

JORNADAS 2020 FORMATO WEBINAR



**DE ACTUALIZACIÓN EN ATENCIÓN FARMACÉUTICA
AL PACIENTE CON PATOLOGÍAS VÍRICAS**

Actualización y Futuro en el Tratamiento de la Infección por VIH

Santiago Moreno

**Servicio de Enfermedades Infecciosas. Hospital U. Ramón y Cajal
Madrid**

ORGANIZA:





1 Tratamiento Antirretroviral Actual



Guidelines 2019/2020

HIV Guidelines.

What to Start.

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



Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

How to Cite the Adult and Adolescent Guidelines:

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>. Accessed [insert date], [insert page number], table number, etc., if applicable.

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the AIDSinfo Web site (<http://aidsinfo.nih.gov>).

Clinical Review & Education

JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults 2020 Recommendations of the International Antiviral Society-USA Panel

Michael S. Saag, MD, Rajesh T. Gandhi, MD, Jennifer F. Hoy, MBBS, Raphael J. Landovitz, MD, Melanie A. Thompson, MD, Paul F. Sax, MD, Dorey M. Smith, MD, Constance A. Benson, MD, Susan H. Buchbinder, MD, Carlos del Rio, MD, Joseph J. Eron Jr, MD, Gerd Fätkenheuer, MD, Hubertus F. Günther, MD, Jean-Michel Molina, MD, Donna M. Jacobsen, BS, Paul A. Volberding, MD

Supplemental content

IMPORTANCE Data on the use of antiretroviral drugs, including new drugs and formulations, for the treatment and prevention of HIV infection continue to guide optimal practices.

OBJECTIVE To evaluate new data and incorporate them into current recommendations for initiating HIV therapy, monitoring individuals starting on therapy, changing regimens, preventing HIV infection for those at risk, and special considerations for older people with HIV.

EVIDENCE REVIEW New evidence was collected since the previous International Antiviral (formerly AIDS) Society-USA recommendations in 2018, including data published or presented at peer-reviewed scientific conferences through August 22, 2020. A volunteer panel of 55 experts in HIV research and patient care considered these data and updated previous recommendations.

FINDINGS From 5316 citations about antiretroviral drugs identified, 549 were included to form the evidence basis for these recommendations. Antiretroviral therapy is recommended as soon as possible for all individuals with HIV who have detectable viremia. Most patients can start with a 3-drug regimen or now a 2-drug regimen, which includes an integrase strand transfer inhibitor. Effective options are available for patients who may be pregnant, those who have specific clinical conditions, such as kidney, liver, or cardiovascular disease, those who have opportunistic diseases, or those who have health care access issues. Recommended for the first time, a long-acting antiretroviral regimen injected once every 4 weeks for treatment or every 8 weeks pending approval by regulatory bodies and availability. For individuals at risk for HIV, preexposure prophylaxis with an oral regimen is recommended or, pending approval by regulatory bodies and availability, with a long-acting injection given every 8 weeks. Monitoring before and during therapy for effectiveness and safety is recommended. Switching therapy for virological failure is relatively rare at this time, and the recommendations for switching therapies for convenience and for other reasons are included. With the survival benefits provided by therapy, recommendations are made for older individuals with HIV. The current coronavirus disease 2019 pandemic poses particular challenges for HIV research, care, and efforts to end the HIV epidemic.

CONCLUSION AND RELEVANCE Advances in HIV prevention and management with antiretroviral drugs continue to improve clinical care and outcomes among individuals at risk for and with HIV.

Author Affiliations. Author affiliations are listed at the end of this article.

Corresponding Author: Michael S. Saag, MD, School of Medicine, University of Alabama at Birmingham, 845 9th St S, 888B 256, Birmingham, AL 35294 (msaag@uab.edu).

JAMA. doi:10.1001/jama.2020.17020
Published online October 14, 2020.

© 2020 American Medical Association. All rights reserved.

E1



EACS
European
AIDS
Clinical
Society

GUIDELINES

Version 10.1

October 2020

English



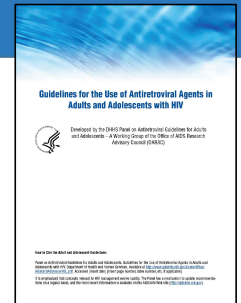
DOCUMENTO DE CONSENSO DE GeSIDA/PLAN NACIONAL SOBRE EL SIDA RESPECTO AL TRATAMIENTO ANTIRRETROVIRAL EN ADULTOS INFECTADOS POR EL VIRUS DE LA INMUNODEFICIENCIA HUMANA

(ACTUALIZACIÓN 2020)

PANEL DE EXPERTOS DE GeSIDA Y
PLAN NACIONAL SOBRE EL SIDA

DHHS Guidelines December, 2019

What to Start: Recommended regimens



Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

INSTI plus 2 NRTIs:

Note: For individuals of childbearing potential, see Table 6b before prescribing one of these regimens.

- BIC/TAF/FTC (AI)
- DTG/ABC/3TC (AI)—if HLA-B*5701 negative
- DTG plus (TAF or TDF)^a plus (FTC or 3TC) (AI)
- RAL plus (TAF or TDF)^a plus (FTC or 3TC) (BI for TDF/[FTC or 3TC], BII for TAF/FTC)

INSTI plus 1 NRTI:

- DTG/3TC (AI), except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

IAS-USA Panel Guidelines 2020

What to Start: Recommended regimens



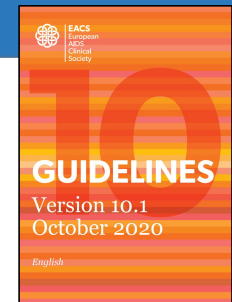
Recommended for Most People With HIV^a

- Bictegravir/tenofovir alafenamide/emtricitabine (evidence rating: A1a)
- Dolutegravir plus (all evidence ratings: A1a)
 - Tenofovir alafenamide/emtricitabine
 - Tenofovir disoproxil fumarate/emtricitabine
 - Tenofovir disoproxil fumarate/lamivudine
- Dolutegravir/lamivudine with caveats^b (evidence rating: A1a)

^b Not recommended for rapid start because baseline laboratory evaluation results must be reviewed before initiation. Also not recommended for patients with chronic hepatitis B or HIV RNA level above 500 000 copies/mL, and perhaps a CD4 cell count below 200/μL, although the latter is unclear. Close monitoring for adherence and virological response is needed. Not recommended for patients being treated for an active opportunistic infection.

EACS Guidelines 2018

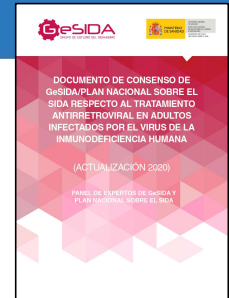
What to Start: Recommended regimens



Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, cardiovascular risk) II (Weight increase (DTG))
TAF/FTC or TDF/FTC or TDF/3TC + DTG		III (Weight increase (DTG, TAF)) IV (TDF: prodrug types. Renal and bone toxicity. TAF dosing)
TAF/FTC/BIC		II (Weight increase (BIC))
TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid		IV (TDF: prodrug types. Renal and bone toxicity. TAF dosing) V (RAL: dosing)
1 NRTI + INSTI		
3TC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL	

