Penn Medicine

Updates in HIV Treatment & Prevention

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Updates in HIV Treatment & Prevention

SOURCES FOR THIS UPDATE

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV (DHHS)

- Last updated 9/12/2024 (from 2020)
- New section on Transplant
- Updates on minor aspects of recommended regimens
- Section on using LA CAB/RPV case by case in pts with VF
- Expanded section on HIV and the older person, substance use and HIV, recs on TB treatment in patients taking ART
- New section on adherence to the continuum of care (importance of social determinants of health, guiding individuals through transitions between different health systems)

IAS-USA Guidelines

- Last updated 12/1/2024 (from 2022)
- New data on doravirine and islatravir
- Updates on minor aspects of first and second line therapies
- Management of Comorbidities, specifically findings from the REPRIEVE trial, which demonstrated significantly fewer major cardiovascular events among people with HIV randomized to pitavastatin compared to placebo
- Weight and Metabolic Considerations: addressing weight gain, hypertension, and diabetes among people with HIV, reflecting the need for ongoing monitoring and management of these conditions.

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society-USA Panel. JAMA 2025;333(7):609-628; Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new. Accessed 5/5/2025; CROI 2025 Abstracts, https://www.croiconference.org/ Accessed 5/5/2025.

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What has not changed for HIV treatment

- ART is recommended for everyone who has HIV, as soon as possible
- ART also reduces the risk of HIV transmission (U=U)
- Recommended initial regimen = INSTI anchor plus a 1- or 2-NRTI backbone
- Initial regimen depends on medical and psychiatric comorbidities, patient preferences, drug interactions
- If a patient fails an ART regimen, assess whether it is due to adherence or resistance
- HIV genotypes are sent at diagnosis/entry into care, and on a failing regimen
- Reassure patients often and early

ART = antiretroviral treatment; U=U is undetectable = untransmittable; INSTI = integrase strand transfer inhibitor; NRTI = nucleoside reverse transcription inhibitor

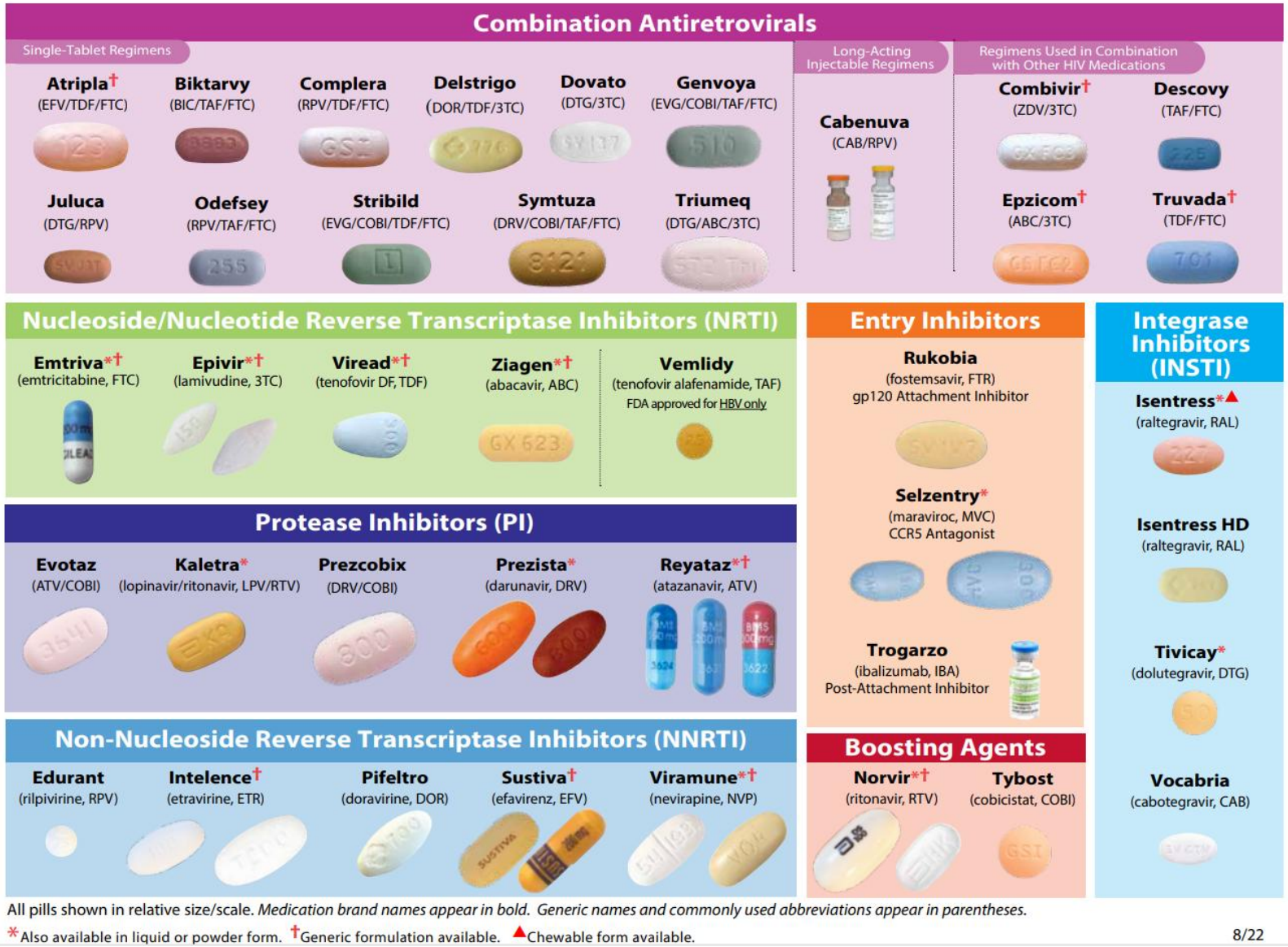
Important things to discuss early & often

- How HIV is passed to others, and *how it is not*
- You can have babies! A family!
- Considering whether to disclose status to family, friends, partners
- Act 148 (Pennsylvania's Confidentiality of HIV-Related Information Act) prohibits providers from sharing any HIV-related information other than with other established health care providers without written permission (i.e. your employer does not need to know)
- You can receive healthcare whether or not you have health insurance

Patients cured of HIV

Timothy Brown “Berlin patient” 2006 - leukemia
Adam Castillejo “London patient” 2019 – Hodgkin’s lymphoma
Mark Franke “Dusseldorf patient” 2019 - leukemia
“NY patient” first female 2022 - leukemia
Paul Edmonds “City of Hope patient” 2022 - leukemia
“Geneva patient” 2023 – leukemia, first patient not to receive double CCRf-delta-32 mutation (had GVHD, received JAK 1/2 inhibitor which has been postulated to reduce the HIV reservoir

HIV Medication Chart



All pills shown in relative size/scale. *Medication brand names appear in bold. Generic names and commonly used abbreviations appear in parentheses.*

*Also available in liquid or powder form. †Generic formulation available. ▲Chewable form available.

