National HIV Curriculum

Cabotegravir, Long-acting Injectable

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Cabotegravir for HIV PrEP

Oral Cabotegravir (Optional)	Cabotegravir Injectable (IM)
	
Oral Cabotegravir 30 mg → INSTI	Cabotegravir (200 mg/mL) 600 mg (3 mL) → INSTI

December 2021: FDA approved as HIV PrEP for at-risk adults and adolescents weighing ≥35 kilograms (77 pounds)

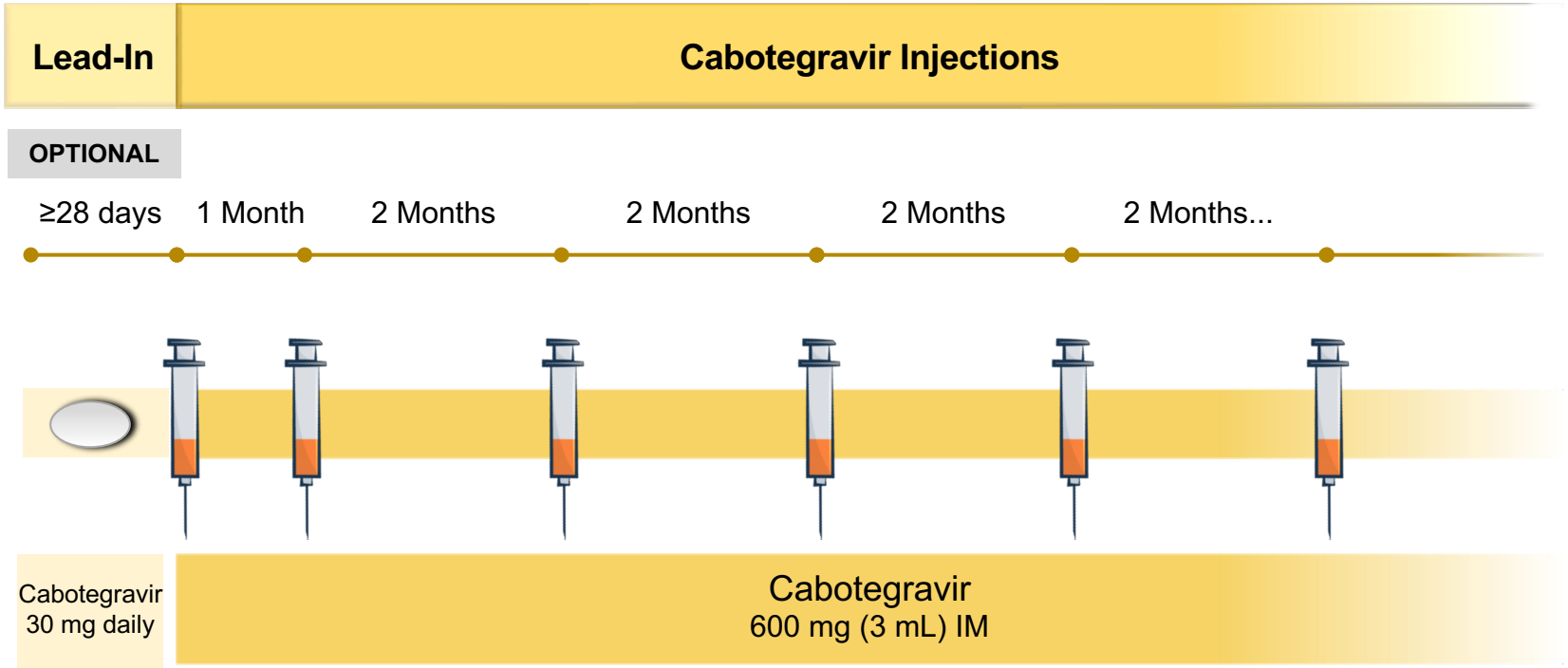
Source: Cabotegravir Prescribing Information.

Cabotegravir 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

Source: Cabotegravir Prescribing Information.

Cabotegravir for HIV PrEP: Prescribing Information

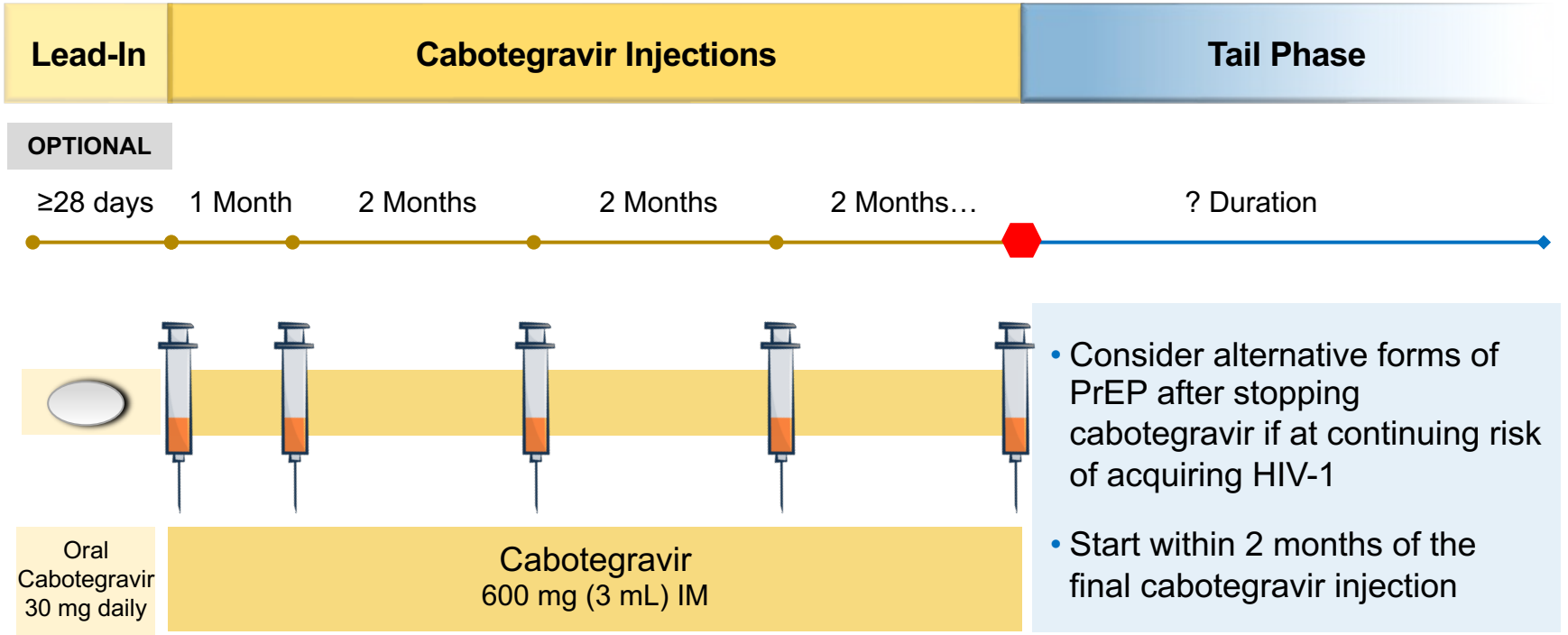


Source: Based on Cabotegravir Prescribing Information. Illustration: David H. Spach, MD