GeSIDA Guidelines 2020

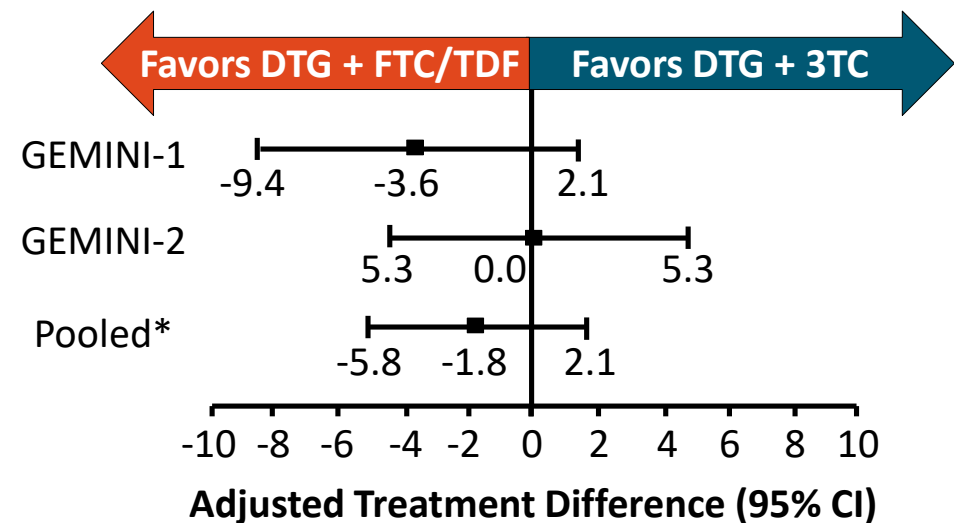
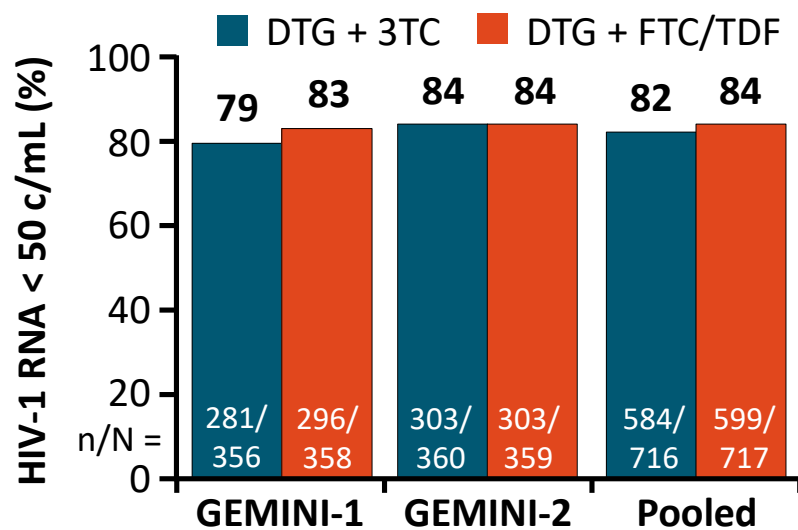
What to Start: Preferred regimens



3er Fármaco	Pauta†	Comentarios‡
Preferentes. Pautas aplicables a la mayoría de los pacientes y que en ensayos clínicos aleatorizados han mostrado una eficacia no inferior a otras pautas también consideradas actualmente como preferentes o superior frente a otras pautas y presentan ventajas adicionales en tolerancia, toxicidad o un bajo riesgo de interacciones farmacológicas		
INI	BIC/FTC/TAF	
	DTG/ABC/3TC	-ABC está contraindicado en pacientes con HLA-B*5701 positivo -DTG no debe utilizarse en mujeres que deseen quedarse embarazadas o mujeres en edad fértil que no utilicen medidas anticonceptivas eficaces. -No utilizar en pacientes con hepatitis B crónica
	DTG+FTC/TAF**	- DTG no debe utilizarse en mujeres que deseen quedarse embarazadas o mujeres en edad fértil que no utilicen medidas anticonceptivas eficaces
	RAL+FTC/TAF*	-RAL puede administrarse indistintamente como 1 comprimido de 400 mg cada 12 horas, o 2 comprimidos de 600 mg (nueva formulación) cada 24 horas
	DTG/3TC	- No recomendado en pacientes con cifra basal de CD4+ menor de 200/ μ L - DTG no debe utilizarse en mujeres que deseen quedarse embarazadas o mujeres en edad fértil que no utilicen medidas anticonceptivas eficaces - No utilizar en pacientes con hepatitis crónica por VHB

GEMINI 1-2: Viral Suppression Through Wk 144 With DTG + 3TC vs DTG + FTC/TDF as Initial ART

- Parallel, international, randomized, double-blind phase III noninferiority studies comparing initial ART with DTG + 3TC (n = 717) vs DTG + FTC/TDF (n = 716)
 - DTG + 3TC noninferior at Wk 48 primary analysis (HIV-1 RNA < 50 copies/mL by ITT-E Snapshot)^[1] and at Wk 96^[2]; current analysis through Wk 144^[3]



*Adjusted for BL HIV-1 RNA ($\leq 100,000$ vs $> 100,000$ copies/mL), BL CD4+ cell count (≤ 200 vs > 200 cells/mm³) and study (GEMINI-1 vs GEMINI-2).

GEMINI 1-2: Virologic Outcomes at Wk 144 Snapshot Analysis

Snapshot Outcome, n (%)	DTG + 3TC (n = 716)	DTG + FTC/TDF (n = 717)
HIV-1 RNA < 50 copies/mL	584 (82)	599 (84)
HIV-1 RNA ≥ 50 copies/mL	23 (3)	21 (3)
▪ Data in window and HIV-1 RNA ≥ 50 copies/mL	4 (< 1)	5 (< 1)
▪ Discontinued for lack of efficacy	10 (1)	4 (< 1)
▪ Discontinued for other reason and HIV-1 RNA ≥ 50 copies/mL	7 (1)	11 (2)
▪ Change in ART	2 (< 1)	1 (< 1)
No virologic data	109 (15)	97 (14)
▪ Discontinued study due to AE or death	29 (4)	32 (4)
▪ Discontinued study for other reasons*	78 (11)	64 (9)
▪ On study but missing data in window	2 (< 1)	1 (< 1)

*Included protocol deviation, loss to follow-up, physician decision, withdrawal by patient, and lack of efficacy.

- **Met CVW criteria:** n = 12 (2%) with DTG + 3TC (1 since Wk 96), n = 9 (1%) with DTG + FTC/TDF (2 since Wk 96)
 - No participant with CVW had treatment-emergent INSTI or NRTI resistance mutations
- 1 patient in DTG + 3TC arm without CVW reported nonadherence and developed M184V at Wk 132 (HIV-1 RNA 61,927 c/mL) and R263R/K at Wk 144 (HIV-1 RNA 135 c/mL), resulting in 1.8-fold change in DTG susceptibility; patient regained virologic suppression after switch to DTG QD + DRV/COBI after Wk 144

GEMINI 1-2: Virologic Response by Baseline Parameters

HIV-1 RNA < 50 c/mL at Wk 144 by Subgroup, % (n/N)	DTG + 3TC	DTG + FTC/TDF
Baseline HIV-1 RNA level, copies/mL		
▪ ≤ 100,000	81 (469/576)	84 (471/564)
▪ > 100,000	82 (115/140)	84 (128/153)
Baseline CD4+ cell count, cells/mm³		
▪ > 200	83 (542/653)	84 (557/662)
▪ ≤ 200	67 (42/63)	76 (42/55)

THE STAT STUDY: Test and Treat (3TC/DTG)

Patients

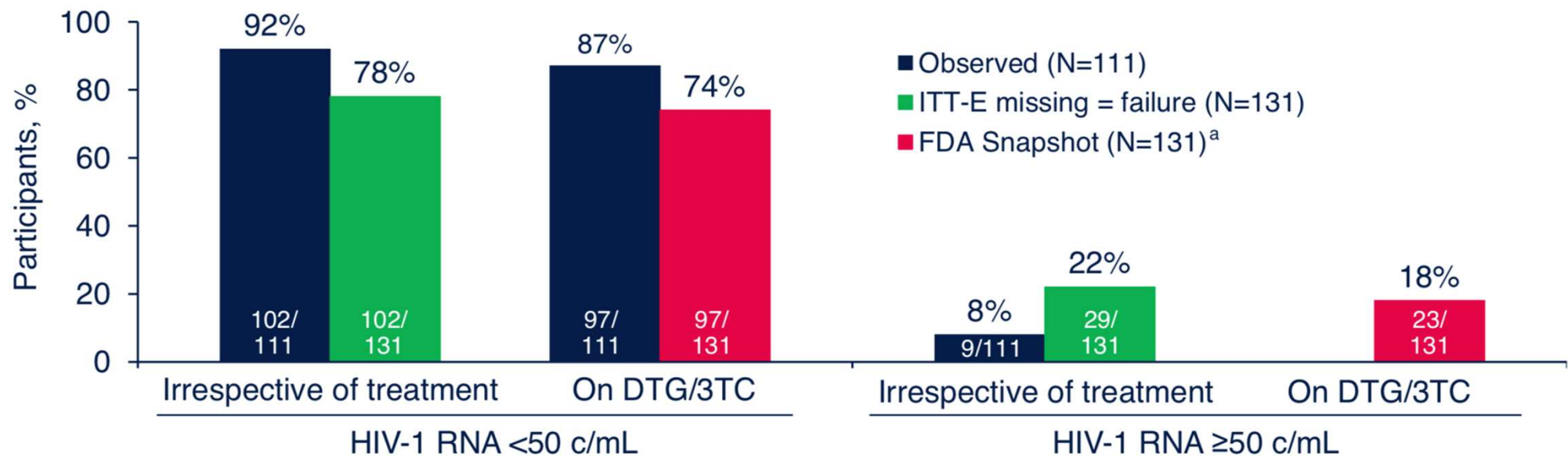
Table 1. Selected Baseline Demographics and Participant Characteristics (ITT-E Population)

