National HIV Curriculum

Cabotegravir (*Apretude*)

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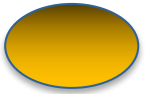
Last Updated: January 8, 2022

AETC AIDS Education & Training Center Program

Cabotegravir (*Apretude*) for HIV PrEP

Oral Cabotegravir (Optional)



Oral Cabotegravir

30 mg

INSTI

Cabotegravir Injectable (IM)

Cabotegravir (200 mg/mL)

600 mg (3 mL)

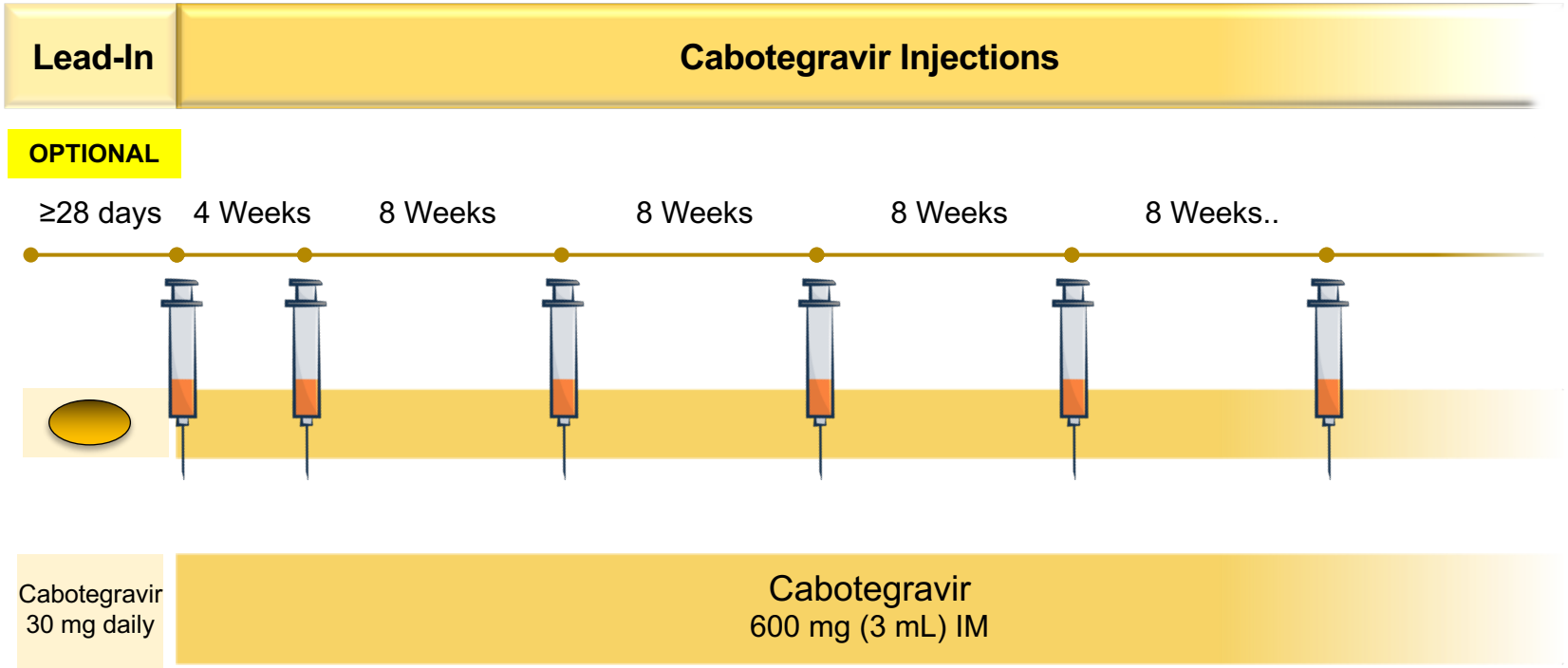
INSTI

December 2021: FDA Approved for PrEP At-risk adults and adolescents weighing ≥35 kilograms (77 pounds)

Dosing with Renal or Hepatic Impairment

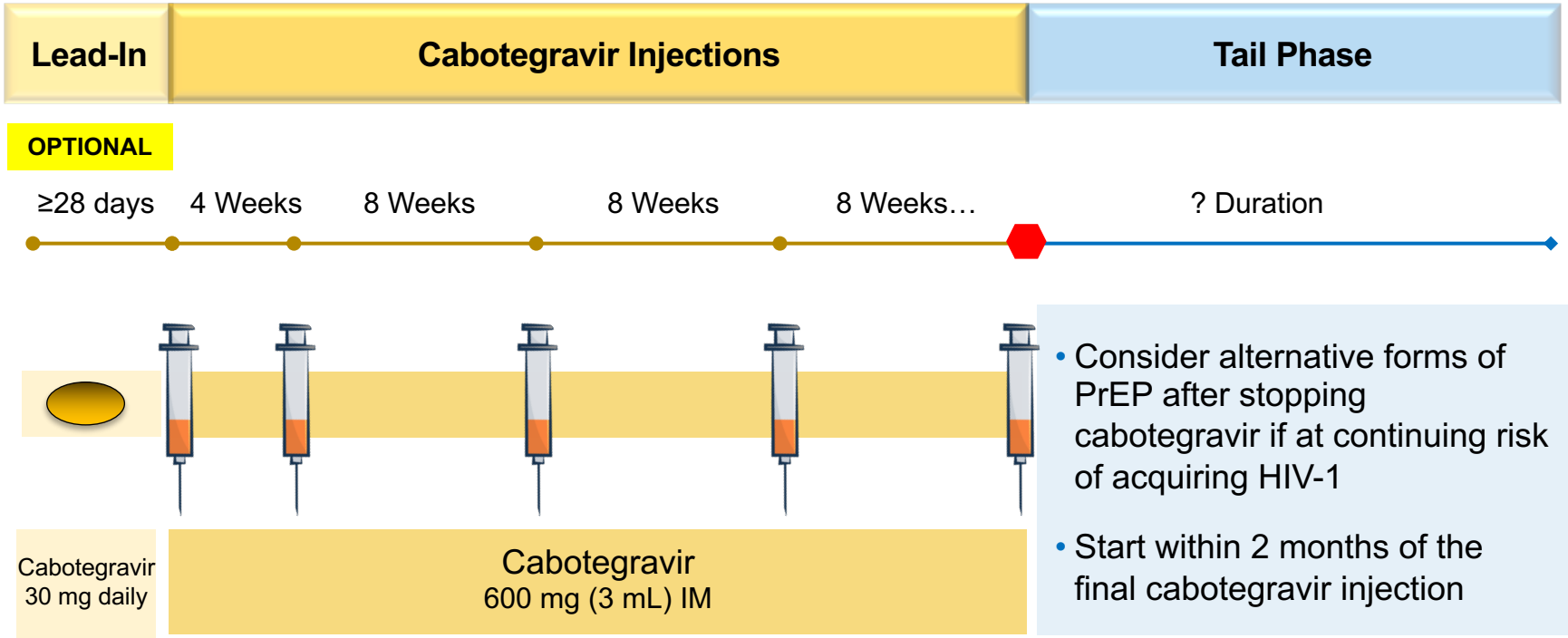
- **Dosing with Renal Insufficiency**
  - Mild (CrCl ≥60 to <90 mL/min): no adjustment
  - Moderate (CrCl ≥30 to <60 mL/min): no adjustment
  - Severe (CrCl 15 to <30 mL/min) or ESRD (<15 mL/min): increased monitoring for adverse effects is recommended
  - Dialysis: not expected to alter cabotegravir levels
- **Dosing with Hepatic Impairment**
  - Mild-to-Moderate (Child A or B): no dose adjustment
  - Severe (Child C): unknown

