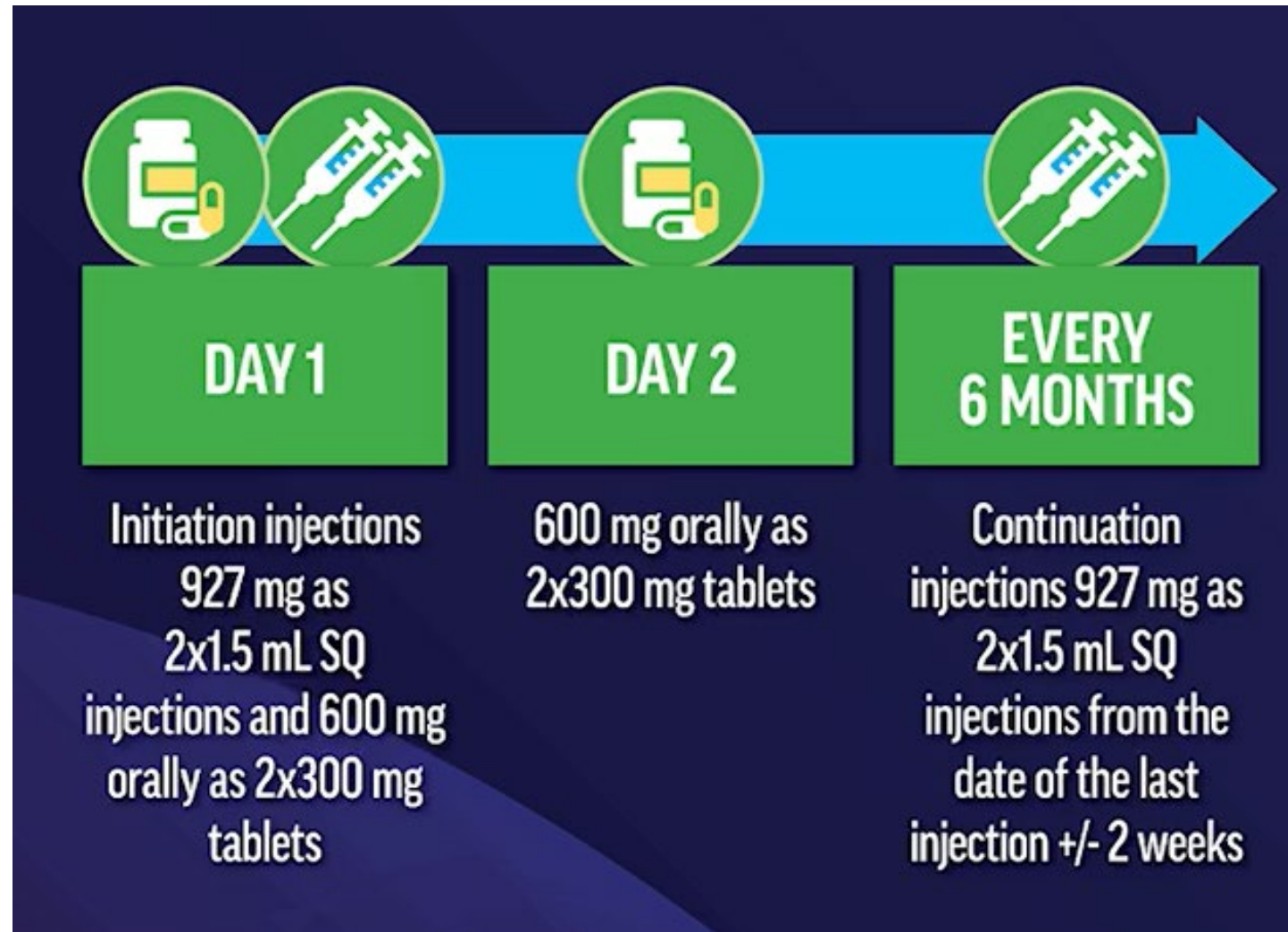
- Recommends lenacapavir for prevention of HIV infection for all routes of sexual exposure

# Lenacapavir-SQ (Yeztugo)

Lenacapavir-SQ	
Indications	Adults and adolescents at risk of HIV who weigh at least 35 kg Recommended for use in PWID who have sexual exposure
Dosing	Day 1: 600 mg PO and 2 injections (927 mg) Day 2: 600 mg PO lenacapavir Administer lenacapavir 927 mg every 26 weeks
Administration	Administered by healthcare provider office subcutaneously



