Top 10 2024 en infección VIH

XIX CURSO EN AVANCES EN INFECCION VIH Y HEPATITIS VIRALES 2024

Vigo, 30 y 31 de mayo 2025

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CIBERINFEC. IMIBIC

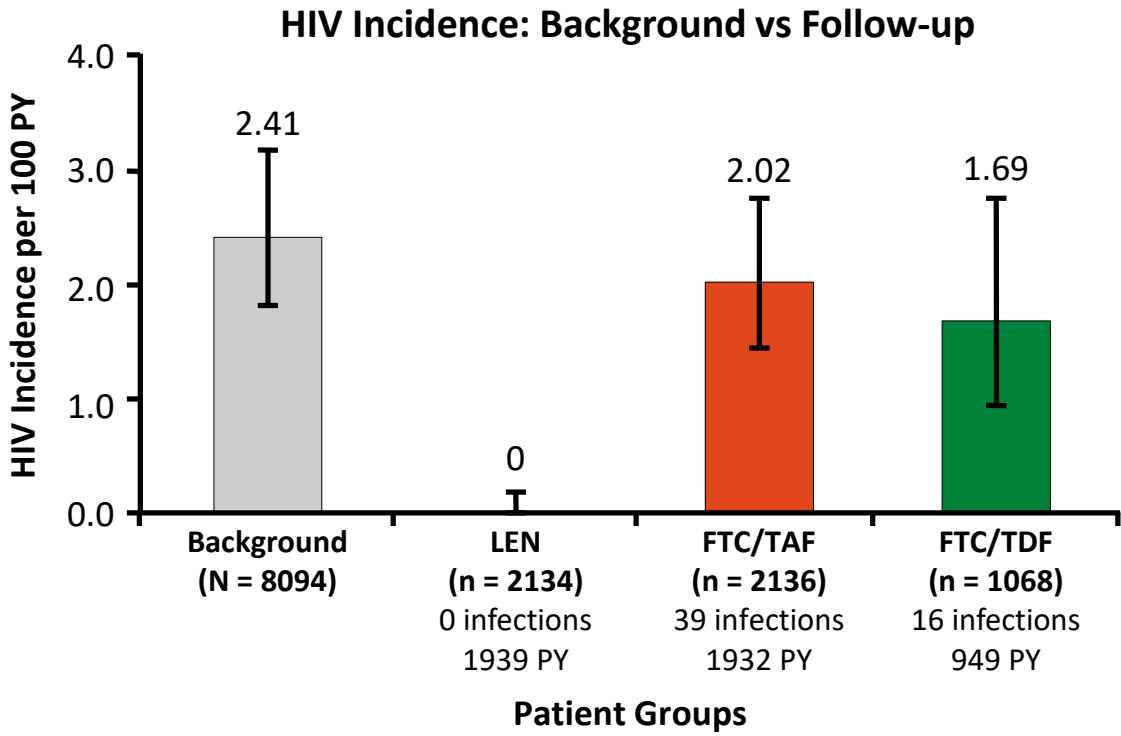
INDICE

TOP 1. PURPOSE 1. PrEp LEN vs TAF/FTC ó TDF/FTC en mujeres CG

Randomized, double-blind phase III trial

LEN* SC (927 mg) SC Q26W
+ FTC/TAF or FTC/TDF placebo oral QD
(n = 2134)

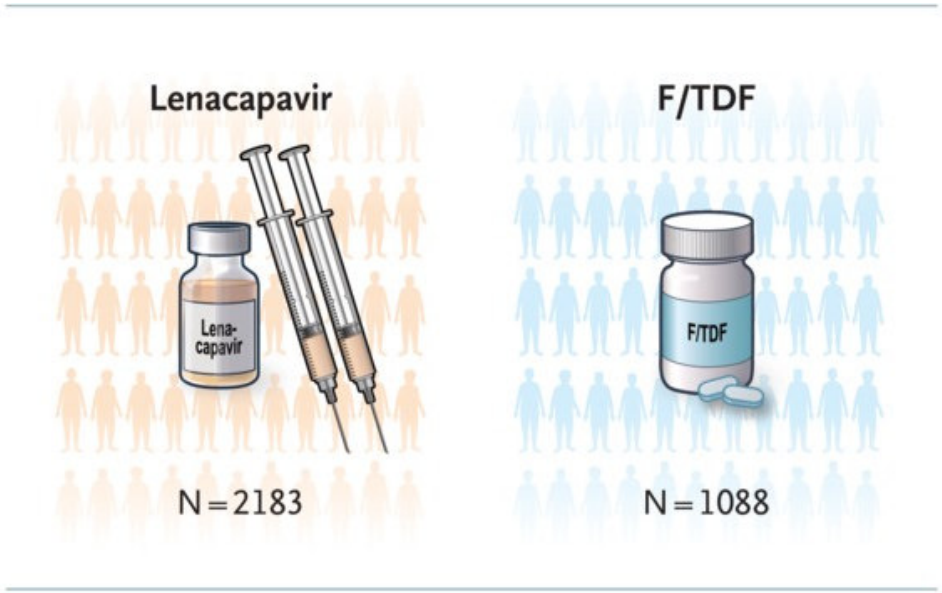
FTC/TAF (200 mg/25 mg) oral QD
+ **LEN placebo** SC Q26W
(n = 2136)