Cabotegravir for HIV PrEP: Prescribing Information*



*Source: Apretude Prescribing Information

Cabotegravir for HIV PrEP: Prescribing Information*

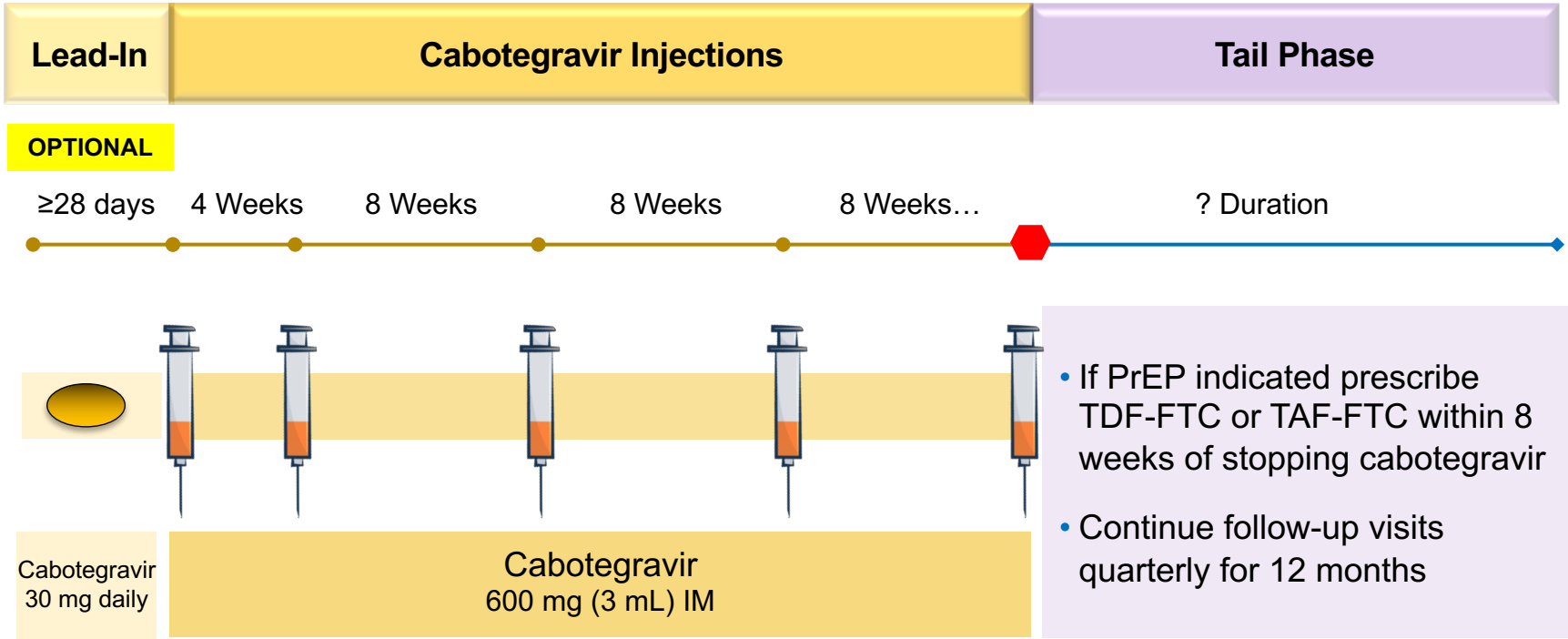


- Consider alternative forms of PrEP after stopping cabotegravir if at continuing risk of acquiring HIV-1
- Start within 2 months of the final cabotegravir injection

