HIV Pre-Exposure Prophylaxis (PrEP)
Lenacapavir

Joanne Stekler, MD MPH
Professor of Medicine
University of Washington

Last Updated: September 25, 2024

Disclosures

September 2024: only FTC/TDF (Truvada), FTC/TAF (Descovy), and CAB-LA (Apretude) are approved by the U.S. Food and Drug Administration (FDA) and only for use in some, but not all, populations.

Lenacapavir is approved for HIV treatment as Sunlenca.

This talk will include discussion of non-FDA approved strategies for HIV prevention.

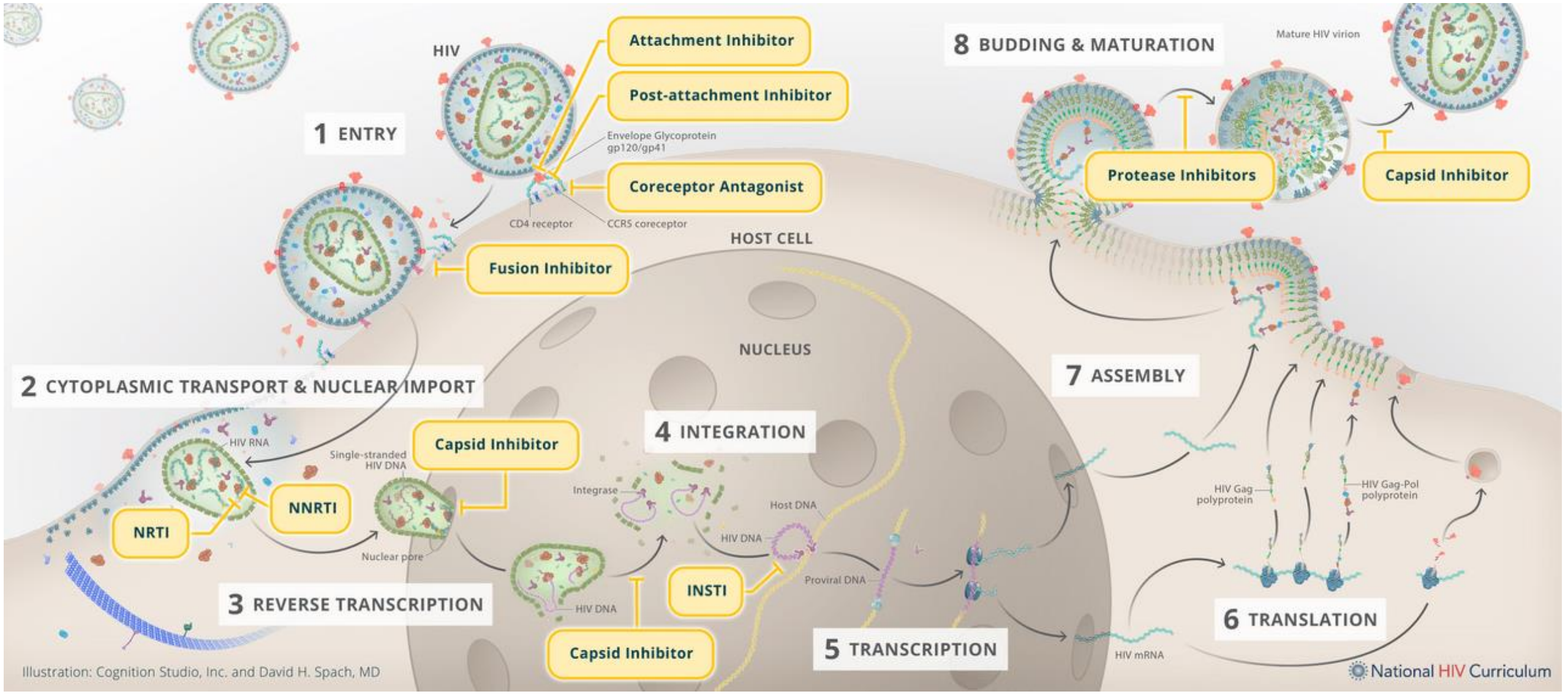
MWAETC

Disclaimer

Funding for this presentation was made possible by 1 TR7HA53202-01-00 from the Human Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. *Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.*

