20ª edición

POSTCROI

Una actualización de la "30th Conference on Retroviruses and Opportunistic Infections"

Nuevos fármacos y PrEP

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Nuevos fármacos antirretrovirales

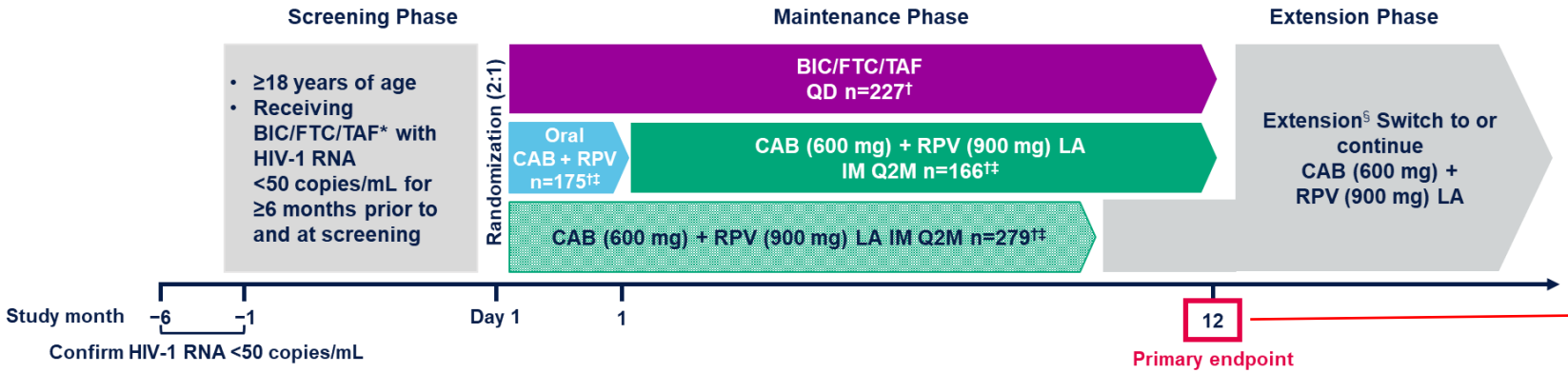
- Cabotegravir/Rilpivirina
- Lenacapavir
- Islatravir

Cabotegravir/Rilpivirina

SOLAR 12-MONTH RESULTS: RANDOMIZED SWITCH TRIAL OF CAB+RPV LA VS ORAL B/FTC/TAF

Moti N. Ramgopal, Antonella Castagna, Charles Cazanave, Vicens Diaz-Brito, Robin Dretler, Shinichi Oka, Olayemi Osiyemi, Kenneth Sutton, Denise Sutherland-Phillips, Alessandro Berni, Christine Latham, Feifan Zhang, Ronald D'Amico, Kimberly Smith, Jean Van Wyk

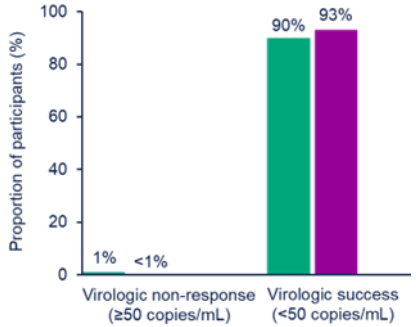
EC Fase 3b, randomizado (2:1), abierto y muticéntrico, de no inferioridad

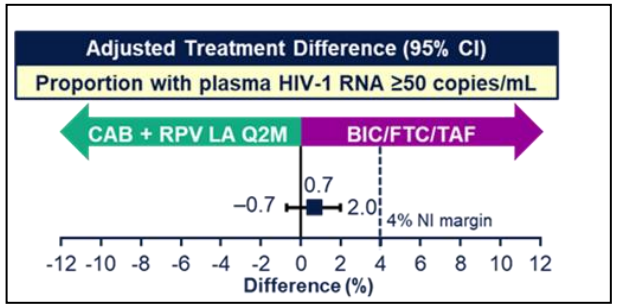


Proporción de participantes con CV ≥50 cop/mL (FDA Snapshot, 4% NI margin)

Características basales

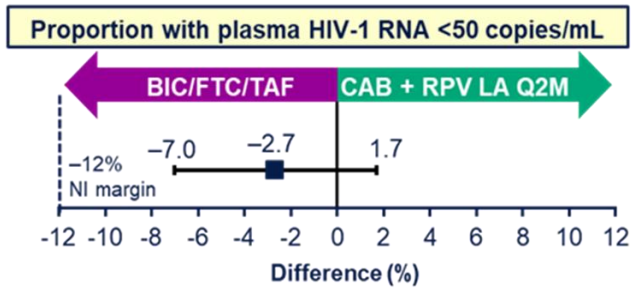
mITT-E population	CAB + RPV LA Q2M (n=447)	BIC/FTC/TAF (n=223)
Median age (range), years	37 (18–74)	37 (18–66)
≥50 years, n (%)	86 (19)	42 (19)
Female (sex at birth), n (%)	77 (17)	41 (18)
Race, n (%)		
Black	95 (21)	49 (22)
White	307 (69)	156 (70)
Asian	23 (5)	11 (5)
Other races*	22 (5)	7 (3)
BMI (kg/m^2), median (IQR)	26.0 (23.2–29.4)	25.4 (23.4–29.6)
Prior duration of ART, median, years	2.58	2.47





CROI 2023, Oral Poster 197

Proporción de participantes con CV <50 cop/mL (FDA Snapshot, -12% NI margin)



Incidencia de FV confirmado (2 CV ≥200 copies/mL consecutivas)

Participants With CVF in the mITT-E Population

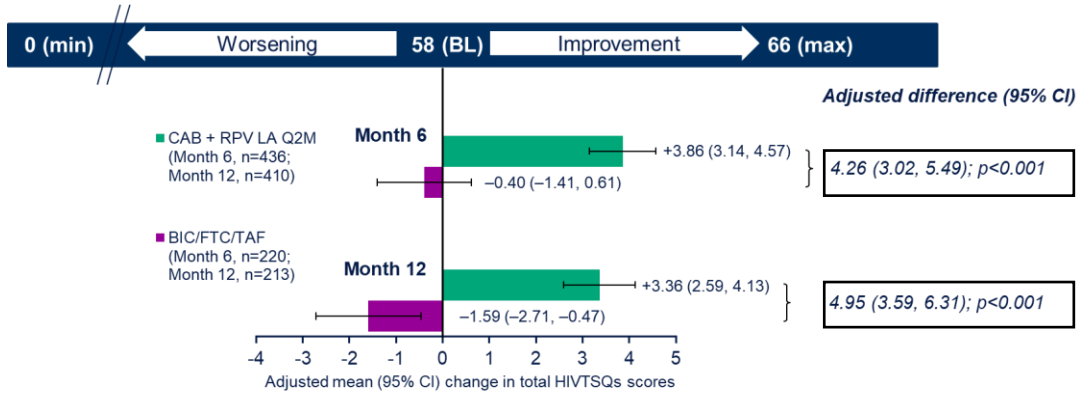
Sex at birth, country	Baseline BMI (kg/m²)	HIV-1 subtype at baseline	Viral load at SVF/CVF (copies/mL)	RPV RAMs observed at baseline (proviral DNA)	INI RAMs observed at baseline (proviral DNA)	RPV RAMs observed at failure (viral RNA)	INI RAMs observed at failure (viral RNA)	Phenotypic resistance (fold-change) to RPV/CAB	SVF timepoint (month)
Male, Italy*	21.5	B	1327/1409	None	None	M230L	Q148R	3.2/3.1	6
Male, Spain†	22.9	AE	6348/419	None	G140G/R	K101E	G118R	1.9/8.4	11

0.4%

Seguridad y tolerabilidad

Parameter, n (%)	CAB + RPV LA Q2M (n=454)	BIC/FTC/TAF (n=227)
Any AE	349 (77)	172 (76)
Drug-related AEs	90 (20)	2 (<1)
Any Grade ≥3 AE	42 (9)	26 (11)
Drug-related	7 (2)	0
Leading to withdrawal	16 (4)	2 (<1)
Drug-related	9 (2)*	0
Any serious AE	21 (5)	15 (7)
Drug-related	3 (<1)†	0

Satisfacción con el tratamiento



A M12 LA CAB/RPV Q2M demostró la no inferioridad en eficacia virológica vs BIC/TAF/FTC.
Ambos fármacos fueron globalmente bien tolerados.
La satisfacción de los participantes fue mayor en la rama CAB/RPV.

CROI 2023, Oral Poster 197

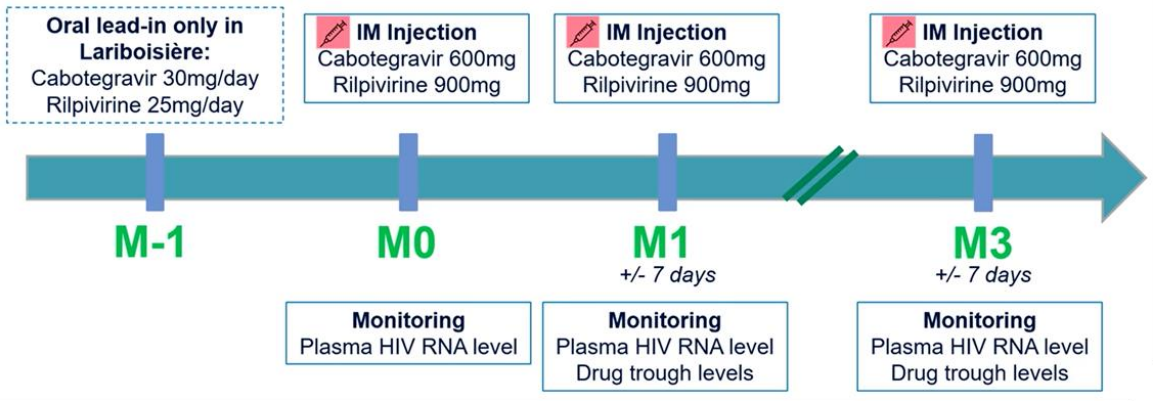
LOW CONCENTRATIONS OF LONG-ACTING CABOTEGRAVIR AND RILPIVIRINE IN PATIENTS WITH HIV

Emma Rubenstein, Myriam Diemer, Lauriane Goldwirt, Caroline Lascoux, Matthieu Lafaurie, Jeremy Zeggagh, Mariagrazia Tateo, Diane Ponscarme, Julien Gras, Blandine Denis, Agathe Rami, Pierre Sellier, Marie-Laure Chaix, Constance Delaugerre, Jean-Michel Molina

Estudio prospectivo de cohortes realizado en 2 hospitales franceses entre marzo 2022 –enero 2023.