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Dosing	Day 1: 600 mg PO and 2 injections (927 mg) Day 2: 600 mg PO lenacapavir Administer lenacapavir 927 mg every 26 weeks
Administration	Administered by healthcare provider office subcutaneously
Common Side Effects	Injection site reactions, subcutaneous nodules, headache, nausea
Time to Efficacy	Unknown, but limited pharmacokinetic data from a phase 1 trial in 14 healthy adults suggest protection is 2 hours after taking the second oral loading dose of lenacapavir
Missed Dose	Can be administered up to 14 days before or after the target date, see next slide for guidance



# Lenacapavir-SQ (Yeztugo)

Dose Missed	Time Since Previous Dose	Recommendation
Day 2 oral initiation dose	Not applicable	Administer as soon as possible
Planned missed injection	>28 weeks	Give lenacapavir 300 mg PO every 7 days for up to 6 months until injections resume. Resume maintenance injection within 7 days after last oral dose
Unplanned missed injection without use of lenacapavir oral tablets	>28 weeks	Restart initiation dosage regimen from day 1



# Monitoring on LEN

Test	Baseline	Q3 mo	Q6 mo	Q12 mo	At discontinuation
HIV	X		X	X	X
Syphilis	X	X*	X	X	MSM/TGW
Gonorrhea	X	X*	X	X	MSM/TGW
Chlamydia	X	X*	X	X	MSM/TGW
Hepatitis B	X				
Hepatitis C	MSM, TGW, PWID			MSM, TGW, PWID	

\*Consider patient risk factors for timing of STI monitoring



# LEN Tail Effect

- Half life of 8-12 weeks
- Prolonged period of residual drug concentrations
- Lasting up to 12 months or longer after the last injection
- Vulnerability to HIV acquisition with resistant virus
  - Use of alternative regimens after discontinuation is advised
- Drug-drug interactions



# LEN Drug-Drug Interactions

## Effect of Other Drugs on LEN

### CYP3A Inducers

- May significantly decrease concentrations of LEN
- Dose modifications of LEN are required when initiating strong/moderate CYP3A4 inducers

### Combined P-gp, UGT1A1, CYP3A inhibitors

- May significantly increase concentrations of LEN
- Concomitant administration **is not recommended**

## Effect of LEN on Other Drugs

### LEN is a moderate inhibitor of CYP3A and a P-gp inhibitor

- May increase concentrations of medications that are substrates of CYP3A or P-gp
- Due to long half-life, may interact with exposure of drugs initiated within 9 months of last dose of LEN



# LEN Logistics and Cost

## Prescription benefits

- Never a local pharmacy
- Specialty pharmacy ships to office
- Insurance may specify which specialty pharmacy you can go through

## Medical benefits

- Specialty pharmacy
- Buy and bill
- Infusion center

## Can help patients find alternative site of care if needed

- <https://prep.advancingaccess.com/hcp/asoc-locator>



# LEN Logistics and Cost

## Average Wholesale Price

- \$2,821 for oral loading dose
- \$16,930 per injection (~\$33,860/year)

## Gilead Advancing Access Copay Savings Program

- Assists **commercially** insured, eligible individuals with their copays via reimbursement
- Copay support covers up to \$8,000 per year including up to \$100 per visit for the injection
- May help lower copay to as little as \$0 for prescribed medications

## Gilead medication assistance program

- Uninsured patients

# Patient Case/Learning Check (Pharmacy Technician ONLY)



Which long-acting injectable must be administered with an oral dose on the first and second day of therapy?

- a. Cabotegravir
- b. Lenacapavir
- c. None of the above

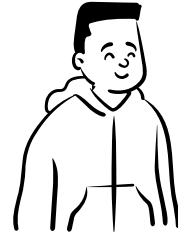
# Patient Case/Learning Check (Pharmacy Technician ONLY)