*Source: Apretude Prescribing Information

2021 CDC PrEP Guidelines

Cabotegravir for HIV PrEP: Monitoring



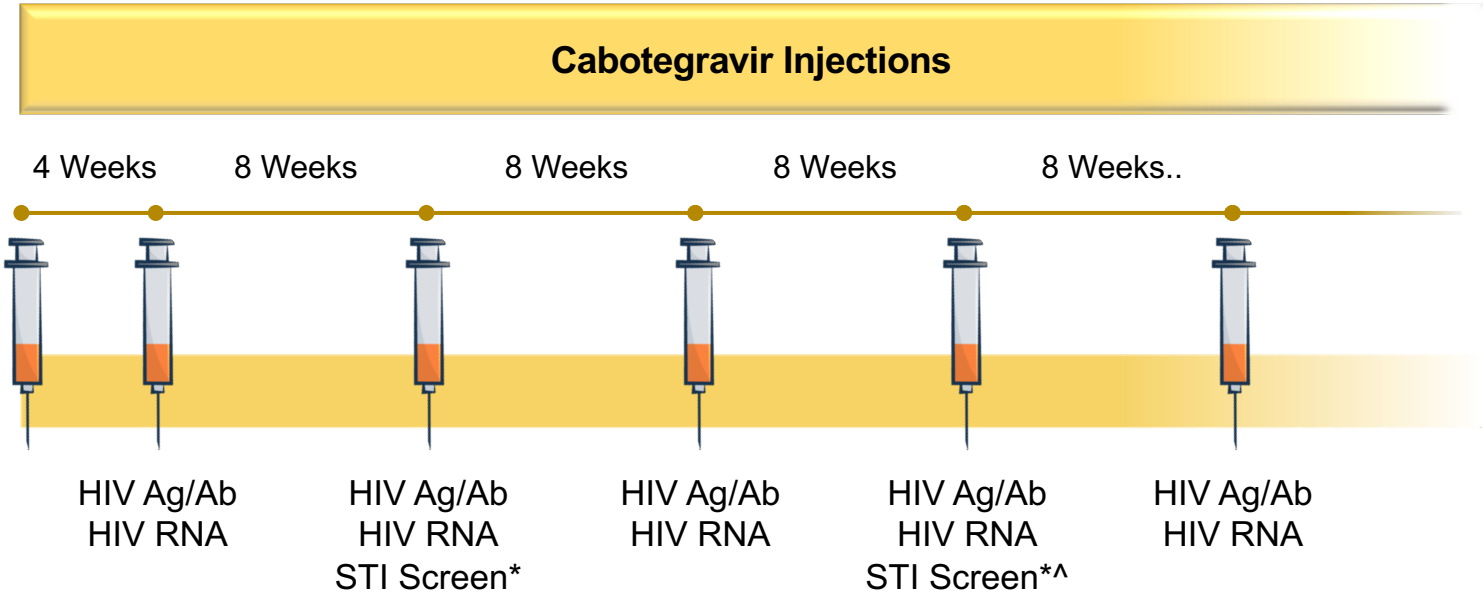
*TDF-FTC = tenofovir DF-emtricitabine; TAF-FTC = tenofovir alafenamide-emtricitabine

Source: CDC Preexposure Prophylaxis for the Prevention of HIV Infection in the U.S.– 2021 Update Clinical Practice Guideline

Cabotegravir Toxicity Monitoring

- Not indicated before starting or monitoring:
  - Creatinine, eCrCl
  - Hepatitis B serology
  - Lipid panels
  - Liver function tests.

Cabotegravir for HIV PrEP: Monitoring



*Bacterial STI screening for MSM and TGW who have sex with men (every 3 months)
^Bacterial STI screening for heterosexually active men and women (every 6 months)

Source: CDC Preexposure Prophylaxis for the Prevention of HIV Infection in the U.S.– 2021 Update Clinical Practice Guideline

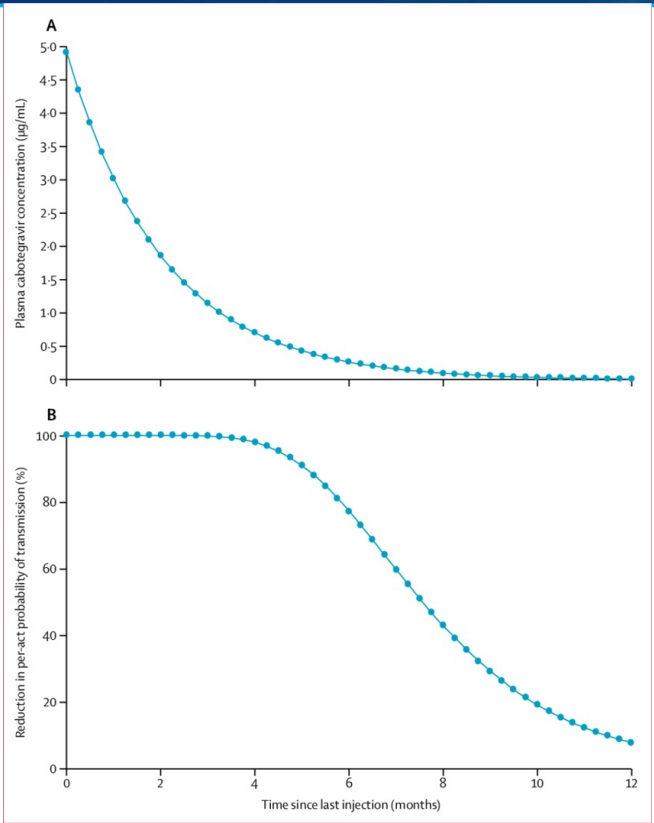


Figure 2: Estimated plasma cabotegravir concentration (A) and reduction in per-act probability of HIV transmission (B), by time since last injection Percentage reduction in per-act HIV transmission after a final long-acting cabotegravir injection was estimated on the basis of half-life values reported by Markowitz and colleagues.

Source: Marshal BDL, et al. Lancet HIV. 2018;5:e498-e505.

