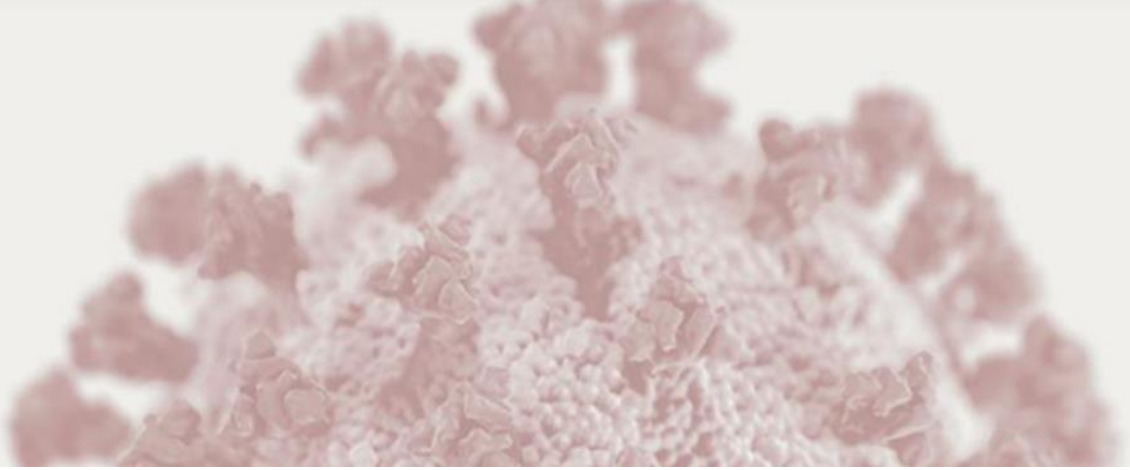
19ª edición

POSTCROI

Una actualización de la "29th Conference on Retroviruses and Opportunistic Infections"



Enfermedades Oportunistas y Virus del Papiloma Humano

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

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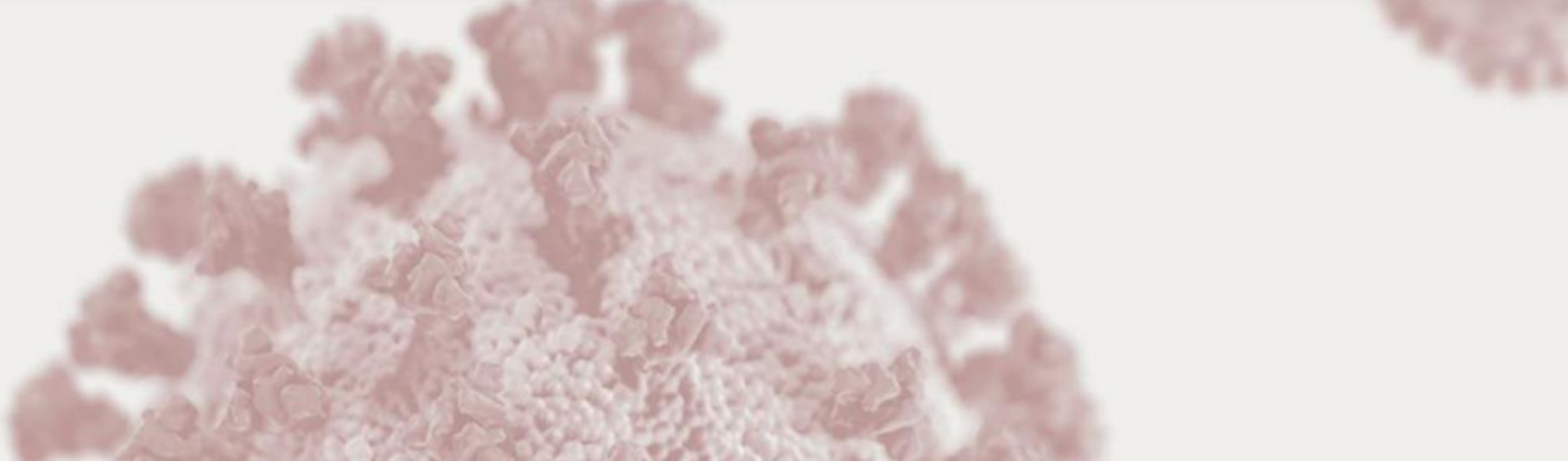


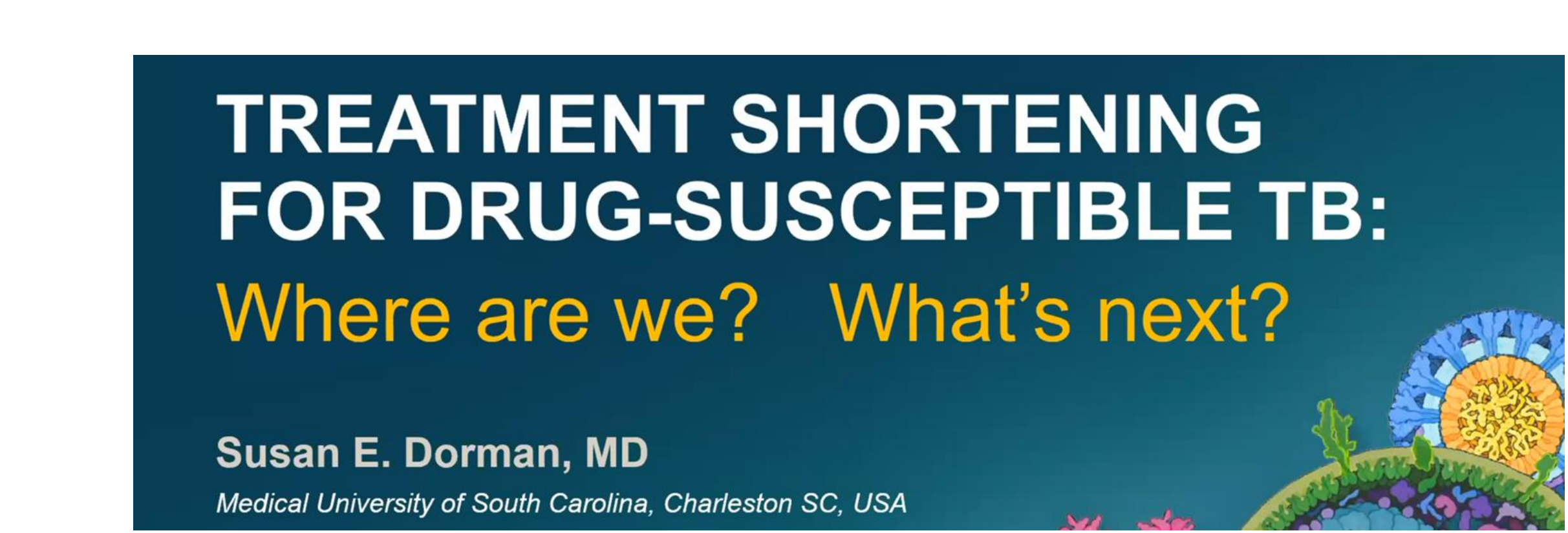
Enfermedades oportunistas

TREATMENT SHORTENING FOR DRUG-SUSCEPTIBLE TB:

Where are we? What's next?

Susan E. Dorman, MD

Medical University of South Carolina, Charleston SC, USA



The NEW ENGLAND JOURNAL of MEDICINE

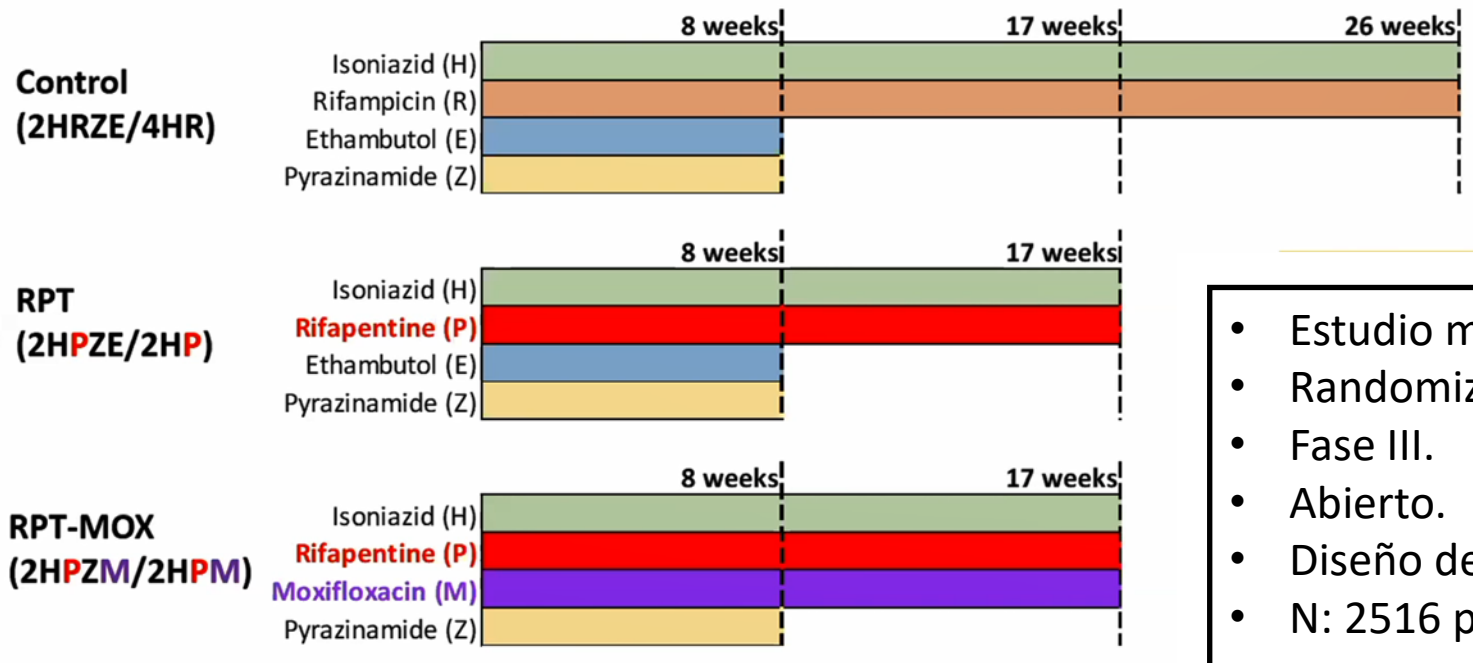
ORIGINAL ARTICLE

Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

S.E. Dorman, P. Nahid, E.V. Kurbatova, P.P.J. Phillips, K. Bryant, K.E. Dooley, M. Engle, S.V. Goldberg, H.T.T. Phan, J. Hakim, J.L. Johnson, M. Lourens, N.A. Martinson, G. Muzanyi, K. Narunsky, S. Nerette, N.V. Nguyen, T.H. Pham, S. Pierre, A.E. Purfield, W. Samaneka, R.M. Savic, I. Sanne, N.A. Scott, J. Shenje, E. Sizemore, A. Vernon, Z. Waja, M. Weiner, S. Swindells, and R.E. Chaisson, for the AIDS Clinical Trials Group and the Tuberculosis Trials Consortium

Dorman S, et al. 2021. NEJM

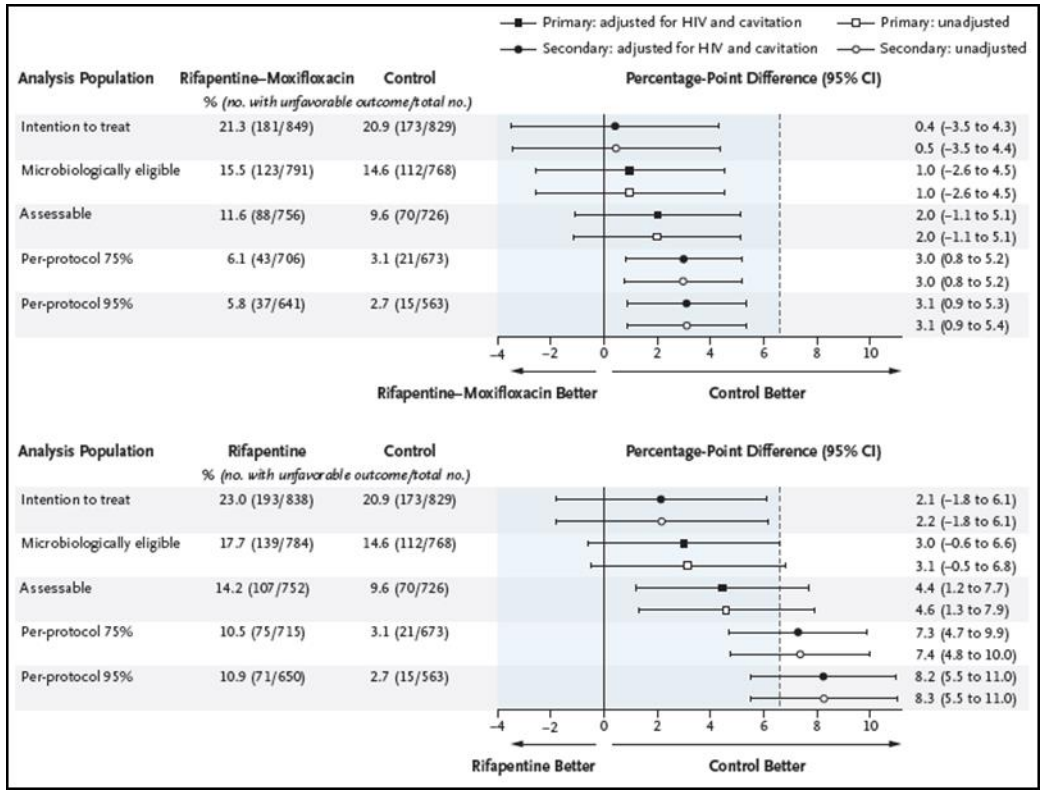
CDC TBTC Study 31 / NIH ACTG 5349:
does high dose daily rifapentine, with or without moxifloxacin, allow treatment shortening to 4 months for DS-PTB in adults & adolescents?