National HIV Curriculum

Prescribing Information

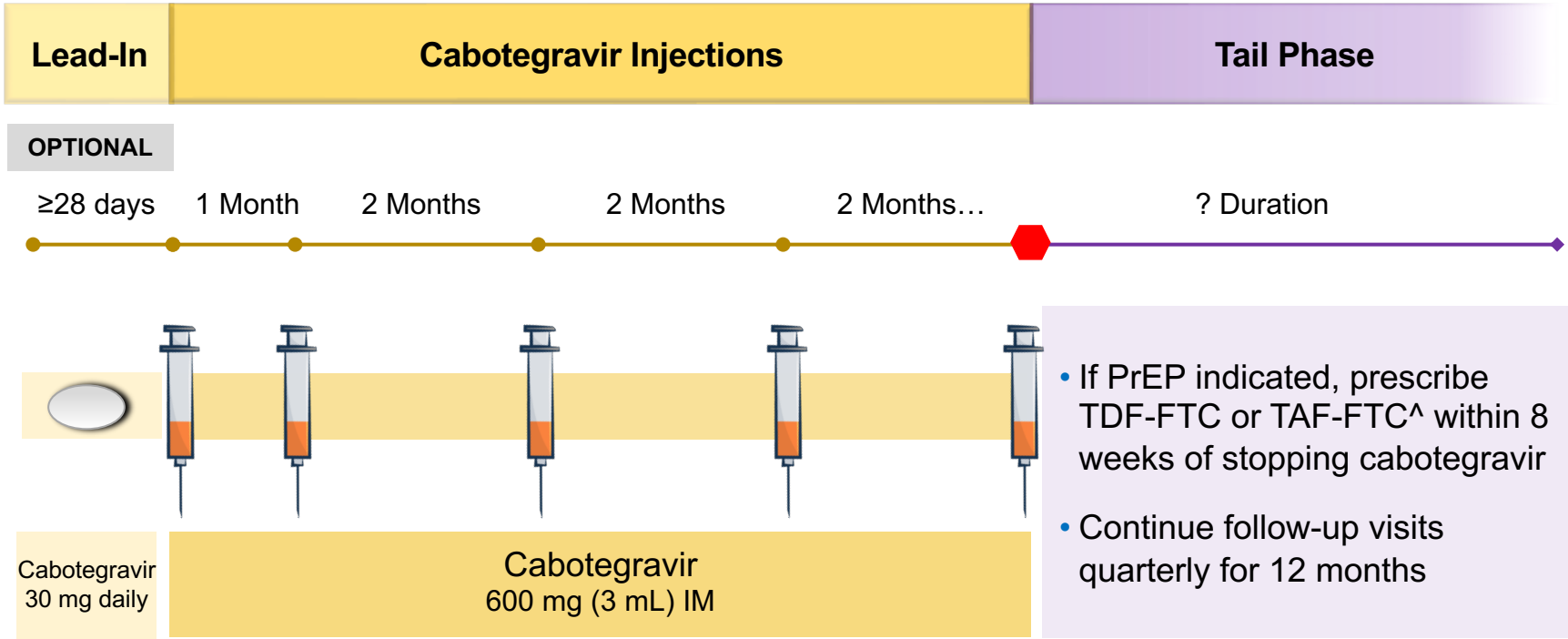
Cabotegravir for HIV PrEP: Tail Phase Recommendations



Source: Based on Cabotegravir Prescribing Information. Illustration: David H. Spach, MD

2021 CDC PrEP Guidelines

Cabotegravir for HIV PrEP: Tail Phase Recommendations



- If PrEP indicated, prescribe TDF-FTC or TAF-FTC^ within 8 weeks of stopping cabotegravir
- Continue follow-up visits quarterly for 12 months

*TDF-FTC = tenofovir DF-emtricitabine; TAF-FTC = tenofovir alafenamide-emtricitabine
^Note that TAF-FTC is not approved as HIV PrEP for individuals at risk from receptive vaginal sex

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

Cabotegravir Baseline Laboratory Monitoring

- Baseline Laboratory Tests Indicated Prior to Starting Cabotegravir:
  - HIV RNA (within 1 week prior to initiation visit)
  - HIV-1/2 antigen-antibody assay
  - STI testing (syphilis, gonorrhea, chlamydia)

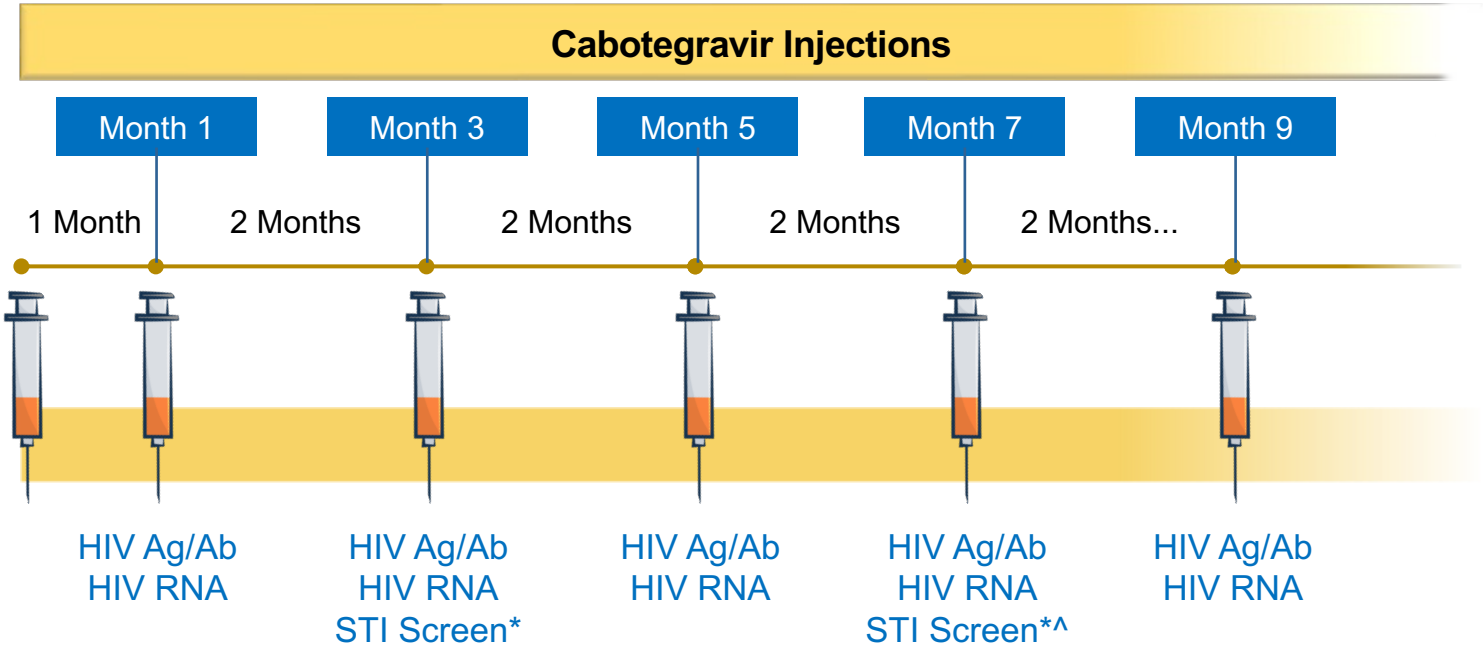
- Baseline Laboratory Tests NOT Indicated Prior to Starting Cabotegravir:
  - Serum creatinine (eCrCl)
  - Hepatitis B serology (HBsAg, anti-HBs, anti-HBc)*
  - Lipid panels
  - Liver function tests

*Note: if person has not previously received HBV immunization, obtaining hepatitis B serologic testing should be done as general health management to determine if hepatitis B vaccine series indicated and to screen for active hepatitis B infection..