8/22

AIDS Education & Training Program, HIV Medication Chart https://aidsetc.org/sites/default/files/media/document/2022-11/HIV%20Medication%20Chart_August%202022.pdf Accessed 5/7/2025.

What to Start: First-line Treatment Regimens

For people who do not have a history of using CAB-LA as PrEP, one of the following regimens is recommended:
Bictegravir/tenofovir alafenamide/emtricitabine **(AI)**
Dolutegravir + (TAF or TDF) + (FTC or 3TC) **(AI)**
Dolutegravir/lamivudine (if VL < 500,000 and no hepatitis B) **(AI)**

For people who have a history of CAB-LA use as PrEP, INSTI genotype resistance testing should be performed before starting ART. If ART is to be started before results of genotypic testing results, the following regimen is recommended:
•DRV/c[c] or DRV/r with (TAF or TDF) plus (FTC or 3TC)—pending the results of the genotype test **(AIII)**

For people who are pregnant:
Dolutegravir + (TAF or TDF) + (FTC or 3TC) **(AI)**
Bictegravir/tenofovir alafenamide/emtricitabine **(AI)**
Darunavir/norvir/TXF/XTC (cannot use cobicistat)

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new. Accessed 5/5/2025

We are in the Injectables era

- Long-acting cabotegravir/rilpiverine (LA CAB/RPV)
  - Approved 2021 as monthly injection, in 2022 every 2 months
  - For virally suppressed patients
- What about in patients who are not virally suppressed?
  - For those unable to take oral ART with advanced HIV disease, LA CAB/RPV may be considered for people with viremia who meet the criteria below when no other treatment options are effective:
    - Unable to take oral ART consistently despite extensive efforts and clinical support
    - High risk of HIV disease progression ($CD4^+$ <200/µL or history AIDS-defining illness)
    - Virus susceptible to both cabotegravir and rilpivirine

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society-USA Panel. JAMA 2025;333(7):609-628.

CROI 2025 Updates

- CARES study
  - Evaluated safety and efficacy of switching from oral HIV therapy to LA CAB/RPV who were virologically suppressed in Africa
  - At weeks 48 and 96, injectable therapy was noninferior to oral HIV therapy (96.9%, 97.3% virologically suppressed, respectively)
- LAPTOP study
  - Assessed the best HIV therapy in treatment-naïve patients with advanced HIV (median CD4 count 41 c/mL) in several countries
  - Integrase-based therapy (bictegravir/TAF/FTC) was non-inferior to darunavir-containing regimen overall, but better virologic response at 48 weeks and better overall tolerability

Kityo. CROI 2025. Abstr 202. Kityo. Lancet Infect Dis. 2024;24:10; Behrens. CROI 2025. Abstr 658.

CROI 2025 Updates

- Switch to doravirine/islatravir (DOR/ISL) from oral ART
  - Islatravir is a nucleoside reverse transcriptase translocation inhibitor
  - Switch to DOR/ISL maintained virologic suppression at 48 weeks (non-inferior)
- Lenacapavir + 2 investigational broadly neutralizing antibodies
  - Every-6-month therapy non-inferior to oral therapy at week 26
- EMBRACE study: CAB + another broadly neutralizing antibody
  - Every-4-month therapy (in conjunction with monthly CAB) maintained virologic suppression in most adults who were sensitive to the bNAb

Colson. CROI 2025. Abstr 204B. 2. Orkin. CROI 2025. Abstr 204A; Ogbuagu. CROI 2025. Abstr 151; Taiwo. CROI 2025. Abstr 203. NCT05996471.

Pipeline: Phase IIa Proof-of Concept Studies

VH-184: Third-Generation INSTI[1,2]

- In vitro activity demonstrated to DTG-and CAB-resistant viruses
- Maximum change from baseline in HIV-1 RNA through Day 10: >2 $\log_{10}$ c/mL decline with 50-mg and 300-mg doses
- AEs grade 1/2; no serious AEs

Plan to investigate as LA injectable for HIV treatment

VH-499: HIV-1 Capsid Inhibitor[3]

- Maximum change from baseline in HIV-1 RNA through Day 11: 1.8-2.2 $\log_{10}$ c/mL decline (highest seen with 250-mg dose)
- 1 participant receiving VH-499 25 mg had an emergent capsid inhibitor RAM (Q67Q/H)
- AEs grade 1/2; no serious AEs