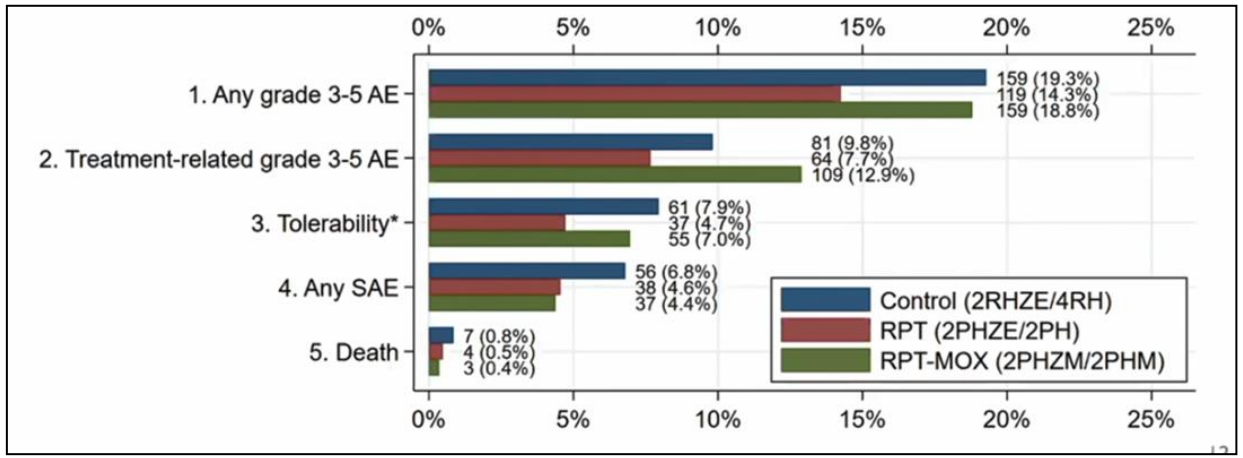


- Estudio multicéntrico.
- Randomizado.
- Fase III.
- Abierto.
- Diseño de no inferioridad.
- N: 2516 participantes.

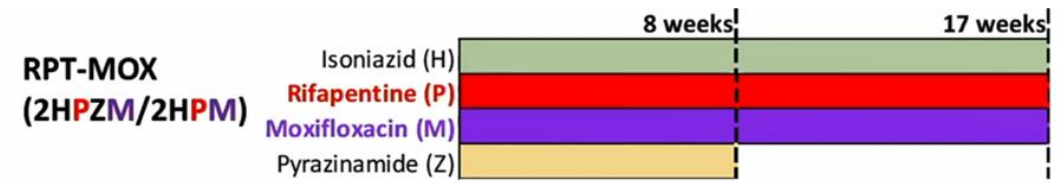
Objetivo primario: supervivencia libre de tuberculosis a los 12 meses

Dorman S, et al. 2021. NEJM





La rama RPT/MOX alcanzó criterio de no inferioridad y resultó una opción segura y bien tolerada.



Dorman S, et al. 2021. NEJM

PATIENT-LEVEL POOLED ANALYSIS OF STUDY 31/A5349, A STRATIFIED MEDICINE APPROACH

Vincent Chang
PhD Candidate
vincent.chang@ucsf.edu

OTHER AUTHORS: Marjorie Imperial, Patrick Phillips, Wendy Carr, Ekaterina Kurbatova, Andrew Vernon, Marc Weiner, Kelly E. Dooley, Susan Dorman, John L. Johnson, Susan Swindells, Richard E. Chaisson, Payam Nahid, Rada M Savic, and the AIDS Clinical Trials Group and the Tuberculosis Trials Consortium

INTRODUCTION

Study 31/A5349 (NCT02410772) was a phase 3 randomized controlled trial assessing 4-month regimens of once-daily isoniazid, rifapentine, and pyrazinamide plus moxifloxacin (HPZ*M*) or ethambutol (HPZE) compared to the 6-month isoniazid, pyrazinamide, ethambutol, and rifampicin standard treatment for drug-sensitive tuberculosis (TB). While HPZM arm successfully demonstrated noninferiority, HPZE arm did not. Nonetheless, 82% of participants receiving HPZE were cured. Through a pooled analysis of patient-level data, we defined phenotypes that are hard to treat and populations who may be treated with the 4-month HPZE regimen.

METHODS

We included 2343 patients in the microbiologically eligible population from all arms in the analysis. Parametric time-to-event analysis identified significant predictors for TB-related unfavorable outcomes, which were used to define low, moderate, and high-risk groups. Post hoc noninferiority analyses were performed on HPZE and HPZM regimens stratified by risk group.

RESULTS

Major risk factors for TB-related unfavorable outcomes in both experimental arms were rifapentine exposure and baseline disease burden, as measured by GeneXpert cycle threshold and disease extent on chest x-ray. Low risk was defined as GeneXpert ≥ 18 ct and disease extent < 50%, with 5% and 3% unfavorable outcomes when treated with HPZE and HPZM regimens respectively (Fig 3). The moderate risk group in HPZM is defined as (GeneXpert ≥ 18 ct and disease extent ≥ 50%) or (GeneXpert < 18 ct and disease extent < 50%) with 4.5% unfavorable outcomes. For HPZE, patients with HIV or diabetes were at higher risk of unfavorable outcomes compared to HIV-negative or non-diabetic patients (HIV: 16.1% unfavorable outcomes vs 8.9%, HR = 1.95 (95% CI: 1.03, 3.7); Diabetes: 43% vs 8.9%, HR = 6.53 (CI: 2.8, 15)). Therefore for HPZE, patients living with HIV or diabetes presenting with moderate-risk baseline disease characteristics were defined as high-risk. The high-risk group for HPZM was defined as GeneXpert < 18 ct and disease extent ≥ 50% with 11.6% unfavorable outcomes. For HPZE, the high-risk group had 19.1% unfavorable outcomes which consisted of these patients along with the aforementioned patients living with HIV or diabetes. Post hoc noninferiority analyses of HPZM and HPZE regimens stratified by risk group demonstrated noninferiority in their respective low and moderate risk groups, while neither experimental regimen demonstrated noninferiority in the high-risk groups (Fig 1) .

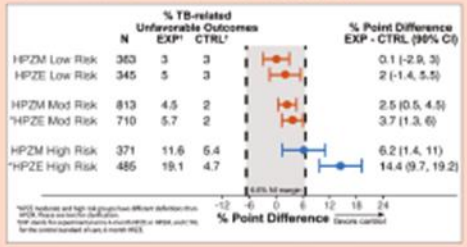


Figure 1. Post-hoc noninferiority analysis of HPZE and HPZM risk groups. Low and moderate risk patients can be treated successfully with 4M HPZE.

THE VAST MAJORITY (70%) OF STUDY 31 DRUG-SENSITIVE TUBERCULOSIS PATIENTS MAY BE TREATED WITH 4-MONTH RIFAPENTINE BASED (HPZE) REGIMEN.

00661

LONGER HPZM TREATMENT DURATIONS AND/OR HIGHER DOSES SHOULD BE FURTHER INVESTIGATED FOR PATIENTS WITH HIGH DISEASE BURDEN.

UCSF University of California San Francisco

Savic Lab

TBTC Tuberculosis Trials Consortium

RISK GROUPS DEFINITIONS

Figure 2. Treatment selection decision tree. Low, moderate, and high-risk groups were defined using most significant baseline predictors for treatment outcome: GeneXpert, chest x-ray disease extent, history of diabetes, and HIV status. Percentage of S31 patients in each risk group are in parantheses in each colored risk group box. Low-risk group and moderate-risk group population were noninferior to equivalent HRZE population (Fig 1). High-risk group did not achieve noninferiority when compared to high-risk HRZE population and therefore higher doses and/or longer treatment durations should be further investigated for these patients. Kaplan Meier curves of stratified by risk group and regimen can be found below in

*Moderate-risk patients living with HIV or diabetes are considered high-risk for HPZE and therefore should not be treated with HPZE. However, treated with HPZM these patients have noninferior outcomes when compared to HRZE standard of care.

KAPLAN MEIER ESTIMATES

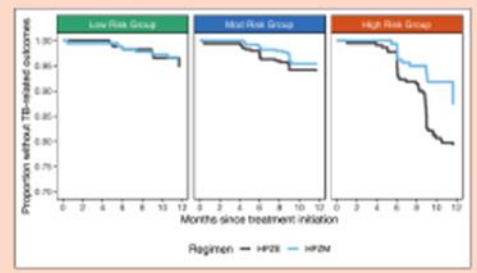


Figure 3. Moxifloxacin is crucial in high-risk group population. Risk group Kaplan-Meier estimates stratified by regimen. The substitution of ethambutol for moxifloxacin is increasingly important going from low to moderate to high-risk group population. In the high-risk group, 11.6% of HPZM patients experienced TB-related unfavorable outcomes compared to 19.1% of HPZE patients at 12 months.

Our post-hoc analysis demonstrates that the HPZE regimen can also be used for the vast majority of patients that present with low or moderate risk characteristics. However, patients living with HIV and/or diabetes should be treated with HPZM.

Although high-risk patients have marked improvement in outcomes with moxifloxacin, further interventions should be investiaged as these patients did not achieve noninferiority compared with equivalent HRZE patients.