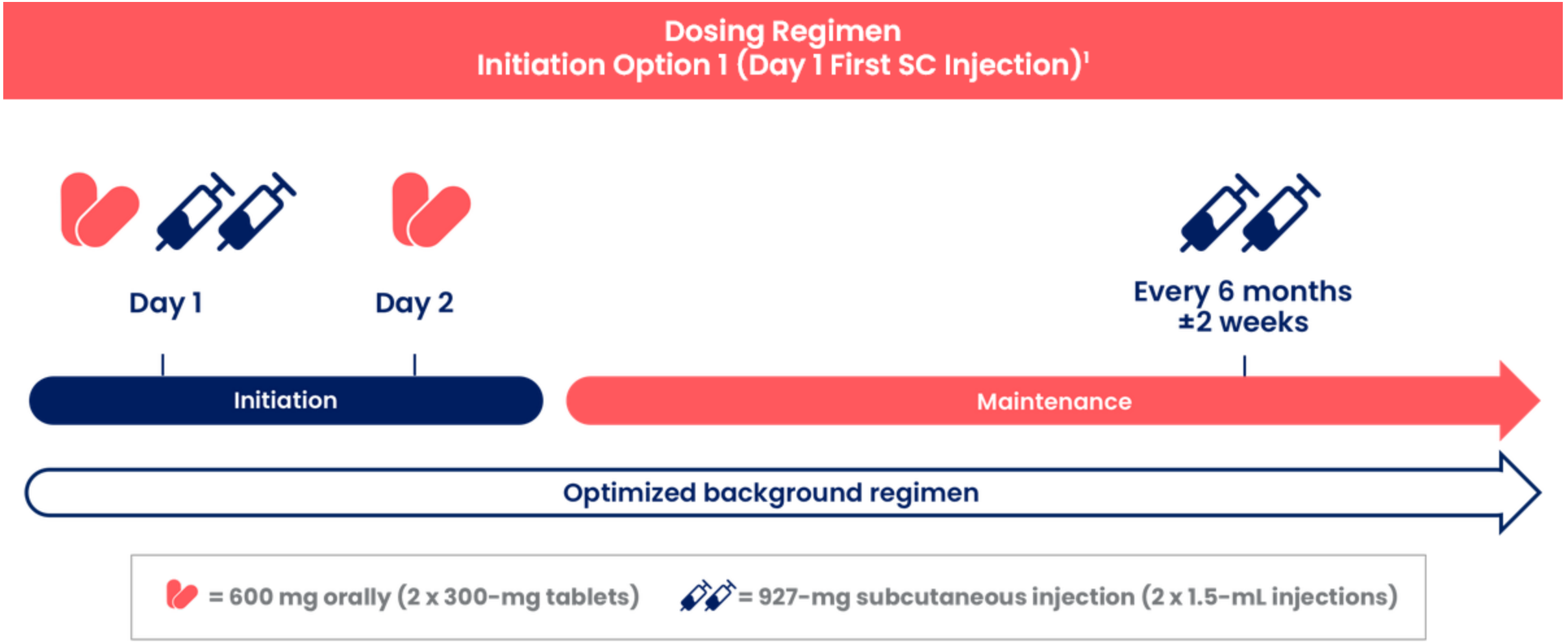
AETC AIDS Education & Training Center Program Mountain West