Plan to investigate as LA injectable for HIV treatment

1. Rogg. CROI 2025. Abstr 152. 2. Rogg. AIDS 2024. Abstr OAB2603. 3. Grisel. CROI 2025. Abstr 153.

HIV Prevention

OLD & NEW

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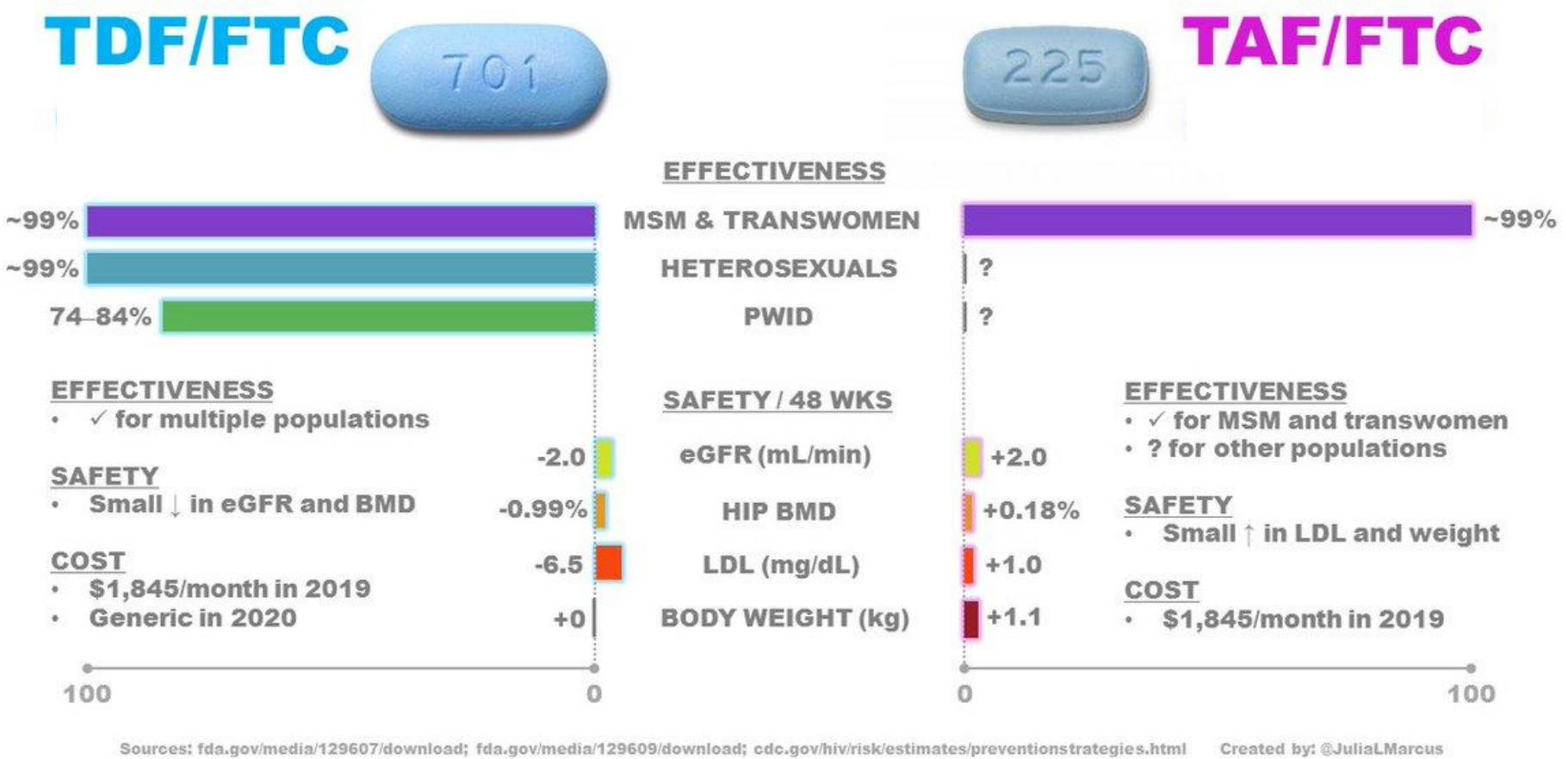
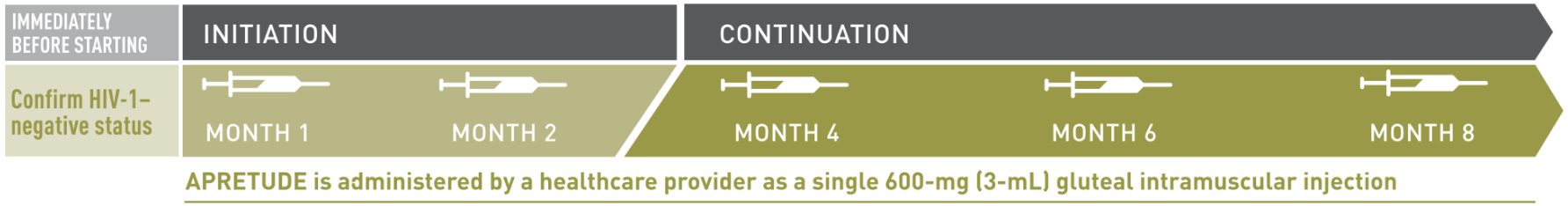
Which medication should I prescribe for PrEP?



Sources: fda.gov/media/129607/download; fda.gov/media/129609/download; cdc.gov/hiv/risk/estimates/preventionstrategies.html Created by: @JuliaLMarcus

LA-Cabotegravir for PrEP Schedule

No safety concerns identified in HTPN 083/084
Oral lead-in therapy now optional



APRETUDE is administered by a healthcare provider as a single 600-mg (3-mL) gluteal intramuscular injection

Injections may be administered +/- 7 days of due date for subsequent injection
Patients unable to come in with in treatment window should be prescribed oral PrEP with either TDF/FTC or TAF/FTC

Tanner MR, et al. *MMWR Recomm Rep*. 2020;69:1-12.

CROI 2025 Updates

- Roll-out of injectable PrEP (cabotegravir) in high HIV prevalence areas
  - PILLAR study: 17 clinics, 85% persistence at 6 months, 73% persistence at 12 months, 0% acquired HIV, 13% acquired STIs
  - Pregnancy outcomes consistent with those expected in this population
  - HIV RNA screening did not perform well in patients on LA-CAB
    - HPTN 084 study showed 75% of positive HIV RNA tests were false positives

Khan. CROI 2025. Abstr 196; Shoptaw. CROI 2025. Abstr 183; Delany-Moretlwe. Lancet. 2022;399:1779; Delany-Moretlwe. CROI 2025. Abstr 195. 3. NCT03164564; Gill. CROI 2025. Abstr 120. NCT04994509; Delany-Moretlwe. AIDS 2022. Abstr OALBX0107.