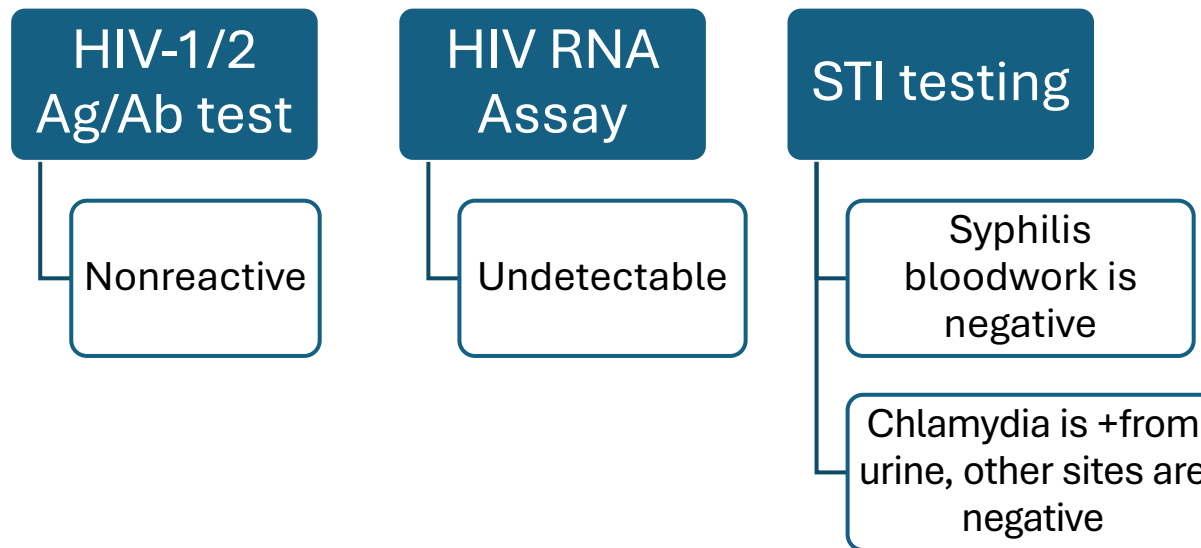
Which long-acting injectable must be administered with an oral dose on the first and second day of therapy?

- a. Cabotegravir
- b. Lenacapavir**
- c. None of the above

# TJ: Follow-up Visit



Patient presents 3 months later. He continued to try oral therapy and tried shifting to the 2-1-1 method but is finding he is missing doses frequently and couldn't follow 2-1-1 method reliably, he is now interested in possible injectable therapy options



# Patient Case/Learning Check

## (Pharmacist and Pharmacy Technician)



Which of the following pairs of statements are correct?

- a. Cabotegravir: SQ injection given every month for two doses, then every 2 months thereafter
- b. Cabotegravir: Required lead-in dose with oral cabotegravir to assess tolerability
- c. Lenacapavir: Most common side effects are known as the "start-up syndrome" of headache, nausea, fatigue
- d. Lenacapavir: SQ injection given every 6 months, with oral dose administered on day 1 and day 2 of starting therapy

# Patient Case/Learning Check

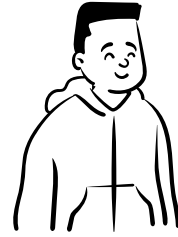
## (Pharmacist and Pharmacy Technician)



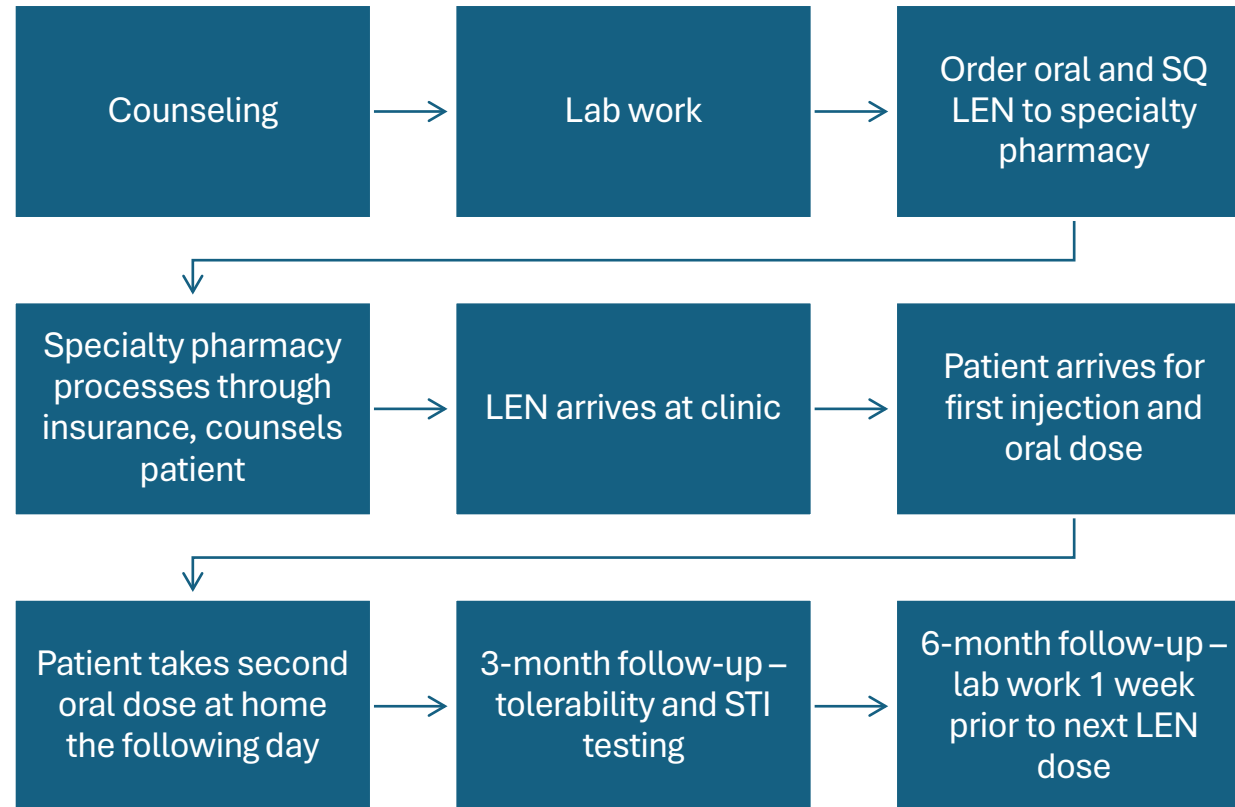
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- c. Lenacapavir: Most common side effects are known as the "start-up syndrome" of headache, nausea, fatigue
- d. **Lenacapavir: SQ injection given every 6 months, with oral dose administered on day 1 and day 2 of starting therapy**