Inclusion criteria

- Plasma HIV-1 RNA <50 copies/mL for at least 6 months
- No previous virological failure with INSTI or NNRTI
- No major INSTI/NNRTI resistance-associated mutations, except K103N
- Positive anti-HBs antibodies



Objetivos

- Determinar las concentraciones valle a M1 y M3.
- Identificar factores asociados a bajas concentraciones valle.

Concentraciones valle bajas
<Q1 en la población agrupada de FLAIR/ATLAS/ATLAS-2M

- Cabotegravir < 1120 ng/mL
- Rilpivirine < 32 ng/mL

Características basales

Characteristics	n=58
Median age, years (IQR)	30 (27 – 34)
Male, n (%)	51 (88)
Median BMI, kg/m² (IQR)	24 (22 – 26)
Geographical origin, n (%)	
Europe	40 (69)
Other	18 (31)
Population groups (%)	
MSM	43 (74)
Heterosexual	13 (22)
IV drug user	2 (3)
Median time since HIV RNA < 50 copies/mL, years (IQR)	8 (3 – 10)
Median CD4 T-cell count, /mm³ (IQR)	694 (529 – 830)
HIV subtype, n (%)	
A (A1)	2 (3)
B	35 (60)
Other	21 (36)
Cumulative RNA/DNA genotype: major NNRTI RAM (K103N), n (%)	3 (5)
Treatment before switch to CAB/RPV combination, n (%)	
INSTI	30 (52)
NNRTI	28 (48)
PI	3 (5)
Oral lead-in with CAB/RPV, n (%)	16 (28)

CROI 2023, Oral Poster 195. [1] Cutrell et al. AIDS. 2021

Follow-up

Evolution	n=58
Median follow-up, months (IQR)	8 (7 – 10)
Patients with viral blip, n (%) At 1 month At 3 months	4 (7) 2 (3) 3/56 (5)
Premature discontinuation, n (%)	4 (7)
Virologic failure, n (%)	1 (2)
Drug-related adverse event, n (%)	2 (3)*
Death, n (%)	1 (2)**

* Pain because of injections (both patients stopped after 3 months); ** Death due to myocardial infarction

Patient with virologic failure
- MSM, 30 years old, BMI 29.4 kg/m^2, HIV subtype CRF02_AG
- Virologically suppressed for 1.8 years with DTG/ABC/3TC, no oral lead-in
- Plasma HIV RNA level 2870 copies/mL at M1, no CAB/RPV RAM
- C_t CAB = 701 ng/mL, C_t RPV = 28 ng/mL at M1

Trough concentrations

	Drug trough concentrations	At 1 month (n=58)	At 3 months (n=56)
CAB	**Trough < 1120 ng/mL**, n (%)	**35 (60)**	**43 (77)**
	Median trough, ng/mL (IQR)	**976 (706 – 1434)**	**701 (440 – 1087)**
	No lead-in (n=42)	*951 (681 – 1196)*	*625 (397 – 880)*
	Lead-in (n=16)	*1213 (908 – 1479)*	*1103 (689 – 1246)*
RPV	**Trough < 32 ng/mL**, n (%)	**16 (28)**	**15 (27)**
	Median trough, ng/mL (IQR)	**48 (29 – 66)**	**43 (32 – 55)**
	No oral rilpivirine before switch (n=25)	*47 (35 – 68)*	*44 (30 – 58)*
	Oral rilpivirine before switch (n=33)	*49 (29 – 62)*	*43 (32 – 53)*

Risk factors for low trough levels

- **Cabotegravir:**

Characteristics	M1 cabotegravir trough level			
	< 1120 ng/mL (n=35)	≥ 1120 ng/mL (n=23)	p	p*
Median age, years (IQR)	29 (26 – 34)	31 (28 – 34)	0.7	
Male, n (%)	29 (83)	22 (96)	0.2	
European origin, n (%)	25 (71)	15 (65)	0.8	
Median BMI, kg/m^2 (IQR)	24 (22 – 27)	22 (20 – 25)	**0.01**	**0.009**
No lead-in, n (%)	29 (83)	13 (57)	**0.04**	**0.02**

* Multivariate analysis

Las concentraciones valle de CAB en mes 1 y 3 fueron bajas, describiéndose como factores de riesgo un IMC elevado y la no realización de lead-in oral

❖ Elevada variabilidad de niveles de concentración valle intra e interindividuales.

PREDICTORS OF POST SWITCH VIREMIA IN PATIENTS ON INJECTABLE CABOTEGRAVIR/RILPIVIRINE

Stephanie Kenney, Nimish Patel, Lucas Hill

Objetivo: evaluar los predictores de CV detectable tras switch a LA CAB/RPV en vida real

Methods

- **Study design**: Retrospective cohort study
- **Population**: Adult PLWH receiving care at the University of California San Diego Owen Clinic
- **Inclusion criteria**:
  - Treatment with LAI CAB/RPV for at least 3 months
  - Availability of both pre- and on-treatment HIV RNA values
  - HIV RNA <200 copies/mL (cpm) at the time of switch to CAB/RPV
  - At least one HIV RNA value collected greater than 21 days after start of LAI CAB/RPV

Viral Load Category	Definition
Blip	At least one viral load 20-199cpm followed by viral load <20cpm
Persistent low-level viremia (pLLV)	At least two consecutive viral loads 20-199cpm
High viral load	At least one viral load ≥200cpm
Continually suppressed	All viral loads < 20cpm

Results

	Total (n=144)	At least one VL ≥20cpm (n=58)	All VL <20 cpm (n=86)	p-value
Median Age (IQR)	44 (34-54)	45 (33-53)	41 (34-54)	0.99
Race (%)				
White	62 (43.1)	27 (46.6)	35 (40.7)	0.51
Black	27 (18.8)	13 (22.4)	14 (16.3)	
Asian	4 (2.8)	1 (1.7)	3 (3.5)	
Other/unknown	51 (35.4)	17 (29.3)	34 (39.5)	
Ethnicity (% Hispanic)	58 (40.3)	27 (46.6)	31 (36.0)	0.46
Female SAB (%)	16 (11.1)	5 (8.6)	11 (12.8)	0.43
Completed oral lead-in (%)	125 (86.8)	49 (84.5)	76 (88.4)	0.50
Late injection or used oral bridge (%)	15 (10.4)	5 (8.6)	10 (11.6)	0.56
CAB/RPV regimen (%)				
Every 1 month only	3 (2.1)	1 (1.7)	2 (2.3)	0.67
Every 2 month only	73 (50.7)	27 (46.6)	46 (53.5)	
Switched to every 2 month	68 (47.2)	30 (51.7)	38 (44.2)	
Median CD4 count (IQR)	745 (520-941)	809 (554-961)	680 (504-923)	0.08
Median BMI (IQR)	26.9 (24.3-30.2)	27.4 (24.6-31.7)	26.4 (24.2-30.0)	0.33
Pre-switch category (%)				
Blip 20-199 cpm	26 (18.1)	12 (20.7)	14 (16.3)	**0.0001**
pLLV	26 (18.1)	17 (29.3)	9 (10.5)	
High viral load	6 (4.2)	2 (3.4)	4 (4.7)	
Always <20 cpm	86 (59.7)	27 (46.6)	59 (68.6)	

In the multivariate regression model:

Having **persistent low level viremia pre-switch** was significantly associated with having at least one VL >20cpm post switch [OR 3.55 (1.54-8.66)]

144 participantes
Media de seguimiento de 278 días
1 Fracaso virológico

Estos datos sugieren que los pacientes con viremia persistente de bajo grado antes del switch a LA CAB/RPV son más propensos a tener al menos 1 determinación con CV detectable tras el switch.