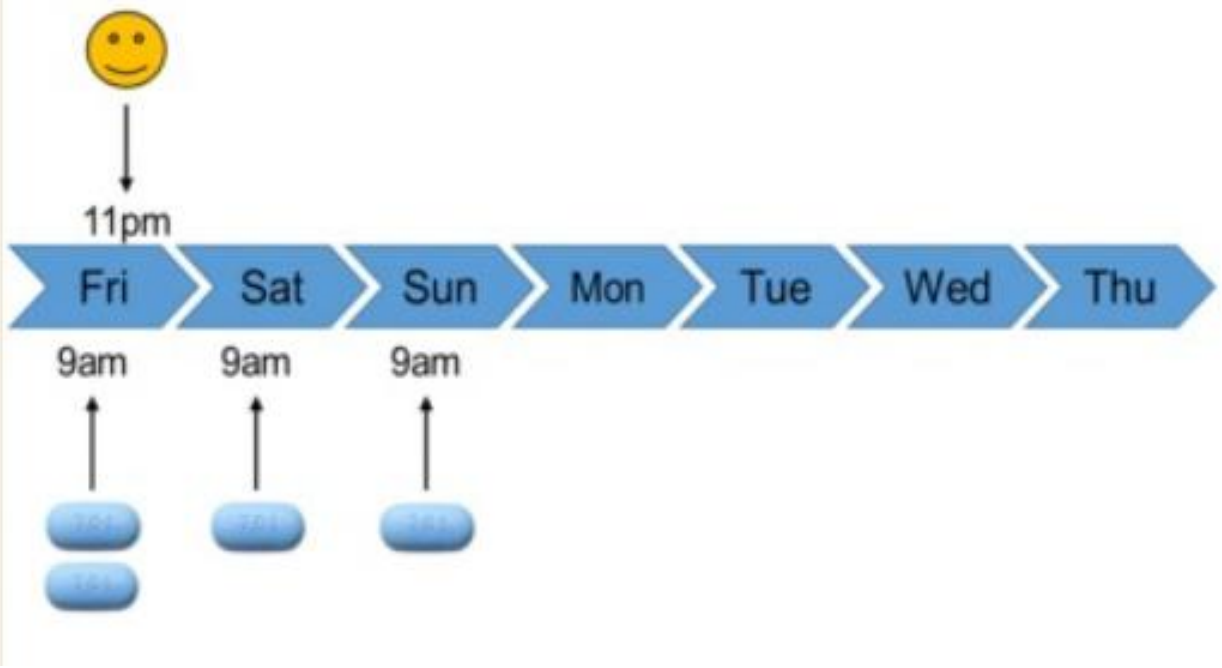
CROI 2025 Updates

- Lenacapavir is on the verge of approval for PrEP
  - PURPOSE 1: lenacapavir is effective in cisgender adolescent girls
- Need to increase access to PrEP among people who inject drugs:
  - HPTN 094: Showed addition of mobile services to a peer health navigation program combined reduced all cause mortality (*P* = .0661)
    - Did not increase MOUD, HIV suppression, PrEP usage
    - Did not decrease HIV acquisition

Khan. CROI 2025. Abstr 196; Shoptaw. CROI 2025. Abstr 183; Delany-Moretlwe. Lancet. 2022;399:1779; Delany-Moretlwe. CROI 2025. Abstr 195. 3. NCT03164564; Gill. CROI 2025. Abstr 120. NCT04994509; Delany-Moretlwe. AIDS 2022. Abstr OALBX0107.

On-demand PrEP

Example 1: One sex episode.
2 PrEP tablets 2-24 hours before sex; 1 PrEP tablet 24 hours after and another 48 hours after the double dose.



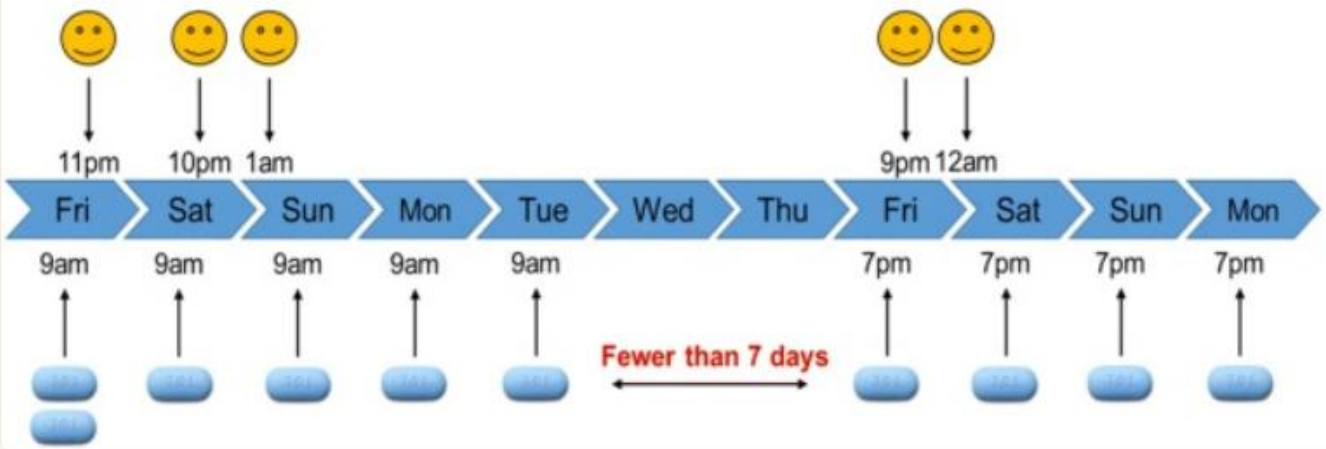
Saberi P and Scott H. J Gen Int Med 2020.

Dosing Schedule

Saberi P and Scott H. J Gen Int Med 2020.