Capsid inhibitors



National HIV Curriculum: https://www.hiv.uw.edu/

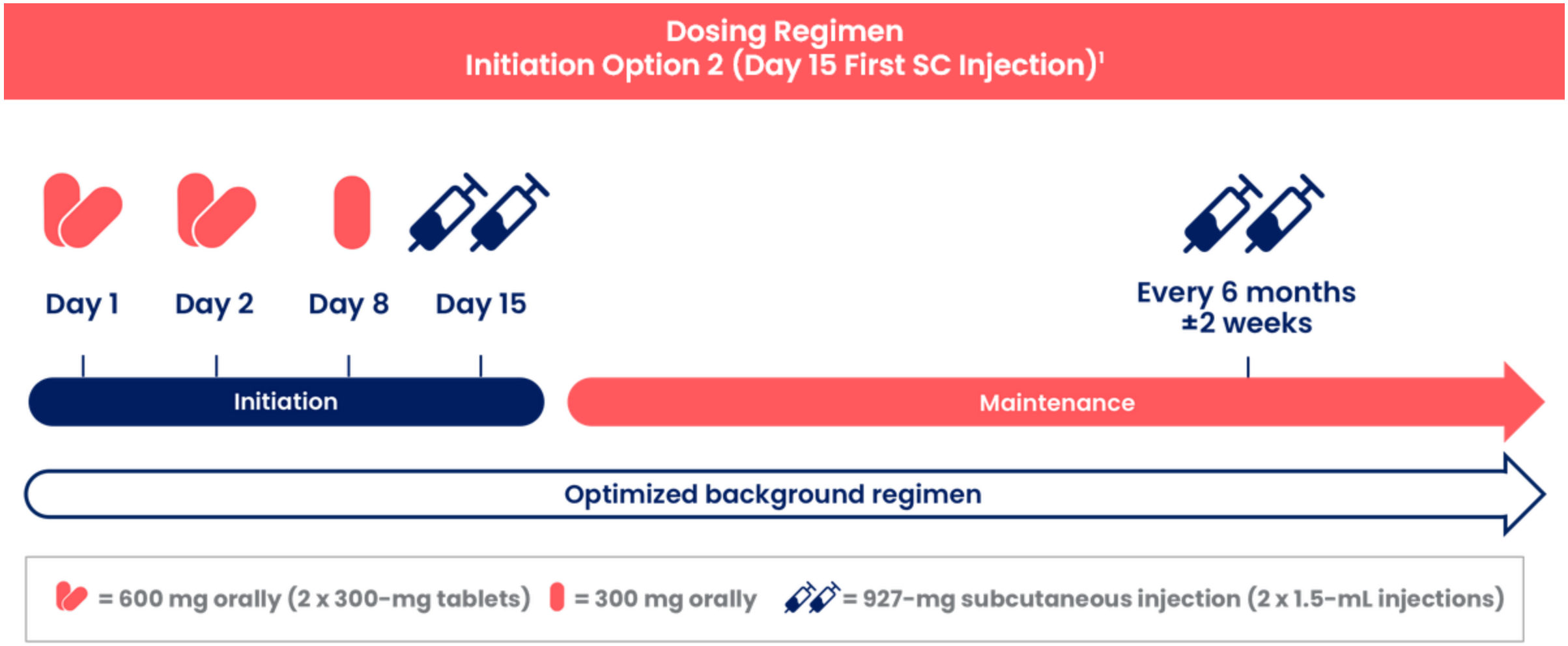
Lenacapavir dosing as HIV treatment (must include at least one other active agent)



https://www.sunlencahcp.com/dosing-and-administration/sunlenca-dosing/

MWAETC

Lenacapavir dosing as HIV treatment (must include at least one other active agent)



https://www.sunlencahcp.com/dosing-and-administration/sunlenca-dosing/

MWAETC

PURPOSE: lenacapavir

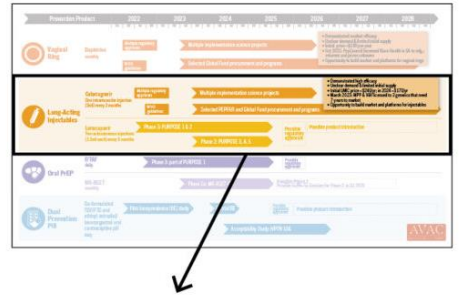
- PURPOSE 1: lenacapavir v FTC/TAF in girls and women
  phase III, n=5639, South Africa and Uganda, 1° completion 2024
- PURPOSE 2: lenacapavir v FTC/TDF in cisMSM, transgender/GNB persons
  phase III, n=3000, US/ex-US sites, 1° completion 2025
- PURPOSE 3: lenacapavir v FTC/TDF in cisgender women in US (HPTN 102)
  phase II, n=250, 1° completion 2027
- PURPOSE 4: lenacapavir v FTC/TDF in PWID in US (HPTN 103)
  phase II, n=250, 1° completion 2027
- PURPOSE 5: lenacapavir persistence in UK and France