# TJ: Follow-up Visit



After discussion of options, patient wishes to move forward with LEN



# Patient Case/Learning Check (Pharmacist ONLY)



Which of the following are counseling points for lenacapavir?

- a. Administration of the injection may cause nodules that persist for months
- b. Discussion of alternative PrEP strategies is not necessary after discontinuation
- c. A lead-in dose of oral lenacapavir is recommended to assess tolerability
- d. Avoid polyvalent cations with the first dose due to drug-drug interactions

# Patient Case/Learning Check (Pharmacist ONLY)



Which of the following are counseling points for lenacapavir?

- a. **Administration of the injection may cause nodules that persist for months**
- b. Discussion of alternative PrEP strategies is not necessary after discontinuation
- c. A lead-in dose of oral lenacapavir is recommended to assess tolerability
- d. Avoid polyvalent cations with the first dose due to drug-drug interactions

# Patient Case/Learning Check (Pharmacist and Pharmacy Technician)



Which of the following lab tests should be completed at least every 6 months while on lenacapavir?

- a. HIV-1/2 ab/ag and STI testing
- b. Lipid panel
- c. Hepatitis B antibodies
- d. Hepatitis C antibody

# Patient Case/Learning Check

## (Pharmacist and Pharmacy Technician)



Which of the following lab tests should be completed at least every 6 months while on lenacapavir?

- a. **HIV-1/2 ab/ag and STI testing**
- b. Lipid panel
- c. Hepatitis B antibodies
- d. Hepatitis C antibody

# Doxy PEP



Doxycycline 200 mg administered orally after condomless sex to prevent syphilis, chlamydia, and gonorrhea

Shown to reduce syphilis and chlamydia by 70% and gonorrhea infections by 50% in MSM and TGW

Insufficient data in individuals who report receptive vaginal sex

Providers should counsel all gay, bisexual, other MSM and TGW with a history of at least 1 STI in the last 12 months about the benefits and harms of Doxy PEP



# Doxy PEP

## Formulation

- Delayed release or immediate release, hyclate or monohydrate
- IR formulations usually cost less

## Administration

- Ideally take within 24 hours after condomless sex, up to 72 hours
- Take with 8 oz water, remain upright 30-60 min
- Milk and positive cations should be avoided within 2 hours

## Adverse effects

- Nausea, GI upset reflux
- Photosensitivity
- May select for antibiotic-resistant organisms

## Supply

- Consider a supply equal to HIV PrEP supply



# HIV PrEP: Quick Comparisons

Type of Exposure	Daily TDF/FTC	On-demand TDF/FTC	Daily TAF/FTC	CAB-IM	LEN-SQ
Insertive anal/vaginal sex	X	X	X	X	X
Receptive anal sex	X	X	X	X	X
Receptive vaginal sex	X			X	X
Injection drug use	X			X*	
Pregnant and breastfeeding	X			X**	X**
Recommended for individuals with CrCl 30-60			X	X	X
Concomitant gender-affirming hormone therapy	X	X	X	X	X

\*TDF/FTC has the strongest evidence for PWID. Patients should also be assessed for sexual routes of exposure to HIV. CAB can be considered for patients who are also at risk from sexual exposures

\*\*Preliminary data in pregnancy and breastfeeding. TDF/FTC is the preferred PrEP option during pregnancy and breastfeeding



# Discontinuing PrEP

- Repeat HIV testing should always be performed after discontinuation
- Protection wanes within 7-10 days after stopping TDF/FTC or TAF/FTC
- When CAB-IM or LEN-SQ is discontinued, oral HIV PrEP should be recommended as high priority during the tail period
- After LAI, continue quarterly follow-up that include HIV testing for at least 12 months

# Expanded Patient Access in Oregon: HB 2292



Requires health plans to cover medications approved for prevention and treatment of HIV without cost-sharing or prior authorization. This also includes services necessary for starting or continuing HIV prevention drugs, such as office visits, testing, vaccinations, and monitoring services.