PATIENT-LEVEL POOLED ANALYSIS OF STUDY 31/A5349, A STRATIFIED MEDICINE APPROACH

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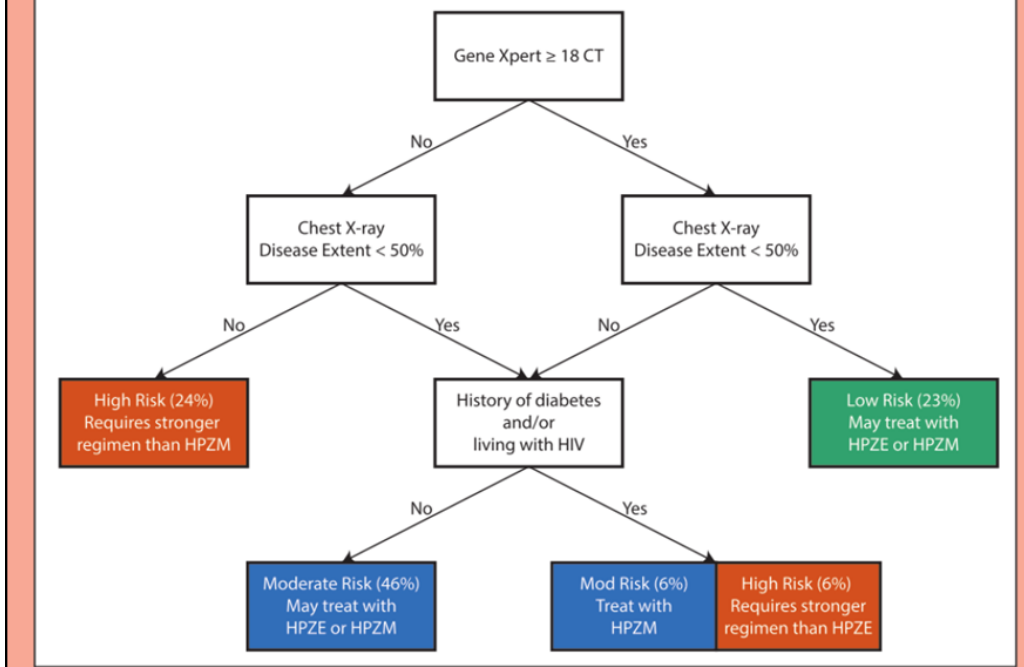
RISK GROUPS DEFINITIONS



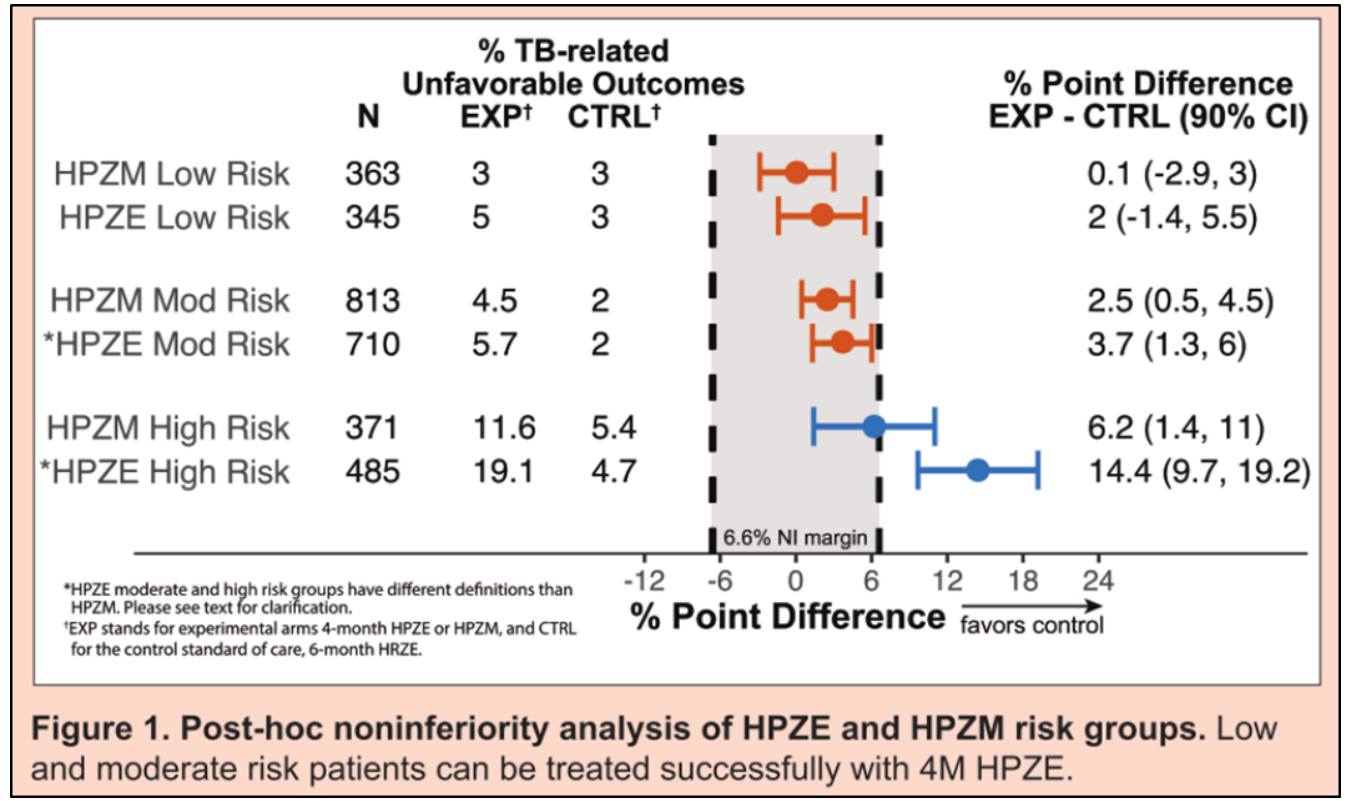
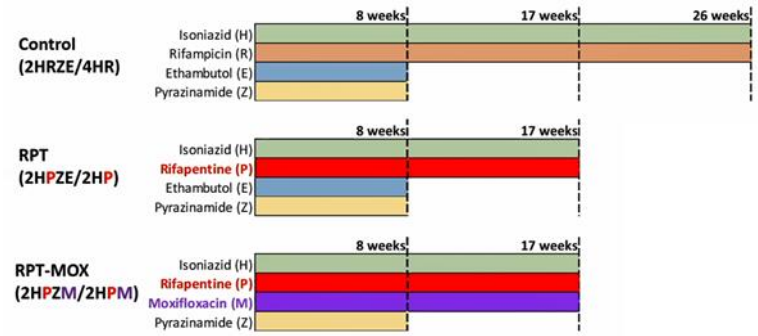


Figure 1. Post-hoc noninferiority analysis of HPZE and HPZM risk groups. Low and moderate risk patients can be treated successfully with 4M HPZE.



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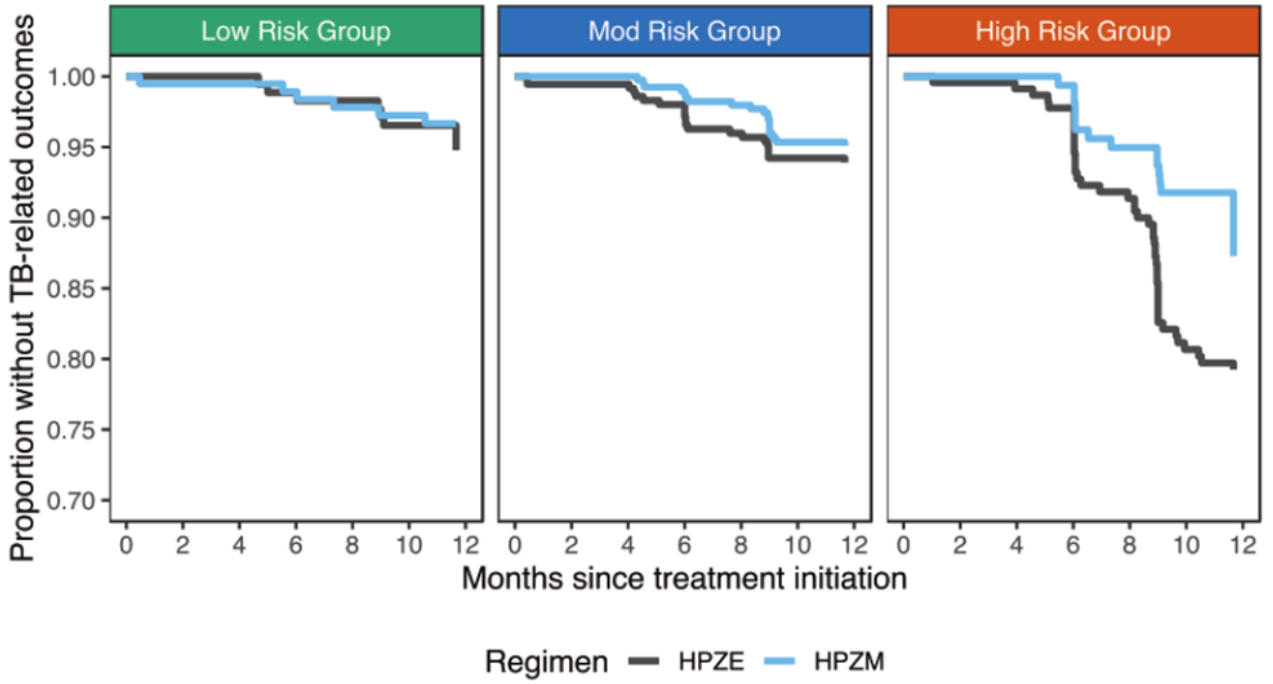
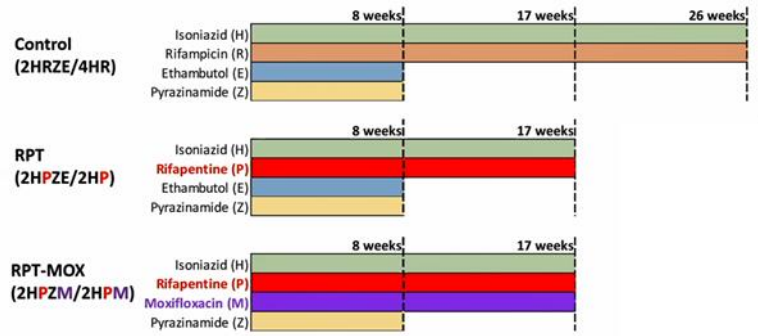


CONCLUSIONES

- Los regímenes de 4 meses basados en RPT pueden ser usado en la gran mayoría de los pacientes que presentan riesgo bajo o moderado.
- Pacientes con VIH y/o DM, deberían recibir tratamiento con RPT-MOX.
- En pacientes de alto riesgo no se alcanzó la no inferioridad comparado con SoC.



CROI 2022

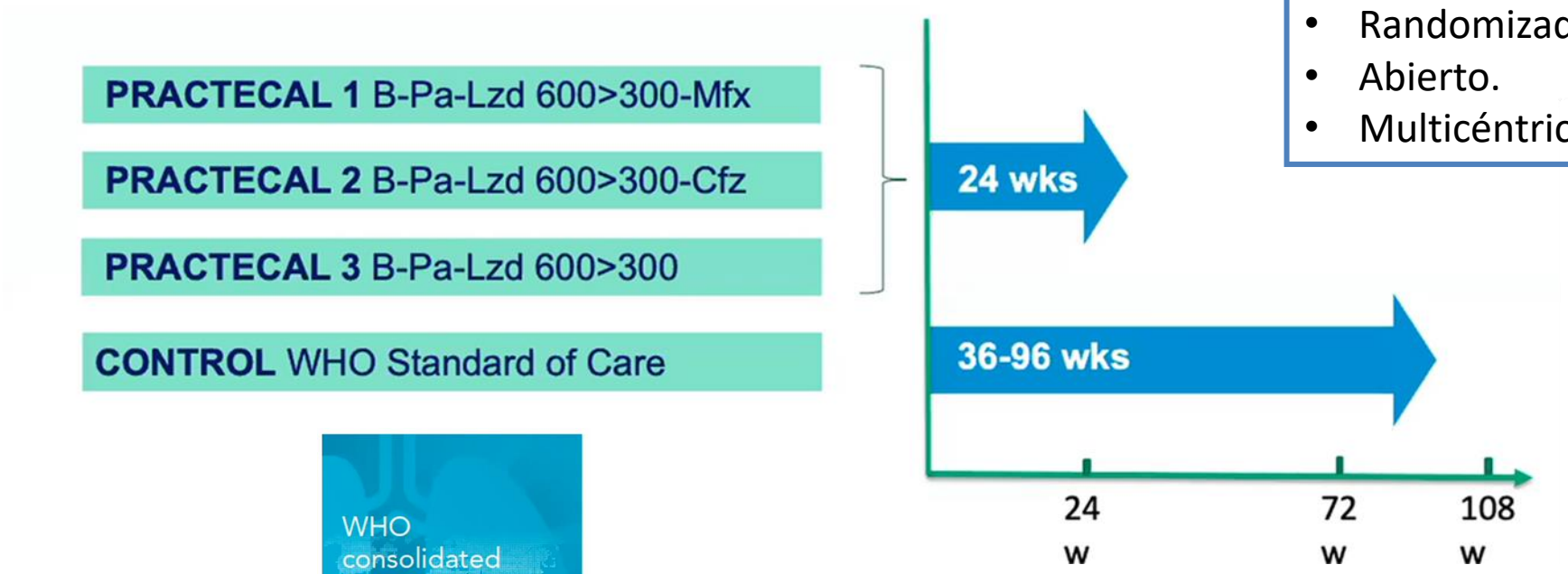
TB-PRACTECAL RESULTS: 24 WEEK ALL-ORAL REGIMENS FOR RIFAMPICIN RESISTANT TUBERCULOSIS

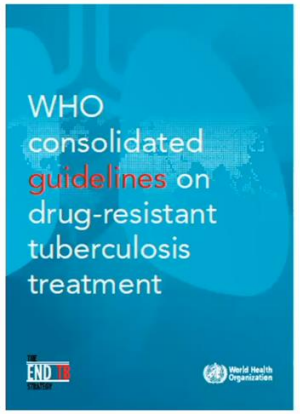
Dr Bern-Thomas Nyang'wa

Médecins sans Frontières
Amsterdam, the Netherlands

Evaluación de la eficacia y seguridad de regimenes que contienen BEDAQUILINA, PRETOMANID y LINEZOLID para el tratamiento de TBC pulmonar resistente a rifampicina confirmada microbiológicamente.