Clinicaltrials.gov, https://www.purposestudies.com/

MWAETC

Overview of Lenacapavir (LEN) for PrEP Trials

- Initial data
- Possible data
- Possible earliest regulatory submissions
- Possible earliest regulatory approval and market entry with product from Gilead
- Possible earliest generic manufacturer(s)



Trial	Population	Location	Size	2022	2023	2024	2025	2026	2027	2028	2029
PURPOSE 1 Phase 3 Injectable lenacapavir & oral F/TAF	Cisgender adolescent girls and young women	South Africa and Uganda	**5,010**	Initial results released in June 2024 demonstrated no infections in the LEN arm							
PURPOSE 2 Phase 3 Injectable lenacapavir	Cisgender men who have sex with men, Transgender women, Transgender men, Gender non-binary	US, South Africa, Peru, Brazil, Mexico, Argentina, and Thailand	**3,000**			Fully enrolled; initial results expected late 2024 or early 202					
PURPOSE 3 **HPTN 102** Phase 2 Injectable lenacapavir	Cisgender women	US	**250**				Currently recruiting; estimated study completed date early 2028				
PURPOSE 4 **HPTN 103** Phase 2 Injectable lenacapavir	People who inject drugs	US	**250**				Currently recruiting; estimated study completed date mid-2027				
PURPOSE 5 Phase 2 Injectable lenacapavir	Cisgender men who have sex with men, Transgender women, Transgender men, Gender non-binary	France and UK	**262**					Enrollment expected to begin in the second half of 2024			