The legislation applies to insurers that offer health benefit plans that reimburse the cost of counseling, prevention services, or screening for sexually transmitted diseases.

Applies to state regulated health plans

- Oregon Medicaid – Fee-for-Service
- Oregon Managed Medicaid Plans (CCO's)
- State regulated commercial plans (e.g. Regence of Oregon, Moda Health, PacificSource, Providence Health Plan)



# Expanded Patient Access in Oregon

## HB 2942

- Oregon Health Authority and CCOs to reimburse pharmacists and pharmacies in the same manner as other health care providers for services related to HIV treatment

## ORS 689.645

- Pharmacist may provide patient care services pursuant to a statewide drug therapy management protocol, including PrEP drug regimens



# Expanded Patient Access in Oregon

- Find Oregon PrEP Providers:
  - <https://www.oraetc.org/prep-provider-list>
- Safeway Pharmacy
  - Eugene
  - Medford
  - McMinnville
  - Woodburn
  - Portland
  - Gresham

**Pre-Exposure Prophylaxis (PrEP) Self-Screening Patient Intake Form**  
(CONFIDENTIAL-Protected Health Information)

Date \_\_\_/\_\_\_/\_\_\_ Date of Birth \_\_\_/\_\_\_/\_\_\_ Age \_\_\_  
Legal Name \_\_\_\_\_ Name \_\_\_\_\_  
Sex Assigned at Birth (circle) M / F Gender Identification (circle) M / F / Other \_\_\_  
Pronouns (circle) She/Her/Hers, He/Him/His, They/Them/Their, Ze/Hir/Hirs, Other \_\_\_\_\_  
Street Address \_\_\_\_\_  
Phone ( ) \_\_\_\_\_ Email Address \_\_\_\_\_  
Healthcare Provider Name \_\_\_\_\_ Phone ( ) \_\_\_\_\_ Fax ( ) \_\_\_\_\_  
Do you have health insurance? Yes / No Insurance Provider Name \_\_\_\_\_  
Any allergies to medications? Yes / No If yes, please list \_\_\_\_\_

**Background Information:** These questions are highly confidential and help the pharmacist to determine if PrEP is right for you and what Human Immunodeficiency Virus (HIV) and Sexually Transmitted Infection (STI) testing is recommended.

**Do you answer yes to any of the following?**       yes  no

1. Do you want to start or continue PrEP?
2. Do you sexually partner with men, women, transgender, or non-binary people?
3. Please estimate how often you use condoms for sex. Please estimate the date of the last time you had sex without a condom. _____% of the time ___/___ last sex without a condom
4. Do you have oral sex? <ul style="list-style-type: none"><li>• Giving- you perform oral sex on someone else</li><li>• Receiving- someone performs oral sex on you</li></ul>
5. Do you have vaginal sex? <ul style="list-style-type: none"><li>• Receptive- you have a vagina and you use it for vaginal sex</li><li>• Insertive- you have a penis and you use it for vaginal sex</li></ul>
6. Do you have anal sex? <ul style="list-style-type: none"><li>• Receptive- someone uses their penis to perform anal sex on you</li><li>• Insertive- you use your penis to perform anal sex on someone else</li></ul>
7. Do you inject drugs?
8. Are you in a relationship with an HIV-positive partner?
9. Do you exchange sex for money or goods? (includes paying for sex)
10. Do you use poppers (inhaled nitrates) and/or methamphetamine for sex?