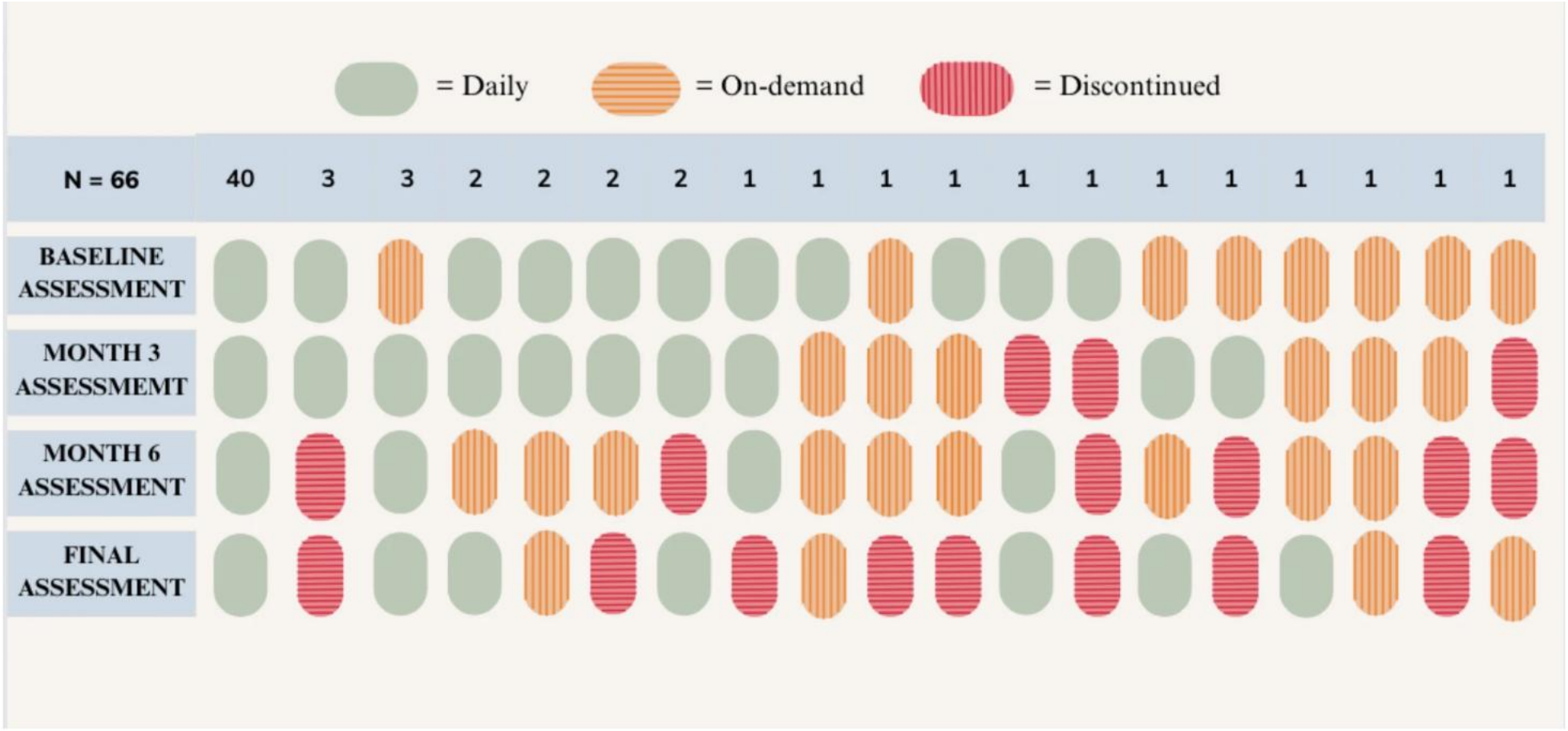
Dosing Schedule

Example 3: Multiple sex episodes in one week.
If there are <7 days between end of one on-demand dosing period and beginning of another, take one single PrEP tablet to restart.
If there are ≥7 since last PrEP dose, start again with 2 PrEP tablets.



Saberi P and Scott H. J Gen Int Med 2020.

Switching back and forth is fairly common



Daily and on-demand PrEP dosing strategy and PrEP discontinuation for participants with complete data at all assessment points in the *PrEP iT!* intervention trial ($n = 66$). Note: Final Assessment conducted 3 to 4 months after month 6 assessment.

Storholm E. AIDS and Behavior 2023

On-Demand FTC/TDF for PrEP in Cisgender Women

- Modeling study seeking to optimize dosing of on-demand TDF/FTC PrEP for women using a previously published PK/PD model of female genitourinary tract tissue

Regimen	TDF/FTC Dosing Instructions	Days Post-Sex		
		5	7	10
2-1-1 (reference)	600/400mg 2 hours pre-sex then 300/200mg 24 & 48 hours after sex	85	46	10
2-2-1	600/400mg 2 hours pre-sex then 600/400mg 24 hours & 300/200mg 48 hours after sex	98.2	68.5	14.1
2-2-2	600/400mg 2 hours pre-sex then 600/400mg 24 & 48 hours after sex	99	77.4	13.8
2-1-1-1	600/400mg 2 hours pre-sex then 300/200mg 24, 48, & 72 hours after sex	99.9	83.7	16.3
2-2-1-1	600/400mg 2 hours pre-sex then 600/400mg 24 hours & 300/200mg 48 & 72 hours after sex	99.8	85.7	19.1
2-2-2-1	600/400mg 2 hours pre-sex then 600/400mg 24 & 48 hours & 300/200mg 72 hours after sex	99.9	90.3	20.8
2-2-2-2	600/400mg 2 hours pre-sex then 600/400mg 24, 48 & 72 hours after sex	99.9	95.4	27.3

1. Cottrell. J Infect Dis. 2016;214:55. 2. Garrett. J Pharmacol Exp Ther. 2018;367:245. 3. Dumond. CROI 2025. Abstr 157.

Other Investigational PrEP Modalities for Cisgender Women

Oral Daily FTC/TAF: PURPOSE-1 Case Control Analysis

- Majority of participants diagnosed with HIV while receiving FTC/TAF had low adherence or decreased adherence over time
  - 1 case likely due to transmitted drug resistance
- Investigators concluded that FTC/TAF efficacious among participants with medium or high adherence
  - 89% lower odds of acquiring HIV if ≥2 doses taken per wk (OR 0.11; 95% CI: 0.012-0.49)