Characteristic	DTG/3TC (N=131)
Time to enrollment since diagnosis, median (range), days	5 (0-15)
HIV-1 RNA, median (range), c/mL, n (%) ^{a,b}	63,056 (<40 to 68,706,840) ^c
<100,000	79 (60)
100,000 to <500,000	32 (24)
500,000 to <1,000,000	9 (7)
≥1,000,000	10 (8)
CD4+ cell count, median (range), cells/mm ^{3b}	389.0 (<20 to 1466) ^d
<200, n (%)	37 (28)
HBV co-infection, n (%) ^{b,e}	7 (5)
M184V resistance mutation, n (%) ^b	1 (<1)

^a1 (<1%) participant had missing plasma HIV-1 RNA results at BL. ^bBL resistance was identified at Week 4, and HIV-1 viral load, CD4+ cell count, and HBV co-infection were identified at Week 1 from samples taken at BL. ^cLower limit of quantification is <40. ^dLower limit of quantification is <20. ^e2 participants with HBV co-infection remained on DTG/3TC.

THE STAT STUDY: Results

Figure 1. Results of Efficacy Analyses: Virologic Outcomes at Week 24



^a11 (8%) of 131 participants had no virologic data at Week 24.

THE STAT STUDY:

Results

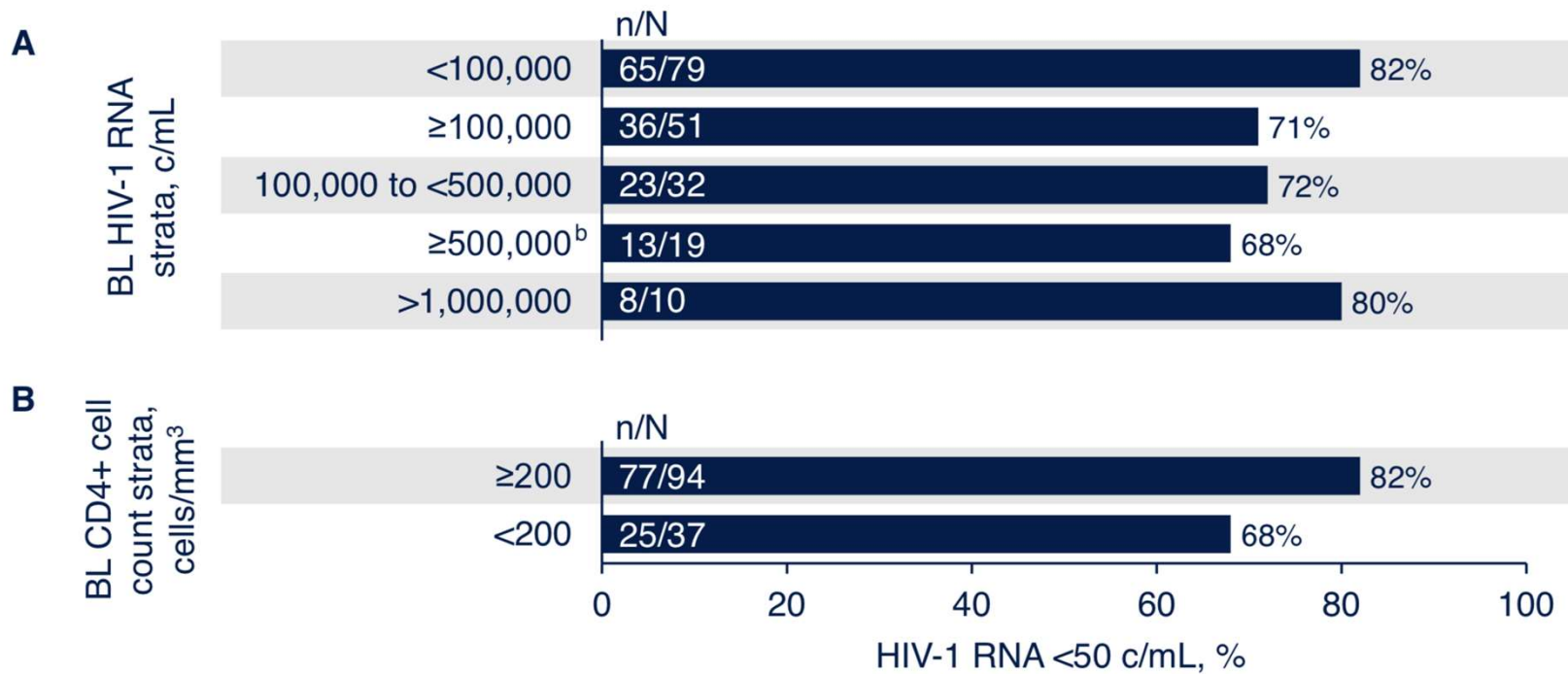
Table 3. Participants Who Switched From DTG/3TC at Any Time Point by Week 24

Reason for switch	Visit window	Modified ART	Plasma HIV-1 RNA at Week 24
BL HBV	Week 1	DTG/3TC + TAF	<40 c/mL
BL HBV	Week 1	BIC/FTC/TAF	NA ^a
BL HBV	Week 4	DTG + TDF/FTC	<40 c/mL
BL HBV	Week 4	BIC/FTC/TAF or DTG + TDF/FTC ^b	49 c/mL
Decision by participant or proxy	Week 4	BIC/FTC/TAF	NA ^c
BL HBV	Week 8	DTG/3TC + TAF	<40 c/mL
BL M184V	Week 8	DTG/RPV	NA ^d
AE (rash)	Week 12; Week 12	COBI/DRV/FTC/TAF; BIC/FTC/TAF ^e	<40 c/mL

^aParticipant on study but missing data in window. Participant had HIV-1 RNA <40 c/mL at Week 36. ^bParticipant participates in another double-blind clinical trial with a tenofovir-based regimen; switched to either Biktarvy or Truvada + Tivicay. ^cParticipant withdrew consent after switch from DTG/3TC. ^dParticipant had HIV-1 RNA 18,752 c/mL at baseline, <40 c/mL on Day 47, switched to DTG/RPV on Day 49, and had last HIV-1 RNA 54 c/mL on Day 57; participant withdrew consent (due to relocation) on Day 106 (Week 12). ^eParticipant switched ART twice.