CROI 2023, Poster 516

HIGH VIROLOGIC SUPPRESSION RATES ON LONG-ACTING ART IN A SAFETY-NET CLINIC POPULATION

Monica Gandhi, Jorge Salazar, Matthew D. Hickey, Katerina Christopoulos, Jon Oskarsson, Mary Shiels, John Szumowski, Janet Grochowski, Francis Munoz-Mayorga, John Sauceda, Elizabeth Imbert, Janet Nguyen, David V. Glidden, Diane V. Havlir

Table 1: Demographics and clinical characteristics of cohort in Ward 86 LA ART program (n=133)

Characteristic	Distribution, n (%)
Age (median, range)	45 (38-45) years
Gender	
Cis Man	117 (88%)
Cis Woman	11 (8%)
Transgender Woman	5 (4%)
Race/ethnicity	
Black	21 (16%)
Latino/a	50 (38%)
White	43 (32%)
Multiracial	19 (14%)
Housing	
Unstable	77 (58%)
Stable	45 (34%)
Homeless	11 (8%)
Insurance	
Medicare or Medicaid or both	130 (98%)
ADAP	3 (2%)
Current stimulant use	44 (33%)
Major mental illness	51 (38%)
Virologically non-suppressed (>30 copies/ml)	57 (43%) with log10 viral load (mean, STD) 4.21 (1.30)
CD4 count (median with interquartile range)	Virologically suppressed 616 (395–818) Virologically non-suppressed 215 (75–402)

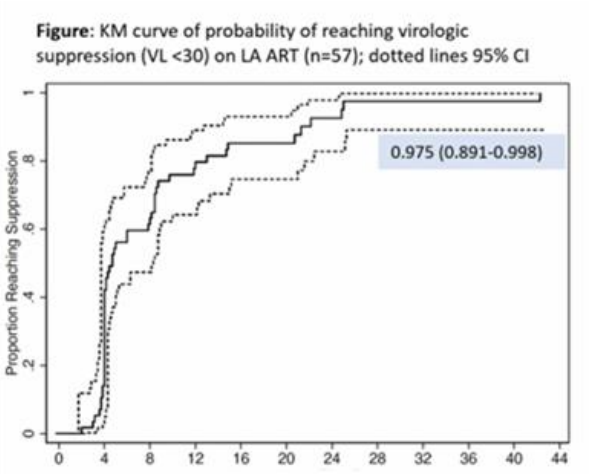
* Note: ADAP is AIDS Drug Assistance Program; Baseline CD4 defined as the CD4 count closest to and including date of first injection. Median time from CD4 count to first injection was 70 (range 0 to 882) days

Estudio descriptivo de administración de LA CAB/RPV con criterios de inclusión muy diferentes a los de los EC:

Inclusion criteria of Ward 86

- Need not be virologically suppressed or take oral ART before injectables
- No RPV or INSTI mutations (strengthened criteria later)
- **Express willingness to come to clinic q4 weeks, contact information, outreach from staff**
- Rigorous protocol, Biweekly review of patients

Resultados



- 55 paciente con CV detectable suprimieron en una media de 33 días.
- 2 FV en primeras 24 semanas, ambas con mutaciones de resistencia.
- 97.5% estaban indetectables a las 26 semanas.

A pesar de las barreras a la adherencia en el entorno del estudio, los resultados son exitosos con tasas de FV similares a los EC

CROI 2023, Poster 518

Lenacapavir

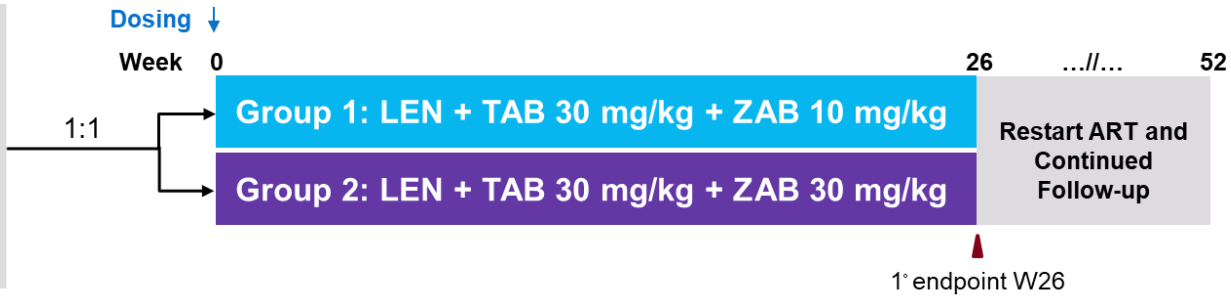
LENACAPAVIR WITH bNAbs GS-5423 AND GS-2872 DOSED EVERY 6 MONTHS IN PEOPLE WITH HIV

Joseph J. Eron, Susan R. Little, Gordon Crofoot, Paul Cook, Peter Ruane, Dushyantha Jayaweera, Edwin DeJesus, Sarah E. Waldman, Megha L. Mehrotra, Laurie A. VanderVeen, Hailin Huang, Sean E. Collins, Jared M. Baeten, Marina Caskey

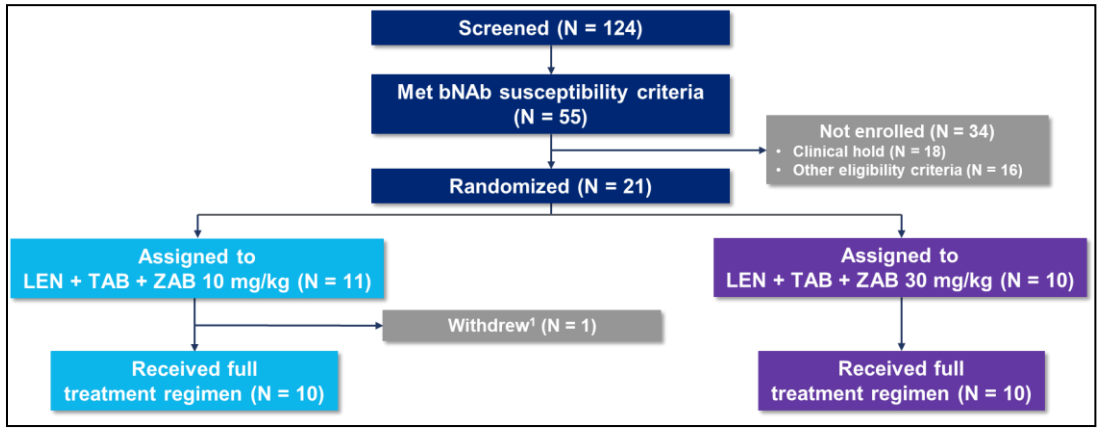
Estudio aleatorizado Fase 1b para evaluar la seguridad y eficacia de un regimen LA (6M) que incluye LENACAPAVIR y 2 bNABs: TEROPAVIMAB y ZINLIRVIMAB

Key Inclusion Criteria

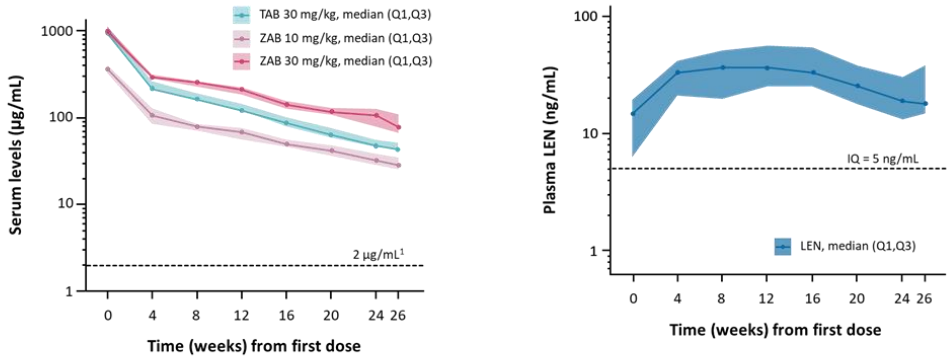
- Adults living with HIV-1
- Virologically suppressed ≥ 18 months
- Viral susceptibility to both TAB and ZAB
- CD4 nadir ≥ 350
- CD4 at entry ≥ 500



	Day 1	Day 2
LEN oral 600 mg		
LEN SC 927 mg		-
TAB IV 30 mg/kg		-
ZAB IV 10 mg/kg or 30 mg/kg		-



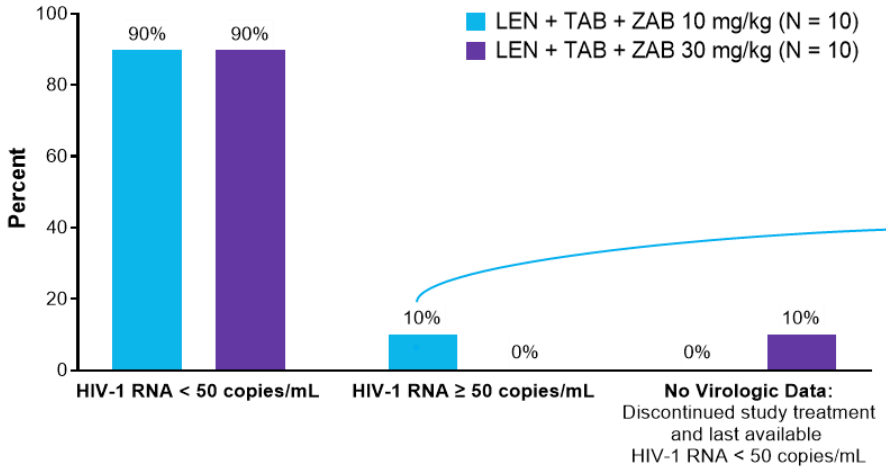
CROI 2023, Oral Poster 193

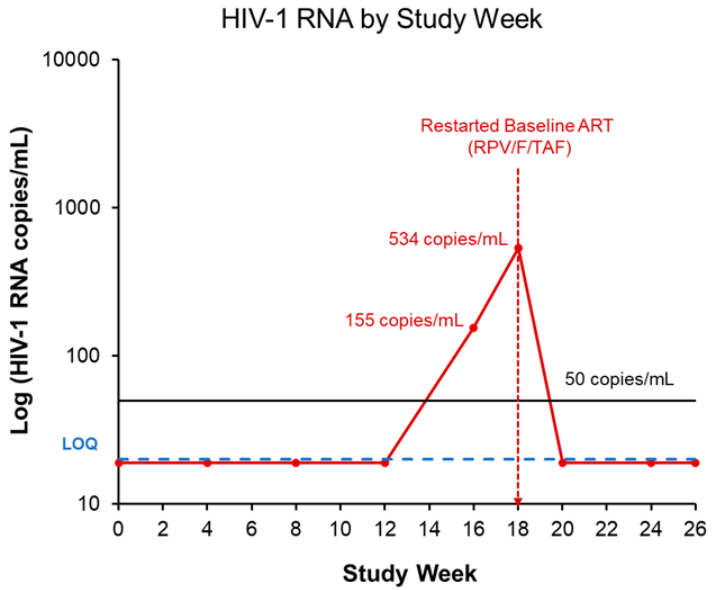


Se mantuvieron concentraciones terapéuticas durante las 26 S

	LEN + TAB + ZAB 10 mg/kg (N = 11)	LEN + TAB + ZAB 30 mg/kg (N = 10)	Total (N = 21)
Any adverse event (AE), n	9	10	19
AEs of any grade occurring in 3 or more study participants			
Injection-site pain, n	5	5	10
Injection-site erythema, n	4	3	7
Injection-site nodule, n	4	2	6
Injection-site induration, n	2	4	6
Injection-site mass, n	3	1	4
COVID-19, n	3	0	3
Upper respiratory tract infection, n	3	0	3

No se produjeron discontinuaciones por AEs





"Este estudio demuestra que la combinación LEN + Teropavimab + Zinlirbimab puede mantener la supresión virológica durante 6 meses en pacientes seleccionados."