Multi-prevention Technology for HIV prevention *and* contraception

- Safety and efficacy reported in macaque model of implant releasing Cabotegravir and medroxyprogesterone

1 Kiweewa. CROI 2025. Abstr 194. 2. Massud. CROI 2025. Abstr 199. This slide adapted from CCO slide with edits.

Slide credit: clinicaloptions.com

Pipeline: Long-Acting PrEP

Once-Yearly Intramuscular LEN[1,2]

- 5000-mg dose (two 5 mL of 500 mg/mL)
- With once-yearly IM, LEN concentrations higher than required for protective efficacy (with twice-yearly SC LEN based on PURPOSE-1 and -2)
- IM LEN safe and well-tolerated; most common AEs were ISRs that improved with ice pretreatment
  - No nodules observed with either formulation

Plan to investigate as LA PrEP option

Once-Monthly MK-8527 (NRTTI)[3]

- Based on a population macaque PK model, ≥6 mg once-monthly dose expected to maintain PK/PD threshold >90%

Plan to investigate as monthly oral PrEP option

1. Jogiraju. CROI 2025. Abstr 154. 2. Jogiraju. Lancet. 2025;[Epub] 3. Kapoor. CROI 2025. Abstr 1232

Recommendations for HIV and STI Prevention

- Serostatus-neutral approach to reduce HIV stigma, ensuring rapid care linkage for individuals diagnosed and PrEP navigation for those who test negative
- Offer PrEP to all sexually active individuals, anyone requesting it, and those using nonprescription drugs or substances, without specific risk criteria or screening tools
- Offer PrEP to all sexual partners of individuals with HIV and to those who share injection drug works with individuals with HIV or of unknown HIV status
    - For monogamous sexual partners of persons with HIV who are known to be receiving ART and have viral loads below 200 copies/mL, it is a reasonable and appropriate decision to defer PrEP; if such a patient requests PrEP; however, it is also reasonable to provide it because of the possibility that there are undisclosed exposures occurring
- Condoms are recommended for all penetrative sexual acts
- Rapid PrEP start if you have a negative HIV test within 7 days, or rapid test on day of start

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society-USA Panel. JAMA 2025;333(7):609-628

Final Thoughts on PrEP

- 3 current options for PrEP
- Expanding options for cisgender women
- Expanding options for 2-1-1 PrEP
- Lenacapavir every 6 months should be approved 6/19/2025, with hopeful approval of lenacapavir every 12 months in 2027
- MK-8527 monthly oral PrEP may be coming too
- Continuing to address adherence, proactive discussion of barriers to care, and making options available to patients are critical

STI Prevention

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Doxycycline for STI prevention (doxyPEP)

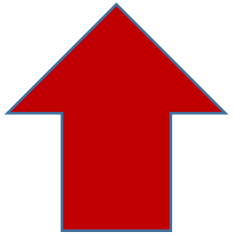
- CDC-recommended for gay, bisexual, other MSM, and transgender women, with history of ≥ 1 bacterial STI (syphilis, chlamydia, or gonorrhea) in the past 12 months
- Doxy-PEP use is rolling out across US and in some countries globally
  - Philadelphia NHBS: 37% heard of doxy-PEP but only 5.5% used in last 12 months
  - More work needed to reach those who are interested and could benefit
- Doxy-PEP reduced use of antibiotics for STI treatment in a real-world setting
  - Criteria for most appropriate use may require refinement for individual clinic or geographic populations
  - Effectiveness for STI prevention is sustained in one of SF's largest SHCs
- Two studies of doxy-P(r)EP found little to no impact on microbiome or emergent antimicrobial resistance

AIDS Education and Training Center, Mountain West. CROI 2025: Updates in HIV Prevention and STIs. https://mwaetc.org/mwaetc-on-demand/presentations/thu-04172025-1200/croi-2025-updates-hiv-prevention-and-stis. Accessed 5/7/2025. CROI conference abstracts e-book. https://www.croiconference.org/wp-content/uploads/sites/2/resources/2025/croi2025-abstract-ebook.pdf. Accessed 5/7/2025. Nassau et al, CROI, poster 1276.

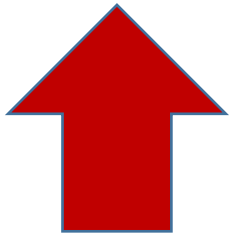
Comorbidities

WEIGHT GAIN, CARDIOMETABOLIC RISK, SUBSTANCE USE DISORDER

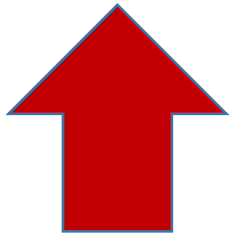
HIV-associated cardiometabolic risk



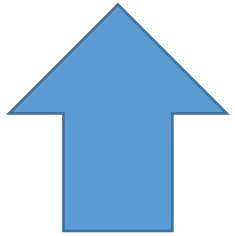
Accelerated atherosclerotic disease



Increased risk cardiovascular and cerebrovascular events



Higher risk of renal disease, including HIV-AN



Higher risk of transmission to partners

Source: HHS Antiretroviral Therapy Guidelines. Clinicalinfo.HIV.gov. Accessed 3/18/2021

Weight Gain and Cardiometabolic Comorbidities

- Document weight and body mass index at baseline and every 6 months for patients initiating/switching to an INSTI- or TAF–based regimen to identify those with excessive weight gain
- Monitor blood pressure at each visit to diagnose and treat incident hypertension
- Changing regimens because of weight gain, hypertension, insulin resistance is not recommended
- People with/at high risk for cardiovascular disease who are receiving an abacavir-containing regimen should switch to a non–abacavir-containing regimen
- Counsel patients beginning ART about potential cardiometabolic complications and the importance of lifestyle changes (exercise and diet), especially:
  - Those at increased likelihood of weight gain with use of INSTI- and TAF–based regimens
  - Those at increased risk for CV disease from hypertension, diabetes, smoking, or other factors

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society-USA Panel. JAMA 2025;333(7):609-628.