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

2021 CDC PrEP Guidelines

Cabotegravir for HIV PrEP: Monitoring on Cabotegravir



*Bacterial STI screening for men who have sex with men and transgender women who have sex with men (every 4 months)
^Bacterial STI screening for heterosexually active women and men (syphilis, gonorrhea, chlamydia every 6 months)

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

Cabotegravir (long-acting injectable) for HIV PrEP
Summary of Key Phase 3 Studies

- **HPTN 083: Cabotegravir versus TDF-FTC for MSM and TGW**
- **HPTN 084: Cabotegravir versus TDF-FTC for Cisgender women**

Abbreviations: HPTN -= HIV Prevention Trials Network; TDF-FTC = tenofovir DF-emtricitabine; MSM = men who have sex with men; TGW = transgender women

IM Cabotegravir versus TDF-FTC for HIV PrEP for MSM and TGW

HPTN 083

National HIV Curriculum

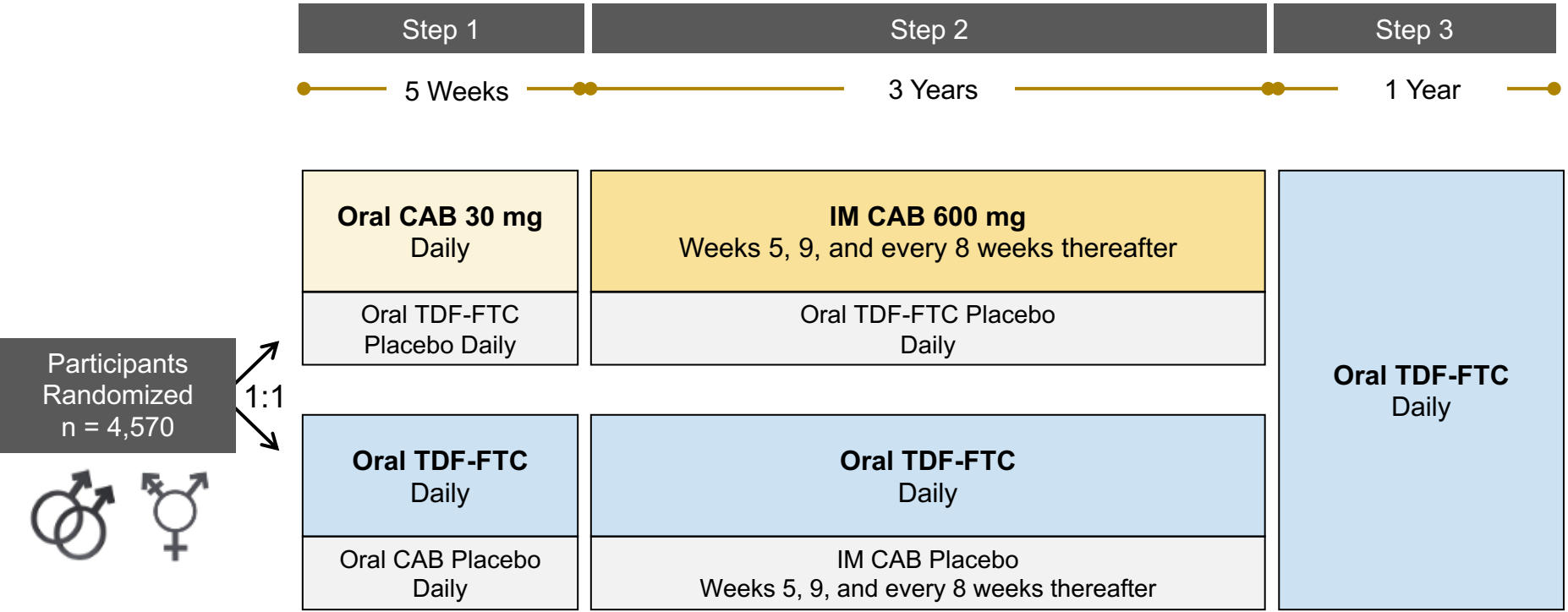
IM Cabotegravir versus TDF-FTC for HIV PrEP for MSM and TGW
HPTN 083: Study Design

- **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 for 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
  - 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/urethral 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 HIV PrEP for 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 HIV PrEP for MSM and TGW
HPTN 083: Study Population

HPTN 083: Selected Baseline Demographics

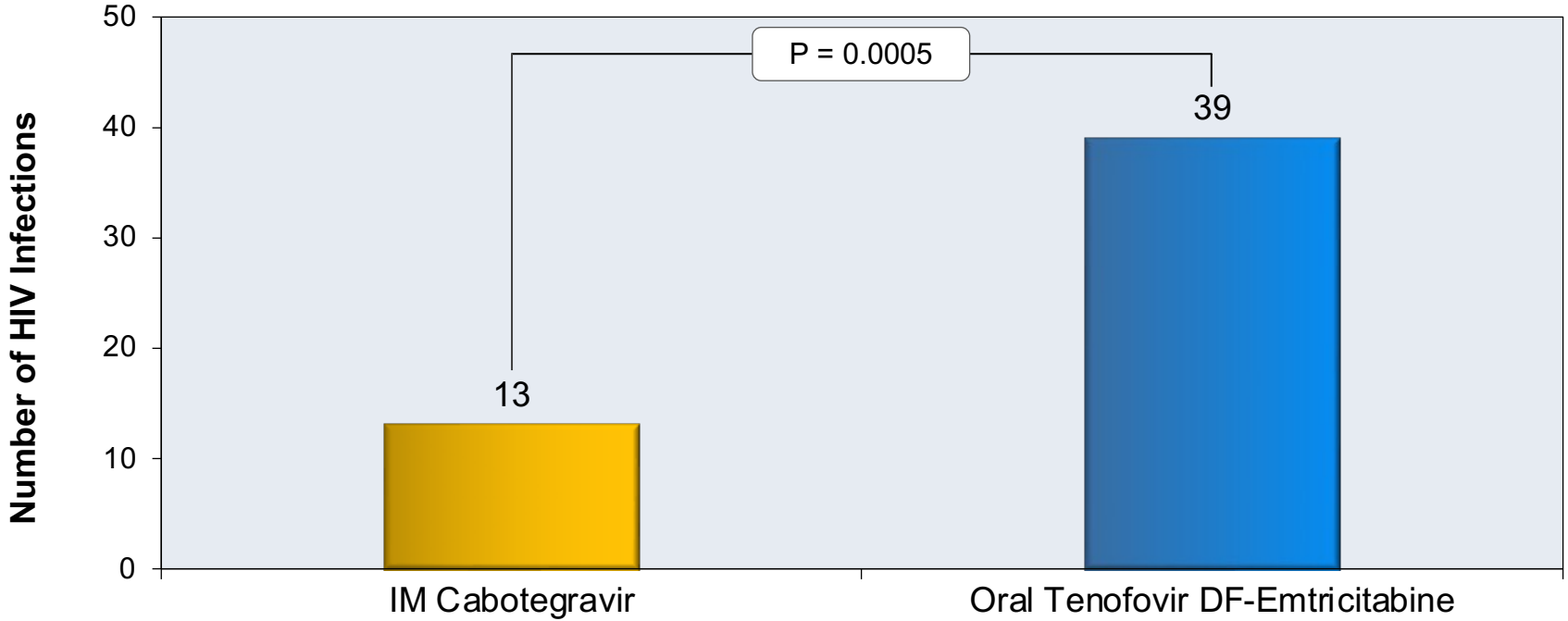
Characteristic	Total (n = 4,566)	Cabotegravir (n = 2,282)	TDF-FTC (n = 2,284)
Cisgender MSM, n (%)	3,992 (87.4)	2,013 (88.2)	1,979 (86.6)
Transgender women, n (%)	570 (12.5)	266 (11.7)	304 (13.3)
Median age (IQR), years, n (%)	26 (22-32)	26 (22-32)	26 (22-32)
Black race, United States, n (%)	845 (49.8)	411 (48.4)	434 (51.1)
Geographic region, n (%)			
United States, n (%)	1,698 (37.2)	849 (37.2)	849 (37.2)
Latin America, n (%)	1,964 (43.0)	980 (42.9)	984 (43.2)
Asia, n (%)	752 (16.5)	375 (16.5)	377 (16.5)
Africa, n (%)	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 HIV PrEP for MSM and TGW
HPTN 083: Results