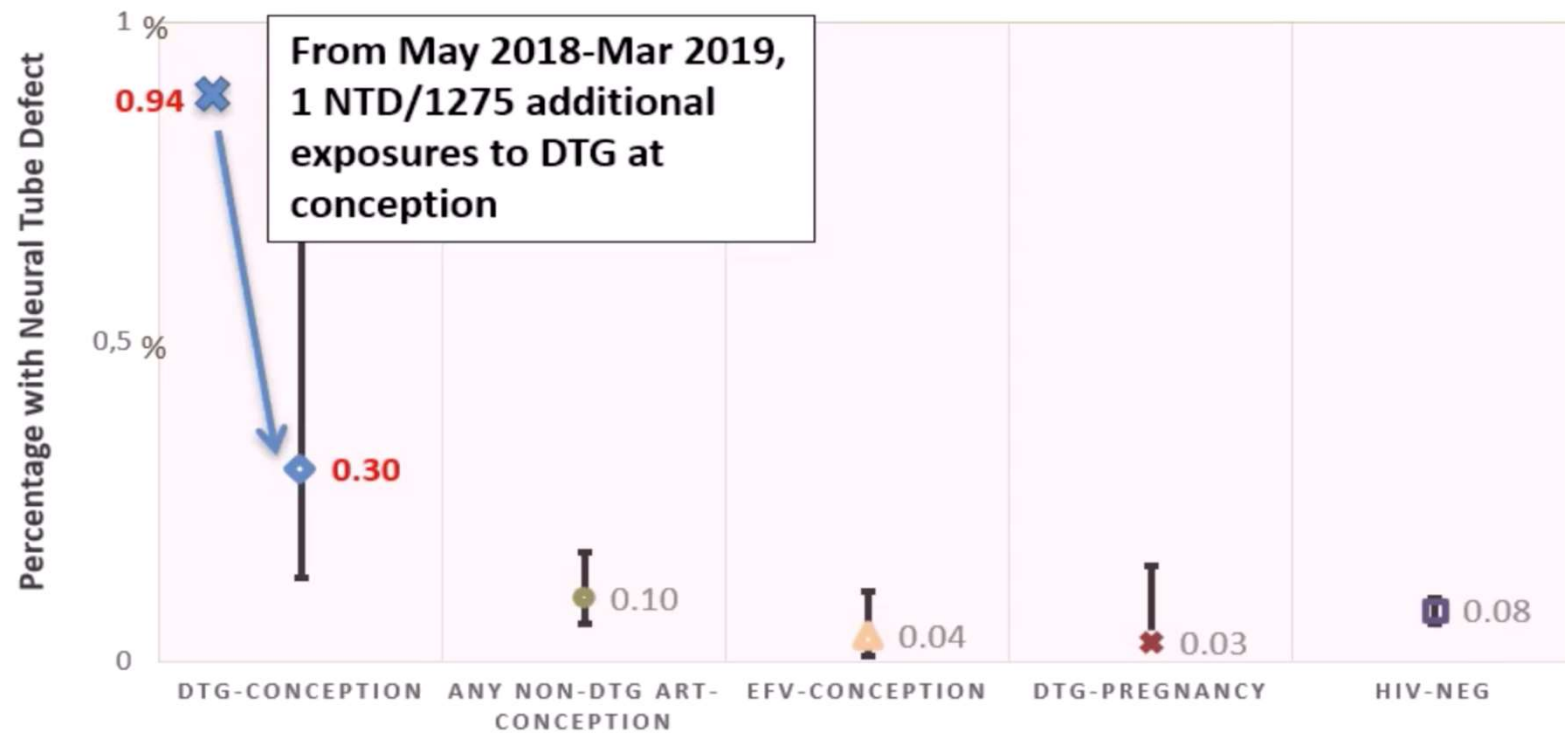
THE STAT STUDY: Results

Figure 2. Proportion of Participants With Plasma HIV-1 RNA <50 c/mL at Week 24 by BL (A) HIV-1 RNA^a and (B) CD4+ Cell Count (ITT-E Missing = Failure Analysis)



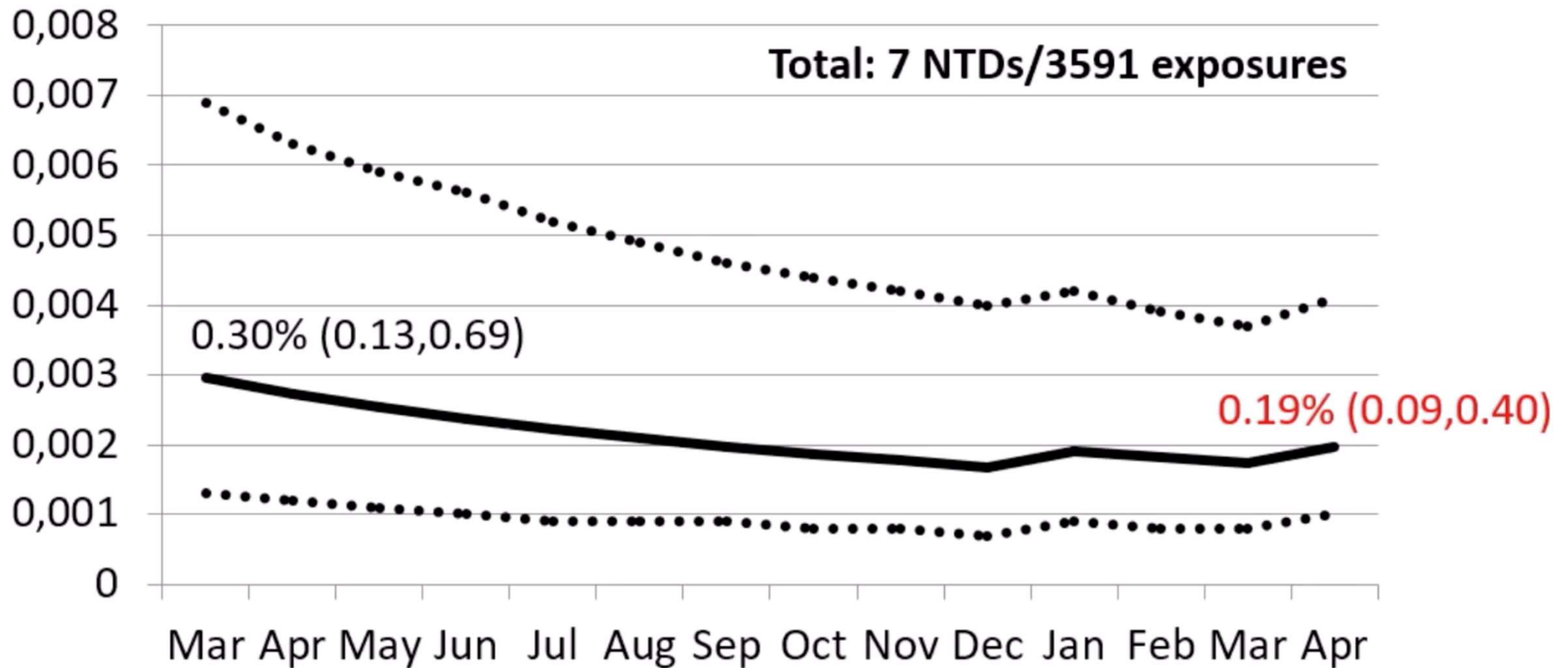
^a1 (<1%) participant had missing plasma HIV-1 RNA results at BL. ^bOf the 19 participants with BL viral load ≥500,000 c/mL, 13 (68%) were suppressed to <50 c/mL, 4 remain on study with viral load >50 c/mL (3 <200 c/mL), and 2 discontinued.

Tsepamo Results as of March 2019




NTDs/Exposures	5/1683	15/14792	3/7959	1/3840	70/89372
% with NTD (95% CI)	0.30% (0.13, 0.69)	0.10% (0.06, 0.17)	0.04% (0.01, 0.11)	0.03% (0.0, 0.15)	0.08% (0.06, 0.10)
Prevalence Difference (95% CI)	ref	0.20% (0.01, 0.59)	0.26% (0.07, 0.66)	0.27% (0.06, 0.67)	0.22% (0.05, 0.62)