REPRIEVE: Risk of Cardiovascular Events With ABC in People With HIV

- Multicenter, randomized, double-blind study of people with HIV (N = 7769)
  - On stable ART for ≥180 days, CD4+ cell count >100 c/mm^3
  - Age 40-75 yr
  - At low to moderate risk of CVD
- Study demonstrated **36% reduction in major adverse cardiovascular events (MACE)** including MI, TIA/stroke, PAD, revascularization, CV death, with **pitavastatin** vs placebo

- **Recommendations:**
  - **People with HIV ages 40-75**
    - **Low-to-Intermediate (<20%) risk**
    - **Start moderate-intensity statin therapy:**
      - **Pitavastatin 4 mg daily**
      - **Atorvastatin 20 mg daily**
      - **Rosuvastatin 10 mg daily**
  - **General population (including HIV)**
    - **High (≥20%) risk**
    - **Start high-intensity statin therapy**
      - **Atorvastatin 40-80 mg daily**
      - **Rosuvastatin 20-40 mg daily**

Fichtenbaum. AIDS 2024. Abstr OAB3406LB. Grinspoon. NEJM. 2023;389:687. Grinspoon. NEJM. 2024;390(17):1626.

Adapted from Currier JS, Optimization of ART in the Setting of Comorbidities; from HIV 101. IAS-USA. Accessed 10/30/2024. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/statin-therapy-people-hiv. Accessed 12/6/2024.

Recommendations for Persons at Risk for and with HIV Who Use Substances and/or with SUD

- Provide screening, diagnosis and treatment for SUDs to all persons at risk for and with HIV
- SUD treatment should be integrated into HIV prevention and treatment services
- Rapid HIV testing and linkage to rapid ART or preexposure prophylaxis provision, when indicated, are recommended for persons who use substances and who have SUDs
- Harm reduction services like naloxone, safe injection education, fentanyl/xylazine drug test strips, referral to syringe programs & safe injection sites should be offered to all persons who use drugs
- Persons who use drugs should be offered oral TDF/FTC for injection drug use risk or oral (TDF/FTC or TAF/FTC) or injectable PrEP (long-acting cabotegravir) to reduce sexual risk of HIV acquisition
- Persons with opioid use and alcohol use disorders should be offered timely initiation of medications for SUD, regardless of HIV and HCV treatment plans
- Peer/patient support staff, telehealth, extended hours, mobile clinics, mobile pharmacies, pharmacy delivery services, walk-in clinic options should be available to persons who use substances/have SUDs who receive HIV treatment or prevention

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society-USA Panel. JAMA 2025;333(7):609-628.

Summary

- We have incredible medications for HIV treatment and prevention
  - Focus on INSTIs and injectable therapies – longer and longer acting!
- Focus is on getting these medications to people
  - Understanding optimal health care delivery models (i.e. peer nav, mobile svc)
  - Promoting equity in HIV treatment and prevention
- Focus is on prevention of comorbidities now that patients live longer
  - Mental health and substance use disorders
  - Cancer contributes to 20-30% deaths in people living with HIV
  - Decreasing cardiovascular risk
  - Caring for older people with HIV involves assessing polypharmacy, cardiovascular risk, neurocognitive dysfunction, screening for depression and anxiety

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society-USA Panel. JAMA 2025;333(7):609-628; Shoptaw. CROI 2025. Abstr 183

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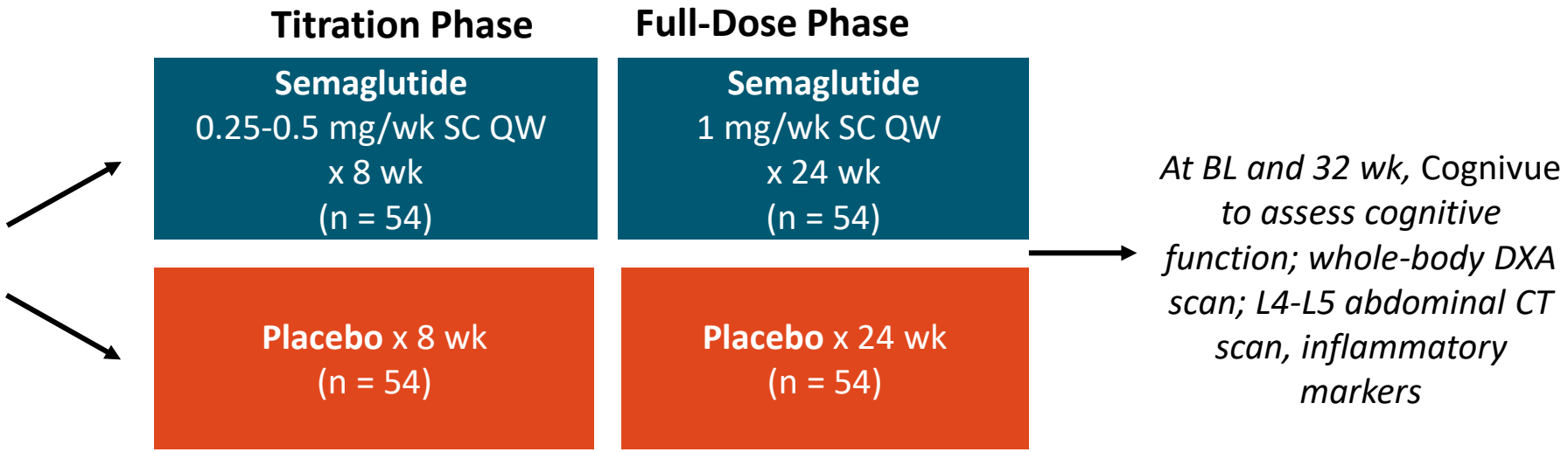
Semaglutide in People Living With HIV: Study Design

- Double-blind, placebo-controlled, randomized phase IIb trial [1-3]