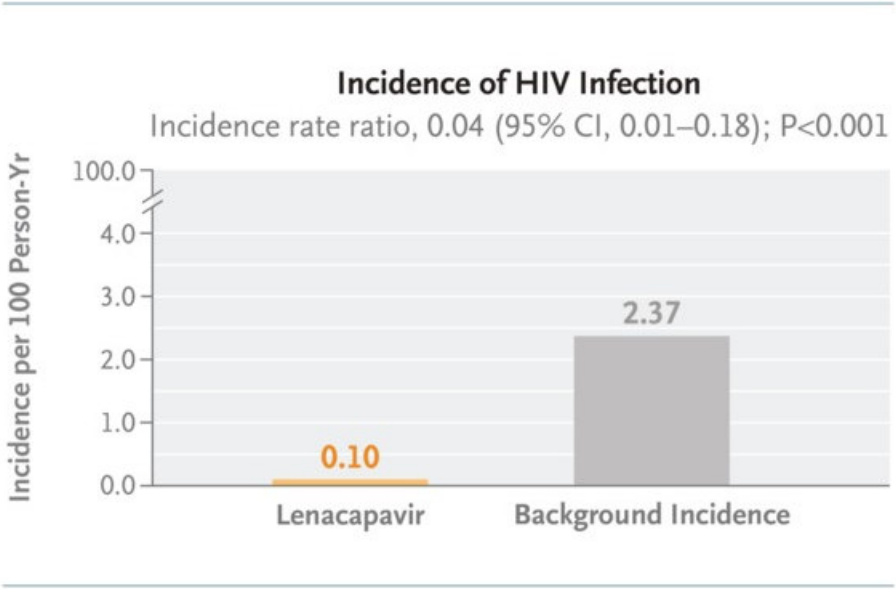


Bekker. NEJM. 2024.

TOP 2. PURPOSE 2. PrEp LEN vs TAF/FTC ó TDF/FTC Hombres > 16 años y personas de diversos generos

Randomized, double-blind phase III trial





Kelley CF et al. N Engl J Med2025;392:1261-1276

Días de tratamiento que exige un régimen PrEp

Régimen	Días de Tratamiento/año
TDF/FTC	365
CAB/RIL	6
LEN	**2**

LEN facilita mucho más la adherencia la posibilidad de TDO

A version of this story appeared in Science, Vol 386, Issue 6727.

RELATED ARTICLE

The biggest science breakthroughs in 2024

BY MEAGAN CANTWELL • MULTIMEDIA • **29 JAN 2025**

2024 BREAKTHROUGH OF THE YEAR

RUNNERS-UP

BREAKDOWNS

VIDEO

Despite decades of progress, HIV still infects more than 1 million people a year, and a vaccine remains stubbornly out of reach. But this year the world got a glimpse of what might be the next best thing: an injectable drug that protects people for 6 months with each shot.

A large efficacy trial in African adolescent girls and young women reported in June that these shots reduced HIV infections to zero—an astonishing 100% efficacy. Any doubts about the finding disappeared 3 months later when a similar trial, conducted across four continents, reported 99.9% efficacy in gender diverse people who have sex with men.

The NEW ENGLAND JOURNAL of MEDICINE

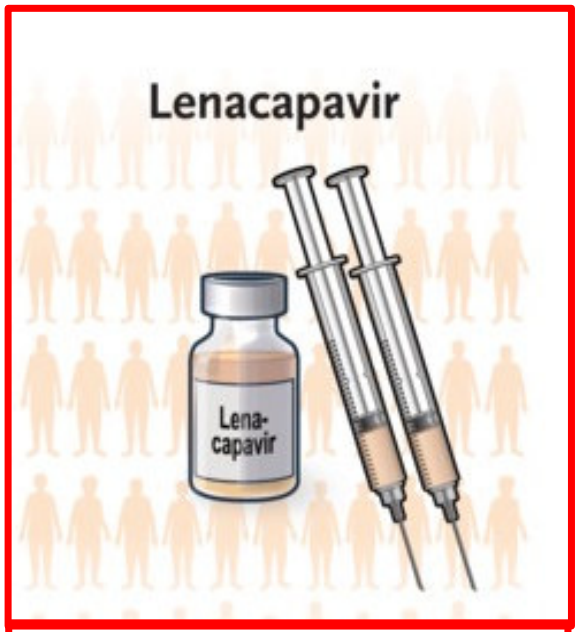
PERSPECTIVE

An HIV Vaccine in the Era of Twice-Yearly Lenacapavir for PrEP — Essential or Irrelevant?

Authors: Lauren P. Jatt, M.D., Nyaradzo M. Mgodi, M.B., Ch.B., M.Med., Susan P. Buchbinder, M.D., Glenda E. Gray, M.B., Ch.B., and James G. Kublin, M.D., M.P.H. Author Info & Affiliations

Published April 19, 2025 | N Engl J Med 2025;392:1561-1563 | DOI: 10.1056/NEJMp2415893 | VOL. 392 NO. 16

TOP 3 Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study



Dosis de 5000 mg (2 iny de 5 mL) IM al año

PK y Seguridad de 2 Formulaciones

- F1 with 5% w/w etanol. N=20
- F2 with 10% w/w etanol. N=20

- La concentración plasmática con ambas formulaciones fue superior a la observada con la administración semestral
- Lo que sugiere que este esquema podría proporcionar una protección duradera con una sola dosis al año.

Plan para investigar como opción de PrEP

Jogiraju V et al. Lancet. 2025

Doxycycline pre-exposure prophylaxis (doxyPrEP) for STI prevention in MSM and trans women on HIV PrEP: The DuDHS Study

Grennan et al., 2024 | *Clinical Infectious Diseases*

TOP 4

IDSA Infectious Diseases Society of America

BACKGROUND: This study examines the feasibility of doxyPrEP in men who have sex with men (MSM) and transgender women on tenofovir/emtricitabine (TDF/FTC) for HIV PrEP.