- EC Fase II-III
- Randomizado.
- Abierto.
- Multicéntrico.





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En Marzo 2021 el DSMB recomendó no continuar randomización

Número de pacientes incluídos

	Control	PRACTECAL arm 1 (BPaLM)	PRACTECAL arm 2 (BPaLC)	PRACTECAL arm 3 (BPaLM)
Total screened	680			
Total randomised	152	151	126	123
ITT population	150	151	126	122
ITT population (72 weeks)	73	72	72	69
mITT population (72 weeks)	66	62	64	60
PP population (72 weeks)	33	57	58	52

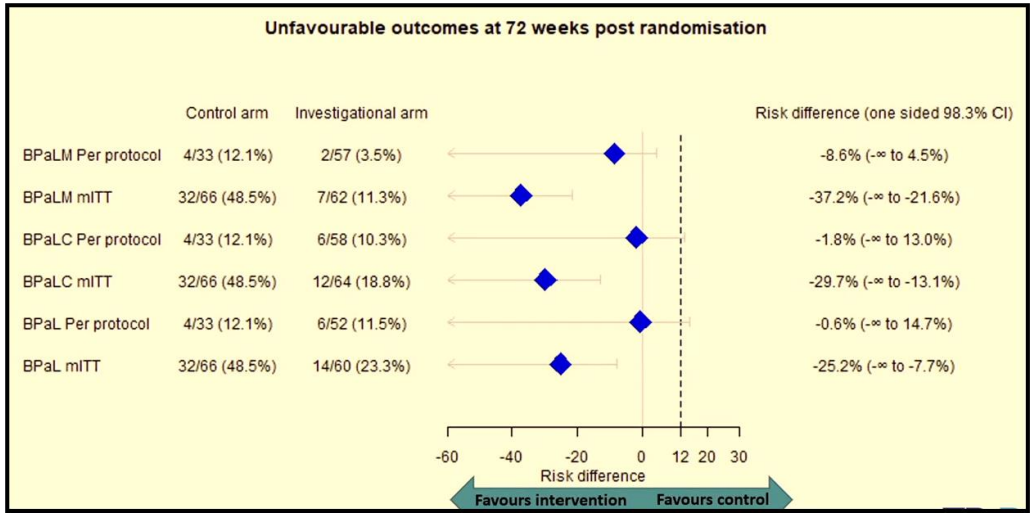
mITT: participantes con número de randomización y medicación administrada al menos una vez, con cultivo de esputo negativo y/o TBC sensible a rifampicina a la inclusión.

Características basales

	Control	Practecal arm-1 BPaLM	Practecal arm-2 BPaLC	Practecal arm-3 BPaL
Total number	66	62	64	60
Age (years), median (range)	36 (19 to 71)	34 (18 to 61)	29 (19 to 63)	34 (18 to 62)
Female, n (%)	33 (50.0)	26 (41.9)	24 (37.5)	28 (46.7)
BMI (kg/m²), median (IQR)	19.2 (17.3 to 22.0)	19.8 (18.1 to 22.1)	18.8 (17.4 to 22.0)	20.5 (18.2 to 22.8)
HIV positive, n (%)	15 (22.7)	14 (22.6)	14 (21.9)	14 (23.3)
CD4 count (cells/µL), median (IQR)	317 (154 to 383)	268 (182 to 364)	394 (112 to 511)	283 (153 to 424)
Smear positive, n (%)	50 (75.8)	40 (64.5)	43 (67.2)	45 (75.0)
Cavity present, n (%)	47 (71.2)	33 (53.2)	39 (60.9)	41 (68.3)
Fluoroquinolone resistant, n (%)	18 (27.7)	17 (28.3)	16 (25.8)	19 (33.9)
QTcF (ms), mean (SD)	398 (18)	396 (18)	393 (20)	398 (18)
ALT (IU/l), median (IQR)	20 (15 to 27)	18 (14 to 27)	18 (15 to 27)	19 (14 to 27)

Resultados de eficacia

	Control	Practecal arm-1 BPaLM	Practecal arm-2 BPaLC	Practecal arm-3 BPaL
Number in mITT population 2	66	62	64	60
Number with no unfavourable outcome	34 (51.5%)	55 (88.7%)	52 (81.3%)	46 (76.7%)
Number with an unfavourable outcome	32 (48.5%)	7 (11.3%)	12 (18.8%)	14 (23.3%)
Risk difference (one-sided 98.3% confidence interval)		-37.2% (-∞ to -21.6%)	-29.7% (-∞ to -13.1%)	-25.2% (-∞ to -7.7%)
Non-inferiority p-value (non-inferiority margin of +12%)		p<0.0001	p<0.0001	p<0.0001
Superiority p-value		p<0.0001	p<0.0001	p = 0.001
Risk ratio (one-sided 98.3% confidence interval)		0.23 (-∞ to 0.52)	0.39 (-∞ to 0.71)	0.48 (-∞ to 0.85)
Deaths	2 (3.0%)	0 (0%)	1 (1.6%)	0 (0%)
Early discontinuations	28 (42.4%)	5 (8.1%)	6 (9.4%)	8 (13.3%)
Adherence issues	3	0	2	2
Adverse event	17	5	4	5
Not meeting inclusion/exclusion criteria	0	0	0	1
Withdrew consent whilst still on treatment	6	0	0	0
Other	2	0	0	0
Treatment failure	0 (0%)	0 (0%)	1 (1.6%)	0 (0%)
Lost to follow-up at 72 weeks	2 (3.0%)	2 (3.2%)	3 (4.7%)	3 (5.0%)
Recurrence	0 (0%)	0 (0%)	1 (1.6%)	3 (5.0%)



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CONCLUSIONES

- 24 semanas de tto oral con regimenes basados en bedaquilina, pretomanid y linezolid, son seguros y eficaces para el tto de TBC resistente a la rifampicina.

- BPALM (rama 1) demuestra no inferioridad *y superiodidad* al SoC.

EFICACIA Rama 1 BPaLM > Rama 2 BPaLC > Rama 3 BPaL > SoC
SEGURIDAD Rama 1 BPaLM > Rama 3 BPaL > Rama 2 BPaLC > SoC

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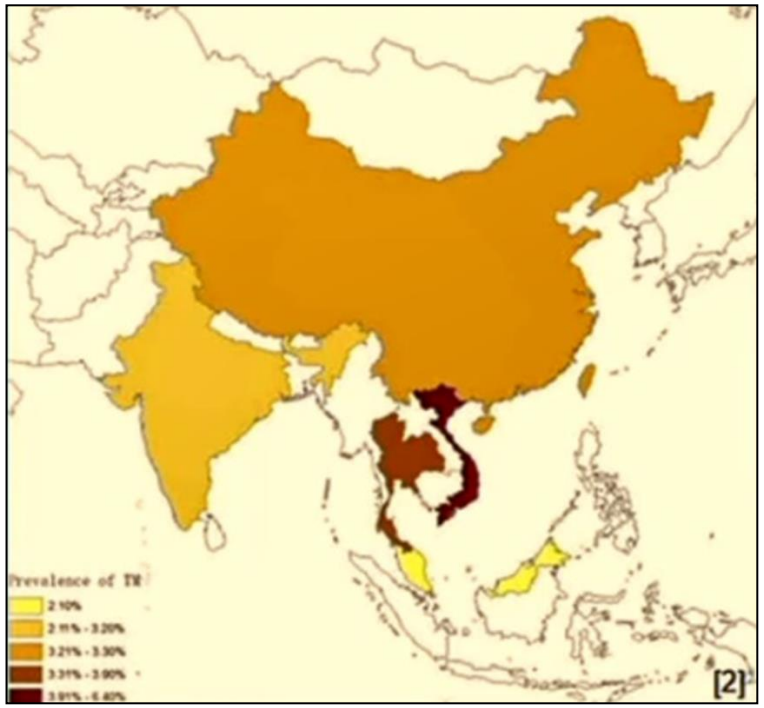
Innovating MDR-TB Treatment

VORICONAZOLE OR AMPHOTERICIN B DEOXYCHOLATE: WHICH IS THE PREFERRED INDUCTION THERAPY?