IM Cabotegravir vs. TDF-FTC for HIV PrEP in MSM and TGW

HPTN 083

National HIV Curriculum

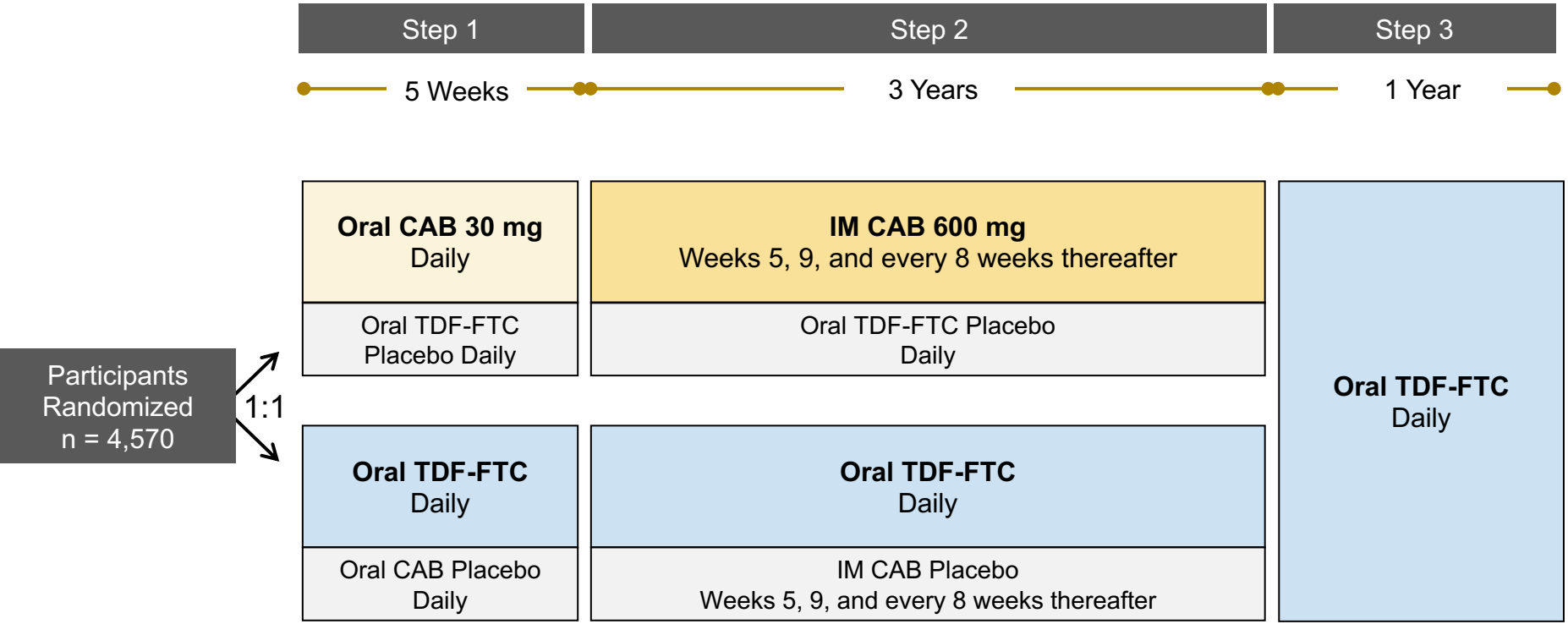
IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Study Design

- **Background**: Phase 2b/3, double-blind, randomized, multinational, trial to assess efficacy of long-acting IM cabotegravir (CAB) compared to daily oral tenofovir DF-emtricitabine (TDF-FTC) for HIV PrEP in men who have sex with men (MSM) and transgender women
- **Setting**
  - 43 global sites
- **Inclusion Criteria**
  - Adult (≥18 years) cisgender MSM and transgender women who have sex with men age
  - Substantial HIV risk*
  - Negative HIV serologic test at enrollment and negative HIV RNA ≤14 days before trial entry
  - Generally good health and CrCl 60 mL/min
  - HBsAg negative and HCV antibody negative
  - No contraindications to gluteal injections
  - No injection drug use within 90 days of trial entry

*Condomless receptive anal intercourse; >5 sex partners, stimulant use, rectal/urthral STI or syphilis ≤6 months; SexPro Score <16 (U.S. only)

Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Study Design



Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

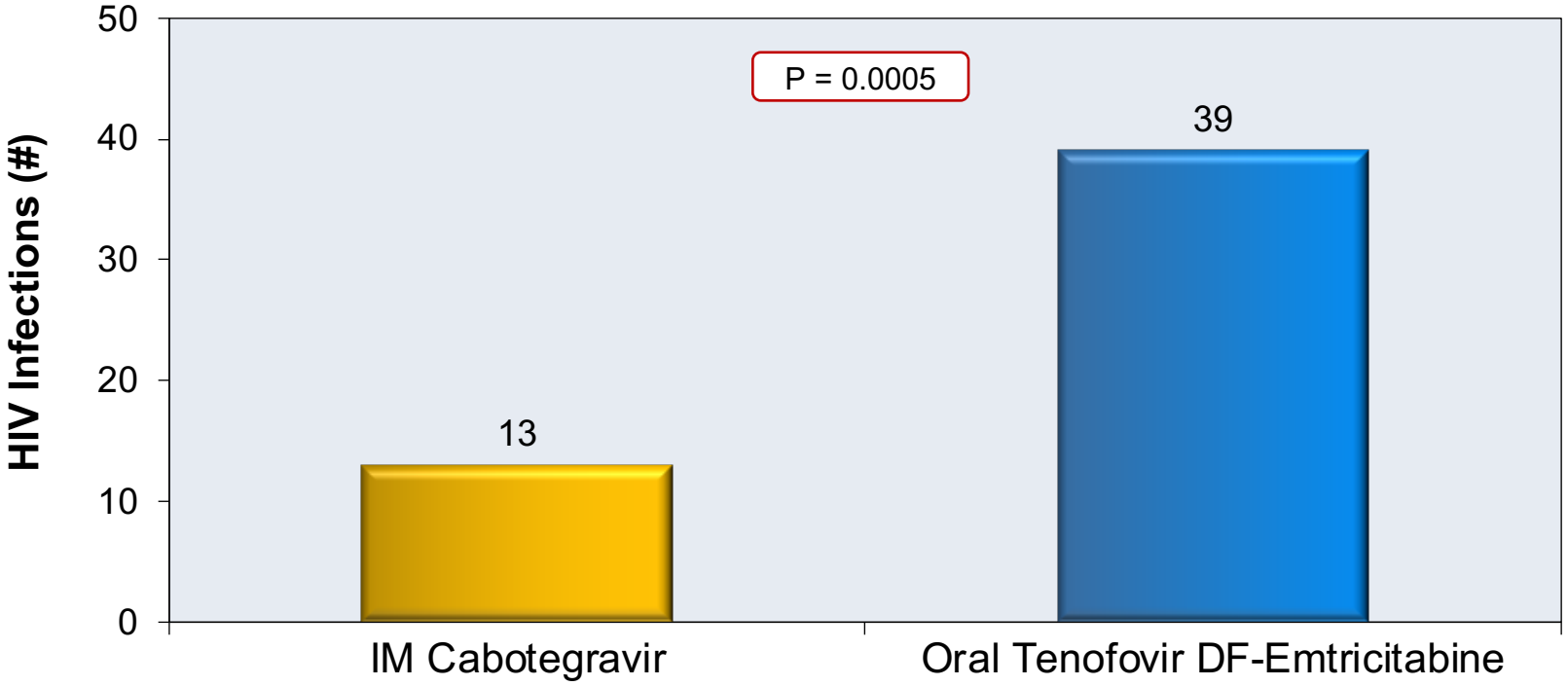
IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Study Population