# Key References and Resources

- [World Health Organization Recommendations on HIV and STI testing](#)
- [World Health Organization Implementation Tool for PrEP](#)
- [World Health Organization Guidelines on Lenacapavir](#)
- [International Antiviral Society-USA Panel Guidelines](#)
- [Centers for Disease Control and Prevention Guidelines](#)
- [Centers for Disease Control and Prevention Guide to Taking a Sexual History](#)
- [US Preventive Services Task Force Guidelines](#)
- [Centers for Disease Control and Prevention Guidance on HIV Testing](#)

# PrEPared in Primary Care: Putting PrEP into Practice

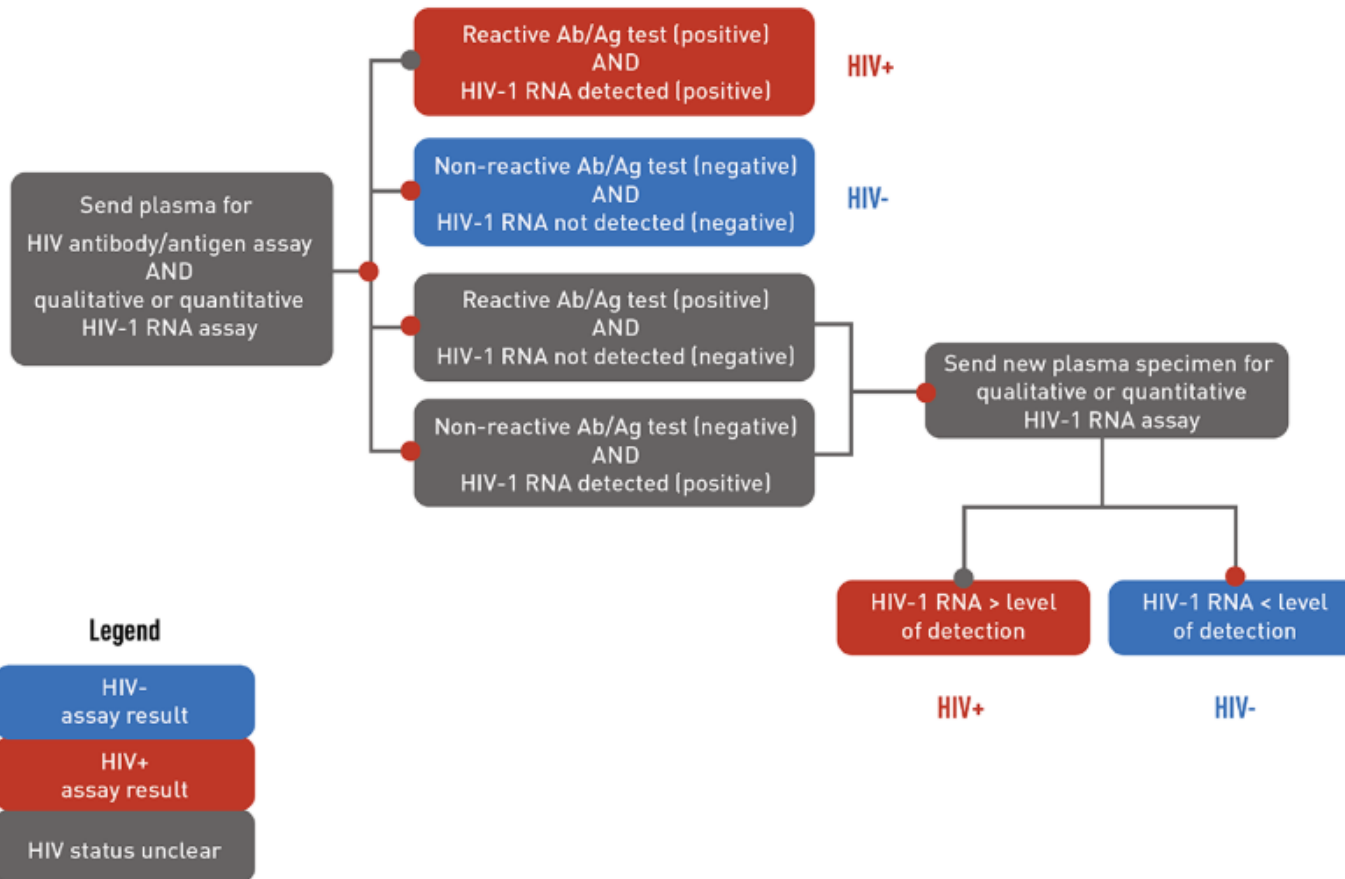
## Questions?