CROI 2023, Oral Poster 193

Islatravir

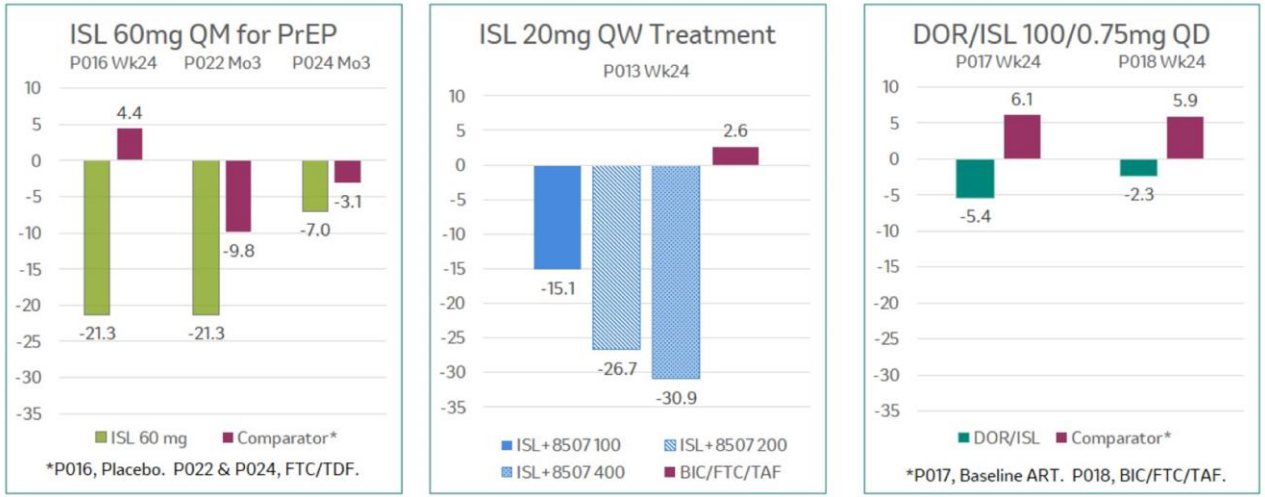
EFFECT OF ISLATRAVIR ON TOTAL LYMPHOCYTE AND LYMPHOCYTE SUBSET COUNT

Kathleen E. Squires, Todd A. Correll, Michael N. Robertson, Stephanie O. Klopfer, Peggy May Tan Hwang, Yun-Ping Zhou, Elizabeth Martin, Elizabeth G. Rhee

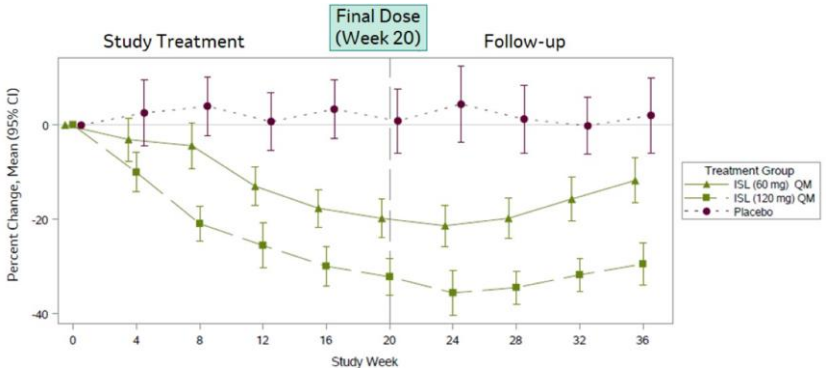
Evalúan los cambios en la cifra linfocitos en distintos EC con islatravir

Study #	Design	Population	Dose	N	Comparator	N
HIV Prevention						
MK8591-016 phase 2	Blinded; 2:2:1 randomization	Adults without HIV	ISL 60 or 120 mg once monthly (QM)	194	Placebo	48
MK8591-022 phase 3	Blinded; 1:1 randomization	Cisgender women	ISL 60 mg QM	362	FTC/TDF	365
MK8591-024 phase 3	Blinded; 2:1 randomization	Cisgender men & transgender women	ISL 60 mg QM	328	FTC/TDF or FTC/TAF	166
HIV-1 Treatment						
MK8591-013 phase 2	Blinded; 1:1:1:1 randomization	Virologically suppressed	ISL 20 mg + 8507 100, 200, or 400 mg once weekly (QW)	121	BIC/FTC/TAF	40
MK8591A-017 phase 3	Open-label; 2:1 randomization	Virologically suppressed	ISL 0.75/DOR 100 mg once daily (QD)	662	Baseline ART	336
MK8591A-018 phase 3	Blinded; 2:1 randomization	Virologically suppressed	ISL 0.75/DOR 100 mg QD	322	BIC/FTC/TAF	319
MK8591-011 phase 2	Blinded; 1:1:1:1 randomization	Treatment-naïve	ISL 0.25, 0.75, or 2.25 mg + DOR 100 mg QD	112	DOR/3TC/TDF	31

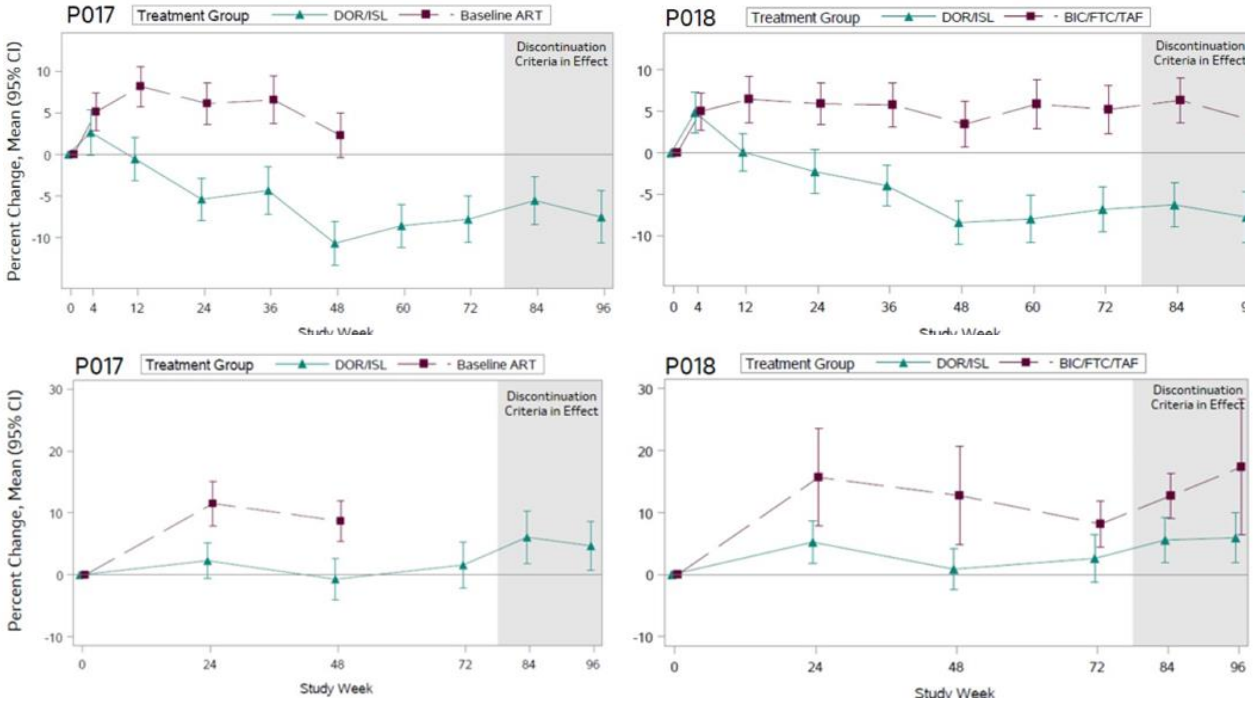
Cambio medio (%) del recuento de linfocitos totales desde la visita basal



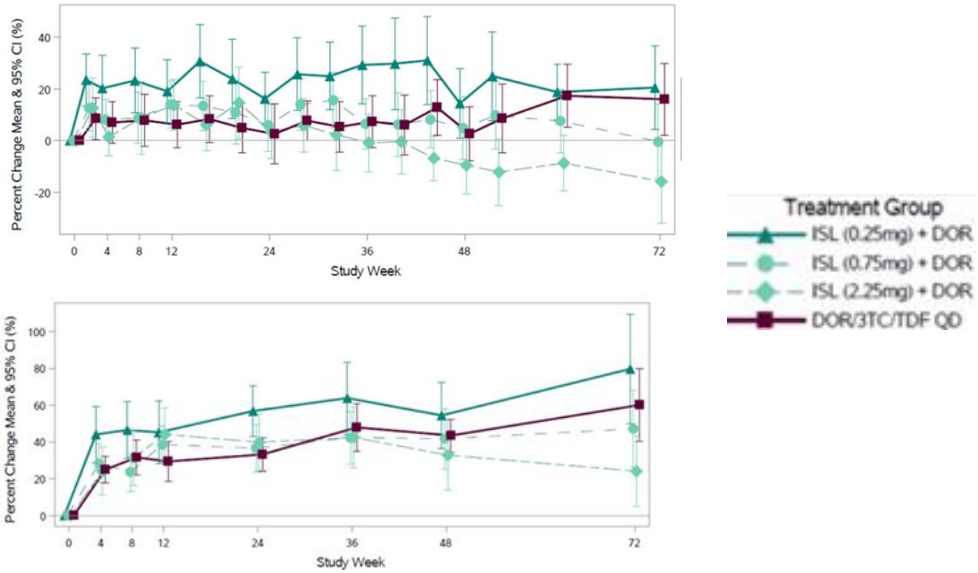
Fase 2 ISLA mensual PrEP: 60 y 120 mg ISLA (linf.)