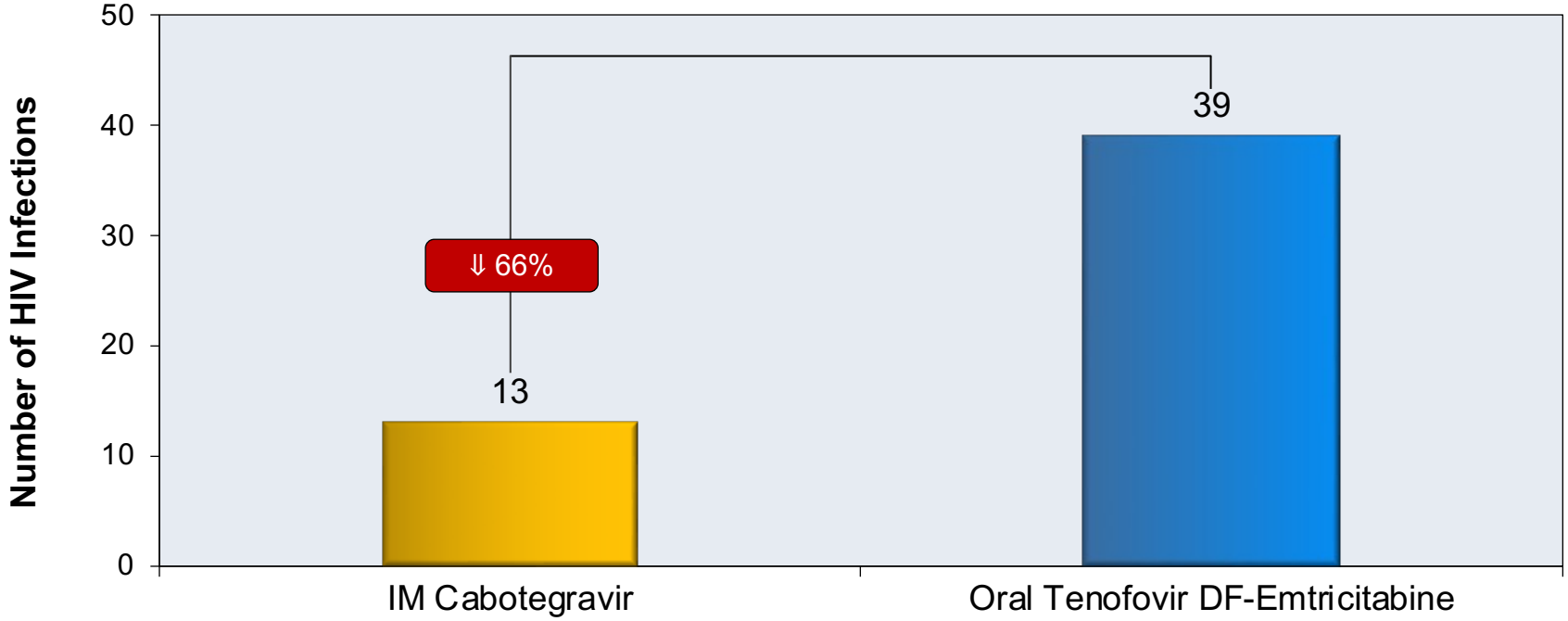
Number of HIV Infections (After Enrollment)



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

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

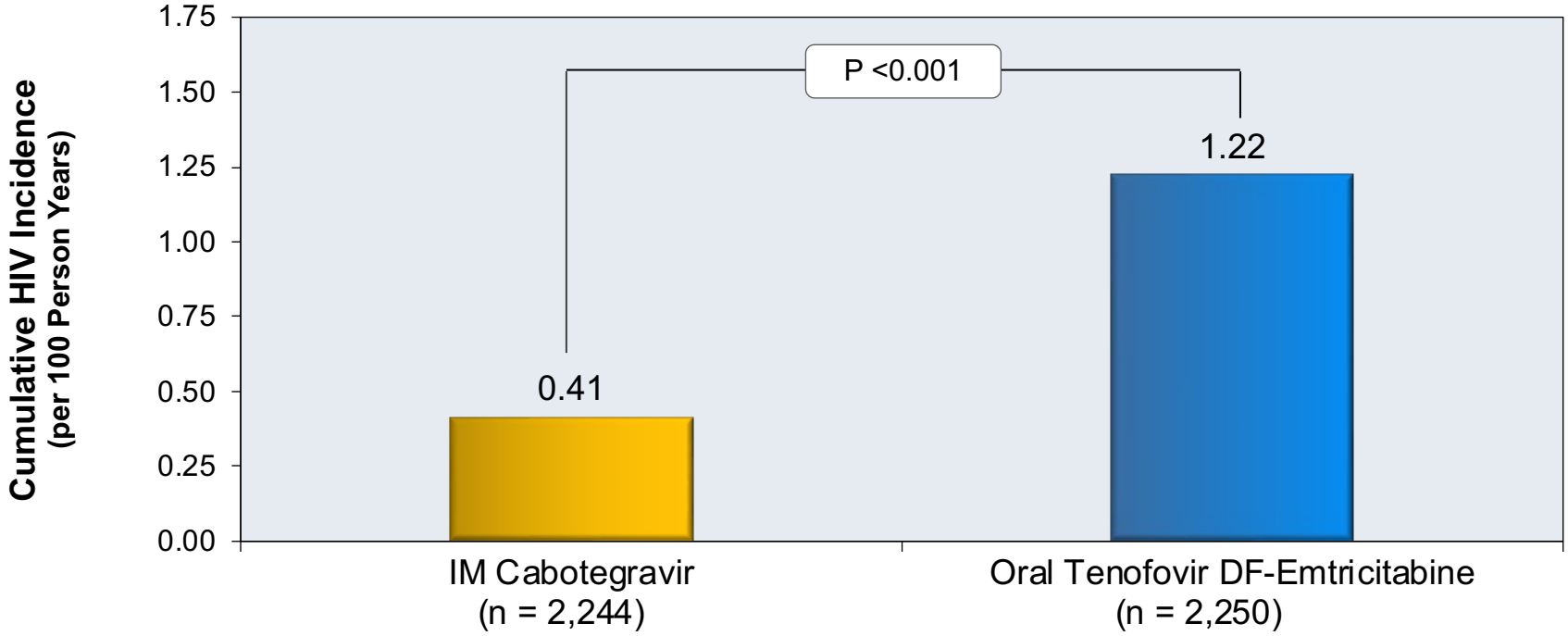
Risk Reduction in HIV Infections (After Enrollment)