# HIV Testing for Patients Previously on PrEP

If the patient has taken oral PrEP or PEP medication in the past 3 months  
OR  
has received a cabotegravir injection in the past 12 months





# Long-acting Early Viral Inhibition (LEVI) Syndrome

- HIV rapid tests and Ag/Ab tests often fail to detect HIV infection in the setting of CAB PrEP
- Viral suppression and delayed Ab expression can persist for months after infection, even after injections are discontinued
- Delayed detection of HIV infection can lead to
  - Unnecessary CAB injections
  - Delayed ART initiation
  - Emergence of INSTI resistance

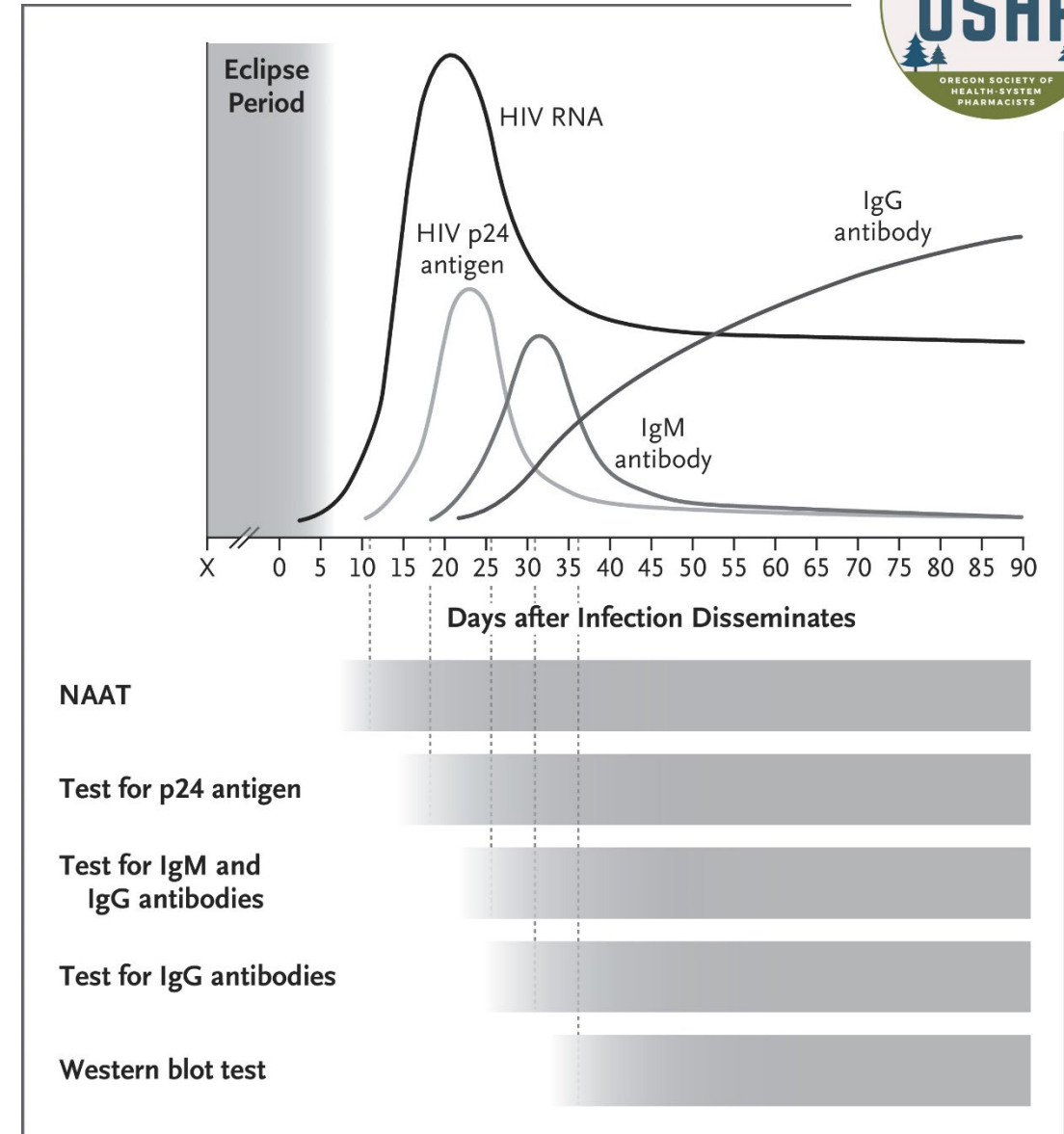
# Long-acting Early Viral Inhibition (LEVI) Syndrome



	AHI	LEVI
<b>Cause</b>	Phase of natural HIV infection	Long-acting anti-viral PrEP agent (prototype: CAB-LA)
<b>Onset</b>	New infection	Infection during PrEP Initiation of PrEP agent during acute/early infection
<b>Viral replication</b>	Explosive	Smoldering
<b>Symptoms</b>	Fever, chills, rash, night sweats, muscle aches, sore throat, fatigue, swollen glands	Minimal, variable, often no symptoms reported
<b>Detection</b>	Ag/Ab assay, RNA assays (including less sensitive POC and pooled tests), DNA assays, total nucleic acid assays	Ultrasensitive RNA assay (often low or undetectable RNA, low/undetectable DNA, diminished/delayed Ab production)
<b>Assay reversion</b>	Rare	Common for many test types
<b>Duration</b>	1-2 weeks (until Ab detection)	Months (until viral breakthrough, drug clearance, or ART start); can persist months after the anti-viral agent is discontinued
<b>Transmission</b>	Very likely	Unlikely (except possibly through blood transfusion)
<b>Drug resistance</b>	No (unless transmitted)	Yes (can emerge early when viral load is low)