NTD Prevalence (95% CI) with DTG at conception, Apr 1, 2019-April 30, 2020



2

Futuro: Nuevos Fármacos



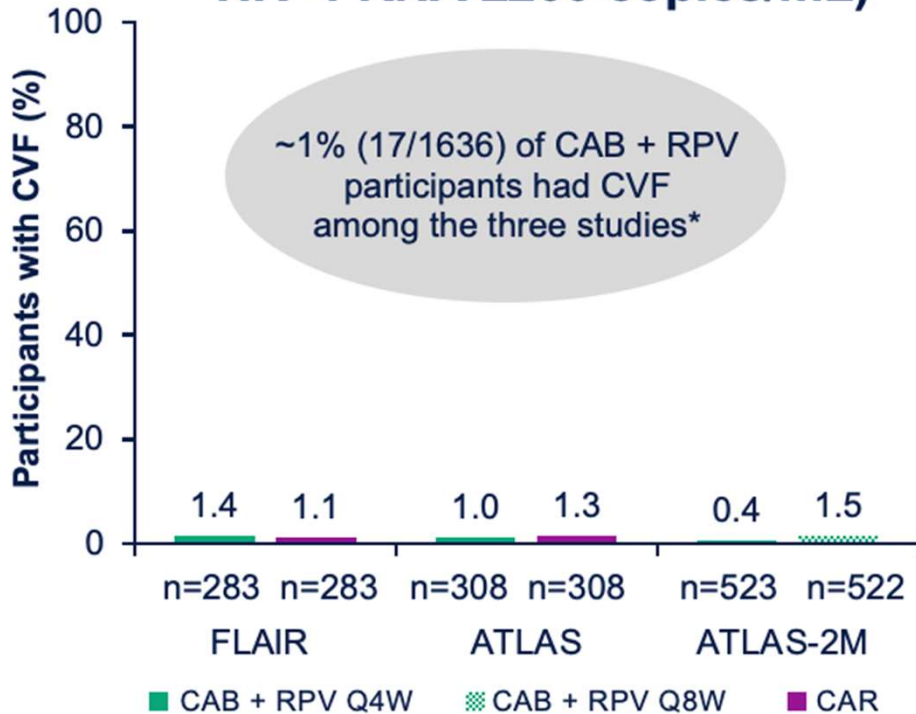
A COMBINATION OF VIRAL
AND PARTICIPANT FACTORS
INFLUENCES VIROLOGIC
OUTCOME TO LONG-ACTING
CABOTEGRAVIR + RILPIVIRINE:
MULTIVARIABLE AND BASELINE
FACTOR ANALYSES ACROSS
ATLAS, FLAIR AND ATLAS-2M
PHASE 3 STUDIES.

Margolis D, et al.

Glasgow 2020

Multivariable Analysis: Participant, Baseline Virus and PK Factors Explored in Relation to CVF Outcome Through Week 48

CVF (two consecutive HIV-1 RNA ≥ 200 copies/mL)



Factors explored in the MVA:

- CAB and RPV PK (i.e. initial trough concentrations at Week 8) and pre-existing resistance mutations,[†] adjusting for the following covariates:
 - Sex at birth
 - BMI
 - HIV-1 subtype
 - Q4W and Q8W regimen

*13 of 17 participants who met the CVF criterion were CAB + RPV naive at study entry and received at least one LA injection were included in the multivariable analysis; three participants with CVF were excluded as they rolled over from ATLAS. An additional participant in FLAIR was excluded because CVF occurred prior to receiving LA injection (withdrawn due to false-positive pregnancy test).

[†]Pre-existing INSTI, as well as L74I polymorphism, RPV and NNRTI RAMs (observed in plasma or peripheral blood mononuclear cells).

BMI, body mass index (kg/m²); CAB, cabotegravir; CAR, current antiretroviral regimen; CVF, confirmed virologic failure; LA, long-acting; MVA, multivariable analysis; NNRTI, non-nucleoside reverse transcriptase inhibitor; PK, pharmacokinetic; Q4W, every 4 weeks; Q8W, every 8 weeks; RAM, resistance-associated mutation; RPV, rilpivirine.

Multivariable Analysis: Four Factors Were Associated With an Increased Odds Ratio of CVF, Three Are Baseline Factors

Parameter	Final Model OR (95% CI), p-value*
RPV RAM(s) at baseline [†]	37.24 (8.44→99), p<0.001
Log ₂ of <i>post hoc</i> Week 8 RPV trough concentration	4.17 (1.59–11.11), p=0.004
Baseline HIV-1 subtype A6/A1	6.59 (1.82–25.26), p=0.005
BMI (kg/m ²) at baseline	1.13 (1.03–1.25), p=0.014
Pre-specified INSTI mutation (excluding L74I non-M mixture) at baseline [‡]	0.11 (0.01–0.83), p=0.029
Log ₂ of <i>post hoc</i> Week 8 CAB trough concentration	Not significant
Female at birth	Not significant
Q8W regimen	Not significant
L74I (non-M mixture) INSTI polymorphism at baseline	Not significant
NNRTI RAM(s) (excluding RPV RAMs) at baseline [‡]	Not significant

*Odds ratios (ORs), 95% penalised profile CIs and penalised likelihood ratio p-values are provided. Covariates with p<0.05 in the final backwards elimination model are presented. CAB and RPV PK parameters were log₂-transformed; therefore, the corresponding ORs are per halving of each variable.

[†]Identified per the IAS–USA 2019 list of mutations.¹

[‡]Identified per the IAS–USA list of mutations associated with resistance to bictegravir, CAB, dolutegravir, elvitegravir or raltegravir and observed mutations during *in vitro* passage of dolutegravir or seen in a previous dolutegravir study (NCT01328041) in INSTI-experienced subjects.

BMI, body mass index (kg/m²); CAB, cabotegravir; CI, confidence interval; CVF, confirmed virologic failure; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; OR, odds ratio; Q8W, every 8 weeks; RAM, resistance-associated mutation; RPV, rilpivirine.

1. Wensing AM, et al. Top Antivir Med. 2019;27(3):111–121.

Multivariable Analysis: A Combination of Baseline RPV RAMs*, Subtype A6/A1 or BMI ≥ 30 Modestly Increased the Risk of Virologic Failure

Factor	CVF, n (%)	HIV-1 RNA <50 copies/mL, n (%)
No baseline factors	3/732 (0.41)	694/732 (95)
Any one baseline factor	1/272 (0.37)	261/272 (96)
Two or more baseline factors	9/35 (26)	25/35 (71)
TOTAL [95% CI]	13/1039 (1.3) [0.67–2.13]	980/1039 (94) [92.74–95.65]

- Sensitivity and specificity of at least two baseline factors is optimal

	PPV	NPV	Sensitivity	Specificity
Two or more factors	26%	99.6%	69%	97.5%
Any one factor	<1%	98%	8%	74%

*Identified per the IAS–USA 2019 list of mutations.¹

BMI, body mass index (kg/m²); CAB, cabotegravir; CI, confidence interval; CVF, confirmed virologic failure; LA, long-acting; NPV, negative predictive values; PPV, positive predictive values; RAM, resistance-associated mutation; RPV, rilpivirine.

1. Wensing AM, et al. *Top Antivir Med.* 2019;27(3):111–121.

JRA

**HPTN 083:
LONG-ACTING INJECTABLE
CABOTEGRAVIR
VERSUS DAILY, ORAL F/TDF
FOR PREP.**

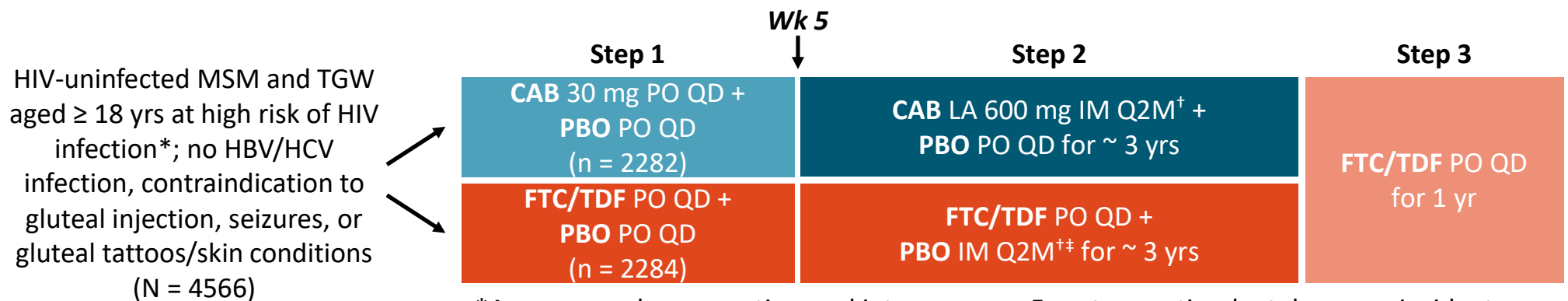
Landovitz R, et al.