Fase 3 ISLA/DORA diario Switch: 0.75 mg ISLA (linf./CD4)



Fase 2b ISLA/DORA diario switch: 0.25, 0.75 y 2.25 mg ISLA (linf./CD4)

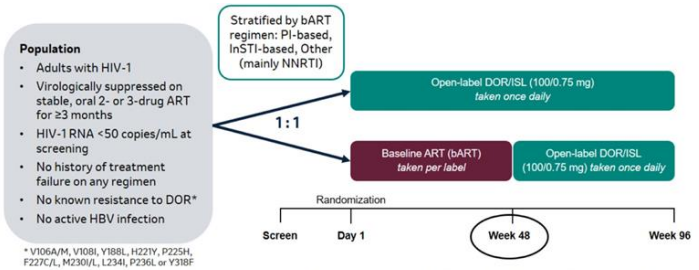


- **Mayor descenso con mayores dosis de ISLA.**
- **En los EC P017 y P018 hay una estabilización entre S48 y S72.**
- **La incidencia de infecciones no aumentó.**

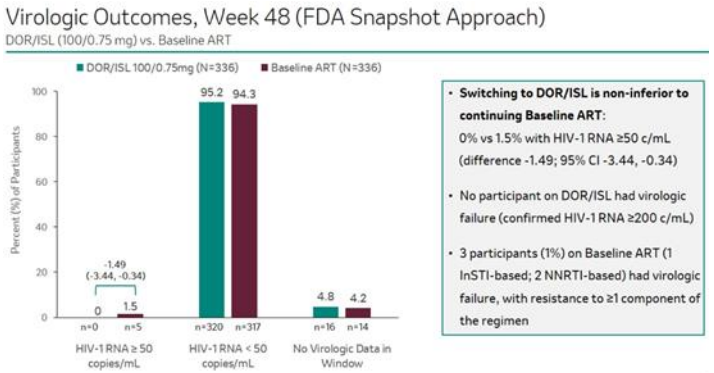
CROI 2023, Oral Poster 192

SWITCH TO DOR/ISL (100/0.75MG) QD: WEEK 48 RESULTS FROM AN OPEN-LABEL PHASE 3 TRIAL

Jean-Michel Molina, Giuliano Rizzardini, Catherine Orrell, Alejandro Afani Saud, Alexandra Calmy, Shinichi Oka, Federico Hinestrosa, Princy Kumar, Pablo Tebas, Sharon Walmsley, Anjana Grandhi, Isaias Noel Gendrano, Karen Eves, Jason Kim, Todd A. Correll

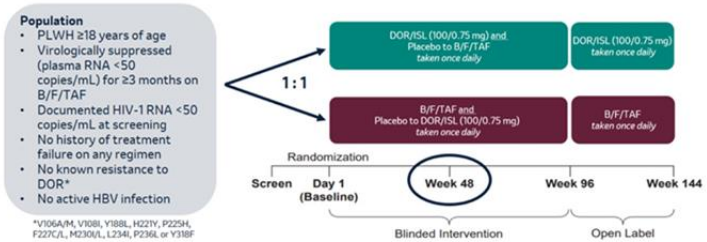


Primary Efficacy Endpoint: HIV-1 RNA ≥50 copies/mL at Week 48 (FDA snapshot approach), non-inferiority margin 4%

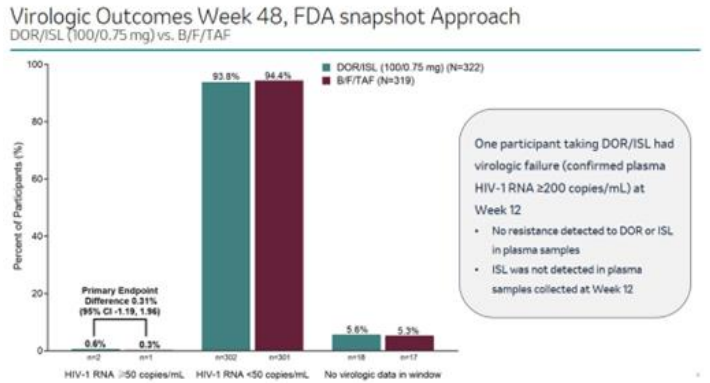


SWITCH TO DOR/ISL (100/0.75MG) QD FROM B/F/TAF: WEEK 48 RESULTS FROM A PHASE 3 TRIAL

Anthony M. Mills, Giuliano Rizzardini, Moti Ramgopal, Olayemi Osiyemi, Johannes R. Bogner, Debbie Hagins, Roger Paredes, Jacques Reynes, Jürgen Rockstroh, Andrew Carr, Feng-Hsiu Su, Stephanie O. Klopfer, Rebeca M. Plank, Michelle C. Fox, Todd A. Correll



Primary Efficacy Endpoint: HIV-1 RNA ≥50 copies/mL at Week 48 (FDA snapshot approach), non-inferiority margin 4%



En semana 48 ambos EC mostraron la no inferioridad de DORA/ISLA (100/0.75 mg) para mantener CV suprimida en comparación con el TAR basal con un perfil de seguridad similar.

❖ Los EC de Fase 3 se continuarán realizando con una dosis de ISLA de 0.25 mg.

PrEP y prevención de otras ITS

- PrEP con LA Cabotegravir

- PEP con Doxiciclina

LA Cabotegravir

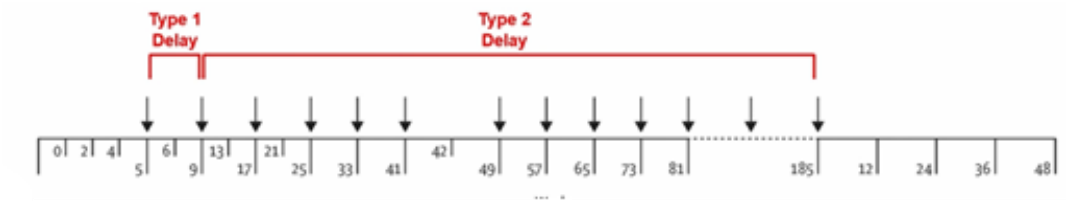
CABOTEGRAVIR PHARMACOLOGY IN THE BACKGROUND OF DELAYED INJECTIONS IN HPTN 084

Mark A. Marzinke, Xu Guo, James Hughes, Brett Hanscom, Estelle Piwowar-Manning, Craig Hendrix, Scott Rose, Jim Rooney, Alex R. Rinehart, Susan Ford, Adeola Adeyeye, Myron S. Cohen, Mina Hosseinipour, Sinead Delany-Moretlwe
Research Group: HPTN 084 Study Team

HPTN084: EC fase 3 aleatorizado que demostró la superioridad de LA CAB Q2M comparado con TDF/FTC para la prevención de VIH en mujeres africanas. Tras un análisis intermedio del DSMB todas las participantes pasaron a la rama LA CAB.

Objetivo: evaluar los episodios con retraso en el momento de la inyección

Retraso Tipo 1: 8-14 semanas entre 1ª y 2ª inyección.
Retraso Tipo 2: 12-18 semanas entre otras dos inyecciones.



224/1614 participantes (12%) tuvieron al menos un retraso.

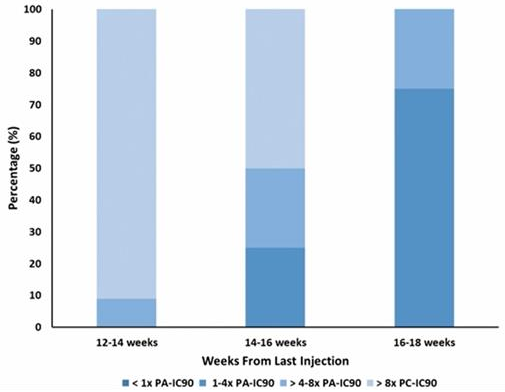
En total 19 retrasos Tipo 1 y 205 tipo 2.

La dosis de LA CAB usada debía alcanzar:

- >4x PA-IC_{90} (0.664 mcg/ml) en 80% de participantes.
- >8x PA-IC_{90} (1.33 mcg/ml) en 50% de participantes.