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

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

Cumulative HIV Incidence (After Enrollment)



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

IM Cabotegravir versus TDF-FTC for HIV PrEP for MSM and TGW
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)

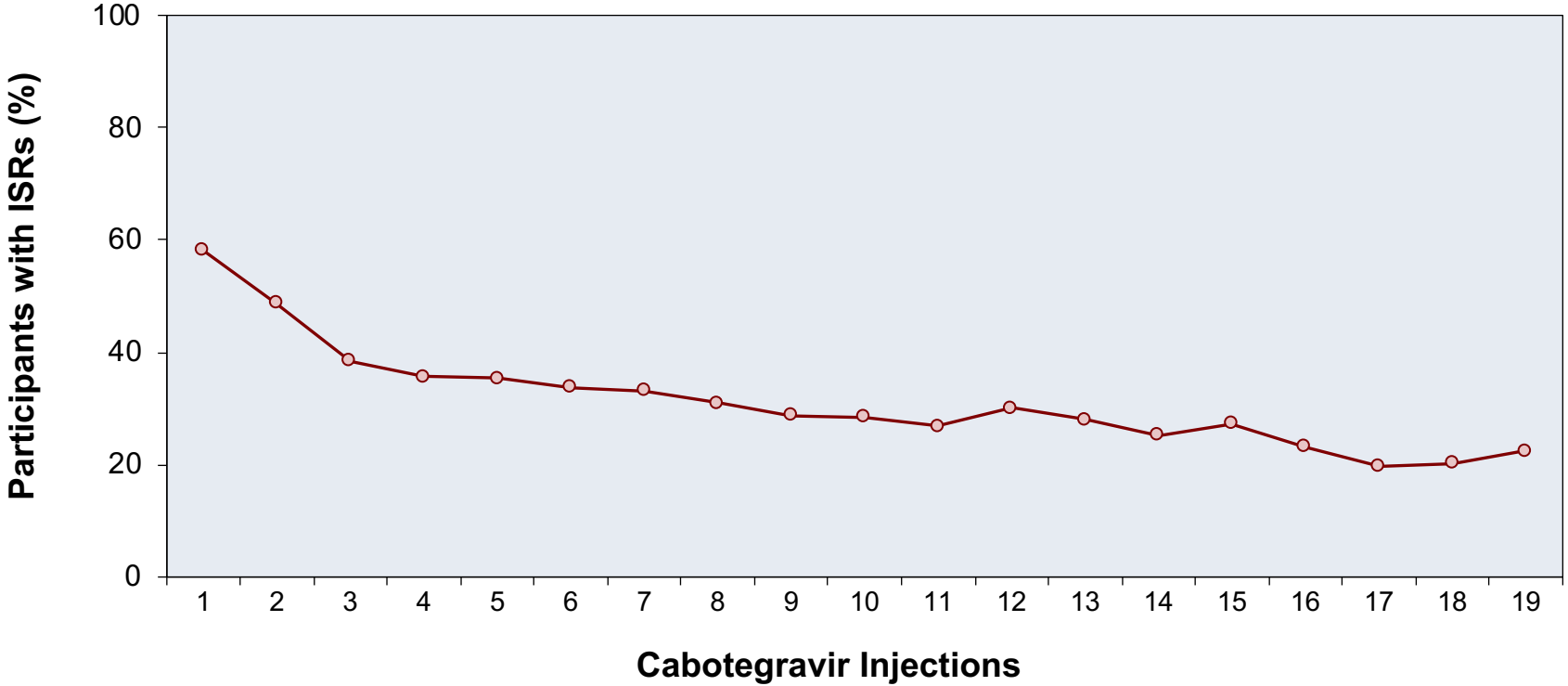
Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

IM Cabotegravir versus TDF-FTC for HIV PrEP for 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 after injection

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

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



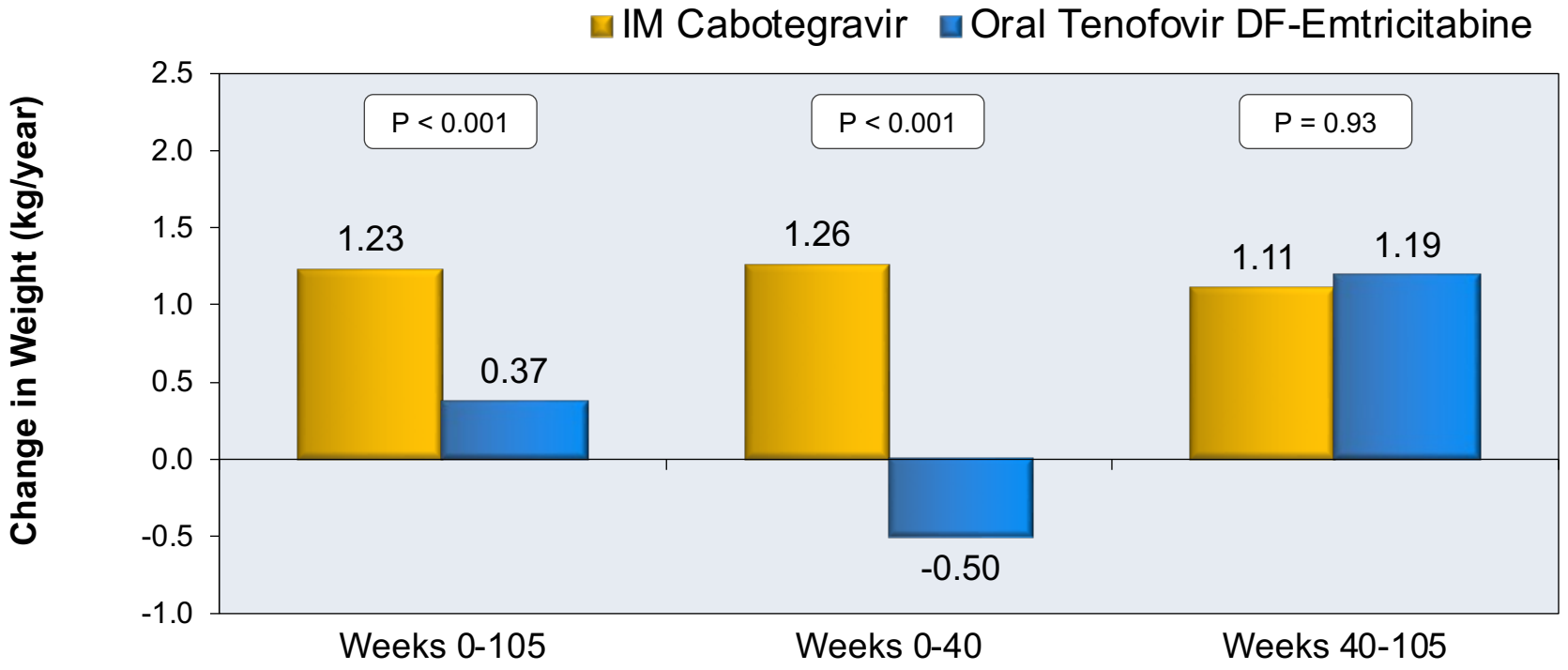
Source: Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