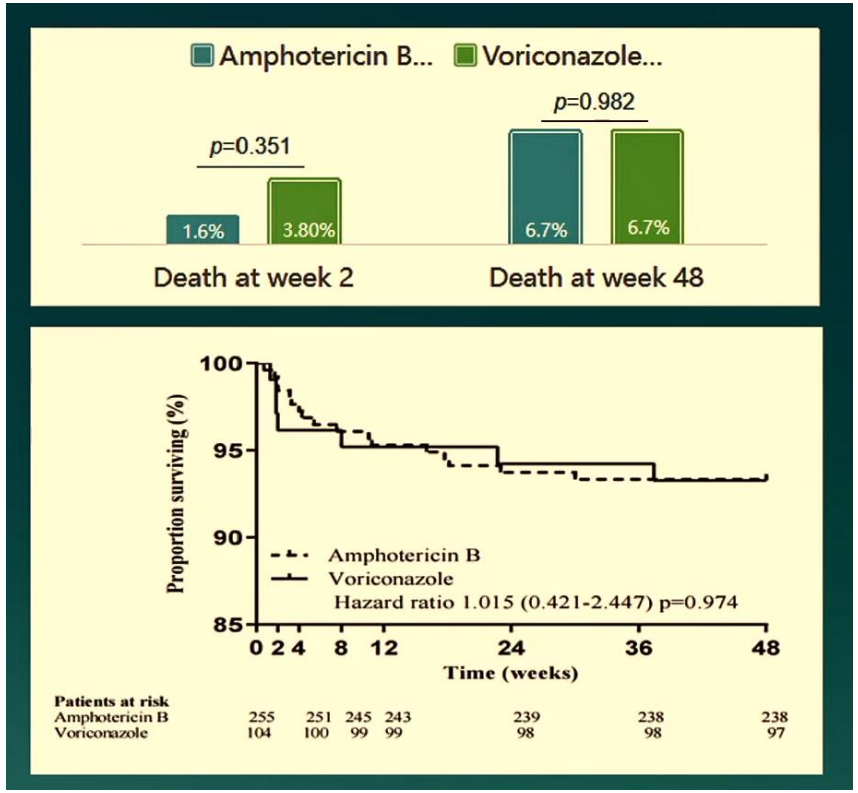
Yaokai Chen

Chongqing Public Health Medical Center, Chongqing, China

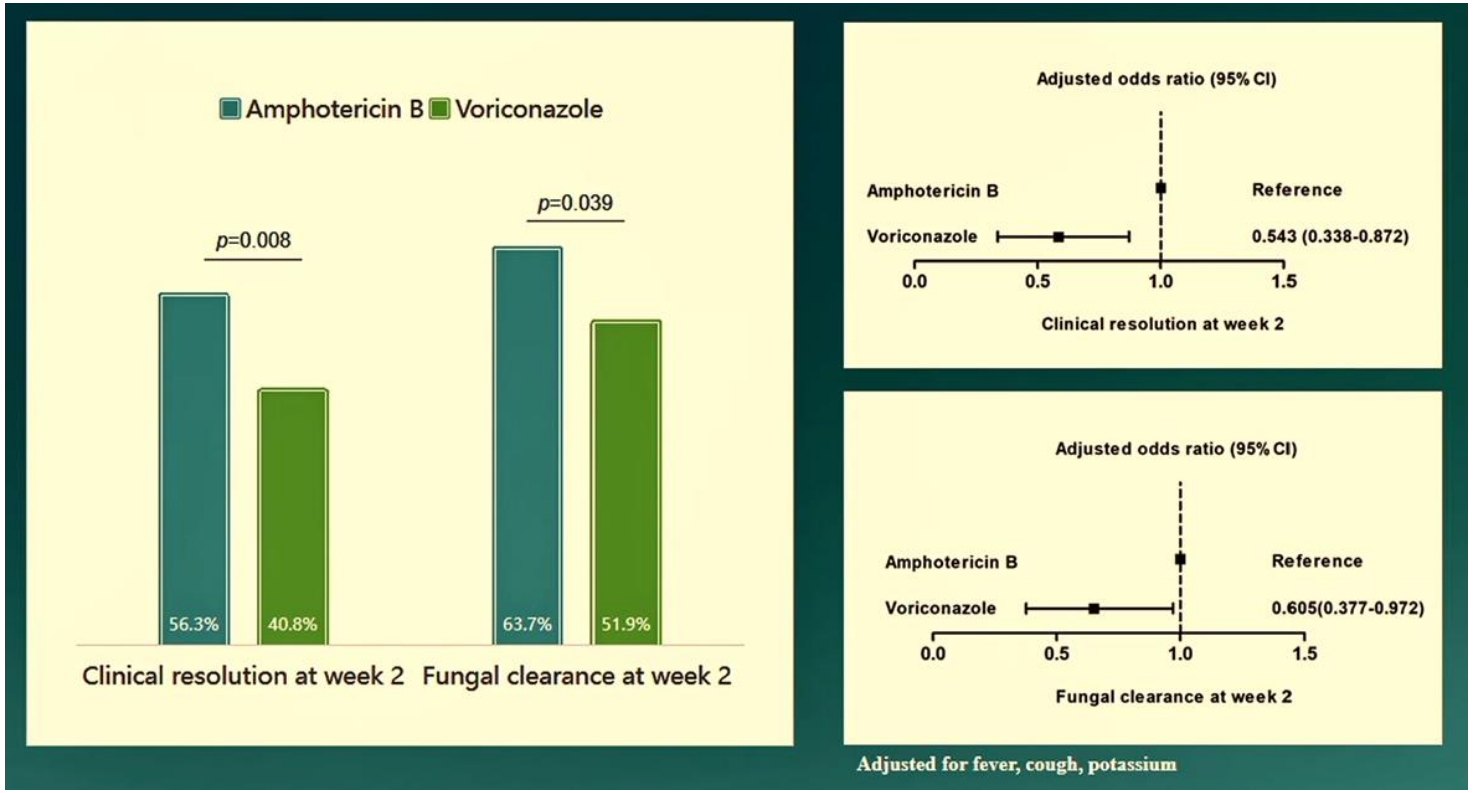


- Estudio de cohortes prospectivo, abierto y multicéntrico (17 hospitales de China).
- Criterios de inclusión: PLWH con diagnóstico de talaromicosis confirmado mediante microscopía convencional, histología o cultivo.

Objetivo primario



Objetivos secundarios



CONCLUSIONES

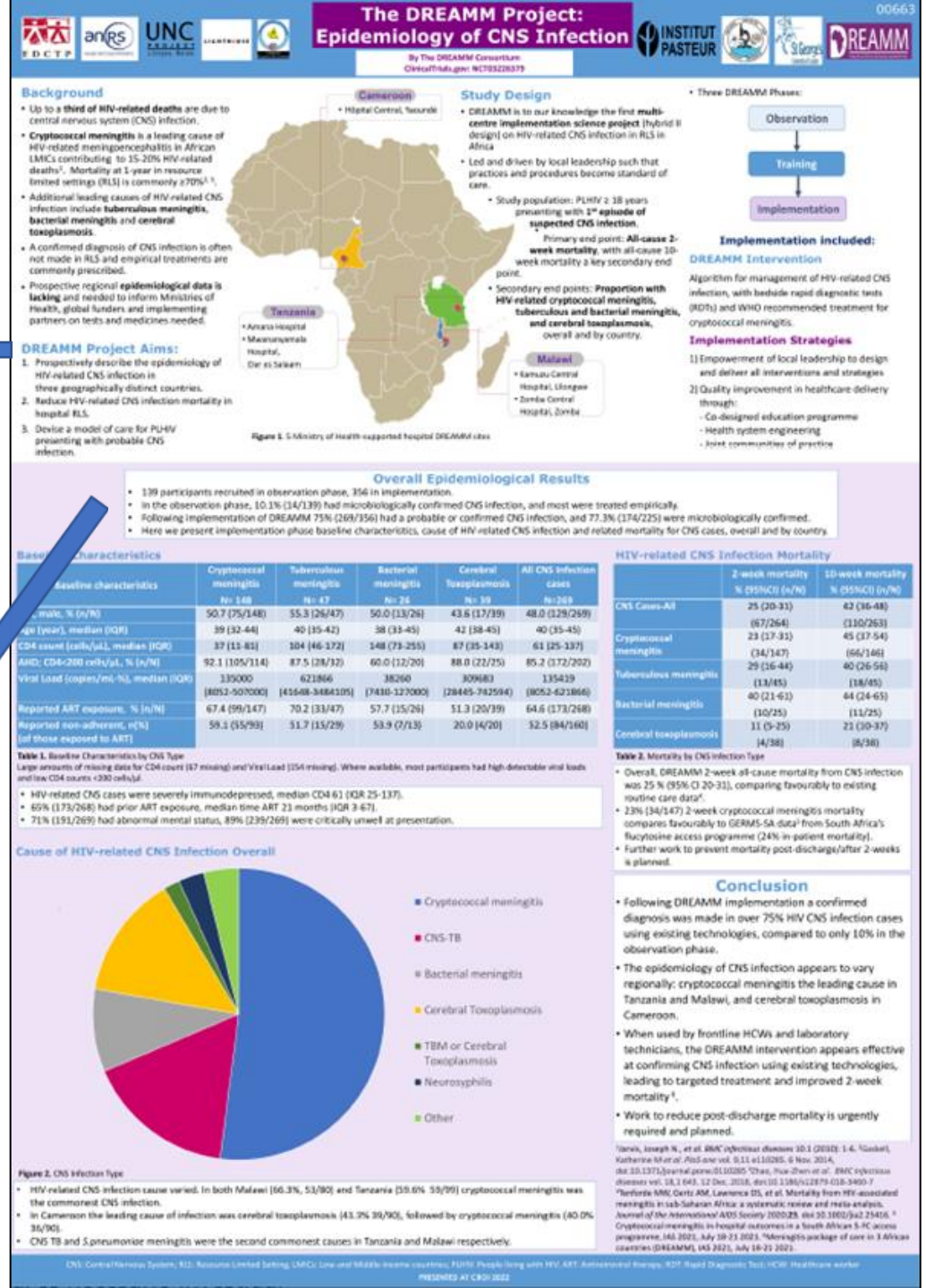
- Similar tasa de mortalidad.
- Con AnfoB desoxicolato se logró aclaramiento fúngico y resolución sintomática más tempranos, pero mayor tasa de mielosupresión.

Objetivos:

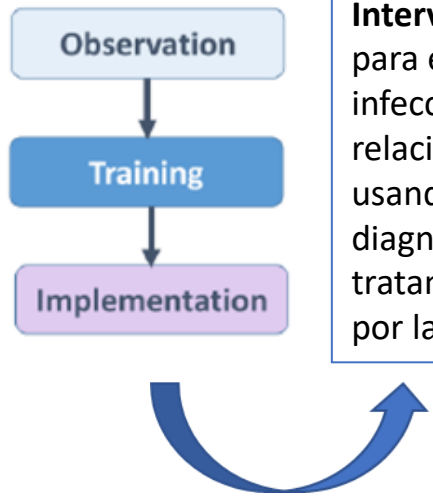
1. Descripción prospectiva de la epidemiología de las infecciones del SNC relacionadas con el VIH en Camerún, Tanzania y Malawi.
2. Reducir la mortalidad intrahospitalaria por estas infecciones.
3. Idear un modelo de cuidados para PLWH que acudan por una probable infección del SNC.

Resultados por fases:

- Reclutamiento:
  - Observación 139.
  - Implementación 356.
- Infección con confirmación micro
  - Observación 10.1%
  - Implementación 77.3%.



Fases



Intervención: algoritmo para el manejo de infecciones del SNC relacionadas con el VIH usando tests de diagnóstico rápido y los tratamientos marcados por la OMS.

CONCLUSIONES

- Tras la implementación de DREAMM más de un 75% de las infecciones del SNC tuvieron diagnóstico.
- La epidemiología de estas infecciones varía por regiones: la meningitis criptocócica fue la causa más frecuente en Tanzania y Malawi y la toxoplasmosis cerebral en Camerún.

La intervención DREAMM demuestra ser efectiva

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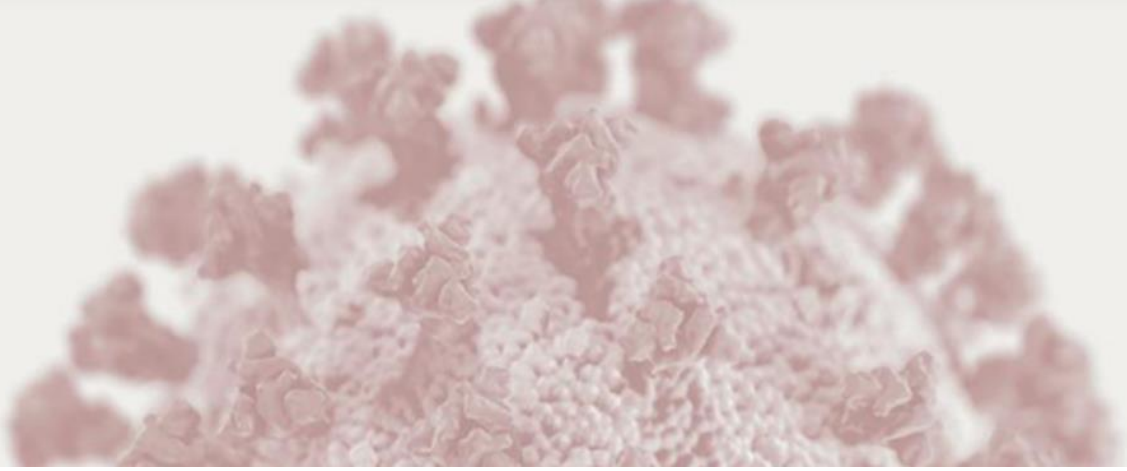


Virus del Papiloma Humano

CROI 2022

Treatment of anal high-grade squamous intraepithelial lesions to prevent anal cancer

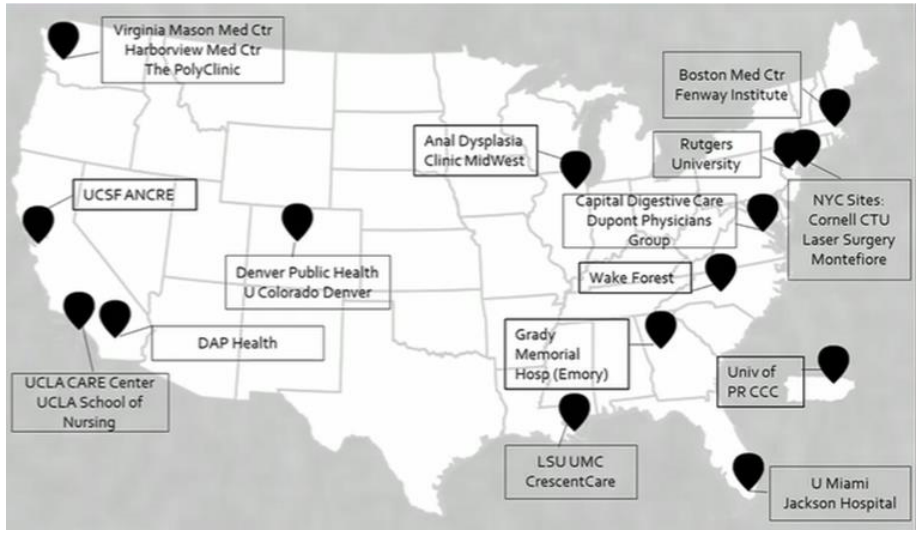
Joel Palefsky, M.D.