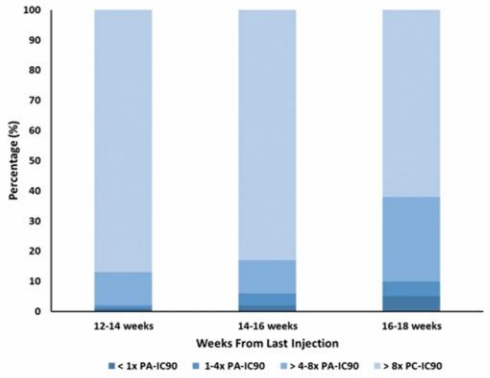
Injection Delays Between 1st and 2nd Injections (Type 1 Delays)

[CAB] Trough	8-10 weeks Between Injections	10-12 weeks Between Injections	12-14 weeks Between Injections
	N=11	N=4	N=4
>8x PA-IC_{90}	10 (91%)	2 (50%)	0 (0%)
>4-8x PA-IC_{90}	1 (9%)	1 (25%)	1 (25%)
1-4x PA-IC_{90}	0 (0%)	1 (25%)	3 (75%)
<1x PA-IC_{90}	0 (0%)	0 (0%)	0 (0%)



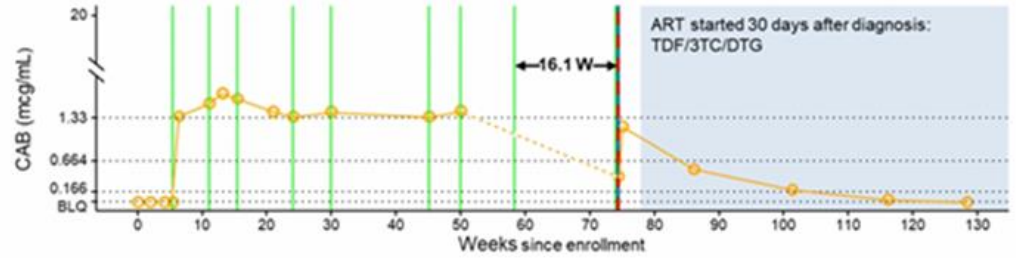
Injection Delays *After* the 2nd Injection (Type 2 Delays)

[CAB] Trough	12-14 weeks Between Injections	14-16 weeks Between Injections	16-18 weeks Between Injections
	N=109	N=57	N=39
>8x PA-IC_{90}	95 (87%)	48 (84%)	24 (62%)
>4-8x PA-IC_{90}	12(11%)	6 (11%)	11 (28%)
1-4x PA-IC_{90}	1 (1%)	2 (4%)	2 (5%)
<1x PA-IC_{90}	1 (1%)	1 (2%)	2 (5%)



Paciente contagiada de VIH durante el estudio

- 3/9 injections occurred late (8.5, 15.1, 16.1 weeks)
- CAB concentration at first HIV positive visit: 0.416 mcg/mL (<4x PA-IC_{90})



Podría haber un periodo de 6 semanas de perdón entre dosis de LA CAB para PrEP en mujeres

HPTN 084 LIFE

CROI 2023, Oral Poster 159

LEVI: Long-acting Early Inhibition Syndrome

THE LEVI SYNDROME: CHARACTERISTICS OF EARLY HIV INFECTION WITH CABOTEGRAVIR FOR PrEP

Susan H. Eshleman, Jessica M. Fogel, Estelle Piwowar-Manning, Brett Hanscom, Alex R. Rinehart, Myron S. Cohen, Marybeth McCauley, Jennifer Farrior, Adeola Adeyeye, Mina Hosseinipour, Beatriz Grinsztejn, Mark A. Marzinke, Sinead Delany-Moretlwe, Raphael J. Landovitz,
Research Group: for the HPTN 083 and 084 Study Teams

HPTN083 y HPTN084 son EC fase 3 aleatorizados que demostraron la superioridad de LA CAB Q2M comparado con TDF/FTC para la prevención de VIH en HSH y mujeres trans y en mujeres cis africanas respectivamente.

Infecciones de VIH durante el HPTN083

Type of case	# Cases
Infected despite on-time injections	**6**
28 other infections	
No recent CAB exposure (within 6 months)	16
HIV+ at enrollment	4
Infected while receiving oral CAB	3
Infected after ≥ 1 delayed injection	3
Infected near the time of CAB re-initiation	2

aprox. la mitad presentaron un retraso en el diagnóstico del VIH

Assay Reversion

	Days since 1st HIV pos visit	Rapid test	Ag/Ab test	Qualitative RNA test (LLOD 30 c/mL)	Confirmatory Ab test	Viral load (LLOQ 40 c/mL or single copy)	DNA test (LLOD 4.09 c/10⁶ cells)
11 months	0	NR	NR	R		6.1	
	42	NR	NR	NR			
	55	NR	NR	R		ND	
	98	NR	NR	NR			
	105	R	R	NR	NEG		Detect <LLOD
	112	NR	R	NR	NEG		
	119	NR	NR	NR			
	132	NR	R	NR	INDET		ND
	195	R	NR	NR			Detect <LLOD
	235	NR	R	NR	INDET		
	280	NR	R	R	NEG	<40	Detect 5.8
	333	R	R	R	INDET	<40	

Comparison of acute HIV infection (AHI) to infections that occur in the setting of long-acting early viral inhibition (LEVI)

	AHI	LEVI
Cause	Phase of natural HIV infection	Long-acting anti-viral PrEP agent (prototype: CAB-LA)
Onset	New infection	Infection during PrEP Initiation of PrEP agent during acute/early infection
Viral replication	Explosive	Smoldering
Symptoms	Fever, chills, rash, night sweats, muscle aches, sore throat, fatigue, swollen glands	Minimal, variable, often no symptoms reported
Detection	Ag/Ab assay, RNA assays (including less sensitive POC and pooled tests), DNA assays, total nucleic acid assays	Ultrasensitive RNA assay (often low or undetectable RNA, low/undetectable DNA, diminished/delayed Ab production)
Assay reversion	Rare	Common for many test types
Duration	1-2 weeks (until Ab detection)	Months (until viral breakthrough, drug clearance, or ART start); can persist months after the anti-viral agent is discontinued
Transmission	Very likely	Unlikely (except possibly through blood transfusion)
Drug resistance	No (unless transmitted)	Yes (can emerge early when viral load is low)

La cuantificación de ARN VIH-1 detecta las infecciones generalmente antes de la aparición de resistencias (ya aprobada por FDA y recomendada por la CDC como método de cribado).

- En estudios futuros se determinará si el Sd. LEVI ocurre también con otros agentes LA en desarrollo para PReP.

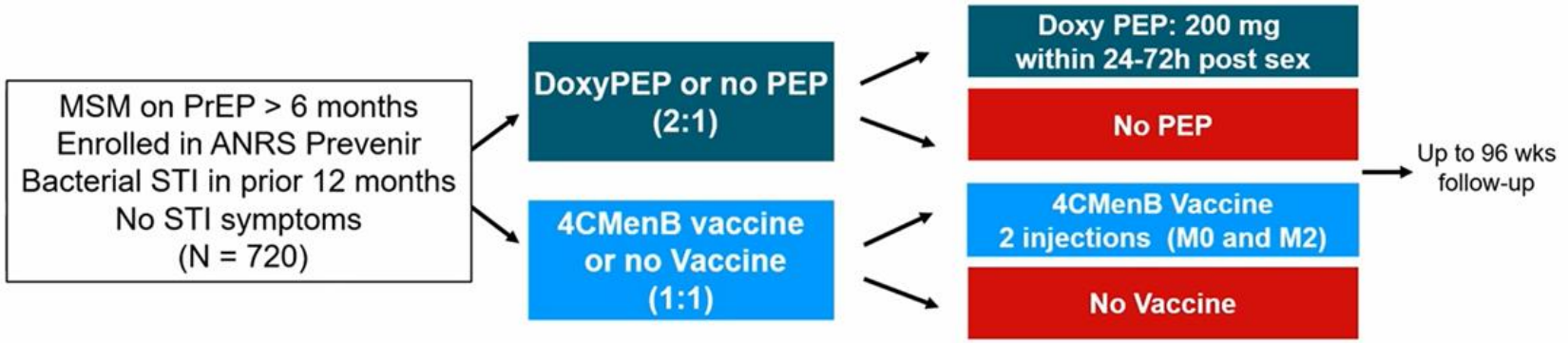
CROI 2023, Oral Poster 160

PEP con doxiciclina

ANRS 174 DOXYVAC: AN OPEN-LABEL RANDOMIZED TRIAL TO PREVENT STIs IN MSM ON PrEP

Jean-Michel Molina, Beatrice Bercot, Lambert Assoumou, Algarte-Genin Michele, Emma Rubenstein, Gilles Pialoux, Christine Katlama, Laure Surgers, Cecile Bebear, Nicolas Dupin, Jean-Paul Viard, Juliette Pavie, Claudine Duvivier, Jade Ghosn, Dominique Costagliola
Research Group: ANRS 174 Doxyvac Group

ANRS 174 DOXYVAC es un EC abierto, aleatorizado de superioridad.



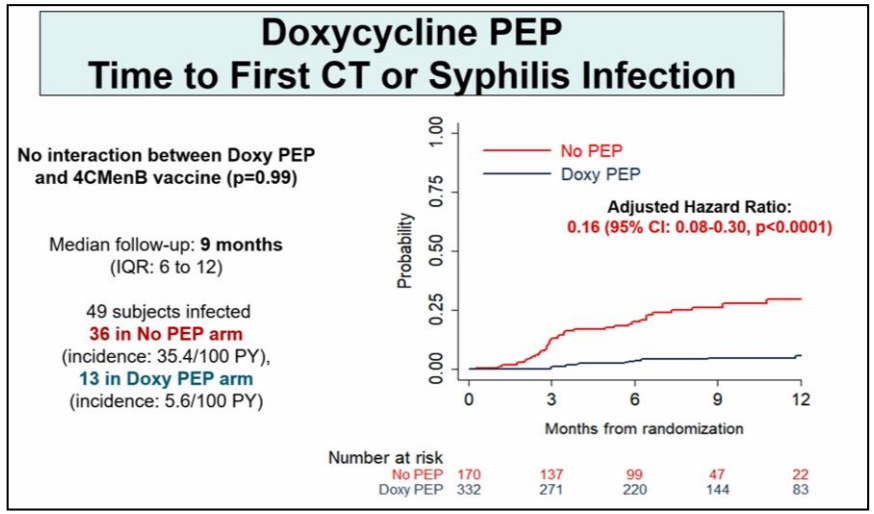
Objetivos primarios

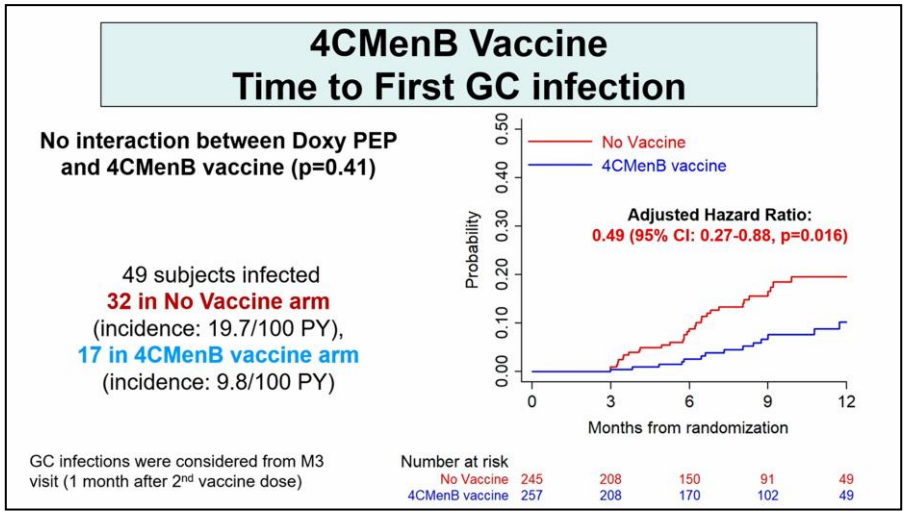
- impacto de DoxyPeP en el tiempo hasta el primer episodio de clamidia o sífilis.
- Impacto de la vacunación 4CMenB en el tiempo hasta el primer episodio de gonorrea.