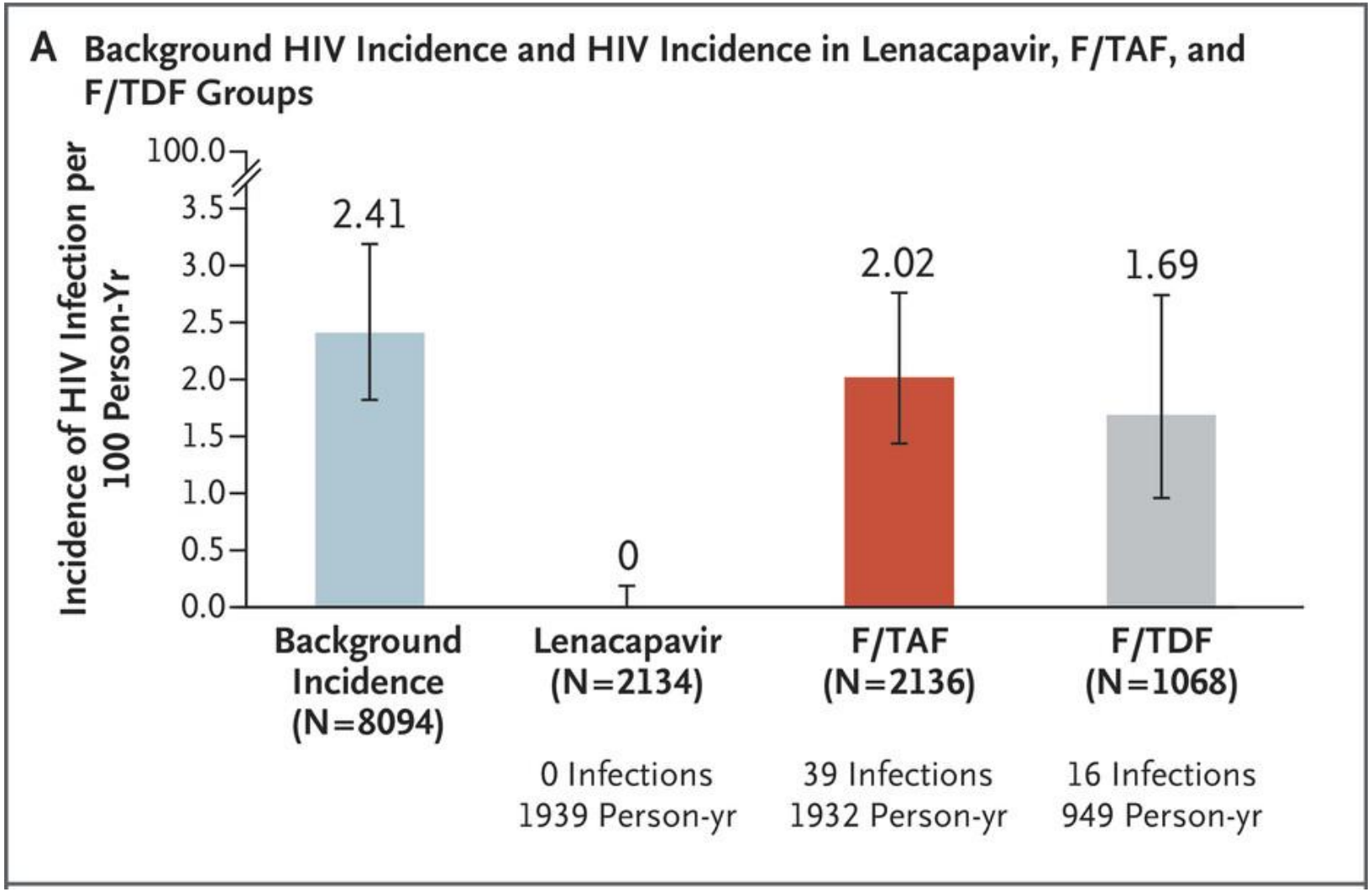
Stopped 6/20 for superiority

Stopped 9/12 for superiority

AVAC
Advocacy. Access. Equity.
Updated June 2024

MWAETC

PURPOSE 1 results



Bekker et al. NEJM 2024 (online ahead of print)

Background incidence (Limiting Antigen-Antibody Avidity Assay)

The bHIV will be estimated by the formula:

$$\hat{\lambda}_0 = \frac{N_{rec}/(N_{+,test}/N_+) - \beta N_+}{N_-(\Omega - \beta T)}$$

T: cutoff time (eg, 2 years) for the definition of true recent infections
Ω: MDRI
β: FRR

The variance of $\hat{\lambda}_0$ in the log scale $\hat{\sigma}^2_{\log(\hat{\lambda}_0)}$ will be estimated by the delta method, as provided by Gao et al.[9] (see below), considering the variance of Ω, β, and the observed counts of N_-, $N_{+,test}$, N_{rec}:

$$\hat{\sigma}^2_{\log(\hat{\lambda}_0)} = \frac{N_{rec}(N_{+,test} - N_{rec})}{N_{+,test}\left(N_{rec} - N_{+,test}\beta\right)^2} + \frac{N}{N_+ N_-} + \sigma^2_\beta \frac{N_{+,test}(N - N_{+,test})}{N\left(N_{rec} - N_{+,test}\beta\right)^2}$$