PARTICIPANTS: 52 HIV-negative MSM and transgender women with a prior history of syphilis.

METHODS

Randomized trial of feasibility of immediate vs. deferred daily doxyPrEP in MSM and trans women receiving TDF/FTC for HIV PrEP, recruited from a single-site in Vancouver, Canada. (Feasibility = self-reported adherence + tolerability)

- ✓ Sexually-active MSM/trans woman
- ✓ Age 19 years or older
- ✓ HIV-negative with prior syphilis
- ✗ Recent (within 30d) HIV PrEP/PEP
- ✗ Chronic Hepatitis B infection
- ✗ Contraindications to doxy, TDF/FTC

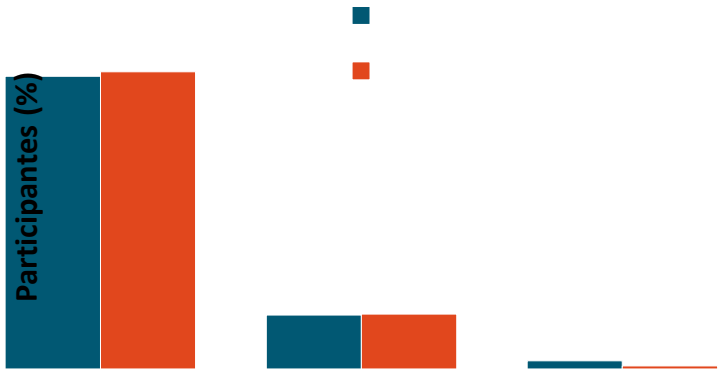
	Immediate arm (n=26): TDF/FTC and doxyPrEP x 48 weeks	Statistical Significance?	Deferred arm (n=26): TDF/FTC x 48 weeks; doxyPrEP start at week 24
Self-reported doxyPrEP adherence at week 48	70.8% 95% CI [52.6-89.0]	No	61.9% 95% CI [41.1-82.7]
Moderate or severe doxyPrEP-related adverse event: n (%)	1 (3%); week 12 nausea (moderate)	No	1 (4%); week 48 nausea (moderate)
Cumulative STI incidence (per 100 person-years) to week 24	31.4 95% CI [8.6-80.3]	Yes* Adj OR: 0.26 95%CI: 0.1-0.75	149.0 95% CI [89.7-232.7]
Staphylococcus aureus resistance to doxycycline (week 48)	4/7 isolates (57.1%)	No	1/2 isolates (50.0%)

CONCLUSION: In a pilot study of 52 MSM and trans women on HIV PrEP, doxyPrEP was feasible, and yielded significant reductions of 74% in overall STI.

Clinical Infectious Diseases https://doi.org/10.1093/cid/ciaf043

TOP 5. Uso en vida real de Doxi-PEP en personas en PrEP (San Francisco)

- Estudio observacional de personas que recibieron PrEP (Magnet Clinic de San Francisco)
  - **Cohorte 1: DoxiPEP**
  - **Cohorte 2: sin DoxiPEP**
  - **Evaluación** 5 meses antes y 5 meses después del inicio del estudio.



Incidencia DE ITS*	DoxyPEP (n = 2524)		Sin DoxyPEP (n = 2068)	
	IP (IC 95 %)	*Valor* P	IP (IC 95 %)	*Valor* P
Cualquier ITS	0,34 (0,28-0,42)	<0,001	1,33 (0,88-2,00)	0,178
Gonorrea	0,56 (0,44-0,71)	<0,001	1,53 (0,92-2,55)	0,099
Clamidia	0,19 (0,13-0,29)	<0,001	1,04 (0,54-2,00)	0,895
Sífilis	0,11 (0,02-0,54)	0,006	1,91 (0,11-32,19)	0,654

El uso de DoxiPEP redujo significativamente la incidencia de ITS.

Scott. CROI 2025. Resumen 163.

TOP 6. A Meta-Analysis of Levofloxacin for Contacts of MDR-TB. Duong T et al. NEJM Evid 2025;4(1) December 18, 2024

Diseño: Análisis combinado de 2 EC F3: eficacia de levofloxacino en expuestos a TB-MDR

- VQUIN: Adultos de Vietnam. No significación estadística*
- TB-CHAMP: niños de Sudáfrica. o significación estadística**

Brazos: levofloxacino o placebo durante 6 meses. Aletaorización 1:1

Objetivo primario: presencia incidental de TB antes de las 54 semanas de seguimiento.

Análisis:

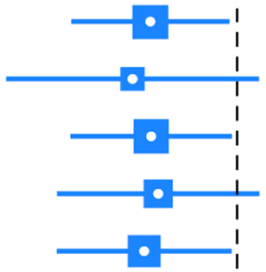
- Metaanálisis Standard de los datos individuales de los participantes en el estudio
- Modelo bayesiano para reanálisis de los datos en cada estudio

* N Engl J Med. 2024; 391:2304-2314. ** N Engl J Med. 2024; 391: 2315-2326

Table 2. Combined Safety Analyses of the VQUIN and TB-CHAMP Trials (Based on Standard Individual Patient Data Meta-Analysis Methods).*