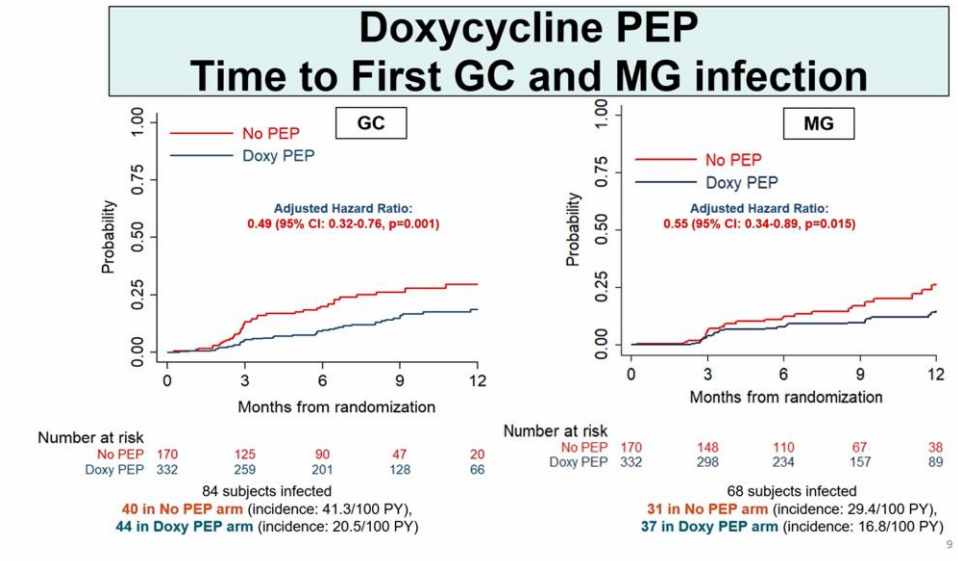
Participants Baseline Characteristics

Median (IQR) or %	Doxy PEP (n = 332)	No PEP (n = 170)	4CMenB vaccine (n = 257)	No Vaccine (n = 245)	Total (n=502)
Age, years	40 (33-48)	39 (33-47)	40 (33-47)	39 (33-48)	**39 (33-47)**
White	79.2	82.9	75.9	85.3	**80.5**
Born in France	84.8	81.7	82.7	84.8	**83.8**
Secondary education	89.1	88.4	90.7	87.0	**88.9**
Employed	87.0	87.5	89.6	84.6	**87.2**
PrEP use, months	42 (32-55)	43 (35-55)	43 (32-55)	42 (33-54)	**42 (32-55)**
No. STIs in prior 12 months	2 (1-2)	2 (1-2)	2 (1-3)	2 (1-2)	**2 (1-2)**
Gonorrheae	67.3	70.1	67.5	69.0	**68.2**
Chlamydiae	50.3	47.9	52.5	46.3	**49.5**
Syphilis	21.5	17.4	20.4	19.8	**20.1**
M. genitalium	3.9	4.2	3.5	4.5	**4.0**
Condomless sex (4 weeks) no.	5 (3-10)	5 (2-10)	5 (2-10)	5 (3-10)	**5 (2-10)**
Partners (last 3 months) no.	10 (5-20)	10 (5-20)	10 (5-20)	10 (5-20)	**10 (5-20)**
Chemsex at last sex act	11.8	10.6	12.5	10.2	**11.4**

CROI 2023, Oral Poster 119; [1]Molina et al, Lancet Inf Dis, 2018; [2]Petoussis-Harris et al, Lancet, 2017; [3]Folaranmi et al, CID, 2017







Con una reducción de la incidencia de clamidia y sífilis de aprox. 80% y de gonorrea de aprox. 55% en sept. 2022 el DSMB paró el estudio y recomendó DoxyPEP y 4cMenB a todos los participantes.

CROI 2023, Oral Poster 119

MUCOSAL PHARMACOLOGY OF DOXYCYCLINE FOR BACTERIAL STI PREVENTION IN MEN AND WOMEN

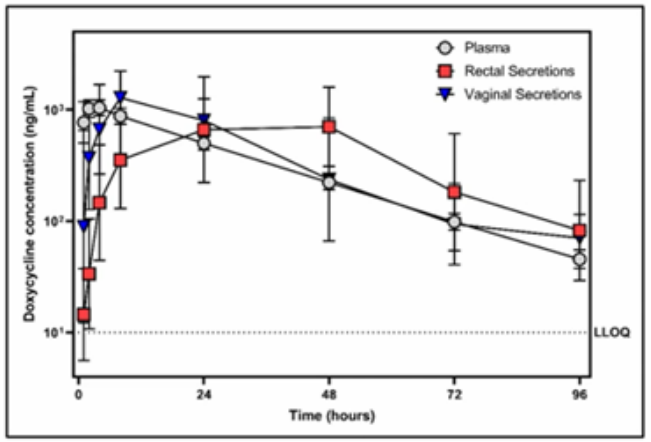
Richard Haaland, Jeffrey Fountain, Chuong Dinh, Tiancheng Edwards, Amy Martin, Deborah Omoyege, Christopher Conway-Washington, Colleen Kelley, Walid Heneine

Objetivo: definir la farmacología de doxiciclina en mucosas tras una dosis oral de 200 mg de doxiciclina de liberación retardada (Doryx®).

	Male (n=11)	Female (n=9)
Age		
Median	38	34

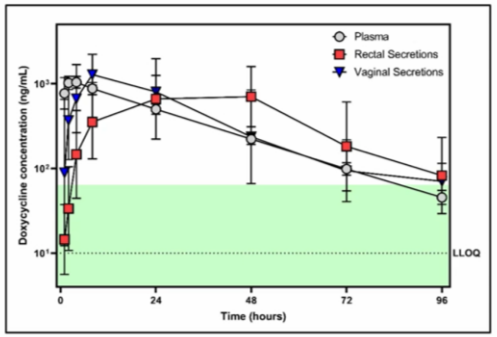
Se recogen muestras de sangre y frotis rectales y/o vaginales durante 7 días después de la administración de doxiciclina

Mucosal Doxycycline Concentrations



	C_{max} (ng/mL) [95% CI]	T_{max}	$AUC_{0\text{-}96h}$ (ng*h/mL) [95% CI]	AUC Ratio (S:P)
Plasma	1042 [889 – 1222]	4 hr	33,951 [29,632 – 38,899]	
Rectal Secretions	704 [311 – 1596]	48 hr	73,511 [34,332 – 156,487]	2.17
Vaginal Secretions	1284 [742 – 2223]	8 hr	58,562 [32,719 – 104,816]	1.72

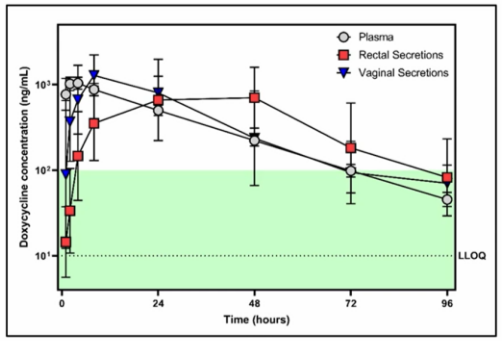
C trachomatis



	Time above MIC value		
	C_{max}	MIC	4x MIC
Plasma	16x	87 hr	44 hr
Rectal Secretions	11x	97 hr	62 hr
Vaginal Secretions	20x	101 hr	45 hr

Minimum Inhibitory Concentrations (MIC):
C trachomatis MIC_{90} = 64 ng/mL Zheng *Sex Transm Dis* 2015

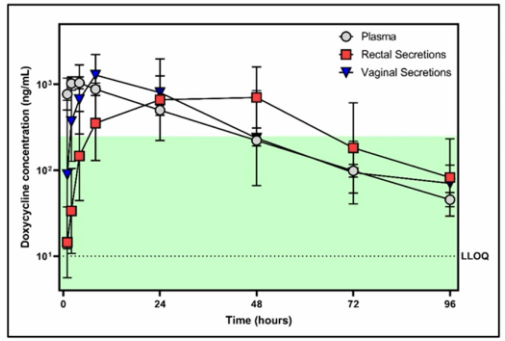
T pallidum



	Time above MIC value		
	C_{max}	MIC	4x MIC
Plasma	10x	71 hr	32 hr
Rectal Secretions	7x	88 hr	51 hr
Vaginal Secretions	12x	70 hr	38 hr

Minimum Inhibitory Concentrations (MIC):
T pallidum MIC_{90} = 100 ng/mL Edmondson *Antimicrob Agents Chemother* 2020

Sensitive *N gonorrhoeae*



	Time above MIC value		
	C_{max}	MIC	4x MIC
Plasma	4x	45 hr	3 hr
Rectal Secretions	3x	62 hr	NA
Vaginal Secretions	5x	45 hr	11 hr

Minimum Inhibitory Concentrations (MIC):
N gonorrhoeae MIC = 250 ng/mL CDC Antimicrob Resist Susc Test

La doxiciclina se distribuye eficientemente en mucosas expuestas y su concentración se mantiene por encima de la CMI para *C. trachomatis* y *T. pallidum* en mayor medida que para *N. gonorrhoeae* sensible.