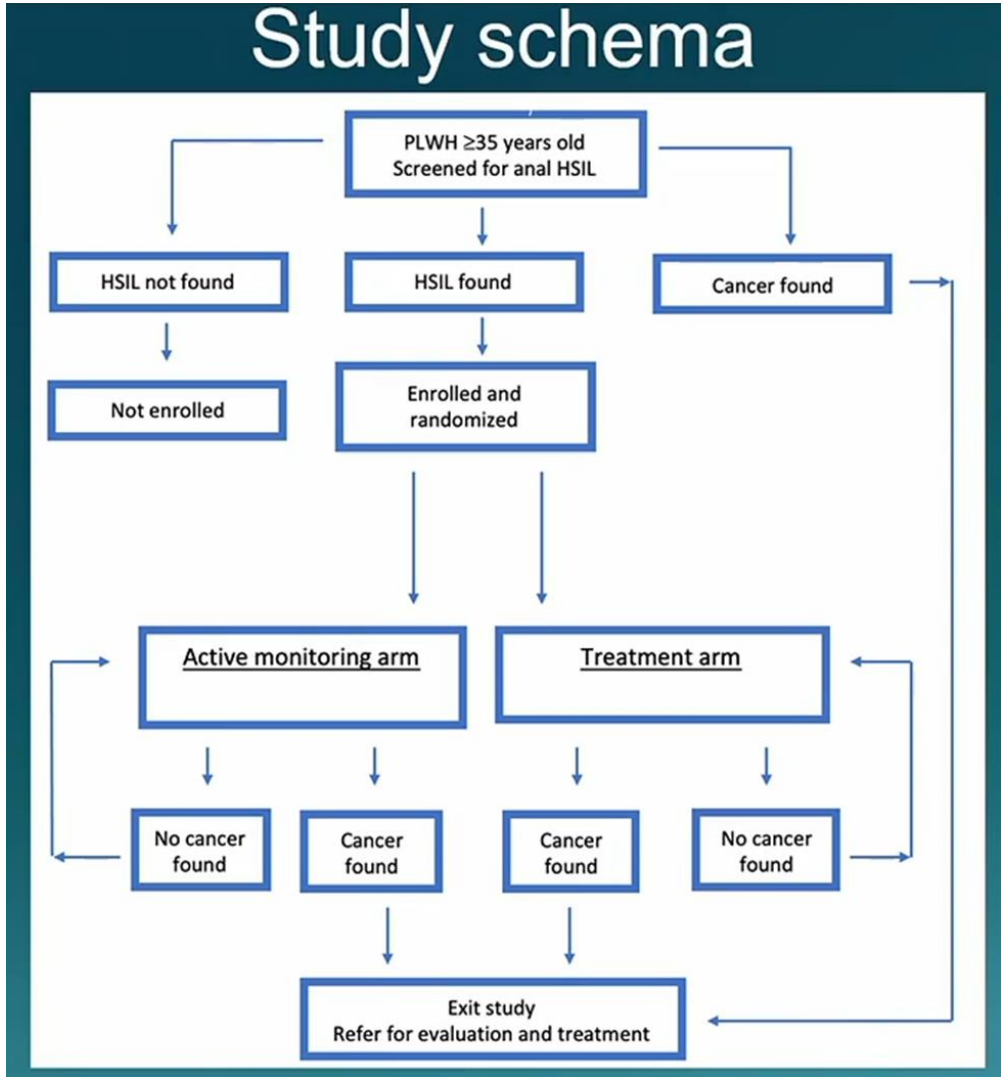
University of California, San Francisco
San Francisco, CA, USA

the ANCHOR study

the ANCHOR study

- Estudio multicéntrico.
- Randomizado.
- N prevista: 2.529 participantes con HSIL por rama para detectar 31 cánceres anales.





Objetivos principales

1. Determinar si el tratamiento de lesiones HSIL es efectivo en la reducción de cáncer anal incidente en PLWH.
2. Determinar la seguridad del tratamiento para HSIL anal.

the ANCHOR study

PACIENTES CRIBADOS

- 10.723 PLWH sept. 2014-agosto 2021
- HSIL histológico: 52.2%
  - 53.3% hombres
  - 45.8% mujeres
- Prevalencia de cáncer anal: 17 (0.16%, 160/100.000 hab./año)

→ El DSMB paró el reclutamiento al alcanzar 32 diagnósticos de cáncer (30 analizados).
→ Media de seguimiento: 25.8 meses.

RAMA DE TRATAMIENTO

Tratamientos recibidos:
- Electrocoagulación 92.2%
- IRC 5.6%
- 5-FU 7%
- Imiquimod 1.2%

Modalidades de tratamiento por paciente:
- 1 modalidad 86%.
- 2 modalidades 10.4%.
- 3 modalidades 1.5%.
- 4 modalidades <0.1%

the ANCHOR study

Demographics of randomized population

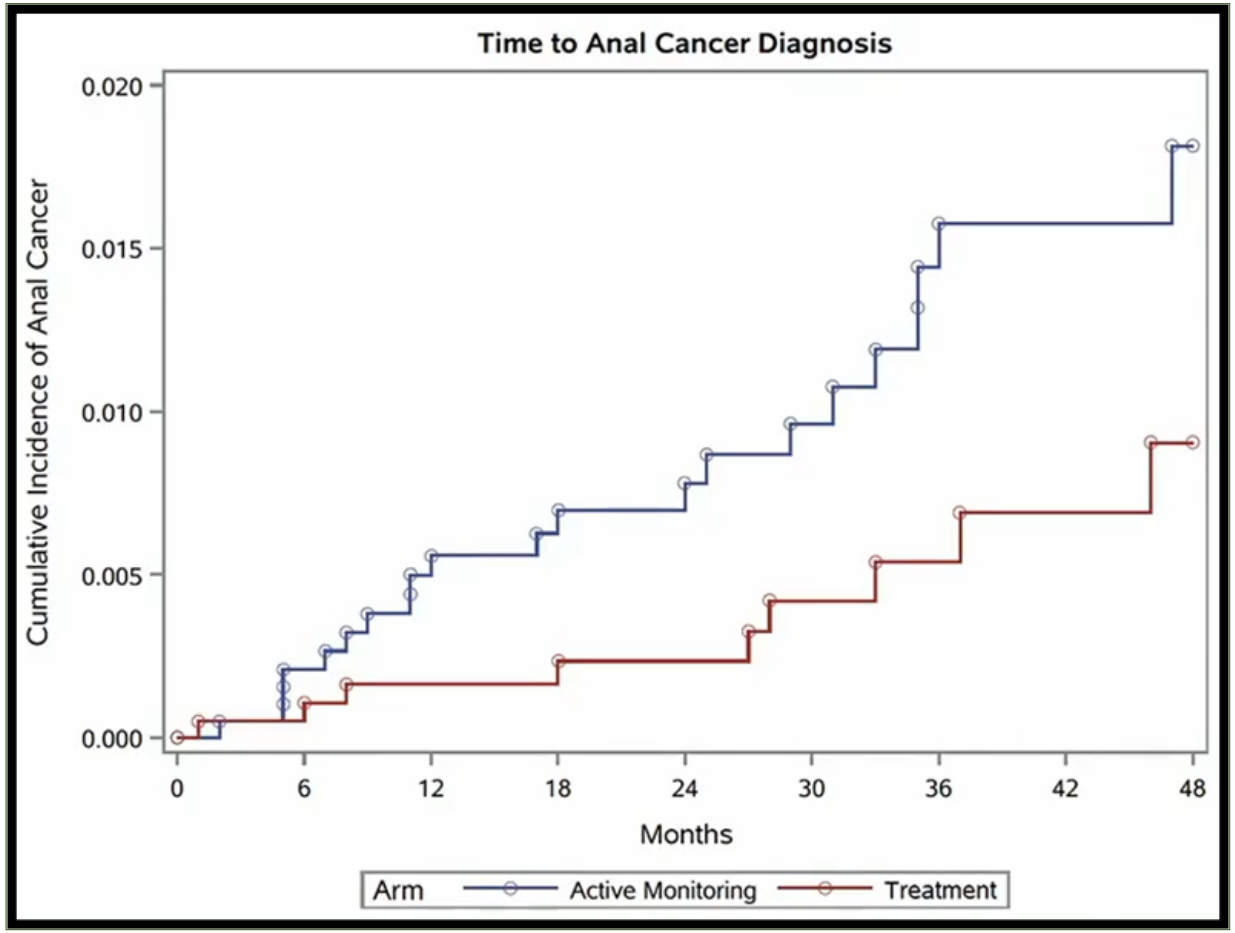
	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Median age at randomization (years, IQR)	51.0 (44.0-57.0)	51.0 (44.0-57.0)	0.79
Median years at randomization since HIV diagnosis (years, IQR)	17.0 (10.0-24.0)	17.0 (10.0-25.0)	0.96
Months of follow-up (median, IQR)	25.3 (11.7 – 42.0)	27.2 (12.0 – 42.1)	0.77
Gender identity N (%)			0.30[2]
Male	1793 (80.5)	1782 (80.3)	
Female	346 (15.5)	365 (16.5)	
Transgender	85 (3.8)	68 (3.1)	
Neither male nor female	2 (0.1)	2 (0.1)	
Decline to answer	1 (0.0)	2(0.1)	

	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Race/ethnicity N (%)			
Non-Hispanic White	695 (31.2)	737 (33.2)	0.37
African-American	935 (42.0)	939 (42.3)	
Hispanic, non-African-American	381 (17.1)	339 (15.3)	
Asian/Pacific Islander	27 (1.2)	29 (1.3)	
Other/Unknown	189 (8.5)	175 (7.9)	
CDC HIV risk group N (%)			
Homosexual	1738 (78.0)	1742 (78.5)	0.74
Heterosexual	532 (23.9)	510 (23.0)	0.48
Injection drug use	152 (6.8)	177 (8.0)	0.14
Transfusion	53 (2.4)	47 (2.1)	0.56
Hemophilia	2 (0.1)	4 (0.2)	0.41
Other high-risk group	34 (1.5)	27 (1.2)	0.37

	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Current smoker N (%)	710 (31.9)	743 (33.5)	0.26
Plasma HIV-1 RNA copies/mL at randomization N (%)			0.27
<50	1852 (83.7)	1800 (81.8)	
51-199	155 (7.0)	160 (7.3)	
200-1000	83 (3.8)	93 (4.2)	
>1000	122 (5.5)	148 (6.7)	
CD4 cells/uL at randomization (median, IQR)	602 (393-827)	607 (410-837)	0.32

	Randomized population N=4,446		P value[1]
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Stratification factors at randomization N (%)			
Nadir CD4 cells/uL			0.88
≤200 cells/uL	1130 (50.7)	1121 (50.5)	
>200 cells/uL	1097 (49.3)	1098 (49.5)	
HSIL size at screening			0.93[8]
>50% of anal canal/perianal region	285 (12.8)	282 (12.7)	
≤50% of anal canal/perianal region	1942 (87.2)	1937(87.3)	

9 cánceres en rama de tratamiento (I: 173/100.000 hab./año).
21 cánceres en rama de seguimiento activo (I: 402/100.000 hab./año).



CONCLUSIONES

- El tratamiento del HSIL es efectivo en reducir la incidencia de cáncer anal.
- Estos datos deberían tenerse en cuenta para incluir el screening y tratamiento de HSIL como SoC.

- Faltan biomarcadores predictores de progresión-regresión de HSIL anal.
- Aún hay que mejorar los tratamientos del HSIL anal.
- Hay que optimizar los algoritmos de cribado de HSIL anal.
- Hay que aumentar los programas de entrenamiento para AAR.
- Estos resultados podrían ser extrapolables a otros grupos de riesgo de cáncer anal.

Results of Anal Dysplasia Screening in People with HIV Younger than 35

00561

Keith Sigel, Michael Gaisa, Yuxin Liu for the Mount Sinai Anal Dysplasia Screening Program

Icahn School of Medicine at Mount Sinai, New York, NY

BACKGROUND

- Anal cancer is a major source of cancer morbidity for people living with HIV (PWH)
- Evolving guidelines recommend initiating anal cancer screening for PWH at age 35.
- Emerging evidence such as the preliminary results of the ANCHOR trial are expanding the evidence base supporting the cancer prevention benefits of anal high-grade squamous intraepithelial lesion (HSIL) treatment.
- Therefore, **the goal of this project** was to determine the outcomes for anal dysplasia screening in people living with HIV (PWH) younger than 35 years of age.