Safety Analysis by Trial	Levofloxacin	Placebo	Estimated Risk Ratio (95% CI†)	P Value for Overall Treatment Effect
Participants who took at least one trial drug dose‡				
VQUIN	960	962		
TB-CHAMP	452	469		
Overall	1412	1431		
Participants with one or more safety end points				
Grade 3 or above adverse event§				
VQUIN	29 (3.0%)	19 (2.0%)	1.55 (0.87 to 2.76)	
TB-CHAMP	14 (3.1%)	23 (4.9%)	0.67 (0.34 to 1.31)	
Overall	43	42	1.07 (0.70 to 1.65)	0.75
Grade 3 or above adverse event at least possibly related to drug§				
VQUIN	10 (1.0%)	2 (0.2%)	5.26 (1.16 to 23.95)	
TB-CHAMP	4 (0.9%)	8 (1.7%)	0.53 (0.16 to 1.70)	
Overall	14	10	1.46 (0.65 to 3.26)	0.36
Any grade 3 or above serious adverse event§				
VQUIN	20 (2.1%)	12 (1.3%)	1.72 (0.85 to 3.49)	
TB-CHAMP	8 (1.8%)	7 (1.5%)	1.23 (0.45 to 3.35)	
Overall	28	19	1.54 (0.87 to 2.74)	0.14
Discontinuation of treatment due to adverse events of any grade				
VQUIN	71 (7.4%)	11 (1.1%)	6.43 (3.42 to 12.09)	
TB-CHAMP	6 (1.3%)	1 (0.2%)	5.25 (0.64 to 43.13)	
Overall	77	12	6.32 (3.43 to 11.63)	<0.001
Musculoskeletal adverse event of any grade				
VQUIN	220 (22.9%)	32 (3.3%)	7.02 (4.67 to 10.56)	
TB-CHAMP	6 (1.3%)	4 (0.9%)	1.35 (0.36 to 5.06)	
Overall	226	36	6.36 (4.30 to 9.42)	<0.001

Analyses*	Levofloxacin n with end point /N	Placebo n with end point /N	Relative Difference in Cumulative Incidence (95% CI/CrI)§
Microbiogically confirmed or clinically defined TB by 54 weeks (primary end point)			
Overall: IPD meta-analysis	8/1474	21/1483	0.41 (0.18 to 0.92), P=0.03
VQUIN: standard analysis	3/1023	9/1018	0.34 (0.09 to 1.25)
VQUIN: Bayesian analysis†	3/1021	9/1015	0.41 (0.18 to 0.95)
TB-CHAMP: standard analysis	5/451	12/465	0.44 (0.16 to 1.26)
TB-CHAMP: Bayesian analysis†	5/448	12/464	0.38 (0.16 to 0.95)



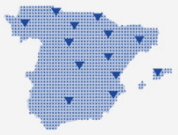
Conclusión: En el metaanálisis, levofloxacino se asoció con una reducción relativa del 60% en la incidencia de TB en adultos y niños del entorno familiar de los contactos con TB-MDR, pero con un riesgo aumentado de efectos adversos musculoesqueléticos.

Real-world effectiveness and safety of BIC/FTC/TAF in comparison with other regimens in people with HIV starting therapy with AIDS-defining conditions. Results from the CORIS Cohort: The ACTUAS II Study.

PEREZ VALERO I et al, 2025 | *Clinical Infectious Diseases*

ACTUAS II — A CoRIS RESEARCH STUDY

Recruitment period: January 2019 ⟷ November 2021



- The study was conducted at **48 Spanish HIV centers.**

- HIV-infected adults with **AIDS-defining conditions.**
- Initiated first-line ART (**BIC/FTC/TAF** or other regimens).
- **Excluded**: Clinical trial participants.

Week 24	VIRAL SUPRESSION (HIV RNA>50 cop/mL)	IMMUNOLOGICAL RECOVERY CD4 count >200 cells/mm3	ART DISCONTINUATION
BIC/FTC/TAF N=90	75.6%	47.7%	4.4%
Significance	**p=0.023**	**p=0.087**	**p<0.001**
Other regimens N=94	56.5%	61.9%	20.2%

Conclusion: In this prospective study, BIC/FTC/TAF demonstrated effectiveness and good tolerability as a first-line ART option for people with HIV and AIDS-defining conditions. Compared to other initial regimens, it was associated with a higher proportion of participants achieving viral suppression within the first 24 weeks and a lower rate of ART discontinuation.

Clinical Infectious Diseases Reference pending – CID-124231 IDSA Infectious Diseases Society of America hivma hiv medicine association

TOP 7. Estudio Dolce

- Objetivo primario: Evaluar la eficacia de DTG/3TC en naive con T4 <200
- Endpoint primario: Proporción de sujetos con ARN-VIH < 50 cop/mL a 48w

✓ **Phase IV, exploratory, open-label , multicenter study including naïve PLWHIV in 11 sites in Argentina and Brazil**

ARV- naïve subjects,
≥18 years old
CD4 ≤ 200 cells/mm3.
HIV-1 RNA >1,000 copies/mL, no upper limit
HB(s)Ag negative
(N=229)

Participants were randomly assigned in a 2:1 ratio

Dual Therapy
DTG + 3TC (STR) QD,
(n=152)

Triple Therapy:
DTG QD + TDF/XTC, QD, FDC
(n=77)

Wk 48
primary endpoint

- **Randomization was stratified by country and by plasma HIV-1 RNA at screening (> or ≤ 100.000 copies/mL).**
- **Treatment period: 48 weeks, followed by a 4 week period to document late adverse events.**