DOXYPEP & ANTIMICROBIAL RESISTANCE IN *N. GONORRHOEAE*, COMMENSAL NEISSERIA, & *S. AUREUS*

Anne F. Luetkemeyer, Deborah Donnell, Julia C. Dombrowski, Stephanie Cohen, Cole Grabow, Clare Brown, Cheryl Malinksi, Sharon K. Martens, Alison Cohee, Veronica Viar, Phong Pham, Susan P. Buchbinder, Diane V. Havlir, Connie Celum, Olusegun O. Soge
Research Group: DoxyPEP Study Team

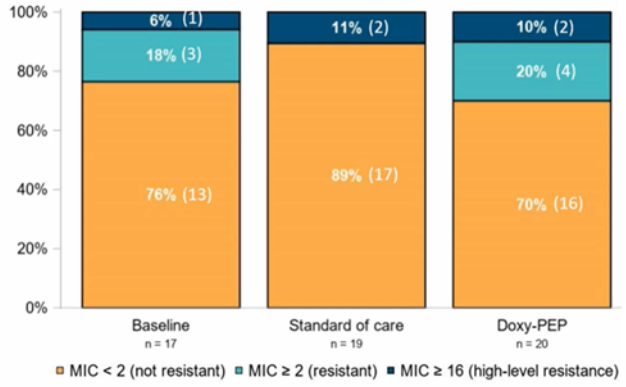
DOXYPEP

EC abierto, aleatorizado 2:1 a doxy-PEP vs. SOC.

En mayo 2022 el DSMB recomendó parar la rama SOC tras demostrarse una reducción de clamidia, sífilis y gonorrea de 65% por trimestre en HSH.

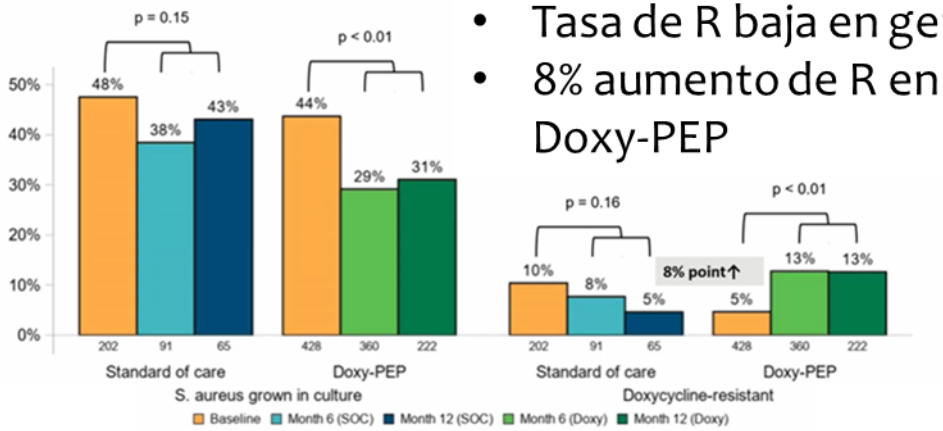
Objetivo: análisis de la aparición de resistencia a doxiciclina de N. gonorrhoeae, S. Aureus y especies no patógenas de neisseria en participantes del estudio doxyPEP.

Tetracycline resistance (TCN-R) in incident GC with culture data



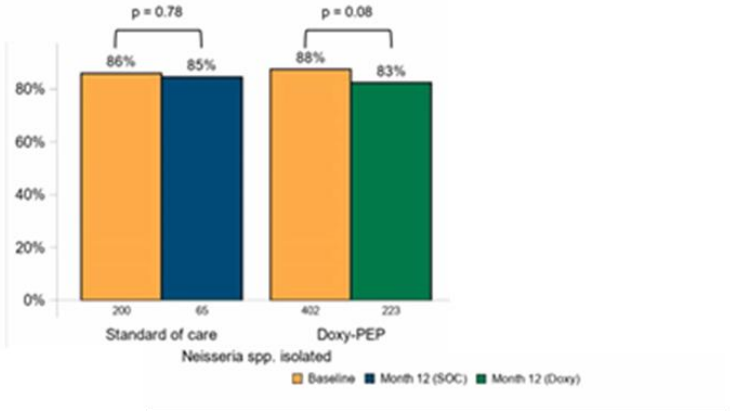
- Incidencia similar en basal y Doxy-PEP.
- Mayor incidencia en Doxy-PEP que en SOC.

S. aureus: 8% absolute increase in doxycycline resistance (doxy-R) in doxy-PEP arm

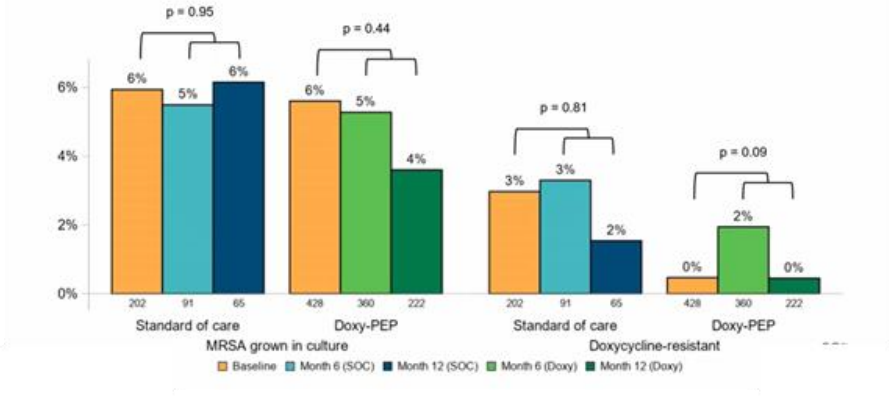


- Tasa de R baja en general.
- 8% aumento de R en rama Doxy-PEP

Commensal *Neisseria* in oropharynx: High rates of colonization & no change with doxy-PEP use



MRSA: No change in doxycycline resistance with doxy-PEP



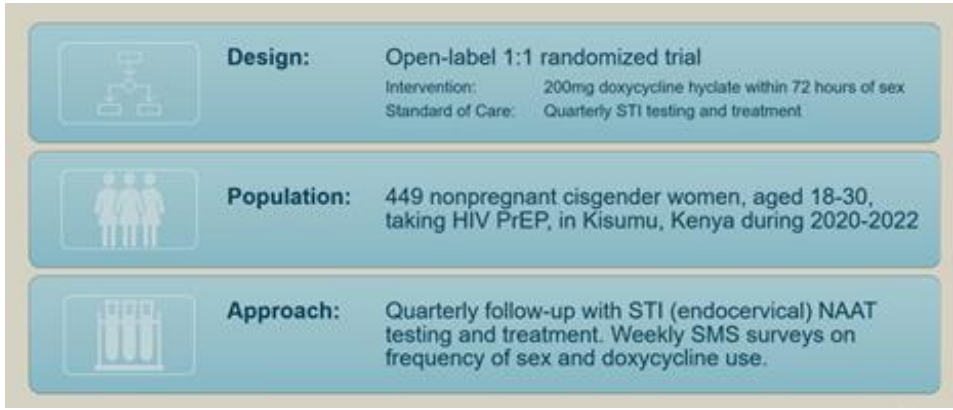
“No encontramos un aumento marcado de la resistencia a la doxiciclina”

CROI 2023, Oral Poster 120

DOXYCYCLINE POSTEXPOSURE PROPHYLAXIS FOR PREVENTION OF STIs AMONG CISGENDER WOMEN

Jenell Stewart, Kevin Oware, Deborah Donnell, Lauren R. Violette, Josephine Odoyo, Caitlin W. Scoville, Olusegun O. Soge, Victor Omollo, Felix Mogaka, Fredricka A. Sesay, R. Scott McClelland, Elizabeth A. Bukusi, Jared M. Baeten
Research Group: the dPEP Kenya Study Team

Objetivo: análisis de la incidencia de clamidia, sífilis y gonorrea



Características basales

	Doxycycline PEP (N=224)	Standard of Care (N = 225)
Age, Median [IQR], years	24 [22-27]	24 [22-27]
Months on HIV PrEP, Median [IQR]	7.5 [4.1-14.9]	7.2 [3.7-13.8]
	% (n)	% (n)
Bacterial STI at baseline	18% (40)	18% (40)
Chlamydia trachomatis	13% (30)	15% (33)
Neisseria gonorrhoeae	5% (10)	3% (7)
Treponema pallidum	0% (0)	1% (2)

Overall STI incidence of 27 per 100 person-years

Analysis	Endpoint	Total	PEP (N=224)	SOC (N=225)	RR	95% CI	P-value
Intention to Treat	All STIs	109	50	59	0.88	0.60-1.29	0.51
	Chlamydia	85	35	50	0.73	0.47-1.13	0.16
	Gonorrhea	31	19	12	1.64	0.78-3.47	0.19

El uso de doxi-PEP en mujeres cis no redujo la incidencia de ITS

Posibles motivos

Diferencias entre tejidos (cervical, uretral, rectal, faríngeo).
Distribución de microorganismos resistentes.
Adherencia a la Doxy-PEP.

CROI 2023, Oral Poster 121

20ª edición

POSTCROI

Una actualización de la "30th Conference on Retroviruses and Opportunistic Infections"

¡ GRACIAS!

Ana C. Silva-Klug

Unitat de VIH i MTS

(Servei de Malalties Infeccioses)

Hospital Universitari de Bellvitge

Bellvitge Hospital Universitari

Institut Català de la Salut

VIH