# HIV Testing Considerations

- The **HIV-1/2 antigen/antibody test with reflex confirmation** is the recommended initial screening test that detects HIV-1 and HIV-2 antibodies plus HIV-1 p24 antigen, followed by an antibody differentiation assay if reactive
  - Can detect acute HIV infection as early as 1-2 weeks after HIV RNA appears and before antibodies develop, because it identifies the p24 antigen that is detectable around 14-16 days post-infection
  - When this initial test is reactive, specimens undergo reflex testing to distinguish between HIV-1 and HIV-2 antibodies
- The **HIV RNA assay** directly detects viral nucleic acid and is used to diagnose acute infection when antibody tests are negative or indeterminate, or when very early infection is suspected before p24 antigen becomes detectable
  - Detects viral RNA approximately 10-12 days after infection, earlier than any antibody or antigen test
  - Particularly valuable for diagnosing acute infection when antigen/antibody test is reactive but assay is negative, indicating infection before antibody development
  - Should be performed if there is high clinical suspicion of an early infection even if the initial antigen/antibody test is nonreactive





# Hepatitis B Screening

HBsAg	Anti-HBs	Anti-HBc	Interpretation	Action
+	-	+	Chronic HBV infection	Referral to hepatitis B-directed care
+	-	-/+	Acute HBV infection (if anti-HBc IgM positive)	Referral to hepatitis B-directed care
-	+	+	Resolved past infection	Counseling reassurance, no further management unless immunocompromised
-	+	-	Immune from vaccination	Reassurance
-	-	-	Susceptible to hepatitis B	Vaccinate
-	-	+	Further evaluation necessary	



# Syphilis Screening

NTT (RPR or VDRL)	TT (TP-PA/EIA)	Interpretation	Clinical Action
Positive (with titer)	Positive	Active syphilis (new diagnosis or reinfection if titer $\geq 4$ fold higher than prior)	Stage infection, treat appropriately
Negative	Positive	Prior treated syphilis, untreated late latent syphilis, very early primary syphilis, or false negative NTT	Review treatment history, if untreated, treat for late latent
Positive (low titer)	Negative	Biologic false-positive	Evaluate for autoimmune disease, pregnancy, acute illness
Negative	Negative	No evidence of syphilis	No treatment needed



# PEP to PrEP Transition

- After 28-day course of nPEP, repeat Ag/Ab test and HIV-1 RNA test
- The transition is most seamless at week 4
  - Start PrEP right away, don't need to wait for the 12-week testing
- Complete labs 12 weeks after the nPEP testing

# LEN Dose Recommendations with CYP3A Inducers



Strong CYP3A Inducers: Schedule for supplemental doses of YEZTUGO <sup>a</sup>	
Time	Dosage
On the day a strong CYP3A inducer is initiated (which should be at least 2 days after YEZTUGO is first initiated)	<b>Supplemental dosage: Step 1</b> <b>927 mg subcutaneously</b> (2 x 1.5-mL injections) AND <b>600 mg orally</b> (2 x 300-mg tablets)
On the day after a strong CYP3A inducer is initiated	<b>Supplemental dosage: Step 2</b> <b>600 mg orally</b> (2 x 300-mg tablets)
If a strong CYP3A inducer is coadministered for longer than 6 months	<b>Subsequent supplemental dosage</b> Every 6 months <sup>b</sup> from initiation of a strong CYP3A inducer, continue to administer supplemental doses of YEZTUGO as described above in Steps 1 and 2

After stopping the strong CYP3A inducer, continue the once-every-6-months

Moderate CYP3A Inducers: Schedule for supplemental doses of YEZTUGO <sup>a</sup>	
Time	Dosage
On the day a moderate CYP3A inducer is initiated	<b>Supplemental dosage</b> <b>463.5 mg subcutaneously</b> (1 x 1.5-mL injection)
If a moderate CYP3A inducer is coadministered for longer than 6 months	<b>Subsequent supplemental dosage</b> Every 6 months <sup>b</sup> from initiation of a moderate CYP3A inducer, continue to administer supplemental dose of YEZTUGO as described above

After stopping the moderate CYP3A inducer, continue the once-every-6-months scheduled continuation injection dosing of YEZTUGO.