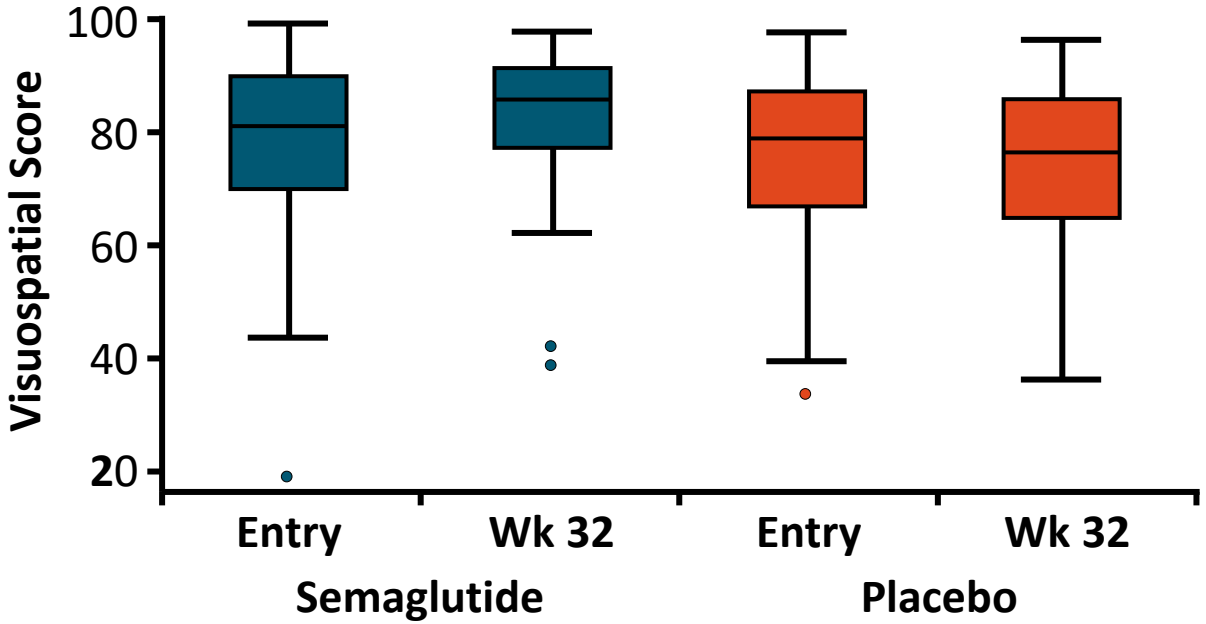


- **Primary endpoint:** changes in adipose tissue quantity at 32 wk (previously reported)[1]
- **Key secondary endpoints:** neurocognitive function, mediators of effects on neurocognitive function (ie, total/visceral adiposity, weight, inflammatory markers)[3]

1. Eckard. Lancet Diabetes Endocrinol. 2024;12:523. 2. NCT04019197. 3.. Atieh. CROI 2025. Abstr 172.

Semaglutide in People Living With HIV: Visuospatial Score

- After adjusting for sex and CD4+ cell count in linear regression analysis, semaglutide was associated with significant improvement in visuospatial score only



- Similar increases were observed in a subgroup with abnormal baseline scores (<75)

- Causal mediation analysis to identify factors with direct effects on visuospatial score
  - Factors considered after adjusting for absolute CD4+ cell count and sex: weight, visceral adipose tissue, hs-CRP, sCD163, and sCD14
- Effect of semaglutide on visuospatial scores mediated by hs-CRP and sCD163

Mediator, *P* value	Total Effect
hs-CRP	.050
sCD163	.049

Atieh. CROI 2025. Abstr 172. Reproduced with permission.

Slide credit: clinicaloptions.com

Switching HIV Therapy with Virologic suppression

•People with HIV and virologic suppression may be receiving regimens that are no longer recommended due to short- and long-term adverse effects, inconvenience, regimen complexity, anticipated drug-drug interactions, progressive kidney disease, risk of cardiovascular disease, or cost. Switching ART to one of the recommended initial ART regimens in these circumstances is frequently the optimal strategy, provided that virologic suppression can be maintained (evidence rating: AIa).

•Individuals with virologic suppression receiving regimens that contain a boosted protease inhibitor and 2 NRTIs can be switched to dolutegravir plus TXF/XTC or BIC/FTC/TAF regardless of known or likely prior resistance to the NRTI pair and provided there is no history of InSTI resistance (evidence rating: AIa).

•Switching individuals receiving boosted protease inhibitors plus 2 NRTIs to NNRTI or first-generation InSTI regimens (raltegravir or elvitegravir) plus 2 NRTIs is not recommended in the presence of previous NRTI resistance (evidence rating: AIa).

•Individuals with NRTI resistance who switch to dual NRTI plus dolutegravir or bictegravir regimens should be monitored more closely in the first year after the switch, especially if there are concerns about taking the new regimen regularly (evidence rating: AIII).

•Injectable long-acting cabotegravir plus long-acting rilpivirine is recommended for persons who experience stigma or other adverse consequences of taking pills daily or in response to strong patient preference (evidence rating: AIb).

•Long-acting cabotegravir plus long-acting rilpivirine is not recommended in individuals with documented or suspected resistance to either agent (evidence rating: AIIa) or with chronic hepatitis B (evidence rating: AIa).

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society-USA Panel. JAMA 2025;333(7):609-628.

Pregnancy Outcomes of Women Exposed to LA CAB for PrEP in HPTN 084

- Randomized, double-blind phase IIb/III trial of LA CAB vs FTC/TDF for PrEP
- In total, 132 confirmed pregnancies over 6477.3 PY
  - Pregnancy IR: 3.2 in unblinded vs 1.3 in blinded period
  - LA CAB: 63 pregnancies/3239.1 PY
  - FTC/TDF: 69 pregnancies/3238.3 PY

Pregnancy Outcome, n*	CAB (n = 63)	FTC/TDF (n = 69)
Live births	31	30
Pregnancy loss		
▪ ≥37 wk	0	0
▪ 20-36 wk	1	2
▪ <20 wk†	9	4
Congenital abnormalities	0	0

*Pregnancies ongoing for 23 women in CAB arm and 34 women in FTC/TDF arm. †Includes ectopic pregnancy, elective terminations, and spontaneous pregnancy loss.

- Pregnancy outcomes consistent with those expected in this population

Delany-Moretlwe. AIDS 2022. Abstr OALBX0107.