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 HIV PrEP for 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

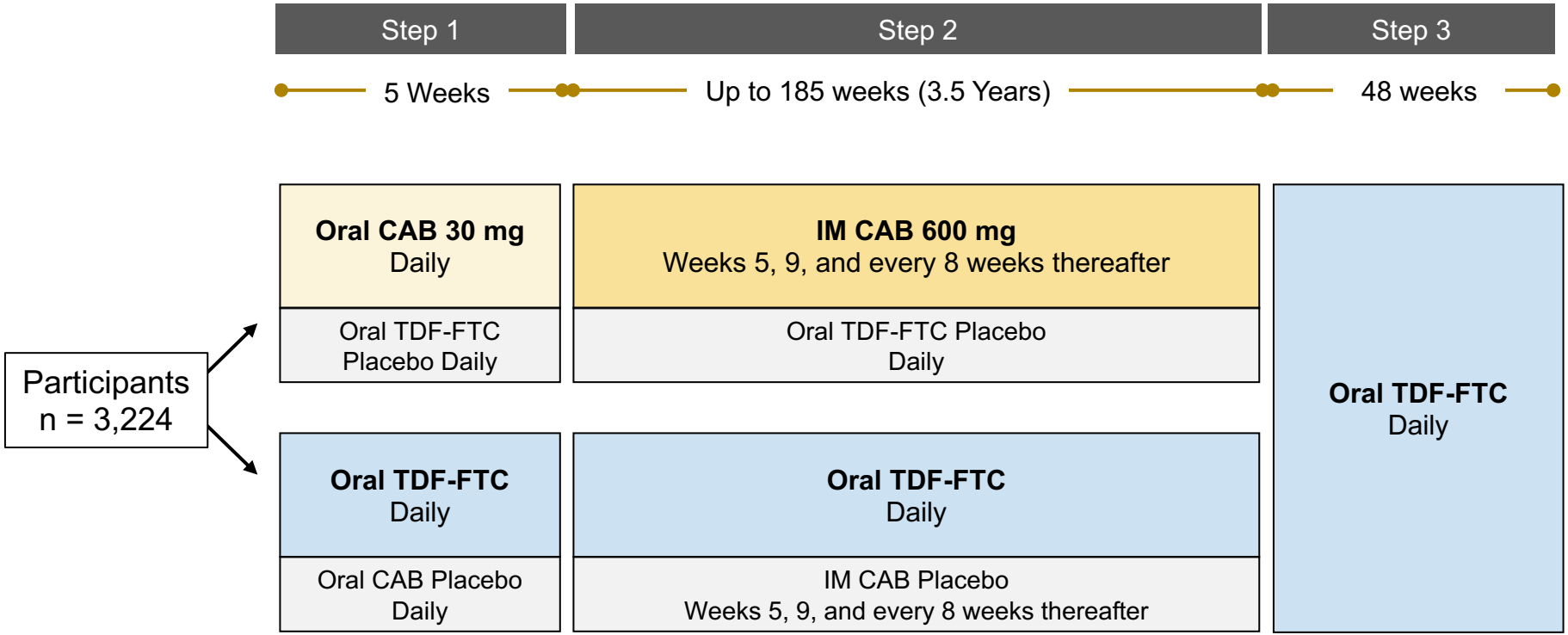
HPTN 084

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 for cisgender women (assigned female sex at birth)
- **Setting**
  - 20 sites in 7 countries in Sub-Saharan Africa
- **Inclusion Criteria**
  - Cisgender women (assigned female sex at birth) 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: Delany-Moretlwe S, et al. Lancet. 2022;399:1779-89.

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



Source: Delany-Moretlwe S, et al. Lancet. 2022;399:1779-89.

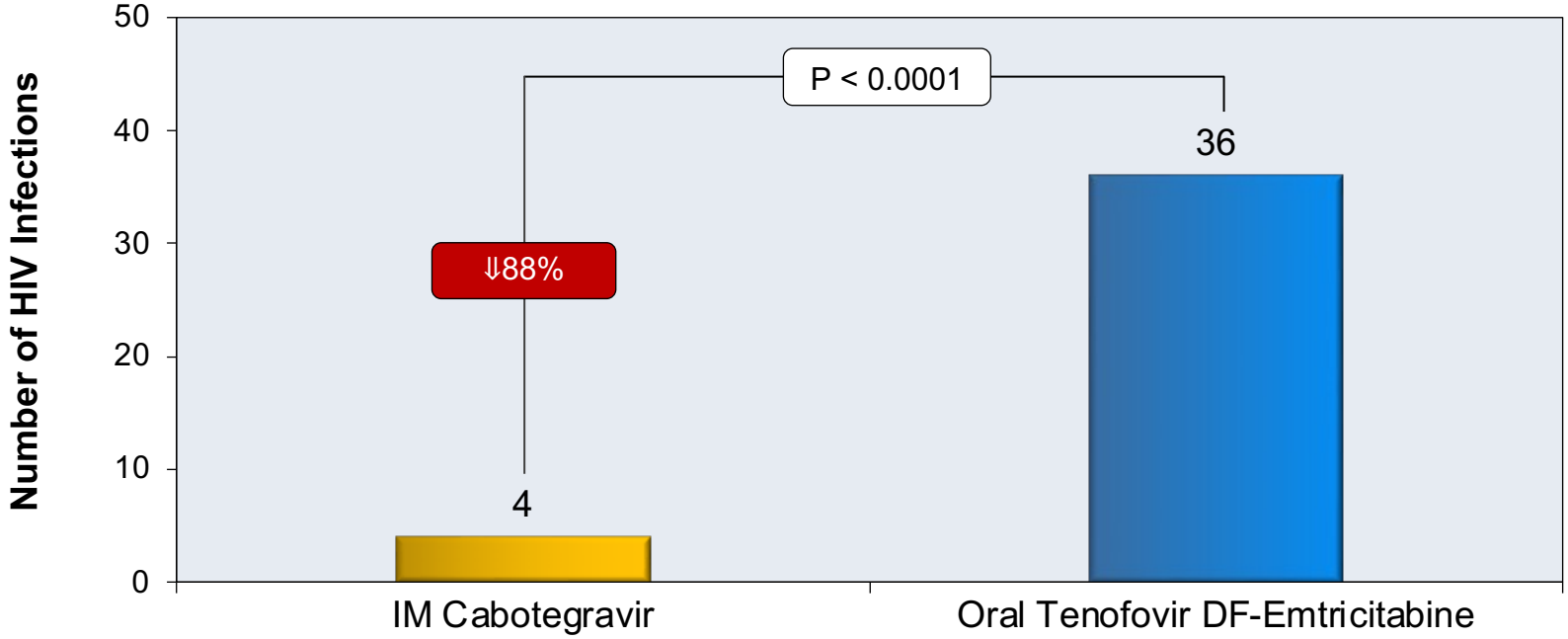
IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Baseline Characteristics

HPTN 084: Selected Baseline Characteristics		
Baseline Characteristics	**Cabotegravir** (n = 1,614)	**TDF-FTC** (n = 1,610)
Median age, years	25	25
Age <25 years, n (%)	814 (50.4%)	816 (50.7%)
Black/African race, n (%)	1,569 (97.2%)	1,554 (96.5%)
Sexual activity in past month (reported)		
>2 sex partners, n (%)	878/1,609 (54.5%)	877/1,609 (54.8%)
Transactional sex, n (%)	658/1,609 (40.9%)	655/1,600 (40.9%)
Partner HIV(+) or unknown, n (%)	542/1,609 (33.7%)	558/1,600 (34.9%)
Anal sex, n (%)	90/1,609 (5.6%)	95/1,600 (5.9%)

Source: Delany-Moretlwe S, et al. Lancet. 2022;399:1779-89.