METHODS

- Between January 2014 and August 2020, we identified initial anal cytology and high-risk HPV (hrHPV) test results for all PWH < 35 years who underwent screening in our health system (**n=1,397**).
- We then collected information on subsequent high-resolution anoscopy (HRA)-guided biopsies and linked cancer registry entries for this cohort.
- Using these data we compared screening and HRA outcomes according to demographics, CD4 count, HPV vaccination status and age subgroups.

Characteristic	
Age, n, %	
<25	143 (10)
25-29	596 (43)
30-34	658 (47)
Men, n, %	1,294 (93)
High-risk HPV	
Any	881 (85) [of 1037]
16/18	446 (43) [of 1037]
Cytology results	
Inadequate	238 (17)
Benign	242 (17)
ASCUS	426 (31)
LSIL	327 (24)
HSIL	156 (11)
HPV vaccination prior to screening	388 (28)
Underwent high-resolution anoscopy	710 (51)
Highest biopsy result, n, %	
Benign	122 (17)
LSIL	299 (42)
HSIL	289 (41)

Table. Cohort characteristics for PWH younger than 35 years undergoing anal dysplasia screening.

For PWH <35 years old, high-risk HPV infection, anal cytologic abnormalities and high-grade intraepithelial lesions were very common.

RESULTS

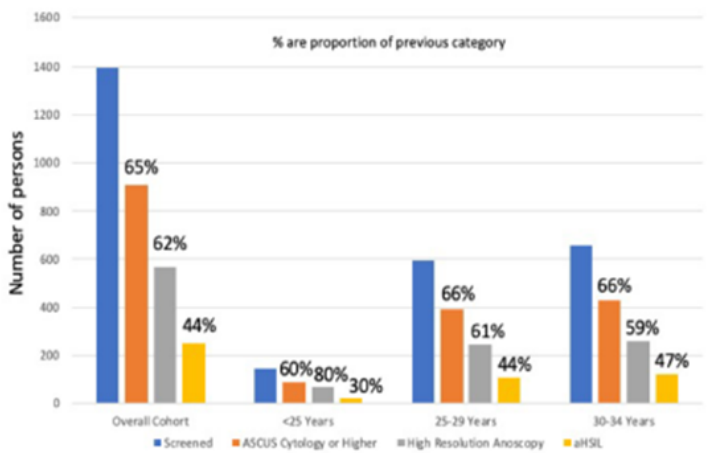


Figure. Anal dysplasia screening results for PWH younger than 35 at initial screen; overall cohort and results stratified by age subgroups.

RESULTS

- Most subjects (66%) had cytologic abnormalities of ASCUS or greater (11% had HSIL cytology).
- 75% of cytology samples were co-tested for hrHPV with 85% of tests positive for any hrHPV type and 43% positive for HPV 16 and/or 18.
- Of subjects with abnormal screening cytology 62% underwent subsequent HRA which yielded anal HSIL in 44%
- Women had substantially less histologic HSIL than men (8% versus 22%; p=0.001).
- There was no significant difference in the proportion of persons diagnosed with histologic HSIL by age subgroup (<25, 25-29, 30-34; p=0.7).
- CD4 count at initial screen was not associated with severity of cytologic abnormalities, hrHPV infection or HSIL diagnosis.
- History of HPV vaccination was associated with lower rates of HPV 16/18 infection (38% in vaccinated versus 45% in unvaccinated, p=0.02) but did not impact rates of overall hrHPV infections or eventual HSIL diagnoses.
- No incident cancers were diagnosed during the follow-up period.

CONCLUSIONS

- High-risk HPV infection, Cytologic abnormalities, and associated histologic HSIL were all common in PWH under age 35.
- HPV 16/18 (along with other high-risk HPV types) were highly prevalent supporting need for continued efforts to vaccinate high-risk persons.
- With emerging evidence regarding the benefits of anal HSIL treatment, the role of screening should be further investigated in this population.

ADDITIONAL KEY INFORMATION

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Results of Anal Dysplasia Screening in People with HIV Younger than 35

00561

Keith Sigel, Michael Gaisa, Yuxin Liu for the Mount Sinai Anal Dysplasia Screening Program
Icahn School of Medicine at Mount Sinai, New York, NY

Determinación de citología anal y VPH-AR en PLWH < 35 años (n=1.397)

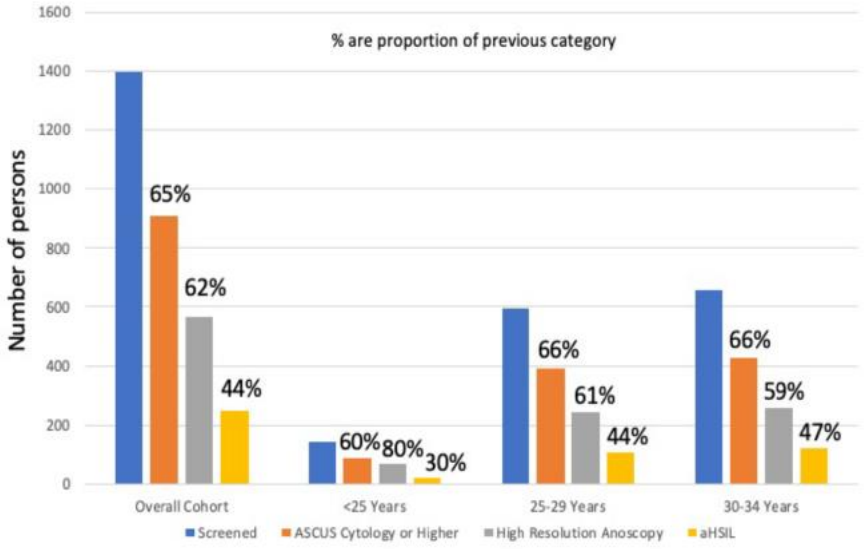


Figure. Anal dysplasia screening results for PWH younger than 35 at initial screen; overall cohort and results stratified by age subgroups.

44% HSIL

CONCLUSIONES

- La infección por VPH-AR, las anomalías citológicas y HSIL histológico asociado son comunes en PLWH <35 años.
- Con el aumento de la evidencia de los beneficios del tratamiento de HSIL, el papel del cribado en este grupo poblacional debería continuar investigándose.

Genital and Anal Cytology-HPV Co-Testing Results From 381 Women Living With HIV

Michael Gaisa MD PhD, Keith Sigel MD PhD, Kevin Weiss MPH, Monica Prasad Hayes MD. Andres Ramirez Zamudio MD, Yuxin Liu MD PhD
Icahn School of Medicine at Mount Sinai, New York, NY, USA

0563

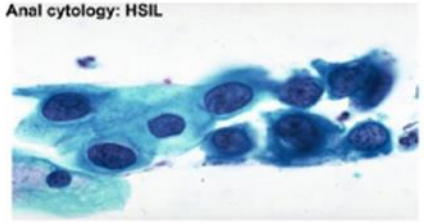
BACKGROUND

- Women living with HIV (WLH) are at increased risk for high-risk human papillomavirus (HR-HPV)-associated cervical and anal cancer.
- While cervical cancer screening has been accepted standard of care, anal cancer screening has not yet been universally adopted.
- Comparative data on cervical and anal HR-HPV positivity and cytological abnormalities are sparse among WLH.

METHODS

- Clinicopathological data were analyzed from 381 WLH, including initial anal and cervical/vaginal cytology/HR-HPV co-testing results obtained within 6 months of one another.
- Rates of and correlation between cervical/vaginal and anal abnormalities were analyzed.
- Significant predictors from logistic regression models were used to create prediction nomograms for anal HR-HPV and HPV16/18 infection.

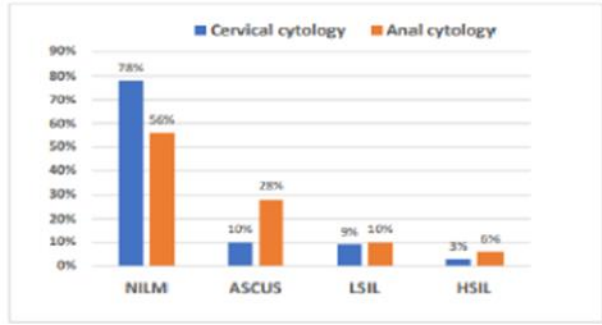
Anal cytology: HSIL



RESULTS

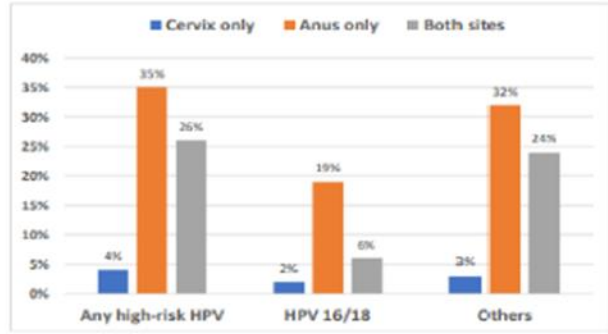
Figure 1: Anal and cervical/vaginal screening results. Data presented as percentage of participants in each category.

A. Cytological diagnoses (47 inadequate samples were excluded).



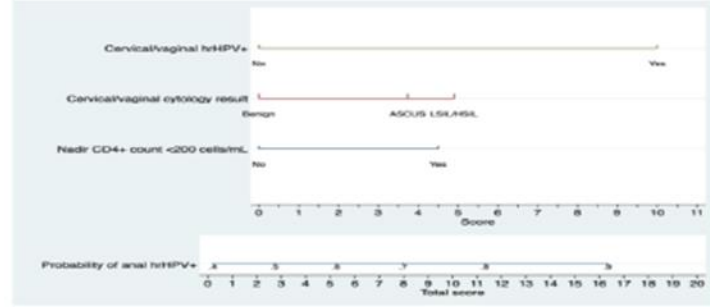
B. High-risk HPV testing results

Others: HPV31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68



- Median age was 49 years (range: 20-81)
- Cytological diagnosis of ASCUS or worse (≥ASCUS) was more prevalent in anus than cervix (44% vs. 22%).
- HR-HPV and HPV16/18 were detected in 65% and 27% of participants, more frequently in anus than cervix (61% vs. 30% and 25% vs. 8%).

Figure 2: Nomogram predicting anal high-risk HPV infection.
To calculate the probability of anal high-risk HPV infection, add the score of each risk factor and then determine the probability based on the total score axis.



A nomogram predicting anal HR-HPV infection based on nadir CD4 T-cell count < 200 cells/mm3, cervical/vaginal cytology ≥ASCUS and cervical/vaginal HR-HPV positivity yielded prediction probabilities ranging from <40% (all predictors absent) to >90% (all predictors present).

CONCLUSIONS

High prevalence of anal HR-HPV infection and cytological abnormalities among WLH underscore the importance of anal cancer screening independent of preceding or concurrent genital disease. Clinical and cervical/vaginal cytological data can help stratify the risk of anal disease via prediction nomograms, although further prospective validation is warranted.

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0563

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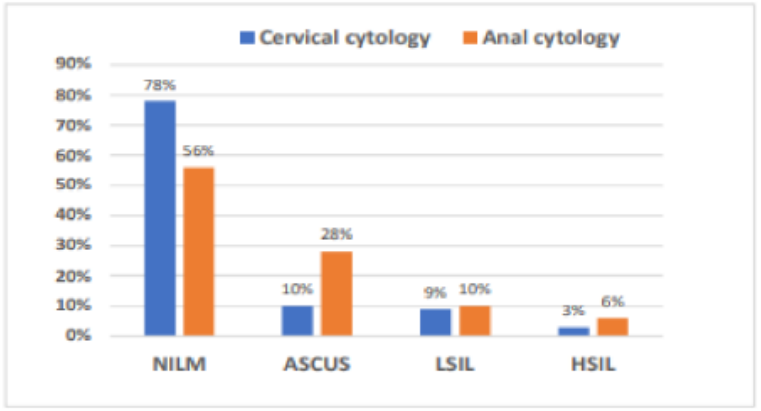
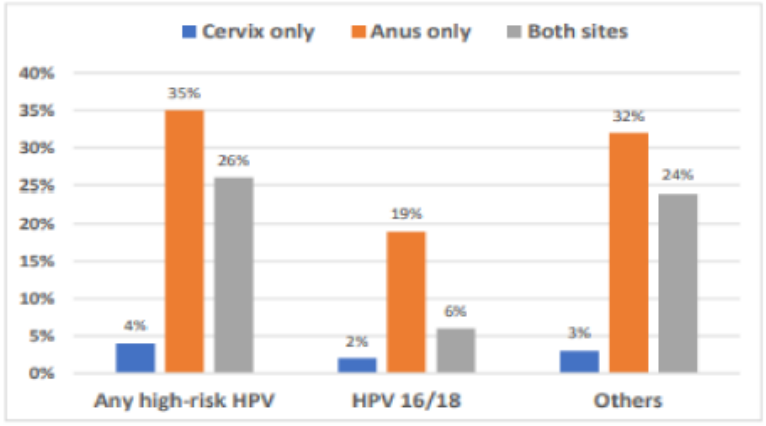


B. High-risk HPV testing results

Others: HPV31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68



Análisis de la correlación entre citología/VPH-AR anal y cervical/vaginal en 381 mujeres con VIH.