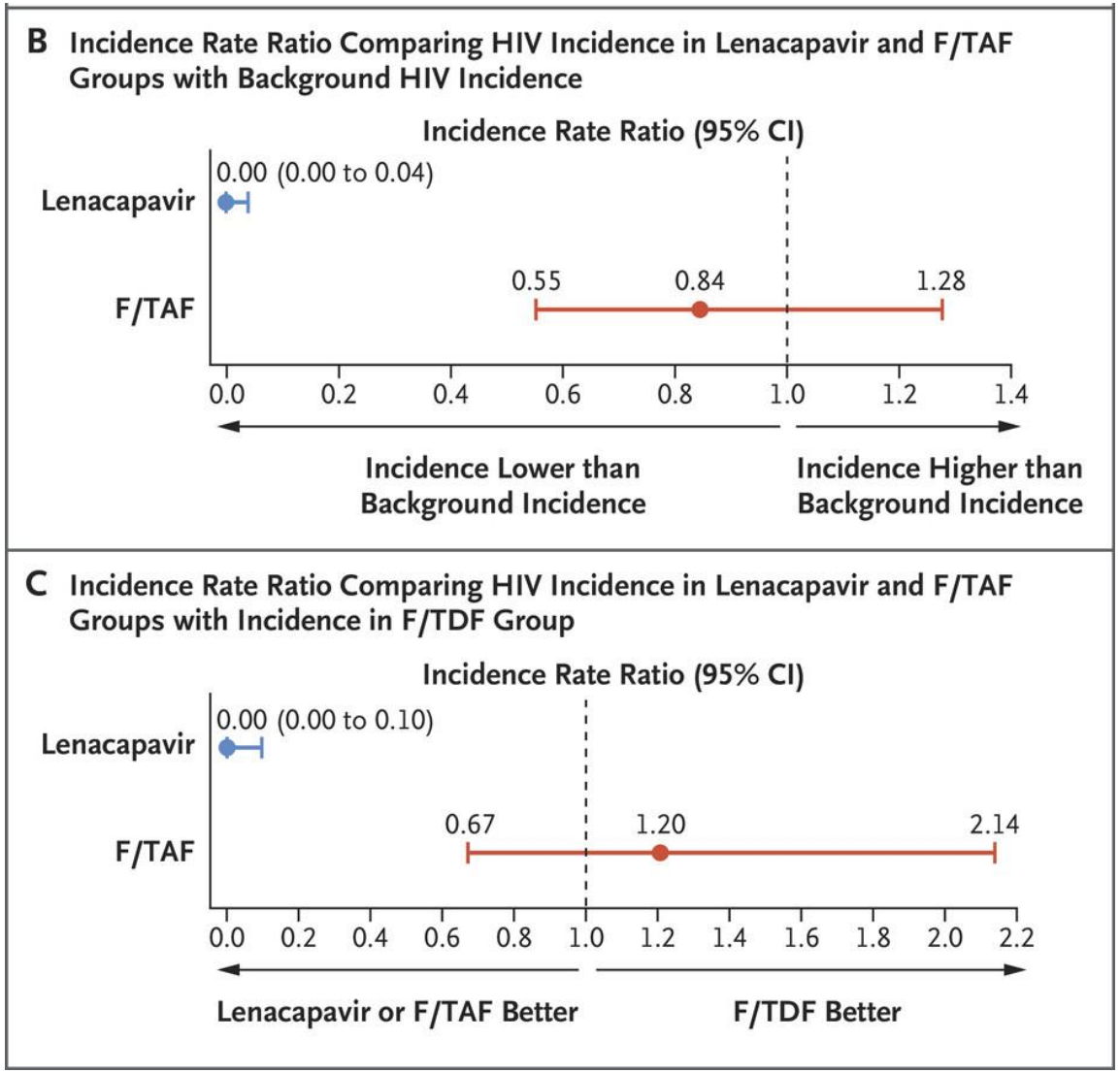
$$= + \frac{\sigma^2_\Omega}{(\Omega - \beta T)^2} + \sigma^2_\beta \left[\frac{N_{+,test}\Omega - N_{rec}T}{(N_{rec} - N_{+,test}\beta)(\Omega - \beta T)}\right]^2$$

The $(1-\alpha) \times 100\%$ confidence interval (CI) for $\log(\lambda_0)$ will be constructed as $\log(\hat{\lambda}_0) \mp z_{\alpha/2}\hat{\sigma}_{\log(\hat{\lambda}_0)}$, and the $(1-\alpha) \times 100\%$ CI for λ_0 will be $\hat{\lambda}_0 \exp\left(\mp z_{\alpha/2}\hat{\sigma}_{\log(\hat{\lambda}_0)}\right)$. Here $z_{\alpha/2}$ is the $(\alpha/2)$-th upper quantile of the standard normal distribution.