Demographics

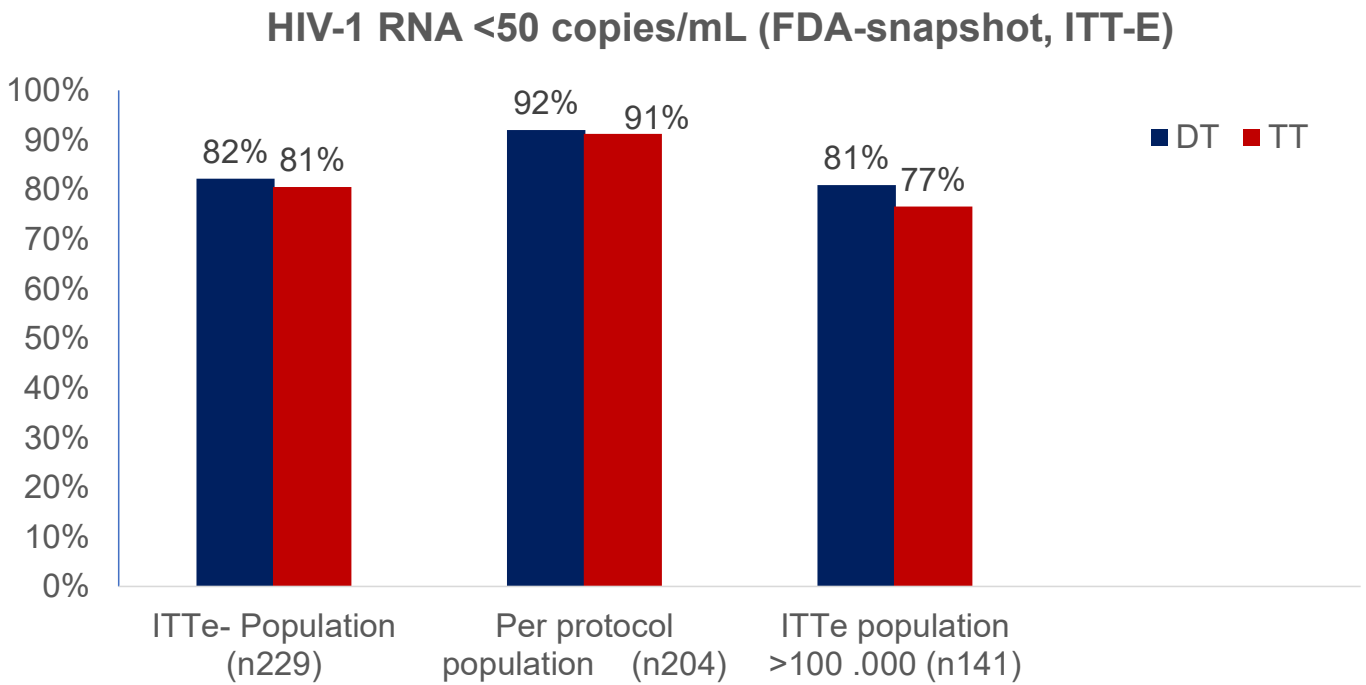
	Total n = 230	Triple therapy (TT) n = 77	Dual therapy (DT) n = 153
Sex at birth [n (%)]			
Female	56 (24.3%)	21 (27.3%)	35 (22.9%)
Male	174 (75.7%)	56 (72.7%)	118 (77.1%)
Age [Median (IQR)]	35 (28, 47)	34 (28, 47)	36 (29, 48)
Race [n (%)]			
Black	35 (15.2%)	9 (11.7%)	26 (17.0%)
Native	8 (3.5%)	0 (0.0%)	8 (5.2%)
Other (Hispanic-Latino/Mixed)	98 (42.6%)	31 (40.3%)	67 (43.8%)
White	89 (38.7%)	37 (48.1%)	52 (34.0%)
Body mass index [Median (IQR)]	**23 (20.0, 25)**	**23 (20.1, 25)**	**22 (19.9, 24)**
Sexual behaviors [n (%)]			
Heterosexual contact	111 (48.3%)	41 (53.2%)	70 (45.8%)
MSM contact	104 (45.2%)	29 (37.7%)	75 (49.0%)
Other	6 (2.6%)	2 (2.6%)	4 (2.6%)
Unknown	9 (3.9%)	5 (6.5%)	4 (2.6%)

Baseline characteristics

	Total n = 230	Triple therapy (TT) n = 77	Dual therapy (DT) n = 153
CD4 count			
CD4 cell count, cells/mL: (median-IQR)	116 (53.3- 188)	128 (58.5 - 200)	109 (48.8 - 177)
CD4% [Median (IQR)]	8 (4, 13)	10 (4.1, 13)	8 (4, 12)
CD4 cells count < = 100 cells/mL	98 (43.4%)	29 (39.2%)	69 (45.4%)
HIV RNA			
HIV-1 viral load (copies/mL) [Median (IQR)]	151,000 (49,027.5, 446,947)	137,084 (43,901 - 419,628)	180,000 (57,309 - 468,691)
HIV RNA, log 10,(median-IQR)	5 (4.7-6)	5 (4.6- 6)	5 (4.8- 6)
HIV RNA, >100,000 c/mL,(n, %)	141 (61.3%)	47 (61.0%)	94 (61.4%)
HIV RNA, =>500,000 c/mL,(n, %)	53 (23.0%)	18 (23.4%)	35 (22.9%)
HIV RNA = > 1,000,000 copies/mL(n, %)	23 (10.0%)	7 (9.1%)	16 (10.5%)
Viral Subtype			
• Subtype B	143 (63.0%)	51 (68.0%)	92 (60.5%)