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

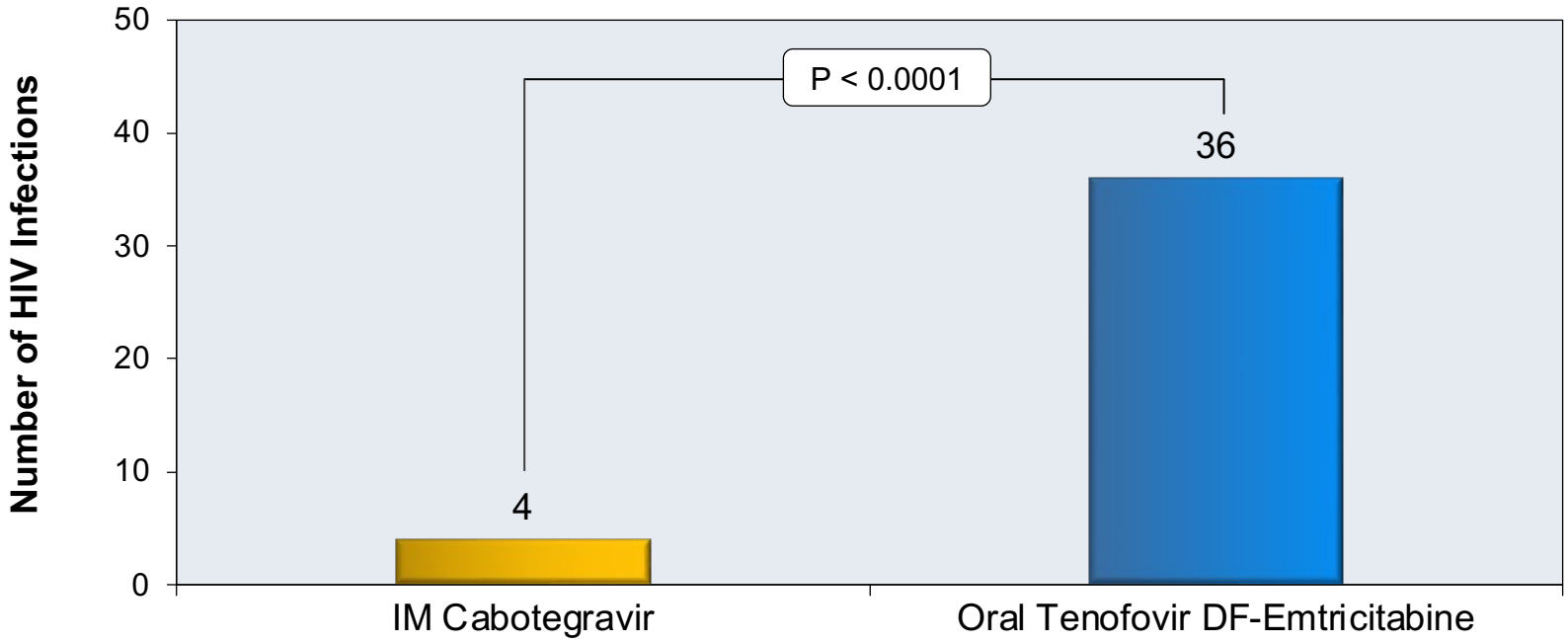
Number of HIV Infections: Risk Reduction



Source: Delany-Moretlwe S, et al. Lancet. 2022;399:1779-89.

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

Number of HIV Infections



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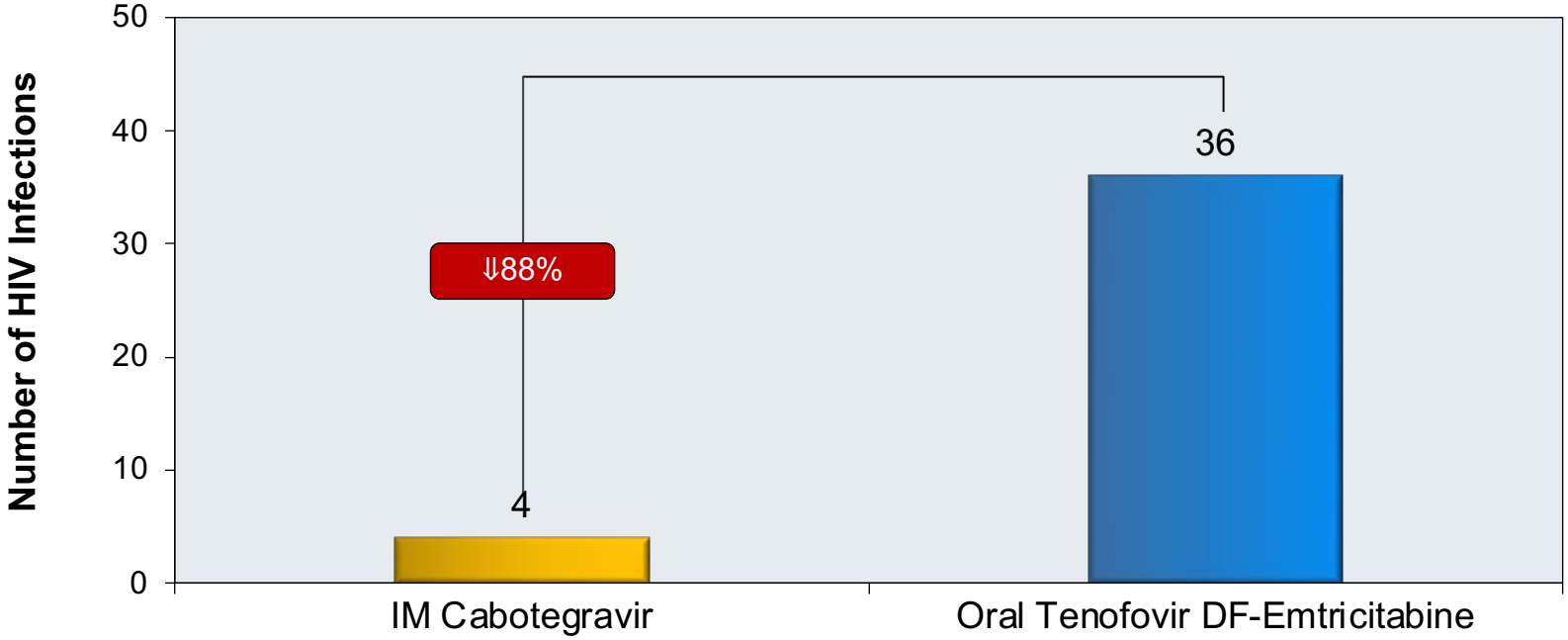
IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women HPTN 084: Results