AIDS 2020



HPTN 083: Study Design

- International, randomized, double-blind phase IIb/III study
 - At interim analysis on May 14, 2020, with 25% of endpoints accrued, DSMB recommended termination of blinded study due to crossing of prespecified O'Brien-Fleming stopping bound
 - Planned N = 5000, with ≥ 50% aged < 30 yrs; ≥ 10% TGW; ≥ 50% black participants in US



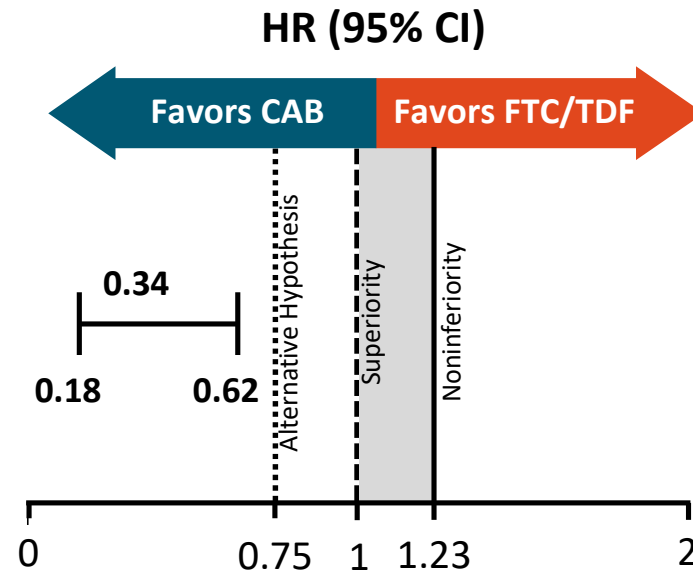
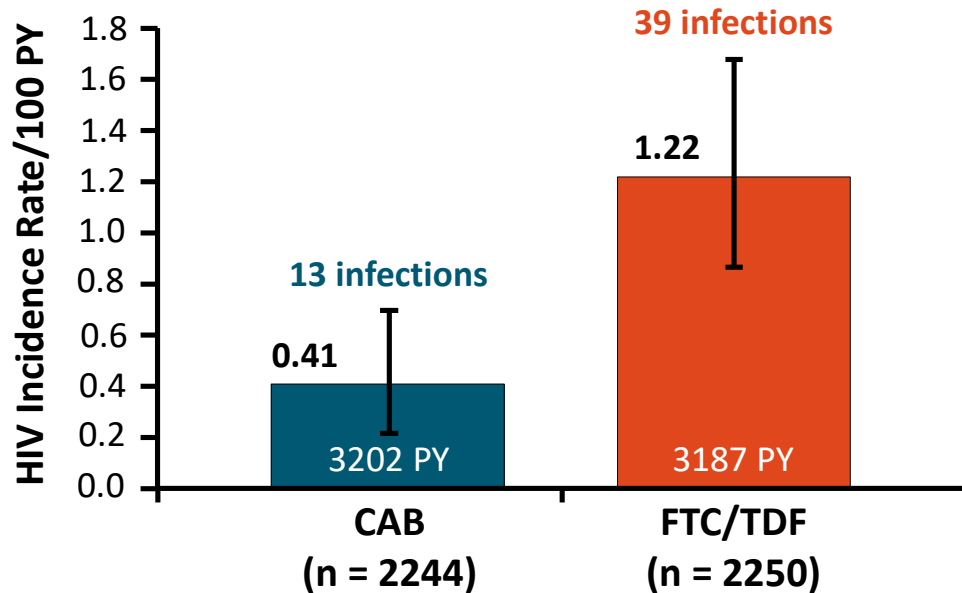
*Any noncondom receptive anal intercourse, > 5 partners, stimulant drug use, incident rectal or urethral STI or incident syphilis in past 6 mos; or SexPro Score ≤ 16 (US only).

[†]First 2 doses given in Wks 5 and 9 then every 2 mos thereafter.

[‡]PBO for CAB injection was a 20% intralipid solution.

HPTN 083: HIV Incidence

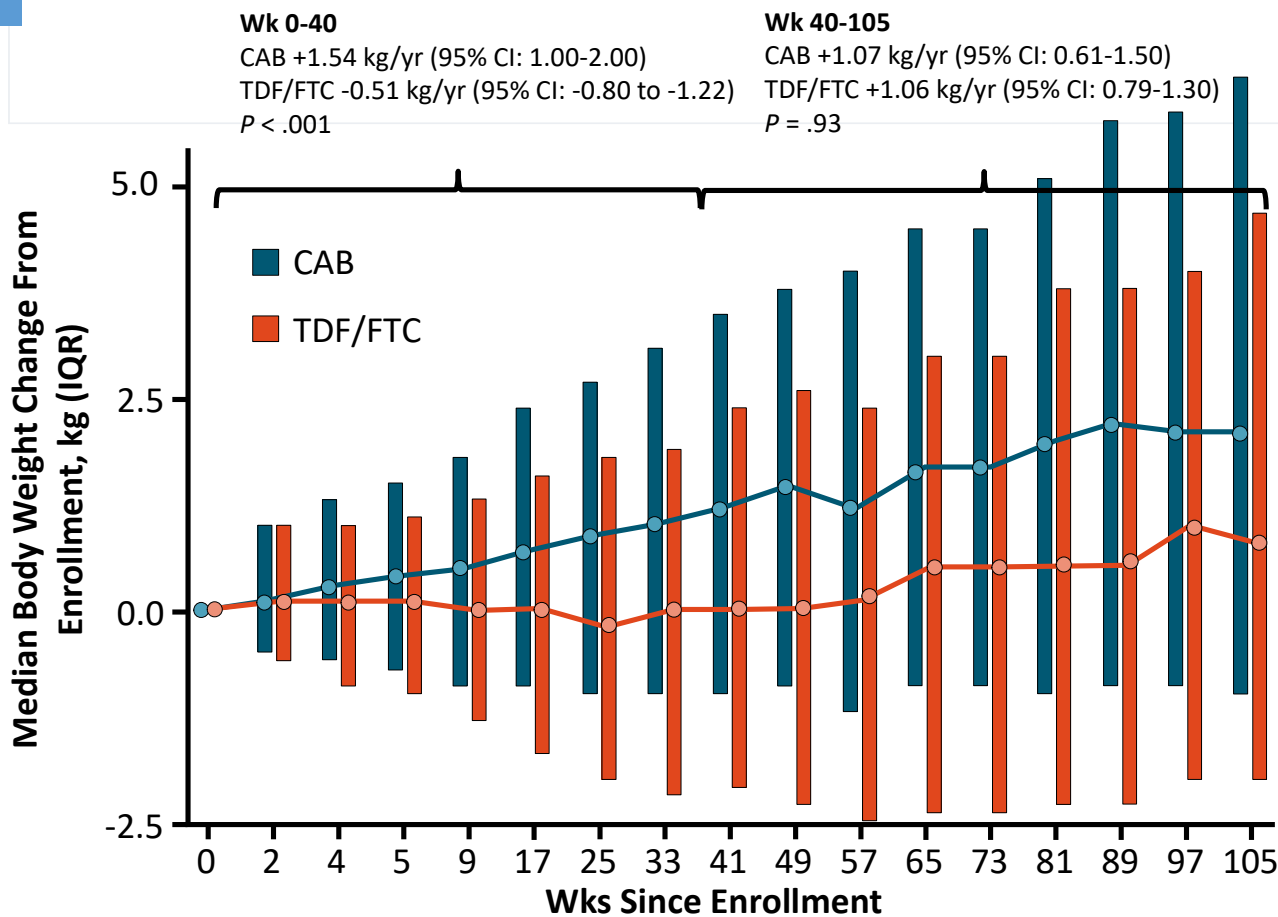
- Pooled incidence: 0.81 per 100 PY (95% CI: 0.61-1.07)
 - 52 HIV infections in 6389 PYFU
- LA CAB met alternative hypothesis (HR: 0.75) and demonstrated statistically significant superiority vs FTC/TDF