CONCLUSIONES

La alta prevalencia de infección por VPH-AR y de anomalías citológicas en mujeres con VIH, subrayan la importancia de realizar cribado de cáncer anal en este grupo poblacional independientemente de la patología genital concurrente.

Immunological Biomarkers Associated With Anal Dysplasia in People Living With HIV

565

Joaquín Burgos[1*], **Cristina Mancebo**[1,3], Núria Massana[1,3], Antonio Astorga-Gamaza[1], Stefania Landolfi[2], Adrian Curran[1], Jorge García[1], Vicenç Falcó[1], María J. Buzón[1], Meritxell Genescà[1*]

[1]Infectious Diseases Department, Vall d'Hebron Hospital Universitari, Institut de Recerca (VHIR), Barcelona, Spain, [2]Pathology Department, Vall d'Hebron Hospital Universitari, Universitat Autònoma de Barcelona, Barcelona, Spain

[3]This authors contributed equally *Corresponding authors: jburgos@vhebron.net (J.B.) and meritxell.genesca@vhir.org (M.G.)

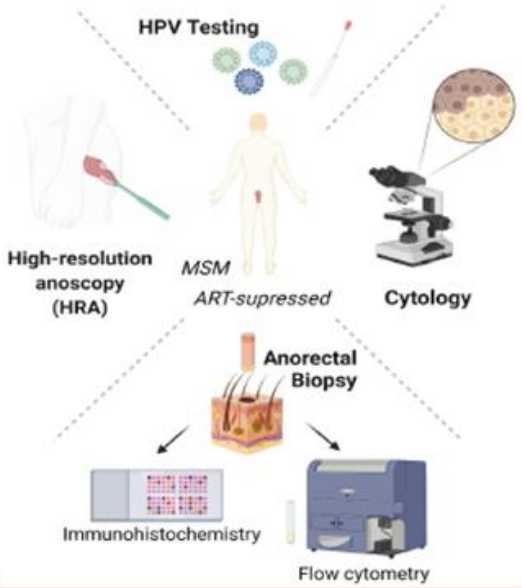
BACKGROUND

Identifying local immunological mechanisms possibly involved in the development of dysplasia and progression to anal cancer could be critical for prevention and treatment of precancerous lesions, as Squamous intraepithelial lesion (SIL), in people at high risk like men who have sex with men (MSM) living with HIV.

METHODS

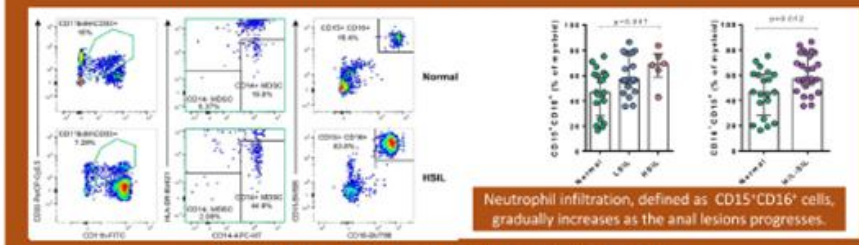
A cross-sectional study of 44 MSM living with HIV and ART-suppressed was performed. 54 anorectal biopsies were obtained for histological analysis and for determining their immunological environment, comparing pathological (LSIL/ HSIL) samples with non-pathological samples. Selected biomarkers were confirmed by immunohistochemistry.

Screening for anal dysplasia and possible biomarkers



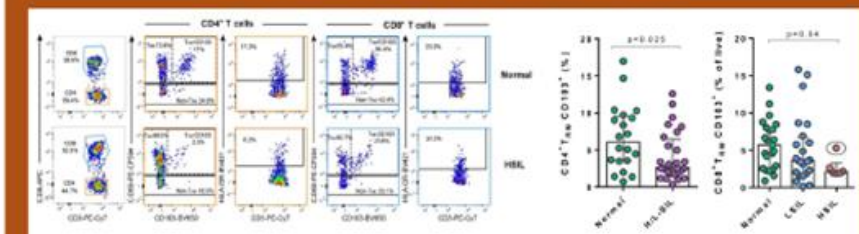
Pathological (L/HSIL) samples are characterized by:

Enriched immune suppressive environment

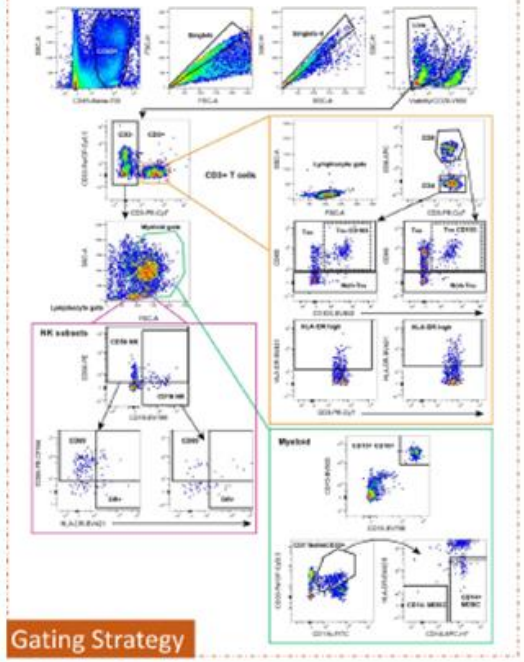


Neutrophil infiltration, defined as CD15$^+$CD16$^+$ cells, gradually increases as the anal lesions progresses.

Depletion of resident antiviral cells



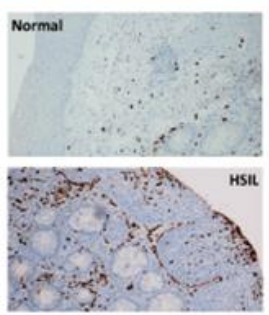
Resident Memory CD103$^+$ CD8$^+$/CD4$^+$ T cells were less frequent in pathological biopsies.



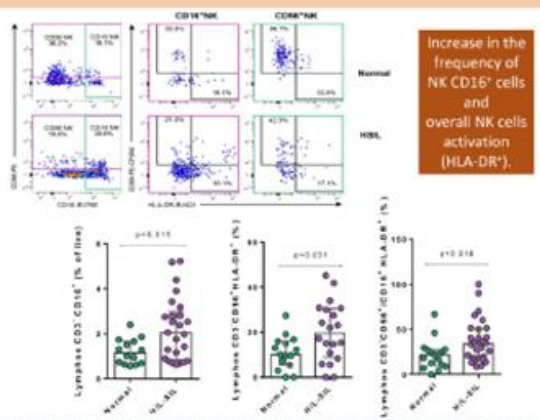
Gating Strategy

RESULTS

Immunohistochemistry



CD15$^+$ cells present in epithelium and underlying lamina propria.



Increase in the frequency of NK CD16$^+$ cells and overall NK cells activation (HLA-DR$^+$).

CONCLUSIONS

- The balance between resident effectors and inflammatory subsets was tilted towards the second in pathological anorectal samples.
- Neutrophil infiltration, determined by CD15 staining, may represent a valuable biomarker to determine the dysplasia's grade.

ADDITIONAL KEY INFORMATION

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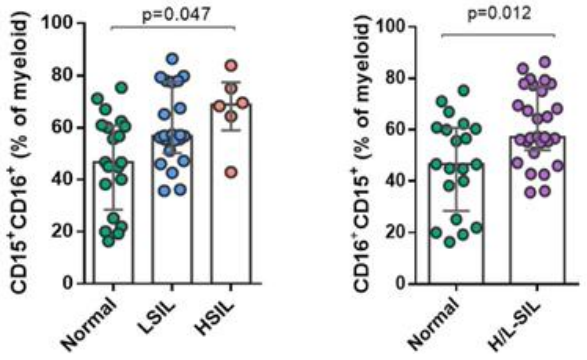
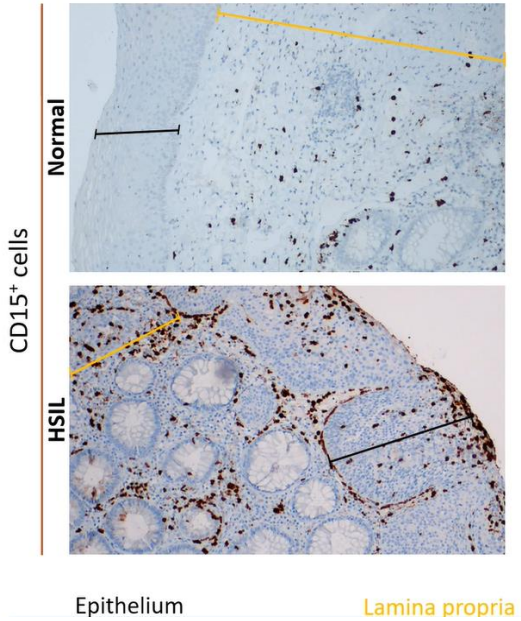
[3]This authors contributed equally *Corresponding authors: jburgos@vhebron.net (J.B.) and meritxell.genesca@vhir.org (M.G.)

- Estudio transversal.
- 44 HSH con VIH y CV indetect.
- 54 biopsias anales.

Determinación del microambiente inmunológico de las muestras histológicas, comparando muestras patológicas (LSIL/HSIL) con no patológicas.





CONCLUSIÓN

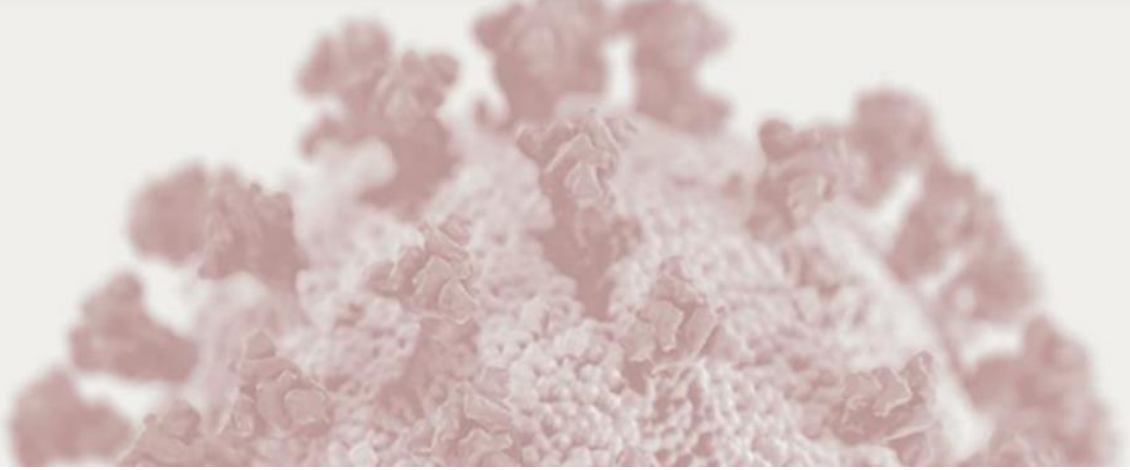
La infiltración neutrofílica, determinada por la tinción de CD15, podría ser un biomarcador útil para determinar el grado de displasia.

Se objetiva un aumento de la infiltración de neutrófilos (células CD15+CD16+) en las muestras patológicas

19ª edición

POSTCROI

Una actualización de la "29th 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