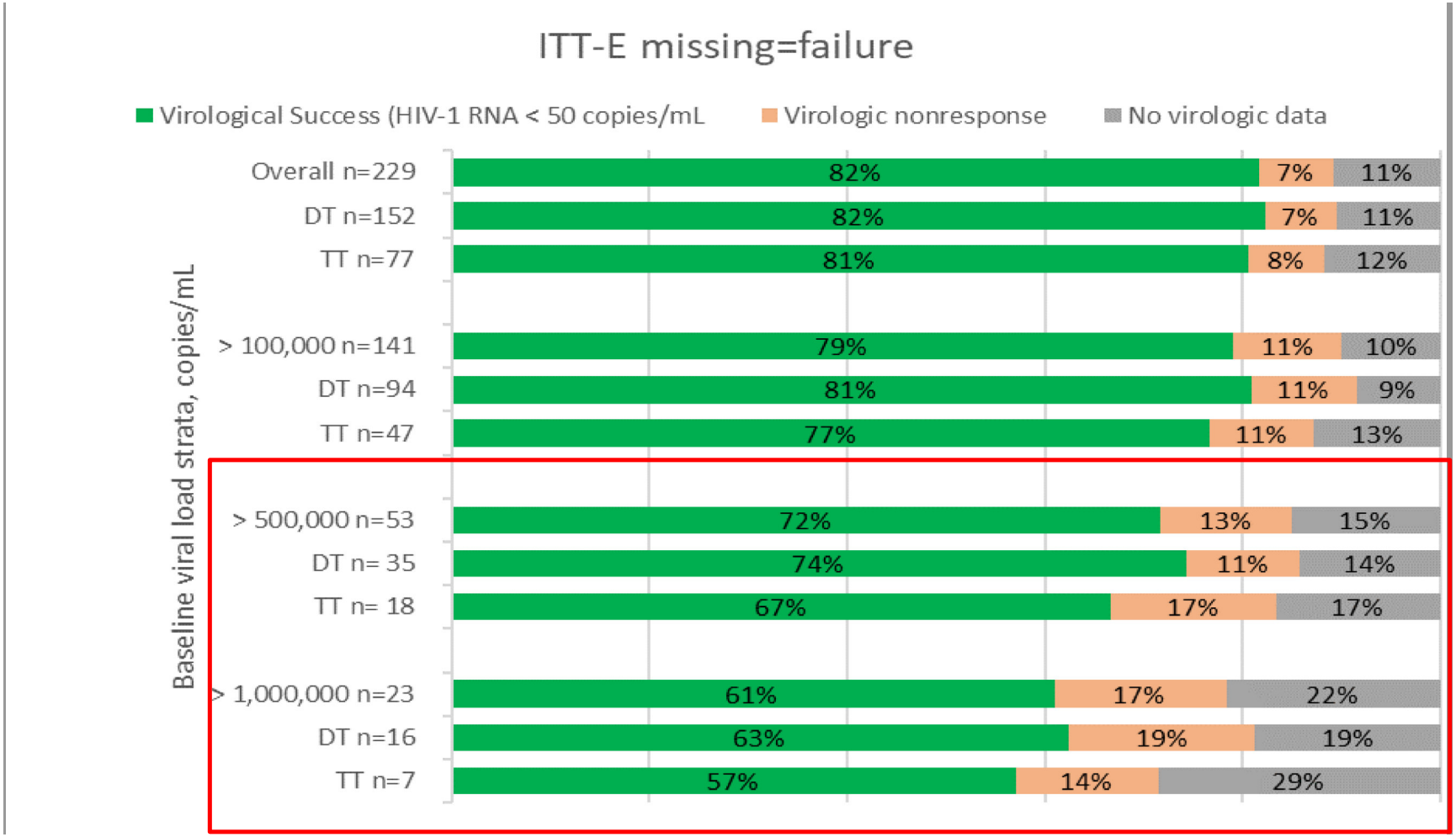
Figueroa MI, et al. O24. HIV Glasgow 2024

Dolce: Eficacia a 48 semanas



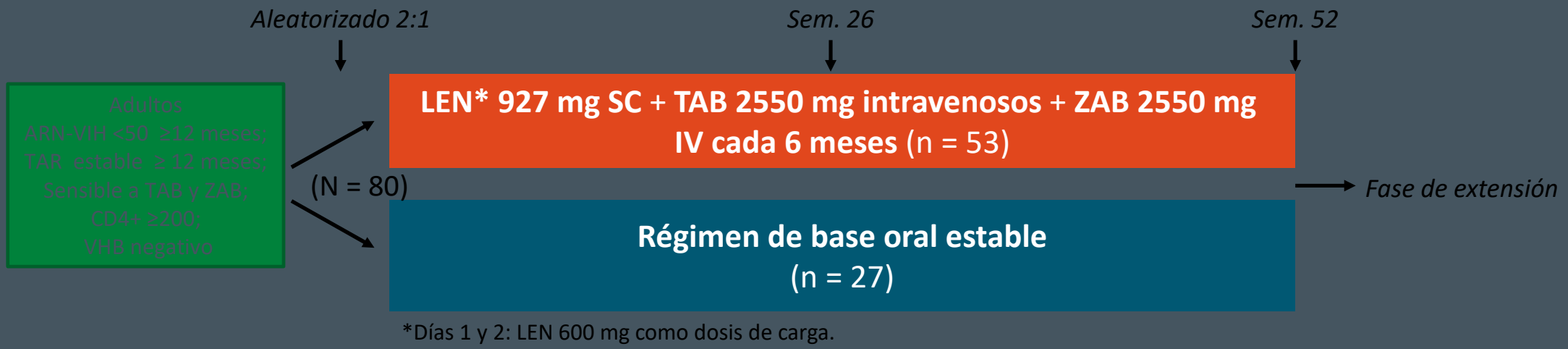
*Cases excluded from the per protocol analysis: 10 VL failures at week 24 or 36 (5 at week 24, and 5 at week 36); and 15 non-virological failures withdrawals from the study.