Bekker et al. NEJM 2024
Parkin et al. Clin Pharmaco Ther 2023; 114(1): 29-40.

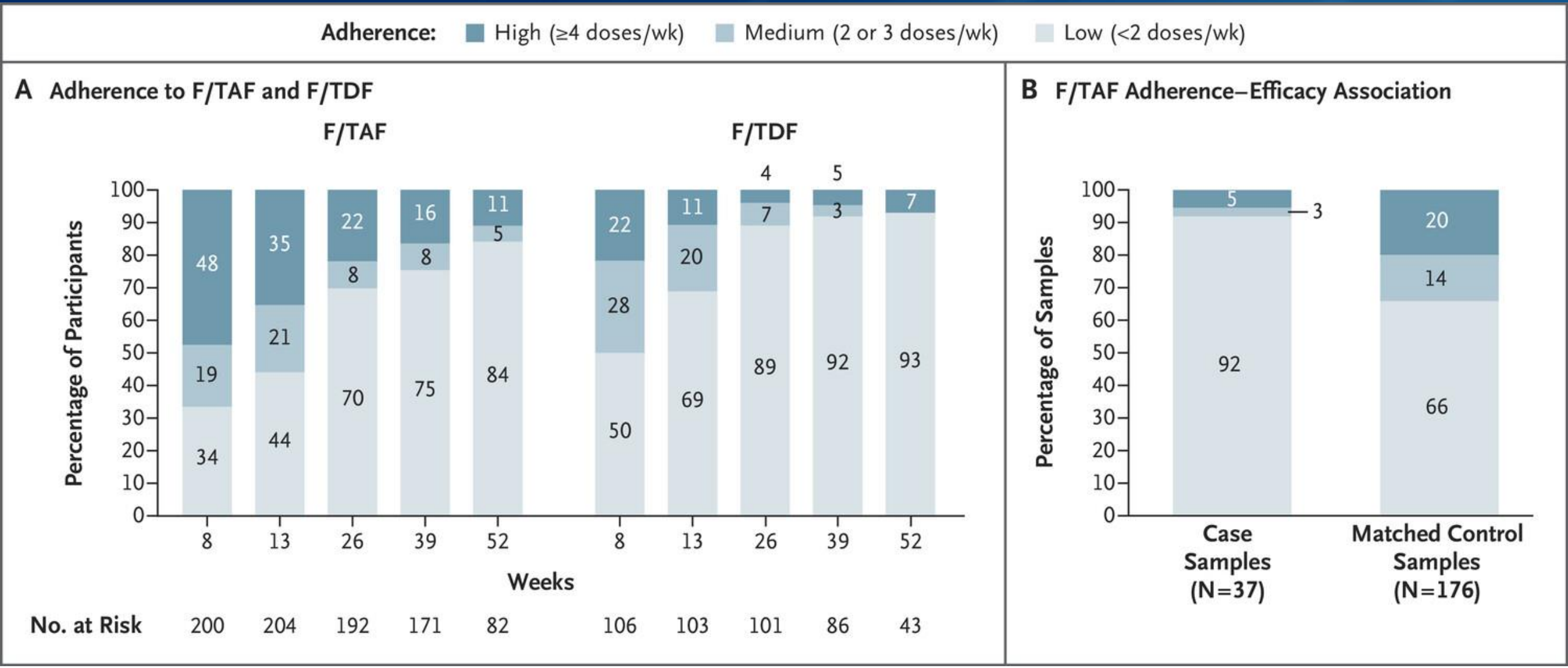
MWAETC

PURPOSE 1 results



Bekker et al. NEJM 2024

PURPOSE 1 results



Bekker et al. NEJM 2024

PURPOSE 1 adverse events

	LEN (n=2138)	F/TAF (n=2137)	F/TDF (n=1070)
Any adverse event excluding injection site reactions	76%	78%	78%
Serious adverse events excluding injection site reactions	3%	4%	3%
Any injection site reaction	69%	35%	34%
Serious injection site reaction	0	0	0
Discontinuation due to reaction	4 (0.2%)	0	0