HPTN 083: Timing of Incident HIV Infections

- **CAB arm: n = 13***
 - Before receiving any study treatment: n = 2
 - During Step 1 (oral CAB lead-in): n = 3
 - During Step 2 (IM CAB): n = 5
 - Following extended on-study hiatus from CAB: n = 5
- **FTC/TDF arm: n = 39[†]**
 - Before receiving any study treatment: n = 3
 - During Step 2 (blinded oral FTC/TDF): n = 39[‡]

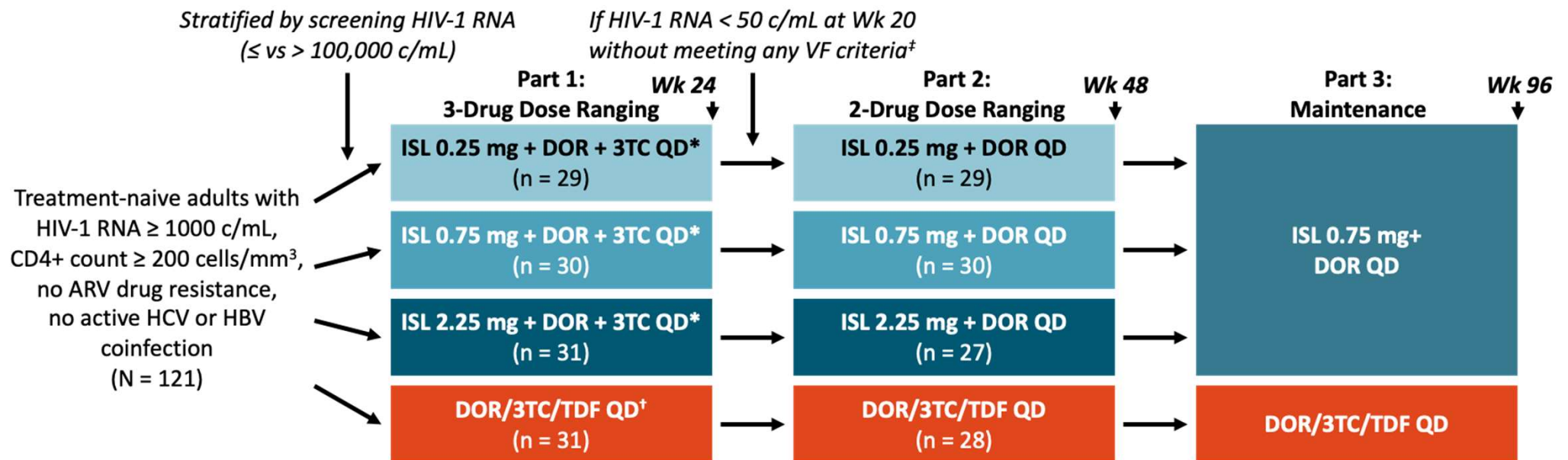
HPTN 083: Change From Baseline in Weight



- Overall, significantly greater median weight increase from BL with CAB vs FTC/TDF (P < .001)
 - CAB: +1.30 kg/yr (95% CI: 0.99-1.60)
 - FTC/TDF: +0.31 kg/yr (95% CI: -0.12 to -0.49)

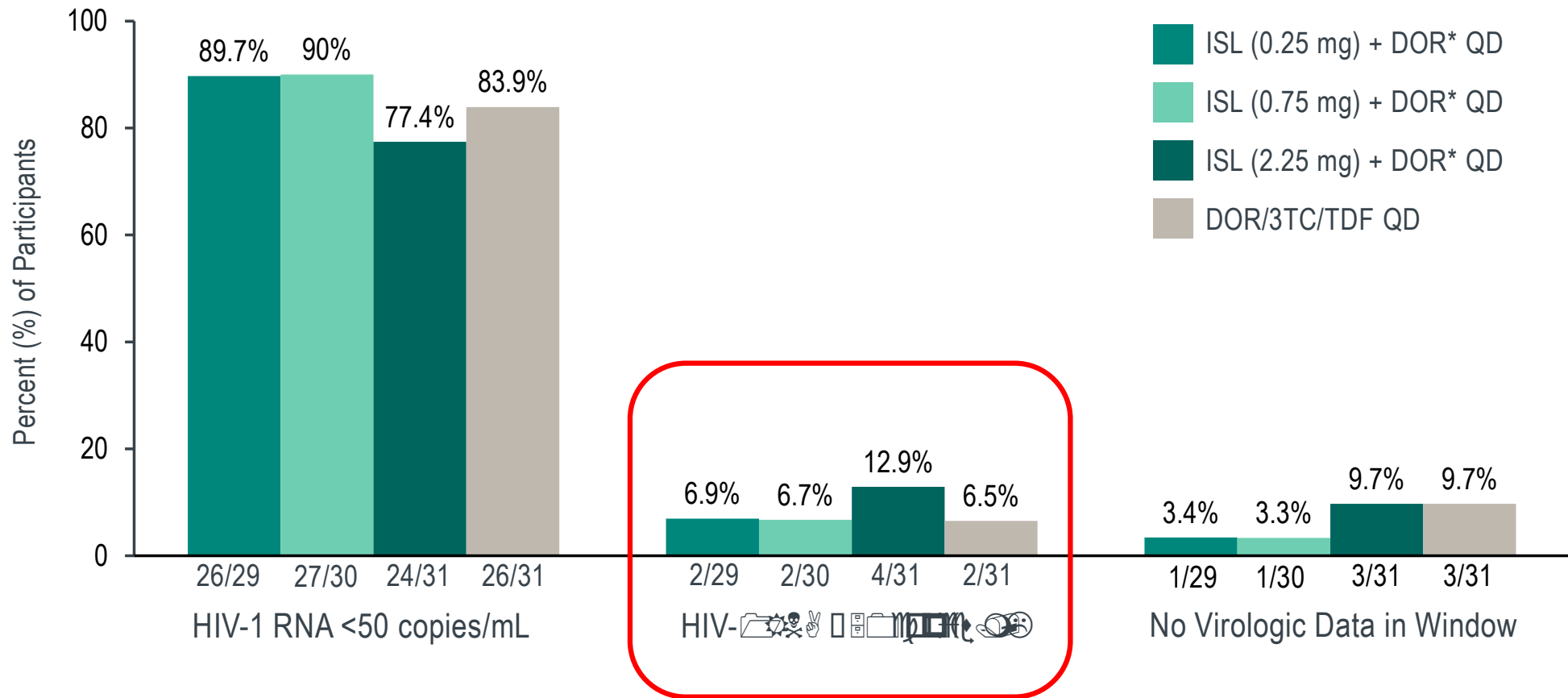
Background

- **Islatravir** (ISL) is the first nucleoside reverse transcriptase translocation inhibitor (NRTTI)
- **P011**: International, randomized, double-blind phase IIb trial



Current Analysis Objective: To characterize participants who discontinued with protocol defined virologic failure.

Virologic Outcomes Through Week 48 (FDA Snapshot Approach)

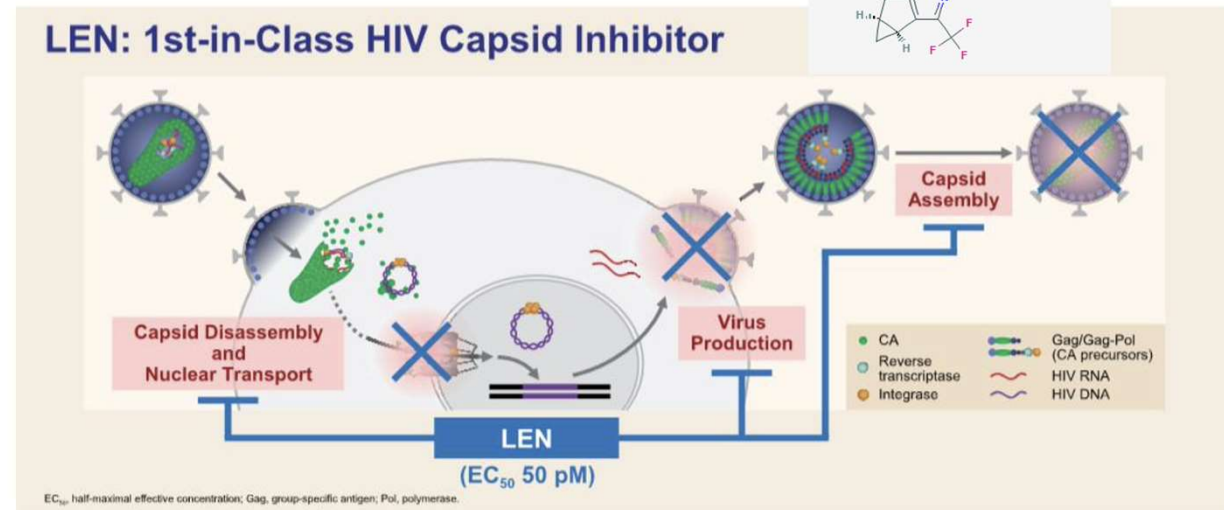


*Participants initially received ISL+DOR+3TC and switched to ISL+ DOR during the week 24-48 period of the study.