Dolce: Eficacia alta carga viral



TOP 8. Lenacapavir, teropavimab y zinlirvimab: eficacia 26w

- Estudio multicéntrico, aleatorizado de fase II; TAB y ZAB son bNAb de investigación



*Días 1 y 2: LEN 600 mg como dosis de carga.

- **Criterio principal de valoración:** ARN del VIH ≥50 copias/ml (FDA Snapshot en 26w)
- **Resultados secundarios:** seguridad; cambio de CD4+ respecto basal.

Lenacapavir, teropavimab y zinlirvimab: eficacia 26w

Parámetro, n (%)	LEN + TAB + ZAB (n = 53)	TAR en la situación basal (n = 27)
ARN del VIH-1 ≥50 copias/ml	1 (1,9)	0
ARN del VIH-1 < 50 cop/ml	51 (96,2)	26 (96,3)
Sin datos virológicos en 26w	1 (1,9)†	1 (3,7)‡

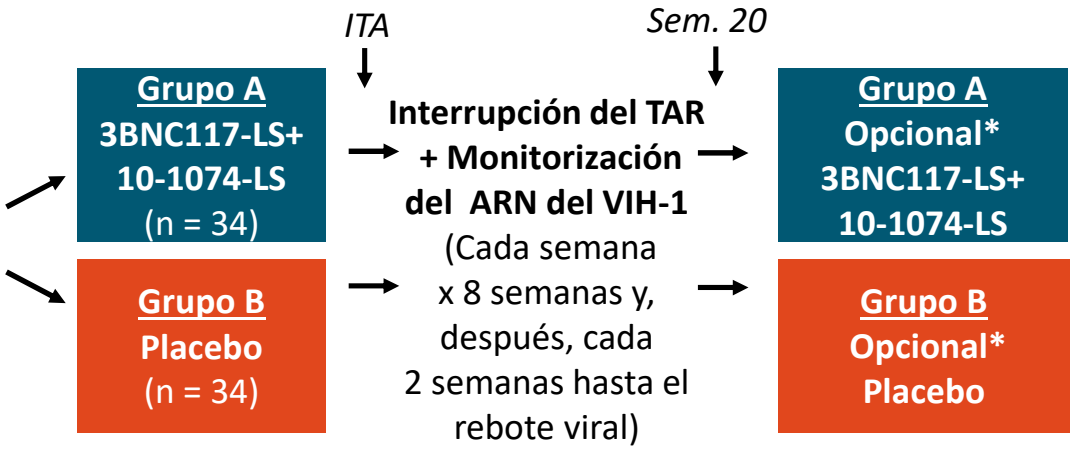
*Último ARN del VIH-1 disponible <50 copias/ml en ambos † Suspendido anticipadamente a discreción del investigador. ‡ Suspendido precozmente debido a carcinoma pancreático metastásico.

- Susceptibilidad a TAB y ZAB: 99 de los analizados.
- Ac emergentes durante tratamiento:
  - Contra TAB: n = 6 (11,3 %)
  - Contra ZAB: n = 9 (17 %)

TOP 9. STUDY RIO:
Efecto de los bNAb en el control del VIH durante la interrupción del TAR

- EECC Fase II controlado con placebo, con doble enmascaramiento, en 2 etapas;
- 3BNC117-LS y 10-1074-LS son bNAb de acción prolongada en investigación.
  - **El análisis actual informa de los datos de la etapa 1**

Edad: 18-69 años con VIH
Nadir CD4: >500 copias/ml
CD4:8 >1 al reclutamiento
No coinfecciones/comorbilidades
ARN-VIV suprimido ≥12 meses



*Después de la sem. 20, segunda dosis con enmascaramiento opcional de bNAb o placebo para individuos que permanecieron virológicamente suprimidos.

Criterios de reanudación de TAR
Repunte viral confirmado;
CD4+ <350 copias/µl;
Preferencia del participante;
síntomas de ITA
Preocupacion por Txdel VIH

- **Criterio de valoración primario:** rebote viral (ARN del VIH-1 >1000 copias/ml) en 20w tras ITA
- **Criterios de valoración secundarios clave:** seguridad, supresión viral a largo plazo

Fidler. CROI 2025. Resumen 107. NCT04319367.