Bekker et al. NEJM 2024

MWAETC

PURPOSE 2 results

- Study stopped after interim analysis on 9/12/2024
- Lenacapavir superior to daily FTC/TDF among Incidence

  LEN: 0.10/100 person-years (n=2 of 2180 participants)

  FTC/TDF: 0.93/100 person-years (n=9 of 1087 participants)

  Background: 2.37/100 person-years
- Risk reduction of 96% compared to background.

"Gilead will begin a series of global regulatory filings by the end of 2024. This could support the initial launch of the first and only twice-yearly HIV prevention choice in 2025."

https://www.gilead.com/news/news-details/2024/gileads-twiceyearly-lenacapavir-for-hiv-prevention-reduced-hiv-infections-by-96-and-demonstrated-superiority-to-daily-truvada

MWAETC

Cost of PrEP medications

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Descovy	25-mg/200-mg tablet	30 tablets	$2,202	$2,643	N/A
Generic	300-mg/200-mg tablet	30 tablets	$25 to $420	$70 to $2,100	$15
Sunlenca	300-mg tablet	4 tablets	$3,250	$3,900	N/A
Sunlenca	300-mg tablet	5 tablets	$4,063	$4,875	N/A
Sunlenca	927-mg injection kit	2 vials (1 kit every 6 months)	$19,500 (every 6 months)	$23,400 (every 6 months)	N/A

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/antiretroviral-therapy-cost-considerations

Cost-effectiveness in Africa: Wu et al. Lancet HIV 2024

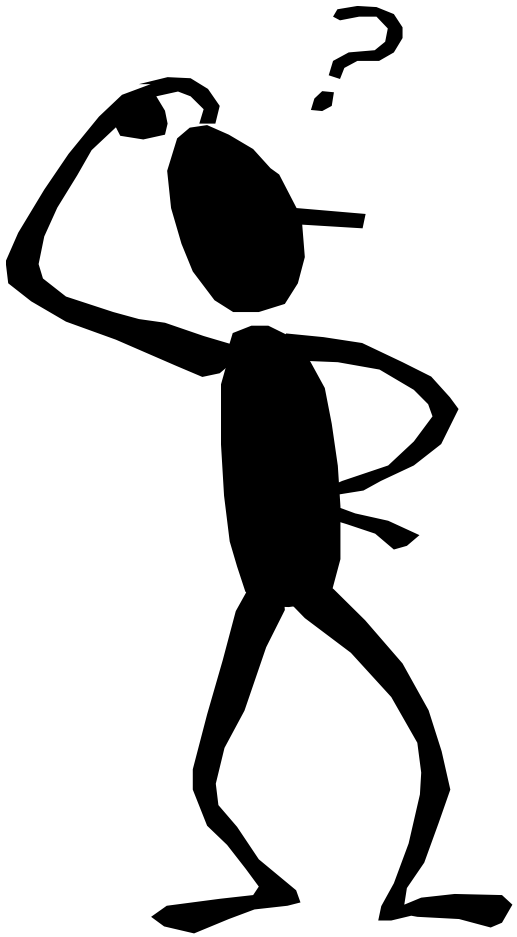
MWAETC

Other questions for LEN implementation as PrEP

- Off-label usage of lenacapavir?
- Adherence monitoring, drug resistance and the “tail”
- Frequency of HIV/STI testing
- Impact on HIV testing results among persons acquiring HIV
- Medication interactions (strong CYP3A inducers)
- Subcutaneous dosing = home administration?
- Insurance coverage

MWAETC

Questions?



Acknowledgment

This Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of award 1 TR7HA53202-01-00 totaling $2,982,063 with 0% financed with non-governmental sources.

AETC AIDS Education & Training Center Program Mountain West