Lenacapavir (GS-6207) PK Study

Lenacapavir

- Novel, 1st in-class selective HIV-1 capsid inhibitor
- EC₅₀: 50 pM
- In clinical development as component of long-acting ART^[1]
- Potent anti-HIV activity observed following single-dose SC administration^[2]
- Oral and SC formulations in development^[3]

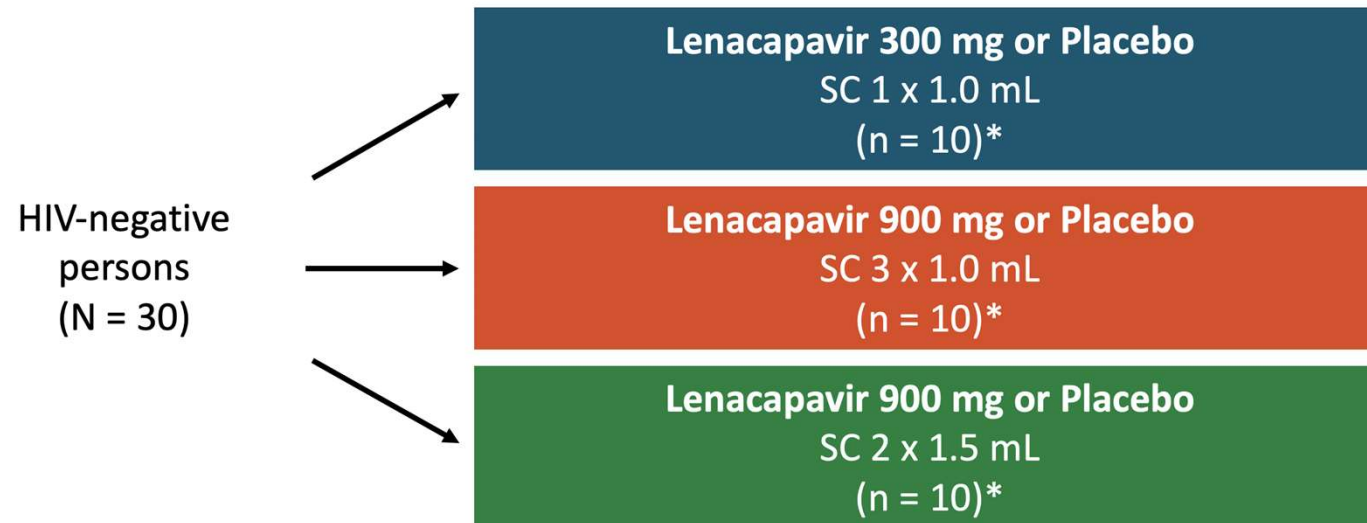


◆ Inhibition of multiple CA-dependent functions essential for viral replication

Current study evaluated tolerability, safety, PK of lenacapavir SC following single-dose administration at escalating doses in HIV-negative volunteers^[4]

Lenacapavir PK Study: Study Design

- Randomized, blinded, placebo-controlled, dose escalation phase I study

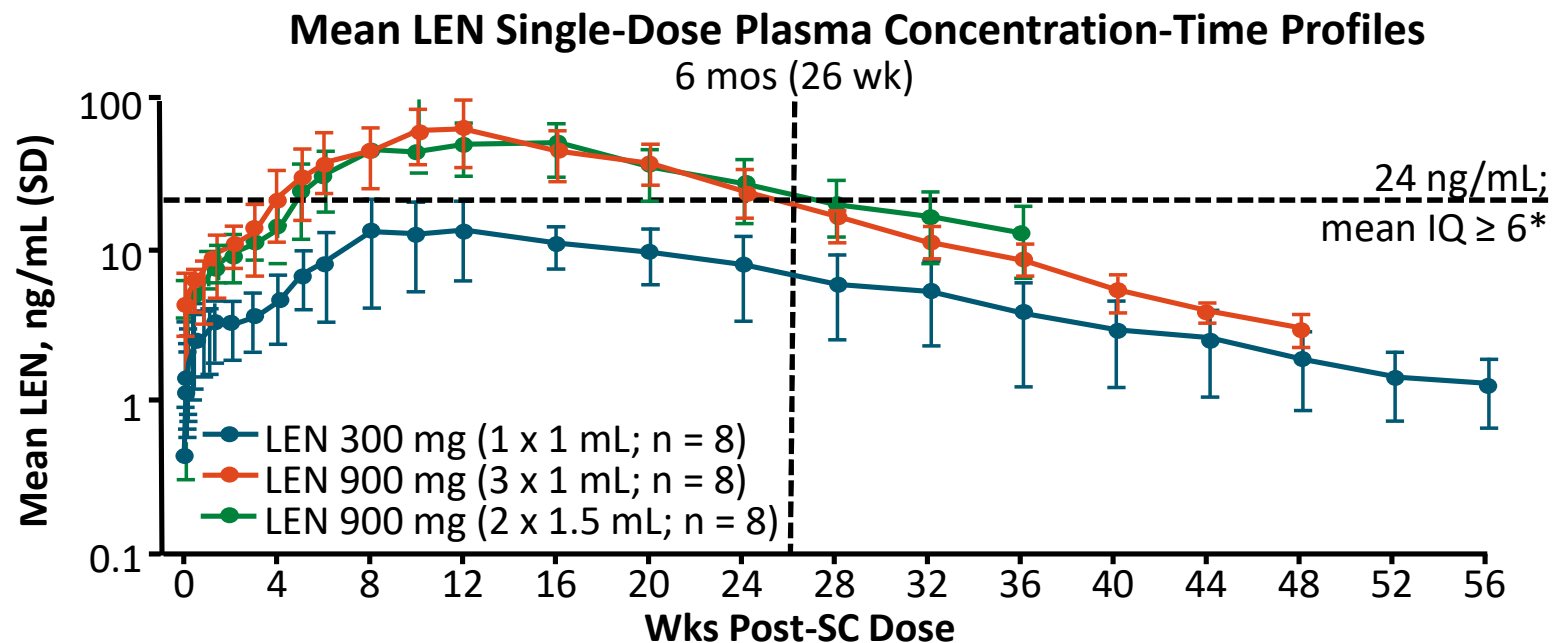


- Endpoints: safety, tolerability, PK
 - PK measured through Day 449

*Participants randomized 4:1 lenacapavir vs placebo. Treatment administered as a single dose.

Lenacapavir PK Study: PK Profile

- Per antiviral activity, mean lenacapavir target plasma concentration is 24 ng/mL, corresponding to mean inhibitory quotient ≥ 6 (range: 6.2-20.3)



*Protein-adjusted EC_{50} : macrophages, 1.16 ng/mL; CD4+ cells, 2.32 ng/mL, MT-4 cells, 3.87 ng/mL.

Conclusiones

- Se incorporan las pautas de dos fármacos como régimen preferente de inicio en todas las guías de tratamiento antirretroviral
- Quedan algunos aspectos aún controvertidos en cuanto a la unanimidad e interpretación por los expertos de las limitaciones de las pautas de dos fármacos
- La incorporación de cabotegravir LA puede ser un avance importante en la PrEP
- El futuro del TAR parece escribirse en clave de fármacos de administración prolongada, con reducción en el número de dosis