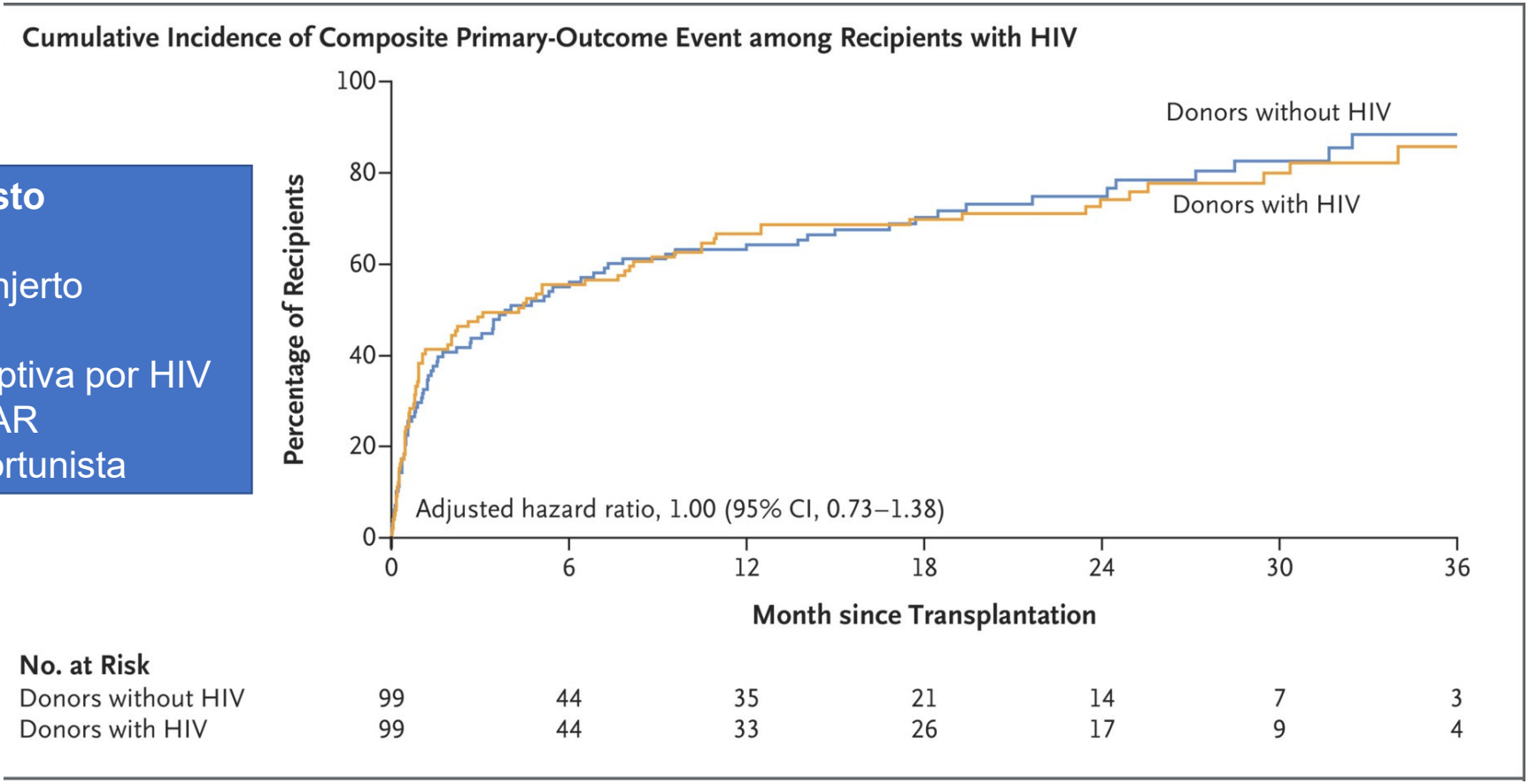
RIO: Rebote viral y resultados de seguridad

- No rebote viral (20w tras ITA): **bNAb** 75 % vs **placebo** 8,8 %; HR: 0,09 (IC 95: 0,04-0,21
- Entre personas en bNAb sin FV en 20w:
  - El 57 % seguía sin FV en 48w (IC95 %: 41 %-80 %).
  - 7 de 29 participantes (24 %) suprimidos sin TAR durante >72 semanas
- Los bNAb o la interrupción del TAR no provocaron AA graves; sin reacciones a la infusión
- Todos los que reiniciaron el TAR lograron resupresión viral (94 % en 12w)

Fidler. CROI 2025. Resumen 107.

TOP 10. Safety of Kidney Transplantation from Donors with HIV
Durand CM et al. N Engl J Med2024;391:1390-1401

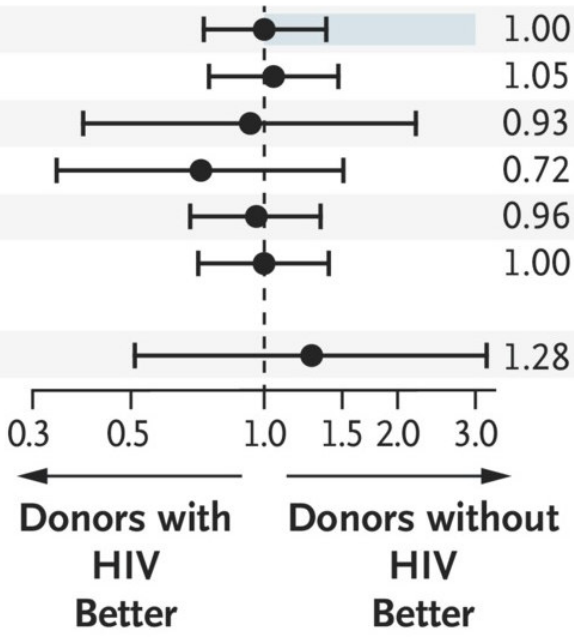
End Point compuesto
- Muerte
- Perdida del injerto
- SAE
- Infección irruptiva por HIV
- Fracaso al TAR
- Infección oportunista



Safety of Kidney Transplantation from Donors with HIV
Durand CM et al. N Engl J Med2024;391:1390-1401

Adjusted Relative Risks of Primary- and Secondary-Outcome Event among Recipients with HIV

Outcome	Donors with HIV	Donors without HIV	Adjusted Relative Risk (95% CI)
	no. of events/no. of recipients		
Primary outcome: composite safety event	79/99	77/99	1.00 (0.73–1.38)
Composite safety event, with additional adjustment	79/99	77/99	1.05 (0.75–1.47)
Death	12/99	11/99	0.93 (0.39–2.20)
Death or graft loss	14/99	17/99	0.72 (0.34–1.51)
Death, graft loss, or first serious adverse event	74/99	76/99	0.96 (0.68–1.34)
Death, graft loss, first serious adverse event, or first opportunistic infection	75/99	76/99	1.00 (0.71–1.40)
Secondary outcome: opportunistic infection	11/99	8/99	1.28 (0.51–3.18)



Podemos utilizar órganos de donantes con VIH de forma segura, con resultados tan buenos como los de donantes sin VIH.