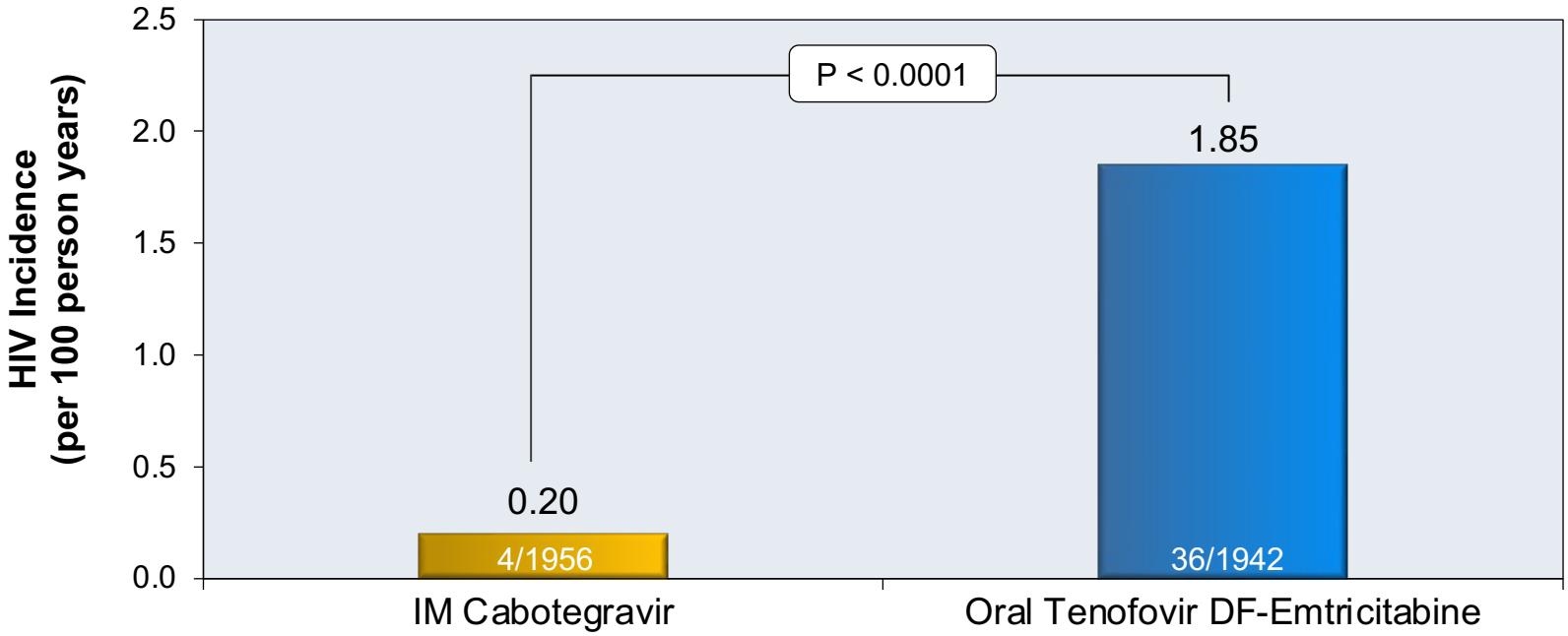
Number of HIV Infections: Risk Reduction



Source: Delany-Moretlwe S, et al. Lancet. 2022;399:1779-89.

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

HIV Incidence



Source: Delany-Moretlwe S, et al. Lancet. 2022;399:1779-89.

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

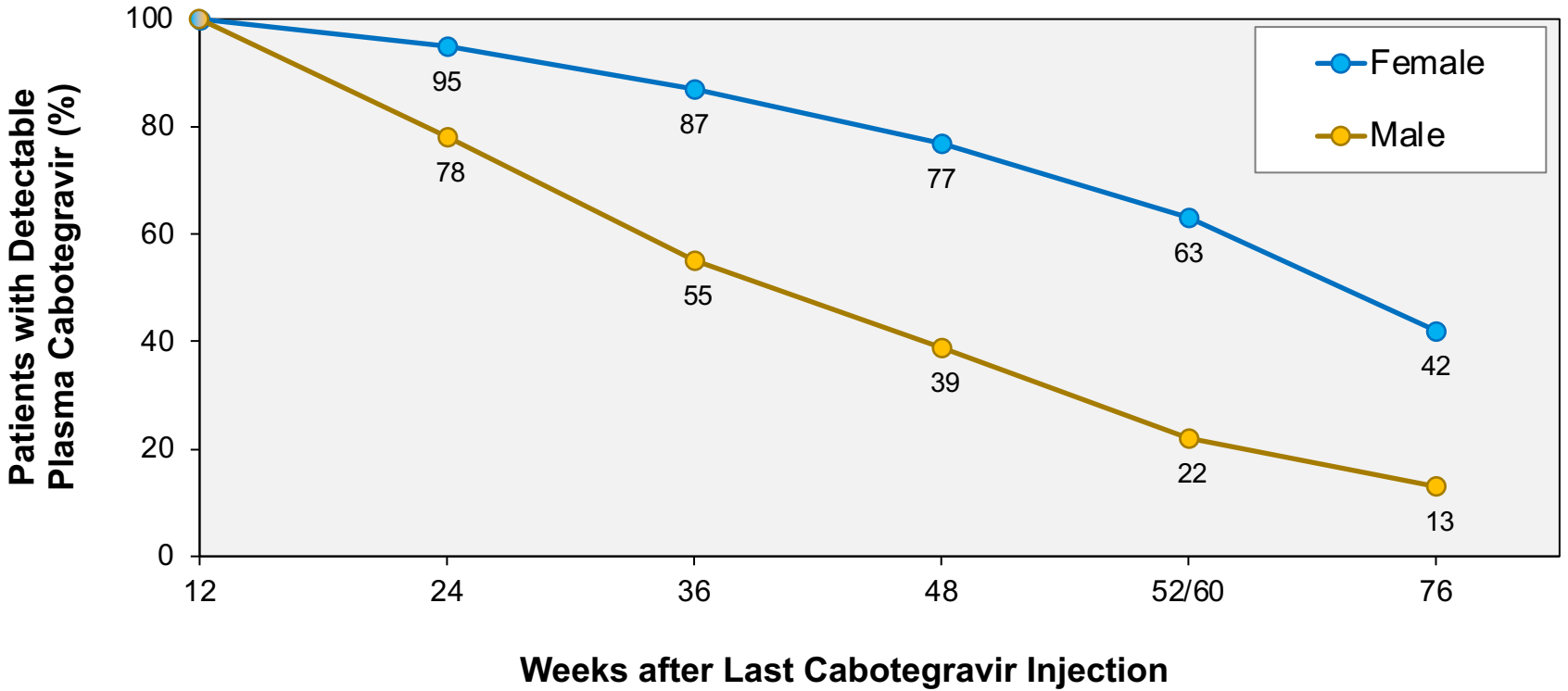
Interpretation: Although both products for HIV prevention were generally safe, well tolerated, and effective, cabotegravir was superior to TDF-FTC in preventing HIV infection in women.

Source: Delany-Moretlwe S, et al. Lancet. 2022;399:1779-89.

IM Cabotegravir Tail-Phase Safety, Tolerability, and Pharmacokinetics

HPTN 077

Cabotegravir Levels After Last Dose of Cabotegravir



Source: Landovitz RJ, et al. Lancet HIV. 2020;7:e472-81.

Acknowledgments

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AETC AIDS Education & Training Center Program

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