HPTN 083: Selected Baseline Demographics			
Characteristic	**Total** (n = 4,566)	**CAB** (n = 2,282)	**TDF-FTC** (n = 2,284)
Cisgender MSM	3,992 (87.4)	2,013 (88.2)	1,979 (86.6)
Transgender Women	570 (12.5)	266 (11.7)	304 (13.3)
Median Age (IQR) Years	26 (22-32)	26 (22-32)	26 (22-32)
Black Race, United States	845 (49.8)	411 (48.4)	434 (51.1)
Geographic Region			
United States	1,698 (37.2)	849 (37.2)	849 (37.2)
Latin America	1,964 (43.0)	980 (42.9)	984 (43.2)
Asia	752 (16.5)	375 (16.5)	377 (16.5)
Africa	152 (3.3)	78 (3.4)	74 (3.2)

*Abbreviations: MSM = men who have sex with men; IQR = interquartile range

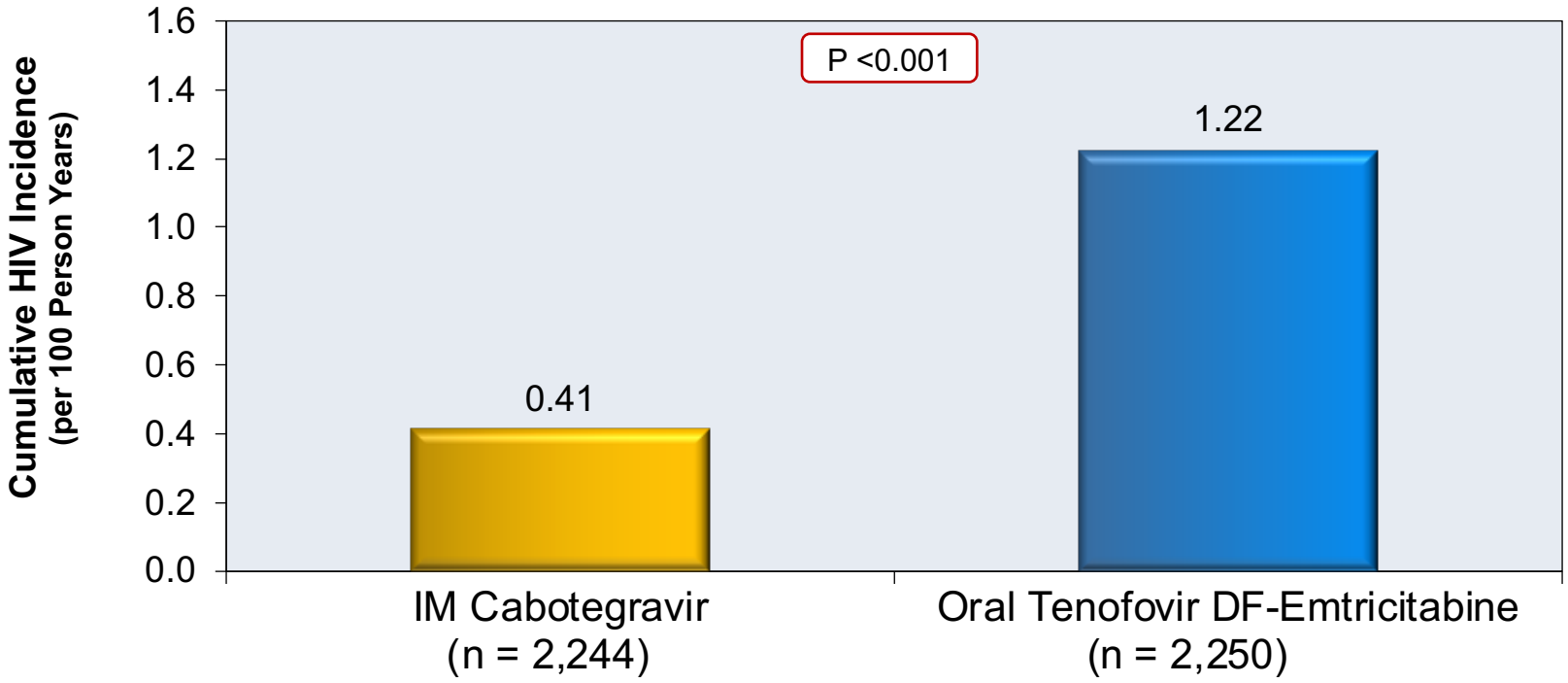
Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Acquisition of HIV After Enrollment



Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Results



Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

HPTN 083: Results

- **When did incident HIV infections occur in CAB arm?**
  - 3 during oral lead-in
  - 5 after “prolonged hiatus” from IM CAB
  - 5 during continuous CAB administration
- **Were drug levels adequate in TDF-FTC arm?**
  - Random sample of 372 participants:
    - 87% detectable plasma tenofovir level
    - 75% levels correlated with high-level protection
    - ≈70% levels suggestive of >4 doses/week (by dried blood spot)

Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW HPTN 083: Cabotegravir Injection Site Reactions

- **Type and Severity of Injection-Site Reactions**
  - Most common pain and tenderness
  - 2.4% chose to discontinue study due to injection reaction
- **Onset**
  - Reactions typically began 1 day after injection
- **Duration**
  - Reactions typically lasted 3-4 days 1 day after injection

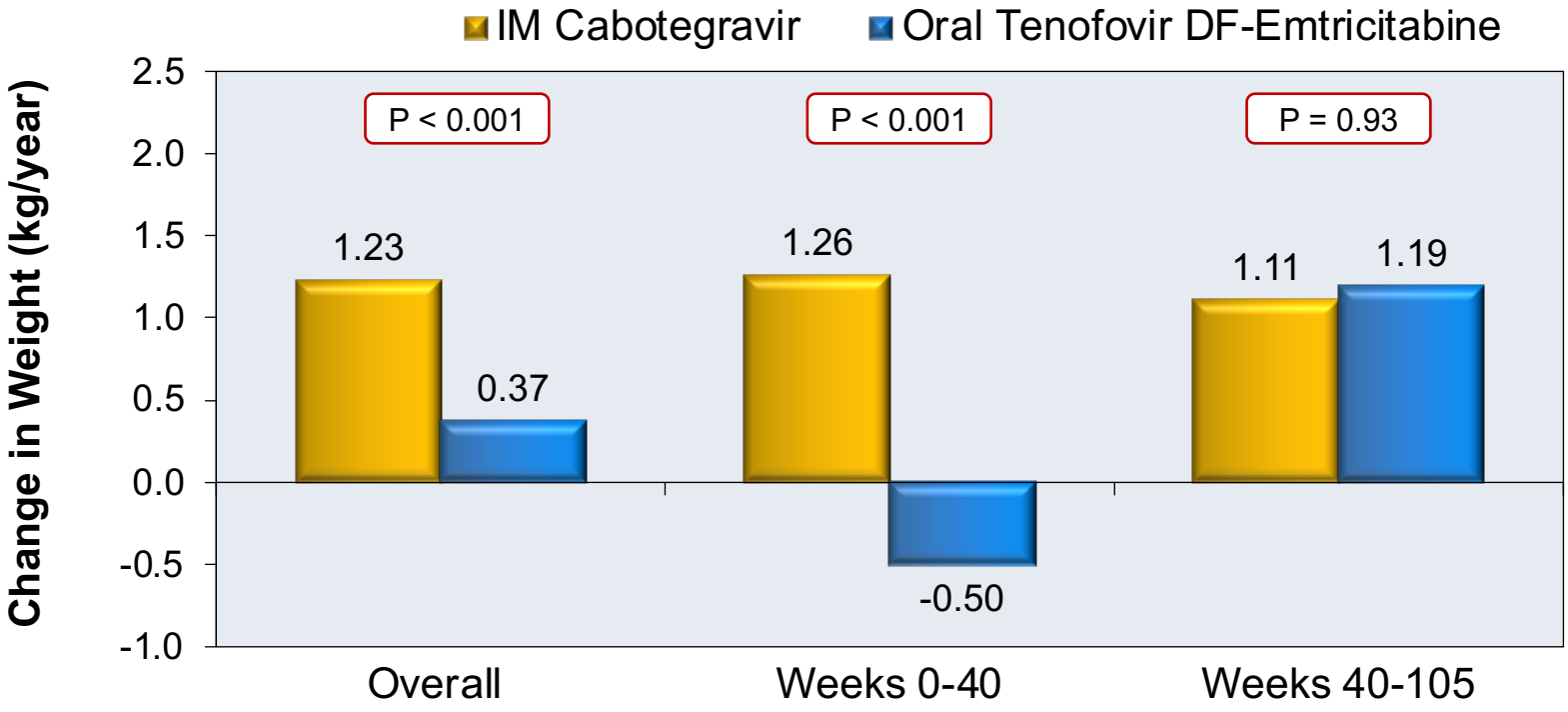
Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW HPTN 083: Results: Resistance with Cabotegravir

- **INSTI Resistance in Cabotegravir Group**
  - 1 at baseline; 4 with incident HIV infections
  - No resistance documented after last injection during “tail phase”

Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Weight Gain



Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

HPTN 083: Conclusions

Conclusions: Long-acting cabotegravir was superior to daily oral Tenofovir DF–emtricitabine in preventing HIV infection among men who have sex with men and transgender women.

Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

IM Cabotegravir vs. TDF-FTC for PrEP in Cisgender Women

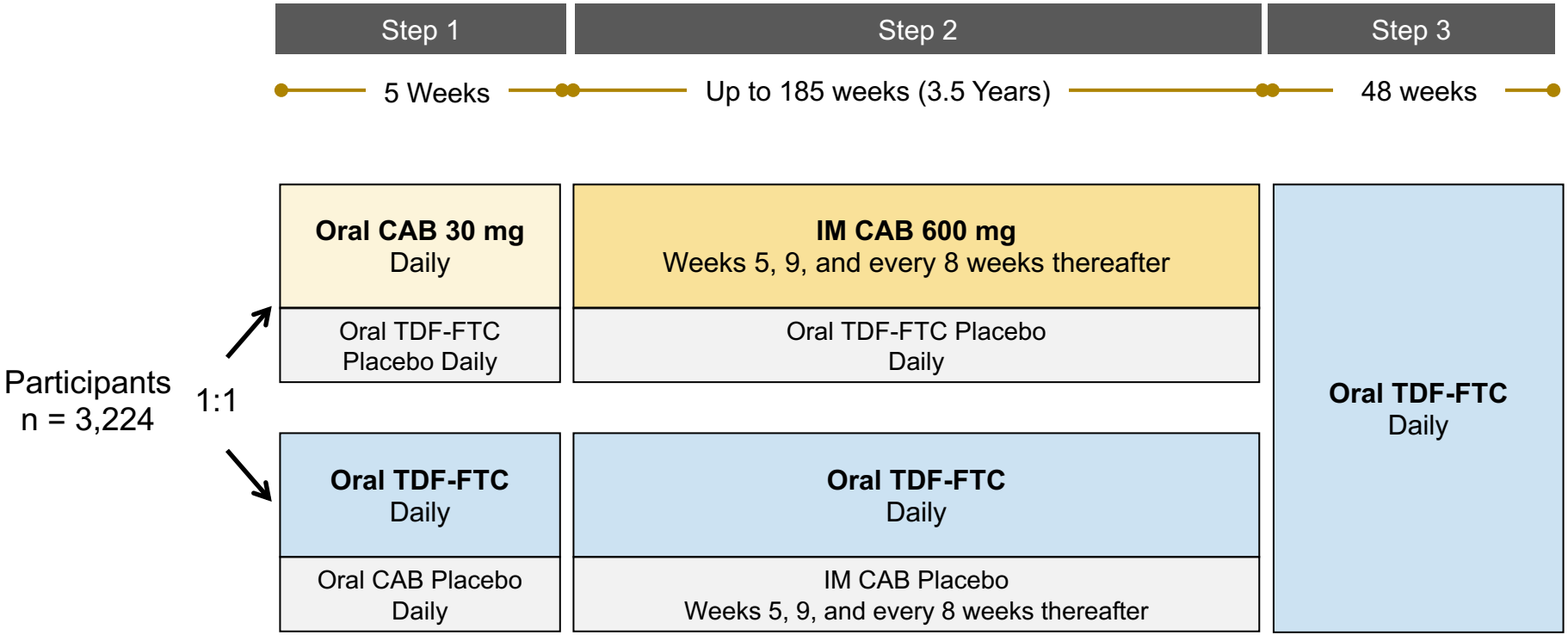
HPTN 084

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Study Design

- **Background**: Phase 3, double blind, randomized, multinational, trial to assess efficacy of long-acting IM cabotegravir (CAB) compared to daily oral tenofovir DF-emtricitabine (TDF-FTC) for HIV PrEP in cisgender women
- **Setting**
  - 20 sites in Sub-Saharan Africa, including 7 in South Africa
- **Inclusion Criteria**
  - Cisgender women (born female) 18-45 years of age
  - Sexually active (e.g vaginal sex on ≥2 separate days in the 30 days prior to screening)
  - HBsAg-negative and willing to receive hepatitis B vaccination
  - HCV antibody negative
  - No contraindications to gluteal injections
  - Creatinine clearance of greater than or equal to 60 mL/min
  - ALT <2 x upper limit of normal (ULN) and total bilirubin ≤ 2.5 x ULN
  - Excluded if pregnant or breastfeeding

Source: Delaney-Mortiwe S, Hosseinipour M. Results Webinar. November 16, 2020.

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Study Design



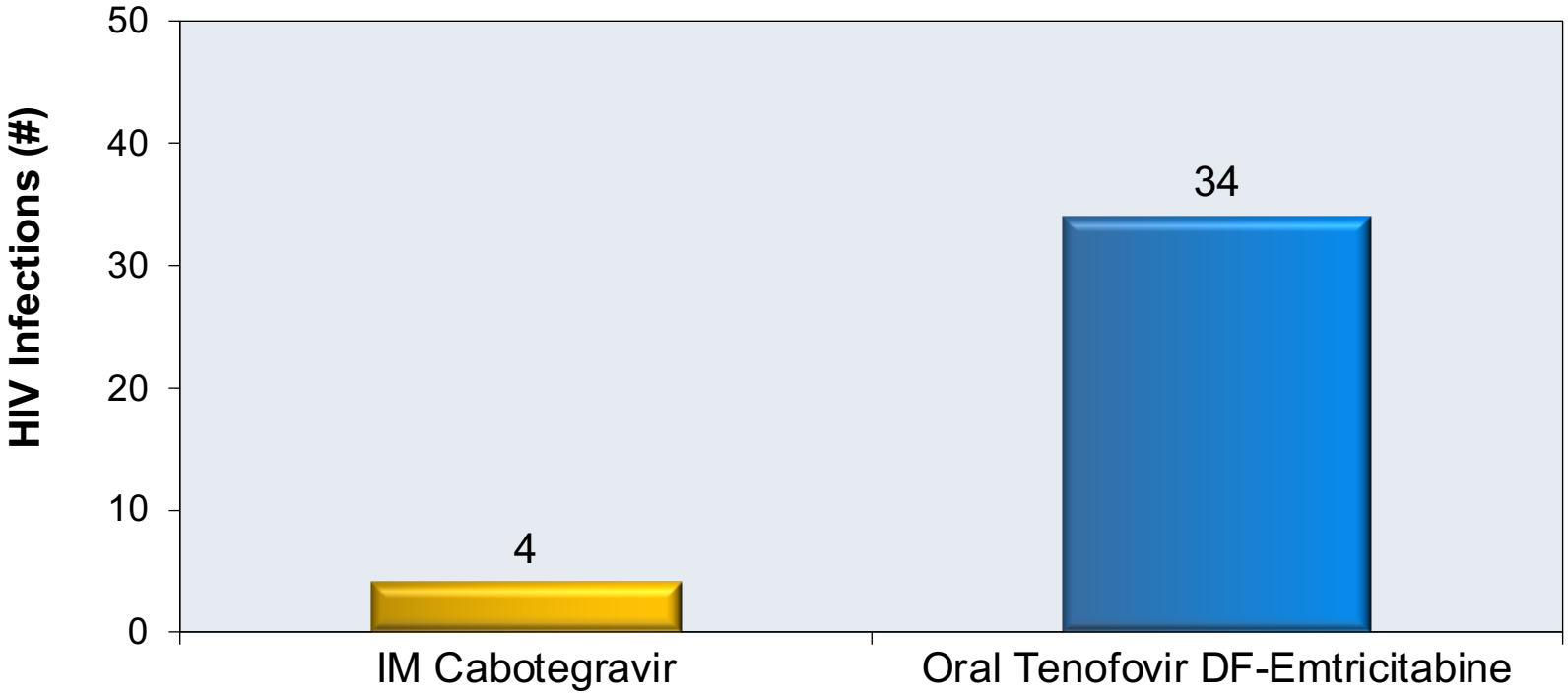
Source: Delaney-Mortiwe S, Hosseinipour M. Results Webinar. November 16, 2020.

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Baseline Characteristics

- **Age**
  - Average age of 26 years
  - 57% were ≤25 years of age
- **Partners**
  - 87% lived with partner
  - 55% reported ≥2 partners in past month
  - 34% had partners that were HIV+ or had unknown status

Source: Delaney-Mortiwe S, Hosseinipour M. Results Webinar. November 16, 2020.

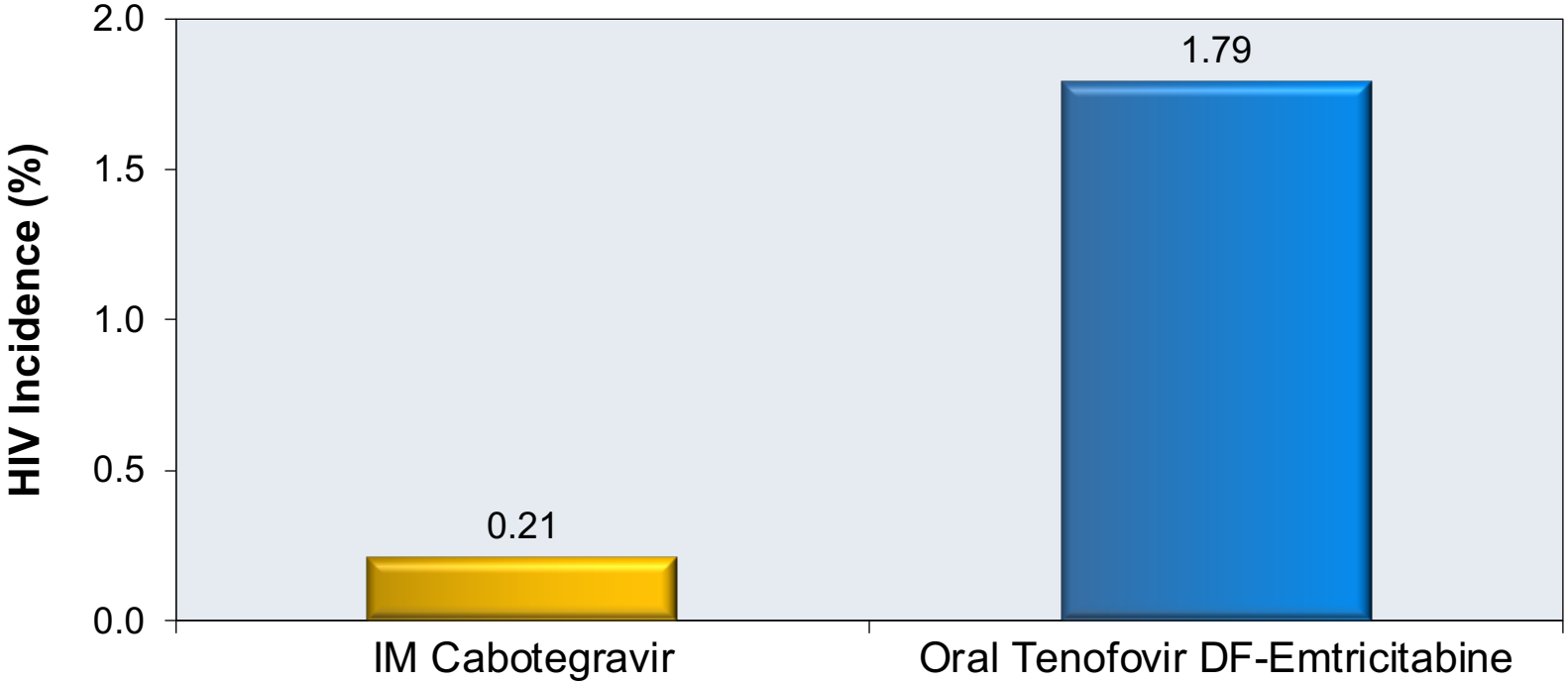
IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Results (n = 3,127 included in analysis)



Source: Delaney-Mortiwe S, Hosseinipour M. Results Webinar. November 16, 2020.

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women

HPTN 084: Results (n = 3,127 included in analysis)



Source: Delaney-Mortiwe S, Hosseinipour M. Results Webinar. November 16, 2020.

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Conclusions

Investigator's Conclusion: Long-acting injectable cabotegravir was more effective than daily oral tenofovir DF-emtricitabine in preventing HIV infection in cisgender women.

Source: Delaney-Mortiwe S, Hosseinipour M. Results Webinar. November 16, 2020.

Acknowledgment

The **National HIV Curriculum** is an AIDS Education and Training Center (AETC) Program supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $800,000 with 0% financed with non-governmental sources. This project is led by the University of Washington's Infectious Diseases Education and Assessment (IDEA) Program.

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